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Full acetals of β-D-glycopyranosylnitromethanes and a 1,2-dideoxy-1-nitroalk-1-enitol derived from common hexoses [1]

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Abstract

Kinetically controlled *O*-isopropylidenation of common 2,6-anhydro-1-deoxy-1-nitroalditols (β-D-glycopyranosylnitromethanes) derived from D-glucose, D-galactose, and D-mannose with 2-methoxypropene in 1,2-dimethoxyethane catalyzed with 4-toluenesulfonic acid afforded high yields of 2,3;4,6-di-*O*-isopropylidene acetals. With D-mannose, the bisacetal was also obtained in quantitative yield by reaction with 2,2-dimethoxypropane. Mono-*O*-benzylidenation of the starting compounds with benzaldehyde dimethyl acetal followed by *O*-isopropylidenation led to 4,6-*O*-benzylidene-2,3-*O*-isopropylidene acetals having better solubilities in non-polar solvents than the di-*O*-isopropylidene acetals. Di-*O*-benzylidenation of β-D-mannopyranosylnitromethane gave both (*endo*-2,3):4,6- and (*exo*-2,3):4,6-di-*O*-benzylidene acetals. Transacetalation of 1-deoxy-1-nitro-D-mannitol with 2,2-dimethoxypropane followed by 2-*O*-acetylation and β-elimination of the acetoxy group afforded (*E*)-1,2-dideoxy-2,4:5,6-di-*O*-isopropylidene-1-nitro-D-*arabino*-hex-1 -enitol.

Keywords: Carbohydrate acetals; D-*arabino*-Hex-1-enitol; 1,2-dideoxy-1-nitro-; *C*-Glycosyl compounds; β-D-Glycopyranosylnitromethanes; Isopropylidenation

1. Introduction

2,6-Anhydro-1-deoxy-1-nitroalditols (glycopyranosylnitromethanes) are convenient precursors for the synthesis of *C*-glycosyl mimics of naturally occurring carbohydrates [1–3]. However, a precondition

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[1] Dedicated to Professor Dr. Hans Paulsen on occasion of his 75th birthday.

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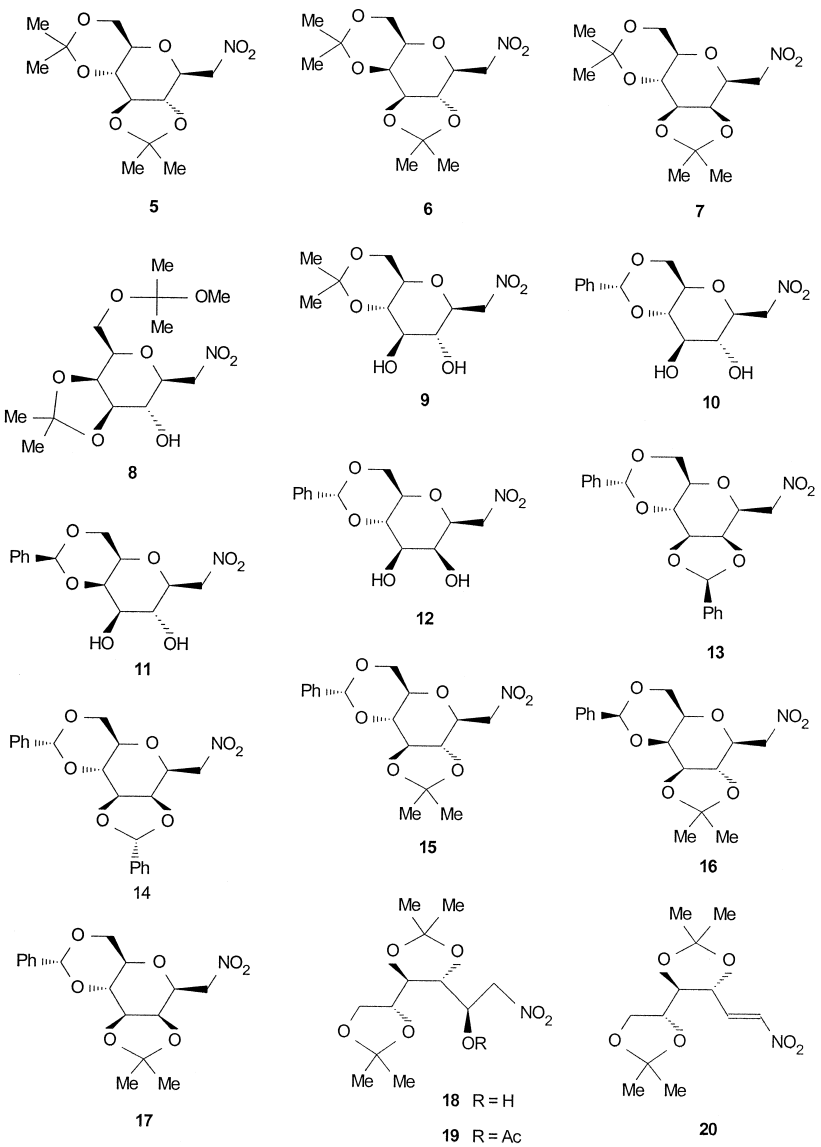
for their use as *C*-glycosyl donors in nucleophilic additions is good solubility and stability of their nitronate forms generated with bases in anhydrous solvents, a condition not fulfilled by their *per*-O-acetates. Here, we introduce full acetals as a new group of β-D-glycopyranosylnitromethanes fully protected with O-isopropylidene groups. Such acetals have previously been prepared from O-glycosides of D-glucose and D-galactose [4–6], but only partial acetals of β-D-glycopyranosylnitromethanes have been described [7,8].

1,2-Dideoxy-1-nitroalk-1-enitol peracetates as acyclic glycose precursors are useful reactive species applicable as acceptors in nucleophilic additions (e.g., Ref. [9]). Their use, however, is limited because of instability of the protecting groups in basic media. Therefore, preparation of a fully O-acetalated nitrohexenitol as a base-stable equivalent to 3,4,5,6-tetra-*O*-acetyl-1,2-dideoxy-1-nitro-D-*arabino*-hex-1-enitol [10] is also described.

2. Results and discussion

Kinetically controlled acetonation was performed essentially under the same conditions applied for di-*O*-isopropylidenation of D-gluco- and D-galactopyranosides [4,5], except for using a more convenient solvent, 1,2-dimethoxyethane, in place of *N*,*N*-dimethylformamide. Treatment of 2,6-anhydro-1-deoxy-1-nitro-D-*glycero*-D-*gulo*-heptitol [11] (β-D-glucopyranosylnitromethane, **1**), 2,6-anhydro-7-de-



Scheme 1.

oxy-7-nitro-L-*glycero*-L-*galacto*-heptitol [11] (β-D-galactopyranosylnitromethane, **2**), and 2,6-anhydro-1-deoxy-1-nitro-D-*glycero*-D-*galacto*-heptitol [12] (β-D-*manno*-pyranosylnitromethane, **3**) with an excess of 2-methoxypropene and a catalytic amount of 4-toluenesulfonic acid in 1,2-dimethoxyethane under anhydrous conditions resulted in almost complete formation of the respective 2,3:4,6-di-*O*-isopropylidene acetals **5–7** (Scheme 1). The reactions were rapid; starting glycosylnitromethanes dissolved within 1 min and reaction was complete (by TLC) in 10–15 min. Diacetals **5–7** were isolated after purification by flash chromatography in 80–90% yields. Prolonged reaction time of **1** and **2** led to complex mixtures of products which were not analyzed in detail; only the prevailing product from the reaction of **2**, characterized as the 3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl) derivative (**8**), was isolated (46% yield).

Comparative thermodynamically controlled isopropylidenation of **1** and **2** with 2,2-dimethoxypropane did not afford appreciable amounts of bisacetals. Rather, 4,6-mono-*O*-isopropylidene derivative **9** was a single product from starting **1**, and a mixture of products not further identified resulted from starting **2**. This acetonation is, however, more convenient and unambiguous for preparation of diacetal **7**, which was obtained from **3** in almost quantitative yield, confirming that *trans*-2,3-diequatorial isopropylidenation is not favorable when 2,2-dimethoxypropane, as opposed to 2-methoxypropene, is used [4].

Similar transacetalation reactions of benzaldehyde dimethyl acetal with glycosylnitromethanes **1–3** resulted in the formation of expected 4,6-*O*-benzylidene acetals **10–12**. With starting **3**, the acetalation occurred further at its *cis* diol site and two di-*O*-benzylidene acetals **13** and **14** which differed in their stereochemistry at the five-membered ring acetal carbon atom were separated by flash chromatography and isolated in respective 50% and 32% yields. Compound **14** was obtained from ether in a form convenient for X-ray crystal structural analysis and measurements were performed at −100°C. The structure was solved by direct methods with the SHELXS-96 program [13] and refined with SHELXL-96 [14]. The refinement was done on F^2 for all reflections. The validated threshold $F > 2\sigma(F)$ was used for calculating R_{obsd} only. All atoms, including hydrogens introduced at theoretical positions using the AFIX option [14], were refined. Table 1 gives the relevant crystallographic data of **14**.[2] The final fractional coordinates of C and O with equivalent thermal parameters are given in Table 2. An ORTEP equivalent illustration of the title compound including the numbering scheme was obtained with PLATON96 [15] and is presented in Fig. 1. It can be seen that **14** is the 2,3-*exo* diastereomer, leaving the correspond-

Table 1
Crystallographic data for **14**[a,b]

	14
Formula	$C_{21}H_{21}NO_7$
Mol wt	399.39
Crystal dimensions (mm)	0.5×0.4×0.2
mp (°C)	195–198
Space group	$P2_1$
Cell parameters (pm, degrees)	
a	545.4(1)
b	1123.8(1)
c	1557.5(1)
β	95.54(1)
Volume *V* (pm^3)	950.2×10^6
Z	2
F (000)	420
Calculated density, D_x ($g\ cm^{-3}$)	1.396
μ (cm^{-1})	8.9
λ (Cu K_α) (pm)	154.178
2Θ range (degrees)	5.7–152.1
Reflections measured	4519
Symmetry independent reflections	3858
Reflections with $F > 2\sigma(F)$)	3777
Number of refined parameters	284
Ratio of valued reflections to parameters	13.6
Final residual factors R[c,d]	
$R_{1(obsd)}$	0.050
$wR_{2(all)}$	0.144
$wR_{2(obsd)}$	0.141
Goodness of fit S[e]	
S_{all}	1.04
S_{obsd}	1.04
Largest difference peak ($e\ pm^{-3}$)	0.26×10^{-6}
Largest difference hole ($e\ pm^{-3}$)	-0.19×10^{-6}
Flack parameter	0.2(2)

[a] Standard deviations in parentheses.
[b] Diffractometer Enraf–Nonius CAD4.
[c] Definitions: $R_1 = \Sigma||F_0|-|F_0|/\Sigma|F_0|$; $wR_2 = [\Sigma w(F_0^2 - F_c^2)^2/\Sigma w(F_0^2)^2]^{1/2}$.
[d] Weighting scheme: $w = 1/[\sigma^2(F_0^2) + (0.1147P)^2 + 0.0948\ P]$ where $P = (F_0^2 + 2F_c^2)/3$.
[e] Definition: $S = [\Sigma w(F_0^2 - F_c^2)^2/(n-p)]^{1/2}$.

[2] Tables of atomic coordinates including anisotropic thermal parameters for the heavy atoms and isotropic ones for the hydrogen atoms, bond lengths, and bond angles have been deposited with the Cambridge Crystallographic Data Centre. These tables may be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Table 2
Fractional positional parameters of C, O and N atoms and the temperature factors (U_{eq}) for **14**[a]

Atom	10^4 x	10^4 y	10^4 z	10^3 U_{eq}
O-2	6515(3)	−62(1)	3350(1)	42(1)
O-3	7881(2)	2578(1)	3474(1)	44(1)
O-4	4439(3)	3248(1)	2665(1)	44(1)
O-5	1740(3)	1141(1)	1801(1)	45(1)
O-7	2013(3)	−902(1)	1574(1)	57(1)
O-11	7824(3)	−1143(2)	5220(2)	74(1)
O-12	11260(3)	−1049(2)	4658(1)	62(1)
N-1	9340(3)	−612(2)	4849(1)	46(1)
C-1	8807(4)	655(2)	4600(1)	45(1)
C-2	6378(3)	728(2)	4054(1)	37(1)
C-3	5796(3)	2009(2)	3780(1)	37(1)
C-4	3823(3)	2138(2)	3020(1)	38(1)
C-5	3941(4)	1139(2)	2370(1)	38(1)
C-6	4241(4)	−63(2)	2813(1)	41(1)
C-7	4241(5)	−1019(2)	2129(2)	56(1)
C-8	7053(3)	3325(2)	2759(1)	40(1)
C-9	1848(4)	228(2)	1179(1)	48(1)
C-81	7794(4)	4605(2)	2891(1)	42(1)
C-82	6571(5)	5333(2)	3429(2)	53(1)
C-83	7240(6)	6526(2)	3509(2)	67(1)
C-84	9051(6)	6985(2)	3047(2)	72(1)
C-85	10241(6)	6258(3)	2516(3)	77(1)
C-86	9629(4)	5052(2)	2435(2)	57(1)
C-91	−416(5)	295(2)	551(1)	52(1)
C-92	−1434(6)	−722(3)	157(2)	69(1)
C-93	−3395(7)	−625(4)	−481(2)	83(1)
C-94	−4375(6)	459(4)	−710(2)	81(1)
C-95	−3433(7)	1471(4)	−300(2)	81(1)
C-96	−1481(6)	1390(3)	331(2)	66(1)

[a]Standard deviations in parentheses.

ing *endo* structure for **13**. The pyranoid ring is found in a slightly flattened $^4C_1$(D) conformation with puckering parameters according to Cremer and Pople [16,17] of $Q = 54.5(2)$ pm, $\theta = 20.4(2)°$ and $\phi = 316.5(6)°$.

In order to obtain full and defined acetals of glycosylnitromethanes **1–3** as single products with better solubilities of their nitronate forms in benzenoid solvents, monobenzylidene acetals **10–12** were treated with 2-methoxypropene. TLC analysis showed that the treatment resulted in rapid formation of 4,6-*O*-benzylidene-2,3-*O*-isopropylidene derivatives **15–17** (complete in 15 min). Derivatives **15–17** were isolated by flash chromatography in 77–88% yields. Derivative **17** was obtained in the same yield also by controlled acid-catalyzed transacetalation reaction of 2,2-dimethoxypropane with **12**. Attempted preparation of **17** by a direct, one-step, regioselective diacetalation of **3** using equimolar amounts of benzaldehyde dimethyl acetal and 2,2-dimethoxypropane led to a complex mixture of products.

Finally, analogical *trans*-acetalation of 1-deoxy-1-nitro-D-mannitol [18] (**4**) with 2,2-dimethoxypropane afforded 1-deoxy-3,4:5,6-di-*O*-isopropylidene-1-nitro-D-mannitol (**18**) in an isolated yield of 70%. Acetylation of **18** under conditions used for a β-D-glucopyranosyl analog [2], but without the catalytic amount of DMAP, gave its 2-*O*-acetyl derivative **19** in addition to the expected nitroalkene, (*E*)-1,2-dideoxy-3,4:5,6-di-*O*-isopropylidene-1-nitro-D-

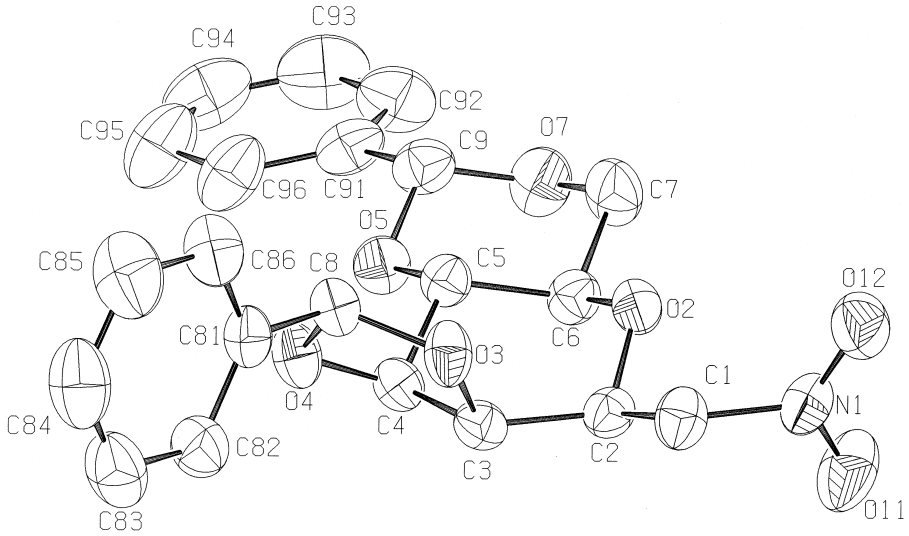


Fig. 1. ORTEP equivalent representation [15] of 2,6-anhydro-1-deoxy-(*exo*-3,4):5,7-di-*O*-benzylidene-1-nitro-D-*glycero*-D-*galacto*-heptitol (**14**).

Table 3
^{13}C chemical shifts of prepared compounds

Compd*	C-1	C-7	C-2–C-6	C(A5)[c]	C(A6)[c]	C(Ph); C(Me); C(OMe)
5[a]	77.5	62.5	79.9, 76.4, 76.2, 73.7, 73.6	112.3	100.0	28.9, 27.0, 26.5, 19.5
6[a]	65.2	79.0	81.9, 78.1, 72.7, 71.9, 69.2	113.4	100.9	30.6, 28.0, 27.9, 20.1
7[b]	75.9	61.6	76.1, 73.7, 73.0, 72.6, 69.4	110.4	99.7	28.9, 28.2, 26.3, 18.7
8[a]	62.8	79.1	81.8, 78.1, 77.6, 76.5, 72.3	111.9	102.4[d]	29.6, 27.7, 25.9, 25.8; 50.0
9[a]	77.9	62.9	78.7, 76.2, 74.7, 72.9, 72.7		100.7	29.3, 19.2
10[a]	78.2	69.0	81.9, 78.0, 75.5, 72.6, 71.3		102.1	139.0, 129.5, 128.7, 127.2
11[a]	69.2	77.8	78.2, 77.2, 74.8, 70.7, 69.7		101.4	139.7, 129.3, 128.6, 127.2
12[a]	77.8	61.7	79.6, 75.6, 71.6, 70.9, 68.9		102.4	139.1, 129.4, 128.7, 127.2
13[b]	77.3	68.9	81.8, 76.9, 75.9, 73.9, 69.2	105.3	102.2	138.9, 138.4, 130.2, 129.5, 129.2, 128.8, 127.6, 127.1
14[b]	77.6	68.9	77.7, 77.3, 74.9, 74.3, 69.3	104.1	102.3	139.9, 138.4, 129.9, 129.6, 129.1, 128.8, 127.1
15[b]	78.9	68.4	80.1, 76.2, 75.6, 75.3, 72.0	112.6	101.6	136.6, 129.2, 128.2, 126.3; 26.7, 26.3
16[a]	70.3	77.9	80.2, 76.8, 74.5, 71.2, 70.5	111.5	100.8	139.5, 129.5, 128.7, 127.2; 26.8, 26.7
16[b]	69.0	76.4	79.8, 75.8, 73.6, 70.2, 69.2	111.6	100.4	137.4, 129.0, 128.3, 126.1; 26.6, 26.4
17[b]	75.8	68.3	80.1, 75.5, 73.6, 73.1, 68.6	110.5	101.8	138.0, 129.0, 128.1, 126.2; 28.2, 26.3

*Recorded in (a) $(CD_3)_2CO$ or in (b) $CDCl_3$ with TMS as an internal standard. [c]Acetal carbon atom in a five-membered 1,3-dioxolane ring (A5) or six-membered 1,3-dioxane ring (A6). [d]Carbon atom of the acyclic acetal.

Table 4
^{1}H chemical shifts of prepared compounds

Compd *	H-1	H-1′	H-2	H-3	H-4	H-5	H-6	H-7	H-7′	H–CPh	H(Ph); H(Me); H(OMe)
5[a]	4.86 dd	4.59 dd	4.45 dt	3.95 dd	3.80 m	3.36 t	3.34 dt	3.82–3.75 m			1.49, 1.41, 1.39, 1.32 s
6[a]	4.42 dd	3.87 dd	3.36 m	4.60 dd	3.77 dd	3.85 t	4.38 dt	4.80 dd	4.68 dd		1.53, 1.48, 1.44, 1.42 s
7[b]	4.72 dd	4.60–4.53 m		4.24 dd	4.14 dd	3.72 dd	3.19 dt	3.91 dd	3.70 dd		1.54, 1.51, 1.42, 1.34 s
8[a]	3.62 d	3.62 d	3.94 m	4.29 dd	4.12 dd	3.50 dd	3.96 m	4.87 dd	4.55 dd		1.52, 1.37, 1.35, 1.34 s; 3.21 s
9[a]	4.93 dd	4.45 dd	4.07 dt	3.53 m	3.34 m	3.45 t	3.29 dt	3.77 dd	3.63 t		1.30, 1.28 s
10[a]	4.96 dd	4.59 dd	4.17 m	3.75 m	3.49 m	4.20 dd	3.52 m	3.68 t	3.45 m	5.58 s	7.51–7.33 m
11[a]	4.09 d	4.09 d	3.62 m	4.30 dd	3.73–3.64 m		4.06 m	4.98 dd	4.63 dd	5.60 s	7.52–7.33 m
12[a]	4.82 dd	4.71 dd	3.90 m	4.07 m	4.46 m	4.69 dd	3.43 m	4.14 dd	3.72 t	5.59 s	7.50–7.34 m
13[b]	5.06 dd	4.74 dd	4.93 dt	4.59 dd	4.53 dd	3.83 dd	3.57 td	4.24 dd	3.72 t	5.98, 5.65 s	7.59–7.34 m
14[b]	5.02 dd	4.70 dd	4.82 dt	4.46 dd	4.74 dd	4.00 dd	3.56 td	4.29 dd	3.78 t	6.27, 5.73 s	7.52–7.36 m
15[b]	4.69 dd	4.49 dd	4.42 m	3.89–3.77 m		4.35 dd	3.51 m	3.80 m	3.30 dd	5.57 s	7.33–7.51 m; 1.48, 1.47 s
16[a]	4.18 d	4.16d	3.65 m	4.67 dd	3.95–3.86 m		4.43 dt	4.88 dd	4.73 dd	5.66 s	7.51–7.32 m; 1.41, 1.29s
16[b]	4.31 dd	4.07 dd	3.47 m	4.54 dd	3.70 dd	3.92 t	4.40 m	4.66 d	4.65 d	5.56 s	7.50–7.32 m; 1.47, 1.45 s
17[b]	4.98 dd	4.66 dd	4.82 dt	4.49 dd	4.35 dd	3.78 dd	3.46 td	4.23 dd	3.73 t	5.68 s	7.50–7.34 m; 1.35, 1.32 s

* Recorded in (a) $(CD_3)_2CO$ or in (b) $CDCl_3$ with TMS as an internal standard.

Table 5
Proton coupling constants of prepared compounds

Compd*	$J_{1,1'}$	$J_{1,2}$	$J_{1',2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{6,7'}$	$J_{7,7'}$
5[a]	13.3	2.4	9.3	9.3	9.2	9.1	9.1	6.3	9.1	n
6[a]	13.0	2.2	1.6	1.3	2.6	9.3	9.3	2.6	9.3	13.5
7[b]	14.1	9.9	2.9	2.5	5.4	7.9	10.1	5.7	10.1	10.9
8[a]	0.0	6.2	6.2	2.2	5.4	7.1	9.7	2.7	9.3	13.2
9[a]	13.2	2.5	9.3	n	n	9.4	9.7	5.4	10.0	10.6
10[a]	13.3	2.5	9.3	n	n	10.1	4.5	9.5	n	10.1
11[a]	0.0	1.7	1.7	1.2	3.2	n	n	2.4	9.5	13.2
12[a]	13.5	3.0	9.2	n	1.4	6.1	4.6	5.0	10.2	10.3
13[b]	13.6	2.5	9.7	2.6	5.9	7.4	9.8	5.1	10.1	10.2
14[b]	13.3	2.1	9.8	2.2	5.2	8.1	9.7	5.1	10.1	10.3
15[b]	12.6	1.7	9.1	10.6	n	10.5	4.8	n	8.6	9.5
16[a]	0.0	1.7	1.5	1.3	2.3	n	9.3	2.6	9.4	13.4
16[b]	12.7	1.3	2.0	1.2	2.7	9.2	9.4	5.5	6.2	0.0
17[b]	13.4	2.4	9.8	2.6	5.5	7.9	9.8	5.2	10.1	10.3

*Recorded in (a) $(CD_3)_2CO$ or in (b) $CDCl_3$ with TMS as an internal standard.
n—Not determined.

arabino-hex-1-enitol (**20**) (**20:19** ratio ca. 1:5 by ^{13}C-NMR). Complete elimination of the acetoxy group under formation of nitroalkene **20** was achieved only after 14 h heating at the reflux temperature of the benzene solution.

^{1}H − and ^{13}C-NMR data for all prepared acetals provided proof of their structures. The ^{13}C chemical shifts (Table 3) of the isopropylidene methyl groups clearly indicated the presence of both 1,3-dioxane and 1,3-dioxolane rings. In accordance with detailed studies by Buchanan et al. [19], 1,3-dioxane structures gave an acetal carbon signal at δ ca. 99–101 and two methyl signals at δ ca. 29–30 and δ ca. 19–20. Corresponding signals in the 1,3-dioxolane arrangement were observed at δ ca. 110–112 (acetal carbon) and δ = ca. 26–28 (both methyl carbon atoms). One signal of the methyl group of the terminal isopropylidene group was observed at δ ca. 24–25 for each compound **18–20**. In agreement with another study by Lipták et al. [20], the size of the acetal rings of benzylidene acetals **10–17** was also apparent from their ^{13}C chemical shifts; respective acetal carbon atoms in 1,3-dioxolane and 1,3-dioxane rings resonated at δ ca. 104–105 and ca. 100–102. Conversion of acetate **19** to nitroalkene **20** was clearly indicated by disappearance of the signals of the acetyl carbon atoms at δ 20.0 and 168.7 and appearance of those of the double bond at δ 138.7 and 139.2. Values of the chemical shifts of the double bond protons of **20**, δ 7.24 and 7.36, are diagnostic of its *E* configuration [21,22]. The corresponding coupling constant, $J_{1,2}$ = 13.3 Hz, also proved this stereochemistry. ^{1}H-NMR data of acetals **5–17** given in Table 4 (chemical shifts) and Table 5 (coupling constants) support the assigned structures.

Use of the full acetals of β-D-glycopyranosylnitromethanes and 1,2-dideoxy-1-nitro-D-*arabino*-hex-1-enitol for Michael additions is in progress.

3. Experimental

General methods and materials.—Melting points were measured on a Kofler stage and are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 polarimeter at 20°C. Microanalyses were obtained using a Perkin–Elmer 240 instrument. NMR spectra were recorded at 295 K on a Bruker AM 300 spectrometer (300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C). TLC was run on glass plates precoated with silica gel L (0.005–0.040 mm, Lachema, Brno, Czech Republic); detection was effected by spraying the chromatograms with 10% ethanolic sulfuric acid and charring them on a hot plate. Flash chromatography was performed using silica gel (0.040–0.100 mm, Lachema).

Commercial benzylidene dimethyl acetal, 2,2-dimethoxypropane, 2-methoxypropene, and 1,2-dimethoxyethane were obtained from Aldrich. β-D-Galactopyranosylnitromethane (**1**), β-D-glucopyranosylnitromethane (**2**), β-D-mannopyranosylnitromethane (**3**), and 1-deoxy-1-nitro-D-mannitol (**4**) were prepared by published procedures [11,12,18].

Isopropylidenation of glycosylnitromethanes with 2-methoxypropene.—A mixture of a glycosylnitromethane (**1–3**; 0.22 g, 1 mmol), Drierite (0.5 g), 4-toluenesulfonic acid (20 mg), and 1,2-dimethoxyethane (10 mL) was stirred 15 min under nitrogen at rt. After addition of 2-methoxypropene (1.0 mL, 10.4 mmol), the reaction mixture was stirred 15 min. Then, $NaHCO_3$ (0.1 g) was added. After stirring 10 min, the neutral mixture was filtered with suction and washed with MeOH (2 × 5 mL). Concentration of filtrates in vacuo afforded a residue which was purified by flash chromatography (eluent: 1:2 v/v ethyl acetate–petroleum ether). Compounds **5–7** were thus prepared.

2,6-Anhydro-1-deoxy-3,4:5,7-di-O-*isopropylidene-1-nitro*-D-glycero-D-gulo-*heptitol* (2,3:4,6-di-*O*-isopropylidene-β-D-glucopyranosylnitromethane) (**5**): yield 0.26 g (87%); mp 71–72°C; $[\alpha]_D$ −18.0° (*c* 1.0, acetone); R_f 0.44 (1:2 v/v ethyl acetate–petroleum ether). Anal. Calcd for $C_{13}H_{21}NO_7$ (303.32): C, 51.48; H, 6.98; N, 4.62. Found: C, 51.33; H, 6.99; N, 4.35.

2,6-Anhydro-7-deoxy-1,3:4,5-di-O-*isopropylidene-7-nitro*-L-glycero-L-galacto-*heptitol* (2,3:4,6-di-*O*-isopropylidene-β-D-galactopyranosylnitromethane) (**6**): yield 0.24 g (80%); solid foam; $[\alpha]_D$ +12.0° (*c* 1.0, acetone); R_f 0.39 (1:2 v/v ethyl acetate–petroleum ether). Anal. Calcd for $C_{13}H_{21}NO_7$ (303.32): C, 51.48; H, 6.98; N, 4.62. Found: C, 51.79; H, 7.00; N, 4.26.

2,6-Anhydro-1-deoxy-3,4:5,7-di-O-*isopropylidene-1-nitro*-D-glycero-D-galacto-*heptitol* (2,3:4,6-di-*O*-isopropylidene-β-D-mannopyranosylnitromethane) (**7**) was obtained directly by crystallization of the evaporation residue: yield 0.27 g (90%); mp 148–150°C; $[\alpha]_D$ −107.0° (*c* 1.0, acetone); R_f 0.48 (1:2 v/v ethyl acetate–petroleum ether). Anal. Calcd for $C_{13}H_{21}NO_7$ (303.32); C, 51.48; H, 6.98; N, 4.62. Found: C, 51.66; H, 7.14; N, 4.44.

2,6-Anhydro-7-deoxy-3,4-O-*isopropylidene-1*-O-*(1-methoxy-1-methylethyl)-7-nitro*-L-glycero-L-galacto-

*heptitol (3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-β-*D*-galactopyranosylnitromethane)* (**8**). —Treatment of β-D-galactopyranosylnitromethane with 2-methoxypropene according to the procedure given above, but prolonged for 2 days, gave **8** as the major product isolated as a solid foam: yield 0.18 g (52%); $[\alpha]_D$ +46.0° (*c* 1.0, acetone); R_f 0.25 (1:2 v/v ethyl acetate petroleum ether). Anal. Calcd for $C_{14}H_{25}NO_8$ (335.36): C, 50.14; H, 7.51; N, 4.18. Found: C, 50.38; H, 7.40; N, 3.86.

Isopropylidenation of glycosylnitromethanes with 2,2-dimethoxypropane.—To a mixture of a glycosylnitromethane (0.22 g, 1 mmol), Drierite (0.5 g), 4-toluenesulfonic acid (20 mg) and 1,2-dimethoxyethane (10 mL) prestirred 15 min at rt, 2,2-dimethoxypropane (1 mL, 8.1 mmol) was added and stirring was continued for 24 h. Then, $NaHCO_3$ (0.1 g) was added, and after stirring 10 min, the neutral mixture was filtered and washed with MeOH (2 × 5 mL). Concentration of filtrates afforded a residue which crystallized from ethanol. Compounds **7** and **9** were thus prepared.

2,6-Anhydro-1-deoxy-3,4:5,7-di-*O*-isopropylidene-1-nitro-D-*glycero*-D-*galacto*-heptitol (2,3:4,6-di-*O*-isopropylidene-β-D-mannopyranosylnitromethane) (**7**) identical with the sample obtained by isopropylidenation with 2-methoxypropene: yield 0.29 g (98%).

2,6-Anhydro-1-deoxy-5,7-*O*-isopropylidene-1-nitro-D-*glycero*-D-*gulo*-heptitol (4,6-*O*-isopropylidene-β-D-glucopyranosylnitromethane) (**9**): yield 0.23 g (87%); mp 144–145°C, $[\alpha]_D$ −27.0° (*c* 1, MeOH); R_f 0.49 (ethyl acetate). Lit. [8] mp 158–159°C, $[\alpha]_D$ −27.6° (*c* 2, MeOH).

Benzylidenation procedure.—A mixture of a glycosylnitromethane **1–3** (0.22 g, 1 mmol), Drierite (0.5 g), 4-toluenesulfonic acid (20 mg) and 1,2-dimethoxyethane (10 mL) was stirred 15 min under nitrogen at rt. After addition of benzaldehyde dimethyl acetal (0.3 mL, 2.0 mmol for monobenzylidenation; 0.6 mL, 4.0 mmol for dibenzylidenation), stirring was continued for 20 h. $NaHCO_3$ (0.2 g) was added, and after stirring 10 min, the neutral mixture was filtered with suction and washed with MeOH (2 × 5 mL). Concentration of filtrates in vacuo afforded a residue which was purified by flash chromatography (eluent: 5:1 v/v ethyl acetate–petroleum ether). Compounds **10–13** were thus prepared.

2,6-Anhydro-5,7-*O*-benzylidene-1-deoxy-1-nitro-D-*glycero*-D-*gulo*-heptitol (4,6-*O*-benzylidene-β-D-glucopyranosylnitromethane) (**10**): yield 0.31 g (96%); mp 212–214°C; $[\alpha]_D$ −30.5° (*c* 4.0, acetone), −36.0° (*c* 0.5, MeOH); R_f 0.55 (5:1 v/v EtOAc–petroleum ether). Lit. [7] mp 211–212°C, $[\alpha]_D^{31}$ −35.4° (*c* 1.3, MeOH); lit. [8] mp 213–214°C, $[\alpha]_D^{20}$ −42.6° (MeOH).

*2,6-Anhydro-1,3-*O*-benzylidene-7-deoxy-7-nitro-*L*-glycero-*L*-galacto-heptitol* (4,6-*O*-benzylidene-β-D-galactopyranosylnitromethane) (**11**): yield 0.28 g (88%); mp 157–159°C, $[\alpha_D$ +10.8° (*c* 4, acetone); R_f 0.32 (5:1 v/v EtOAc–petroleum ether). Anal. Calcd for $C_{14}H_{17}NO_7$ (311.29): C, 54.02; H, 5.50; N, 4.50. Found: C, 53.85; H, 5.76; N, 4.33.

*2,6-Anhydro-5,7-*O*-benzylidene-1-deoxy-1-nitro-D-glycero-D-galacto-heptitol* (4,6-*O*-benzylidene-β-D-mannopyranosylnitromethane) (**12**): yield 0.15 g (47%); mp 173–174°C; $[\alpha]_D$ −35.0° (*c* 4.0, acetone); R_f 0.54 (5:1 v/v EtOAc–petroleum ether). Anal. Calcd for $C_{14}H_{17}NO_7$ (311.29): C, 54.02; H, 5.50; N, 4.50. Found: C, 53.55; H, 5.58; N, 4.44.

*2,6-Anhydro-1-deoxy-(*endo-*3,4):5,7-di-*O*-benzylidene-1-nitro-D-glycero-D-galacto-heptitol* [(*endo*-2,3):4,6-di-*O*-benzylidene-β-D-mannopyrano- sylnitromethane] (**13**): yield 0.20 g (50%); mp 77–80°C; $[\alpha]_D$ −149° (*c* 2.0, acetone); R_f 0.79 and 0.27 (EtOAc–petroleum ether, 5:1 v/v and 1:2 v/v, respectively). Anal. Calcd for $C_{21}H_{21}NO_7$ (399.40): C, 63.15; H, 5.30; N, 3.51. Found: C, 63.01; H, 5.42; N, 3.45.

*2,6-Anhydro-1-deoxy-(*exo-*3,4):5,7-di-*O*-benzylidene-1-nitro-D-glycero-D-galacto-heptitol* [(*exo*-2,3):4,6-di-*O*-benzylidene-β-D-mannopyranosylnitromethane] (**14**): yield 0.13 g (32%); mp 195–198°C; $[\alpha]_D$ −117° (*c* 1.0, acetone); R_f 0.79 and 0.42 (EtOAc–petroleum ether, 5:1 v/v and 1:2 v/v, respectively). Anal. Calcd for $C_{21}H_{21}NO_7$ (399.40): C, 63.15; H, 5.30; N, 3.51. Found: C, 63.35; H, 5.49; N, 3.50.

*Isopropylidenation of 4,6-*O*-benzylidene-glycosylnitromethanes*.—A mixture of Drierite (0.25 g), 4-toluenesulfonic acid (10 mg) and 1,2-dimethoxyethane (5 mL) was stirred 15 min under nitrogen at room temperature. After addition of 2-methoxypropane (0.5 mL, 5.2 mmol) and a 4,6-*O*-benzylidene-glycosylnitromethane **10–12** (0.16 g, 0.5 mmol), stirring was continued for 15 min. Then, $NaHCO_3$ (0.1 g) was added, and after stirring 10 min, the neutral mixture was filtered with suction and washed with MeOH (2 × 5 mL). Concentration of filtrates in vacuo afforded a residue that was purified by flash chromatography (eluent: 1:2 v/v ethyl acetate–petroleum ether). Compounds **15–17** were prepared using this procedure.

*2,6-Anhydro-5,7-*O*-benzylidene-1-deoxy-3,4-*O*-isopropylidene-1-nitro-D-glycero-D-gulo-heptitol*

(4,6-*O*-benzylidene-2,3-*O*-isopropylidene-β-D-gluco-pyranosylnitromethane) (**15**) as a solid foam: yield 0.14 g (77%); $[\alpha]_D$ −24.0° (*c* 1.5, acetone); R_f 0.43 (EtOAc–petroleum ether, 3:2). Anal. Calcd for $C_{17}H_{21}NO_7$ (351.37): C, 58.11; H, 6.02; N, 3.99. Found: C, 58.19; H, 5.99; N, 3.78.

2,6-Anhydro-1,3-O-*benzylidene-7-deoxy-4,5*-O-*isopropylidene-7-nitro*-L-glycero-L-galacto-*heptitol* (4,6-*O*-benzylidene-2,3-*O*-isopropylidene-β-D-galacto-pyranosylnitromethane) (**16**): yield 0.16 g (88%), had mp 155–156°C, $[\alpha]_D$ +7.7° (*c* 1.3, acetone); R_f 0.39 (EtOAc–petroleum ether, 3:2). Anal. Calcd for $C_{17}H_{21}NO_7$ (351.37): C, 58.11; H. 6.02; N, 3.99. Found: C, 58.14; H, 6.15; N, 4.00.

2,6-Anhydro-5,7-O-*benzylidene-1-deoxy-3,4*-O-*isopropylidene-1-nitro*-D-glycero-D-galacto-*heptitol* (4,6-*O*-benzylidene-2,3-*O*-isopropylidene-β-D-manno-pyranosylnitromethane) (**17**): yield 0.16 g (88%); mp 132–133°C, $[\alpha]_D$ −95.0° (*c* 1.0, acetone); R_f 0.44 (3:2 v/v EtOAc–petroleum ether). Anal. Calcd for $C_{17}H_{21}NO_7$ (351.37): C, 58.11; H, 6.02; N, 3.99. Found: C, 57.94; H, 6.31; N, 3.66. The foregoing isopropylidenation procedure with **12**, with the exception of using 2,2-dimethoxypropane (0.5 mL) in a 2 h reaction in place of 2-methoxypropene, gave **17** (yield 0.16 g, 88%) identical with the sample described above.

Treatment of 1-deoxy-1-nitro-D-mannitol (0.42 g, 2 mmol) according to the procedure for isopropylidenation of glycosylnitromethanes with 2,2-dimethoxypropane using twofold amounts of reaction components afforded 1-deoxy-3,4:5,6-di-*O*-isopropylidene-1-nitro-D-mannitol (**18**) as a syrup: yield 0.41 g (70%); $[\alpha]_D$ −13.0° (*c* 1.0, acetone); R_f 0.51 (1:2 v/v EtOAc–petroleum ether). ^{13}C-NMR ($CDCl_3$): δ 110.3, 110.1 (2 CMe_2), 80.8, 80.2, 75.9, 69.7 (C-2, C-3, C-4, C-5), 78.3 (C-1), 67.6 (C-6), 26.6, 26.5, 26.2, 24.8 (4 Me).

*(*E*)-1,2-Dideoxy-3,4:5,6-di*-O-*isopropylidene-1-nitro*-D-arabino-*hex-1-enitol* (**20**).—Acetic anhydride (0.8 mL) and pyridine (0.5 mL) were added to a solution of **18** (0.4 g) in $CHCl_3$ (10 mL) at 0°C. After 2 d at rt, cold aqueous M HCl (10 mL) was added. The organic phase was washed with a second 10 mL portion of cold M HCl and then with saturated aqueous $NaHCO_3$ (2 × 10 mL) and water (10 mL), dried (Na_2SO_4), and concentrated to give a mixture of 2-*O*-acetyl-1-deoxy-3,4:5,6-di-*O*-isopropylidene-1-nitro-D-mannitol (**19**), R_f 0.55 (1:2 v/v EtOAc–petroleum ether), and nitroalkene **20** (0.4 g) in an approx. 5:1 ratio (by ^{13}C-NMR spectroscopy). ^{13}C-NMR ($CDCl_3$) of **19**: δ 168.7 (CO), 109.9, 109.3 (2 CMe_2), 78.8, 78.7, 76.2, 74.6, 69.0, 66.9 (C-1, C-2, C-3, C-4, C-5, C-6), 26.5, 26.4, 25.9, 24.6 (4 isopropylidene Me), 20.0 (acetyl Me).

The residue containing **19** and **20** was dissolved in dry benzene (10 mL), and the solution was heated 14 h at the reflux temperature in the presence of $NaHCO_3$ (0.4 g). The cooled reaction mixture was filtered and evaporated to give syrupy **20**: yield 0.31 g (94%); $[\alpha]_D$ +5.0° (*c* 1.4, acetone); R_f 0.66 (1:2 v/v EtOAc–petroleum ether). ^{1}H-NMR ($CDCl_3$): δ 7.36 (dd, 1 H, $J_{1,2}$ 13.3 Hz, $J_{2,3}$ 3.6 Hz, H-2), 7.24 (dd, 1 H, $J_{1,3}$ 1.7 Hz, H-1), 4.63 (ddd, 1 H, $J_{3,4}$ 8.1 Hz, H-3), 4.16 (m, 1 H, $J_{5,6}$ 6.05 Hz, H-6), 4.11 (m, 1 H, $J_{5,6'}$ 3.65 Hz, H-5), 3.97 (dd, 1 H, $J_{6,6'}$ 8.3 Hz, H-6′), 3.68 (t, 1 H, $J_{4,5}$ 8.2 Hz, H-4), 1.44, 1.43, 1.42, 1.36 (4 s, 12 H, 4 CH_3); ^{13}C-NMR ($CDCl_3$): δ 139.2 (C-1), 138.7 (C-2), 110.5, 109.6 (2 CMe_2), 80.8, 76.6, 76.3 (C-3, C-4, C-5), 67.3 (C-6), 26.4, 26.3, 26.1, 24.8 (4 Me). Anal. Calcd for $C_{12}H_{19}NO_6$: C, 52.74; H, 7.01, N, 5.13. Found: C, 52.51, H, 7.16, N, 4.87.

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