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Synthesis of Diuloses by Chain Elongation of Aldonoyl Chlorides

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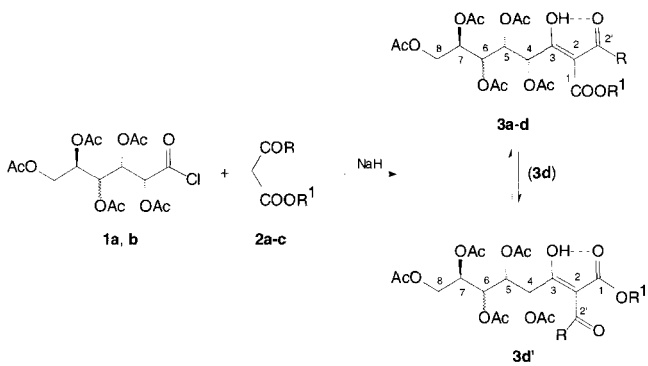
Abstract. 2,3,4,5,6-Penta-*O*-acetyl-*D*-galactonic acid chloride (**1a**) and *D*-gluconic acid chloride (**1b**), respectively, react with alkyl acetoacetates and benzoylacetates **2**, respectively, to yield derivatives **3** of diuloses with an alkoxycarbonyl group in the branch. Decarboalkoxylation of these compounds gives 1,3-didesoxy-nono-2,4-diuloses **4a,b** and 2-deoxy-octo-1,3-diuloses **4c**, respectively. Compound **4a** and diazomethane react to furnish the corresponding methyl enol ether **5a** and **5b**.

Progress in antiviral chemotherapy was accomplished by the recognition that potent antiviral activity is displayed by some analogues of the natural nucleosides in which the ribose unit is replaced by an acyclic residue [1–3]. Important compounds of this type include the guanosine analogues, *aciclovir*, which is in clinical use against herpes infections, *ganciclovir* and the adenosine analogue (*S*)-9-(2,3-dihydroxy-propyl)adenine.

In this paper the preparations of building blocks for the syntheses of similar acyclic *C*-nucleoside analogues are described. The syntheses of 1,3-dideoxy-nono-2,4-diuloses and 2-deoxy-octo-1,3-diuloses, respectively, were achieved by C-chain elongation of 2,3,4,5,6-penta-*O*-acetyl-*D*-galactonic or *D*-gluconic acid chloride (**1a** or **1b**) with 1,3-dicarbonyl compounds. Those deoxy-diuloses with structure features of acetyl- or benzoylacetone should be suitable for the synthesis of heterocycles.

The reaction of 2,3,4,5,6-penta-*O*-acetyl-*D*-galactonic or *D*-gluconic acid chloride (**1a** or **1b**) with alkyl acetoacetates **2a,b** and ethyl benzoylacetate (**2c**), respectively, in the presence of sodium hydride led to alkyl 4,5,6,7,8-penta-*O*-acetyl-2-deoxy-2-acyl-*D-galacto*-(or *D-gluco*-)oct-3-ulosonate (**3a–d**, Scheme 1). Using three equivalents of acylacetic acid ester and base and one equivalent of aldonic acid chloride the formation of *O*-acylated products was almost avoided.

Probably, there is a fast equilibrium between the two H-bridge stabilized enolic structures in the solution of **3a–c** in $CDCl_3$. Therefore, these tautomers cannot be distinguished in the ^1H NMR and ^{13}C NMR spectra. In the ^{13}C NMR spectra signals at 107 and 194 to 196 ppm suggest the presence of a sp^2 C-2 and C-2'/C-3 carbon, respectively. For compound **3d** the NMR spectra suggest the presence of two isomers **3d** and **3d'**. The proportions of the both diastereomers are 1.6 : 1. The NMR data do not allow any assignment to one isomer.



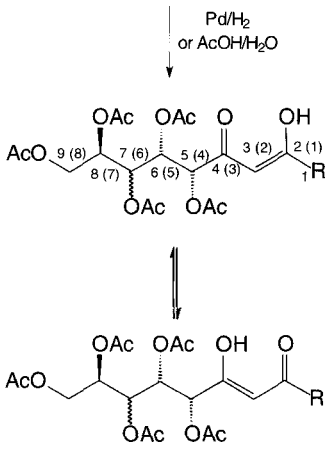
	1a	1b	2a	2b	2c	3a	3b	3c	3d,3d'
config.	D-galacto	D-gluco				D-galacto	D-gluco	D-galacto	
R			Me	Me	Ph	Me	Me	Me	Ph
R^1			Me	Bzl	Et	Et	Et	Bzl	Et

Through hydrogenation with palladium/charcoal [4-6] of benzyl 2-acetyl-4,5,6,7,8-penta-*O*-acetyl-2-deoxy-*D-galacto*-oct-3-ulosonate (**3c**) the corresponding branched octulonic acid was obtained. As described for the free 2-acylacetic acid [7], these compound un-

derwent spontaneous decarboxylation at room temperature giving the 1,3-dideoxy-nono-2,4-diulose **4a** in a yield of 86%.

According to the decarboalkoxylation of malonates with propionic acid [8], heating the octulosonic acid ester **3a,b,d** in acetic acid as solvent with a trace of water furnishes the 1,3-dideoxy-nono-2,4-diuloses and 2-deoxy-octo-1,3-diulose **4a–c** in very good yields.

3a-d



4a,b,c

	config.	R
4a	D-galacto	Me
4b	D-gluco	Me
4c	D-galacto	Ph

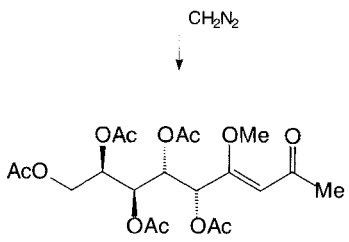
^{1}H NMR and ^{13}C NMR spectra show signals for enolic forms **4a–c**. Also in this case, there is a fast equilibrium between the two enolic structures stabilized by H-bridges, and these tautomers cannot be distinguished in the ^{1}H NMR and ^{13}C NMR spectra. In a $CDCl_3$ solution compound **4a** shows signals at 97.1 and 189.1/190.2 ppm suggesting the presence of sp^2 C-3 and C-2/C-4 carbon, respectively.

Compound **4a** was subjected to X-ray analysis at 293 *K*. The relevant crystallographic data for **4a** are given in Table 1. The structure was solved by direct methods in the usual way with the help of the Siemens program XS [9], and refined with SHELXL-93 [10]. All non-hydrogen atoms were refined anisotropically, hydrogens introduced at theoretical positions and refined according to the riding model. An ORTEP drawing of **4a** with 50% probability of the thermal ellipsoids is shown in Figure 1, which gives the numbering scheme of the atoms.

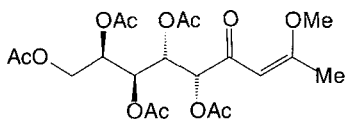
We obtained the corresponding methyl enol ether **5a** and **5b** from 4,5,6,7,8-penta-*O*-acetyl-1,2-dideoxy-*D*-*galacto*-nono-2,4-diulose (**4a**) using diazomethane and Al_2O_3 [11]. The crystallographic data for **5a** and **5b** are given in Table 1. ORTEP drawings of **5a** and **5b** are shown in Figure 2.

We thank the Fonds der Chemischen Industrie for financial support.

4a



5a



5b

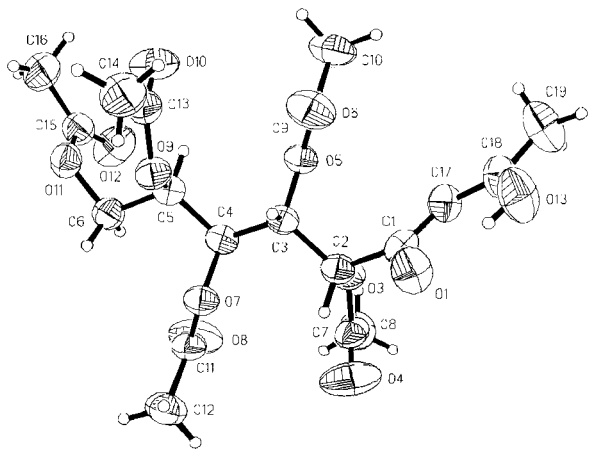


Fig. 1 ORTREP drawing of **4a**

Experimental

Melting points were determined with a BOETIUS melting point apparatus and are corrected. Specific rotations were determined with a Polar LμP (IBZ Messtechnik). IR spectra were recorded with a Nicolet 205 FT-IR spectrometer. ^{1}H 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 ^{1}H, ^{13}C, COSY experiments. The mass spectra were recorded on an AMD 402/3 spectrometer. For column chromatography Merck Silica gel 60 (63–200 μm) was used. Toluene/ethylacetate = 2:1 was used as eluent. TLC was performed on silica gel 60 F_{254} (Merck) with detection by UV light (λ = 254 nm) and/or staining by heating. A mixture of toluene/ethylacetate = 1:2 was used as eluent, if not stated otherwise. Elemental analyses were carried out on a Leco CHNS-932.

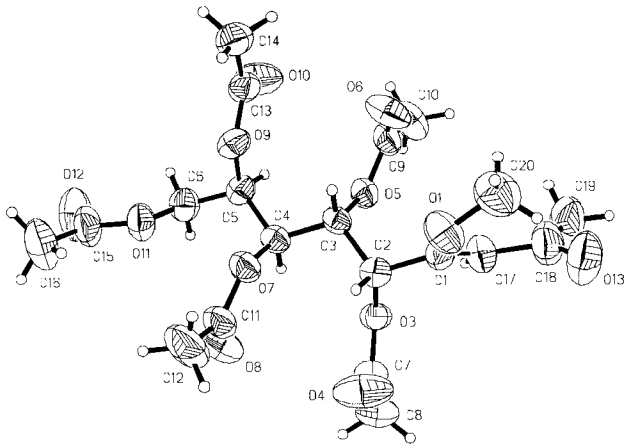
2,3,4,5,6-Penta-*O*-acetyl-*D*-galactonic acid chloride (**1a**) and 2,3,4,5,6-Penta-*O*-acetyl-*D*-gluconic acid chloride (**1b**) were prepared according to a literature procedure [12, 13].

Tab. 1 Crystallographic data for 5,6,7,8,9-penta-*O*-acetyl-1,3-dideoxy-*D-galacto*-nono-2,4-diulose (**4a**), 5,6,7,8,9-penta-*O*-acetyl-1,3-dideoxy-4-*O*-methyl-*D-galacto*-non-3-en-2-ulose (**5a**) and 5,6,7,8,9-penta-*O*-acetyl-1,3-dideoxy-2-*O*-methyl-*D-galacto*-non-2-en-4-ulose (**5b**)

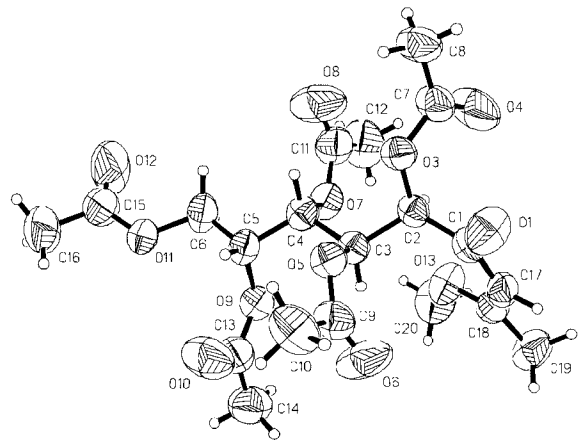
Compound	**4a**	**5a**	**5b**
Crystal size (mm)	0.66×0.5 ×0.42	0.64×0.28 × 0.2	0.84×0.46 ×0.15
Space group	$P2_1$	$P2_1$	$P2_12_12_1$
Cell parameters (Å, degrees) [a]			
a	5.965 (1)	10.085 (2)	8.046 (2)
b	20.997 (2)	23.146 (5)	8.836 (1)
c	9.429 (1)	11.488 (3)	33.996 (3)
β	104.17 (1)	115.88 (2)	
Volume (Å^3) [a]	1154.0 (3)	2412.7 (9)	2416.9 (4)
Z	2	4	4
F(000)	472	976	976
Density D_x (Mg m^{-3})	1.295	1.268	1.265
λ(Mo Kα) (Å)	0.71073	0.71073	0.71073
μ (cm^{-1})	1.09	1.06	1.06
2 Θrange (degrees)	3.88–45	3.5–45	4.8–45
Symmetry independent reflections	2998	6302	3165
Observed reflections with $I>2\ \sigma(I)$	2859	4794	2350
Number of refined parameters	288	591	296
Ratio of parameters to valued reflections	10.41	10.66	10.69
$R1_{(obs)}$	0.0479	0.0653	0.0654

[a] Standard deviations given in parentheses.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited wih the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 101169. 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@chemcrys.cam.ac.uk).



Compound **5a**



Compound **5b**

Fig. 2 ORTEP drawings of **5a** and **5b**

Alkyl Oct-3-ulosonates 3a–d (General Procedure)

30 mmol ethyl or benzyl acetoacetate (**2a,b**) and ethyl benzoylacetate (**2c**), respectively, dissolved in 30 ml toluene were carefully dropped into a suspension of sodium hydride (0.72 g, 30 mmol) in toluene (80 ml) while the solution was heavily stirred. After foaming decreased and stirring for additional 10 minutes 2,3,4,5,6-penta-*O*-acetyl-*D*-galactonic (or -gluconic) acid chloride **1a** or **1b** (4.24 g, 10 mmol) dissolved in 30 ml toluene was added. The solution was stirred for 30 minutes and washed with water (150 ml) containing $NaHSO_4$ (10 g). The layers were separated and the organic layer was washed 2x with water. The solution was dried with $MgSO_4$ and the solvent was evaporated.

Ethyl 2-Acetyl-4,5,6,7,8-penta-O-acetyl-2-deoxy-D-galacto-oct-3-ulosonate (**3a**)

2a and **1a** were used to react in toluene as described above. After drying and evaporation of the solvent the compound was crystallized from ether and recrystallized from ethanol giving **3a** as a white solid (1.78 g, 34.3%). *m.p.* 100–102 °C; R_f = 0.74; $[\alpha]_D^{20}$ –29.4° (*c* = 1.0, chloroform). – IR (KBr): ν/cm^{-1} = 1692 (C=C–OH). – ^{1}H NMR ($CDCl_3$): δ/ppm = 1.31 (t, J = 7,3 Hz, 3H, $C\underline{H}_3CH_2$), 1.97–2.13 (5s, 15H, OAc), 2.40 (s, 3H, $C\underline{H}_3$C-2'), 3.90 (dd, $J_{8,8'}$ = 11.6 Hz, $J_{7,8'}$ = 7.3 Hz, 1H, H-8'), 4.25 (q, 2H, $CH_3C\underline{H}_2$), 4.27 (dd, $J_{7,8}$ = 5.2 Hz, 1H, H-8), 5.35 (m, $J_{6,7}$ = 2.1 Hz, 1H, H-7), 5.52 (dd, $J_{5,6}$ = 9.8 Hz, 1H, H-6), 5.69 (dd, $J_{4,5}$ = 1.5 Hz, 1H, H-5), 5.76 (d, 1H, H-4), 14.1 (s, OH). – ^{13}C NMR ($CDCl_3$): δ/ppm = 13.9 ($\underline{C}H_3CH_2$), 20.1–20.4 ($\underline{C}H_3CO$), 25.6 ($\underline{C}H_3$C-2'), 60.7 ($CH_3\underline{C}H_2$), 61.8 (C-8), 67.4 (C-7), 67.6 (C-6), 67.9 (C-5), 71.3 (C-4), 107.0 (C-2), 165.6 (C-1), 169.3–170.2 ($CH_3\underline{C}O$), 194.5, 195.9 (C-2'/C-3). – MS(DCI/isobutan): *m/z* (%) = 519 (90, [MH$^+$]), 459 (100).

$C_{22}H_{30}O_{14}$	Calcd.:	C 50.97 H 5.83
(518.5)	Found:	C 50.86 H 5.79.

Ethyl 2-Acetyl-4,5,6,7,8-penta-O-acetyl-2-deoxy-D-gluco-oct-3-ulosonate (**3b**)

2a and **1b** were used to react in toluene as described above. After drying and evaporation of the solvent the residue was dissolved in ether (800 ml) and extracted 2× with saturated aqueous $NaHCO_3$. The combined $NaHCO_3$ layers were acidified with 5% HCl until pH < 2 and extracted 2× with ether (400 ml). The combined ether layers were dried over Na_2SO_4 and the solution was concentrated. After crystallizing the product for 2 days at 4 °C and recrystallization from ethanol **3b** was obtained as a white solid (2.15 g, 41.5%): *m.p.* 96–98 °C; R_f = 0.74; $[\alpha]_D^{20}$ +3.1° (*c* = 1.0, chloroform). – IR (KBr):

ν/cm^{-1} = 1677 (C=C–OH). – ^{1}H NMR ($CDCl_3$): δ/ppm = 1.33 (t, J= 7,3 Hz, 3H, $C\underline{H}_3CH_2$), 1.99 – 2.11 (s, 15H, OAc), 2.40 (s, 3H, $C\underline{H}_3$C-2'), 4.19 (dd, $J_{8,8'}$ = 12.4 Hz, $J_{7,8'}$ = 6.2 Hz, 1H, H-8'), 4.27 (q, 2H, $CH_3C\underline{H}_2$), 4.34 (dd, $J_{7,8}$ = 2.6 Hz, 1H, H-8), 5.13 (m, $J_{6,7}$ = 6.7 Hz, 1H, H-7), 5.49 (dd, $J_{5,6}$ = 4.9 Hz, 1H, H-6), 5.76 (dd, $J_{4,5}$ = 2.7 Hz, 1H, H-5), 5.98 (d, 1H, H-4), 14.2 (s, OH). – ^{13}C NMR ($CDCl_3$): δ/ppm = 14.1 ($\underline{C}H_3CH_2$), 20.2 – 20.7 ($\underline{C}H_3CO$), 25.7 ($\underline{C}H_3$C-2'), 61.1 ($CH_3\underline{C}H_2$), 61.7 (C-8), 68.4 (C-7), 69.0 (C-6), 69.8 (C-5), 73.3 (C-4), 107.2 (C-2), 166.0 (C-1), 169.5 – 170.4 ($CH_3\underline{C}O$), 193.9, 196.0 (C-2', C-3). – MS(DCI/isobutan): m/z (%) = 519 (81, [MH$^+$]), 431 (100).

$C_{22}H_{30}O_{14}$ Calcd.: C 50.97 H 5.83
518.5 Found: C 51.16 H 5.80.

Benzyl 2-Acetyl-4,5,6,7,8-penta-O-acetyl-2-deoxy-D-galacto-oct-3-ulosonate (**3c**)

2b and **1a** were used to react in toluene as described above. After drying and evaporation of the solvent the residue was dissolved in ether (800 ml) and extracted 2× with saturated aqueous $NaHCO_3$. The combined $NaHCO_3$ layers were acidified with 5% HCl until pH < 2 and extracted 2x with ether (400 ml). The combined ether layers were dried over Na_2SO_4 and the solution was concentrated. After crystallizing the product for 2 days at 4 °C and recrystallization from ethanol **3c** was obtained as a white solid (0.93 g, 16.1%): *m.p.* 92 – 94 °C; R_f = 0.77; $[\alpha]_D^{20}$ – 22.5° (c = 1.0, chloroform). – IR (KBr): ν/cm^{-1} = 1705 (C=C–OH). – ^{1}H NMR ($CDCl_3$): δ/ppm = 1.99 – 2.15 (5s, 15H, OAc), 2.35 (s, 3H, $C\underline{H}_3$C-2'), 3.93 (dd, $J_{8,8'}$ = 11.6 Hz, $J_{7,8'}$ = 7.3 Hz, 1H, H-8'), 4.27 (dd, $J_{7,8}$ = 5.2 Hz, 1H, H-8), 5.30 (AB, J = 12.5 Hz, 2H, $C\underline{H}_2$Ph), 5.38 (m, $J_{6,7}$ = 2.1 Hz, 1H, H-7), 5.54 (dd, $J_{5,6}$ = 9.8 Hz, 1H, H-6), 5.72 (dd, $J_{4,5}$ = 1.5 Hz, 1H, H-5), 5.91 (d, 1H, H-4), 7.29 – 7.40 (m, 5H, Ph), 14.06 (s, OH). – ^{13}C NMR ($CDCl_3$): δ/ppm = 20.2 – 20.6 ($\underline{C}H_3CO$), 25.9 ($\underline{C}H_3$C-2'), 62.0 (C-8), 66.7 (Ph$\underline{C}H_2$), 67.7 (C-7), 67.8 (C-6), 68.1 (C-5), 71.5 (C-4), 106.9 (C-2), 128.0, 128.3, 128.7, 135.5 (Ph), 165.8 (C-1), 169.6 – 170.3 ($CH_3\underline{C}O$), 195.0, 196.1 (C-2'/C-3). – MS(DCI/isobutan): m/z (%) = 581 (35, [M$^+$ + H]), 61 (100).

$C_{27}H_{32}O_{14}$ Calcd.: C 55.86 H 5.56
(580.5) Found: C 55.91 H 5.55.

Ethyl 4,5,6,7,8-Penta-O-acetyl-2-benzoyl-2-deoxy-D-galacto-oct-3-ulosonate (**3d**)

2c and **1a** were used to react in toluene as described above. After drying and evaporation of the solvent the residue was dissolved in ether (800 ml) and extracted 2× with saturated aqueous $NaHCO_3$. The combined $NaHCO_3$ layers were acidified with 5% HCl until pH < 2 and extracted 2× with ether (400 ml). The combined ether layers were dried over Na_2SO_4 and the solution was concentrated. After crystallization the product for 2 days at 4 °C and recrystallization from ethanol **3d** was obtained as a white solid (1.1 g, 18%): *m.p.* 113 – 121 °C; R_f = 0.58; $[\alpha]_D^{20}$ –6.1° (c = 1.0, chloroform). – IR (KBr): ν/cm^{-1} = 1678 (C=C–OH); there are 2 tautomers (**3d** and **3d'**) in $CDCl_3$ distinguished by intensity (1.6:1). – ^{1}H NMR ($CDCl_3$): δ/ppm = 0.81 (t, J = 7,3 Hz, 3H, **3d**-$C\underline{H}_3CH_2$), 0.89 (t, J = 7,3 Hz, 3H, **3d'**-$C\underline{H}_3CH_2$), 1.76, 1.99 – 2.18 (10s, 15H, OAc), 3.86 (dd, $J_{8,8'}$ = 11.4 Hz, $J_{7,8'}$ = 7.3 Hz, 1H, **3d**-H-8'), 3.89 (dd, $J_{8,8'}$ = 11.4 Hz, $J_{7,8'}$ = 7.3 Hz, 1H, **3d'**-H-8'), 3.94 (q, 2H, **3d**-$CH_3C\underline{H}_2$), 4.05 (q, 2H, **3d'**-$CH_3C\underline{H}_2$), 4.22 (dd, $J_{7,8}$ = 5.4 Hz, 1H, **3d'**-H-8), 4.29 (dd, $J_{7,8}$ = 5.4 Hz, 1H, **3d**-H-8), 5.37 (m, $J_{6,7}$ = 1.8 Hz, 1H, **3d'**-H-7), 5.40 (m, $J_{6,7}$ = 2.1 Hz, 1H, **3d**-H-7), 5.41 (d, 1H, **3d'**-H-4), 5.42 (dd, $J_{4,5}$ = 2.1 Hz, 1H, **3d'**-H-5), 5.57 (dd, $J_{5,6}$ = 9.8 Hz, 1H, **3d**-H-6), 5.62 (dd, $J_{5,6}$ = 9.8 Hz, 1H, **3d'**-H-6), 5.80 (d, 1H, **3d**-H-4), 5.85 (dd, $J_{4,5}$ = 1.5 Hz, 1H, **3d**-H-5), 7.35 – 7.79 (m, 5H, Ph), 13.3 (s, 1H, **3d'**-OH), 14.9 (s, 1H, **3d**-OH). – ^{13}C NMR ($CDCl_3$): δ/ppm = 13.2 (**3d**-$\underline{C}H_3CH_2$), 13.4 (**3d'**-$\underline{C}H_3CH_2$), 20.1 – 20.7 ($\underline{C}H_3CO$), 60.9 (**3d**-$CH_3\underline{C}H_2$), 61.5 (**3d'**-$CH_3\underline{C}H_2$), 61.9 (**3d'**-C-8), 62.0 (**3d**-C-8), 67.6 (**3d'**-C-7), 67.7 (**3d**-C-7), 67.8 (**3d'**-C-6), 68.1 (**3d**-C-6), 68.2 (**3d**-C-5), 68.7 (**3d'**-C-5), 68.9 (**3d'**-C-4), 71.1 (**3d**-C-4), 106.1 (**3d'**-C-2), 107.2 (**3d**-C-2), 127.8 – 139.0 (Ph), 162.0 (**3d'**-C-1), 166.8 (**3d**-C-1), 169.7 – 171.1 ($CH_3\underline{C}O$), 169.8, 190.5, 191.8, 192.4 (**3d**-C-2'/C-3, **3d'**-C-2'/C-3). – MS(DCI/isobutan): m/z (%) = 581 (77, [MH$^+$]), 459 (100).

$C_{27}H_{32}O_{14}$ Calcd.: C 55.86 H 5.56
(580.5) Found: C 55.89 H 5.56.

1,3-Dideoxy-nono-2,4-diuloses and 2-Deoxy-octo-1,3-diulose (General Procedure)

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

Method B. Alkyl oct-3-ulosonate **3a**,**b**,**d** (10 mmol) was dissolved in acetic acid (40 ml, containing a trace of water) and the solution was refluxed for 1h. After cooling the solvent was evaporated, the syrup was dissolved in toluene and again evaporated *in vacuo* until the residue was free of acetic acid. The product crystallizes from ether and was recrystallized in methanol and ethanol, respectively.

5,6,7,8,9-Penta-O-acetyl-1,3-dideoxy-D-galacto-nono-2,4-diulose (**4a**)

3c (5.8 g, 10 mmol, method A) and **3a** (5.2 g, 10 mmol, method B), respectively, were used to react as described above and yielded **4a** as a white solid (3.84 g, 86.1%, method A and 2.50 g, 56%, method B, respectively): *M.p.* 118 – 120 °C; R_f = 0.75; $[\alpha]_D^{20}$ + 40.8° (c = 1.0, chloroform). – IR (KBr): ν/cm^{-1} = 1615 (C=C). – ^{1}H NMR ($CDCl_3$): δ/ppm = 2.03 – 2.16 (5s, 15H, OAc), 2.17 (s, 3H, H-1), 3.84 (dd, $J_{9,9'}$ = 11.6 Hz, $J_{8,9'}$ = 7.3 Hz, 1H, H-9'), 4.25 (dd, $J_{8,9}$ = 5.2 Hz, 1H, H-9), 5.18 (d, 1H, H-5), 5.25 (m, $J_{7,8}$ = 2.1 Hz, 1H, H-8), 5.39 (dd, $J_{6,7}$ = 9.9 Hz, 1H, H-7), 5.55 (s, 1H, H-3), 5.61 (dd, $J_{5,6}$ = 2.1 Hz, 1H, H-6), 14.9 (s, 1H, OH). – ^{13}C NMR ($CDCl_3$): δ/ppm = 20.2 – 20.7 ($\underline{C}H_3CO$), 23.9 (C-1), 62.0 (C-9), 67.5 (C-8), 67.7 (C-7), 67.9 (C-6), 72.2 (C-5), 97.1 (C-3), 168.8 – 170.3 ($CH_3\underline{C}O$), 189.1, 190.2 (C-2/C-4). – MS(DCI/isobutan): m/z (%) = 447 (83, [MH$^+$]), 387 (100).

$C_{19}H_{26}O_{12}$ Calcd.: C 51.12 H 5.87
(446.4) Found: C 51.05 H 5.76.

5,6,7,8,9-Penta-O-acetyl-1,3-dideoxy-D-gluco-nono-2,4-diulose (**4b**)

3b (5.2 g, 10 mmol, method B) was used to react as described above and yielded **4b** as a white solid (3.38 g, 73.6%): *m.p.* 87 – 89 °C; R_f = 0.75; $[\alpha]_D^{20}$ +45.2° (c = 1.0, chloroform). – IR

(KBr): ν/cm^{-1} = 1598 (C=C). – ^{1}H NMR ($CDCl_3$): δ/ppm = 2.02–2.07 (s, 15H, OAc), 2.17 (s, 3H, H-1), 4.08 (dd, $J_{9,9'}$ = 12.2 Hz, $J_{8,9'}$ = 5.8 Hz, 1H, H-9'), 4.29 (dd, $J_{8,9}$ = 4.0 Hz, 1H, H-9), 5.04 (m, $J_{7,8}$ = 6.4 Hz, 1H, H-8), 5.30 (d, 1H, H-5), 5.41 (dd, $J_{6,7}$ = 4.9 Hz, 1H, H-7), 5.56 (s, 1H, H-3), 5.60 (dd, $J_{5,6}$ = 4.9 Hz, 1H, H-6), 14.8 (s, 1H, OH). – ^{13}C NMR ($CDCl_3$): δ/ppm = 20.3–20.6 ($\underline{C}H_3CO$), 23.9 (C-1), 61.5 (C-9), 68.8 (C-8), 69.0 (C-7), 69.4 (C-6), 73.1 (C-5), 97.7 (C-3), 169.3–170.4 ($CH_3\underline{C}O$), 189.0, 189.6 (C-2/C-4). – MS(DCI/isobutan): m/z (%) = 447 (88, [MH$^+$]), 387 (100).

$C_{19}H_{26}O_{12}$	Calcd.:	C 51.12	H 5.87
446.4	Found:	C 51.11	H 5.84.

4,5,6,7,8-Penta-O-acetyl-2-deoxy-1-phenyl-D-galacto-octo-1,3-diulose (**4c**)

3d (5.8 g, 10 mmol, method B) was used to react as described above and yielded **4c** as a colorless syrup (4.83 g, 95%), which crystallizes after several weeks: *m.p.* 78-84 °C; R_f = 0.81, R_f (toluene/ethyl acetate 2:1) = 0,63; $[\alpha]_D^{20}$ +45.2° (c = 1.0, chloroform). – IR (KBr): ν/cm^{-1} = 1688 (C=C–OH), 1603 (C=C). – ^{1}H NMR ($CDCl_3$): δ/ppm = 1.95–2.21 (5s, 15H, OAc), 3.86 (dd, $J_{8,8'}$ = 11.6 Hz, $J_{7,8'}$ = 7.3 Hz, 1H, H-8'), 4.28 (dd, $J_{7,8}$ = 5.2 Hz, 1H, H-8), 5.28 (m, $J_{6,7}$ = 2.1 Hz, 1H, H-7), 5.32 (d, 1H, H-4), 5.44 (dd, $J_{5,6}$ = 10.1 Hz, 1H, H-6), 5.70 (dd, $J_{4,5}$ = 2.1 Hz, 1H, H-5), 6.22 (s, 1H, H-2), 7.41–7.85 (m, 5H, Ph), 15.5 (s, 1H, OH). – ^{13}C NMR ($CDCl_3$): δ/ppm = 20.3–20.7 ($\underline{C}H_3CO$), 62.0 (C-8), 67.5 (C-7), 67.7 (C-6), 68.0 (C-5), 72.7 (C-4), 93.4 (C-2), 127.1–132.9 (Ph), 168.8–170.3 ($CH_3\underline{C}O$), 182.1, 191.7 (C-1/C-3). – MS(DCI/isobutan): m/z (%) = 509 (100, [MH$^+$]).

$C_{24}H_{28}O_{12}$	Calcd.:	C 56.69	H 5.55
(508.5)	Found:	C 56.54	H 5.54.

5,6,7,8,9-Penta-O-acetyl-1,3-dideoxy-4-O-methyl-D-galacto-non-3-en-2-ulose (**5a**) and *5,6,7,8,9-Penta-O-acetyl-1,3-dideoxy-2-O-methyl-D-galacto-non-2-en-4-ulose* (**5b**)

Etheric diazomethane solution was added to **4a** (2.0 g, 4.5 mmol) dissolved in acetone containing Al_2O_3 (0.5 g) until the color of the diazomethane remains. The excess of diazomethane was removed by a low volume of acetic acid, that was added and the Al_2O_3 was filtered off. After evaporation of the solvent the residue furnished after column chromatography **5a** (1.15 g, 55.5%) crystallized from ethanol, and **5b** (0.71 g, 34.3%) crystallized from ether as colorless crystals.

5a: *M.p.* 147–149 °C; R_f = 0.70; $[\alpha]_D^{20}$ –3.8° (c = 1.0, chloroform). – IR (KBr): ν/cm^{-1} = 1658, 1627 (C=C–OMe). – ^{1}H NMR ($CDCl_3$): δ/ppm = 2.02–2.11 (5s, 15H, OAc), 2.17 (s, 3H, H-1), 3.83 (s, 3H, OMe), 3.83 (dd, $J_{9,9'}$ = 11.6 Hz, $J_{8,9'}$ = 7.3 Hz, 1H, H-9'), 4.25 (dd, $J_{8,9}$ = 4.9 Hz, 1H, H-9), 5.24 (d, 1H, H-5), 5.30 (m, $J_{7,8}$ = 1.5 Hz, 1H, H-8), 5.35 (s, 1H, H-3), 5.37 (t, $J_{6,7}$ = 0.8 Hz, 1H, H-7), 5.37 (t, $J_{5,6}$ = 1.1 Hz, 1H, H-5). – ^{13}C NMR ($CDCl_3$): δ/ppm = 20.3–20.6 ($\underline{C}H_3CO$), 31.3 (C-1), 61.0 (OMe), 62.0 (C-9), 67.6 (C-8), 67.8 (C-7, C-6), 68.9 (C-5), 106.0 (C-3), 163.2 (C-4), 169.1–170.3 ($CH_3\underline{C}O$), 195.8 (C-2). – MS(DCI/isobutan): m/z (%) = 461 (100, [MH$^+$]).

$C_{20}H_{28}O_{12}$	Calcd.:	C 52.17	H 6.13
(460.4)	Found:	C 52.23	H 6.10.

5b: *m.p.* 156–158 °C; R_f = 0.30, R_f (toluene/ethyl acetate 1:4) = 0.43; $[\alpha]_D^{20}$ +7.3° (c = 1.0, chloroform). – IR (KBr): ν/cm^{-1} = 1658, 1613 (C=C–OMe). – ^{1}H NMR ($CDCl_3$): δ/ppm = 2.03–2.12 (5s, 15H, OAc), 2.05 (d, $J_{1,3}$ = 0.6 Hz, 3H, H-1), 3.88 (s, 3H, OMe), 3.89 (dd, $J_{9,9'}$ = 11.6 Hz, $J_{8,9'}$ = 7.3 Hz, 1H, H-9'), 4.22 (dd, $J_{8,9}$ = 5.2 Hz, 1H, H-9), 5.16 (q, 1H, H-3), 5.26 (m, $J_{7,8}$ = 2.1 Hz, 1H, H-8), 5.44 (dd, $J_{6,7}$ = 9.8 Hz, 1H, H-7), 5.50 (d, 1H, H-5), 5.72 (dd, $J_{5,6}$ = 1.8 Hz, 1H, H-6). – ^{13}C NMR ($CDCl_3$): δ/ppm = 20.2–20.7 ($\underline{C}H_3CO$), 20.5 (C-1), 55.7 (OMe), 62.0 (C-9), 67.6 (C-8), 67.8 (C-7), 67.9 (C-6), 75.6 (C-5), 94.5 (C-3), 168.9–170.3 ($CH_3\underline{C}O$), 176.5 (C-2), 190.9 (C-4). – MS(DCI/isobutan): m/z (%) = 461 (100, [MH$^+$]).

$C_{20}H_{28}O_{12}$	Calcd.:	C 52.17	H 6.13
(460.4)	Found:	C 52.27	H 5.99.

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