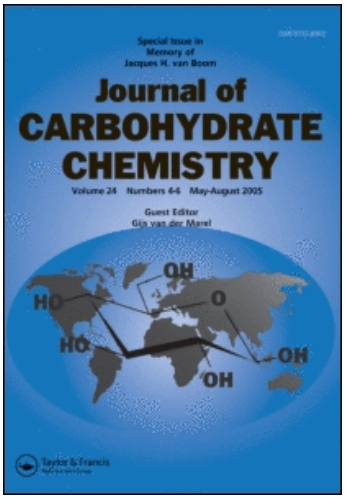

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Synthesis of Blocked Sugars Bearing a Terminal 1-Cyanovinyl Group

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SYNTHESIS OF BLOCKED SUGARS BEARING A TERMINAL 1-CYANOVINYL GROUP

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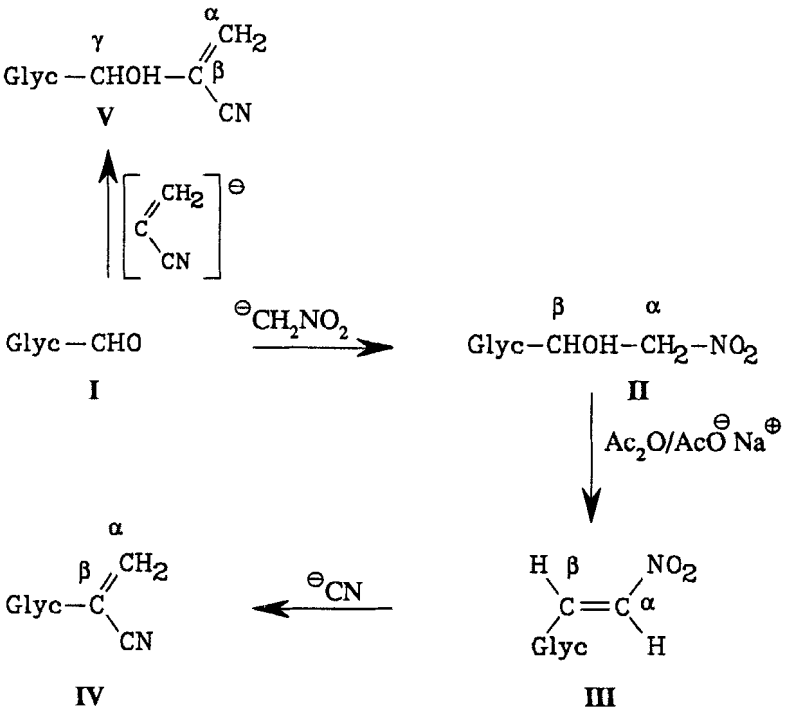
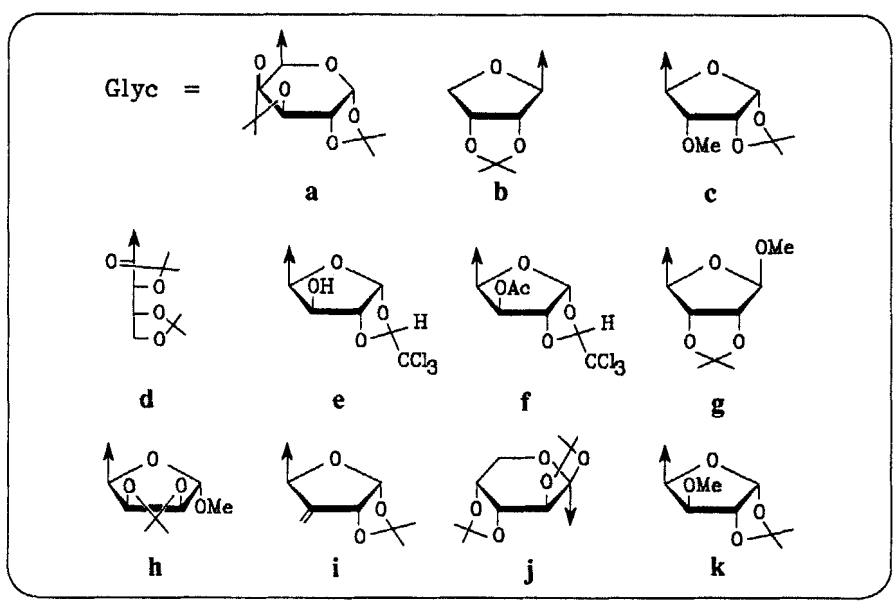
ABSTRACT

A series of blocked sugar aldehydes treated with the conjugate base of nitromethane afforded the expected nitrosugars **1-7**, whose configuration at the new asymmetric centre was assigned by CD. Nitroenoses **8-14**, obtained from the corresponding saturated β-hydroxy nitrosugars, reacted with potassium cyanide, afforded the terminal 1-cyanovinyl sugar derivatives **15-23**. Another route to 1-cyanovinylic sugars bearing a free hydroxy group (**24** and **25**) consisted in reacting aldehydo sugars with the conjugate base of acrylonitrile. The 1-cyanovinyl sugars are soft electrophiles which react with hydroxylamines to give the product of a conjugate addition (**27** and **28**). The interest of these compounds resides in their often selective toxicity towards cells, viruses or bacteria.

INTRODUCTION

Most active antiviral compounds are nucleosides. Paradoxically, we found[1] that sugars bearing a terminal 1-cyanovinyl group, lost most of their cytotoxicity and antiviral properties upon nucleosidation. Moreover, the study of the cytotoxic, antiviral and antimicrobial properties of a series of blocked sugars bearing this electrophilic group, showed[2] a strong dependence of the biological properties of these compounds, on the structure of the sugar moiety. As some of these compounds showed promising antiviral properties, they appeared as possible leads toward the development of new types of non-nucleosidic antiviral





SCHEME 1

compounds. To undertake a quantitative structure-activity relationship (QSAR) study, we needed a large number of cyanovinylic sugars, the synthesis of some being described here.

RESULTS AND DISCUSSION

The synthetic pathways to the 1-cyanovinylic sugars are summarized in SCHEME 1 and TABLE 1.

TABLE I. Origin or Structure of the Main Compounds Cited

Glyc	I	II	III	IV	V
a	Ref. 3	1	8	15	
b	Ref. 4	2	9	16	
c			Ref. 5	17	
d			Ref. 6	18	
e	Ref. 7	3			
f			10[a]	19	
g	Ref. 8	4	11	20	
h	Ref. 9	5	12	21	
i	Ref 10	6	13	22	
j	Ref. 8	7	14	23	24
k	Ref. 11				25

a. Obtained from 3.

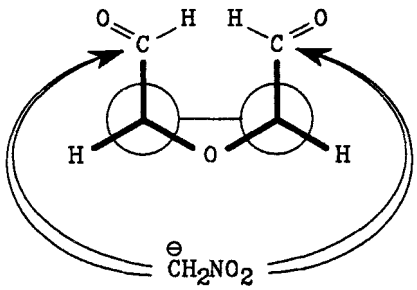
Treatment of aldehydosugars I with the conjugate base of nitromethane, gave in fair to good yields the expected nitrosugars **1-7** (TABLE 2). The reaction always afforded one preponderant or exclusive isomer. As the $J_{\beta,\gamma}$ ^{1}H NMR coupling is not, in this situation, a viable means of determining the configuration, owing to a *partial conformational annulation of the configurational difference*,[12] we resorted to circular dichroism (CD) measurements to establish the configuration of the new asymmetric carbon. In CD spectra of nitroalcohols, negative θ values at *ca* 275 and 310 nm correspond to an *R* configuration of the β carbon atom.[13]

From these configurations (TABLE 2) it could be deduced that the nucleophile attack should take place from the less hindered side of the molecule (the side of the ring oxygen), with the carbonyl oxygen away from the ring oxygen (SCHEME 2).

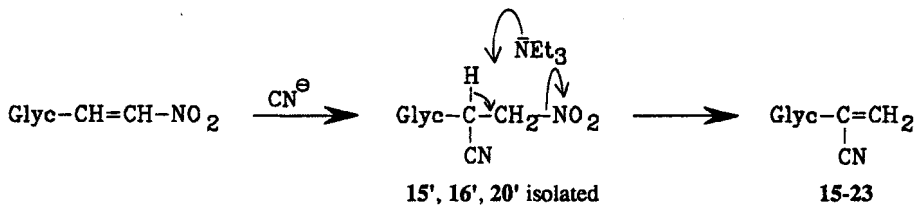
TABLE 2. Some Properties of the Major (or Unique) Isomer of Nitrosugars **1-7**

compd	yield	mp	θ (λ)	configuration	$J_{\beta,\gamma}$	MF (MW)	elementary analysis
1	71	syrup	-1840 (279) - 690 (310)	α-D-*glycero*- D-*galacto*	8	$C_{13}H_{21}NO_8$ (319.31)	Calcd: C, 48.90; H, 6.63; N, 4.39 Found: C, 48.62; H, 6.82; N, 4.13
2	82	74.3-75.6	+1610 (275) + 640 (310)	D-*allo*	8	$C_9H_{15}NO_6$ (232.22)	Calcd: C, 46.35; H, 6.48; N, 6.01 Found: C, 46.29; H, 6.55; N, 5.96
3[a]	66	135.4-154.6				$C_8H_{10}Cl_3NO_7$ (338.53)	Calcd: C, 28.38; H, 2.98; Cl, 31.42; N, 4.14 Found: C, 28.30; H, 2.95; Cl, 31.24; N, 4.06
4	57	116.8-116.9	-3010 (272) -1504 (310)	β-D-*allo*	6	$C_{10}H_{17}NO_7$ (263.25)	Calcd: C, 45.63; H, 6.51; N, 5.32 Found: C, 45.64; H, 6.48; N, 5.40
5	83	syrup	-1610 (273) - 710 (310)	α-D-*manno*	7	$C_{10}H_{17}NO_7$ (263.25)	Calcd: C, 45.63; H, 6.51; N, 5.32 Found: C, 45.70; H, 6.49; N, 5.29
6	44[b]	syrup	-2030 (278) - 830 (310)	α-D-*ribo*	5	$C_{10}H_{15}NO_6$ (245.23)	Calcd: C, 48.98; H, 6.17; N, 5.71 Found: C, 49.14; H, 6.15; N, 5.67
7	94	109.0-110.8	-1380 (280) - 920 (310)	β-D-*manno*	-	$C_{13}H_{21}NO_8$ (319.31)	Calcd: C, 48.90; H, 6.63; N, 4.39 Found: C, 49.04; H, 6.71; N, 4.41

a. Unresolvable mixture (4:1) of the two epimers. b. 16% of the second isomer were also isolated.



SCHEME 2



SCHEME 3

As the most populated conformation of aldehydosugars is one where the O=C-C-O torsional angle is close to 0°,[5] the stereochemistry of the reaction is clearly not controlled by the starting compounds but by the transition state whose most favourable topography is when the incipient negative charge on the carbonyl oxygen is away from the ring oxygen. Notable quantities of the second isomer were obtained when both sides of the molecule were accessible (**6**) or in the special case where a hydroxyl group was present (**3**). It should be noted that the accessibility is governed by stereoelectronic rather than purely steric factors, as shown by the fact that 1,2-*O*-isopropylidene-α-D-*ribo*-pentodialdo-1,4-furanose gave a mixture of isomers.[5]

Upon acetylation, the nitrosugars **1-7** underwent elimination to the corresponding nitroenoses. The yields obtained and the properties of nitroenoses **8-14** are collected in TABLE 3. As shown by the values of their $J_{\alpha,\beta}$ ^{1}H NMR coupling constants, their configuration is *E*. The small value of their $J_{\beta,\gamma}$ is in accordance with the preponderance of the conformation where the double bond and the C_γ-O bond are eclipsed, as established by quantum mechanics calculations[14] for terminal (*E*)-unsaturated sugars bearing an electro-withdrawing group on their terminal carbon.

Upon treatment with potassium cyanide in the presence of a phase transfer catalyst, **8** gave a mixture of the 1-cyanovinyl derivative **15** and the corresponding α-nitromethylnitrile

TABLE 3. Some Data Relative to Nitroenose Derivatives **8-14**

compd	yield	mp	$[\alpha]_D$ (c, temp)	$J_{\alpha,\beta}$	$J_{\beta,\gamma}$	$J_{\alpha,\gamma}$	MF	elementary analysis
8	82	140.0-140.5	-55.2 (1.05, 23)	13.5	3.5	2.5	$C_{13}H_{19}NO_7$ (301.30)	Calcd: C, 51.82; H, 6,36; N, 4.65 Found: C, 51.85; H, 6.35; N, 4.68
9	92	58.7-59.5	-96.5 (1.3, 22)	14.0	3	< 0.5	$C_9H_{13}NO_5$ (215.21)	Calcd: C, 50.23; H, 6.09; N, 6.51 Found: C, 50.35; H, 6.06; N, 6.53
10	57	140.9-142.2	+39.8 (1.3, 23)	13.0	3	1.5	$C_{10}H_{10}Cl_3NO_7$ (362.55)	Calcd: C, 33.13; H, 2,78; Cl, 29.34; N, 3.86 Found: C, 33.26; H, 2.84; Cl, 29.09; N, 3.85
11	54	syrup[a]	-47.7 (0.9, 25)	14.0	6.0	0.7	$C_{10}H_{15}NO_6$ (245.23)	Calcd: C, 48.98; H, 6.17; N, 5.71 Found: C, 49.14; H, 6.04; N, 5.81
12	48	43.6-47.9	0 (0.9, 29)	14.0	4.0	1.2	$C_{10}H_{15}NO_6$ (245.23)	Calcd: C, 48.98; H, 6.17; N, 5.71 Found: C, 48.91; H, 6.12; N, 5.57
13	51	80.8-81.8	+104.6 (1.1, 21)	13.0	3.0	< 0.5	$C_{10}H_{13}NO_5$ (227.22)	Calcd: C, 52.86; H, 5.77; N, 6.16 Found: C, 52.75; H, 5.71; N, 6.25
14	75	78.0-78.7	-36.6 (1.4, 22)	13.3	---	---	$C_{13}H_{19}NO_7$ (301.30)	Calcd: C, 51.82; H, 6.36; N, 4.65 Found: C, 51.80; H, 6.37; N, 4.68

a, bp 120 °C (10^{-2} mm Hg)

15', whereas **11** led exclusively to the addition compound **20'**. Heating of **20'** with triethylamine promoted an elimination to **20** (SCHEME 3).

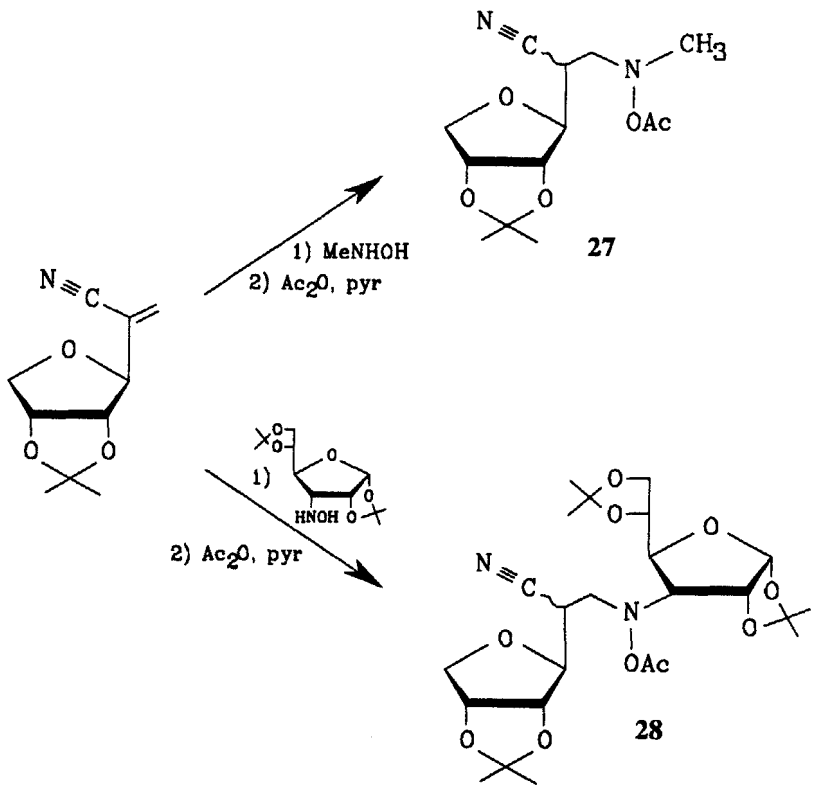
In the other cases, the elimination reaction was run immediately after the addition and the intermediate α-nitromethylnitrile not isolated except in the reaction with **9** where, besides **16** (74%), a small amount of the intermediate **16'** (6.6%) was isolated.

The first examples of 1-cyanovinylic sugars of type **IV**, have been described by Paulsen[15] some time ago, but their physicochemical mainly conformational properties, which should play an important role in their interesting biological activity, were not known. In this instance, the NMR spectroscopy is not of much help as the only usable coupling constants, the allylic $J_{\alpha,\gamma}$, are restricted to a small range of absolute values[16] (0-3 Hz). The observed values were small (sum of the two $J_{\alpha,\gamma} < 1$ Hz) for **17**, **18** and **22**, intermediate (1-3 Hz) for **16**, **19**, **20** and **21**, large (> 3 Hz) for **15**. These data indicated a tendency to an increase of the $J_{\alpha,\gamma}$ value with the steric hindrance on the β side of the sugar with the notable exception of **16** for which small couplings were expected.

The molecules should populate two almost degenerate (from a NMR point of view) pairs of conformers : one ($J_{\alpha,\gamma} \sim 0$ Hz) in which either the C≡N or the C=C bond eclipses the C_γ-H bond, the other ($J_{\alpha,\gamma} \sim 2$ Hz) in which the C_γ-O bond is eclipsed by one of these two groups. The increase of the volume of the groups on the β side should direct the population toward the rotamers where the conjugated system eclipses the C_γ-O bond thus increasing $J_{\alpha,\gamma}$. A partial confirmation of these proposals were found in the X-ray diffraction data[17] of **19**, compound of intermediate $J_{\alpha,\gamma}$ values, which indicated a O-C_γ-C_β-C_α dihedral angle ($\Phi_{\beta,\gamma}$) of 12.6°. Since the more important factors thought to be operative here, were of steric or electrostatic origin, the problem was submitted to a molecular mechanics analysis using CHARMm[18] and QUANTA.[19]

The energy minimization of **15**, led to the expected conformation with a $\Phi_{\beta,\gamma}$ value of 6.9°. About the same conformation ($\Phi_{\beta,\gamma}$ 8.6°) was found for **22**. This discrepancy with experimental results, not very significant given the small differences in energy at stake, could be due to an overweighting in this case, of the electrostatic potential term. It is probable that the level of steric compression of the transition state of the reactions of these compounds with biological nucleophiles is still more relevant to their chemotherapeutic activity.

The synthesis of a novel type of 1-cyanovinylic sugars, bearing a hydroxy group at the γ position (**24** and **25**), has been conducted by reacting an aldehydo sugar with propenenitrile in the presence of a base. A carbonyl analog (**26**), bearing an acetyl group instead of a cyano has been prepared by substituting butenone to acrylonitrile in the preceding reaction. In these reactions, only the major isomer, of unknown configuration, has been isolated in moderate yield.



SCHEME 4

The major interest of all these compounds is their reactivity toward soft nucleophiles. This most probably constitutes the reason of the high, often selective, toxicity of this group of substances.

Excellent models of nucleophiles acting mostly on electrophilic sp^2 carbons, are the hydroxylamines whose selective nucleophilicity is generally attributed to the α-effect.[20]

For example, treated with *N*-methylhydroxylamine, then acetylated, **16** gave a 14:1 mixture of two isomers (SCHEME 4) whose NMR spectra were very similar. The most significative differences were the $J_{2,3}$ couplings (8 Hz for the major isomer, 4 Hz for the minor), and the appearance of the H-2-H_2C-N system (A_2M with two equal couplings of 6.5 Hz for the major isomer, AMX system with coupling of 6.5 and 8 Hz for the minor isomer).

A careful examination of molecular models showed that the *2R* configuration (D-*altro*) was the more in accordance with an antiperiplanar conformation, the CH_2-N(OAc)Me chain extending away from the rest of the molecule, so allowing two isoenergetic rapidly

exchanging conformations around the C-2-CH_2 bond. On this basis, the D-*altro* configuration was provisionally assigned to the major isomer. An exploration of the conformational hyperspace generated by 10° increments rotations around both concerned bonds (C_2-C_3 and C_2-CH_2) using CHARMm and QUANTA[19] was undertaken. It showed for the (*2R*) isomer, two almost isoenergetic conformations about the C-2-C-3 bond (H-2-H-3 dihedral angles 180° (67.45 kcal/mol) and -80° (67.17 kcal/mol)) whereas for the (*2S*) isomer the synclinal conformation was found 0.75 kcal/mol more stable than the antiperiplanar one, thus confirming the attribution, as far as this kind of treatment does not neglect too significant factors.

The reaction could be used to prepare disaccharides analogs as **28**.

EXPERIMENTAL

General Procedures. See ref. 21. A Jasco model *J*-20 spectropolarimeter has been used for the circular dichroism measurements and a Silicon Graphics IRIS 4D/50 GT workstation, for the molecular modelling experiments.

Chain-extension using nitromethane. To a solution of the starting aldehydosugar (27 mmol) in methanol (150 mL), nitromethane (4.9 g, 80.3 mmol) and sodium methoxide (4.34 g, 80.3 mmol) were added. After 3 h at 0 °C, the solution was neutralized (Dowex 50 H^+), filtered, concentrated and purified by dry column chromatography (ether/hexane 4:1 or AcOEt/hexane 1:5 to 2:3). Solid nitrosugars were recrystallized either from chloroform-hexane or ether-hexane.

Preparation of the nitroenoses III. To a solution of 20 mmol of one of the nitro derivatives **II** in acetic anhydride (50 mL), sodium acetate (10 g, 122 mmol) was added at 0 °C. After 24 h at room temperature, the reaction mixture was evacuated under vacuum, extracted with ether and the ether extracts concentrated, purified by dry column chromatography (ether/hexane 1:3, or AcOEt/hexane 1:15 to 1:3).

6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-*C*-methylidene-α-D-*galacto*-heptopyranurononitrile (15). To a solution of potassium cyanide (4.2 g, 64.5 mmol) and tetrabutylammonium bromide (130 mg, 0.4 mmol) in water (27 mL), brought at pH 7-7.5 (HCl 10%), a solution of **8** (603 mg, 2 mmol) in a mixture of THF (27 mL) and toluene (56 mL) was added. After 3 d at room temperature under stirring, the organic phases were dried (Na_2SO_4), concentrated and separated by dry column chromatography (AcOEt/hexane 1:5) to give 390 mg (59%) of **15'**, 140 mg of a mixture **15** and **15'** and 60 mg of **15** (total yield *ca* 93%): mp 94.3-94.6 °C; R_F: 0.53 (AcOEt/hexane 1:2); $[\alpha]_D^{23}$ -93.6° (c 0.8, $CHCl_3$); UV (EtOH) 204 (6670). IR (KBr) 3118 (ν=CH), 2986, 2937, 2909 (ν-CH), 2228 (νC ≡N), 1623 (νC=C), 1388, 1379 (δCMe_2), 1255, 1216, 1176, 1069, 1003. ^{1}H NMR (C_6D_6) 1.01, 1.12, 1.30, 1.46 (*4s*, 4x3H, 2CMe_2), 4.10 (*dd*, 1H, $J_{1,2}$ 5 Hz, $J_{2,3}$ 2.2 Hz, H-C_2), 4.17 (*dd*, 1H, $J_{3,4}$ 7.7 Hz, $J_{4,5}$ 2 Hz, H-C_4), 4.41 (*dd*, 1H, H-C_3), 4.47 (*q*, 1H, $J_{5,6'a} = J_{5,6'b}$ 1.8 Hz, H-C_5), 5.47 (*d*, 1H, H-C_1), 5.60 (*d*, 1H, Ha-C_6), 5.80 (*d*, 1H, Hb-C_6). MS: *m/z* 59 (86), 65 (14), 71 (45), 85 (67), 92 (14), 100 (60), 113 (100), 120 (63), 136 (9), 142 (18), 166 (4), 178 (1), 194 (2), 208 (16), 224 (0.5), 266 (22), 281 (0.5, $M^{+\cdot}$).

Anal. calcd for $C_{14}H_{19}NO_5$ (281.31): C, 59.78; H, 6.81; N, 4.98. Found: C, 59.76; H, 6.83; N, 4.98.

6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-*C*-nitromethyl-α-D-*glycero*-D-*galacto*- (or β-L-*glycero*-D-*galacto*)-heptopyranurononitrile (15'). Obtained as described for the preparation of **15** : mp 153.5-154.0 °C; R_F: 0.47 (AcOEt/hexane 1:2); $[\alpha]_D^{27}$ -62.5° (c 0.9, $CHCl_3$) UV (EtOH) 205 (3570); IR (KBr) 2996, 2937, 2924 (ν-CH), 2256 (νC≡N), 1563 or 1543 ($\nu_{as}NO_2$), 1386, 1376 (δCMe_2 and ν_sNO_2), 1258, 1214, 1064, 1045, 1008. ^{1}H NMR 1.33, 1.40, 1.48, 1.53 (*4s*, 4x3H, 2CMe_2), 3.68 (*ddd*, 1H, $J_{5,6}$ 10.5 Hz, $J_{6,6'a}$ 6 Hz, $J_{6,6'b}$ 4.8 Hz, H-C_6), 4.09 (*dd*, 1H, $J_{4,5}$ 1.5 Hz, H-C_5), 4.38 (*dd*, 1H, $J_{1,2}$ 5 Hz, $J_{2,3}$ 2.8 Hz, H-C_2), 4.45 (*dd*, 1H, $J_{3,4}$ 7.3 Hz, H-C_4), 4.70 (*dd*, 1H, $J_{6'a,6'b}$ 15.5 Hz, Ha-$C_{6'}$), 4.71 (*dd*, 1H, H-C_3), 4.78 (*dd*, 1H, Hb-C_7), 5.49 (*d*, 1H, H-C_1). MS: *m/z* 59 (100), 71 (31), 85 (39), 100 (37), 106 (14), 113 (26), 120 (41), 149 (18), 159 (2), 184 (2), 210 (3), 225 (2), 239 (1), 255 (4), 267 (1), 280 (1), 297 (1), 313 (10, $M^{+\cdot}$ - CH_3^+).

Anal. calcd for $C_{14}H_{20}N_2O_7$ (328.32): C, 51.22; H, 6.14; N, 8.53. Found: C, 51.31; H, 6.11; N, 8.51.

3,6-Anhydro-3,4,5,6-tetrahydroxy-4,5-*O*-isopropylidene-2-methylidene-D-*ribo*-hexanenitrile (16). To a solution of potassium cyanide (6.192 g, 95.1 mmol) and tetrabutylammonium bromide (540 mg, 1.68 mmol) in water (100 mL), brought at pH 7-7.5 (HCl 10%), a solution of **9** (1.62 g, 7.53 mmol) in toluene (400 mL) was added. After 22 h under stirring at room temperature, the organic phase and the $CHCl_3$ washings (3x100 mL) of the aqueous phase were collected, dried (Na_2SO_4), concentrated to 1/3 of their initial volume, and heated for 2 h at 50 °C with triethylamine (4 mL, 28.7 mmol). Evaporation of the solvent and dry column chromatography (ether/hexane 1:5) gave **16'** (120 mg 6.6%) and **16** (1.09 g, 74%), whose short-path distillation (110 °C, 9.10 mm Hg) gave crystals: mp 77.3-77.4 °C; R_F: 0.65 (ether/hexane 1:5); $[\alpha]_D^{25}$ -67.8° (c 1.1, $CHCl_3$), UV (EtOH) 205 (7760); IR (KBr) 3114, 3042 (ν=CH), 3002, 2992, 2953, 2940, 2883, 2855 (ν-CH), 2228 (νC≡N), 1623 (νC=C), 1387, 1379 (δCMe_2), 1276, 1209, 1161, 1104, 1090, 1058. ^{1}H NMR 1.31, 1.51 (*2s*, 2x3H, CMe_2), 3.92 (*dd*, 1H, $J_{6a,6b}$ 11 Hz, $J_{5,6a}$ 3 Hz, Ha-C_6), 4.06 (*dd*, 1H, $J_{5,6b}$ 1.5 Hz, Hb-C_6), 4.58 (*m*, 1H, $J_{3,4}$ ~ 1.7 Hz, $J_{2'a,3}$ 2 Hz, $J_{2'b,3}$ 2 Hz, H-C_3), 4.83 (*m*, 2H, $J_{4,5}$ ~ 6.3 Hz, H-C_5, H-C_4), 6.02 (*d*, 1H, Ha-$C_{2'}$), 6.05 (*d*, 1H, Hb-$C_{2'}$). MS: *m/z* 59 (92), 69 (72), 81 (36), 92 (17), 111 (9), 120 (56), 137 (10), 149 (8), 180 (100, $M^{+\cdot}$ - CH_3^+).

Anal. calcd for $C_{10}H_{13}NO_3$ (195.22): C, 61.53; H, 6.71; N, 7.17. Found: C, 61.49; H, 6.79; N, 7.24.

3,6-Anhydro-2-deoxy-3,4,5,6-tetrahydroxy-4,5-*O*-isopropylidene-2-nitromethyl-D-*altro* (or D-*allo*)-hexanenitrile (16'). Obtained as described for the preparation of **16**: mp 105.0-106.0°C; R_F: 0.4 (ether/hexane 1:5); $[\alpha]_D^{25}$ -42.6° (c 0.9, $CHCl_3$); UV (EtOH) 206 (5800); IR (KBr) 3048, 2978, 2934 (ν-CH), 2247 (νC≡N), 1562 ($\nu_{as}NO_2$), 1389, 1379 (δCMe_2), 1379 (ν_sNO_2), 870 (νC-N), 1271, 1228, 1213, 1110, 1090, 1058. ^{1}H NMR 1.38, 1.52 (*2s*, 2x3H, CMe_2), 3.50 (*ddd*, 1H, $J_{2'a,2}$ 7 Hz, $J_{2'b,2}$ 6.5 Hz, $J_{2,3}$ 9.5 Hz, H-C_2), 3.90 (*dd*, 1H, $J_{6a,6b}$ 11.5 Hz, $J_{5,6a}$ 4.2 Hz, Ha-C_6), 4.09 (*dd*, 1H, $J_{5,6b}$ 1.2 Hz, Hb-C_6), 4.19 (*dd*, 1H, $J_{3,4}$ 2 Hz, H-C_3), 4,69 (*m*, 2H, $J_{2'a,2'b}$ ~ 15 Hz, H_2-$C_{2'}$); 4.80 (*dd*, 1H, $J_{4,5}$ 6.3 Hz, H-C_4), 4.92 (*ddd*, 1H, H-C_5). MS: *m/z* 59 (49), 69 (28), 81 (14), 92 (7), 106 (42), 120 (54), 227 (100, $M^{+\cdot}$ - CH_3^+).

Anal. calcd for $C_{10}H_{14}N_2O_5$ (242.23): C, 49.59; H, 5.83; N, 11.56. Found: C, 49.46; H, 5.82; N, 11.44.

5-Deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-*C*-methylidene-α-D-*ribo*-hexofuranurononitrile (17). Prepared as described for **16** from *(E)*-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-6-*C*-nitro-α-D-*ribo*-hex-5-eno-1,4-furanose[5] (400 mg, 1.53 mmol), potassium cyanide (1.26 g, 19.3 mmol), tetrabutylammonium bromide (110 mg, 0.34 mmol), triethylamine (0.7 mL, 5 mmol), water (20 mL) and toluene (80 mL). Dry column chromatography (ether/hexane 1:1) afforded 255 mg (68%) of **17**: mp 89.9-90.4 °C; R_F: 0.25 (ether/hexane 1:1); $[\alpha]_D^{21}$ +80,3° (c 1.2, $CHCl_3$); UV (EtOH) 203 (8120); IR (KBr) 3120 (ν=CH), 2996, 2957, 2940, 2917 (ν-CH), 2840 (νOMe), 2226 (νC ≡ N), 1629 (νC=C), 1388, 1374 (δCMe_2), 1216, 1166, 1116,

1080, 1065, 1027. ^{1}H NMR 1.26, 1.48 (*2s*, 2x3H, CMe_2), 3.40 (*s*, 3H, OMe), 3.58 (*dd*, 1H, $J_{2,3}$ 4.2 Hz, $J_{3,4}$ 9 Hz, H-C_3), 4.33 (*broad d*, 1H, $J_{4,5'}$ ~ 0.5 Hz, H-C_4), 4.66 (*t*, 1H, $J_{1,2}$ 3.8 Hz, H-C_2), 5.73 (*d*, 1H, H-C_1), 6.02 (*broad s*, 2H, $H_2C_{5'}$). MS: *m/z* 51 (9), 59 (64), 68 (13), 77 (13), 85 (61), 94 (30), 109 (100), 136 (6), 149 (9), 178 (13), 210 (33, $M^{\cdot+}$ - CH_3^+).

Anal. calcd for $C_{11}H_{15}NO_4$ (225.25): C, 58.66; H, 6.71; N, 6.22. Found: C, 58.62; H, 6.78; N, 6.29.

3,4,5,6-Tetrahydroxy-3,4:5,6-di-*O*-isopropylidene-2-methylidene-D-*arabino*-hexanenitrile (18). Prepared as described for **16** (but allowing 48 h for the cyanidation step), from *(E)*-3,4:5,6-di-*O*-isopropylidene-1-nitro-D-*arabino*-hex-1-en-3,4,5,6-tetrol[6] (273 mg, 10 mmol), potassium cyanide (7.5 g, 115.2 mmol), tetrabutylammonium bromide (640 mg, 1.99 mmol), triethylamine (2.5 mL, 17.9 mmol), water (125 mL), toluene (480 mL) and THF (150 mL). After dry column chromatography (AcOEt/hexane 1:9) and several short-path distillations (130 °C, 1 mmHg), 650 mg (26%) of **18** were obtained: mp 36.5-39.1 °C; R_F: 0.4 (AcOEt/hexane 1:3); $[\alpha]_D^{21}$ -22.7° (c 1.8, $CHCl_3$); UV (EtOH) 203 (6430); IR (KBr) 3114 (ν=CH), 2990, 2927 (νCH), 2229 (νC≡N), 1667 (νC=C), 1383, 1373 (δCMe_2), 1245, 1218, 1154, 1075. ^{1}H NMR 1.32, 1.39, 1.42, 1.48 (*4s*, 4x3H, $2CMe_2$), 3.95-4.13 (*m*, 4H, H-C_4, H-C5, H_2C_6), 4.45 (*d*, 1H, $J_{3,4}$ 7.5 Hz, H-C_3), 6.06 (*d*, 1H, $J_{2'a,3}$ < 0.5 Hz, Ha-$C_{2'}$), 6.13 (*d*, 1H, $J_{2'b,3}$ 0.5 Hz, Hb-$C_{2'}$). MS: *m/z* 49 (100), 57 (22), 71 (11), 84 (7), 101 (33), 123 (9), 152 (2), 165 (0.5), 180 (4), 238 (7, $M^{\cdot+}$ - CH_3^+).

Anal. calcd for $C_{13}H_{19}NO_4$ (253.30): C, 61.64; H, 7.56; N, 5.53. Found: C, 61.54; H, 7.46; N, 5.51.

3-*O*-Acetyl-5-deoxy-5-*C*-methylidene-1,2-*O*-(trichloro-2,2,2-ethylidene)-α-D-*xylo*-hexofuranurononitrile (19). Prepared as described for **16** (but allowing 72 h for the cyanidation step) from **10** (770 mg, 2.12 mmol), potassium cyanide (4.521 g, 69.4 mmol), tetrabutylammonium bromide (140 g, 0.43 mmol), triethylamine (0.5 mL, 3.6 mmol), water (30 mL), toluene (60 mL) and THF (30 mL). After dry column chromatography (AcOEt/hexane 1:5) and recrystallization (ether/hexane), 530 mg (70%) of **19** were obtained: mp 119.1-120.7 °C; R_F: 0.4 (AcOEt/hexane 1:2); $[\alpha]_D^{24}$ +20.8° (c 1.1, $CHCl_3$); UV (EtOH) 204 (7750); IR (KBr) 3125, 3026 (ν=CH), 3009, 2975, 2915 (ν-CH), 2229 (νC≡N), 1756 (νC=O), 1626 (νC=C), 1373, 1220, 1163, 1110, 1093, 1050. ^{1}H NMR 2.14 (*s*, 3H, OAc), 4.81 (*d*,1H, $J_{1,2}$ 4 Hz, H-C_2), 5.22 (*broad d*, 1H, $J_{4,5'a} = J_{4,5'b}$ ~ 1 Hz, $J_{3,4}$ 3,5 Hz, H-C_4), 5.37 (*s*, 1H, $CHCCl_3$), 5.57 (*d*, 1H, H-C_3), 6.12 (*broad s*, 1H, Ha-$C_{5'}$), 6.16 (*broad s*, 1H, Hb-$C_{5'}$), 6.24 (*d*, 1H, H-C_1). MS: *m/z* 53 (16), 59 (25), 65 (14), 71 (100), 82 (39), 96 (11), 108 (88), 124 (46), 136 (41), 153 (32), 164 (14), 178 (7), 188 (14), 217 (64), 246 (34), 262 (43), 282 (9), 306 (16), 343 (13, $M^{\cdot+}$).

Anal. calcd for $C_{11}H_{10}Cl_3NO_5$ (342.57): C, 38.57; H, 2.94; Cl, 31.05; N, 4.09. Found: C, 38.58; H, 3.02; Cl, 31.11; N, 4.03.

Methyl-5-deoxy-2,3-*O*-isopropylidene-5-*C*-nitromethyl-β-D-*allo* (or α-L-*talo*)-hexofuranosidurononitrile (20'). A mixture of **11** (550 mg, 2.25 mmol), potassium cyanide (1.5 g, 23 mmol), tetrabutylammonium bromide (130 mg, 0.4 mmol), water (20 mL) and toluene (95 mL) was stirred overnight at room temperature. The organic phase and the washings (2x30 mL of chloroform) of the aqueous layer were collected, dried (Na_2SO_4), concentrated and purified by dry column chromatography (AcOEt/hexane 3:20) to give 415 mg (82%) of **20'**, whose analytical sample was obtained by short-path distillation (120 °C, 10^{-2} mm Hg): mp 66.4-67.1 °C; R_F: 0.2 (AcOEt/hexane 1:5); $[\alpha]_D^{21}$ -57,4° (c 1.4, $CHCl_3$); UV (EtOH) 205 (4240); IR (KBr) 2992, 2942 (ν-CH), 2842 (νOMe), 2250 (νC ≡ N), 1560 ($\nu_{as}NO_2$), 1377 (δCMe_2 and ν_sNO_2), 867 (νC-N), 1212, 1106, 1094, 1063. ^{1}H NMR 1.34, 1.48 (*2s*, 2x3H, CMe_2), 3.39 (*s*, 3H, OMe), 3.55 (*ddd*, 1H, $J_{5,5'a}$ 8.3 Hz, $J_{3,5'b}$ 4.5 Hz, $J_{4,5}$ 11 Hz, H-C_5), 4.32 (*broad d*, 1H, $J_{2,4}$ ~ 1 Hz, $J_{3,4}$ 0 Hz, H-C_4), 4.70 (*d*, 1H, $J_{2,3}$ 6 Hz,

H-C_3), 4.70 (*dd*, 1H, $J_{5'a,5'b}$ 15.3 Hz, Ha-$C_{5'}$), 4.79 (*dd*, 1H, Hb-$C_{5'}$), 4.93 (*broad d*, 1H, H-C_2), 5,02 (*s*, 1H, H-C_1). MS: *m/z* 54 (23), 59 (100), 71 (17), 80 (7), 85 (34), 93 (2), 108 (9), 122 (29), 136 (13), 143 (1), 150 (11), 157 (5), 166 (0,5), 173 (3), 183 (0,5), 197 (1), 225 (0,5), 241 (0,5), 257 (26, $M^{+\cdot}$ - CH_3^+).

Anal. calcd for $C_{11}H_{16}N_2O_6$ (272.26): C, 48.53; H, 5.92; N, 10.29. Found: C, 48.71; H, 5.90; N, 10.21.

Methyl-5-deoxy-2,3-*O*-isopropylidene-5-*C*-methylidene-α-D-*ribo*-hexofuranosidurononitrile (20). A solution of **20'** (365 mg, 1.34 mmol) and triethylamine (0.5 mL, 3.6 mmol) in toluene (50 mL) is kept at 50 °C for 2 h, concentrated and purified by dry column chromatography (AcOEt/hexane 1:10), then by short-path distillation (110 °C, 10^{-2} mm Hg) to give 220 mg (73%) of **20**: bp 110 °C (10^{-2} mm Hg); R_F: 0.35 (AcOEt/hexane 1:5); IR (KBr) 3113 (ν=CH), 2991,2941 (ν-CH), 2840 (νOMe), 2225 (νC≡N), 1653 (νC=C), 1384, 1375 (δCMe_2), 1213, 1111, 1093, 1040. ^{1}H NMR 1.33, 1.51 (*2s*, 2x3H, CMe_2), 3.43 (*s*, 3H, OMe), 4.44 (*d*, 1H, $J_{1,2}$ < 0.5 Hz, $J_{2,3}$ 6 Hz, H-C_2), 4.75 (*q*, 1H, $J_{3,4} = J_{4,5'a} = J_{4,5'b}$ 1.5 Hz, H-C_4), 4.89 (*dd*, 1H, H-C_3), 5.07 (*s*, 1H, H-C_1), 6.07 (*d*, 1H, Ha-$C_{5'}$), 6.10 (*d*, 1H, Hb-$C_{5'}$). MS: *m/z* 51 (17), 57 (98), 65 (14), 69 (51), 77 (28), 81 (25), 85 (32), 91 (23), 97 (25), 107 (25), 115 (16), 122 (16), 133 (9), 149 (74), 159 (19), 173 (39), 193 (100), 210 (19, $M^{+\cdot}$ - CH_3^+).

Anal. calcd for $C_{11}H_{15}NO_4$ (225.25): C, 58.66; H, 6.71; N, 6.22. Found: C, 58.75; H, 6.74; N, 6.27.

Methyl-5-deoxy-2,3-*O*-isopropylidene-5-*C*-methylidene-α-D-*lyxo*-hexofuranosidurononitrile (21). Prepared as described for **16** [but with a reduced time (5 h) and an increased pH (9-9.5) for the cyanidation step], from **12** (560 mg, 2.28 mmol), potassium cyanide (1.62 g, 24.9 mmol), tetrabutylammonium bromide (152 mg, 0.47 mmol), water (30 mL), toluene (60 mL), THF (30 mL) and triethylamine (0.5 mL, 3.6 mmol). Dry column chromatography (AcOEt/hexane 1:5) afforded 260 mg (51%) of **21**: mp 68.9-70.2 °C; R_F: 0.55 (AcOEt/hexane 1:2); $[\alpha]_D^{26}$ +14.7° (c 2.2, $CHCl_3$); UV (EtOH) 204 (5830); IR (KBr) 3127 (ν=CH), 2942, 2918, 2901 (ν-CH), 2838 (νOMe), 2229 (νC ≡N), 1625 (νC=C), 1378, 1213, 1204, 1161, 1112, 1100, 1085, 1032. ^{1}H NMR 1.29, 1.47 (*2s*, 2x3H, CMe_2), 3.34 (*s*, 3H, OMe), 4.52 (*broad d*, 1H, $J_{4,5'a}$ 1.5 Hz, $J_{4,5'b}$ 1.1 Hz, $J_{3,4}$ 4 Hz, H-C_4), 4.61 (*d*, 1H, $J_{2,3}$ 6 Hz, $J_{1,2}$ ~ 0 Hz, H-C_2), 4.82 (*dd*, 1H, H-C_3), 5.01 (*s*, 1H, H-C_1), 6.08 (*d*, 1H, Ha-$C_{5'}$), 6.13 (*d*, 1H, Hb-$C_{5'}$).

Anal. calcd for $C_{11}H_{15}NO_4$ (225.25): C, 58.66; H, 6.71; N, 6.22. Found: C, 58.70; H, 6.74; N, 6.14.

3,5-Dideoxy-1,2-*O*-isopropylidene-3,5-*C*,*C*-dimethylidene-α-D-*erythro*-hexofuranurononitrile (22). Prepared as described for **16**, from **13** (100 mg, 0.88 mmol), potassium cyanide (660 mg, 10.1 mmol), tetrabutylammonium bromide (57 mg, 0.18 mmol), water (11 mL), toluene (42 mL) and triethylamine (0.4 mL, 2.9 mmol). A dry column chromatography (AcOEt/hexane 1:4), followed by a short-path distillation (100 °C, 8.10^{-2} mm Hg), afforded 65 mg (36%) of **22**: bp 100 °C, 8.10^{-2} mm Hg; R_F: 0.4 (AcOEt/hexane 1:3); $[\alpha]_D^{22}$ +103.9° (c 0.4, $CHCl_3$); UV (EtOH) 204 (5810); IR (KBr) 3115, 3088 (ν=CH), 2990, 2938 (ν-CH), 2231 (νC ≡N), 1384, 1375 (δCMe_2), 1218, 1163, 1052, 1022. ^{1}H NMR 1.48, 1.63 (*2s*, 2x3H, CMe_2), 4.96 (*broad d*, 1H, $J_{1,2}$ 4 Hz, $J_{2,4}$ ~ $J_{2,3'a}$ 0.5-1 Hz, H-C_2), 5.21 (*m*, 2H, $J_{4,3'b}$ ~ 1 Hz, $J_{3'a,3'b}$ ~ 2 Hz, $J_{4,5'a}$ < 0.5 Hz, $J_{4,5'b}$ < 0.5 Hz, Ha-$C_{3'}$ and H-C_4), 5.60 (*broad s*, 1H, Hb-$C_{3'}$), 5.96 (*d*, 1H, H-C_1), 6.02 (*broad s*, 1H, Ha-$C_{5'}$), 6.12 (*broad s*, 1H, Hb-$C_{5'}$). MS: *m/z* 55 (100), 69 (61), 73 (45), 79 (20), 83 (37), 91 (20), 97 (27), 105 (12), 111 (18), 129 (18), 135 (9), 143 (11), 149 (18), 157 (7), 185 (9), 199 (95), 207 (43, $M^{+\cdot}$).

Anal. calcd for $C_{11}H_{13}NO_3$ (207.23): C, 63.76; H, 6.32; N, 6.76. Found: C, 63.68; H, 6.39; N, 6.65.

2-Deoxy-3,4:5,6-di-*O*-isopropylidene-2-*C*-methylidene-β-D-*arabino*-hept-3-ulopyrananonitrile (23). Prepared as described for **16** (but allowing 96 h for the cyanidation step), from **14** (904 mg, 3 mmol), potassium cyanide (4g, 61.4 mmol), tetrabutylammonium bromide (192 mg, 0.6 mmol), water (38 mL),

toluene (144 mL), THF (70 mL) and triethylamine (0.5 mL, 3.6 mmol). A dry column chromatography (AcOEt/hexane 1:10), afforded 430 mg (51%) of **23**: mp 75.0-76.9 °C; R_F: 0.6 (AcOEt/hexane 1:2); $[\alpha]_D^{21}$ -26.6° (c 1.05, $CHCl_3$); UV (EtOH) 208 (5370); IR (KBr) 3119 (ν=CH), 2991, 2944, 2891 (ν-CH), 2229 (νC≡N), 1387, 1376 (δCMe_2), 1255, 1208, 1184, 1166, 1112, 1073, 1041, 1001. ^{1}H NMR 1.32, 1.42, 1.48, 1.58 (*4s*, 4x3H, 2CMe_2), 3.90 (*dd*, 1H, $J_{7a,7b}$ 12 Hz, $J_{6,7a}$ 1 Hz, Ha-C_7), 3.98 (*dd*, 1H, $J_{6,7b}$ 2 Hz, Hb-C_7), 4.27 (*ddd*, 1H, $J_{5,6}$ 8.3 Hz, H-C_6), 4.40 (*d*, 1H, $J_{4,5}$ 2.5 Hz, H-C_4), 4.62 (*dd*, 1H, H-C_5), 6.20 (*d*, 1H, $J_{2'a,2'b}$ 0.5 Hz, Ha-$C_{2'}$), 6.48 (*d*, 1H, Hb-$C_{2'}$). MS: *m/z* 52 (87), 59 (100), 69 (85), 80 (94), 85 (79), 95 (11), 100 (21), 113 (20), 136 (39), 148 (68), 166 (24), 171 (3), 188 (0.5), 208 (44), 224 (0.5), 266 (73), 281 (0.5, $M^{\cdot+}$).

Anal. calcd for $C_{14}H_{19}NO_5$ (281.31): C, 59.78; H, 6.81; N, 4.98. Found: C, 59.70; H, 6.83; N, 5.00.

4,5:6,7-Di-*O*-isopropylidene-2-*C*-methylidene-2-β-D-*gluco* (or β-D-*manno*)-oct-4-ulo-4,8-pyranononitrile (24). A mixture of 2,3:4,5-di-*O*-isopropylidene-aldehydo-β-D-*arabino*-hex-4-ulo-2,6-pyranose[8] (1.55 g, 6 mmol), 1,4-diazabicyclo[2,2,2]octane (74 mg, 0.66 mmol) and acrylonitrile (430 mg, 8.11 mmol), was stirred 20 h at room temperature, then extracted with ether (50 mL). The ether extract washed (HCl 1N, then aq satd $NaHCO_3$, then water), dried (Na_2SO_4), filtered and concentrated, afforded, after dry column chromatography (AcOEt/hexane 1:3) and crystallization (ether/hexane), 1.07 g (57%) of the major isomer of **24**: mp 113.5-115.0 °C; R_F: 0.35 (AcOEt/hexane 1:2); $[\alpha]_D^{24}$ -6.4° (c 0.9, $CHCl_3$); UV (EtOH) 205 (7250); IR (KBr) 3512, 3412 (νOH), 3118 (ν=CH), 2992, 2941, 2903 (ν-CH), 2223 (νC≡N), 1635 (νC=C), 1390, 1374 (δCMe_2), 1252, 1215, 1169, 1104, 1072, 1001. ^{1}H NMR 1.36, 1.48, 1.52, 1.58 (*4s*, 4x3H, 2CMe_2), 2.93 (*d*, 1H, $J_{3,OH}$ 8 Hz, C_3-OH exchangeable), 3.82 (*broad d*, 1H, $J_{7,8a}$ ~ 1 Hz, $J_{8a,8b}$ 13 Hz, Ha-C_8), 3.94 (*dd*, 1H, $J_{7,8b}$ 2 Hz, Hb-C_8), 4.28 (*broad dd*, 1H $J_{6,7}$ 8 Hz, H-C_7), 4.41 (*broad d*, 1H, $J_{2'a,3}$ 1 Hz, $J_{2'b,3}$ 0.5 Hz, H-C_3), 4,53 (*d*, 1H, $J_{5,6}$ 2.5 Hz, H-C_5), 4,68 (*dd*, 1H, H-C_6), 6.10 (*broad s*, 1H, Ha-$C_{2'}$), 6.16 (*broad s*, 1H, Hb-$C_{2'}$). MS: *m/z* 59 (100), 85 (61), 97 (10), 113 (33), 150 (9), 171 (95), 229 (40), 296 (92, $M^{\cdot+}$ - CH_3^+).

Anal. calcd for $C_{15}H_{21}NO_6$ (311.34): C, 57.87; H, 6.80; N, 4.50. Found: C, 57.84; H, 6.76; N, 4.58.

6-Deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-6-*C*-methylidene-α-D-*gluco* (or β-L-*ido*)-hepto-1,4-furanurononitrile (25). Prepared as described for **24** from 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdo-1,4-furanose[11] (1.212 g, 6 mmol), 1,4-diazabicyclo[2,2,2]octane (74 mg, 0.66 mmol) and acrylonitrile (330 mg, 6.2 mmol), yield 560 mg (37%) of the major isomer: bp 120 °C (10^{-2} mm Hg); R_F: 0.15 (AcOEt/hexane 1:2); $[\alpha]_D^{22}$ -44.8° (c 2.7, $CHCl_3$); UV (EtOH) 205 (4560); IR (KBr) 3460 (νOH), 3110 (ν=CH), 2990, 2938 (ν-CH), 2836 (νOMe), 2227 (νC ≡N), 1623 (νC=C), 1384, 1376 (δCMe_2), 1218, 1165, 1117, 1079, 1024. ^{1}H NMR 1.36, 1.51 (*2s*, 2x3H, CMe_2), 3.46 (*s*, 3H, OMe), 3.60 (*broad s*, 1H, C_5-OH exchangeable), 3.98 (*d*, 1H, $J_{3,4}$ 3.5 Hz, H-C_3), 4.28 (*dd*, 1H, $J_{4,5}$ 5.5 Hz, H-C_4), 4.62 (*m*, 2H, H-C_2, H-C_5), 5.98 (*d*, 1H, $J_{1,2}$ 4 Hz, H-C_1), 6.12 (*broad s*, 2H, H_2-$C_{6'}$). MS: *m/z* 59 (73), 71 (27), 81 (10), 87 (100), 97 (4), 107 (14), 122 (1), 127 (5), 132 (0.5), 139 (3), 149 (8), 155 (0.5), 167 (2), 173 (26), 181 (0.5), 191 (0.5), 202 (0.5), 215 (0.5), 231 (0.5), 240 (4, $M^{\cdot+}$ - CH_3^+).

Anal. calcd for $C_{12}H_{17}NO_5$ (255.27): C, 56.46; H, 6.71; N, 5.49. Found: C, 56.39; H, 6.71; N, 5.42.

6,8-Deoxy-1,2-*O*-isopropylidene-3-*O*-méthyl-6-*C*-methylidene-α-D-*gluco*- (or β-L-*ido*)-octo-1,4-furanos-7-ulose (26). Prepared and purified as described for **24**, from 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdo-1,4-furanose[11] (706 mg, 3.5 mmol), 1,4-diazabicyclo[2,2,2]hexane (37 mg, 0.33 mmol) and but-3-en-2-one (252 mg, 0.33 mmol), yield 470 mg (45%) of the major isomer: mp 111.2-113.3 °C; R_F: 0.4 (AcOEt/hexane 1:1); $[\alpha]_D^{22}$ -66.2° (c 1.3, $CHCl_3$); UV (EtOH) 215 (6800); IR (KBr) 3478 (νOH), 3116

(ν=CH), 2991, 2923, 2892 (ν-CH), 2830 (νOMe), 1665 (νC=O), 1641 (νC=C), 1386, 1375 (δCMe$_2$), 1220, 1117, 1081, 1023. ^{1}H NMR 1,31, 1.47 (*2s*, 2x3H, CMe$_2$), 2.41 (*s*, 3H, H$_3$C$_8$), 3.48 (*s*, 3H, OMe), 3.73 (*d*, 1H, $J_{5,OH}$ 9 Hz, C$_5$-OH exchangeable), 3.82 (*d*, 1H, $J_{3,4}$ 3 Hz, H-C$_3$), 4.32 (*dd*, 1H, $J_{4,5}$ 8 Hz, H-C$_4$), 4.58 (*d*, 1H, $J_{1,2}$ 4 Hz, H-C$_2$), 4.72 (*broad t*, $J_{5,6'a}$ 1 Hz, H-C$_5$), 5.90 (*d*, 1H, H-C$_1$), 6.16 (*d*, 1H, Ha-C$_{6'}$), 6.24 (*s*, 1H, Hb-C$_{6'}$). MS: *m/z* 59 (40), 73 (6), 87 (100), 99 (16), 115 (20), 155 (8), 173 (72), 211 (8), 257 (20), 273 (2, M^{+}).

Anal. calcd for $C_{13}H_{20}O_6$ (272.30): C, 57.34; H, 7.40. Found: C, 57.22; H, 7.39.

2-(*N*-Acetoxy-*N*-methylaminomethyl)-3,6-anhydro-4,5-*O*-isopropylidene-3,4,5,6-tetrahydroxy-D-*altro* (and D-*allo*)-hexanenitrile (27). A solution of **16** (710 mg, 3.64 mmol), *N*-methylhydroxylamine hydrochloride (510 mg, 6.19 mmol) and triethylamine (1 mL, 7.2 mmol) in THF (20 mL), was kept 72 h at room temperature, filtered and concentrated. The residue was treated for 20 h at room temperature with pyridine (50 mL) and acetic anhydride (20 mL), and the reaction mixture coevaporated with toluene, then purified by dry column chromatography (ether/hexane 3:1) followed by short-path distillation (160 °C, 5.10^{-4} mm Hg), gave 710 mg (69%) of the D-*altro* (*2R*) isomer, while 50 mg (5%) of the D-*allo* isomer were obtained from the faster-moving fractions of the column chromatography. D-*altro isomer*: bp 160 °C (5.10^{-4} mm Hg); R$_F$: 0.18 (ether/hexane 3:1); UV (EtOH) 204 (1110), 270 (125); IR (KBr) 2988, 2939, 2885 (n-CH), 2243 (νC ≡ N), 1761 (νC=O), 1383, 1372 (δCMe$_2$), 1226, 1189, 1091, 1054. ^{1}H NMR 1.33, 1.50 (*2s*, 2x3H, CMe$_2$), 2.08 (*s*, 3H, Ac), 2.80 (*s*, 3H, NMe), 2.92 (*dt*, 1H, $J_{2,2'}$ 6.5 Hz, $J_{2,3}$ 8 Hz, H-C$_2$), 3.15 (*d*, 2H, H$_2$-C$_{2'}$), 3.95 (*dd*, 1H, $J_{6a,6b}$ 11 Hz, $J_{5,6a}$ 4 Hz, Ha-C$_6$), 4.00 (*dd*, 1H, $J_{5,6b}$ 2 Hz, Hb-C$_6$), 4.16 (*dd*, 1H, $J_{3,4}$ 2 Hz, H-C$_3$), 4.78 (*dd*, 1H, $J_{4,5}$ 6 Hz, H-C$_4$), 4.88 (*ddd*, 1H, H-C$_5$). MS: *m/z* 60 (100), 102 (11), 150 (7), 167 (57), 184 (46), 209 (21), 227 (57), 242 (50), 269 (44), 284 (6, M^{+}). D-*allo isomer*: syrup; R$_F$: 0.22 (ether/hexane 3:1); IR (KBr) : 2989, 2938, 2881 (ν-CH), 2246 (νC≡N), 1761 (νC=O), 1383, 1373 (δCMe$_2$), 1224, 1190, 1096. ^{1}H NMR : 1.30, 1.48 (*2s*, 2x3H, CMe$_2$), 2,03 (*s*, 3H, Ac), 2.78 (*s*, 3H, NMe), 2.94 (*ddd*, 1H, $J_{2,2'a}$ 5.8 Hz, $J_{2,2'b}$ 8 Hz, $J_{2,3}$ 4 Hz, H-C$_2$), 3.08 (*dd*, 1H, $J_{2'a,2'b}$ 13.8 Hz, Ha-C$_{2'}$), 3.21 (*dd*, 1H, Hb-C$_{2'}$), 3.97 (*dd*, 1H, $J_{6a,6b}$ 10.5 Hz, $J_{5,6a}$ 2.2 Hz, Ha-C$_6$), 4.16 (*dd*, 1H, $J_{3,4}$ 2.7 Hz, H-C$_3$), 4.21 (*dd*, 1H, $J_{5,6b}$ 4.8 Hz, Hb-C$_6$), 4.71 (*dd*, 1H, $J_{4,5}$ 6.2 Hz, H-C$_4$), 4.92 (*ddd*, 1H, H-C$_5$).

Anal. calcd for $C_{13}H_{20}N_2O_5$ (284.31): C, 54.92; H, 7.09; N, 9.85. Found: C, 55.00; H, 7.17; N, 9.84.

2-(*N*-Acetoxy-3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-allofuranos-3'-ylaminomethyl)-3,6-anhydro-3,4,5,6-tetrahydroxy-4,5-*O*-isopropylidene-D-*altro* (and D-*allo*)-hexanenitrile (28). To a solution of **16** (195 mg, 1 mmol) in THF (5 mL), 3-deoxy-3-(*N*-hydroxyamino)-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (275 mg, 1 mmol) and triethylamine (0.2 mL, 1.4 mmol), were added. After 2 d refluxing, the reaction mixture, treated with Dowex 50 [H^{+}], filtered and concentrated was dissolved in a mixture of pyridine (10 mL) and acetic anhydride (5 mL), and left overnight at room temperature. A dry column chromatography (ether/hexane 2:1) afforded 240 mg (47%) of a mixture of the two isomers of **28**: mp 118.4-121 °C; R$_F$ 0.15 (ether/hexane 2:1); UV (EtOH) 200 (870), 270 (2142); IR (KBr) 2995, 2870 (ν-CH), 2230 (νC ≡ N), 1760 (νC=O), 1385, 1370 (δCMe$_2$), 1210, 1160, 1110, 1080, 1050. ^{1}H NMR : ^{1}H NMR : 2 stereoisomers *A* and *B* (*A*/*B* = 5/6). 1.29, 1.30, 1.32, 1.40, 1.48, 1.51 (*6s*, 2CMe$_2$, (*A* and *B*)), 2.02 (*s*, 3H, OAc *(B)*), 2.04 (*s*, 3H, OAc *(A)*), 2.90 (*dt*, $J_{2,HaHbCN}$ 5 Hz, $J_{2,HaHbCN} = J_{2,3}$ 7.7 Hz, H-C$_2$ *(B)*), 2.92 (*ddd*, $J_{2,HaHbCN}$ 7.2 Hz, $J_{2,HaHbCN}$ 5 Hz, $J_{2,3}$ 6 Hz, H-C$_2$ *(A)*), 3.27 (*dd*, $J_{2,3}$ 5 Hz, $J_{3,4}$ 8.8 Hz, H-C$_3$ *(A)*), 3.32 (*dd*, $J_{2,3}$ 5 Hz, $J_{3,4}$ 8.8 Hz, H-C$_3$ *(B)*), 3.42 (*dd*, $J_{HaHbCN,HaHbCN}$ 14 Hz, HaHbCN *(B)*), 3.50 (*dd*, $J_{HaHbCN,HaHbCN}$ 14 Hz, HaHbCN *(A)*), 3.58 (*ddd*, 1H, HaHbCN (*A* and *B*)), 3.88-4.25 (*m*, 7H, H-C$_{3'}$, H-C$_{4'}$, H-C$_{5'}$, H$_2$-C$_{6'}$, H$_2$-C$_6$, (*A* and *B*)), 4.70-4.77 (*m*, 2H, $J_{4,5}$ 6 Hz, H-C$_4$, H-C$_{2'}$ (*A* and *B*)), 4.84 (*ddd*, 1H, $J_{5,6a}$, 2.5 Hz, $J_{5,6b}$, 3.2 Hz,

H-C_5 *(B)*), 4.90 (*ddd*, 1H, $J_{5,6a}$ 2 Hz, $J_{5,6b}$ 4.5 Hz, H-C_5 *(A)*), 5.69 (*d*, 1H, $J_{1',2'}$ 4 Hz, H-$C_{1'}$ *(B)*), 5.71 (*d*, 1H, $J_{1',2'}$ 4 Hz, H-$C_{1'}$ *(A)*).

Anal. calcd for $C_{24}H_{36}N_2O_{10}$ (512.56): C, 56.24; H, 7.08; N, 5.47. Found: C, 56.24; H, 7.11; N, 5.40.

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