Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

2,3:4,6-Di-*O*-isopropylidene-*α*-L-sorbofuranose and 2,3-*O*-isopropylidene-*α*-L-sorbofuranose

Vratislav Langer,[a]* Bohumil Steiner[b] and Miroslav Koóš[b]*

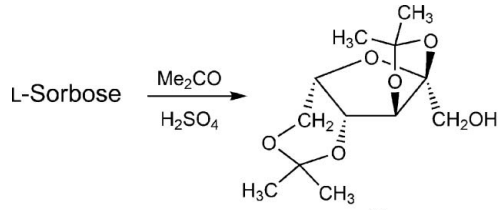
[a]Environmental Inorganic Chemistry, Department of Chemical and Biological Engineering, Chalmers University of Technology, SE-412 96 Göteborg, Sweden, and [b]Institute of Chemistry, Centre of Excellence GLYCOMED, Slovak Academy of Sciences, Dúbravská cesta 9, SK-845 38 Bratislava, Slovakia
Correspondence e-mail: langer@chalmers.se, chemmiro@savba.sk

Received 26 February 2009
Accepted 6 March 2009
Online 14 March 2009

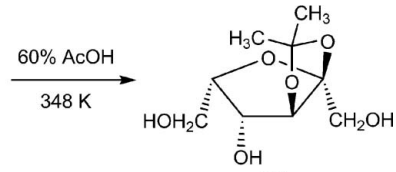
In the title compounds, $C_{12}H_{20}O_6$, (I), and $C_9H_{16}O_6$, (II), the five-membered furanose ring adopts a $^4T_3$ conformation and the five-membered 1,3-dioxolane ring adopts an E_3 conformation. The six-membered 1,3-dioxane ring in (I) adopts an almost ideal $^OC_3$ conformation. The hydrogen-bonding patterns for these compounds differ substantially: (I) features just one intramolecular O—H···O hydrogen bond [O···O = 2.933 (3) Å], whereas (II) exhibits, apart from the corresponding intramolecular O—H···O hydrogen bond [O···O = 2.7638 (13) Å], two intermolecular bonds of this type [O···O = 2.7708 (13) and 2.7730 (12) Å]. This study illustrates both the similarity between the conformations of furanose, 1,3-dioxolane and 1,3-dioxane rings in analogous isopropylidene-substituted carbohydrate structures and the only negligible influence of the presence of a 1,3-dioxane ring on the conformations of furanose and 1,3-dioxolane rings. In addition, in comparison with reported analogs, replacement of the –CH_2OH group at the C1-furanose position by another group can considerably affect the conformation of the 1,3-dioxolane ring.

Comment

The title isopropylidene derivatives of L-sorbofuranose, namely 2,3:4,6-di-*O*-isopropylidene-*α*-L-sorbofuranose, (I), and 2,3-*O*-isopropylidene-*α*-L-sorbofuranose, (II), are useful intermediates in organic synthesis. They have been used as starting materials for the stepwise synthesis of 1-deoxynojirimycin (Beaupere *et al.*, 1989), the 6,6-difluoro analog (Szarek *et al.*, 1997) and *N*-butyl-1-deoxynojirimycin (*N*-Bu DNJ, Zavesca®) (Boucheron *et al.*, 2005; Godin *et al.*, 2002), known as a very efficient glycosidase inhibitor used, *inter alia*, as a therapeutic agent in the treatment of lysosomal disease. In the context of studies on the synthesis of imino-sugar derivatives related to nojirimycin and mannojirimycin, we have prepared (I) from L-sorbose using acetone as an isopropylidenation agent and concentrated sulfuric acid as a catalyst. Subsequent selective acid hydrolysis of the 4,6-*O*-isopropylidene group in (I) afforded the monoisopropylidene-substituted compound (II).



(I)



(II)

The molecular structures of (I) and (II) are illustrated in Figs. 1 and 2, respectively [the numbering of atoms corresponds to the numbering according to the IUPAC Nomenclature of Carbohydrates (McNaught, 1996)]. The puckering parameters (Cremer & Pople, 1975) Q = 0.250 (2) Å and φ = 112.2 (6)°, and the relevant torsion angles (see Table 3) are indicative of an E_3 (E_{O3}) conformation for the O2/C2/C3/O3/C7 five-membered 1,3-dioxolane ring in (I). Considering the values for (I) of the relevant torsion angles (Table 3) and the puckering parameters Q = 0.370 (3) Å and φ = 127.0 (4)°, the five-membered O5/C2–C5 furanose ring adopts a $^4T_3$ ($^{C5}T_{C4}$)

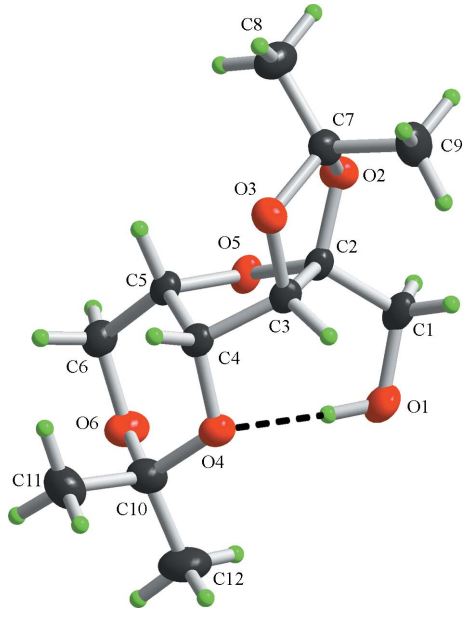


Figure 1
A view of (I), showing the atom-numbering scheme. Displacement ellipsoids are shown at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The intramolecular O—H···O hydrogen bond is shown as a dashed line.

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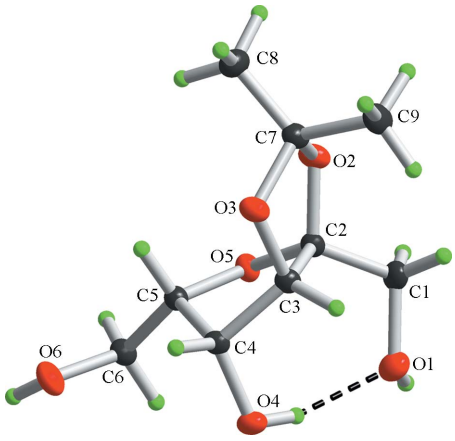

Figure 2
A view of (II), showing the atom-numbering scheme. Displacement ellipsoids are shown at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The intramolecular O—H···O hydrogen bond is shown as a dashed line.

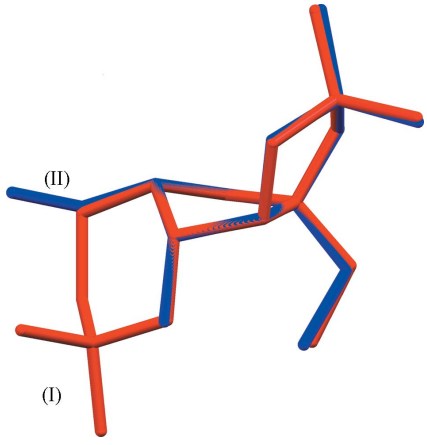

Figure 3
A projection of (I) (red in the online version of the paper) and (II) (blue) with the furanose ring fitted as a common fragment. H atoms have been omitted for clarity.

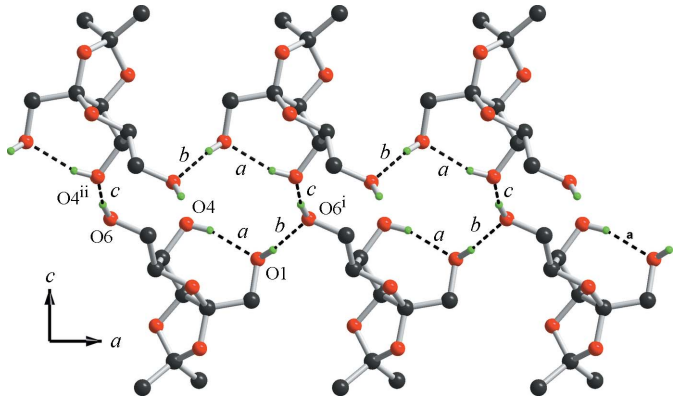

Figure 4
The hydrogen bonding in (II) depicted as dashed lines. H atoms not involved in the strong hydrogen bonds have been omitted for clarity. Symmetry codes and geometric details are listed in Table 2.

conformation, with atom C4 lying in the *exo* and C5 the *endo* direction with respect to the O5/C2/C3 reference plane. Based on the values of relevant torsion angles (Table 3) and the puckering parameters Q = 0.509 (3) Å, φ = 300.0 (19)° and θ = 8.7 (3)°, the O4/C4–C6/O6/C10 six-membered 1,3-dioxane ring adopts an almost ideal ${}^{O}C_3$ (${}^{O4}C_{C6}$) conformation slightly shifted to the E_5 direction. Similarly, for compound (II), the puckering parameters Q = 0.2810 (11) Å and φ = 110.4 (2)°, and the relevant torsion angles (Table 3) are indicative of an E_3 (E_{O3}) conformation for the O2/C2/C3/O3/C7 five-membered 1,3-dioxolane ring. Analogously, considering the values of the relevant torsion angles (Table 3) and the puckering parameters Q = 0.3958 (11) Å and φ = 123.07 (16)°, the five-membered O5/C2–C5 furanose ring adopts a ${}^{4}T_3$ (${}^{C5}T_{C4}$) conformation.

To date, only a few crystal structures of this general type have been described. Among them, the most closely related structure is 2,3:4,6-di-*O*-isopropylidene-α-L-*xylo*-hex-2-ulosonic acid (2,3:4,6-di-*O*-isopropylidene-2-keto-L-gulonic acid) [CSD (Allen, 2002) refcode DIPKGA; Takagi & Jeffrey, 1978]. Related structures include 1-phthalimido-1-deoxy-2,3:4,6-di-*O*-isopropylidene-α-L-sorbofuranose (refcode PHISOR; Glass & Johnson, 1976), *cis*-6-(2-deoxy-3,5-*O*-isopropylidene-1,2-isopropylidenedioxy-β-L-*xylo*-furanosyl)-2,3-dimethyl-1,2,5-oxadiazinane (refcode XAKKUP; Gravestock *et al.*, 2000) and [2*R*,3*S*,4*S*,5*S*,5(2*S*,3*S*,4*R*,5*S*)]-5-(2,3,4-trihydroxy-5-hydroxymethyl-2,3:4,5′-di-*O*-isopropylidene-2-tetrahydrofuranyl)-4-methyl-2-phenyltetrahydrofuran-3-carbaldehyde (refcode TEZHAI; Kollmann *et al.*, 2007) which have the exocyclic –CH_2OH group replaced by a more complicated organic functionality and, finally, (2,3-*O*-isopropylidene-α-L-sorbofuranose)trimethylplatinum(IV) tetrafluoroborate (refcode GOZJEK; Junicke *et al.*, 1999) which is a metal–carbohydrate complex where 2,3-*O*-isopropylidene-α-L-sorbofuranose represents a tridentate ligand coordinated to the Pt^{IV} centre *via* the hydroxyl groups at the C1, C4 and C6 positions.

A comparison of (I) and (II) with these structures shows only small differences in the conformation of the furanose ring. Only TEZHAI exhibits the ${}^{4}E$ (C4 furanose atom in an *endo* direction) conformation, while the ${}^{4}T_3$ conformation was observed for the other structures. Conformational similarity can also be seen for the 1,3-dioxane ring in (I) and in related structures. Thus, in (I), PHISOR, TEZHAI and DIPKGA, the ${}^{O}C_3$ conformation is slightly distorted to the E_5 direction, while a slight shift in the ${}^{4}H_5$ direction is observed for XAKKUP. Regarding the 1,3-dioxolane ring, its conformation is considerably affected by the substitution at the C1 furanose position (–CH_2OH *versus* another substituent). In this respect, the 1,3-dioxolane ring in (I), (II) and GOZJEK adopts the E_3 (O3 atom in an *endo* direction) conformation, while other conformations observed are ${}^{4}T_3$ (for TEZHAI and XAKKUP), ${}^{3}E$ (for DIPKGA) and ${}^{4}T_3$ shifted halfway to the ${}^{4}E$ direction (for PHISOR).

Although the presence of a 1,3-dioxane ring fused to a furanose ring at the 4,6-positions imposes some conformational rigidity on (I), its influence on the conformations of the furanose (in a significant shift of $E_3 \rightarrow {}^{4}T_3$) and 1,3-dioxolane rings is, as seen from comparison with (II), negligible (see Fig. 3). The most dramatic change in the conformation is

apparent in the C2—C1—O1—H1 torsion angle, which has values of 8 and 127° for (I) and (II), respectively.

The hydrogen-bonding patterns are very different in the two compounds. For (I), there is one strong intramolecular O—H···O hydrogen bond (Fig. 1) and some weak intermolecular C—H···O hydrogen bonds (see Table 1 for details). For (II), there are strong O—H···O hydrogen bonds, one intramolecular (denoted as *a* in Table 2) and two intermolecular (*b* and *c*), together with other weak intermolecular C—H···O hydrogen bonds (Table 2). On the first-level graph-set, defined by Bernstein *et al.* (1995) and Grell *et al.* (1999), string $S(7)$ (bond *a*) and chains $C(8)$ (*b*) and $C(6)$ (*c*) were identified. On the second-level graph-set, chains $C_2^2(9)$ and $C_2^2(14)$ formed by hydrogen bonds *b* and *c* could be recognized. On the third-level graph set, rings $R_5^5(21)$ can be found (*a*, *b* and *c*; see Fig. 4 and Table 2).

Experimental

Compound (I) was prepared according to a slight modification of the procedure of Slobodin (1947) (fast neutralization under efficient cooling using NaOH instead of $KHCO_3$; four extractions with ethyl acetate instead of 11 extractions with $CHCl_3$ was deemed sufficient). Compound (II) was obtained by heating (I) in 60% acetic acid at 348 K for 40 min, followed by evaporation of the solvent under reduced pressure and crystallization of the product from a mixture of ethyl acetate and hexane. The analytical data for (I) and (II) were in accordance with those published previously (Szarek *et al.*, 1997; Beaupere *et al.*, 1989). Colourless single crystals of a quality adequate for diffraction analysis were obtained by slow crystallization of (I) from a 2:1 (*v*/*v*) mixture of diethyl ether and *n*-hexane under moderate cooling in a refrigerator. Analogous crystallization using a mixture of ethyl acetate and *n*-hexane (2:1 *v*/*v*) afforded suitable crystals of (II).

Compound (I)

Crystal data

$C_{12}H_{20}O_6$
M_r = 260.28
Orthorhombic, $P2_12_12_1$
a = 6.7203 (16) Å
b = 9.286 (2) Å
c = 21.972 (5) Å
V = 1371.1 (6) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 153 (2) K
0.78 × 0.48 × 0.32 mm

Data collection

Bruker SMART CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.440, T_{max} = 0.969
15054 measured reflections
1483 independent reflections
1236 reflections with $I > 2\sigma(I)$
R_{int} = 0.067

Table 1
Hydrogen-bond geometry (Å, °) for (I).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···O4	0.84	2.17	2.933 (3)	151
C1—H1*A*···O5^{i}	0.99	2.59	3.551 (3)	165
C4—H4···O1^{ii}	1.00	2.49	3.278 (3)	135
C8—H8*A*···O5^{iii}	0.98	2.50	3.462 (3)	166

Symmetry codes: (i) $x+\frac{1}{2}, -y+\frac{3}{2}, -z$; (ii) $x-1, y, z$; (iii) $x-\frac{1}{2}, -y+\frac{3}{2}, -z$.

Table 2
Hydrogen-bonding geometry for (II) (Å, °).

Label	*D*—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
a	O4—H4···O1	0.84	1.95	2.7638 (13)	164
b	O1—H1···O6^{i}	0.84	1.94	2.7708 (13)	168
c	O6—H6···O4^{ii}	0.84	1.95	2.7730 (12)	165
d	C8—H8*A*···O5^{iii}	0.98	2.45	3.3682 (15)	155
e	C9—H9*C*···O3^{iv}	0.98	2.55	3.4508 (16)	154

Symmetry codes: (i) $x+1, y, z$; (ii) $-x+1, y-\frac{1}{2}, -z+\frac{1}{2}$; (iii) $x-\frac{1}{2}, -y+\frac{1}{2}, -z$; (iv) $x+\frac{1}{2}, -y+\frac{3}{2}, -z$.

Table 3
Selected torsion angles (°) for (I) and (II).

	(I)	(II)
O2—C2—C3—O3	13.8 (2)	16.32 (11)
C7—O3—C3—C2	−25.6 (2)	−29.03 (10)
C3—O3—C7—O2	27.7 (2)	30.81 (11)
C2—O2—C7—O3	−18.3 (2)	−19.73 (12)
C7—O2—C2—C3	2.7 (2)	2.05 (12)
O5—C2—C3—C4	10.8 (2)	13.88 (11)
C2—C3—C4—C5	−29.7 (2)	−32.62 (10)
C3—C4—C5—O5	38.5 (2)	40.80 (10)
C2—O5—C5—C4	−33.6 (2)	−34.03 (10)
C5—O5—C2—C3	14.5 (2)	12.61 (11)
O4—C4—C5—C6	44.4 (3)	
C4—C5—C6—O6	−45.0 (3)	
C10—O6—C6—C5	53.1 (3)	
C6—O6—C10—O4	−59.2 (3)	
C4—O4—C10—O6	59.8 (3)	
C10—O4—C4—C5	−52.7 (3)	

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.037
$wR(F^2)$ = 0.098
S = 1.00
1483 reflections
168 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}

Compound (II)

Crystal data

$C_9H_{16}O_6$
M_r = 220.22
Orthorhombic, $P2_12_12_1$
a = 6.7321 (3) Å
b = 9.1945 (5) Å
c = 17.0658 (9) Å
V = 1056.34 (9) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.12 mm^{-1}
T = 153 (2) K
1.08 × 1.06 × 0.54 mm

Data collection

Bruker SMART CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.690, T_{max} = 0.940
19061 measured reflections
2219 independent reflections
2019 reflections with $I > 2\sigma(I)$
R_{int} = 0.037

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.031
$wR(F^2)$ = 0.082
S = 1.00
2219 reflections
141 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.27 e Å^{-3}
$\Delta\rho_{min}$ = −0.23 e Å^{-3}

In the absence of significant resonant scattering, the Friedel-equivalent reflections were merged for compounds (I) and (II), and therefore the absolute configuration of the molecules in (I) and (II) were not determined by diffraction techniques. However, the absolute configuration at chiral atoms C2, C3, C4 and C5 in (I) and (II) was assigned on the basis of the known arrangement in L-sorbofuranose derivatives, because isopropylidenation at O4 and O6 does not affect the arrangements of atoms O3, O4 and O5 with respect to the furanose ring in (I) and acetonation at O2 and O3 affords preferentially the *cis*-2,3-*O*-isopropylidenated product with an α configuration at anomeric atom C2. For secondary H atoms, the C—H distance was fixed at 0.99 Å and for tertiary at 1.00 Å. For the methyl groups, the C—H distances (0.98 Å) and C—C—H angles (109.5°) were kept fixed. The O—H distances (0.84 Å) and C—O—H angles (109.5°) were also fixed. Isotropic displacement parameters were constrained to $U_{iso}(H) = 1.2U_{eq}(C)$, $1.5U_{eq}(C_{methyl})$ and $1.5U_{eq}(O)$.

For both compounds, data collection: *SMART* (Bruker, 2003); cell refinement: *SAINT* (Bruker, 2003); data reduction: *SAINT* and *SADABS* (Sheldrick, 2003); program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXTL*; molecular graphics: *DIAMOND* (Brandenburg, 2008); software used to prepare material for publication: *SHELXTL*.

The financial support of this work by the Scientific Grant Agency (VEGA, Slovak Academy of Sciences, grant No. 2/0128/08) and by the Slovak Research and Development Agency (APVV, Ministry of Education, grant No. APVV-0366–07) is gratefully acknowledged.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG3193). Services for accessing these data are described at the back of the journal.

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