Synthesis of 4-Octuloses, VI[+]

4-Octulose Derivatives, Prepared from L-Sorbose, as Key Intermediates in the Stereoselective Synthesis of *C*-Glycoside and Polyhydroxyindolizidine Analogues

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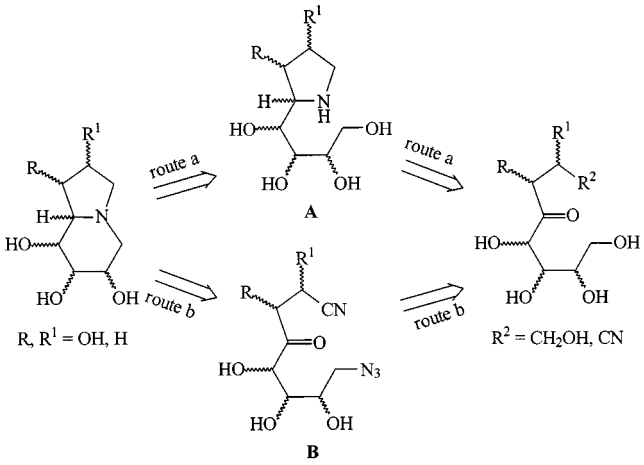
Reactions of **1** and **12** with *p*-toluenesulfonyl chloride in pyridine gave the corresponding 1-*O*-*p*-toluenesulfonyl derivatives **2** and **13** in yields of 91% and 60%, respectively. Compound **12** was also transformed into **14** by treatment with I_2/Ph_3P/imidazole in anhydrous dichloromethane. Treatment of compounds **12** and **13/14** with NaN_3 in DMF furnished the respective 1-azido-1-deoxy derivatives **3** and **15**, which were then deacetonated to give the free 4-octuloses **4** and **16**. These were subsequently hydrogenated in the presence of 10% Pd/C to afford the expected polyhydroxylated branched-chain pyrrolidines **5** and **17**. Attempted OH → OMes transformation at C-8 in the *N*–Cbz-protected pyrrolidines **7** and **19** was unsuccessful and an internal anhydration process took place to yield the corresponding *C*-glycoside-like furanoses **9** and **20**. On the other hand, **23** was transformed into the D-*ribo* analogue **25** through reduction of the intermediate 4,6-diulose **24**. Finally, deprotection of **25** in acid medium to give the free 4-ulose **26**, followed by hydrogenation of the latter in the presence of 10% Pd/C in methanol, allowed the preparation of (6*S*,7*S*,8*S*,8a*S*)-6,7,8-trihydroxy-8a-methoxyindolizidin-3-one (**27**).

Introduction

The bicyclic skeleton of indolizidine occurs extensively in Nature since a high proportion of alkaloids incorporate this moiety. Polyhydroxyindolizidines are important inhibitors of glycosidases, enzymes that are essential in the biosynthetic processing of polysaccharides and glycoproteins, and thus may be considered as potential chemotherapeutic agents against viral infections, cancer, malaria, and diabetes.[2] Given that the activity of such compounds as glycosidase inhibitors cannot reliably be predicted, the synthesis of their natural and nonnatural analogues is of great importance for establishing structure−activity relationships.[3]

Our group has recently reported on the highly stereoselective synthesis of some derivatives of 4-octulose, 2-deoxy-4-octulose,[4] and 2,3-dideoxy-4-octulosononitriles,[1] using common hexuloses (D-fructose and L-sorbose) as chiral starting materials for the synthesis of polyhydroxyindolizidines.[1,5] Moreover, from the retrosynthetic analysis shown in Scheme 1, it can be seen that 4-octuloses, due to the diversity of their functional groups, may be considered as excellent intermediates for the stereoselective synthesis of the aforementioned polyhydroxyindolizidines, as these groups can easily be transformed into appropriate functionalities allowing construction of the indolizidine skeleton. Two possible synthetic routes are outlined in Scheme1, involving construction of either a polyhydroxylated branched-chain pyrrolidine (**A**) (route *a*) or a suitably functionalized 4-octulosononitrile (**B**) (route *b*) as an intermediate. Intermediates of type **A** are cyclized to the bicyclic indolizidine system in two steps, whereas for intermediates of type **B** only one step is required. In the present study, both routes were used according to the natures of the starting 4-octulose derivatives.



Scheme 1. Retrosynthetic analysis

Results and Discussion

On the basis of previous reports and in accordance with route *a* in Scheme 1, our first objective was a $-CH_2OH \rightarrow -CH_2N_3$ modification at C-1 of the protected 4-octuloses

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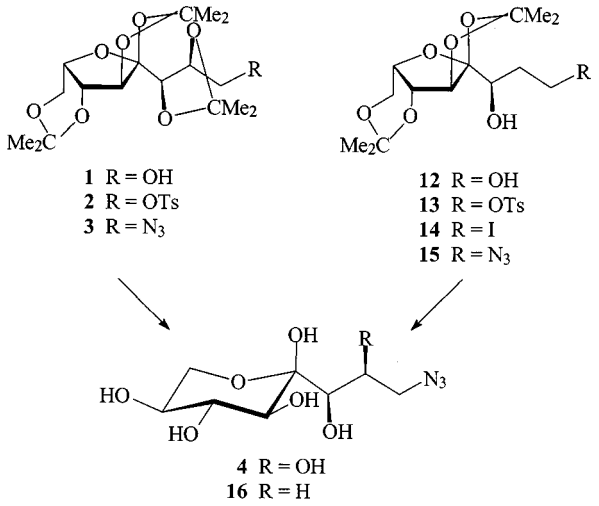
1 and **12** by introducing a good leaving group (e.g. iodide or *p*-toluenesulfonyloxy) and then displacing this with azide. Thus, 2,3:4,5:6,8-tri-*O*-isopropylidene-α-L-*glycero*-D-*galacto*-oct-4-ulofuranose (**1**)[4c] was transformed into the corresponding 1-*O*-*p*-toluenesulfonyl derivative **2** in 91% yield. When the same reaction was performed on the related 2-deoxy-L-*gulo*-oct-4-ulofuranose (**12**),[4d] only a moderate yield (60%) of the corresponding 1-*O*-*p*-toluenesulfonyl derivative **13** was obtained. In this case, it proved preferable to proceed via the 1-deoxy-1-iodo derivative **14**, which was prepared in 90% yield by reaction of **12** with I_2/Ph_3P/imidazole. It was found that the iodide leaving group could not be introduced into compound **1** in this way. These results reveal that both steric effects and the presence of a free hydroxyl at C-3 are important factors in determining the yields of the above transformations.

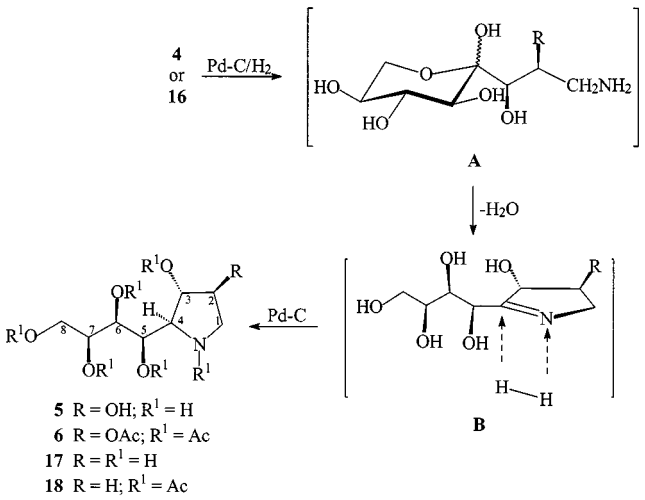
Compounds **2** and **13/14** were allowed to react with sodium azide in DMF to afford the corresponding 1-azido-1-deoxy derivatives **3** and **15**, respectively. Deacetonation of **3** and **15** in acid media then gave the free octuloses **4** and **16**, respectively (Scheme 2), mainly in their α-pyranoid forms, as evidenced by ^{13}C-NMR spectroscopy.



Scheme 2. *N*-Functionalization of 4-octuloses at C-1

Catalytic hydrogenations of **4** and **16** in the presence of 10% Pd/C gave a single product in each case, which were identified as 1,4-dideoxy-1,4-imino-L-*threo*-L-*altro*-octitol (**5**) and 1,2,4-trideoxy-1,4-imino-L-*glycero*-D-*talo*-octitol (**17**), respectively. The formation of **5** and **17** can be envisaged as proceeding by reduction of N_3 to NH_2 to produce the corresponding 1-amino-1-deoxy-4-octuloses (intermediates **A**, not isolated), nucleophilic attack of the newly formed C-1 amino group on the carbonyl group at C-4 to give the cyclic pyrrolinic intermediate **B**, and finally hydrogenation to give the observed products (Scheme 3).

The structures of **5** and **17**, and hence the stereochemistries at the newly formed stereogenic centres (C-4), were determined on the basis of their analytical and spectroscopic data, as well as those of their peracetylated derivatives (**6** and **18**). Thus, the small $J_{3,4}$ values for **6** and **18** (3.9 and ca. 0 Hz, respectively) indicate a *trans* relationship between



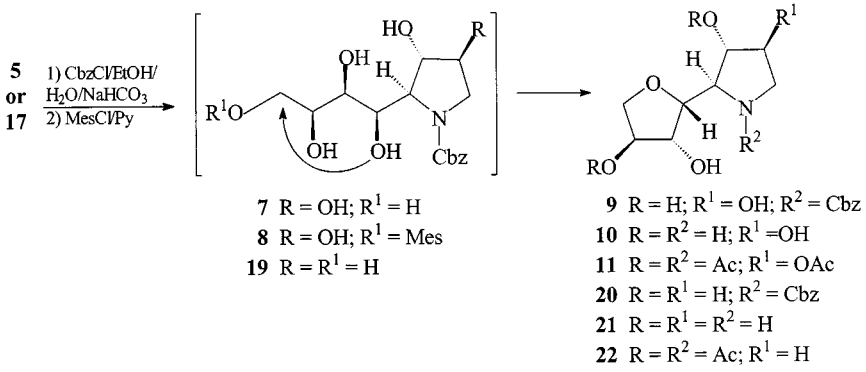
Scheme 3. Synthesis of polyhydroxylated branched-chain pyrrolidines **5** and **17** with indication of the stereochemistry

3-H and 4-H, in accordance with the proposed configurations.

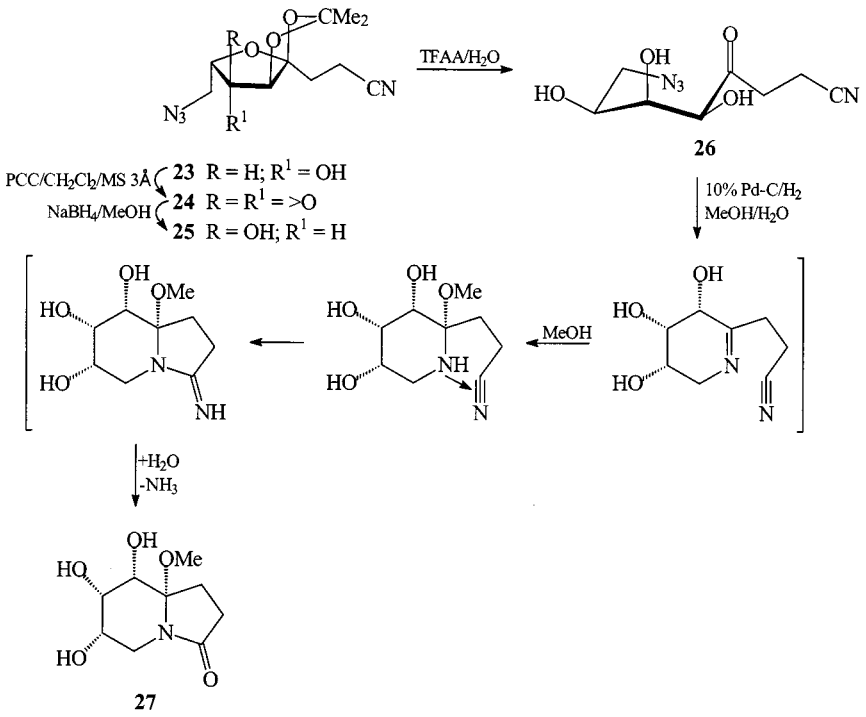
The high stereoselectivity observed for the hydrogenation of the Δ^1-pyrroline intermediates **B** is in accordance with that previously reported by our group[5] and other authors.[6] The hydrogen molecule approaches the same face as occupied by the substituent at C-3, resulting in a product with a *trans* relationship between C-3 and C-4. The presence of the hydroxy group at C-3 seems to be crucial for the stereocontrol of the hydrogenation; in the absence of such a substituent the stereoselectivity is reduced and a mixture of two diastereomeric pyrrolidines is obtained.[7]

Our next objective was to construct the indolizidine system through the application of a well-established synthetic protocol.[5] This involved selective *N*−Cbz protection, chemoselective transformation of 8-OH into a mesitylenesulfonyloxy group, and finally hydrogenolysis of the *N*−Cbz group in order to promote further cyclization to the bicyclic system. Thus, compounds **5** and **17** were selectively *N*-protected as benzyloxycarbonyl derivatives **7** and **19**, respectively. However, attempts to prepare the corresponding 8-*O*-mesitylenesulfonyloxy derivatives were partly unsuccessful. Instead of the desired derivatization, an internal anhydrization process took place, presumably involving attack of the 5-OH group at C-8, with formation of the corresponding *C*-glycoside-like furanoses **9** and **20**, respectively (Scheme 4). This unexpected cyclization seems to be general and is apparently favoured with a *xylo*[1] configuration at C-5 to C-8 of the polyhydroxy chain. It is not observed with an *arabino*[5] configuration of the chain. A similar process in analogous compounds has previously been reported by other authors,[8] where it was attributed to steric factors. Compounds **9** and **20** were deprotected to give **10** and **21**, which were characterized as their acetyl derivatives **11** and **22**, respectively.

Finally, on the basis of the above results we envisaged a new strategy for preparing novel indolizidines that avoids the aforementioned undesirable cyclization. This involves inversion of the configuration at C-6 of a 4-octulose and the



Scheme 4. Formation of either 5,8-anhydro-1,4-dideoxy- or -1,2,4-trideoxy-1,4-iminooctitols



Scheme 5. Synthetic route for polyhydroxyindolizidin-3-one **27**

application of the protocol[1] (route *b*) outlined in Scheme 1, where the indolizidine skeleton is formed by a double cyclization with the participation of three functional groups, specifically nitrile at C-1, keto at C-4, and azido at C-8. Thus, 8-azido-2,3,8-trideoxy-4,5-*O*-isopropylidene-α-L-*xylo*-oct-4-ulofuranose (**23**)[1] was oxidized with PCC in dichloromethane to give the corresponding 4,6-diulofuranose **24** and its hydrated form (see Experimental Section). Reduction of **24** with sodium tetrahydroborate in methanol proceeded with high stereofacial control in favour of the β-face, presumably owing to the presence of the 4,5-*O*-isopropylidene group, which blocks approach of the hydride at the α-face. Consequently, solely 8-azido-2,3,8-trideoxy-4,5-*O*-isopropylidene-α-L-*ribo*-oct-4-ulofuranose (**25**) was obtained, which was subsequently deacetonated to give the intermediate free 4-octulose derivative **26**. The final step involved hydrogenation of **26** in the hope of obtaining the required indolizidine, but (6*S*,7*S*,8*S*,8a*S*)-6,7,8-trihydroxy-8a-methoxyindolizidin-3-one (**27**) was produced instead.[9]

The formation of **27** may be rationalized in terms of fast reduction of the 8-azido function to an amino group with subsequent formation of a Δ^1-piperidine intermediate, which then undergoes addition of a solvent molecule (methanol) to give the corresponding piperidine (Scheme 5). Intramolecular addition of the piperidine NH to the cyano group presumably then afforded a cyclic amidine-like intermediate, which, instead of undergoing hydrogenolytic deamination to give the indolizidine skeleton,[1,10] was hydrolyzed to give the indolizidin-3-one **27**. This type of solvent addition has previously been observed by other authors.[11]

Experimental Section

General Remarks: Melting points were determined with a Gallenkamp apparatus and are uncorrected. − Organic solutions were dried with $MgSO_4$ prior to concentration under reduced pressure. − ^{1}H- and ^{13}C-NMR spectra were recorded with Bruker AMX-

Table 1. ^{1}H NMR spectroscopic data; chemical shifts (δ) with multiplicities

	1-H	1′-H	2-H	2′-H	3-H	4-H	5-H	6-H	7-H	8-H	8′-H	CMe_2
2	4.43 dd	4.11 dd	4.42 m	–	4.04 br. d	–	4.41 s	4.28 d	4.04 m	3.98 dd	3.82 d	1.47 s, 1.39 s, 1.36 s, 1.35 s, 1.33 s
3	3.77 dd	3.37 dd	4.43 ddd	–	4.10 d	–	4.44 s	4.30 d	4.06 dd	4.02 dd	3.92 d	1.49 s, 1.47 s, 1.41 s, 1.39 s, 1.38 s, 1.35 s
6[a]	4.05 dd	3.28 dd	5.19 ddd	–	5.44 br. dd	4.26 br. t	5.65 dd	5.45 dd	5.26 m	4.22 dd	3.97 dd	–
9	3.83 dd	3.39 d	4.11 br. d	–	4.38 s	3.92 d	4.23 dd	3.87 br. d	4.19 br. d	4.11 br. dd	3.63 d	–
11[b]	3.99 dd	3.66 d	5.20 br. d	–	5.69 d	3.81 dd	4.33 d	3.98 s	5.20 br. d	4.26 dd	3.74 d	–
13	4.32–4.20 m		2.26 dddd	1.80 dddd	3.90 dd	–	4.42 s	4.27 br. d	4.07 br. dd	4.03 dd	3.97 d	1.47 s, 1.40 s, 1.36 s, 1.32 s
14	3.42 ddd	3.32 dt	2.41 ddt	1.98 dddd	3.93 br. d	–	4.46 s	4.30 d	4.11 br. d	4.06 dd	4.01 d	1.49 s, 1.41 s, 1.39 s, 1.38 s
15	3.53 m		2.18 ddt	1.76 ddt	3.93 dd	–	4.47 s	4.30 d	4.11 br. d	4.06 dd	4.01 d	1.49 s, 1.41 s, 1.39 s, 1.35 s
18[c]	3.52 dt	3.44 dt	2.26 m	2.10 m	5.36 d	4.10 br. s	5.69 dd	5.53 dd	5.42 br. ddd	4.24 dd	4.01 dd	–
20	3.67–3.59 m	3.48 t	2.16 ddt	1.91 dd	4.50 d	3.91 d	3.67–3.59 m	3.85 br. s	4.17 d	4.10 dd	3.67–3.59 m	–
22[d]	4.30 br. d	3.48 dd	2.37 m	2.12 m	5.54 d	3.62 d	3.61 dd	3.97 d	5.17 d	4.28 dd	3.72 d	–
25	–	–	2.59 m		2.19 m	–	4.43 d	3.95 m		3.69 dd	3.34 dd	1.55 s, 1.41 s

[a] AcO and AcN groups at δ = 2.17, 2.10, 2.09, 2.07, 2.03, 2.0. – [b] AcO and AcN groups at δ = 2.12, 2.11, 2.07, 2.05. – [c] AcO and AcN groups at δ = 2.18, 2.05, 2.03, 2.02, 2.00. – [d] AcO and AcN groups at δ = 2.14, 2.05, 2.04.

300, AM-300, ARX-400, and AMX-500 spectrometers with samples in $CDCl_3$ solution (Me_4Si as internal reference). – IR spectra were recorded with a Perkin–Elmer 782 instrument. – Mass spectra were obtained with Hewlett-Packard HP-5988A, Fisons model Platform II, and VG Autospec-Q mass spectrometers. – Optical rotations were measured for solutions in $CHCl_3$ (1-dm tube) with a Jasco DIP-370 polarimeter. – TLC was performed on precoated silica gel 60 F_{254} aluminium-backed sheets with detection by charring with H_2SO_4 (A) or by treatment with phosphomolybdic acid (B) or ninhydrin (C). – Column chromatography was performed on silica gel (Merck, 7734).

2,3:4,5:6,8-Tri-*O*-isopropylidene-1-*O*-*p*-toluenesulfonyl-α-L-*glycero*-D-*galacto*-oct-4-ulofuranose (2): To an ice/water-cooled solution of 2,3:4,5:6,8-tri-*O*-isopropylidene-α-L-*glycero*-D-*galacto*-oct-4-ulofuranose (**1**,[4c] 5.26 g, 14.6 mmol) in dry dichloromethane (50 mL) containing triethylamine (6 mL, 43.3 mmol), *p*-toluenesulfonyl chloride (3.0 g, 15.73 mmol) was added portionwise with stirring and then the mixture was set aside at room temperature for 24 h. Subsequent TLC analysis (diethyl ether/hexane, 2:1; detection by method A) revealed the presence of a main faster moving compound. The mixture was poured into ice/water and the resulting solution was left for 1 h. It was then extracted with diethyl ether (3 × 50 mL) and the combined extracts were washed with 10% aq. hydrochloric acid, water, saturated $NaHCO_3$ solution, and further water. After concentration to dryness, the residue was subjected to column chromatography (diethyl ether/hexane, 1:2) to afford pure **2** (6.8 g, 91%) as a syrup. – $[\alpha]_D^{25} = -18$ (c = 1.2). – IR (film): $\tilde{\nu}$ = 1601, 1385, 1373 (CMe_2), 666 cm^{-1} (aromatic). – NMR: See Table 1, Table 2 and Table 3. – $C_{24}H_{34}O_{10}S$ (514.6): calcd. C 56.02, H 6.66, S 6.23; found C 55.85, H 6.81, S 6.13.

1-Azido-1-deoxy-2,3:4,5:6,8-tri-*O*-isopropylidene-α-L-*glycero*-D-*galacto*-oct-4-ulofuranose (3): To a stirred solution of **2** (6.7 g, 13 mmol) in dry DMF (35 mL), NaN_3 (2.55 g, 39.2 mmol) was added and the mixture was heated at 100 °C for 15 h. Thereafter, TLC analysis (diethyl ether/hexane, 2:1; detection by method A) revealed the presence of a new compound of higher mobility. The reaction mixture was concentrated, diluted with water, and extracted with diethyl ether (4 × 50 mL). The combined extracts were washed with brine and water, concentrated to dryness, and the residue was chromatographed (diethyl ether/hexane, 1:3) to afford crystalline **3** (4.52 g, 90%); m.p. 62–64 °C (from diethyl ether/hexane). – $[\alpha]_D^{25} = -47$ (c = 1.1). – IR (KBr): $\tilde{\nu}$ = 2101 (N_3); 1385, 1373 cm^{-1} (CMe_2). – NMR: See Table 1, Table 2 and Table 3. – $C_{17}H_{27}N_3O_7$ (385.4): calcd. C 52.98, H 7.06, N 10.90; found C 52.86, H 7.41, N 11.04.

Table 2. ^{1}H-NMR-spectroscopic data, coupling constants (Hz)

	$J_{1,1'}$	$J_{1,2}$	$J_{1',2}$	$J_{1,2'}$	$J_{1',2'}$	$J_{2,2'}$	$J_{2,3}$	$J_{2',3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8}$	$J_{7,8'}$	$J_{8,8'}$
2	11.1	1.9	6.1	–	–	–	8.1	–	–	–	0.0	2.3	2.4	0.0	13.2
3	13.1	2.4	5.4	–	–	–	8.3	–	–	–	0.0	2.3	2.2	0.0	13.2
6	11.8	7.6	5.1	–	–	–	2.7	–	3.9	4.0	7.2	3.9	5.1	6.7	11.6
9	12.0	5.2	0.0	–	–	–	0.0	–	0.0	9.9	2.3	0.0	4.1	0.0	9.4
11	12.6	5.7	0.0	–	–	–	0.0	–	2.4	10.5	0.0	0.0	4.2	0.0	10.4
13	–	9.5	6.9	5.6	4.6	14.7	2.7	10.3	–	–	0.0	3.6	2.3	0.0	13.4
14	7.4	9.7	9.6	4.5	7.3	14.5	2.7	10.0	–	–	0.0	2.2	2.1	0.0	13.5
15	–	8.0	8.0	6.0	6.0	14.2	2.7	9.8	–	–	0.0	2.2	2.0	0.0	13.5
18	10.0	10.0	10.0	7.7	2.3	–	5.0	0.0	0.0	1.9	8.0	3.6	5.4	6.6	11.5
20	9.7	–	9.7	7.1	0.0	13.6	3.8	0.0	0.0	9.8	0.0	0.0	4.0	0.0	9.4
22	10.0	–	2.4	–	0.0	–	3.9	0.0	0.0	10.3	1.6	0.0	4.2	0.0	10.4
25	–	–	–	–	–	–	–	–	–	–	4.1	–	2.4	3.7	13.6

1,4-Dideoxy-1,4-imino-L-*threo*-L-*altro*-octitol (5): A suspension of **3** (4.0 g, 10.4 mmol) in 50% aq. trifluoroacetic acid (20 mL) was stirred at room temperature for 24 h, in the course of which it became a clear solution. Subsequent TLC analysis (chloroform/methanol, 5:2; detection by method A) showed the presence of only one product of lower mobility. The mixture was concentrated and the remaining trifluoroacetic acid was removed by repeated co-distillation with water. The residue was chromatographed (chloroform/methanol, 10:1) to yield 1-azido-1-deoxy-L-*glycero*-D-*galacto*-4-octulose (**4**, 2.63 g, quantitative) as a syrup. – IR (film): $\tilde{\nu}$ = 3372 (OH), 2112 cm^{-1} (N_3). – ^{13}C NMR ([D$_4$]MeOH): δ (inter alia) = 104.4 (C-4, α-Fu), 99.3 (C-4, α-Pyr), 63.2 (C-8, α-Pyr), 62.2 (C-8, α-Fu), 58.3 (C-1, α-Fu), 55.0 (C-1, α-Pyr). – HRMS (LSIMS); *m*/*z*: 288.08077 [M^+ + Na] (calcd. 288.08077).

Compound **4** (2.6 g, 9.80 mmol) in water (100 mL) was hydrogenated at 4 atm in the presence of 10% Pd/C (500 mg) for 13 h. Subsequent TLC analysis (chloroform/methanol, 5:2; detection by method B) revealed that **4** had been completely consumed and showed the presence of a nonmobile compound. Further TLC (2-propanol/methanol/aq. ammonia, 2:1:1) showed the presence of one major product. The catalyst was filtered off and washed with

Table 3. ^{13}C-NMR-spectroscopic data

	C-1	C-2	C-3	C-5	C-6	C-7	C-8	C-4	*C*Me$_2$	C*Me*$_2$
2	70.4	← 85.4,	76.1,	75.2,	73.2,	and 72.8 →	60.1	113.0	112.9, 110.8, 97.4	29.0, 27.6, 27.3, 26.6, 26.4, 18.8
3	53.0	← 85.5,	76.9,	76.5,	73.2,	and 72.7 →	60.2	113.2	113.0, 110.6, 97.4	29.0, 27.6, 27.4, 26.7, 26.5, 18.7
5	50.9	77.7	78.9	71.2	72.5	71.8	62.7	65.6	−	−
6[a]	51.8	← 75.9, 75.8 →		← 69.7, 69.6, and 68.5 →			61.7	61.9	−	−
9[b]	54.9	76.6	78.6	81.2	77.2	77.6	74.5	65.6	−	−
11[c]	53.4	← 79.7,	79.4,	77.0,	75.2,	and 73.6 →	71.7	60.9	−	−
13	68.1	31.1	84.7	← 73.2,	72.6,	68.7 →	60.4	115.7	112.6, 97.5	28.9, 27.8, 27.0, 18.7
14	3.21	35.7	84.8	← 73.1,	72.6,	72.2 →	60.4	115.8	112.6, 97.5	29.0, 27.8, 27.1, 18.8
15	48.8	31.0	84.7	← 73.2,	72.6,	69.8 →	60.4	116.0	112.6, 97.5	28.9, 27.9, 27.1, 18.7
18[d]	45.9	31.4	← 73.7,	70.3,	70.0,	68.4 →	61.6	63.7	−	−
20[e]	46.0	32.2	← 82.1,	77.4,	77.3,	73.7 →	74.9	66.1	−	−
22[f]	46.4	29.6	← 80.8,	79.1,	75.5,	73.6 →	72.0	61.3	−	−
25	119.3	12.0	34.0	81.2	80.3	71.9	50.5	113.2	111.6	27.0, 26.8
27	26.1	30.1	170.6	37.0	66.4	72.9	72.8, 96.9 (8a)	−	−	−

[a] AcO and AcN groups at δ = 170.5, 170.1, 169.8, 22.3, 20.9, 20.8, 20.7, 20.6. − [b] Cbz group at δ = 158.9 (C=O) and 68.7 (Ph*C*H$_2$). − [c] AcO and AcN groups at δ = 172.0, 169.8, 169.6, 169.2, 22.7, 21.1, 21.0. − [d] AcO and AcN groups at δ = 170.5, 170.4, 170.1, 169.9, 169.3, 22.5, 21.0, 20.9, 20.8, 20.7, 20.6. − [e] Cbz group at δ = 158.8 (C=O) and 68.6 (Ph*C*H$_2$). − [f] AcO and AcN groups at δ = 172.2, 170.2, 169.9, 22.6, 21.2, 21.1.

water and the combined filtrate and washings were concentrated. Column chromatography (2-propanol/methanol/aq. ammonia, 2:1:1) of the residue afforded the title compound **5** (2.02 g, 91%) as a colourless solid foam, which was characterized as its peracetyl derivative (see below). − NMR: See Table 3. − HRMS (LSIMS); *m*/*z*: 246.09533 [M$^+$ + Na] (calcd. 246.09536).

Conventional acetylation of **5** (50 mg, 0.22 mmol) in dry pyridine (2 mL) by overnight treatment with acetic anhydride (1 mL) and a catalytic amount of DMAP gave, after the usual workup and column chromatography (diethyl ether/acetone, 10:1), the corresponding *N*-acetyl-2,3,5,6,7,8-hexa-*O*-acetyl derivative **6** (91 mg, 85%) as a colourless syrup. − $[\alpha]_D^{25}$ = +10 (*c* = 0.7). − IR (film): $\tilde{\nu}$ = 1762, 1757, 1748 (MeCOO), 1661 cm^{-1} (MeCON). − NMR: See Table 1, Table 2 and Table 3. − HRMS (LSIMS); *m*/*z*: 540.16814 [M$^+$ + Na] (calcd. 540.16931).

***N*-Benzyloxycarbonyl-1,4-dideoxy-1,4-imino-L-*threo*-L-*altro*-octitol(7):** To an ice/water-cooled solution of **5** (1.95 g, 8.8 mmol) in water (15 mL) containing sodium hydrogen carbonate (1 g) and sodium carbonate (1 g), benzyl chloroformate (2 mL, 14 mmol) was added dropwise with stirring. After 24 h, TLC analysis (2-propanol/methanol/aq. ammonia, 6:2:1; detection by method B) revealed the presence of a faster moving compound. The mixture was acidified (to pH = 4−5) with 1 N aq. hydrochloric acid and then extracted with diethyl ether. The aqueous phase was concentrated and the residue was applied to a silica gel column and chromatographed (2-propanol/methanol/aq. ammonia, 15:2:1 → 6:2:1) to give **7** (2.88 g, 92%) as a syrup. − $[\alpha]_D^{25}$ = +32 (*c* = 0.3, MeOH). − IR (film): $\tilde{\nu}$ = 3374 (OH); 1680, 1675 cm^{-1} (NCbz). − ^{1}H NMR ([D$_4$]MeOH): δ (inter alia) = 7.45−7.35 (m, 5 H, *Ph*CH$_2$), 5.20 (s, 2 H, PhC*H*$_2$). − ^{13}C NMR: δ = 158.4 (C=O), 137.9, 129.5, 129.1, 128.9 (*Ph*CH$_2$), 77.5, 76.4, 74.3, 71.8, 71.5 (C-2,3,5,6,7), 69.2 (C-4), 68.4 (Ph*C*H$_2$), 64.0 (C-8), 54.7 (C-1).

5,8-Anhydro-*N*-benzyloxycarbonyl-1,4-dideoxy-1,4-imino-L-*threo*-L-*altro*-octitol (9): To an ice/water-cooled solution of **7** (1.0 g, 2.8 mmol) in dry pyridine (15 mL), DMAP (50 mg) and mesitylenesulfonyl chloride (1.0 g, 4.57 mmol) were added portionwise with stirring and then the mixture was set aside at room temperature for 15 h. Subsequent TLC analysis (chloroform/methanol, 7:1; detection by method B) revealed the presence of two faster-moving compounds. Methanol (5 mL) was added, and the mixture was left at room temperature for 1 h and then concentrated. Column chromatography (dichloromethane → dichloromethane/methanol, 20:1) of the residue afforded first syrupy *N*-benzyloxycarbonyl-1,4-dideoxy-1,4-imino-8-*O*-mesitylenesulfonyl-L-*threo*-L-*altro*-octitol (**8**, 80 mg, 5%). − $[\alpha]_D^{25}$ = +29 (*c* = 0.9). − IR (film): $\tilde{\nu}$ = 3396 (OH), 1681 cm^{-1} (NCbz). − ^{1}H NMR: δ (inter alia) = 7.40−7.30 (m, 5 H, *Ph*CH$_2$), 6.97 (s, 2 H, Mes), 5.14 and 5.10 (2 d, 2 H, *J* = 12.3 Hz, PhC*H*$_2$), 4.16 (dd, 1 H, $J_{7,8}$ = 4.2 Hz, $J_{8,8'}$ = 9.7 Hz, 8-H), 4.02 (dd, 1 H, $J_{1,2}$ = 5.9 Hz, $J_{1,1'}$ = 13 Hz, 1-H), 3.62 (d, 1 H, 8′-H), 3.59 (dd, 1 H, $J_{1',2}$ = 2.6 Hz, 1′-H), 2.61 and 2.30 (2 s, 9 H, Mes). − ^{13}C NMR: δ = 156.7 (C=O), 143.9, 140.1, 135.7, 132.0, 128.7, 128.5, 128.0 (Mes and *Ph*CH$_2$), 81.4, 80.2, 77.1, 76.2, 73.8 (C-2,3,5,6,7), 73.8 (C-8), 68.1 (Ph*C*H$_2$), 63.2 (C-4), 51.2 (C-1), 22.8, 22.6, 21.1 (Mes). − HRMS (LSIMS); *m*/*z*: 562.17247 [M$^+$ + Na] (calcd. 562.17229).

Syrupy **9** was eluted subsequently and was crystallized from dichloromethane (645 mg, 68%); m.p. 193−194 °C. − $[\alpha]_D^{27}$ = +23 (*c* = 0.9, MeOH). − IR (KBr): $\tilde{\nu}$ = 3413, 3339 (OH), 1675, 1670 cm^{-1} (NCbz). − $C_{16}H_{21}NO_7$ (339.3): calcd. C 56.63, H 6.24, N 4.13; found C 56.96, H 6.07, N 4.16.

5,8-Anhydro-1,4-dideoxy-1,4-imino-L-*threo*-L-*altro*-octitol (10): A solution of **9** (200 mg, 0.59 mmol) in dry methanol (25 mL) containing 10% Pd/C (40 mg) was hydrogenated at 75 psi for 4 h. Subsequent TLC analysis (chloroform/methanol, 7:1; detection by method B) revealed that **9** had been completely consumed and that a nonmobile product was present. Further TLC (2-propanol/methanol/aq. ammonia, 2:1:0.5; detection by method C) revealed the presence of only one product. The catalyst was filtered off, washed with methanol, and the combined filtrate and washings were concentrated to dryness. Chromatographic workup of the residue (2-propanol/methanol/aq. ammonia, 5:1:0.5) afforded crystalline **10** (110 mg, 91%); m.p. 153−154 °C (dec.). − $[\alpha]_D^{27}$ = −2; $[\alpha]_{405}^{28}$ = −18 (*c* = 0.45, MeOH). − IR (KBr): $\tilde{\nu}$ = 3355, 3268 cm^{-1} (OH and NH). − ^{1}H NMR ([D$_4$]MeOH): δ = 4.15 (dd, 1 H, $J_{7,8}$ = 3.9 Hz, 8-H), 4.13−4.01 (m, 5 H, 2-,3-,5-,6-,7-H), 3.66 (dd, 1 H, $J_{7,8'}$ = 3.7 Hz, $J_{8,8'}$ = 11.7 Hz, 8′-H), 3.28 (dd, 1 H, 4-H), 3.17 (br. ddd, 1 H, $J_{1,1'}$ = 11.4 Hz, 1-H), 2.85 (br. dt, 1 H, 1′-H). − ^{13}C NMR: δ = 81.7, 80.9, 78.8, 78.6, 78.2 (C-2,3,5,6,7), 74.6 (C-8), 65.6 (C-4), 52.4 (C-1). − $C_8H_{15}NO_5$ (205.2): calcd. C 46.82, H 7.37, N 6.83; found C 47.24, H 7.58, N 6.54.

Conventional acetylation of **10** (50 mg, 0.24 mmol) in dry dichloromethane (5 mL) by overnight treatment with acetic anhydride (0.2 mL) and triethylamine (0.5 mL) gave, after the usual workup and column chromatography (diethyl ether), the corresponding *N*-acetyl-2,3,7-tri-*O*-acetyl derivative **11** (70 mg, 77%) as a colourless syrup. − $[\alpha]_D^{27}$ = +12 (*c* = 1.2). − IR (film): $\tilde{\nu}$ = 3284 (OH), 1748 (MeCOO), 1635 cm^{-1} (MeCON). − NMR: See Table 1, Table 2 and Table 3. − HRMS (LSIMS): *m*/*z* = 396.12704 [M^+ + Na] (calcd. 396.12704).

2-Deoxy-4,5:6,8-di-*O*-isopropylidene-1-*O*-*p*-toluenesulfonyl-α-L-*gulo*-oct-4-ulofuranose (13): To an ice/water-cooled solution of 2-deoxy-4,5:6,8-di-*O*-isopropylidene-α-L-*gulo*-oct-4-ulofuranose (**12**,[4d] 3.0 g, 9.86 mmol) in dry dichloromethane (50 mL) and triethylamine (2.5 mL), *p*-toluenesulfonyl chloride (2.1 g, 11 mmol) was added portionwise with stirring and then the mixture was set aside at room temperature for 24 h. Subsequent TLC analysis (diethyl ether; detection by method A) revealed the presence of a faster moving compound. The mixture was poured into ice/water and the resulting solution was left for 1 h. It was then extracted with diethyl ether (3 × 50 mL) and the combined extracts were washed with 10% aq. hydrochloric acid, water, saturated $NaHCO_3$ solution, and further water, and then concentrated to dryness. Chromatographic workup of the residue (diethyl ether/hexane, 1:1) afforded **13** (2.7 g, 60%) as a colourless syrup. − $[\alpha]_D^{25}$ = +13; $[\alpha]_{405}^{26}$ = +30 (*c* = 1.2). − IR (film): $\tilde{\nu}$ = 3529 (OH), 1385, 1374, 1360 cm^{-1} (CMe_2). − NMR: See Table 1, Table 2 and Table 3. − HRMS (LSIMS): *m*/*z* = 459.16787 [M^+ + 1] (calcd. 459.16888).

1,2-Dideoxy-1-iodo-4,5:6,8-di-*O*-isopropylidene-α-L-*gulo*-oct-4-ulofuranose (14): To a stirred solution of **12** (1.56 g, 5.12 mmol) in anhydrous dichloromethane (15 mL), a solution of iodine (1.42 g, 5.6 mmol), triphenylphosphane (1.47 g, 5.6 mmol), and imidazole (694 mg, 10.2 mmol) in the same solvent (40 mL) was added at room temperature. After 4 h, TLC analysis (diethyl ether/hexane, 3:2; detection by UV) revealed the presence of a faster moving compound. The mixture was filtered and concentrated. Column chromatography (diethyl ether/hexane, 1:1) of the residue gave syrupy **14** (1.91 g, 90%), which was crystallized from hexane; m.p. 77−78 °C. − $[\alpha]_D^{28}$ = +28 (*c* = 1). − IR (KBr): $\tilde{\nu}$ = 3520 (OH), 1388, 1374 cm^{-1} (CMe_2). − NMR: See Table 1, Table 2 and Table 3. − $C_{14}H_{23}IO_6$ (414.2): calcd. C 40.59, H 5.60; found C 40.95, H 5.70.

1-Azido-1,2-dideoxy-4,5:6,8-di-*O*-isopropylidene-α-L-*gulo*-oct-4-ulofuranose (15): (a) To a stirred solution of **13** (2.95 g, 6.43 mmol) in dry DMF (40 mL), sodium azide (1.05 g, 16 mmol) was added and the mixture was heated at 80 °C for 15 h. Subsequent TLC analysis (diethyl ether; detection by method A) revealed that **13** had been completely consumed and showed the presence of a faster moving compound. The reaction mixture was concentrated, diluted with water, and extracted with diethyl ether (4 × 50 mL). The combined extracts were washed with brine and water, and then concentrated to dryness. Chromatographic workup of the residue (diethyl ether/hexane, 1:2) afforded crystalline **15** (2.0 g, 94%); m.p. 72−74 °C. − $[\alpha]_D^{24}$ = +20 (*c* = 0.8). − IR (KBr): $\tilde{\nu}$ = 3538 (OH), 2104 (N_3), 1387, 1376 cm^{-1} (CMe_2). − NMR: See Table 1, Table 2 and Table 3. − $C_{14}H_{23}N_3O_6$ (329.3): calcd. C 51.05, H 7.04, N 12.76; found C 51.29, H 7.54, N 12.53.

(b) Treatment of compound **14** (1.47 g, 3.55 mmol) in dry DMF (35 mL) with sodium azide (2.55 g, 39.2 mmol) as above gave **15** (1.11 g, 95%).

1,2,4-Trideoxy-1,4-imino-L-*glycero*-D-*talo*-octitol (17): A suspension of **15** (2.0 g, 6.07 mmol) in 50% aq. trifluoroacetic acid (15 mL) was stirred at room temperature for 24 h, in the course of which it became a clear solution. Subsequent TLC analysis (chloroform/methanol, 5:1; detection by method A) showed the presence of only one product of lower mobility. The mixture was concentrated and the remaining trifluoroacetic acid removed by repeated co-distillation with water. The residue was chromatographed (chloroform/methanol, 10:1) to yield 1-azido-1,2-dideoxy-L-*gulo*-4-octulose (**16**, 1.31 g, 87%) as a syrup. − ^{13}C NMR ([D_4]MeOH): δ (inter alia) = 98.9 (C-4, α-Pyr), 76.3, 73.4, 72.7, 71.4 (C-3,5,6,7, α-Pyr), 63.4 (C-8, α-Pyr), 49.8 (C-1, α-Pyr), 31.1 (C-2, α-Pyr).

Compound **16** (1.14 g, 4.57 mmol) in water (60 mL) and methanol (20 mL) was hydrogenated at 4 atm in the presence of 10% Pd/C (150 mg) for 18 h. Subsequent TLC analysis (chloroform/methanol, 5:2; detection by method B) revealed that **16** had been completely consumed and showed the presence of a nonmobile compound. Further TLC (2-propanol/methanol/aq. ammonia, 6:2:1; detection by method B) showed the presence of one major product. The catalyst was filtered off and washed with water, and the combined filtrate and washings were concentrated. Column chromatography (2-propanol/methanol/aq. ammonia, 6:2:1) of the residue afforded the title compound (**17**, 850 mg, 90%), which was characterized as its peracetyl derivative (see below).

Conventional acetylation of **17** (93 mg, 0.45 mmol) in dry pyridine (1 mL) by overnight treatment with acetic anhydride (1 mL) and a catalytic amount of DMAP gave, after the usual workup and column chromatography (diethyl ether/acetone, 5:1) the corresponding *N*-acetyl-3,5,6,7,8-penta-*O*-acetyl derivative **18** (150 mg, 73%), which was crystallized from diethyl ether/hexane; m.p. 99−100 °C. − $[\alpha]_D^{27}$ = +17 (*c* = 1). − IR (KBr): $\tilde{\nu}$ = 1757, 1748, 1740 (MeCOO), 1658 cm^{-1} (MeCON). − NMR: See Table 1, Table 2 and Table 3. − $C_{20}H_{29}NO_{11}$ (459.4): calcd. C 52.28, H 6.36, N 3.05; found C 52.43, H 6.21, N 3.12.

***N*-Benzyloxycarbonyl-1,2,4-trideoxy-1,4-imino-L-*glycero*-D-*talo*-octitol (19):** To an ice/water-cooled solution of **17** (800 mg, 3.86 mmol) in water (10 mL) containing sodium hydrogen carbonate (400 mg) and sodium carbonate (400 mg), benzyl chloroformate (1.2 mL, 8.41 mmol) was added dropwise with stirring. After 30 h, TLC analysis (2-propanol/methanol/ammonia, 6:2:1; detection by method B) revealed the presence of a faster moving compound. The mixture was acidified (to pH = 4−5) with 1 N aq. hydrochloric acid and then extracted with diethyl ether. The aqueous phase was concentrated and the residue was applied to a silica gel column and chromatographed (2-propanol/methanol/aq. ammonia, 10:2:1 → 6:2:1) to give **19** (980 mg, 74%) as a syrup. − $[\alpha]_D^{26}$ = +22 (*c* = 0.3, MeOH). − IR (film): $\tilde{\nu}$ = 3169, 3157 (OH), 1680, 1675 cm^{-1} (NCbz). − ^1H NMR ([D_4]MeOH): δ (inter alia) = 7.42−7.25 (m, 5 H, *Ph*CH_2), 5.15 (s, 2 H, PhCH_2), 4.52 (d, 1 H, 5-H), 2.19 (m, 1 H, 2-H), 1.89 (m, 1 H, 2′-H). − ^{13}C NMR: δ = 158.6 (C=O), 138.0, 129.5, 129.1, 128.8 (*Ph*CH_2), 74.5, 73.0, 72.8, 71.4, 69.8 (C-3,4,5,6,7), 68.4 (Ph*C*H_2), 64.0 (C-8), 46.0 (C-1), 32.8 (C-2).

5,8-Anhydro-*N*-benzyloxycarbonyl-1,2,4-trideoxy-1,4-imino-L-*glycero*-D-*talo*-octitol (20): To an ice/water-cooled solution of **19** (220 mg, 0.65 mmol) in dry pyridine (5 mL), mesitylenesulfonyl chloride (240 mg, 1.10 mmol) was added portionwise with stirring and then the mixture was set aside at room temperature for 18 h. Subsequent TLC analysis (chloroform/methanol, 10:1; detection by method B) revealed the presence a faster moving compound. Methanol (5 mL) was added, and the mixture was left at room temperature for 1 h and then concentrated. Column chromatography (dichloromethane → dichloromethane/methanol, 20:1) of the residue afforded **20** (135 mg, 65%). − $[\alpha]_D^{23}$ = +27 (*c* = 0.9, MeOH). − IR (film): $\tilde{\nu}$ = 3389 (OH), 1680, 1669 cm^{-1} (NCbz). − NMR: See Table 1, Table 2 and Table3. − HRMS (LSIMS); *m*/*z*: 346.12711 [M^+ + Na] (calcd. 346.12666).

5,8-Anhydro-1,2,4-trideoxy-1,4-imino-L-*glycero*-D-*talo*-octitol (21): A solution of **20** (100 mg, 0.31 mmol) in dry methanol (15 mL) containing 10% Pd/C (40 mg) was hydrogenated at 75 psi for 6 h. Subsequent TLC analysis (chloroform/methanol, 7:1; detection by method B) revealed that **20** had been completely consumed and that a nonmobile product was present. Further TLC (2-propanol/methanol/aq. ammonia, 6:1:0.5; detection by method C) revealed the presence of only one product. The catalyst was filtered off, washed with methanol, and the combined filtrate and washings were concentrated to dryness. Chromatographic workup of the residue (2-propanol/methanol/aq. ammonia, 5:1:0.5) afforded **21** (52 mg, 89%), which was characterized as its triacetyl derivative.

Conventional acetylation of **21** (35 mg, 0.11 mmol) in dry dichloromethane (4 mL) by overnight treatment with acetic anhydride (0.1 mL) and triethylamine (0.3 mL) gave, after the usual workup and column chromatography (diethyl ether/hexane, 1:1), the corresponding *N*-acetyl-3,7-di-*O*-acetyl derivative (**22**, 35 mg, 79%) as a colourless syrup. − $[\alpha]_D^{24} = -14$ ($c = 1$). − IR (film): $\tilde{\nu}$ = 3270 (OH), 1748, 1740 (MeCOO), 1628 cm^{-1} (MeCON). − NMR: See Table 1, Table 2and Table 3. − $C_{14}H_{21}NO_7$ (315.3): calcd. C 53.32, H 6.71, N 4.44; found C 53.43, H 6.57, N 4.32.

8-Azido-2,3,8-trideoxy-4,5-*O*-isopropylidene-α-L-*ribo*-oct-4-ulofuranosononitrile (25): To a stirred solution of 8-azido-2,3,8-trideoxy-4,5-*O*-isopropylidene-α-L-*xylo*-oct-4-ulofuranosononitrile (**23**,[1] 970 mg, 3.62 mmol) in anhydrous dichloromethane (20 mL) were added 4-Å molecular sieves (2 g) and pyridinium chlorochromate (2.0 g, 9 mmol). Stirring was continued for 4 h at room temperature, whereupon TLC analysis (diethyl ether) showed the presence of a new product of slightly lower mobility. The mixture was diluted with diethyl ether (40 mL), filtered through silica gel, and concentrated. Column chromatography (diethyl ether/hexane, 1:1 → 3:1) of the residue gave syrupy 8-azido-2,3,8-trideoxy-4,5-*O*-isopropylidene-α-L-*erythro*-oct-4,6-diulofuranosononitrile (**24**, 860 mg, 89%) and its hydrated form in a ratio of ca. 3:4, as evidenced by ^{1}H NMR. − $[\alpha]_D^{28} = -67$ ($c = 1.2$). − IR (film): $\tilde{\nu}$ = 3439 (OH), 2252 (CN), 2114 (N_3), 1779 (CO), 1386, 1377 cm^{-1} (CMe_2). − ^{1}H NMR: δ (inter alia) = 4.52 (dt, 1 H, $J_{5,7} = 1.1$ Hz, 7-H), 4.28 (s, 1 H, OH, hydrated form), 4.21 (d, 1 H, 5-H), 4.06 (s, 1 H, 5-H, hydrated form), 4.04 (dd, 1 H, 7-H, hydrated form), 3.82 (s, 1 H, OH, hydrated form), 3.70 (dd, 1 H, $J_{7,8} = 3.2$ Hz, 8-H), 3.65 (dd, 1 H, $J_{7,8} = 4.3$ Hz, 8-H, hydrated form), 3.60 (dd, 1 H, $J_{7,8'} = 3.1$ Hz, $J_{8,8'} = 13.2$ Hz, 8′-H), 3.54 (dd, 1 H, $J_{7,8'} = 5.3$, $J_{8,8'} = 13.4$ Hz, 8′-H, hydrated form), 1.54 and 1.38 (2 s, 6 H, CMe_2, hydrated form), 1.44 and 1.42 (2 s, 6 H, CMe_2). − ^{13}C NMR: δ = 208.7 (C-6), 119.8 (C-1, hydrated form), 119.2 (C-1), 114.8 (C-4), 113.0 (C-4, hydrated form), 111.8 (*C*Me_2, hydrated form), 110.4 (*C*Me_2), 100.5 (C-6, hydrated form), 85.1 and 79.0 (C-5,7, hydrated form), 78.9 and 78.7 (C-5,7), 51.2 (C-8), 48.4 (C-8, hydrated form), 33.8 (C-3, hydrated form), 33.3 (C-3), 27.9, 27.8, 23.3, and 26.8 (CMe_2), 12.0 (C-2, hydrated form), 11.8 (C-2).

To a cooled (−20 °C) solution of **24** (820 mg, 3.1 mmol) in anhydrous methanol (25 mL), sodium tetrahydroborate (120 mg, 3.2 mmol) was added portionwise with stirring. After 10 min, the mixture was neutralized with acetic acid and then concentrated. Chromatographic workup of the residue (diethyl ether/hexane, 3:1) afforded **25** (780 mg, quantitative) as a syrup. − $[\alpha]_D^{25} = -76$ ($c = 2.7$). − IR (film): $\tilde{\nu}$ = 3462 (OH), 2251 (CN), 2107 (N_3), 1386, 1373 cm^{-1} (CMe_2). − NMR: See Table 1, Table 2 and Table 3. − HRMS (LSIMS): *m*/*z* = 291.10685 [M^+ + Na] (calcd. 291.10693).

8-Azido-2,3,8-trideoxy-L-*ribo*-oct-4-ulosononitrile (26): A suspension of **25** (780 mg, 2.9 mmol) in 50% aq. trifluoroacetic acid (10 mL) was stirred at 40 °C for 6 h, in the course of which it became a clear solution. Subsequent TLC analysis (diethyl ether; detection by method A) revealed the presence of just one product of lower mobility. The mixture was concentrated and the remaining trifluoroacetic acid was removed by repeated co-distillation with water. The residue was chromatographed (diethyl ether → diethyl ether/methanol, 20:1) to yield **26** (550 mg, 83%) as a syrup. − $[\alpha]_D^{25} = -36$ ($c = 1.2$, methanol). − IR (film): $\tilde{\nu}$ = 3417 (OH), 2254 (CN), 2112 cm^{-1} (N_3). − ^{13}C NMR ([D_4]MeOH): δ (inter alia) = 209.7 (C-4, keto form), 121.4 and 121.3 (C-1, α,β-Fu), 120.5 (C-1, keto form), 82.9 and 82.7 (C-5, α,β-Fu), 80.0 (C-5, keto form), 75.6, 74.6, 74.0, 72.7 (C-6,7, α,β-Fu), 75.4 (C-6, keto form), 70.8 (C-7, keto form), 55.6 (C-8, keto form), 55.1 and 53.3 (C-8, α,β-Fu), 35.8 (C-3, keto form), 35.4 and 32.6 (C-3, α,β-Fu), 12.4 and 12.1 (C-2, α,β-Fu), 11.7 (C-2, keto form). − HRMS (LSIMS); *m*/*z*: 251.07490 [M^+ + Na] (calcd. 251.07563).

(6*S*,7*S*,8*S*,8a*S*)-6,7,8-Trihydroxy-8a-methoxyindolizidin-3-one (27): Compound **26** (240 mg, 1.05 mmol), dissolved in methanol/water (7:1; 25 mL) containing triethylamine (0.3 mL) and 10% Pd/C (50 mg), was hydrogenated at 4 atm for 48 h. Subsequent TLC analysis (2-propanol/methanol/aq. ammonia, 6:2:1; detection by method C) revealed that **26** had been completely consumed and showed the presence of a nonmobile compound. The catalyst was filtered off, washed with water, and the combined filtrate and washings were concentrated to dryness. Chromatographic workup of the residue (2-propanol/methanol/aq. ammonia, 6:2:1 → methanol/water, 1:1) afforded crystalline **27** (210 mg, 92%); m.p. 146−147 °C (dec.). − $[\alpha]_D^{27}$ +22.4 ($c = 0.8$, water). − IR (KBr): $\tilde{\nu}$ = 3486, 3437, 3305 (OH); 1676, 1661 cm^{-1} (CO). − ^{1}H NMR (D_2O, 500 MHz): δ = 4.10 (br. t, 1 H, $J_{6,7} = 2.8$ Hz, 7-H), 3.94 (br. dd, 1 H, 5β-H), 3.77 (m, 1 H, 6-H), 3.73 (d, 1 H, $J_{7,8} = 3.1$ Hz, 8-H), 3.21 (s, 3 H, OMe), 2.88 (br. t, 1 H, $J_{5\alpha,5\beta} \approx J_{5\alpha,6} = 11.4$ Hz, 5α-H), 2.80−2.50 (2 m, 2 H, 2α-,2β-H), 2.40−2.20 (2 m, 2 H, 1α-,1β-H). − ^{13}C NMR (D_2O/[D_6]acetone): δ = 170.6 (C-3), 96.9 (C-8a), 72.9 (C-7), 72.8 (C-8), 66.4 (C-6), 48.6 (OMe), 37.0 (C-5), 30.1 (C-2), 26.1 (C-1). − MS (CI, CH_4): *m*/*z* (%) = 218 [M^+ + 1] (13.6), 201 [M^+ + 1 − OH] (3.5), 186 [M^+ + 1 − MeOH] (18.4), 170 (3.0), 167 [M^+ − MeOH − H_2O] (100). − $C_9H_{15}NO_5$ (217.2): calcd. C 49.76, H 6.96, N 6.45; found C 49.62, H 7.27, N 6.59.

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