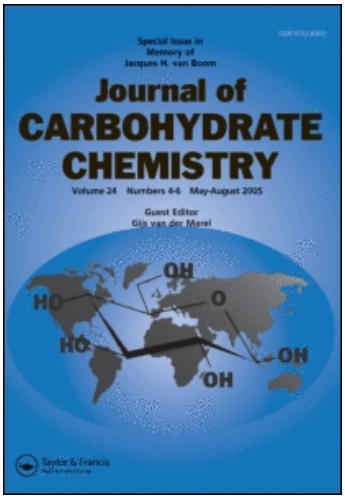

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SYNTHESIS AND REACTIONS OF DERIVATIVES OF 2-DEOXYOCT-3-ULOSONIC ACIDS

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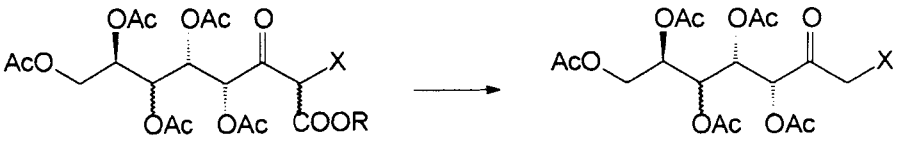
ABSTRACT

Decarboalkoxylations of branched chain 2-deoxyoct-3-ulosonic acid derivatives furnished the unbranched 2-deoxyoct-3-ulosonic acid esters and nitriles, respectively. The O-methylation and halogenation of 2-deoxyoct-3-ulosonates are described.

INTRODUCTION

In a previous communication (this issue) we reported the synthesis of 2-alkoxycarbonyl-2-deoxyoct-3-ulosonic acid esters and nitriles **1** by C-chain elongation of 2,3,4,5,6-penta-*O*-acetyl-D-galactonic or D-gluconic acid chloride with derivatives of malonic acid. [1] This paper describes the preparation of 2-deoxyoct-3-ulosonic acid esters and nitriles **4 - 6**, **13 - 15** by removal of the 2-alkoxycarbonyl group of branched chain 2-deoxyoct-3-ulosonates **1 - 3**, **7 - 12** (Scheme 1). Further reactions of the unbranched 2-deoxyoct-3-ulosonic acid esters to provide new precursors for the synthesis of C-nucleoside and acyclonucleoside analogues are reported.



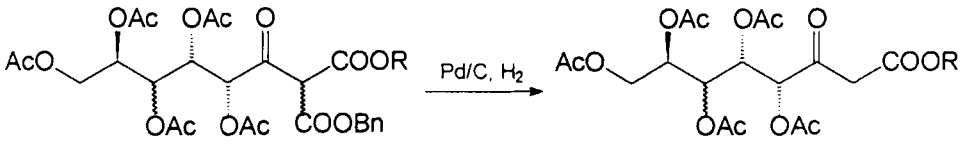
1 - 3, 7 - 12 **4 - 6, 13 - 15**

X = $COOR^1$, CN
R, R^1 = Alkyl

Scheme 1

RESULTS AND DISCUSSION

Through the hydrogenation of the 2-alkoxycarbonyl-2-deoxyoct-3-ulosonic acid benzyl esters **1-3** with hydrogen and palladium/charcoal[2,3,4] the free 2-alkoxycarbonyl-2-deoxy-oct-3-ulosonic acids could be obtained, undergoing spontaneous decarboxylation at room temperature[5] to yield the alkyl 2-deoxyoct-3-ulosonates **4 - 6** (Scheme 2).



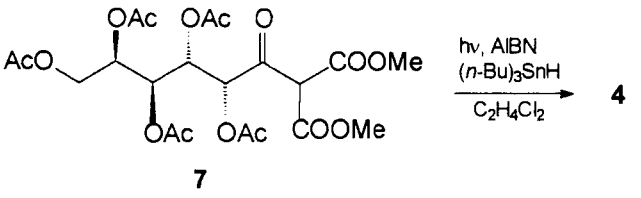
1 - 3 **4 - 6**

	config.	R
1	D-*galacto*	Me
2	D-*gluco*	Me
3	D-*galacto*	Et

	config.	R
4	D-*galacto*	Me
5	D-*gluco*	Me
6	D-*galacto*	Et

Scheme 2

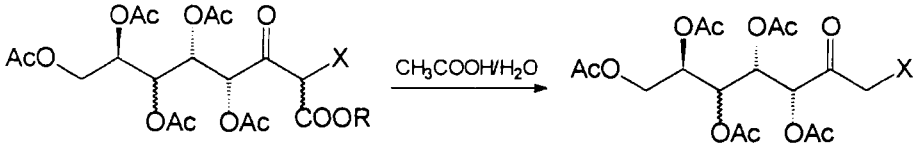
Another way of synthesizing 2-deoxyoct-3-ulosonic acid esters was by radical decarboalkoxylation. Compound **7** was treated with tri-*n*-butyl tin hydride and azobisisobutyronitrile in dichloroethane to give **4** in 29% yield. The low yield could be attributed to side reactions of the intermediary existing radicals (Scheme 3).



7

Scheme 3

Similar to the decarboalkoxylation of malonates with propionic acid,[6] heating the octulosonic acid ester **7** - **12** in acetic acid, as solvent, with a trace of water furnishes the octulosonic acid derivatives **4** - **6**, **13** - **15** in acceptable yields (Scheme 4).



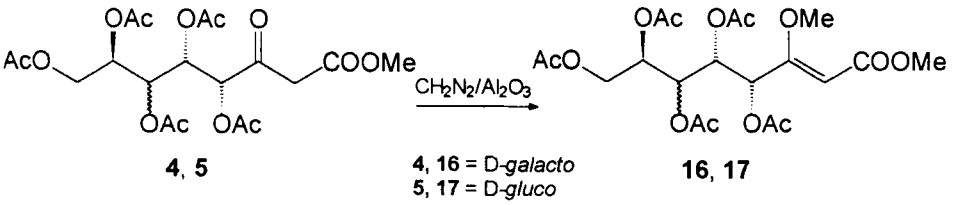
7 - 12 **4 - 6, 13 - 15**

	config.	R	X
7	D-*galacto*	Me	COOMe
8	D-*gluco*	Me	COOMe
9	D-*galacto*	Et	COOEt
10	D-*gluco*	Et	COOEt
11	D-*galacto*	Et	CN
12	D-*gluco*	Et	CN

	config.	X
4	D-*galacto*	COOMe
5	D-*gluco*	COOMe
6	D-*galacto*	COOEt
13	D-*gluco*	COOEt
14	D-*galacto*	CN
15	D-*gluco*	CN

Scheme 4

We obtained the corresponding methyl enol ether **16** and **17** from the acetylated methyl 2-deoxyoct-3-ulosonates **4** and **5**, respectively, using diazomethane and Al_2O_3 (Scheme 5).[7] The crystallographic data for **16** are provided in Table 1. The ORTEP drawing of **16** is illustrated in Figure 1, confirming that the *Z*-configuration had been constituted.[8,9]



Scheme 5

Table 1 Crystallographic data for Methyl 4,5,6,7,8-Penta-*O*-acetyl-2-deoxy-3-*O*-methyl-D-*galacto*-oct-2(*Z*)-enoate (**16**)

Crystal size (mm)	0.8 x 0.38 x 0.36	μ (cm^{-1})	1.11
Space group	$P2_12_12_1$	2 Θ range (degrees)	4.4 - 47
Cell parameters (Å, degrees)[a]		Symmetry independent reflections	3336
a	8.446 (1)	Observed reflections with $I>2\ \sigma(I)$	2850
b	15.554 (2)	Number of refined parameters	326
c	18.373 (1)	Ratio of parameters to valued reflections	10.23
Volume (Å^3)[a]	2413.6 (4)	$R1_{(obs)}$	0.0533
Z	4		
F(000)	1008		
Density D_x (Mg m^{-3})	1.311		
λ (Mo Kα) (Å)	0.71073		

a. Standard deviations given in parentheses.

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-101340. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: Int. code +(1223) 336-033; e-mail: deposit@ccdc.cam.ac.uk).

Like ethyl acetoacetate,[10] the 4,5,6,7,8-penta-*O*-acetyl-2-deoxy-D-*galacto*-oct-3-ulosonic acid methyl (**4**) and ethyl esters (**6**) were brominated in chloroform/diethyl ether giving 4,5,6,7,8-penta-*O*-acetyl-2-bromo-2-deoxy-D-*galacto*-oct-3-ulosonic acid methyl (**18** / 87%) and ethyl esters (**19** / 76%) in high yields (Scheme 6).

If the brominations of **4** and **6** are carried out in pure chloroform, the reaction begins slowly and the yields are 50% and less, because there is a low concentration of the enol form in chloroform. This was uncovered by ^{1}H NMR spectroscopy recorded in

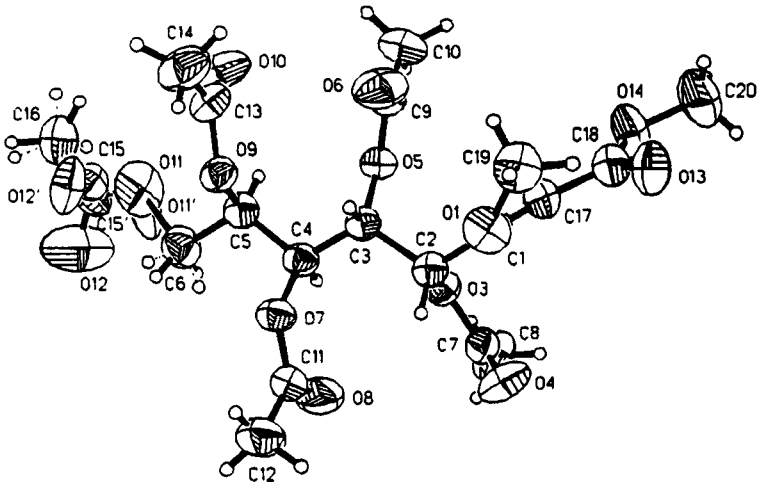
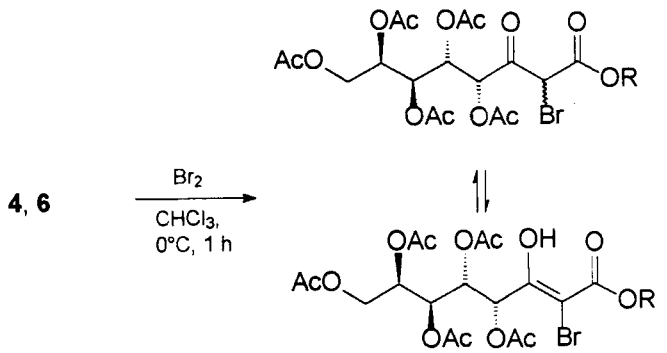


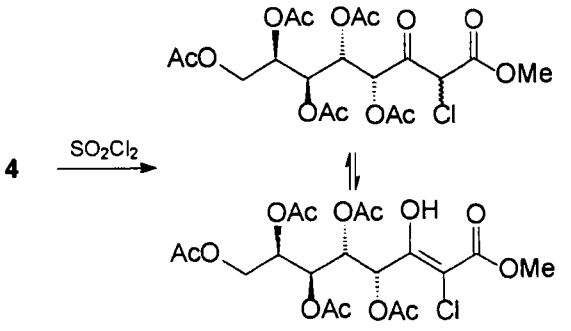
Fig. 1. ORTEP drawing of **16**

deuteriochloroform. If dry diethyl ether is used as solvent, the color of bromine disappears right after addition. Maximum yields could be reached in dry chloroform containing 10-20% dry diethyl ether.



Scheme 6

On the other hand, 4,5,6,7,8-penta-*O*-acetyl-2-deoxy-D-*galacto*-oct-3-ulosonic acid methyl ester (**4**) was chlorinated in sulfuryl chloride[11] giving 4,5,6,7,8-penta-*O*-



20

Scheme 7

acetyl-2-chloro-2-deoxy-D-*galacto*-oct-3-ulosonic acid methyl ester (**20**). The separation of a side product 4,5,6,7,8-penta-*O*-acetyl-2,2-dichloro-2-deoxy-D-*galacto*-oct-3-ulosonic acid methyl ester was conducted by fractional crystallization (Scheme 7).

There is a rapid equilibrium between the keto and enol tautomers in the solutions of **18**, **19** and **20**, respectively, in $CDCl_3$. Therefore, in their ^{13}C NMR spectra only one signal of C-2 and C-3, for each, was found.

EXPERIMENTAL

General Procedures. Melting points were determined with a BOETIUS melting point apparatus and have been corrected. Specific rotations were determined with a Polar LμP (IBZ Messtechnik). IR spectra were recorded with a Nicolet 205 FT-IR spectrometer. ^1H NMR (300.133 MHz and 250.133 MHz, respectively) and ^{13}C NMR (75.466 MHz and 62.896 MHz, respectively) were obtained on Bruker instruments WM 300 and AC 250, respectively. The ^{13}C NMR spectra were determined by DEPT and/or ^1H, ^{13}C, COSY experiments. ^1H and ^{13}C chemical shifts (δ) are given in ppm relative to the solvent signal. The mass spectra were recorded on an AMD 402/3 spectrometer. For column chromatography Merck Silica gel 60 (63 - 200 mesh) was used. Toluene/ethyl acetate = 2:1 was used as eluent. TLC was performed on silica gel 60 GF_{254} (Merck) with detection by UV light (λ = 254 nm) and/or staining by heating. If not otherwise

described, a mixture of toluene/ethyl acetate = 1:2 was used as eluent. Elemental analyses was carried out on a Leco CHNS-932.

General decarboalkoxylation procedure of substituted alkyl 2-deoxyoct-3-ulosonates 1 - 3, 7 - 12.

Method A. Benzyl oct-3-ulosonates **1-3** (10 mmol) are dissolved in ethyl acetate (50 mL), a small catalytic amount of 10% palladium on charcoal is added and the solution is stirred over night under hydrogen atmosphere. After adding ethyl acetate (50 mL) and stirring further 10 minutes, the catalyst is filtered off and the solution evaporated. The product crystallizes from ether and is recrystallized from methanol and ethanol, respectively.

Method B. Alkyl oct-3-ulosonates **7-12** (10 mmol) and tri-*n*-butyl tin hydride (4 mL) are heated >100 °C by a lamp, azobisisobutyronitrile (0.5 g) is added and the mixture is heated for 30 minutes. 1,2-Dichloroethane (10 mL) is then added and the mixture refluxed for a further 20 h, adding a small amount of azobisisobutyronitrile every 30 minutes. After cooling, the solvent is evaporated and the residue is purified by column chromatography. The product crystallizes from ether and is recrystallized from methanol.

Method C. Alkyl oct-3-ulosonates **7-12** (10 mmol) are dissolved in acetic acid (40 mL, containing a trace of water) and the solution is refluxed for 1h. After cooling, the solvent is evaporated, the syrup is dissolved in toluene and again evaporated until the residue contains no more acetic acid. The product crystallizes from ether and is recrystallized from methanol and ethanol, respectively.

Methyl 4,5,6,7,8-Penta-*O*-acetyl-2-deoxy-D-*galacto*-oct-3-ulosonate (4). **1**[1] (6.0 g, 10 mmol, method A) and **7**[1] (5.2 g, 10 mmol, method B or C), respectively, were used to react as described above and yielded **4** as a white solid, 3.01 g, 70.4% (method A), 1.33 g, 28.8% (method B) and 2.92 g, 63.2% (method C), respectively: mp 129-132 °C; R_f = 0.74; $[\alpha]_D^{20}$ -3.5° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 2.02 - 2.18 (5s, 15H, OAc), 3.49 (AB, $J_{2,2'}$ = 15.8 Hz, 1H, H-2'), 3.62 (AB, 1H, H-2), 3.86 (dd, $J_{8,8'}$ = 11.6 Hz, $J_{7,8'}$ = 7.4 Hz, 1H, H-8'), 3.73 (s, 3H, OMe), 4.26 (dd, $J_{7,8}$ = 5.2 Hz, 1H, H-8), 5.29 (m, $J_{6,7}$ = 2.0 Hz, 1H, H-7), 5.38 (d, 1H, H-4), 5.43 (dd, $J_{5,6}$ = 9.9 Hz, 1H, H-6), 5.62 (dd, $J_{4,5}$ = 1.9 Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$) δ 20.4 - 20.7 (CH_3CO), 46.4 (C-2), 52.6 (OMe), 61.9 (C-8), 67.1 (C-7), 67.4 (C-6), 67.6 (C-5), 74.6 (C-4), 166.4 (C-1), 169.5 -

170.4 (CH_3CO), 196.5 (C-3). Mass spectrum (DCI/isobutane: *m/z* (%) = 463 (6, $[M+H]^+$), 403 (100).

Anal. Calcd for $C_{19}H_{26}O_{13}$: C, 49.35; H, 5.67; Found: C, 49.37; H, 5.67.

Methyl 4,5,6,7,8-Penta-*O*-acetyl-2-deoxy-D-*gluco*-oct-3-ulosonate (5). **2**[1] (6.0 g, 10 mmol, method A) and **8**[1] (5.2 g, 10 mmol, method C), respectively, were used to react as described above and yielded **5** as a white solid, 1.42 g, 30.8% (method A) and 2.02 g, 43.7% (method C), respectively): mp 115-119 °C; R_f = 0.74; $[\alpha]_D^{20}$ +13.6° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 2.03 - 2.17 (5s, 15H, OAc), 3.54 (AB, $J_{2,2'}$ = 15.9 Hz, 1H, H-2'), 3.56 (AB, 1H, H-2), 3.71 (s, 3H, OMe), 4.09 (dd, $J_{8,8'}$ = 12.5 Hz, $J_{7,8'}$ = 5.8 Hz, 1H, H-8'), 4.30 (dd, $J_{7,8}$ = 3.7 Hz, 1H, H-8), 5.06 (m, $J_{6,7}$ = 6.4 Hz, 1H, H-7), 5.43 (d, 1H, H-4), 5.45 (dd, $J_{5,6}$ = 4.6 Hz, 1H, H-6), 5.59 (dd, $J_{4,5}$ = 4.3 Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$) δ 20.2 - 20.7 (CH_3CO), 46.6 (C-2), 52.5 (OMe), 61.6 (C-8), 68.5 (C-7), 69.1 (C-5), 69.7 (C-6), 74.8 (C-4), 166.4 (C-1), 169.5 - 169.7 (CH_3CO), 196.2 (C-3). Mass spectrum (DCI/isobutane): *m/z* (%) = 463 (30, $[M+H]^+$), 403 (100).

Anal. Calcd for $C_{19}H_{26}O_{13}$: C, 49.35; H, 5.67; Found: C, 49.29; H, 5.59.

Ethyl 4,5,6,7,8-Penta-*O*-acetyl-2-deoxy-D-*galacto*-oct-3-ulosonate (6). **3**[1] (6.1 g, 10 mmol, method A) and **9**[1] (5.5 g, 10 mmol, method C), respectively, were used to react as described above and yielded **6** as a white solid, 3.33 g, 70.0% (method A) and 2.09 g, 43.9% (method C), respectively: mp 92-94 °C; R_f = 0.79; $[\alpha]_D^{20}$ +2.3° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.25 (t, J = 7.3 Hz, 3H, CH_3CH_2), 2.00 - 2.15 (5s, 15H, OAc), 3.46 (AB, $J_{2,2'}$ = 15.6 Hz, 1H, H-2'), 3.58 (AB, 1H, 2-H), 3.86 (dd, $J_{8,8'}$ = 11.6 Hz, $J_{7,8'}$ = 7.0 Hz, 1H, H-8'), 4.16 (q, 2H, CH_3CH_2), 4.25 (dd, $J_{7,8}$ = 5.2 Hz, 1H, H-8), 5.27 (m, $J_{6,7}$ = 2.1 Hz, 1H, H-7), 5.38 (d, 1H, H-4), 5.40 (dd, $J_{5,6}$ = 9.8 Hz, 1H, H-6), 5.61 (dd, $J_{4,5}$ = 2.1 Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$) δ 14.0 (CH_3CH_2), 20.4 - 20.7 (CH_3CO), 46.7 (C-2), 61.7 (CH_3CH_2), 61.9 (C-8), 67.1 (C-7), 67.3 (C-6), 67.6 (C-5), 74.5 (C-4), 165.9 (C-1), 169.5 - 170.4 (CH_3CO), 196.7 (C-3). Mass spectrum (DCI/isobutane): *m/z* (%) = 477 (21, $[M+H]^+$, 417 (100).

Anal. Calcd for $C_{20}H_{28}O_{13}$: C, 50.42; H, 5.92; Found: C, 50.45; H, 5.98.

Ethyl 4,5,6,7,8-Penta-*O*-acetyl-2-deoxy-D-*gluco*-oct-3-ulosonate (13). **10**[1] (5.5 g, 10 mmol, method C) was used to react as described above and yielded **13** as a colorless syrup (3.90 g, 82.0%), which crystallized after several weeks: mp 45-49 °C; R_f

= 0.79; $[\alpha]_D^{20}$ -4.5° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, J = 7.3 Hz, 3H, CH_3CH_2), 1.99 - 2.16 (s, 15H, OAc), 3.61 (AB, $J_{2,2'}$ = 16.5 Hz, 1H, H-2'), 3.82 (AB, 1H, H-2), 4.10 (q, 2H, CH_3CH_2), 4.13 (dd, $J_{8,8'}$ = 12.2 Hz, $J_{7,8'}$ = 6.1 Hz, 1H, H-8'), 4.28 (dd, $J_{7,8}$ = 3.4 Hz, 1H, H-8), 5.02 (m, $J_{6,7}$ = 6.1 Hz, 1H, H-7), 5.39 (dd, $J_{5,6}$ = 4.6 Hz, 1H, H-6), 5.47 (d, 1H, H-4), 5.58 (dd, $J_{4,5}$ = 3.7 Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$) δ 13.8 (CH_3CH_2), 20.0 - 20.4 (CH_3CO), 45.9 (C-2), 60.7 (C-8), 61.1 (CH_3CH_2), 67.4 (C-7), 68.4 (C-6), 68.8 (C-5), 75.3 (C-4), 165.9 (C-1), 169.2 - 169.9 (CH_3CO), 196.8 (C-3). Mass spectrum (DCI/isobutane): *m/z* (%) = 477 (41, $[M+H]^+$), 417 (100).

Anal. Calcd for $C_{20}H_{28}O_{13}$: C, 50.42; H, 5.92; Found: C, 50.45; H, 5.97.

4,5,6,7,8-Penta-*O*-acetyl-2-deoxy-D-*galacto*-oct-3-ulosononitrile (14). 11[1] (5.0 g, 10 mmol, method C) was used to react as described above and yielded **14** as a white solid (3.27 g, 76.3%): mp 137-139 °C; R_f = 0.62; $[\alpha]_D^{20}$ -17.9° (*c* 1.0, chloroform); IR (KBr) 2264 (CN); ^{1}H NMR ($CDCl_3$) δ 2.00 - 2.16 (5s, 15H, OAc), 3.60 (AB, $J_{2,2'}$ = 19.6 Hz, 1H, H-2'), 3.61 (AB, 1H, H-2), 3.87 (dd, $J_{8,8'}$ = 11.7 Hz, $J_{7,8'}$ = 7.4 Hz, 1H, H-8'), 4.24 (dd, $J_{7,8}$ = 5.3 Hz, 1H, H-8), 5.20 (d, 1H, H-4), 5.34 (m, $J_{6,7}$ = 1.8 Hz, 1H, H-7), 5.43 (dd, $J_{4,5}$ = 1.5 Hz, 1H, H-5), 5.45 (dd, $J_{5,6}$ = 9.8 Hz, 1H, H-6); ^{13}C NMR ($CDCl_3$) δ 20.1 - 20.5 (CH_3CO), 29.5 (C-2), 61.8 (C-8), 67.1 (C-5), 67.6 (C-7), 67.7 (C-6), 74.0 (C-4), 112.7 (C-1), 169.3 - 170.2 (CH_3CO), 191.3 (C-3). Mass spectrum (DCI/isobutane): *m/z* = 430 (8, $[M+H]^+$), 370 (100).

Anal. Calcd for $C_{18}H_{23}NO_{11}$: C, 50.35; H, 5.40; N, 3.26; Found: C, 50.38; H, 5.45; N, 3.35.

4,5,6,7,8-Penta-*O*-acetyl-2-deoxy-D-*gluco*-oct-3-ulosononitrile (15). 12[1] (5.0 g, 10 mol, method C) was used to react as described above and yielded **15** as a white solid (3.03 g, 71.4%): mp 135-136 °C; R_f = 0.62; $[\alpha]_D^{20}$ +13.6° (*c* 1.0, chloroform); IR (KBr) 2265 (CN); ^{1}H NMR ($CDCl_3$) δ 2.03 - 2.16 (5s, 15H, OAc), 3.63 (AB, $J_{2,2'}$ = 19.8 Hz, 1H, H-2'), 3.66 (AB, 1H, H-2), 4.07 (dd, $J_{8,8'}$ = 12.5 Hz, $J_{7,8'}$ = 5.5 Hz, 1H, H-8'), 4.29 (dd, $J_{7,8}$ = 3.0 Hz, 1H, H-8), 5.06 (m, $J_{6,7}$ = 6.9 Hz, 1H, H-7), 5.30 (d, 1H, H-4), 5.41 (dd, $J_{5,6}$ = 4.0 Hz, 1H, H-6), 5.51 (dd, $J_{4,5}$ = 4.3 Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$) δ 20.1 - 20.6 (CH_3CO), 30.0 (C-2), 61.6 (C-8), 68.1 (C-7), 68.6 (C-6), 68.9 (C-5), 74.4 (C-4), 112.7 (C-1), 169.5 - 170.5 (CH_3CO), 191.6 (C-3). Mass spectrum (DCI/isobutane): *m/z* (%) = 430 (5, $[M+H]^+$), 370 (100).

Anal. Calcd for $C_{18}H_{23}NO_{11}$: C, 50.35; H, 5.40; N, 3.26; Found: C, 50.33; H, 5.45; N, 3.28.

General O-methylation procedure of methyl 2-deoxyoct-3-ulosonates 4, 5. Ethereal diazomethane solution is added to **4**, **5** (1 mmol) dissolved in acetone containing Al_2O_3 (0.5 g) until the color of the diazomethane remains. The excess of diazomethane is removed by a low volume of acetic acid, that is added and the Al_2O_3 was filtered off. The solvent is evaporated and the product is crystallized from ether and recrystallized by dissolving the solid in a low volume of acetone and adding ether to this solution.

Methyl 4,5,6,7,8-Penta-*O*-acetyl-2-deoxy-3-*O*-methyl-D-*galacto*-oct-2(*Z*)-enoate (16). **4** (0.46 g, 1 mmol) was used to react with diazomethane as described above and yielded **16** as a white solid (0.37 g, 77.6%): mp 95-98 °C; R_f = 0.75; $[\alpha]_D^{20}$ +12.1° (*c* 1.0, chloroform); IR (KBr) 1646 (C=C-O-Me); ^{1}H NMR ($CDCl_3$) δ 1.99 - 2.10 (5s, 15H, OAc), 3.63, 3.90 (s, 6H, OMe), 3.84 (dd, $J_{8,8'}$ = 11.6 Hz, $J_{7,8'}$ = 7.3 Hz, 1H, H-8'), 4.25 (dd, $J_{7,8}$ = 4.9 Hz, 1H, H-8), 5.05 (s, 1H, H-2), 5.14 (d, 1H, H-4), 5.30 (m, $J_{6,7}$ = 1.5 Hz, 1H, H-7), 5.37 (t, $J_{5,6}$ = 1.8 Hz, 1H, H-6), 5.37 (t, $J_{4,5}$ = 1.5 Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$) δ 20.3 - 20.6 (CH_3CO), 51.2, 62.0 (OMe), 62.0 (C-8), 67.6 (C-7), 67.7 (C-6), 67.8 (C-5), 70.0 (C-4), 94.7 (C-2), 164.7 (C-1), 164.9 (C-3), 169.2 - 170.3 (CH_3CO). Mass spectrum (DCI/isobutane): *m/z* (%) = 477 (93, $[M+H]^+$), 403 (100).

Anal. Calcd for $C_{20}H_{28}O_{13}$: C, 50.42; H, 5.92; Found: C, 50.65; H, 5.84.

Methyl 4,5,6,7,8-Penta-*O*-acetyl-2-deoxy-3-*O*-methyl-D-*gluco*-oct-2(*Z*)-enoate (17). **5** (0.46 g, 1 mmol) was used to react with diazomethane as described above and yielded after column chromatography **17** as a colorless syrup (0.33 g, 69.2%), which solidifies after several month: mp 61-65 °C; R_f = 0.75; $[\alpha]_D^{20}$ +32.9° (*c* 1.0, chloroform); IR (KBr) 1657 (C=C-O-Me); ^{1}H NMR ($CDCl_3$) δ 2.01 - 2.12 (5s, 15H, OAc), 3.63, 3.90 (s, 6H, OMe), 4.08 (dd, $J_{8,8'}$ = 12.2 Hz, $J_{7,8'}$ = 5.8 Hz, 1H, H-8'), 4.25 (dd, $J_{7,8}$ = 4.3 Hz, 1H, H-8), 5.02 (m, $J_{6,7}$ = 6.1 Hz, 1H, H-7), 5.14 (s, 1H, H-2), 5.27 (d, 1H, H-4), 5.35 (dd, $J_{5,6}$ = 5.2 Hz, 1H, H-6), 5.48 (t, $J_{4,5}$ = 4.8 Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$) δ 20.4 - 20.7 (CH_3CO), 51.3, 62.1 (OMe), 61.4 (C-8), 68.6 (C-7), 69.2 (C-5), 69.4 (C-6), 72.5 (C-4), 96.6 (C-2), 163.9 (C-1), 164.8 (C-3), 169.3 - 170.4 (CH_3CO). Mass spectrum (DCI/isobutane): *m/z* = 477 (71, $[M+H]^+$), 403 (100).

Anal. Calcd for $C_{20}H_{28}O_{13}$: C, 50.42; H, 5.92; Found: C, 50.74; H, 5.84.

General bromination procedure of alkyl 2-deoxy-D-*galacto*-oct-3-ulosonates 4, 6. Bromine (0.28 mL, 5.5 mmol) is dropped into a stirred solution of **4**, **6** (5 mmol) dissolved in chloroform (50 mL) containing diethyl ether (5 mL). After 1 h at 0 °C the solution is washed with 5% Na_2SO_3 solution (100 mL), the layers are separated and the aqueous layer is washed with another chloroform (30 mL). The combined organic layers are washed another two times with water, dried and the solvent is evaporated. The product crystallizes from ether and is recrystallized in methanol and ethanol respectively.

Methyl 4,5,6,7,8-Penta-*O*-acetyl-2-bromo-2-deoxy-D-*galacto*-oct-3-ulosonate (18). **4** (4.6 g, 10 mmol) was brominated as described above and yielded **18** as a white solid (4.69 g, 86.7%): mp 121-123 °C; R_f = 0.73; $[\alpha]_D^{20}$ +11.3° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.99 - 2.15 (5s, 15H, OAc), 3.79 (s, 3H, OMe), 3.82 (dd, $J_{8,8'}$ = 11.6 Hz, $J_{7,8'}$ = 7.3 Hz, 1H, H-8'), 4.24 (dd, $J_{7,8}$ = 5.2 Hz, 1H, H-8), 5.09 (s, 1H, H-2), 5.22 (m, $J_{6,7}$ = 2.1 Hz, 1H, H-7), 5.33 (dd, $J_{5,6}$ = 9.8 Hz, 1H, H-6), 5.61 (d, 1H, H-4), 5.63 (dd, $J_{4,5}$ = 2.1 Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$) δ 20.4 - 20.7 (CH_3CO), 46.9 (C-2), 53.9 (OMe), 61.9 (C-8), 67.3 (C-7), 67.4 (C-6), 67.9 (C-5), 72.8 (C-4), 164.5 (C-1), 169.2 - 170.3 (CH_3CO), 192.3 (C-3). Mass spectrum (DCI/isobutane): *m/z* (%) = 543, 541 (3, 2, $[M+H]^+$), 403 (100).

Anal. Calcd for $C_{19}H_{25}BrO_{13}$: C, 42.16; H, 4.65; Found: C, 42.59; H, 4.73.

Ethyl 4,5,6,7,8-Penta-*O*-acetyl-2-bromo-2-deoxy-D-*galacto*-oct-3-ulosonate (19). **6** (2.4 g, 5 mmol) was brominated as described above and yielded **19** as a white solid (2.1 g, 75.7%): mp 116-119 °C; R_f = 0.79; $[\alpha]_D^{20}$ +24.6° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J = 7.3 Hz, 3H, CH_3CH_2), 1.99 - 2.15 (5s, 15H, OAc), 3.83 (dd, $J_{8,8'}$ = 11.6 Hz, $J_{7,8'}$ = 7.3 Hz, 1H, H-8'), 4.24 (dd, $J_{7,8}$ = 5.2 Hz, 1H, H-8), 4.25 (q, 2H, CH_3CH_2), 5.08 (s, 1H, H-2), 5.22 (m, $J_{6,7}$ = 2.1 Hz, 1H, H-7), 5.34 (dd, $J_{5,6}$ = 9.8 Hz, 1H, H-6), 5.64 (d, 1H, H-4), 5.65 (dd, $J_{4,5}$ = 1.8 Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$) δ 13.8 (CH_3CH_2), 20.4 - 20.7 (CH_3CO), 46.9 (C-2), 61.9 (C-8), 63.5 (CH_3CH_2), 67.3 (C-7), 67.4 (C-6), 67.9 (C-5), 72.8 (C-4), 164.0 (C-1), 169.2 - 170.4 (CH_3CO), 192.5 (C-3). Mass spectrum (DCI/isobutane): *m/z* (%) = 557, 555 (0.5, 0.4, $[M+H]^+$), 61 (100).

Anal. Calcd for $C_{20}H_{27}BrO_{13}$: C, 43.26; H, 4.90; Found: C, 43.08; H, 4.75.

Methyl 4,5,6,7,8-Penta-*O*-acetyl-2-chloro-2-deoxy-D-*galacto*-oct-3-ulosonate (20). **4** (0.462 g, 1 mmol) was dissolved in sulfuryl chloride (1 mL) and stirred for 1 h.

After heating the solution to reflux for 2 minutes, diethyl ether was added to crystallize the product. The solution was stored 2 h at 4 °C for complete crystallization. Recrystallizing the substance from ethanol gave **20** as a white solid (0.23 g, 46.7%): mp 134-138 °C; R_f = 0.69; $[\alpha]_D^{20}$ -8.1° (*c* 1.0. chloroform); ^{1}H NMR ($CDCl_3$) δ 2.00 - 2.15 (5s, 15H, OAc), 3.82 (s, 3H, OMe), 3.85 (dd, $J_{8,8'}$ = 11.6 Hz, $J_{7,8'}$ = 7.3 Hz, 1H, H-8'), 4.25 (dd, $J_{7,8}$ = 5.2 Hz, 1H, H-8), 5.17 (s, 1H, H-2), 5.27 (m, $J_{6,7}$ = 2.1 Hz, 1H, H-7), 5.39 (dd, $J_{5,6}$ = 9.5 Hz, 1H, H-6), 5.58 (d, 1H, H-4), 5.59 (dd, $J_{4,5}$ = 1.2 Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$) δ 20.2 - 20.7 (CH_3CO), 53.9 (OMe), 59.6 (C-2), 61.8 (C-8), 67.5 (C-7, C-6), 67.6 (C-5), 72.8 (C-4), 164.4 (C-1), 169.4 - 170.3 (CH_3CO), 191.8 (C-3). Mass spectrum (DCI/isobutane): *m/z* (%) = 499, 497 (3, 5, $[M+H]^+$), 439, 437 (36, 100).

Anal. Calcd for $C_{19}H_{25}ClO_{13}$: C, 45.93; H, 5.07; Cl, 7.14; Found: C, 45.87; H, 4.97; Cl, 7.45.

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