Crystal Structure of Methyl 4-amino-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-α-L-talopyranoside

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Abstract: The structure of methyl 4-amino-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-α-L-talopyranoside was established by X-ray analysis confirming a *talo* configuration at C-4 and suggesting a $^1C_4$ conformation of the pyranose ring. The values of relevant torsion angles and calculated puckering parameters revealed a distortion into the direction of ^5E conformation, thus indicating a flattening at C-2.

Keywords: Amino nitrile, methyl talopyranoside, amino sugar, X-ray analysis.

Introduction

The amino sugars represent a very important class of organic compounds primarily because of their biological role in living organisms. Their presence in bacteria and all tissues and fluids of pluricellular organisms as well as their association with many proteins and lipids suggests a great medicinal importance. The rapid increase of knowledge in the field of relationship between structure of amino sugar-containing compounds and biological activity requires availability many of suitable synthetically prepared model compounds with well established structures.

Within our research on synthesis of new amino sugar derivatives, we have prepared [1] two sugar amino nitriles – methyl 4-amino-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-α-L-talopyranoside (**1**) and methyl 4-amino-4-cyano-4,6-dideoxy-2,3-*O*-isopropylidene-β-D-allopyranoside (**2**) which are structurally related to naturally occurring biologically important Perosamine (**3**) (Figure 1). Because of the difficulties in unambiguous establishing the configuration at C-4 position of the pyranose ring (*talo* versus *manno* for **1** and *allo* versus *gulo* for **2**) by NMR methods, X-ray analysis of corresponding *N*-acetylated derivative **4** was presented [1] and recently, we have also published [2] the crystal structure of *N*-acetylated derivative **5**.
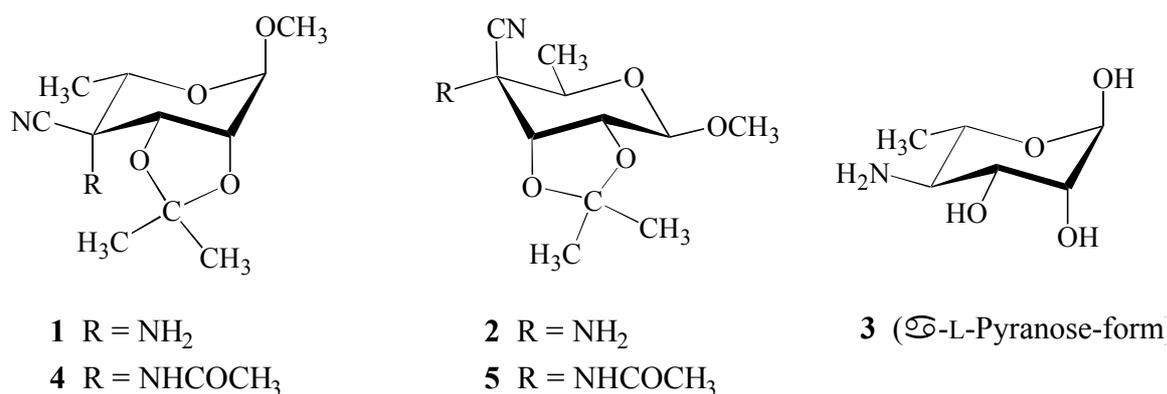

1 R = NH$_2$
4 R = NHCOCH$_3$

2 R = NH$_2$
5 R = NHCOCH$_3$

3 (⊘-L-Pyranose-form)

Figure 1.

Finally, we were successful in generating suitable crystals of the *N*-unprotected amino nitrile **1** and thus complete this structural study by presentation of the corresponding X-ray analysis data.

Results and Discussion

Structure Elucidation

The title compound **1** was fully characterized by ^{1}H and ^{13}C NMR, EIMS, CIMS, [α]$_D$, TLC, mp and elemental analysis data [1]. The coupling constants $J_{1,2}$ of 0 Hz and $J_{2,3}$ of 6.5 Hz suggest a $^1C_4$ conformation with an axial glycosidic methoxyl group, H-3 and H-5, an equatorial H-1 and H-2 and favoured 2,3-*cis* stereochemistry for the isopropylidene group. Because the data obtained from NMR measurements were unsufficient, X-ray analysis was used to determine unambiguously correct actual configuration at C-4 and simultaneously, conformation of the pyranose ring.

X-ray Analysis

The relevant crystallographic data and structure refinement are given in Table 1. The bond lengths and bond angles are listed in Table 2. A list of selected torsion angles is given in Table 3. The final

positional parameters are summarized in Table 4. Perspective view and the numbering of the atoms is depicted in Figure 2. The hydrogen atoms were refined isotropically in idealized positions riding on the atom to which they are attached.
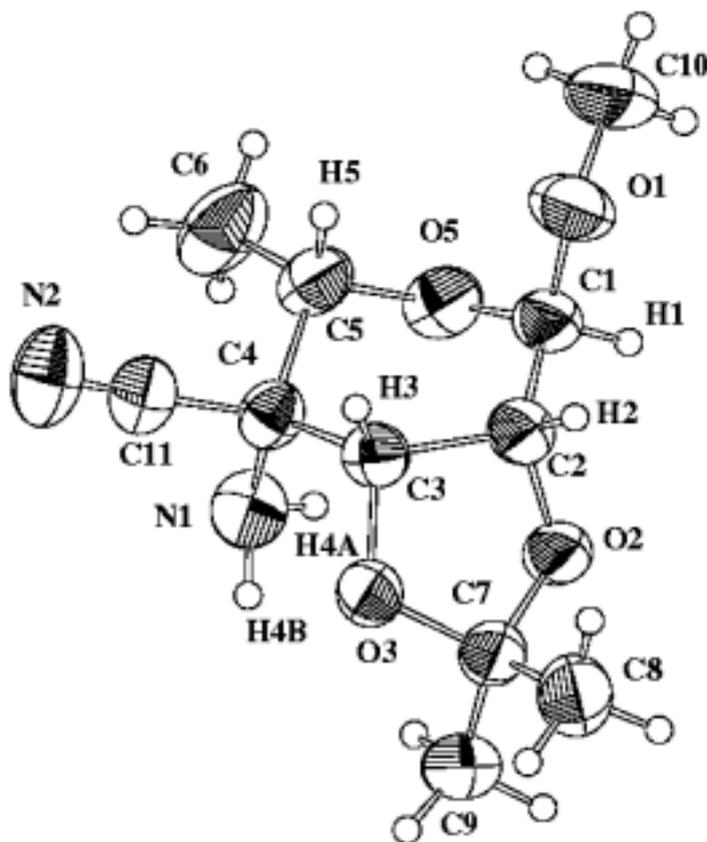

Figure 2. ZORTEP plot and atomic numbering of compound **1**.

The analysis of ring conformation by calculating puckering parameters [Q = 0.544(2) Å, θ = 151.3 (2)°, φ = 126.1(4)°] according to Cremer and Pople [3] has shown that pyranose ring in **1** adopt a $^1C_4$ conformation which is slightly distorted into the direction of ^5E [4,5], thus indicating a considerable flattening at C-2.

The values of selected relevant torsion angles [O3–C3–C4–C11 = 85.07(18)°, C3–C4–C5–C6 = –179.59(19)°] clearly demonstrate a *talo* configuration respecting the above mentioned conformation of the pyranose ring. On the other hand, torsion angle O1–C1–C2–O2 = –152.71(14)° indicates an α-L-anomeric linkage. Additionally, the values of torsion angles H1–C1–C2–H2 = 83.2° and H2–C2–C3–H3 = 29.4° obtained from X-ray analysis are in good agreement with those obtained from ^{1}H NMR measurements. According to Karplus curve [6], observed vicinal coupling constants $J_{1,2}$ = 0 Hz and $J_{2,3}$ = 6.5 Hz correlate with dihedral angles of about 90° and 28°, respectively.

Analysis of the molecular packing in the unit cell revealed a weak intermolecular interaction [C(8) – H(8B)…O(5) = 3.534(3)Å, C(8) – H(8B) = 0.96Å, H(8B)…O(5) = 2.585Å, C(8) – H(8B)…O(5) = 170°, symmetry code = 2-x+y,1-x,1/3+z] which probably stabilizes the crystal structure.

Acknowledgements

Experimental

General

The synthesis and relevant data of analytical methods as well as instruments used for the preparation and characterization of the title amino nitrile **1** have already been published [1]. An analytical sample of **1** was used for generation of suitable crystals. These were obtained by slow crystallization from a mixture of ethyl acetate–hexane (1:2, v/v) at room temperature.

X-ray Analysis

Crystal and experimental data for compound **1** are given in Table 1. The structure was solved by direct methods and refined by anisotropic full-matrix least-squares technique. The choice of space group and hence the absolute configuration of the compound (1-*R*, 2-*R*, 3-*S*, 4-*R*, 5-*S*) was based on the fact that configuration on positions 1, 2, 3 and 5 of pyranose ring is known and could not change. The crystallographic computations were performed with Bruker SHELXTL [7]. The ZORTEP program [8] was used for the molecular graphics drawing.

Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. The corresponding deposition number is CCDC 143616. Copies of the data can be obtained free of charge on request to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Tel.: +44-1223-336408, Fax: +44-1223 336-033).

Table 1. Crystal and experimental data for compound **1**[a]

Empirical formula	$C_{11}H_{18}N_2O_4$
Formula weight	242.27
Temperature, *T* (K)	296(2)
Wavelength, λ (Å)	0.71073
Crystal system	Trigonal

Space group	P3$_2$
Unit cell dimensions (Å)	$a = 10.29620(10)$ $\alpha = \beta = 90°$
	$b = 10.29620(10)$
	$c = 10.8118(2)$ $\gamma = 120°$
Volume, V (Å^3)	996.62(2)
Formula units per unit cell, Z	3
Calculated density, D_x (g cm^{-3})	1.216
Absorption coefficient, μ (mm^{-1})	0.093
F(000)	390
Crystal size (mm)	1.00 (max) 0.21 (min)
Diffractometer	Siemens SMART CCD
Theta range for data collection (˚)	2.28—27.17
Index ranges	$-13 \leq h \leq 13, -13 \leq k \leq 13, -13 \leq l \leq 13$
Reflections collected	11057
Independent reflections [$I > 2\sigma(I)$]	2902 (R$_{int}$ = 0.0246)
Refinement method	Full-matrix least-squares
Minimization of	$\Sigma w \, (|F_o| - |F_c|)^2$
Data / parameters	2902 / 182
Goodness of fit (all)	1.028
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0375$ w$R2 = 0.0897$
R indices (all data)	$R1 = 0.0475$ w$R2 = 0.0963$
Largest diff. peak and hole	0.086 and -0.149 (e Å^{-3})

[a] Standard deviations in parentheses.

Table 2. Selected bond lengths [in Å] and bond angles [in °] for compound **1**[a]

O5–C1	1.406(2)	C2–C3–C4	114.65(14)
O5–C5	1.437(2)	O1–C1–O5	112.29(15)
O2–C2	1.419(2)	O1–C1–C2	106.30(15)
O2–C7	1.423(2)	O5–C1–C2	113.09(14)
O3–C3	1.420(2)	O2–C7–O3	104.82(12)
O3–C7	1.454(2)	O2–C7–C9	108.34(17)
O1–C1	1.404(2)	O3–C7–C9	109.91(16)
O1–C10	1.433(3)	O2–C7–C8	111.78(16)
C3–C2	1.530(2)	O3–C7–C8	109.10(17)
C3–C4	1.563(2)	C9–C7–C8	112.60(18)
N1–C4	1.450(2)	N2–C11–C4	176.6(2)
C1–C2	1.519(2)	O5–C5–C6	107.37(17)

C7–C9	1.505(3)	O5–C5–C4	106.70(13)
C7–C8	1.510(3)	C6–C5–C4	113.9(2)
C11–N2	1.136(3)	N1–C4–C11	107.76(16)
C11–C4	1.485(2)	N1–C4–C5	109.84(16)
C5–C6	1.510(3)	C11–C4–C5	108.38(15)
C5–C4	1.545(3)	N1–C4–C3	116.12(15)
C1–O5–C5	113.91(14)	C11–C4–C3	106.49(14)
C2–O2–C7	106.33(13)	C5–C4–C3	107.98(15)
C3–O3–C7	109.19(12)	O2–C2–C1	108.93(14)
C1–O1–C10	113.01(19)	O2–C2–C3	102.59(12)
O3–C3–C2	103.59(13)	C1–C2–C3	116.68(15)
O3–C3–C4	109.92(13)		

^a Standard deviations in parentheses.

Table 3. Selected torsion angles [in °] for compound **1**^a

C1–C2 – C3–C4	28.0(2)
H1–C1 – C2–H2	83.2
H2–C2 – C3–H3	29.4
C3–C4 – C5–O5	62.08(17)
C3–C2 – O2–C7	–37.35(16)
C3–C4 – C5–C6	–179.59(19)
O1–C1 – C2–O2	–152.71(14)
O2–C2 – C3–O3	28.82(16)
C10–O1 – C1–O5	–61.5(2)
C10–O1 – C1–C2	174.32(19)
O3–C3 – C4–C11	85.07(18)

^a Standard deviations in parentheses.

Table 4. Atomic coordinates (x 10⁴) and equivalent isotropic displacement parameters (Å² x 10³) for compound **1**^a

Atom	x	y	z	U(eq)
O5	6111.7(13)	247.3(16)	4509.9(11)	57.5(3)
O2	9554.1(13)	2224.3(14)	4448.5(11)	53.4(3)
O3	9820.0(12)	1926.3(14)	6505.3(11)	51.6(3)
O1	6342.0(17)	2618.0(19)	4597.9(14)	70.8(4)
C3	8375.7(18)	1759.9(18)	6340.1(15)	45.4(4)

H3	8203	2334	6977	50(5)
N1	7550(2)	–998.2(18)	5960(2)	59.9(4)
H4A	7490(30)	–1010(30)	5170(30)	70(7)
H4B	8550(40)	–690(40)	6170(30)	107(10)
C1	7050.2(19)	1793(2)	4307.8(17)	52.2(4)
H1	7328	1948	3431	49(5)
C7	10646.0(18)	2418(2)	5348.3(17)	54.8(4)
C11	6810(2)	–251(2)	7778.6(18)	57.1(4)
N2	6545(3)	–434(2)	8805.6(18)	80.0(5)
C5	5720(2)	–146(2)	5785.1(18)	57.7(5)
H5	5411	527	6153	64(6)
C4	7147.1(19)	67.8(18)	6441.0(15)	47.7(4)
C2	8479.5(19)	2465(2)	5071.8(16)	48.3(4)
H2	8874	3545	5170	54(5)
C6	4424(3)	–1738(3)	5817(3)	88.0(8)
H6A	3566	–1780	5427	119(11)
H6B	4186	–2064	6660	93(8)
H6C	4696	–2381	5383	89(9)
C9	11261(3)	1410(3)	5015(2)	73.3(6)
H9A	10447	406	4896	79(8)
H9B	11895	1421	5670	97(9)
H9C	11833	1761	4265	91(8)
C8	11857(2)	4041(3)	5468(2)	75.1(7)
H8A	12362	4392	4689	120(12)
H8B	12565	4130	6087	86(8)
H8C	11414	4632	5704	69(7)
C10	5039(3)	2210(4)	3857(3)	94.5(9)
H10A	5288	2233	2999	117(11)
H10B	4692	2906	4001	110(11)
H10C	4264	1217	4075	107(10)

[a] Standard deviations in parentheses.

References and Notes

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Sample Availability: The title compound is available from the corresponding author.