ELSEVIER

Carbohydrate Research 264 (1994) 191–198

CARBOHYDRATE RESEARCH

Conformations and structure studies of sugar lactones in the solid state. Part II. The molecular structure of α-D-glucosaccharino-γ-lactone: 2-*C*-methyl-D-*ribo*-pentono-1,4-lactone ☆

M. Ashraf Shalaby [a,*], Frank R. Fronczek [a], Ezzat S. Younathan [a], Graheme J.B. Williams [b], Leo H. Straver [c]

[a] *Departments of Biochemistry and Chemistry, Louisiana State University, Baton Rouge, LA 70803, USA*
[b] *Enraf–Nonius, 390 Central Avenue, Bohemia, NY 11716, USA*
[c] *Nonius B.V., P.O. Box 811, 2624 Delft, Netherlands*

Received 27 January 1994; accepted 9 May 1994

Abstract

The crystal structure of 2-*C*-methyl-D-*ribo*-pentono-1,4-lactone (α-D-glucosaccharino-γ-lactone, **1**) has been determined by single-crystal X-ray diffraction. The crystals are orthorhombic, space group $P2_12_12_1$ with $a=7.7429(6)$, $b=8.3373(7)$, $c=11.3258(7)$ Å, $V=731.1(2)$ Å^3 (Cu$K\alpha$, $\lambda=1.54184$ Å), $\mu=10.82$ cm^{-1}, $D_c=1.473$ g cm^{-3}, and $Z=4$. The structure was refined to $R=0.0307$ and $R_w=0.0424$ for 876 observed reflections. Compound **1** has the D-*ribo* configuration, in agreement with an earlier deduction from chemical evidence. The lactone ring adopts the $^3T_2$ conformation, with puckering parameters $\varphi=279.8(9)°$ and $q=0.32(5)$ Å. The orientation of the methyl group about the C-2–C-3 bond is gauche–trans, with the C-6–C-2–C-3–O-3 and C-6–C-2–C-3–C-4 torsion angles being $-81.3(2)°$ and $154.7(1)°$, respectively. The molecules are linked in the crystal in a two-dimensional intermolecular hydrogen bonding network that involves all hydroxyl groups as well as the carbonyl oxygen atom.

Keywords: D-*ribo*-Pentono-1,4-lactone, 2-*C*-methyl; α-D-Glucosaccharino-γ-lactone; X-ray crystal structure

1. Introduction

2-*C*-Methyl-D-*ribo*-pentono-1,4-lactone [1,2] (α-D-glucosaccharino-γ-lactone, **1**) prepared by the action of calcium hydroxide on D-fructose or ''inverted' sucrose, is a compound

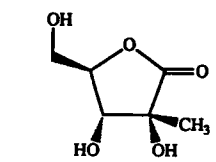
☆ For Part I, see Ref. [13].

* Corresponding author (present address): Center for Advanced Materials, Lawrence Berkeley Laboratory, University of California–Berkeley, Berkeley, CA 94720, USA.

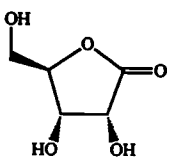
SSDI 0008-6215(94)00196-M

of diverse synthetic utilities [3–6]. Most used of these has been the application of **1** as a chiral template for the synthesis of new anthracyclinones of potent antitumor activities [7].

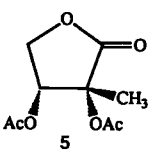
The free acid was first isolated in the mid-nineteenth century as the crystalline calcium salt [8], and identified as a 2-*C*-methyl aldonic acid [9] by reducing lactone **1** with hydrogen iodide in the presence of red phosphorus to 2-*C*-methyl glutaric acid. The configuration of the acid was assigned to the D-*ribo* configuration upon correlating the configuration of **1** with that of the branched-chain sugar hamamelose, 2-*C*-(hydroxymethyl)-D-ribose, and converting each into 5-deoxy-2-*C*-methyl-D-ribitol [10,11]. The aim of the present work was to confirm this assignment and determine the conformation and 3D molecular structure of **1**. The results obtained are compared with those of closely related structures, namely, D-ribono-1,4-lactone (**2**) [12], L-rhamnono-1,4-lactone (**3**) [13], L-mannono-1,4-lactone (**4**) [13], and 2,3-di-*O*-acetyl-2-*C*-methylerythrono-1,4-lactone (**5**) [14].



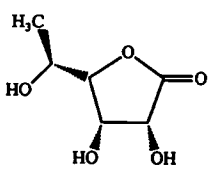
1



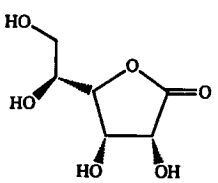
2



5



3



4

2. Experimental

The crystalline sample of α-D-glucosaccharino-γ-lactone (**1**) was kindly provided by Professor H.S. El Khadem from the late Dr. H.S. Isbell's collection of rare sugars at The American University, Washington DC.

Data collection and processing.—A colorless fragment with dimensions of $0.25 \times 0.30 \times 0.35$ mm was used for the structure determination. Intensity data were collected on an Enraf–Nonius CAD4-MACH diffractometer equipped with graphite-monochromated Cu$K\alpha$ radiation ($\lambda = 1.54184$ Å) at 24°C. Unit-cell parameters were obtained from setting angles of 25 reflections having $22° < 2\theta < 108°$. The crystal data are summarized in Table 1. A total of 904 reflections was measured by $\omega - 2\theta$ scans (one octant having $4° < 2\theta < 148.5°$) and variable scan rates (2.4–16.5 deg min^{-1}), 887 unique data were obtained; 876 reflections with $I < 1\sigma(I)$ were used in the refinement. Crystal stability was monitored by recording three standard reflections every 2 h, and no significant variation was observed. Absorption corrections were based on a series of ψ scans, and the minimum relative transmission coefficient was 88.4%. Systematic absences uniquely specified that the crystal belongs to orthorhombic space group $P2_12_12_1$ with $Z = 4$.

Table 1
Crystallographic data for 2-*C*-methyl-D-*ribo*-pentono-1,4-lactone (**1**)

Molecular formula	$C_6H_{10}O_5$
Molecular weight	162.1
Melting point (°C)	160–161
Crystal dimensions (mm)	$0.25 \times 0.30 \times 0.35$
Space group	$P2_12_12_1$
Cell dimensions (Å)	
a	7.7429(6)
b	8.3373(7)
c	11.3258(7)
Volume (Å^3)	731.1(2)
Z (molecules/cell)	4
θ_{max} (°)	74.25
μ (cm^{-1})	10.82
Radiation (graphite monochromator)	Cu$K\alpha$
Calculated density (g cm^{-3})	1.473
Unique reflections	887
$I > 1\sigma(I)$	876
S (141 variables)	2.976
Final residual factors	
R	0.031
R_w	0.042

Structure analysis.—The structure was solved by direct methods using the program MULTAN-80 [15] which revealed the position of all nonhydrogen atoms. It was refined by full-matrix least squares based upon F with $w = 4F_o^2 [\sigma^2(I) + (0.02\ F_o^2)^2]^{-1}$ using the MolEN programs [16]. Nonhydrogen atoms were refined anisotropically. The hydrogen atoms were located from difference maps and were refined isotropically. Atomic coordinates and equivalent isotropic thermal parameters, along with their esds, are given in Table 2 [1]. Final $R = 0.0307$ for 876 observed data (0.031 for all 887 data), $R_w = 0.0424$, and $S = 2.976$ for 141 variables. In the final cycle of refinement, the maximum shift was 0.01σ, maximum residual density 0.19, minimum -0.15 eÅ^{-3}, and extinction coefficient $g = 3.02(6) \times 10^{-5}$ where the factor $(1 + gI_c)^{-1}$ was applied to F_c. All calculations were performed on a VAX 3600 computer. Atomic scattering factors were obtained from the International Tables for X-ray Crystallography [17]. Refinement of the L isomer under identical circumstances yielded $R = 0.0311$, $R_w = 0.0430$, and $S = 3.017$.

3. Discussion

The structure of α-D-glucosaccharino-γ-lactone molecule (**1**), as observed in the crystal, is represented as an ORTEP [18] drawing (Fig. 1), which also shows the atom numbering

[1] Lists of observed and calculated structure-amplitudes, anisotropic thermal parameters, and torsion angles for **1** have been deposited with the Cambridge Crystallographic Data Centre and may be obtained on request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Table 2
Atomic coordinates and isotropic [a] thermal parameters for 2-*C*-methyl-D-*ribo*-pentono-1,4-lactone (**1**)

Atom	*x*	*y*	*z*	B_{iso} (Å^2)
O-1	0.2549(2)	0.2549(1)	0.6125(1)	2.90(2)
O-2	0.1831(1)	0.6195(1)	0.5715(1)	2.43(2)
O-3	0.4334(2)	0.7951(1)	0.6818(1)	2.50(2)
O-4	0.4865(1)	0.3972(1)	0.56259(9)	2.22(2)
O-5	0.8509(1)	0.5144(1)	0.5150(1)	2.51(2)
C-1	0.3313(2)	0.3798(2)	0.6143(1)	1.97(2)
C-2	0.2703(2)	0.5395(2)	0.6657(1)	1.90(2)
C-3	0.4427(2)	0.6267(2)	0.6819(1)	1.86(2)
C-4	0.5530(2)	0.5590(2)	0.5815(1)	1.90(2)
C-5	0.7414(2)	0.5488(2)	0.6135(1)	2.42(3)
C-6	0.1604(2)	0.5226(2)	0.7750(1)	2.96(3)
H-2OH	0.082(3)	0.562(2)	0.557(2)	5.3(5)
H-3OH	0.388(3)	0.825(2)	0.622(2)	4.6(5)
H-5OH	0.828(3)	0.431(3)	0.493(2)	4.5(5)
H-3	0.490(2)	0.594(2)	0.758(2)	1.9(3)
H-4	0.540(2)	0.616(2)	0.509(1)	2.0(3)
H-5a	0.791(2)	0.650(3)	0.638(1)	3.8(4)
H-5b	0.758(3)	0.471(2)	0.677(2)	3.3(4)
H-6a	0.216(3)	0.473(3)	0.836(2)	5.4(5)
H-6b	0.124(3)	0.632(3)	0.807(2)	4.4(5)
H-6c	0.054(3)	0.453(2)	0.764(2)	3.2(4)

[a] Equivalent isotropic thermal parameters are given for nonhydrogen atoms. The definition of this quantity is $B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* a_i \cdot a_j$.

in the molecule. The bond lengths, bond angles, and selected torsion angles are listed in Table 3.

Inspection of the molecular structure of **1** reveals that the molecule has the D-*ribo* configuration, and is present in the γ-lactone form. The lactone group is nearly planar, as shown by the torsion angles of 5.0(2)° and −178.0(1)° between the bonds adjacent to C-

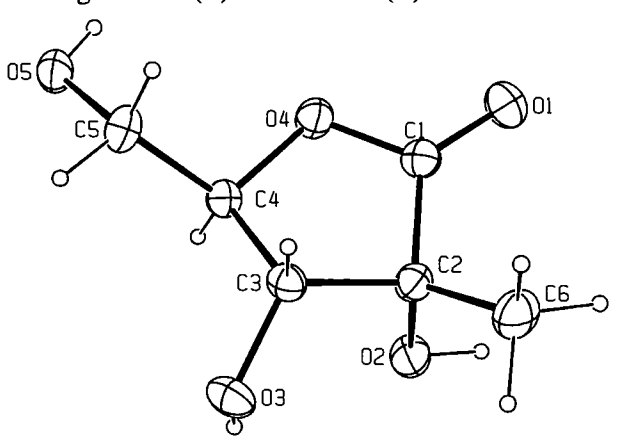


Fig. 1. Molecular structure and atomic numbering of 2-*C*-methyl-D-*ribo*-pentono-1,4-lactone (**1**). Nonhydrogen atoms are represented with 40% ellipsoids and hydrogen atoms with circles of arbitrary radius.

Table 3
Bond lengths, bond angles, and selected torsion angles in 2-*C*-methyl-D-*ribo*-pentono-1,4-lactone (**1**)

Atoms	Length (Å)	Atoms	Length (Å)
O-1–C-1	1.198(2)	C-1–C-2	1.529(2)
O-2–C-2	1.428(2)	C-2–C-3	1.531(2)
O-3–C-3	1.405(2)	C-2–C-6	1.509(2)
O-4–C-1	1.345(2)	C-3–C-4	1.530(2)
O-4–C-4	1.460(2)	C-4–C-5	1.505(2)
O-5–C-5	1.430(2)		
Atoms	Angle (deg)	Atoms	Angle (deg)
C-1–O-4–C-4	110.5(1)	C-3–C-2–C-6	115.9(1)
O-1–C-1–O-4	121.8(1)	O-3–C-3–C-2	115.4(1)
O-1–C-1–C-2	127.7(1)	O-3–C-3–C-4	113.4(1)
O-4–C-1–C-2	110.4(1)	C-2–C-3–C-4	102.8(1)
O-2–C-2–C-1	105.6(1)	O-4–C-4–C-3	104.7(1)
O-2–C-2–C-3	106.2(1)	O-4–C-4–C-5	109.0(1)
O-2–C-2–C-6	113.0(1)	C-3–C-4–C-5	112.5(1)
C-1–C-2–C-3	101.0(1)	O-5–C-5–C-4	113.5(1)
C-1–C-2–C-6	113.9(1)		
C-4–O-4–C-1–O-1	−178.0(1)	C-4–O-4–C-1–C-2	5.0(2)
C-1–O-4–C-4–C-3	15.8(1)	C-1–O-4–C-4–C-5	136.4(1)
O-1–C-1–C-2–O-2	−89.7(2)	O-4–C-1–C-2–C-3	−23.4(1)
O-2–C-2–C-3–O-3	45.1(1)	C-1–C-2–C-3–C-4	31.1(1)
C-6–C-2–C-3–O-4	−81.3(2)	C-6–C-2–C-3–C-4	154.7(1)

1–O-4. The C-1–O-4 bond is shorter and O-4–C-4 is longer than the normal C–O single bond length of 1.425 Å [19]. Such characteristics, which have been observed in other 1,4-lactones (see Table 4), is attributable to the sp^2 hybridization of C-1 and to contributions from the valence-bond resonance form C^+–O=C–O^-.

The C–C bond distances are normal, ranging from 1.505(2) to 1.531(1) Å, as are the C–OH bonds, 1.405(2) to 1.430(2) Å, which are consistent with those values reported for other carbohydrates [20–22]. The ring angles at the carbon atoms of the lactone ring range from 102.8(1) to 105.6(1)° with the exception of the carbonyl atom, C-1, is larger, 110.4(1)°, as would be expected from the sp^2 hybridization of the carbon atom.

Table 4
Puckering parameters, conformations, and C–O bond lengths and torsion angles for some 1,4-lactone rings

Compound	Puckering paramters		Confor-mation	Bond length (Å)			Torsion angle (deg)	
	φ (deg)	q (Å)		C-1–O-1	C-1–O-4	C-4–O-4	C-4–O-4–C-1–O-1	O-1–C-1–C-2–O-2
1	279.8	0.32	$^3T_2$	1.198(2)	1.345(2)	1.460(2)	−178	−89.7
2	99	0.38	$^2T_3$	1.203(1)	1.354(1)	1.467(1)	+172.7	−25.5
3	103.1	0.39	E_3–$^2T_3$	1.203(2)	1.342(2)	1.470(2)	+175.4	28.5
4	106.6	0.42	E_3	1.204(1)	1.344(1)	1.474(1)	+179.0	−26.5
5	337	0.13	E_4–$^3T_4$	1.203(7)	1.320(9)	1.429(8)	+171.6	−57.7

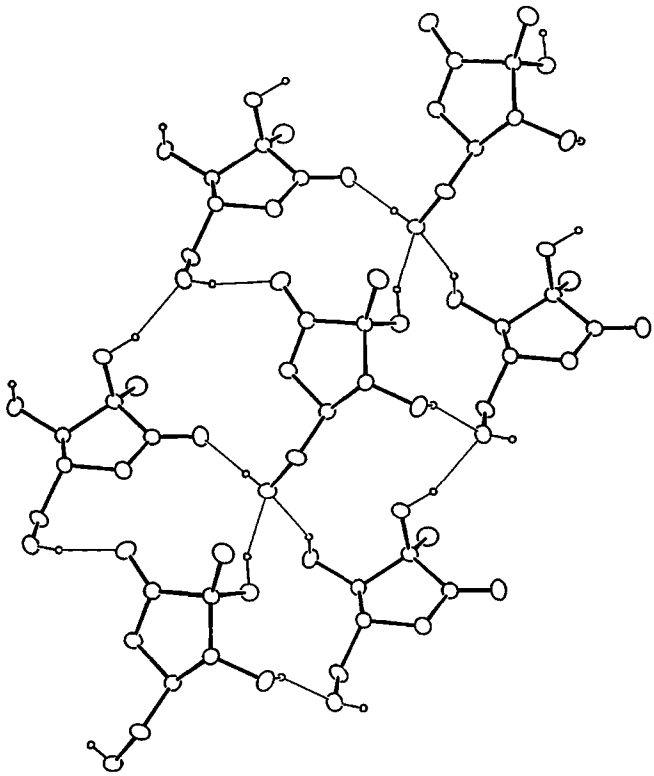


Fig. 2. The hydrogen-bonding scheme of in the crystal of 2-*C*-methyl-D-*ribo*-pentono-1,4-lactone (**1**). Hydrogen atoms not involved in hydrogen bonding are omitted.

The lactone ring adopts the twist $^3T_2$ conformation, with a phase angle (P) of 10.03° and a pseudorotation amplitude (τ_m) [23] of 31.58°. The corresponding puckering parameters as defined by Cremer and Pople [24] are $\varphi = 279.8°$ and $q = 0.32$ Å. Analysis of the deviations of the ring atoms from the least-squares plane defined by C-1–O-4–C-4 places C-2 and C-3 at positions 0.126(1) Å above and 0.404(1) Å below the plane, respectively.

Table 4 shows a comparison between the ring conformation of the title compound (**1**) with those of the closely related 1,4-lactone structures **2**, **3**, **4**, and **5**. The data clearly show that when the lactone group is planar, the γ-lactone ring is constrained to have an envelope conformation E_3, which is less strained than the planar lactone ring. Thus, the lactone ring

Table 5
Geometry of the hydrogen bonds [a] in 2-*C*-methyl-D-*ribo*-pentono-1,4-lactone (**1**)

D [b]···A	Acceptor symmetry	O···O (Å)	O–H (Å)	H···O (Å)	O–H···O (deg)
O-5–H···O-1	$0.5+x, 0.5-y, 1-z$	2.770(2)	0.76(2)	2.03(2)	163(2)
O-2–H···O-5	$x-1, y, z$	2.793(2)	0.94(2)	1.89(3)	161(2)
O-3–H···O-5	$x-0.5, 1.5-y, 1-z$	2.811(2)	0.80(2)	2.07(2)	154(2)

[a] Estimated standard deviation in parentheses.
[b] D, donor; A, acceptor.

of **4** adopts a near perfect envelope conformation E_3, with the C-4–O-4–C-1–O-1 torsion angle being 179°, whereas a distortion from the ideal envelope toward the direction of the twist conformation was observed in the crystal structure of **2**, **3**, and **5** as results of the small deviations from exact planarity of their lactone groups. In the present structure, it was interesting to observe that although the lactone group is nearly planar [torsion angle magnitude 178.0(1)°], the lactone ring is deviated toward the twist conformation. This discrepancy can presumably be attributed to the 1,3-interaction between the bulky pseudoaxial substituents at C-2 and C-4. The structure apparently undergoes a rotation around the C-2–C-3 bond to avoid such interaction, thus forcing the ring towards a twist conformation, and tilting C-2 endo and C-3 exo with respect to the C-1–O-4–C-4 plane. The orientation of the methyl group about the C-2–C-3 bond is gauche–trans, with the C-6–C-2–C-3–O-3 and C-6–C-2–C-3–C-4 torsion angles being $-81.3(2)°$ and $154.7(1)°$, respectively.

The molecules are linked in the crystal in a two-dimensional intermolecular hydrogen bonding network in which each molecule participates in a six O–H···O hydrogen bonds. The hydrogen bond interactions are illustrated in Fig. 2, and the relevant hydrogen–oxygen and oxygen–oxygen distances are listed in Table 5, together with angles about the H atoms. Of the three hydroxyl groups, OH-5 participates in three hydrogen bonds, one as donor and two as acceptor, while OH-2 and OH-3 participate as hydrogen-bond donors only, and the carbonyl oxygen atom participates as an acceptor.

Acknowledgements

We are indebted to Professor Hassan S. El Khadem of The American University, Washington DC, for supplying the sample of α-D-glucosaccharino-γ-lactone (**1**). This work was supported, in part, by grant No. DK 40401 from the National Institutes of Health.

References

[1] R.L. Whistler and J.N. BeMiller, *Adv. Carbohydr. Chem.*, 13 (1958) 289–291.
[2] A.J. Feast, B. Linderg, and O. Theander, *Acta Chem. Scand.*, 19 (1965) 1127–1134.
[3] A.G.M. Barrett, B.C.B. Bezuidenhoudt, D. Dhanak, A.F. Gasiecki, A.R. Howell, A.C. Lee, and Mark A. Russell, *J. Org. Chem.*, 54 (1989) 3321–3328.
[4] R.E. Ireland, R.C. Anderson, R. Badoud, B.J. Fitzsimmons, G.J. McGarvey, S. Thaisrivongs, and C.S. Wilcox, *J. Am. Chem. Soc.*, 105 (1983) 1988–2006.
[5] R.E. Ireland, S. Thaisrivongs, and C.S. Wilcox, *J. Am. Chem. Soc.*, 102 (1980) 1155–1157.
[6] F. Bennani, J.-C. Florent, M. Koch, C. Monneret, *Tetrahedron*, 40 (1984) 4669–4676.
[7] B. Deguin, J. Florent, and C. Monneret, *J. Org. Chem.*, 56 (1991) 405–411.
[8] J.C. Sowden, *Adv. Carbohydr. Chem.*, 12 (1957) 35–79.
[9] H. Kiliani, *Liebigs Ann. Chem.*, 218 (1883) 361.
[10] J.C. Sowden and D.R. Strobach, *J. Am. Chem. Soc.*, 82 (1960) 3707–3708.
[11] A.B. Foster, T.D. Inch, J. Leehmann, and J.M. Webber, *J. Chem. Soc.*, (1964) 948–952.
[12] Y. Kinoshita, J.R. Ruble, and G.A. Jeffrey, *Carbohydr. Res.*, 92 (1981) 1–7.
[13] M.A. Shalaby, F.R. Fronczek, and E.S. Younathan, *Carbohydr. Res.*, CAR 12158.
[14] A. Conde, E. Moreno, and R. Marquez, *Acta Crystallogr., Sect. B*, 36 (1980) 1713–1715.

[15] P. Main, S.J. Fiske, S.E. Hull, L. Lessinger, G. Germain, J.P. Declercq, and M.M. Woolfson, MULTAN-80, A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data, Universities of York, England and Louvain, Belgium.
[16] C.K. Fair, MolEN, An Interactive Structure Solution Procedure, Enraf–Nonius, Delft, The Netherlands, 1990.
[17] D.T. Cromer and J.T. Waber, International Tables for X-Ray Crystallography, Vol. IV, Tables 2. 2B and 2.3.1, The Kynoch Press, Birmingham, England, 1974 (current distributor, Kluwer Academic Publishers, Dordrecht).
[18] C.K. Johnson, ORTEP II, Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1976.
[19] M.A. Shalaby, F.R. Fronczek, and E.S. Younathan, *Carbohydr. Res.*, CAR 12157.
[20] G.A. Jeffery and A.D. French, *Chem. Soc. Spec. Publ.*, 6 (1978) 183–223.
[21] F.H. Allen, *Acta Crystallogr., Sect. B*, 42 (1986) 515–522.
[22] F.H. Allen, O. Kennard, D.G. Watson, L. Brammer, A.G. Orpen, and R. Taylor, *J. Chem. Soc., Perkin Trans.* 2, (1987) S1–S19.
[23] C. Altona and M. Sundaralingam, *J. Am. Chem. Soc.*, 94 (1972) 8205–8212.
[24] D. Cremer and J.A. Pople, *J. Am. Chem. Soc.*, 97 (1975) 1354–1358.