Carbohydrate Research 343 (2008) 2336–2339

Contents lists available at ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

Note

Crystal structure of β-D-psicopyranose

Anna Kwiecień *, Katarzyna Ślepokura, Tadeusz Lis

Faculty of Chemistry, University of Wrocław, 14 F. Joliot–Curie St., 50–383 Wrocław, Poland

ARTICLE INFO

Article history:
Received 24 April 2008
Accepted 13 May 2008
Available online 21 May 2008

Keywords:
D-Psicose
Rare sugars
Ketohexose
X-ray crystal structure

ABSTRACT

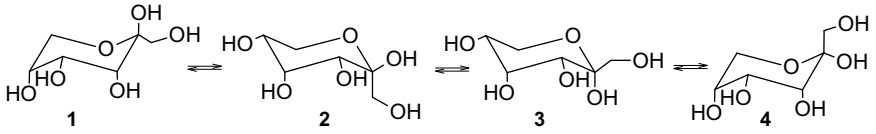
Here, we report the crystal structure of D-psicose, $C_6H_{12}O_6$, one of the rare sugars. The compound crystallizes as the β-anomer with rarely observed in pyranose carbohydrate structures *trans–gauche* orientation of the hydroxymethyl group relative to the pyranosyl ring. The crystal system is orthorhombic, space group $P2_12_12_1$, $Z = 4$, with cell dimensions $a = 7.727(2)$, $b = 8.672(2)$, $c = 11.123(3)$ Å, $V = 745.3(3)$ Å^3. The pyranosyl ring adopts chair $^2C_5$ conformation. The crystal structure at 100(2) K is stabilized by three-dimensional network of O–H···O and C–H···O intermolecular hydrogen bonds.

D-Psicose (also known as D-ribo-2-ketohexose; D-ribohexulose; D-allulose; D-erythrohexulose; pseudofructose), $C_6H_{12}O_6$, belongs to a group of rare sugars and occurs in small amounts in nature. Recently, these sugars have attracted significant attention due to a variety of applications such as non- or low-caloric carbohydrate sweeteners or bulking agents for potential use in the food industry.[1,2] D-Psicose, one of the epimers of D-fructose, has been separated and identified as a nonfermentable substance in cane molasses.[3]

It was observed that D-psicose possesses a strong scavenging activity towards reactive oxygen species (ROS). Some biochemical evidence shows that overproduction of ROS, which causes oxidative stress, can contribute to the development of Parkinson's disease, a neurodegenerative disorder. Several studies show that natural antioxidants may be used as therapeutic agents for neurodegenerative diseases because of their ability to reverse neuronal cell death in vitro. Results of certain studies suggest that D-psicose may play a potential role as the neuroprotective agent for this kind of disease.[4] What is more, the results propose that products containing D-psicose, for example, healthy food diets, nutrient supplements and drugs, may have neuroprotective function and prevent further neuronal degeneration in patients. It has been already shown that D-psicose is a useful carbohydrate for healthy food diets.[5–8]

A few structures of aldohexoses (such as glucose, galactose, talose, mannose and allose) and ketohexoses (fructose, tagatose and sorbose) are deposited in the Cambridge Structural Database (CSD).[9] Some information about the molecular structure of carbohydrates are also available from NMR data, both in solid phase and in solution.[10] We have performed a single-crystal X-ray structural analysis of a commercially available sample of D-psicose (Sigma, P8043). The details of both the structural and conformational analysis and the intermolecular interactions are presented herein.

In a solution of D-psicose, both conformational and anomeric equilibria are possible:[11]



Transformation **1**⇄**2** and **3**⇄**4** shows a conformational equilibrium that depends not only on steric effects but also on the anomeric effect. Transformation **2** ⇄ **3** shows an anomeric equilibrium.

For the crystalline state, we can establish the preferred conformation using the single-crystal X-ray method to determine both the molecular structure and the conformation. Figure 1 presents the molecular structure and the atom numbering scheme of D-psicose in the crystal. The sugar crystallizes as the β-anomer with the O6–C2–C3–C4–C5–C6 of the pyranosyl ring adopting the chair $^2C_5$ conformation. Cremer–Pople puckering parameters ($Q = 0.568(2)$ Å, $\Theta = 177.8(2)°$, $\Phi = 358(3)°$) and the appropriate torsion angles (Table 1) confirm an almost ideal chair

* Corresponding author.
E-mail address: aniuta04@gmail.com (A. Kwiecień).

0008-6215/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2008.05.012

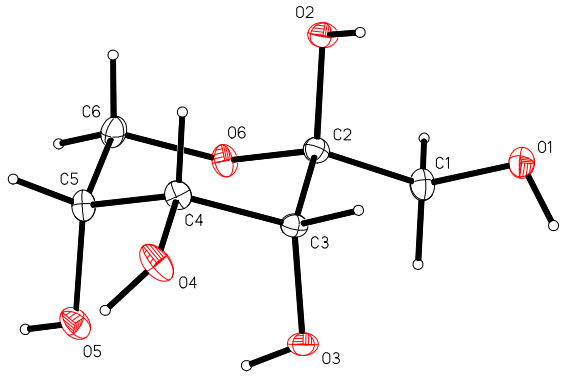


Figure 1. The molecular structure of β-D-psicopyranose showing the atom numbering scheme. Displacement ellipsoids are shown at the 50% probability level.

Table 1
Selected geometrical parameters (Å, °) for β-D-psicopyranose

Bond lengths			
O1–C1	1.427(2)	O5–C5	1.430(2)
O2–C2	1.410(2)	O6–C2	1.426(2)
O3–C3	1.433(2)	O6–C6	1.446(2)
O4–C4	1.424(2)		
Valence angles			
C2–O6–C6	114.6(1)	O2–C2–C3	110.1(1)
O2–C2–O6	107.4(1)	O6–C2–C3	110.4(1)
O2–C2–C1	110.6(1)	C1–C2–C3	113.6(1)
O6–C2–C1	104.4(1)		
Endocyclic torsion angles			
C6–O6–C2–C3	57.6(2)	C3–C4–C5–C6	−55.7(2)
O6–C2–C3–C4	−55.1(2)	C2–O6–C6–C5	−58.5(2)
C2–C3–C4–C5	55.6(2)	C4–C5–C6–O6	55.4(2)
Other torsion angles			
C6–O6–C2–O2	−62.4(2)	C1–C2–C3–C4	−172.0(1)
C6–O6–C2–C1	−179.9(1)	O3–C3–C4–O4	56.2(2)
O1–C1–C2–O2	57.0(2)	C2–C3–C4–O4	−179.2(1)
O1–C1–C2–O6	172.3(1)	O3–C3–C4–C5	−68.9(2)
O1–C1–C2–C3	−67.4(2)	O4–C4–C5–O5	−58.0(2)
O2–C2–C3–O3	−171.9(1)	C3–C4–C5–O5	65.8(2)
O6–C2–C3–O3	69.7(2)	O4–C4–C5–C6	−179.5(1)
C1–C2–C3–O3	−47.2(2)	O5–C5–C6–O6	−62.9(2)
O2–C2–C3–C4	63.3(2)		

conformation. It is to be noted here that the chair conformation of the pyranosyl ring is also observed in three other ketohexoses: in α-L-sorbose[12] and β-D-fructose[13] the conformation is $^{2}C_{5}$, and in α-D-tagatose[14] it is $^{5}C_{2}$. In its derivatives the D-psicose moiety can adopt other forms and conformations, for example, the chair $^{1}C_{4}$ conformation in 1,2:4,5-di-*O*-isopropylidene-3-*C*-(5-phenyl-1,2,4-oxadiazol-3-yl)-β-D-psicopyranose,[15] or envelope E_{O} conformation in 1,2:3,4-di-*O*-isopropylidene-β-D-psicofuranose.[16]

The polar O2–H2 hydroxyl group bonded to the anomeric carbon C2 is located in the axial position, which is the result of the anomeric effect. The C–O bond lengths in the crystal of D-psicose are in the range between 1.410(2) and 1.446(2) Å. The mean C–O distance of 1.428 Å harmonizes with literature data for α-L-sorbose (1.424 Å)[12] and β-D-fructose (1.421 Å).[13] The shortest C–O distance is 1.410(2) Å and occurs in the exocyclic C2–O2 anomeric bond. This anomeric shortening is accompanied by a slight shortening of the adjacent endocyclic C2–O6 bond (1.426(2) Å), with the C6–O6 distance being significantly longer (1.446(2) Å). The C–C bond lengths in β-D-psicopyranose range from 1.522(2) to 1.549(2) Å. The mean C–C value of 1.531 Å is in good agreement with data reported for D-tagatose (1.53 Å).[14]

The C–C–C valence angles range from 108.9(1)° to 113.6(1)° (mean 110.7°), the C–C–O angles are from 104.4(1)° to 112.4(1)° (mean 110.2°), and both are close to the tetrahedral value. The most significant deviation from the average value for C–C–O angles

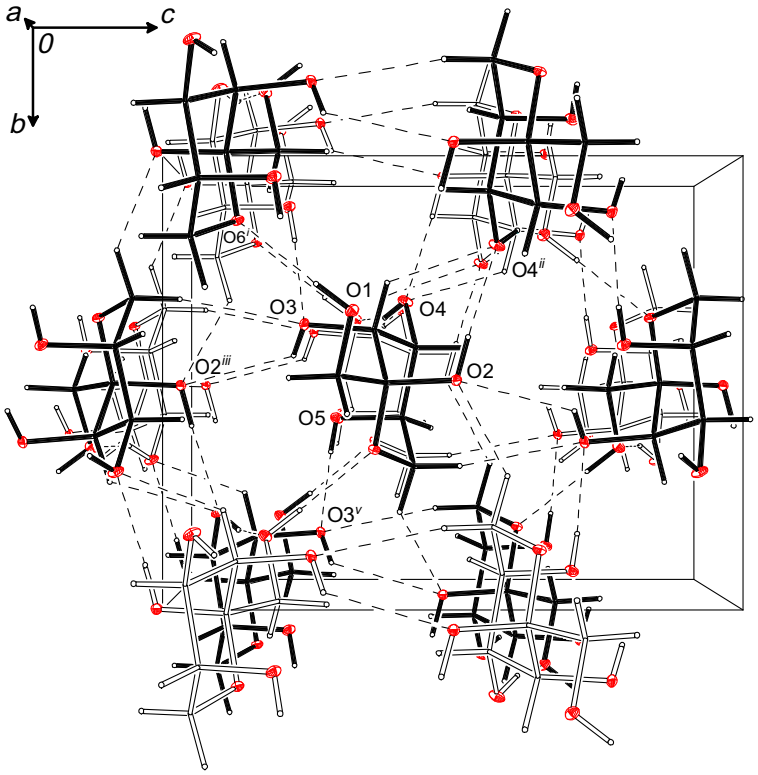


Figure 2. Molecular packing diagram in the crystal of β-D-psicose; viewed along the *a*-axis.

Table 2
Geometry of proposed hydrogen bonds and close contacts for β-D-psicose (Å, °)

D–H···A (Å)	D–H (Å)	H···A (Å)	D···A (Å)	(D–H···A) (°)
O1–H1···O6^{i}	0.85(3)	1.90(3)	2.725(2)	167(3)
O2–H2···O4^{ii}	0.86(3)	1.85(3)	2.712(2)	177(3)
O3–H3···O5	0.80(3)	2.07(2)	2.718(2)	138(2)
O3–H3···O2^{iii}	0.80(3)	2.54(2)	3.109(2)	129(2)
O4–H4···O1^{iv}	0.84(2)	1.95(2)	2.721(2)	153(2)
O5–H5···O3^{v}	0.76(2)	2.09(3)	2.840(2)	169(2)
C1–H1B···O5^{vi}	0.93(2)	2.71(2)	3.368(2)	128(2)
C3–H3A···O4^{ii}	1.03(2)	2.54(2)	3.285(2)	129(2)
C6–H6A···O2^{vii}	1.00(2)	2.54(2)	3.316(2)	134(2)
C6–H6B···O3^{viii}	0.94(2)	2.57(2)	3.505(2)	170(2)

Symmetry codes: (i) $-x+2$, $y-1/2$, $-z+1/2$; (ii) $x+1/2$, $-y+1/2$, $-z+1$; (iii) $-x+3/2$, $-y+1$, $z-1/2$; (iv) $x-1$, y, z; (v) $-x+1$, $y+1/2$, $-z+1/2$; (vi) $x+1$, y, z; (vii) $x-1/2$, $-y+3/2$, $-z+1$; (viii) $-x+3/2$, $-y+1$, $z+1/2$.

occurs in the exocyclic C1–C2–O6 angle (Table 1). A comparable deviation can be found in other ketohexoses. For example, in β-D-fructopyranose, this angle is 104.6(2)°.[13] The anomeric effect contributes to increasing the value of the C2–O6–C6 angle in comparison with the other endocyclic valence angles.

The orientation of the C1–O1 hydroxymethyl group relative to the pyranosyl ring is defined by the O1–C1–C2–O6 and O1–C1–C2–C3 torsion angles (Table 1), which indicate a *trans–gauche* (*tg*) conformation. Therefore, the orientation of the C2-bonded hydroxyl and hydroxymethyl groups in relation to each other is *synclinal* (O1–C1–C2–O2 torsion angle of 57.0(2)°). It is emphasized that such *trans–gauche* orientation of $-CH_2OH$ is rarely observed in pyranose carbohydrate structures.[9]

It is to be noted here that the crystallographic results for the structure of D-psicose are in good agreement with the NMR spectral data obtained for the title compound. Experimental data for a commercially available sample of D-psicose (Sigma, P8043) measured in D_2O, with a sample concentration of 100 mM, at a temperature of 298 K and at pH 7.4, measured at Bruker DMX 400 are available from the Madison Metabolomics Consortium Database.[17]

The molecular structure of β-D-psicose is stabilized by intramolecular O3–H3···O5 hydrogen interactions formed between two hydroxyl groups (Table 2). The adjacent molecules are joined to each other by the extensive network of intermolecular O–H···O hydrogen bonds, in which all the psicose hydroxyl groups are hydrogen donors and all of oxygen atoms act as acceptors. In addition, some of the C–H groups are also involved in the intermolecular interactions of C–H···O type. The packing diagram of β-D-psicose crystal shown in Figure 2 reveals the arrangement of the molecules within the crystal lattice in a kind of piles along the *a*-axis due to O4–H4···O1^{iv} contacts. The piles are additionally stabilized by the C1–H1B···O5^{vi} close contacts and interact with-one another by the other hydrogen interactions of the geometry given in Table 2. All that gives rise to the extensive three-dimensional hydrogen-bonding network.

1. Experimental

Diffraction data were collected at 100(2) K on a KM4CCD diffractometer with Mo Kα radiation ($\lambda = 0.71073$ Å). A summary of the conditions for the data collection and the structure refinement parameters is given in Table 3. Data collection, cell refinement and data reduction and analysis were carried out with the KM4CCD software (Oxford Diffraction, Poland): CrysAlis CCD and CrysAlis RED, respectively.[18] The crystal structure was solved by direct methods using the SHELXS-97[19] and refined by a full-matrix least-squares method using the program SHELXTL v. 6.12[19] with anisotropic thermal parameters for nonhydrogen atoms. Positions of hydrogen atoms were found in difference Fourier maps and then refined. Friedel opposites for analyzed crystal were merged, and the absolute configuration was established on the basis of the known stereochemistry. The figures were made with the XP[20] program. Cremer–Pople parameters were calculated using the PLATON Program.[21]

Table 3
Crystal data and structure refinement details for the crystal of β-D-psicopyranose

Crystal data	
Empirical formula	$C_6H_{12}O_6$
Formula weight (g mol^{-1})	180.16
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
a (Å)	7.727(2)
b (Å)	8.672(2)
c (Å)	11.123(3)
V (Å^3)	745.3(3)
Z	4
D_{calc} (g cm^{-3})	1.605
μ (mm^{-1})	0.146
$F(000)$	384
Crystal size (mm)	0.34 × 0.16 × 0.11
Crystal colour and form	Colourless plate
Data collection	
Diffractometer	Kuma KM4CCD
Data collection method	ω scans
Monochromator	graphite
Radiation type	MoKα
Wavelength, λ (Å)	0.71073
T (K)	100(2)
θ Range (°)	2.98–36.60
Indexes range	$-12 \leqslant h \leqslant 12$, $-14 \leqslant k \leqslant 14$, $-14 \leqslant l \leqslant 18$
Measured reflections	13,034
Independent reflections	2035
Observed reflections ($I > 2\sigma(I)$)	1854
R_{int}	0.0407
Refinement	
Refinement on	F^2
Data/restraints/parameters	2035/0/157
$R(F_o^2 > 2\sigma(F_o^2))$	$R_1 = 0.0395$; $wR_2 = 0.0855$
R (all data)	$R_1 = 0.0462$; $wR_2 = 0.0882$
GooF = S	1.068
Weighting parameter a/b	0.0515/0.0738
$\Delta\rho_{max}/\Delta\rho_{min}$ (e Å^{-3})	0.44/−0.22

$R_1 = \sum ||F_o| - |F_c|| / \sum |F_o|$; $wR_2 = \sqrt{\sum[w(F_o^2 - F_c^2)^2] / \sum[w(F_o^2)^2]}$; weighting scheme: $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$ where $P = (F_o^2 + 2F_c^2)/3$.

Supplementary data

Complete crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 685386. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK. (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via www.ccdc.cam.ac.uk). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2008.05.012.

References

1. Livesey, G.; Brown, J. C. *Jpn. J. Nutr.* **1996**, *126*, 1601–1609.
2. Matsuo, T.; Suzuki, H.; Hashiguchi, M.; Izumori, K. *J. Nutr. Sci. Vitamin (Tokyo)* **2002**, *48*, 77–80.
3. Zerban, F. W.; Sattler, L. *Ind. Eng. Chem.* **1942**, *34*, 1180–1188.
4. Takata, M. K.; Yamaguchi, F.; Nakanose, K.; Watanabe, Y.; Hatano, N.; Tsukamoto, I.; Nagata, M.; Izumori, K.; Tokuda, M. *J. Biosci. Bioeng.* **2005**, *100*, 511–516.
5. Sun, Y.; Hayakawa, S.; Ogawa, M.; Izumori, K. *Food Control* **2007**, *18*, 220–227.
6. Matsuo, T.; Baba, Y.; Hashiguchi, M.; Takeshita, K.; Izumori, K.; Suzuki, H. *J. Clin. Biochem. Nutr.* **2001**, *30*, 55–65.

7. Matsuo, T.; Izumori, K.. *J. Oleo Sci.* **2004**, *53*, 453–460.
8. Sun, Y.; Hayakawa, S.; Izumori, K. *J. Food Sci.* **2004**, *69*, C427–C434.
9. Cambridge Structural Database (CSD): Allen, F. H. *Acta Crystallogr., Sect. B* **2002**, *58*, 380–388.
10. Chen, Y. Y.; Lou, S. Y.; Hung, S. C.; Chan, S. I.; Tzou, D. L. M. *Carbohydr. Res.* **2005**, *340*, 723–729.
11. Nowakowski, A.; Wiśniewski, A. *Wiadomości Chemiczne* **2005**, *59*, 613–638.
12. Kim, S. H.; Rosenstein, R. D. *Acta Crystallogr.* **1967**, *22*, 648–656.
13. Kanters, J. A.; Roelofsen, G.; Alblas, B. P.; Meinders, I. *Acta Crystallogr., Sect. B* **1977**, *33*, 665–672.
14. Takagi, S.; Rosenstein, R. D. *Carbohydr. Res.* **1969**, *11*, 156–158.
15. Yu, J.; Zhang, S.; Li, Z.; Lu, W.; Zhou, R.; Liu, Y.; Cai, M. *Carbohydr. Res.* **2003**, *338*, 257–261.
16. Watkin, D. J.; Glawar, A. F. G.; Soengas, R.; Izumori, K.; Wormald, M. R.; Dwek, R. A.; Fleet, G. W. J. *Acta Crystallogr., Sect. E* **2005**, *61*, o2949–o2951.
17. Cui, Q.; Lewis, I. A.; Hegeman, A. D.; Anderson, M. E.; Li, J.; Schulte, C. F.; Westler, W. M.; Eghbalnia, H. R.; Sussman, M. R.; Markley, J. L. *Nat. Biotechnol.* **2008**, *26*, 162.
18. Xcalibur PX/KM4CCD software. CRYSALIS CCD and CRYSALIS RED, *Ver.* 1.171; Oxford Diffraction: Poland, 2006.
19. Sheldrick, G. M. *Acta Crystallogr., Sect. A* **2008**, *64*, 112–122.
20. XP–INTERACTIVE MOLECULAR GRAPHICS, v. 5.1; Bruker Analytical X-ray System, 1998.
21. Spek, A. L. PLATON—*A Multipurpose Crystallographic Tool*; Utrecht University: Utrecht, 2003; Spek, A. L. *J. Appl. Crystallogr.* **2003**, *36*, 7–13.