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CARBOHYDRATE RESEARCH

4-Amino-4-cyano-4,6-dideoxy sugar derivatives from methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose via Strecker-type reaction

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Abstract

Application of the Strecker reaction to methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose resulted in the formation of methyl 4-amino-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-α-L-talopyranoside, methyl 4-amino-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-β-D-allopyranoside and methyl 4-cyano-6-deoxy-2,3-*O*-isopropylidene-α-L-talopyranoside. Their proportionality and yields depend on the reaction conditions used. Additionally, 4-amino-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-α-L-talopyranoside can be prepared favourably from preformed methyl 4-cyano-6-deoxy-2,3-*O*-isopropylidene-α-L-talopyranoside. The crystal structure of methyl 4-acetamido-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-α-L-talopyranoside is also presented.

Keywords: Sugar amino nitriles; Methyl 2,3-*O*-isopropylidene-hexopyranosid-4-uloses; Strecker reaction; X-ray analysis

1. Introduction

In theory, the Strecker reaction represents a general route to sugar amino nitriles and acids if suitably O-protected sugar carbonyl compounds are available, but the practical applicability of this method is highly reduced, since in most cases, an epimeric mixture of products results from the reaction. Furthermore, the overall yields are often low. On the other hand, it is possible in many cases to obtain one desirable epimer in preponderance or there is a possibility to separate both epimers by crystallization or chromatography affording thus an access also to unfavourable but sometimes not so easily available very important compounds what makes this method still attractive.

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Although the amino nitrile synthesis involving C-1 carbonyl groups of saccharides is very well known [1], less attention has been paid till now to the study of reactions employing another carbonyl group in the saccharide while the C-1 carbonyl and hydroxyl groups at remaining positions are suitably protected [2–4].

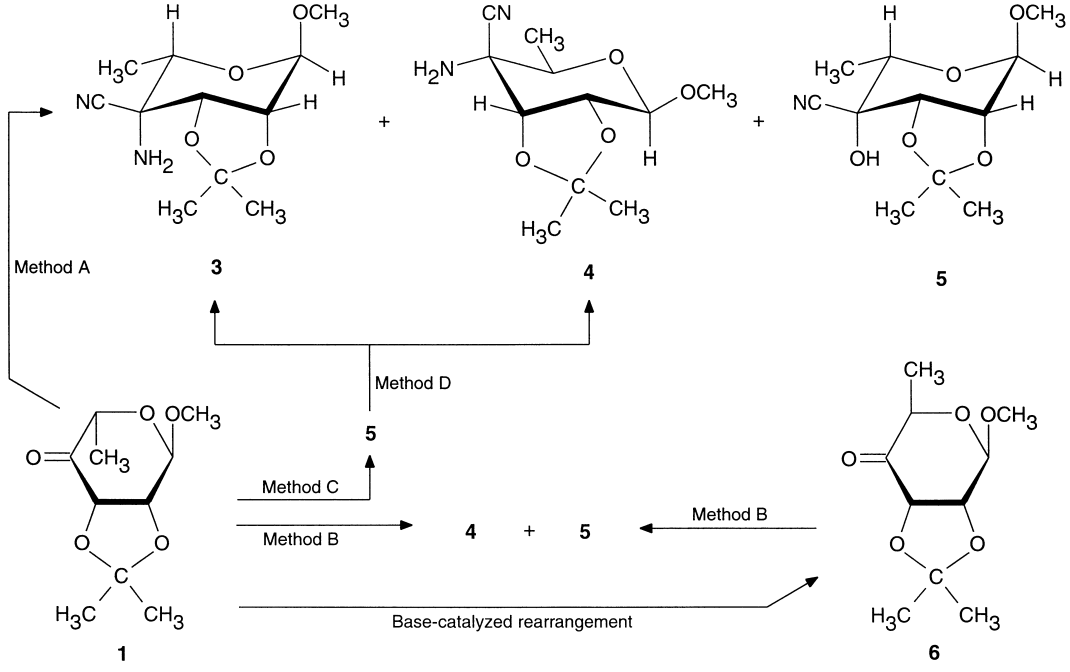
The amino sugars are of interest primarily because of their occurrence in antibiotics. Many of them have been found in bacterial organisms. Their presence as components of high-molecular-weight compounds identified in living organisms suggests a biological and medical importance of these molecules. To understand the mechanisms of amino sugar bioactivity, synthetically prepared suitable model compounds are needed.

With respect to the diversity of this class of compounds, we have started with the preparation of 4-amino-4-cyano-4-deoxy-L-*rhamno* derivatives, which are structurally related to perosamine. Subsequently, a series of sugar amino nitriles will be prepared starting from uloses of properly protected glucose, mannose, and galactose derivatives. Transformation of these amino nitriles into amino acids followed by linking to afford corresponding oligosaccharides, will be studied in the future.

2. Results and discussion

As a starting material we have used methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose (**1**) [5–11] prepared by oxidation of methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-mannopyranoside (**2**) [6,12–17] using pyridinium dichromate–acetic anhydride according to the procedure given for various uloses [18]. This method increased the yield of **1** up to 75% in comparison with only 35% reported [11] for the method using CrO_3–pyridine as an oxidant.

Reaction of the ketone **1** with potassium cyanide, ammonia and ammonium chloride afforded two or three products depending on the reaction conditions (Scheme 1). When the reaction was performed at 40 °C for a long time (method A), methyl 4-amino-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-α-L-talopyranoside (**3**) was formed as the major product together with a minority of methyl 4-amino-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-β-D-allopyranoside (**4**) and small amount of methyl 4-cyano-6-deoxy-2,3-*O*-isopropylidene-α-L-talopyranoside (**5**). Application of a shorter reaction time and room temperature (method B) led to the formation of a major amount of **5** and small amount of **4**. Cyanohydrin **5** was



Scheme 1.

formed exclusively when **1** was reacted with potassium cyanide and ammonium carbonate at room temperature (method C). It was found that amino nitriles **3** (major) and **4** can be also obtained starting from preformed cyanohydrin **5** applying ammonia and ammonium chloride as reactants and longer heating at 40 °C (method D). The overall yield of **3** from this two-steps procedure (**1**→**5**→**3**+**4**) is essentially the same as that of the straightforward preparation (**1**→**3**+**4**+**5**) (method A). However, regarding the presence of only two reaction products with high predominance of compound **3**, the two-step procedure is more advantageous for the isolation and purification of **3** by column chromatography.

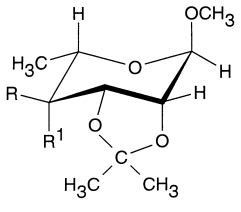
The formation of product **4** can be explained as follows: In addition to the usual Strecker reaction of ketone **1**, a competitive base-catalyzed isomerization at the C-5 position of the pyranose ring takes place [8,19,20] (a similar isomerization at C-5 was also observed in methyl 2,3-*O*-isopropylidene-6-*O*-methyl-α-L-*lyxo*-hexopyranosid-4-ulose during the Wittig reaction [21]) and the subsequent Strecker reaction of the so formed methyl 6-deoxy-2,3-*O*-isopropylidene-β-D-*ribo*-hexopyranosid-4-ulose (**6**) affords amino nitrile **4**. This assumption was confirmed by the synthesis of amino nitrile **4** from 4-ulose **6** itself which was prepared independently prior to the Strecker reaction (Scheme 1). In this case, the amino nitrile **4** was obtained almost exclusively both at 40 °C and room temperature. Moreover, isolation of cyanohydrin **5** (about 5%) suggests that the base-catalyzed isomerization at C-5 in **1** and **6** is a reversible process.

The isolation of amino nitriles and cyanohydrins only with L-*talo* (**3** and **5**) and D-*allo* (**4**) configuration (the other possible L-*manno* and D-*gulo* isomers were not detected) indicates the high stereoselectivity of the reaction at the C-4 ketone group. In addition, a comparison of the molar ratio of the amino nitriles **3** and **4** (~5:1 for method A, ~18:1 for method D) suggests that the amino nitrile formation at C-4 is faster than the base-catalyzed rearrangement at C-5.

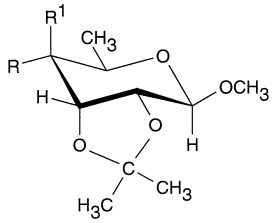
Even though the preparation of ketone **6** from ketone **1** is known [8,19,20], the described separation of these compounds from the reaction mixture is suitable only for small scale preparations. Therefore, we have used a two-steps procedure utilizing a reduction of the mixture of ketones **1** and **6** with $NaBH_4$ in the first step to afford the corresponding known methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-talopyranoside (**7**) [6,9] and methyl 6-deoxy-2,3-*O*-isopropylidene-β-D-allopyranoside **8** [8,20,22] (Scheme 2). These compounds are very easily separable by column chromatography and in the next step, they are oxidized with pyridinium dichromate–acetic anhydride to give the desirable pure ketones **1** or **6**.

The structure of the prepared compounds was determined on the basis of ^1H and ^{13}C NMR spectral data. These are summarized in Tables 1 and 2. The complete spectral data of some already known compounds are also included because they have not yet been fully or even not at all published till now. The EI and CI (pyridine) mass spectra of the selected compounds were also confirmative.

The ^1H NMR spectra of **3** and its *N*-acetyl derivative **9** showed coupling constants for the anomeric proton ($J_{1,2}$) of ~0 Hz suggesting the $^1C_4$ conformation with an axial glycosidic methoxyl group, H-3 and H-5 (α-L-*talo* or α-L-*manno* configuration) [11]. Moreover, the chemical shift of δ 2.10 for the CH_3 protons in the acetamido group of **9** support an axial position of an acetamido group of *talo* configuration rather than an equatorial which would be present in the *manno* isomer [23,24]. On the other hand, coupling constants $J_{1,2}$ of ~7 Hz in **4** and **10** indicate a significant change at the anomeric position. Although enolization at C-3 is also possible under the Strecker reaction conditions, the configuration at C-3 remains unchanged because a 2,3-*cis* stereochemistry is favoured for the isopropylidene group as observed in similar base-catalyzed isomerizations [25,26]. Considering that C-1, C-2, and C-3 positions were not attacked and that inversion took place only at C-5, the significant difference in the coupling constant values for anomeric protons in comparison with those reported for **3** and **9** can be explained by the inversion of a $^1C_4$ to a $^4C_1$ conformation with



2 R = OH, R^1 = H
7 R = H, R^1 = OH
9 R = CN, R^1 = $NHCOCH_3$



8 R = OH, R^1 = H
10 R = $NHCOCH_3$, R^1 = CN

Scheme 2.

Table 1
^{1}H Chemical shifts and coupling constants of the prepared sugars (in $CDCl_3$)

Compd	Chemical shifts (δ, ppm)										
	H-1	H-2	H-3	H-4	H-5	H-6	OMe	CMe_2		Others	
1	4.84(s)	4.43(s)	—	—	4.25(q)	1.40(d)	3.47(s)	1.48(s)	1.38(s)	—	
2	4.86(s)	4.13(d)	4.08(dd)	3.38(dd)	3.63(m)	1.31(d)	3.39(s)	1.53(s)	1.36(s)	—	
3	4.91(s)	4.10(d)	4.41(d)	—	4.01(q)	1.49(d)	3.40(s)	1.58(s)	1.40(s)	1.69(bs)[a]	
4	4.38(d)	4.04(dd)	4.50(d)	—	3.70(q)	1.46(d)	3.51(s)	1.54(s)	1.41(s)	2.05(bs)[a]	
5	4.99(s)	4.20(d)	4.26(d)	—	3.76(q)	1.46(d)	3.40(s)	1.76(s)	1.38(s)	3.58(s)[b]	
6[c]	4.42(d)	4.35(dd)	4.29(d)	—	4.16(q)	1.23(d)	3.13(s)	1.47(s)	1.14(s)	—	
7	4.93(s)	3.56(d)	4.21(dd)	4.03(dd)	3.83(m)	1.33(d)	3.40(s)	1.59(s)	1.38(s)	2.28(bs)[b]	
8	4.49(d)	3.70(dd)	4.53(dd)	4.10(t)	3.71(m)	1.40(d)	3.54(s)	1.59(s)	1.44(s)	2.20(bs)[b]	
9	4.90(s)	4.14(d)	4.57(d)	—	4.13(q)	1.43(d)	3.41(s)	1.52(s)	1.37(s)	5.71(bs)[d]	2.10(s)[e]
10	4.40(d)	4.12(dd)	4.90(d)	—	3.84(q)	1.50(d)	3.53(s)	1.54(s)	1.38(s)	5.83(bs)[d]	2.07(s)[e]

Compd	Coupling constants (J, Hz)				
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$
1	0	—	—	—	6.8
2	0	5.7	7.2	9.4	6.3
3	0	6.5	—	—	6.3
4	6.9	5.1	—	—	6.3
5	0	6.4	—	—	6.2
6[c]	3.9	7.9	—	—	6.9
7	0	4.9	6.4	1.2	6.6
8	5.6	3.8	5.9	5.9	5.9
9	0	6.3	—	—	6.4
10	6.9	5.2	—	—	6.3

[a] Chemical shift for protons of NH_2 group.
[b] Chemical shift for proton of OH group.
[c] Measured in C_6D_6.
[d] Chemical shift for proton of acetamido group.
[e] Chemical shift for protons of CH_3 group in acetyl.

an equatorial glycosidic methoxyl group and H-3, and an axial H-5 (β-D-*allo* or β-D-*gulo* configuration).

Because of the obvious difficulties in unambiguous establishing the configuration of compounds **3** (*talo* versus *manno*) and **4** (*allo* versus *gulo*) at C-4 by NMR methods, suitable crystals of corresponding *N*-acetylated compounds **9** and **10** were subjected to X-ray analysis. This confirmed the α-L-*talo* configuration of **9** and the β-D-*allo* configuration of **10**. The structure of compound **9** and the numbering of the atoms is shown in Fig. 1. The H-positions have been put at calculated positions. The relevant crystallographic data for **9** are given in Table 3. The bond lengths and bond angles are

Table 2
^{13}C Chemical shifts of the prepared sugars (in $CDCl_3$)

Compd	Chemical shifts (δ, ppm)										
	C-1	C-2	C-3	C-4	C-5	C-6	OMe	CMe_2	$C(CH_3)_2$		CN
1	97.9	75.7	78.5	204.3	69.5	15.7	55.6	111.1	26.5	25.3	—
2	98.0	75.7	78.4	74.3	65.5	17.3	54.7	109.3	27.9	26.0	—
3	98.3	73.3	76.0	53.8	64.9	15.3	55.2	109.9	25.8	24.8	120.8
4	103.2	75.5	77.2	56.8	70.9	15.2	56.9	110.7	27.8	26.1	119.0
5	98.5	79.4	75.9	75.1	65.2	14.8	55.3	111.3	25.9	25.2	118.2
6	101.9	75.5	78.3	206.6	74.7	17.3	56.6	112.0	26.5	24.8	—
7	98.4	72.9	73.1	66.7	64.2	16.6	54.9	109.1	25.7	25.1	—
8	101.8	74.5	76.6	70.8	69.9	18.3	56.5	101.8	27.4	25.6	—
9[a]	98.3	73.4	76.8	52.8	66.3	15.5	55.4	110.0	25.9	24.7	117.2
10[b]	103.2	74.9	75.0	55.6	70.3	16.6	57.0	111.1	27.9	26.1	115.1

[a] 168.9 and 23.7 ppm for C=O and CH_3 in acetyl.
[b] 169.4 and 23.3 ppm for C=O and CH_3 in acetyl.

Table 3
Crystal and experimental data for methyl 4-acetamido-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-α-L-talopyranoside (**9**)

Formula	$C_{13}H_{20}N_2O_5$
Formula weight	284.31
Crystal system	monoclinic
Space group	$P2_1$
Unit-cell dimensions (Å)	$a = 8.7357(2)$
	$b = 8.5982(2)$
	$c = 9.95500(10)$
	$\beta = 104.0671(14)$
Unit-cell volume V (Å^3)	725.31(2)
Formula units per unit cell, Z	2
F(000)	304
Calculated density D_x (g cm^{-3})	1.302
Radiation	MoK α
Wavelength, λ (Å)	0.7103
Linear absorption coefficient (cm^{-1})	1
Temperature, T (K)	173(2)
Crystal description	colourless prism
Crystal size (mm)	0.46 (max)
	0.42 (min)
Diffractometer	Siemens SMART CCD
Unit-cell determination	
No. of reflections used	2582
Θ-range (°)	2.11–23.21
Intensity data collection	
Θ_{max} (°)	23.11
Range of h	−9–9
Range of k	−9–9
Range of l	−7–11
Scan mode	ω
Scan range, $\Delta\omega$	0.3
Total number of reflections	1887
No. of independent reflections, $[l > 2\sigma(l)]$	1856
Structure refinement	
Minimization of	$\Sigma w(\|F_o\| - \|F_c\|)^2$
Anisotropic thermal parameters	All non-hydrogen atoms
Isotropic thermal parameters	Hydrogen atoms
No. of refined parameters	206
Weighting scheme	$\left[\sigma^2\left(\|F_o\|^2\right) + (0.0378P)^2 + 0.1454P\right]^{-1}$
	where $P = \left(\|F_o\|^2 + 2\|F_c\|^2\right)/3$
$R = \Sigma \parallel F_o\| - \|F_c \parallel / \Sigma\|F_o\|$	0.0242
$R_w = \left[\Sigma w(\|F_o\| - \|F_c\|)^2 / \Sigma w\|F_o\|^2\right]^{1/2}$	0.0646
$S = \left[\Sigma w(\|F_o\| - \|F_c\|)^2 / (N_{obs} - N_{var})\right]^{1/2}$	1.020
Final $(\Delta/\sigma)_{max}$	0.001
Final $\Delta\rho_{min}$ and $\Delta\rho_{max}$ (e Å^{-3})	−0.119 and 0.131

listed in Table 4. A list of selected torsion angles is given in Table 5. The final positional parameters are summarized in Table 6. The X-ray data suggest for **9** a $^1C_4$ conformation which is distorted into the direction of ^5E, thus indicating a considerable flattening at C-2. A similar situation is observed in the related structures having an α-L-*rhamno* configuration [27–29]. The more detailed X-ray analysis study of **10** will be published elsewhere [30].

3. Experimental

General methods.—^{1}H and ^{13}C NMR spectra (in $CDCl_3$, internal standard Me_4Si) were recorded on a Bruker Avance DPX 300 instrument operating at 300.13 and 75.46 MHz working frequencies, respectively. For the assignments of signals, 1D NOESY and C–H heterocorrelated experiments were used. The quaternary carbon atoms were identified on the basis of a semiselective INEPT

experiment and a 1D INADEQUATE pulse sequence technique. The EI and CI (using pyridine as a reactive gas) mass spectra (70 eV) were obtained on a Finnigan MAT SSQ 710 instrument. Specific optical rotations were determined on a Perkin–Elmer 241 polarimeter (10 cm cell). Microanalyses were performed on a Fisons EA 1108 analyzer. Melting points were determined with a Boetius PHMK 05 microscope. All reactions were monitored by TLC on Silica Gel plates (E. Merck) using the following solvents: 3:2 EtOAc–hexane (eluent A) and 6:1 $CHCl_3$–Me_2CO (eluent B). Visualization was affected with iodine vapour or H_2SO_4. Column chromatography was performed as flash chromatography on Silica Gel 60 (E. Merck, 230–400 mesh) with the same eluents.

X-ray techniques.—Crystal and experimental data for compound **9** are listed in Table 3. The structure was solved by direct methods and refined by a full-matrix least-squares technique. The crystallographic computations were performed with SHELX86 [31] and SHELX93 [32]. The ZORTEP program [33] was used for the illustration.

Table 4
Bond lengths [in Å] and bond angles [in °] for methyl 4-acetamido-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-α-L-talopyranoside (**9**)

N-1–C-12	1.358(2)
N-1–C-4	1.456(2)
C-1–O-1	1.405(2)
C-1–O-5	1.416(2)
C-1–C-2	1.526(2)
O-1–C-10	1.440(2)
C-2–O-2	1.433(2)
C-2–C-3	1.521(2)
N-2–C-11	1.146(2)
C-12–C-13	1.504(3)
O-3–C-3	1.421(2)
O-3–C-8	1.458(2)
C-3–C-4	1.565(2)
C-4–C-11	1.476(2)
C-4–C-5	1.555(2)
O-2–C-7	1.446(2)
O-5–C-5	1.433(2)
C-5–C-6	1.512(2)
C-7–C-9	1.503(3)
C-7–C-8	1.509(3)
C-12–O-4	1.225(2)
C-12–N-1–C-4	125.50(14)
O-1–C-1–O-5	112.24(12)
O-1–C-1–C-2	103.57(14)
O-5–C-1–C-2	112.87(14)
C-1–O-1–C-10	113.11(14)
O-2–C-2–C-3	101.24(13)
O-2–C-2–C-1	113.34(13)
C-3–C-2–C-1	115.51(13)
C-3–O-3–C-7	108.68(12)
O-3–C-3–C-2	103.36(13)
O-3–C-3–C-4	111.94(14)
C-2–C-3–C-4	113.09(14)
N-1–C-4–C-11	111.69(14)
N-1–C-4–C-5	111.14(14)
C-11–C-4–C-5	111.37(13)
N-1–C-4–C-3	110.51(12)
C-11–C-4–C-3	105.33(14)
C-5–C-4–C-3	106.53(13)
C-2–O-2–C-7	103.75(12)
C-1–O-5–C-5	113.63(13)
O-5–C-5–C-6	107.14(14)
O-5–C-5–C-4	106.17(11)
C-6–C-5–C-4	114.91(14)
O-2–C-7–O-3	103.87(11)
O-2–C-7–C-9	109.74(15)
O-3–C-7–C-9	109.68(14)
O-2–C-7–C-8	111.44(14)
O-3–C-7–C-8	109.59(14)
C-9–C-7–C-8	112.18(14)
O-4–C-12–N-1	122.4(2)
O-4–C-12–C-13	22.5(2)
N-1–C-12–C-13	15.0(2)
N-2–C-11–C-4	170.1(2)

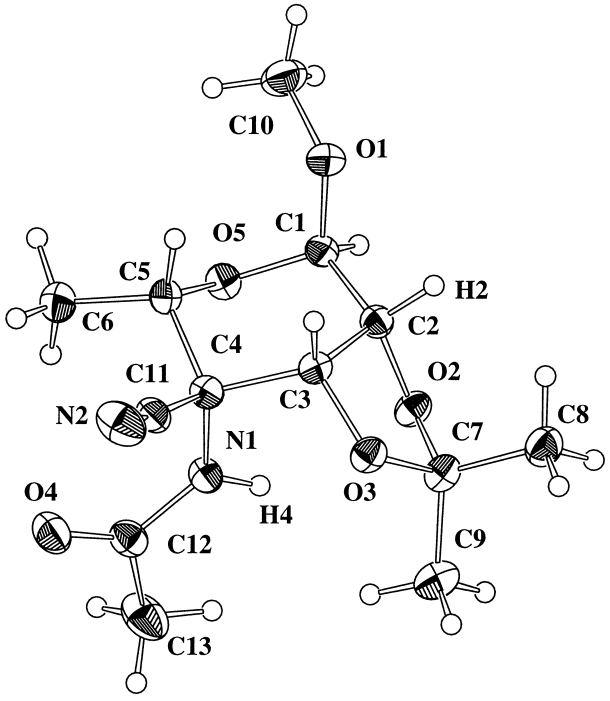


Fig. 1. ZORTEP plot and atomic numbering of methyl 4-acetamido-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-α-L-talopyranoside (**9**).

Table 5
Selected torsion angles (in °) for methyl 4-acetamido-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-α-L-talopyranoside (**9**)

C-10–O-1–C-1–O-5	−62.31
C-10–O-1–C-1–C-2	175.66
C-13–C-12–N-1–C-4	177.21
O-4–C-12–N-1–C-4	−3.01
O-2–C-2–C-3–O-3	34.93
O-3–C-3–C-4–C-11	75.39

Table 6
Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for compound **9**

Atom	x	y	z	U(eq)
N-1	8459(2)	6346(2)	1832(2)	227(3)
C-1	5959(2)	9018(2)	2819(2)	219(4)
O-1	6223(1)	10385(1)	3617(1)	274(3)
C-2	6540(2)	9433(2)	1537(2)	213(4)
N-2	12029(2)	8313(2)	3039(2)	389(4)
C-13	8380(2)	3637(2)	1176(2)	415(5)
O-3	8416(1)	9077(2)	283(1)	240(3)
C-3	8301(2)	9226(2)	1677(2)	201(4)
C-4	9002(2)	7780(2)	2573(2)	208(4)
O-2	5896(1)	8457(1)	370(1)	234(3)
O-5	6754(1)	7720(1)	3544(1)	238(3)
C-5	8436(2)	7892(2)	3935(2)	229(4)
C-7	6839(2)	8822(2)	−598(2)	234(4)
C-10	5644(2)	10293(3)	4851(2)	367(5)
C-8	6269(2)	10285(2)	−1401(2)	303(5)
C-9	6863(2)	7453(2)	−1531(2)	322(5)
C-12	9231(2)	4962(2)	2026(2)	257(4)
O-4	10527(1)	4807(2)	2831(1)	319(3)
C-11	10730(2)	7953(2)	2840(2)	248(4)
C-6	9072(2)	6641(2)	4991(2)	323(5)
H-4	7554(2)	6378(2)	1206(2)	37(6)
H-2	6250(2)	10537(2)	1279(2)	19(4)
H-1	4801(2)	8799(2)	2540(2)	12(4)
H-13A	7396(2)	4020(2)	567(2)	101(11)
H-13B	8137(2)	2835(2)	1792(2)	141(16)
H-13C	9050(2)	3194(2)	614(2)	132(14)
H-3	8871(2)	10185(2)	2094(2)	15(4)
H-5	8712(2)	8938(2)	4364(2)	6(4)
H-10A	5735(15)	11315(5)	5300(8)	54(7)
H-10B	6269(11)	9531(12)	5488(7)	55(7)
H-10C	4535(6)	9970(16)	4605(3)	74(9)
H-8A	7000(8)	10566(8)	−1968(9)	31(5)
H-8B	6220(13)	11132(4)	−754(2)	28(5)
H-8C	5216(6)	10106(5)	−2002(9)	37(5)
H-9A	7575(12)	7672(6)	−2132(9)	43(6)
H-9B	5796(4)	7266(10)	−2102(10)	47(6)
H-9C	7234(15)	6530(4)	−969(2)	54(7)
H-6A	10229(2)	6661(9)	5221(9)	38(6)
H-6B	8700(11)	5621(3)	4605(5)	26(5)
H-6C	8701(11)	6828(8)	5830(5)	36(5)

Methyl 6-deoxy-2,3-O-*isopropylidene*-α-L-lyxo-*hexopyranosid-4-ulose* (**1**).—Methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-mannopyranoside (**2**; 14.0 g, 64.1 mmol) in dry CH_2Cl_2 (250 mL) was added dropwise in the course of 1 h to a stirred and cooled (10 °C) solution of pyridinium dichromate (16.9 g, 45 mmol) and Ac_2O (18 mL) in dry CH_2Cl_2 (250 mL) followed by heating under reflux for 2 h. After cooling to room temperature, the mixture was diluted with EtOAc (100 mL) and the solution was concentrated. The dark residue was added to the top of a silica gel column (4.5×30 cm) to remove chromium salts and the product was thoroughly eluted with EtOAc in one fraction (R_f 0.78, eluent A). After concentration, the residue was co-concentrated with toluene in order to remove any Ac_2O, HOAc or pyridine. The ketone **1** (10.4 g, 75%) was obtained as a colourless liquid; $[\alpha]_D$ −101.4° (*c* 1, MeOH), lit. −105.8° [8], −101° [11]. Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found: C, 55.49; H, 7.50.

Alternatively, 4-ulose **1** was prepared (~75% yield) from methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-talopyranoside (**7**) using the same oxidative procedure as above.

General procedures for the preparation of amino nitriles.—Method A. Dry ammonia gas was introduced to a magnetically stirred mixture of methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose (**1**; 8.65 g, 40 mmol), NaCN (3.93 g, 80.0 mmol) and NH_4Cl (4.28 g, 80.0 mmol) in dry MeOH (700 mL). The mixture was stirred at 40 °C for 4 days. After concentration, the residue was dissolved in water (100 mL). Extraction with $CHCl_3$ (3×100 mL) and evaporation of the solvent afforded the crude reaction product which was chromatographed on a silica gel column (4.5×55 cm, eluent A).

Method B. The mixture of reactants as above was stirred at 25 °C for 20 h followed by the same work-up as described in Method A.

Method C. A mixture of methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose (**1**; 8.65 g, 40 mmol), $(NH_4)_2CO_3$ (7.69 g, 80 mmol) and NaCN (3.93 g, 80 mmol) in dry MeOH (200 mL) was stirred at 25 °C for 24 h. The solution was concentrated and the residue was dissolved in water (100 mL). Extraction with Et_2O (3×100 mL) and evaporation of the solvent afforded the crude reaction product which was recrystallized from EtOAc–hexane.

Method D. Dry ammonia gas was introduced to a magnetically stirred mixture of methyl 4-cyano-6-deoxy-2,3-*O*-isopropylidene-α-L-talopyranoside (**5**; 9.73 g, 40 mmol) and NH_4Cl (4.28 g, 80 mmol) in dry MeOH (700 mL). The mixture was stirred at 40 °C for 4 days followed by the same work-up as in Method A.

Methyl 4-amino-4-cyano-4,6-dideoxy-2,3-O-*isopropylidene*-α-L-*talopyranoside* (**3**).—The fractions having R_f 0.75 (eluent A) from column chromatography (method A) were collected and evaporated to yield crude **3**. Recrystallization from EtOAc–hexane gave amino nitrile **3** as colourless needles (5.22 g, 54%); mp 76–78 °C; $[\alpha]_D$ −13° (*c* 1.0, MeOH). Anal. Calcd for $C_{11}H_{18}N_2O_4$: C, 54.53; H, 7.49; N, 11.56. Found: C, 54.61; H, 7.55; N, 11.50.

Alternatively, the amino nitrile **3** (7.10 g, 73%) was obtained by column chromatography (as above) of the crude reaction product from method D.

Methyl 4-amino-4-cyano-4,6-dideoxy-2,3-O-*isopropylidene-β*-D-*allopyranoside* (**4**).—The fractions with R_f 0.51 (eluent A) from column chromatography (method A) were collected and evaporated to give crude 4. Recrystallization from EtOAc–hexane yielded **4** as a white amorphous solid (1.15 g, 12%); mp 60–62 °C; $[\alpha]_D$ −59° (*c* 1.0, MeOH). Anal. Calcd for $C_{11}H_{18}N_2O_4$: C, 54.53; H, 7.49; N, 11.56. Found: C, 54.45; H, 7.53; N, 11.51.

Alternatively, the amino nitrile **4** was obtained by column chromatography (as above) of the crude reaction product from method B (0.21 g, 2%) or from method D (0.40 g, 4%). More conveniently, compound **4** (48% yield) was prepared from methyl 6-deoxy-2,3-*O*-isopropylidene-*β*-D-*ribo*-hexopyranosid-4-ulose (**6**) applying the reaction conditions of method B.

Methyl 4-cyano-6-deoxy-2,3-O-*isopropylidene-α*-L-*talopyranoside* (**5**).—The fractions with R_f 0.68 (eluent A) from column chromatography (method A) were collected and evaporated to afford crude **5**. Recrystallization from EtOAc–hexane yielded **5** as white needles (0.31 g, 3%); mp 205–206 °C; $[\alpha]_D$ −12° (*c* 1.0, MeOH). Anal. Calcd for $C_{11}H_{17}NO_5$: C, 54.31; H, 7.04; N, 5.76. Found: C, 54.23; H, 7.11; N, 5.80.

Alternatively, the cyanohydrin **5** was obtained by column chromatography (as above) of the crude reaction product from method B (4.78 g, 49%) or more conveniently applying method C (7.09 g, 73%). In addition, compound **5** can be prepared (5% yield) from 4-ulose **6** applying the reaction conditions of method B.

Methyl 6-deoxy-2,3-O-*isopropylidene-β*-D-*ribo-hexopyranosid-4-ulose* (**6**).—Starting from methyl 6-deoxy-2,3-*O*-isopropylidene-*β*-D-allopyranoside (**8**; 7.0 g, 32 mmol) and application of the same oxidative procedure as described for the preparation of **1** afforded **6** (5.3 g, 77%) as an oil which solidified; mp 42–43 °C, lit. 42–43 °C [8], 39–41 °C [19], 40–42 °C [20]; $[\alpha]_D$ +35° (*c* 1, $CHCl_3$), lit. +36° (*c* 0.4, $CHCl_3$) [8], +52° ($CHCl_3$) [19]. Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found: C, 55.67; H, 7.51.

Methyl 6-deoxy-2,3-O-*isopropylidene-α*-L-*talopyranoside* (**7**) *and methyl 6-deoxy-2,3*-O-*isopropylidene-β*-D-*allopyranoside* (**8**).—A mixture of ketones **1** and **6** (5.41 g, 25 mmol) obtained from **1** (6.70 g, 31 mmol) after isomerization using KOH was reduced with $NaBH_4$ (2.35 g, 62.1 mmol) in MeOH (200 mL) according to the described method [8]. The crude reaction product was chromatographed on a column of silica gel (4.5×40 cm) with 9:1 toluene–MeOH as an eluent. The fractions having R_f 0.46 were collected and evaporated to give **7** (2.80 g, 51%) as a colourless oil; $[\alpha]_D$ −26° (*c* 1, MeOH), lit. −49° (*c* 1.3, MeOH) [9]. Anal. Calcd for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 55.13; H, 8.35. The fractions with R_f 0.31 afforded after evaporation **8** (2.52 g, 46%) as a colourless oil; $[\alpha]_D$ −98° (*c* 1, MeOH), $[\alpha]_D$ −46° (*c* 1, $CHCl_3$), lit. −50° (*c* 0.45, $CHCl_3$) [8]. Anal. Calcd for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 55.11; H, 8.29.

Methyl 4-acetamido-4-cyano-4,6-dideoxy-2,3-O-*isopropylidene-α*-L-*talopyranoside* (**9**).—Acetylation of **3** (1.21 g, 5 mmol) with Ac_2O (7 mL) in pyridine (15 mL) overnight followed by concentration and co-concentration with toluene gave, after recrystallization from EtOAc–hexane, **9** (1.26 g, 89%) as white needles (R_f 0.51, eluent B); mp 145–146 °C; $[\alpha]_D$ +22° (*c* 1, MeOH); EIMS (70 eV): *m*/*z* 285 $[M+1]^+$, 269 $[M–Me]^+$, 253, 240, 227, 211, 182, 167, 153, 125, 124, 115, 109, 85, 82, 73, 59, 43 (100%). CIMS: *m*/*z* 364 $(M+80)^+$. Anal. Calcd for $C_{13}H_{20}N_2O_5$: C, 54.92; H, 7.09; N, 9.85. Found: C, 54.86; H, 7.07; N, 9.81.

Methyl 4-acetamido-4-cyano-4,6-dideoxy-2,3-O-*isopropylidene-β*-D-*allopyranoside* (**10**).—Acetylation of **4** (1.21 g, 5 mmol) with Ac_2O (7 mL) in pyridine (15 mL) overnight followed by concentration and co-concentration with toluene gave, after recrystallization from EtOAc–hexane, **10** (1.29 g, 91%) as white needles (R_f 0.30, eluent B); mp 201–202 °C; $[\alpha]_D$ +38° (*c* 1, MeOH); EIMS (70 eV): *m*/*z* 269 $[M–Me]^+$, 240, 227, 195, 182, 167, 125, 124, 115, 109, 100, 85, 82, 59, 43 (100%). CIMS: *m*/*z* 364 $(M+80)^+$. Anal. Calcd for $C_{13}H_{20}N_2O_5$: C, 54.92; H, 7.09; N, 9.85. Found: C, 55.00; H, 7.12; N, 9.81.

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