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Note

Synthesis and geometry of methyl (methyl 4-*O*-acetyl-3-azido-2,3-dideoxy-α/β-D-*arabino*- and -α/β-D-*ribo*-hexopyranosid)uronates

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Abstract—The synthesis of methyl (methyl 4-*O*-acetyl-3-azido-2,3-dideoxy-α/β-D-*arabino*- and -α/β-D-*ribo*-hexopyranosid)uronates is presented. High resolution ^{1}H and ^{13}C NMR spectral data for all diastereoisomers and single-crystal X-ray diffraction analysis for methyl (methyl 3-azido-2,3-dideoxy-β-D-*arabino*-hexopyranosid)uronate are reported. The planarity of the 4-OAc and 5-COOMe groups as well as the orientations of the aglycone and azide groups in the crystal lattice is discussed. The influence of the 5-COOMe group on the pyranose ring conformation is considered.

Keywords: Sugar amino acid; X-ray diffraction; Anomeric effect; Mesomeric effect; Hybridization; Conformational equilibrium

Sugar amino acids (SAAs) are sugar moieties bearing both an amino group and a carboxyl group on a carbohydrate framework.[1,2] Neuraminic acid, muraminic acid and glycosaminuronic acids are naturally occurring sugar amino acids, which are structural elements of oligosaccharides and glycoproteins.[3] Derivatives of glycosaminuronic acids can be found in certain antibiotics, for example, cancomycins, ezomycin A and gougerotin.[3] Synthetic SAAs have been used extensively in mimetic studies of peptides,[4] oligosaccharides,[5,6] oligonucleotides[7,8] and cyclodextrins.[1,9] Mixed oligomers of furanoid SAAs and amino acids, especially in the cyclic form, have been extensively studied because of their biological activity.[10,11] SAAs are also very useful as polyfunctional scaffolds, where the carboxyl, amino and hydroxyl termini allow structural diversities akin to biologically active molecules to be created.[2,3] The rigid pyranose ring system of a monosaccharide amino acid can be used as a molecular template to display pharmacophoric groups in a well-defined spatial orientation.[12] The synthesis of glycosaminuronic acids usually involves the selective oxidation of the primary hydroxyl group in the amino- or azido-sugar.[4,7,12–15]

Acetylated glycals treated with a 0.02 M equiv of mercuric sulfate in a solvent consisting of 5 mM sulfuric acid and 1,4-dioxane are converted into α,β-unsaturated aldehydes.[16] It has been reported that the conjugate addition of hydrazoic acid to α,β-unsaturated aldehydes derived from tri-*O*-acetyl-D-glucal,[17–19] tri-*O*-acetyl-D-galactal,[20] di-*O*-acetyl-L-rhamnal[21,22] and di-*O*-acetyl-L-arabinal[23] is a convenient method for the preparation of 3-azido-2,3-dideoxy hexopyranoses and pentofuranoses. Here, a simple and efficient synthesis of methyl (methyl 4-*O*-acetyl-3-azido-2,3-dideoxy-α/β-D-*arabino*- and -α/β-D-*ribo*-hexopyranosid)uronates—new precursors of sugar amino acids—is reported. This synthesis is based on the addition of hydrazoic acid to the α,β-unsaturated aldehyde derived from methyl 3,4-di-*O*-acetyl-2,6-anhydro-5-deoxy-D-*lyxo*-hex-5-enopyranonate (commercial name methyl 3,4-di-*O*-acetyl-D-glucuronal). Single-crystal X-ray diffraction data for methyl (methyl 4-*O*-acetyl-3-azido-2,3-dideoxy-β-D-*arabino*-hexopyranosid)uronate are also reported, and the conformation of the synthesized precursors of sugar amino acids is discussed. The application of sugar amino acids as polyfunctional scaffolds requires the pyranose ring to be rigid with a

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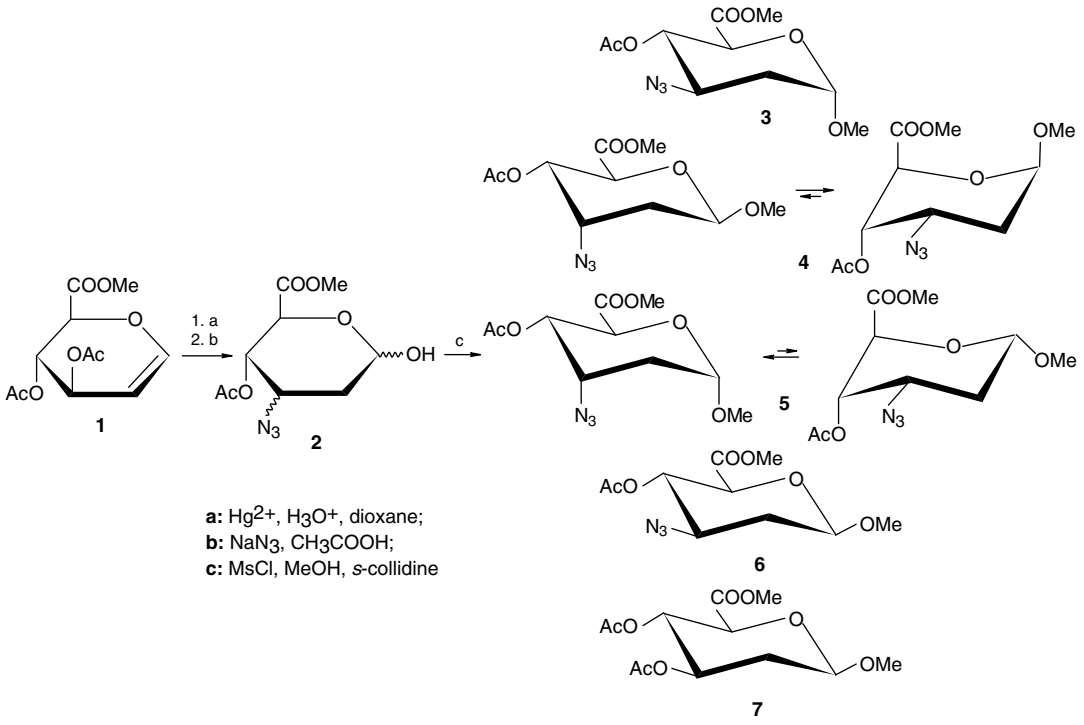
well-defined spatial orientation. Hence, discussion on the influence of the 5-methoxycarbonyl group on the pyranose ring conformation is important.



The addition of hydrazoic acid to the α,β-unsaturated aldehyde derived from methyl 3,4-di-*O*-acetyl-2,6-anhydro-5-deoxy-D-*lyxo*-hex-5-enopyranonate (**1**), followed by glycosylation of methanol, yielded a mixture of products that were separated and identified as methyl (methyl 4-*O*-acetyl-3-azido-2,3-dideoxy-α-D-*arabino*- (**3**), -β-D-*ribo*- (**4**), -α-D-*ribo*- (**5**), and -β-D-*arabino*-hexopyranosid)uronates (**6**) and methyl (methyl 3,4-di-*O*-acetyl-2-deoxy-β-D-*arabino*-hexopyranosid)uronate (**7**). Compound **7** is a by-product formed in the reaction mixture as a result of competitive acetic acid addition.

The NMR spectra of **3**–**7** (Tables 1–3) provide ample confirmation of their configurations and conformations in solution. Thus, the $J_{2a,3} = 12.70$ Hz, $J_{3,4} \sim J_{4,5} =$ 9.28 Hz or 9.77 Hz coupling constants indicate a D-*arabino* structure and a $^4C_1$ conformation of **3** and **6**. The $J_{1,2a} = 2.93$ Hz coupling constant is diagnostic for the α configuration of **3**, as is the $J_{1,2a} = 9.77$ Hz coupling constant for the β configuration of **6**. The β-D-*arabino* configuration of **7** is confirmed by the $J_{1,2a}$, $J_{2a,3}$, $J_{3,4}$

Table 1. Chemical shifts (ppm) in the ^{1}H NMR spectra of **3**–**7**

	H1	H2a	H2e	H3	H4	H5	OAc	OCH_3	$COOCH_3$
3	4.93 (d)	1.79 (td)	2.17 (m)	3.99 (ddd)	4.99 (t)	4.23 (d)	2.13 (s)	3.40 (s)	3.77 (s)
4	4.82 (dd)	1.94 (dt)	2.17 (m)	4.14 (dt)	5.38 (dd)	4.42 (d)	2.16 (s)	3.45 (s)	3.79 (s)
5	4.85 (t)	2.11 (m)		3.98 (q)	5.22 (dd)	4.66 (d)	2.14 (s)	3.48 (s)	3.80 (s)
6	4.51 (dd)	1.74 (td)	2.26 (ddd)	3.68 (ddd)	5.01 (t)	3.93 (d)	2.12 (s)	3.52 (s)	3.77 (s)
7	4.54 (dd)	1.79 (q)	2.35 (ddd)	5.07 (td)	5.13 (t)	3.97 (d)	2.05 (s)	3.52 (s)	3.77 (s)

Table 2. The ^{1}H–^{1}H coupling constants (Hz) for **3**–**7**

		$J_{1,2a}$	$J_{1,2e}$	$J_{2a,2e}$	$J_{2a,3}$	$J_{2e,3}$	$J_{3,4}$	$J_{4,5}$
3	α-D-*arabino*	2.93	n.d.	13.18	12.70	4.88	9.77	9.77
4	β-D-*ribo*	3.42	4.39	13.18	8.79	3.91	3.42	4.88
5	α-D-*ribo*	3.91		n.d.	4.89		3.42	7.81
6	β-D-*arabino*	9.77	1.95	13.18	12.70	4.88	9.77	9.28
7	β-D-*arabino*	9.76	1.95	12.70	10.74	4.88	9.28	9.28

n.d. not determined.

Table 3. Chemical shifts (ppm) in the ^{13}C NMR spectra of **3**–**6**

	C1	C2	C3	C4	C5	OCH_3	OAc		$COOCH_3$	
							CH_3	C=O	C=O	CH_3
3	98.06	34.71	57.23	71.56	69.37	55.68	20.88	168.80–170.21		53.09
4	99.81	32.25	53.65	69.28	71.93	57.18	21.03			52.66
5	97.77	32.16	55.54	69.46	68.44	56.53	20.87	169.31	170.06	52.92
6	101.04	35.65	59.43	71.50	73.93	57.30	20.87	167.95	169.88	53.06

and $J_{4,5} = 9$–10 Hz coupling constants. Worthy of notice is that $J_{2a,3} = 10.74$ Hz coupling constant in the case of **7** is significantly lower than $J_{2a,3} = 12$–13 Hz coupling constant in the case of **3**–**6**. Such a difference is probably due to the different electronegativity of substituents bound to the C3 carbon atom. The respective coupling constants of **4** and **5** confirm their D-*ribo* structure and simultaneously indicate the $^4C_1 \rightleftarrows {}^1C_4$ conformational equilibrium for these compounds. Thus, the $J_{4,5} = 7.81$, $J_{3,4} = 3.42$ and $J_{2a,3} = 4.89$ Hz coupling constants are diagnostic for the D-*ribo* configuration of **5** with the conformational equilibrium shifted in the $^4C_1$ direction. The $J_{1,2a}$ coupling constant of 3.91 Hz confirms these assignments and indicates an α configuration for glycoside **5**. This configuration of **5** is also reflected by the high positive optical rotation ($[\alpha]_D^{20}$ +133). Similarly, the $J_{4,5} = 4.88$, $J_{3,4} = 3.42$ and $J_{2a,3} = 8.79$ Hz coupling constants indicate the D-*ribo* configuration of **4** with the conformational equilibrium shifted a little in the $^1C_4$ direction. These assignments are in agreement with the $J_{1,2a}$ coupling constant 3.42 Hz, which is indicative rather of the equatorial orientation of the H1 proton and consequently of the β configuration of **4**. Glycosides **4** and **5** differ solely in their anomeric carbon atom configuration. The results thus show that the *endo*-anomeric effect definitely affects the conformational equilibrium of **4** and **5**.

The findings presented in this paper show that the $^4C_1$ conformation is preferably adopted by methyl (methyl 4-*O*-acetyl-3-azido-2,3-dideoxyhexopyranosid)uronates with a D-*arabino* configuration, whereas the same $^4C_1$ conformation is not stable enough for analogous compounds with the D-*ribo* configuration. These findings are surprising, because other methyl 4-*O*-acetyl-3-azido-2,3-dideoxyhexopyranosides with the D-*ribo* configuration, which we previously reported, adopted the $^4C_1$ conformation in solution.[20,24] This means that the 5-COOMe group, unlike the 5-CH_2X group (X = OH, OAc, OTs, I), influences the conformational preferences of the pyranose ring. What is the reason for this difference? Most probably, the planarity of the 5-$COOCH_3$ group makes it less bulky than the typical 5-CH_2X group. The different van der Waals radii of these groups mean that unfavourable 1,3-diaxial interactions in the case of the 5-$COOCH_3$ group are not as strong as in the case of the 5-CH_2X group. Hence, the equatorial orientation of the 5-$COOCH_3$ group is not so important for the stability of the $^4C_1$ conformation (D) as the equatorial orientation of the 5-CH_2X group is. We also noted this particular effect of the 5-$COOCH_3$ group on conformational stability in the case of methyl 3,4-di-*O*-acetyl-2,6-anhydro-5-deoxy-D-*lyxo*-hex-5-enopyranonate (3,4-di-*O*-acetyl-D-glucuronal).[25]

In the crystal, **6** adopts the $^4C_1$ chair conformation[26,27] (Fig. 1) with ring-puckering parameters[28,29] $Q = 0.575(3)$ Å, $\theta = 5.7(3)$ Å and $\varphi = 326(3)°$. This conformation is the same as the one adopted by **6** in chloroform solution. Although the anomeric effect does not take place in the $^4C_1$ form of **6**, such a conformation is optimal because of the equatorial orientation of the 3-N_3, 4-OAc and 5-COOMe groups.

Studies of the crystal structure of **6** lead to certain inferences. Crucial to any discussion of the geometry is the fact that the 4-OAc group is almost planar in the region of the C4, O12, C13, O14 and C15 atoms. This is demonstrated by the C4–O12–C13–C15 torsion angle of 174.9° as well as the C4–O12–C13–O14 torsion angle of 2.8° (Table 6). Such an extensive planarity of the OAc group is not restricted solely to the crystal structure. Our geometry optimizations for methyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-hex-5-enopyranosides at the B3LYP level of density functional theory show the same planarity for the C4-OAc group.[30] Neither is this restricted to the OAc group bound to the C4 carbon atom. Analysis of our previously reported structures, that is, *S*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(*Z*)-hydroxyimino-β-D-*lyxo*-hexopyranosyl]-thiophenol, methyl 2,5-di-*O*-acetyl-β-D-glucofuranosidurono-6,3-lactone, 1,2,5-tri-*O*-acetyl-β-D-gluco-

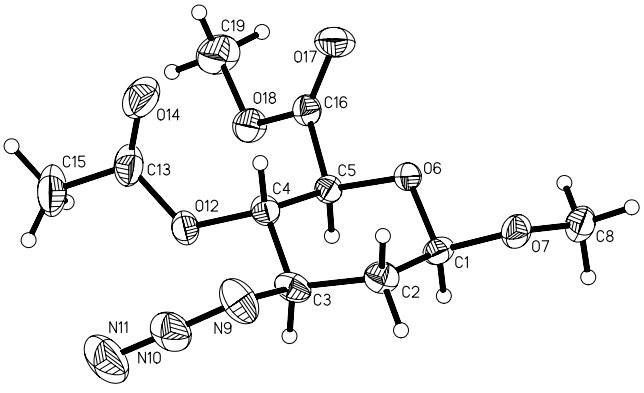


Figure 1. Structures of **6** showing 25% probability displacements for ellipsoids.

furanurono-6,3-lactone and methyl 3,4-di-*O*-acetyl-2,6-anhydro-5-deoxy-D-*lyxo*-hex-5-enopyranonate, deposited in the CCDC data base,[31] confirms that all OAc groups are planar starting from the carbon atom to which they are bound. This planarity is probably due to the mesomeric effect that causes the O12 oxygen lone pair of electrons to delocalize onto the O14 carbonyl oxygen atom. Such a delocalization stabilizes the compound and increases the O12–C13 rotational barrier. On the other hand, this mesomeric effect requires the O12 oxygen atom to be sp^2 hybridized. Indeed, the C4-O12-C13 valence angle of 117.5° (Table 6) is more suited to sp^2 than to sp^3 hybridization.

The 5-$COOCH_3$ group in the crystal state of **6** displays analogous planarity. In the case of the 5-methoxycarbonyl group, the C5, C16, O17, O18 and C19 atoms lie in almost the same plane (the C5–C16–O18–C19 torsion angle 176.1°, the O17–C16–O18–C19 torsion angle 2.4°; Table 6). This indicates that the O18 oxygen atom appears to be sp^2 hybridized, which is confirmed by the C16–O18–C19 valence angle of 117.0° (Table 6).

Comparison of the respective bond lengths in the crystal structure of **6** (Table 6) provides additional confirmation of this delocalization of the non-carbonyl oxygen lone pair of electrons onto the carbonyl oxygen. Hence, the measured C–O bond lengths in **6** can be divided into three categories. In the first, both carbon and oxygen atoms are sp^3 hybridized and the length of the C–O bond is 1.41–1.44 Å (O6–C1, O12–C4, C5–O6, C19–O18). In the second, both carbon and oxygen atoms are sp^2 hybridized and the length of the C–O bond is 1.20 Å (C16–O17, C13–O14). In the third category, the carbon atom is sp^2 hybridized and the hybridization of the oxygen atom is between sp^3 and sp^2. In this case the length of the C–O bond is 1.33–1.35 Å (O12–C13, O18–C16).

Another finding concerns the geometry of aglycone. The methyl group in the crystal structure of **6** is oriented almost antiperiplanarly to the C2 carbon atom (the C2–C1–O7–C8 torsion angle 166.2°). Such an orientation of the methyl group is typical of all the methyl glycosides that we have synthesized and crystallographically analyzed: methyl 3-azido-2,3-dideoxy-α-D-*lyxo*-hexopyranoside, methyl 3-azido-2,3-dideoxy-4,6-di-*O*-*p*-tolylsulfonyl-α-D-*lyxo*-hexopyranoside and methyl 2,5-di-*O*-acetyl-β-D-glucofuranosidurono-6,3-lactone (the respective C2–C1–O7–C8 torsion angles are equal to 169.9°,

Table 4. Crystal data and structure refinement for **6**

Empirical formula	$C_{10}H_{15}O_6N_3$
Formula weight	273.25
Temperature (K)	295(2)
Wavelength (Å)	0.71073
Crystal system	monoclinic
Space group	$P2_1$
Unit cell dimensions	
a (Å)	8.315(3)
b (Å)	8.383(2)
c (Å)	10.017(3)
β (°)	96.88(3)
V (Å^3)	693.2(4)
Z	2
D_{calcd} (Mg m^{-3})	1.309
Absorption coefficient (mm^{-1})	0.109
$F(000)$	288
Crystal size (mm)	$0.6 \times 0.4 \times 0.3$
θ Range for data collection (°)	2.05–25.02
Limiting indices	$-9 \leqslant h \leqslant 9$, $0 \leqslant k \leqslant 9$, $0 \leqslant l \leqslant 11$
Reflections collected/unique	1378/1302 [$R_{int} = 0.0109$]
Completeness $2\theta = 50.24°$ (%)	99.1
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	1302/1/176
Goodness-of-fit on F^2	1.026
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0336$
	$wR_2 = 0.0828$
R indices (all data)	$R_1 = 0.0591$
	$wR_2 = 0.0938$
Absolute structure parameter	−0.03(6)
Extinction coefficient	0.039(7)
Largest difference in peak and hole (e Å^{-3})	0.146 and −0.121

Table 5. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters (Å$^2 \times 10^3$) for **6**

Atom	x	y	z	U(eq)
C1	4789(3)	3699(3)	4322(2)	47(1)
C2	6560(3)	3915(4)	4239(3)	55(1)
C3	7546(3)	3278(4)	5485(3)	54(1)
C4	6953(3)	3954(3)	6726(3)	47(1)
C5	5137(3)	3667(3)	6691(2)	41(1)
O6	4350(2)	4405(2)	5520(2)	44(1)
O7	3921(2)	4483(3)	3262(2)	55(1)
C8	2262(4)	4064(4)	3058(3)	65(1)
N9	9239(3)	3746(5)	5415(3)	85(1)
N10	10252(4)	3002(4)	6131(4)	84(1)
N11	11307(4)	2425(6)	6735(5)	122(2)
O12	7795(2)	3148(2)	7864(2)	55(1)
C13	8212(4)	4014(5)	8983(3)	71(1)
O14	7965(4)	5415(4)	9049(3)	94(1)
C15	8938(5)	2988(6)	10107(4)	105(2)
C16	4462(3)	4397(4)	7864(3)	48(1)
O17	3813(3)	5671(3)	7879(2)	75(1)
O18	4717(3)	3443(3)	8926(2)	61(1)
C19	4227(5)	4023(6)	10168(3)	90(1)
H1A	4514	2562	4296	56
H2A	6793	5039	4139	66
H2B	6856	3359	3455	66
H3A	7466	2112	5499	65
H4A	7182	5100	6786	56
H5A	4915	2518	6663	49
H8A	1719	4697	2342	98
H8B	1782	4255	3868	98
H8C	2158	2955	2825	98
H15A	9277	3640	10877	158
H15B	9857	2434	9839	158
H15C	8149	2229	10330	158
H19A	4604	3305	10884	135
H19B	3067	4090	10088	135
H19C	4685	5061	10360	135

U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

Table 6. Selected bond lengths (Å), valence angles (°) and torsion angles (°) for **6**

Bond length (Å)	
C1–O7	1.378(3)
C1–O6	1.424(3)
C1–C2	1.495(4)
C2–C3	1.506(4)
C3–N9	1.471(4)
C3–C4	1.502(4)
C4–O12	1.433(3)
C4–C5	1.525(4)
C5–O6	1.415(3)
C5–C16	1.493(4)
O7–C8	1.415(4)
N9–N10	1.212(5)
N10–N11	1.115(5)
O12–C13	1.346(4)
C13–O14	1.196(5)
C13–C15	1.485(5)
C16–O17	1.198(4)
C16–O18	1.327(4)
O18–C19	1.439(4)
Valence angles (°)	
O7–C1–O6	106.7(2)
O7–C1–C2	109.1(2)
O6–C1–C2	110.5(2)
C1–C2–C3	110.7(2)
N9–C3–C4	110.5(3)
N9–C3–C2	107.2(2)
C4–C3–C2	110.6(2)
O12–C4–C3	107.7(2)
O12–C4–C5	109.3(2)
C3–C4–C5	110.1(2)
O6–C5–C16	107.0(2)
O6–C5–C4	107.9(2)
C16–C5–C4	112.5(2)
C5–O6–C1	112.1(2)
C1–O7–C8	113.9(2)
N10–N9–C3	115.8(3)
N11–N10–N9	172.2(4)
C13–O12–C4	117.5(2)
O14–C13–O12	123.1(3)
O14–C13–C15	125.7(4)
O12–C13–C15	111.1(4)
O17–C16–O18	123.8(3)
O17–C16–C5	126.0(3)
O18–C16–C5	110.1(3)
C16–O18–C19	117.0(3)
Torsion angles (°)	
O7–C1–C2–C3	171.9(2)
O6–C1–C2–C3	54.8(3)
C1–C2–C3–N9	−171.8(3)
C1–C2–C3–C4	−51.3(3)
N9–C3–C4–O12	−68.9(3)
C2–C3–C4–O12	172.6(2)
N9–C3–C4–C5	172.0(2)
C2–C3–C4–C5	53.5(3)
O12–C4–C5–O6	−177.0(2)
C3–C4–C5–O6	−58.9(3)
O12–C4–C5–C16	65.2(3)
C3–C4–C5–C16	−176.7(2)
C16–C5–O6–C1	−174.6(2)
C4–C5–O6–C1	64.1(3)
O7–C1–O6–C5	178.4(2)
C2–C1–O6–C5	−63.0(3)
O6–C1–O7–C8	−74.4(3)
C2–C1–O7–C8	166.2(2)
C4–C3–N9–N10	78.0(4)
C2–C3–N9–N10	−161.4(3)
C3–N9–N10–N11	−179.0(4)
C3–C4–O12–C13	143.0(3)
C5–C4–O12–C13	−97.3(3)
C4–O12–C13–O14	−2.8(5)
C4–O12–C13–C15	174.9(3)
O6–C5–C16–O17	−22.2(4)
C4–C5–C16–O17	96.2(3)
O6–C5–C16–O18	159.4(2)
C4–C5–C16–O18	−82.2(3)
O17–C16–O18–C19	−2.4(5)
C5–C16–O18–C19	176.1(3)
H1A–C1–C2–H2A	172.1
H1A–C1–C2–H2B	53.8
H2A–C2–C3–H3A	169.7
H2B–C2–C3–H3A	51.3
H3A–C3–C4–H4A	171.5
H4A–C4–C5–H5A	178.0

176.4° and 173.9°). Such a conformational preference of the methyl group probably results from the *exo*-anomeric effect, an important factor influencing the geometry of the glycosides.

The azide group is almost linear, which is demonstrated by the N11–N10–N9 valence angle of 172.2°. This linearity is caused by the sp hybridization of the N10 nitrogen atom and is also observed in other crystal structures of azidosugars.[32–34]

There are no hydrogen bonds in the crystal lattice of **6**.

1. Experimental

1.1. General methods

Melting points are uncorrected. IR spectra were recorded as Nujol mulls with a Bruker IFS 66 spectrophotometer; ^{1}H and ^{13}C NMR spectra ($CDCl_3$, internal Me_4Si) on a Unity Plus 500 (500/125 MHz) instrument; positive-ion mode MALDITOF mass spectra on a Bruker Biflex III spectrometer; elemental analyses on a Carlo Erba EA1108 instrument. Thin-layer chromatography (TLC) was performed on E. Merck Kieselgel 60 F-254 plates using eluent system A, 3:1 (v/v) CCl_4–acetone, and column chromatography on MN Kieselgel 60 (<0.08 mm) with eluent system B, 5:1 (v/v) petroleum ether–EtOAc.

1.2. Methyl 3,4-di-*O*-acetyl-2,6-anhydro-5-deoxy-D-*lyxo*-hex-5-enopyranonate (1)

This was synthesized as previously reported.[25]

1.3. Methyl (methyl 4-*O*-acetyl-3-azido-2,3-dideoxy-α-D-arabino- (3), -β-D-*ribo*- (4), -α-D-*ribo*- (5), and -β-D-*arabino*-hexopyranosid)uronates (6) and methyl (methyl 3,4-di-*O*-acetyl-2-deoxy-β-D-*arabino*-hexopyranosid)uronate (7)

A mixture of **1** (2.3 g, 0.009 mol), 1,4-dioxane (14 mL), 5 mM aq H_2SO_4 (50 mL) and $HgSO_4$ (115 mg, 0.39 mmol) was stirred at rt. Substrate **1** disappeared after 24 h (TLC, solvent A) and then CH_3COOH (15 mL) and NaN_3 (7.2 g, 0.11 M) were added. The reaction mixture was stirred for another 24 h until the new substrate (**2**) disappeared (TLC, solvent A), and then was diluted with water and extracted with chloroform. The organic solution was washed with satd aq $NaHCO_3$ and water, and dried over $MgSO_4$. Concentration under reduced pressure yielded the crude product (2.14 g), which was then dissolved in CH_2Cl_2 (35 mL). *s*-Collidine (6 mL) and methanesulfonyl chloride (2 mL) were added to this solution and the reaction mixture was stirred. After 10 min abs CH_3OH (6 mL) was added and stirring was continued for 24 h at rt. When the end of reaction was verified by TLC (solvent A), the reaction mixture was diluted with CH_2Cl_2, washed with 1 M aq HCl, then with satd aq $NaHCO_3$ and water, and dried over $MgSO_4$. Concentration under reduced pressure led to the crude product (2.19 g), which was purified by chromatography (solvent B) to yield first a mixture of **3** and **4** (0.678 g, 28%, syrup); $R_f = 0.51$ (solvent B); IR: *v* 2955, 2844 (C–H), 2105 (N_3), 1750 (ester C=O), 1372 (ester CH_3), 1226 (ester C–O) cm^{-1}; MALDITOF-MS: *m*/*z* 273.1 $[M]^+$, 296.1 $[M+Na]^+$. Anal. Calcd for $C_{10}H_{15}N_3O_6$: C, 43.96; H, 5.53; N, 15.38. Found: C, 44.16; H, 5.52; N, 15.30.

Eluted second was **5** (0.242 g, 10%, syrup); $[\alpha]_D^{20}$ +133 (*c* 1, $CHCl_3$); $R_f = 0.42$ (solvent B); IR: *v* 2956, 2847 (C–H), 2107 (N_3), 1750 (ester C=O), 1374 (ester CH_3), 1230 (ester C–O) cm^{-1}; MALDITOF-MS: *m*/*z* 273.1 $[M]^+$, 296.1 $[M+Na]^+$. Anal. Calcd for $C_{10}H_{15}N_3O_6$: C, 43.96; H, 5.53; N, 15.38. Found: C, 44.01; H, 5.52; N, 15.50.

Eluted third was **6** (0.945 g, 39%, mp 64–65 °C); $[\alpha]_D^{20}$ −32 (*c* 1, $CHCl_3$); $R_f = 0.33$ (solvent B); IR: *v* 2922, 2851 (C–H), 2101 (N_3), 1747 (ester C=O), 1372 (ester CH_3), 1256, 1221 (ester C–O) cm^{-1}; MALDITOF-MS: *m*/*z* 273.1 $[M]^+$, 296.1 $[M+Na]^+$. Anal. Calcd for $C_{10}H_{15}N_3O_6$: C, 43.96; H, 5.53; N, 15.38. Found: C, 44.17; H, 5.58; N, 15.29.

Eluted fourth was **7** (0.096 g, 4%, mp 121–123 °C); $R_f = 0.26$ (solvent B); IR: *v* 2923, 2852 (C–H), 1749 (ester C=O), 1371 (ester CH_3), 1241, 1222 (ester C–O) cm^{-1}.

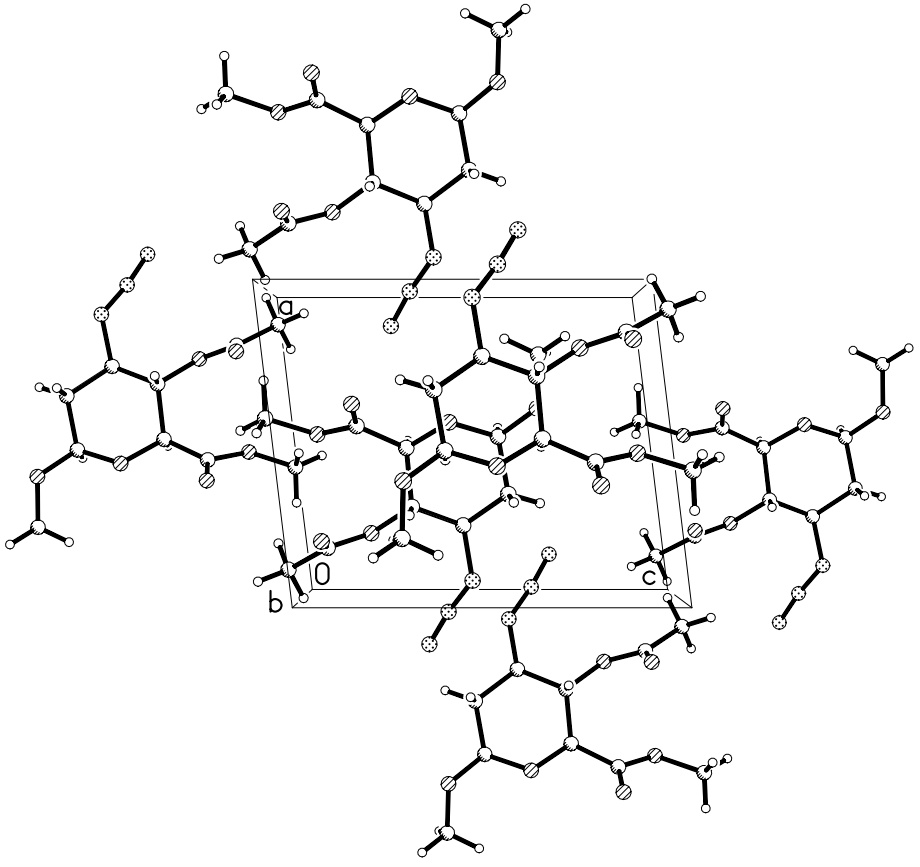


Figure 2. Molecular packing of **6** (view along *b*-axis).

1.4. Description of the crystal structure of 6

Diffraction data were collected at room temperature (295 K) on a KUMA KM-4 four circle diffractometer[35] with MoKα radiation ($\lambda = 0.71073$ Å) using the $2\theta/\omega$ scan mode. Initial phase angles were determined using the SHELXS program.[36] All H atoms were located geometrically and refined using a riding model with C–H = 0.97–0.98 Å, and $U_{iso}(H) = 1.2U_{eq}(C)$ (C–H = 0.96 Å and $U_{iso}(H) = 1.5U_{eq}(C)$ in the case of the methyl H atoms). Crystallographic data, data collection and structure refinement are given in Table 4, the coordinates of atoms and their isotropic temperature factors in Table 5 and a selection of the crystal's important geometric parameters in Table 6.

The crystal structure was refined to $R_1 = 0.0591$ (1378 reflections—all unique reflections) and $R_1 = 0.0336$ (1302 reflections with $F_o > 2\sigma(F_o)$) by the full-matrix least-squares method using SHELXL-97[37] based on 176 parameters. The compound structure showing the conformation and atom numbering system is illustrated in Figure 1.[38] The molecular packing in the crystal, illustrated in Figure 2, was established with the aid of PLUTO-78.[39] The computational material for publication was prepared using the PLATON program.[29]

Supplementary data

Full crystallographic details, excluding structures features, have been deposited (Deposition No. CCDC 652689) with the Cambridge Crystallographic Data Center. These data may be obtained, on request, from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (tel.: +44-1223-336408; fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www:http://www.ccdc.cam.ac.uk).

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References

1. Locardi, E.; Stöckle, M.; Gruner, S.; Kessler, H. *J. Am. Chem. Soc.* **2001**, *123*, 8189–8196.
2. Chakraborty, T. K.; Srinivasu, P.; Tapadar, S.; Mohan, B. K. *J. Chem. Sci.* **2004**, *116*, 187–207.
3. Gruner, S. A. W.; Locardi, E.; Lohof, E.; Kessler, H. *Chem. Rev.* **2002**, *102*, 491–514.
4. Graf von Roedern, E.; Lohof, E.; Hessler, G.; Hoffmann, M.; Kessler, H. *J. Am. Chem. Soc.* **1996**, *118*, 10156–10167.
5. Suhara, Y.; Ichikawa, M.; Hildreth, J. E. K.; Ichikawa, Y. *Tetrahedron Lett.* **1996**, *37*, 2549–2552.
6. Nishimura, S.-I.; Nomura, S.; Yamada, K. *Chem. Commun.* **1998**, 617–618.
7. Goodnow, R. A., Jr.; Richou, A.-R.; Tam, S. *Tetrahedron Lett.* **1997**, *38*, 3195–3198.
8. Goodnow, R. A., Jr.; Tam, S.; Pruess, D. L.; McComas, W. W. *Tetrahedron Lett.* **1997**, *38*, 3199–3202.
9. Menand, M.; Blais, J.-C.; Hamon, L.; Valery, J.-M.; Xie, J. *J. Org. Chem.* **2005**, *70*, 4423–4430.
10. Gruner, S. A. W.; Kéri, G.; Schwab, R.; Venetianer, A.; Kessler, H. *Org. Lett.* **2001**, *3*, 3723–3725.
11. Gruner, S. A. W.; Truffault, V.; Voll, G.; Locardi, E.; Stöckle, M.; Kessler, H. *Chem. Eur. J.* **2002**, *8*, 4365–4376.
12. Jain, R.; Kamau, M.; Wang, Ch.; Ippolito, R.; Wang, H.; Dulina, R.; Anderson, J.; Gange, D.; Sofia, M. J. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2185–2189.
13. Györgydeák, Z.; Thiem, J. *Carbohydr. Res.* **1995**, *268*, 85–92.
14. Xie, J. *Carbohydr. Res.* **2003**, *338*, 399–406.
15. Ying, L.; Gervay-Hague, J. *Carbohydr. Res.* **2004**, *339*, 367–375.
16. Gonzalez, F.; Lesage, S.; Perlin, A. S. *Carbohydr. Res.* **1975**, *42*, 267–274.
17. Hansen, P.; Lau, J.; Pedersen, E. B.; Nielsen, C. M. *Liebigs. Ann. Chem.* **1990**, 1079–1082.
18. Daley, L.; Roger, P.; Monneret, C. *J. Carbohydr. Chem.* **1997**, *16*, 25–48.
19. Dąbrowska, A.; Dokurno, P.; Konitz, A.; Smiatacz, Z. *Carbohydr. Res.* **2000**, *323*, 230–234.
20. Liberek, B.; Dąbrowska, A.; Frankowski, R.; Matuszewska, M.; Smiatacz, Z. *Carbohydr. Res.* **2002**, *337*, 1803–1810.
21. Florent, J.-C.; Monneret, C. *J. Chem. Soc., Chem. Commun.* **1987**, 1171–1172.
22. Grynkiewicz, G.; Fokt, I.; Skibicki, P.; Przewloka, T.; Szeja, W.; Pribe, W. *Polish J. Chem.* **2005**, *79*, 335–347.
23. Wengel, J.; Lau, J.; Pedersen, E. B.; Nielsen, C. M. *J. Org. Chem.* **1991**, *56*, 3591–3594.
24. Liberek, B.; Dąbrowska, A.; Frankowski, R.; Smiatacz, Z. *J. Carbohydr. Chem.* **2004**, *23*, 425–442.
25. Liberek, B.; Tuwalska, D.; Konitz, A.; Sikorski, A. *Carbohydr. Res.* **2007**, *342*, 1280–1284.
26. Evans, G. G.; Boeyens, J. A. *Acta Crystallogr., Sect. B* **1989**, *45*, 581–590.
27. Saenger, W. *Principles of Nucleic Acid Structure*; Springer: New York, 1983, p 19.
28. Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354–1358.
29. Spek, A. L. *J. Appl. Crystallogr.* **2003**, *36*, 7–13.
30. Liberek, B.; Nowacki, A. *J. Phys. Chem. A.* **2007**, *111*, 4397–4403.
31. Cambridge Structural Database, November 2005, Version 5.27.
32. Dąbrowska, A.; Konitz, A.; Smiatacz, Z. *Carbohydr. Res.* **2002**, *337*, 175–181.
33. Harding, C. C.; Shallard-Brown, H.; Watkin, D. J.; Soengas, R.; Fleet, G. W. J. *Acta Crystallogr., Sect. E* **2004**, *60*, o2334–o2336.
34. Liberek, B.; Sikorski, A.; Konitz, A. *Carbohydr. Res.* **2005**, *340*, 143–147.
35. Kuma KM-4 Software User's Guide. Version 3.1. Kuma Diffraction, Wrocław, Poland, 1989.

36. Sheldrick, G. M. *Acta Crystallogr., Sect. A* **1990**, *46*, 467–473.
37. Sheldrick, G. M. SHELXL-97. Program for Crystal Structure Refinement; University of Göttingen: Göttingen, 1997.
38. Johnson C. K. ORTEP II; Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, TN, USA, 1976.
39. Mortherwell, S.; Clegg, S. PLUTO-78; Program for Drawing and Molecular Structure; University of Cambridge: UK, 1978.