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Conformations of methyl 2,5-di-*O*-acetyl-β-D-glucofuranosidurono-6,3-lactone and 1,2,5-tri-*O*-acetyl-β-D-glucofuranurono-6,3-lactone in the crystal structure and in solution

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Abstract—The single-crystal X-ray diffraction and high-resolution ^{1}H and ^{13}C NMR spectral data for methyl 2,5-di-*O*-acetyl-β-D-glucofuranosidurono-6,3-lactone and 1,2,5-tri-*O*-acetyl-β-D-glucofuranurono-6,3-lactone are reported. The lactones were synthesized as byproducts of reactions carried out to obtain methyl 1,2,3,4-tetra-*O*-acetyl-D-glucopyranuronate. The conformations of these lactones in the crystal structure and in solution are discussed. A $^1T_2$-like conformation was found to be the preferred form for these lactones in both the crystal lattice and in solution.

Keywords: β-D-Glucofuranurono-6,3-lactone; X-ray diffraction; Single-crystal; Coupling constant; Torsion angle; $^1T_2$ Conformation; Anomeric effect

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1. Introduction

Despite their ubiquity in biological structures, furanosides have received much less attention than pyranosides with regards to conformational analysis. This is because different conformations of five-membered rings have quite similar energies,[1] whereas six-membered rings are normally present in a single, low-energy chair conformation. Therefore, conformations of pyranosides in solution are easily identified, for example, by NMR techniques, which is not the case with furanosides.

Furanose rings exist as mixtures of ideal envelope (*E*) conformations with four atoms in a plane or twist (*T*) forms with three atoms in a plane (Fig. 1). Since such a description may be inadequate for intermediate conformations, a particular furanose ring conformer is usually described by two parameters: the amplitude of pseudorotation τ_m,[2,3] defined as an upper limit for the endocyclic torsion angle (maximum torsion angle θ_m[4]) and the pseudorotational phase angle (*P*).[2–4] The pseudorotation phase angle *P* is calculated from the endocyclic torsion angles, θ_0, θ_1, θ_2, θ_3, and θ_4, according to Eq. 1:[4]

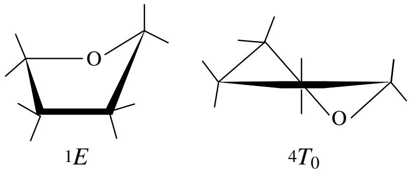

Figure 1. Examples of furanose ring conformations: *left*, envelope; *right*, twist.

$$\tan P = [(\theta_4 + \theta_1) - (\theta_3 + \theta_0)]/[2\theta_2(\sin 36^\circ + \sin 72^\circ)] \quad (1)$$

The phase angle *P* is defined to be 0° when θ_2 is maximally positive, which corresponds to the $^3T_2$ conformation and returns to the same point at $P = 360^\circ$ (Fig. 2).

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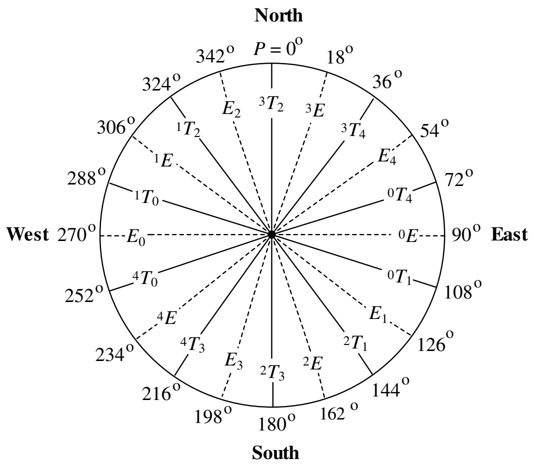


Figure 2. Pseudorotational itinerary for a D-aldofuranose ring.

The five torsion angles are related from the phase angle P by Eq. 2:[4]

$$\theta_j = \theta_m \cos(P + j\delta) \tag{2}$$

where $j = 0, 1, 2, 3$, or 4, $\delta = 720°/5 = 144°$ and θ_m is the maximum torsion angle[4] (the amplitude of pseudorotation τ_m[2,3]), derived by setting $j = 0$, Eq. 3:[4]

$$\theta_m = \theta_0 / \cos P \tag{3}$$

Two opposite conformers of the furanose ring, in which the signs of all torsion angles are reversed (e.g., $^3T_2$ and $^2T_3$ forms), exist in equilibrium in solution. One of these opposite forms is present in the northern hemisphere of the pseudorotational wheel, the other in the southern hemisphere. Interconversion between such conformers occurs via the eastern or western pathway of the pseudorotation itinerary, which depends on the identity and orientation of the substituents on the ring.[2]

Conformational analysis of a furanose ring based on NMR studies is complicated because two furanose conformers are equilibrating rapidly on the NMR scale, and averaging of coupling constants occurs. Thus, using ^{1}H–^{1}H NMR coupling constants, we can usually predict the region of the pseudorotational itinerary in which the favored conformers will be found. For example, the coupling constants of the β-D-galactofuranose derivatives described in the literature, like the majority of their furanoid solution geometries, fall within the $^4E \leftrightharpoons {}^4T_0 \leftrightharpoons E_0 \leftrightharpoons {}^1T_0$ range, that is, in the western part of the pseudorotational itinerary.[5] $^3J_{H,H}$ data, though not indicating any particular conformation, can be successfully used for making conformational comparisons between different furanosides,[6] since they provide information about the axial or equatorial preferences of substituents, for example, an aglycone. Computational investigations of furanoid ring conformations often confirm NMR-derived data, but they also suggest, which region of the pseudorotational itinerary is the most favored one.[5] Combining NMR studies with theoretical calculations seems to be an accurate methodology for determining the preferred conformers of the furanose ring.[2,7] A least-squares minimization program, PSEUROT 6.2,[8] with the use of intracyclic ring $^3J_{H,H}$ data, calculates the N/S ratio and provides P values from which the ring forms can be determined.[2]

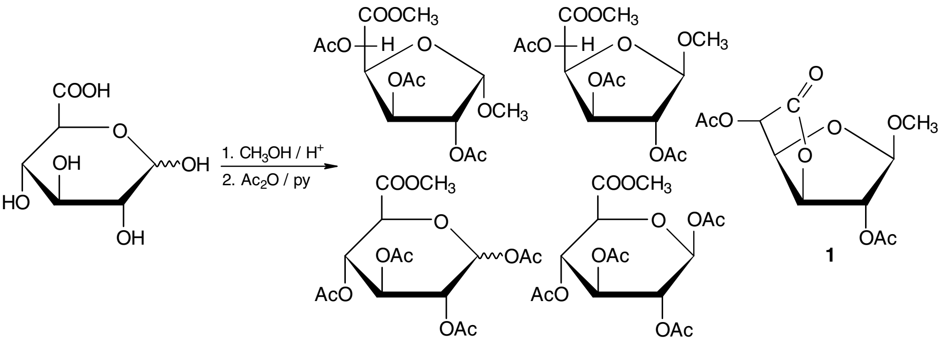
Important findings concerning the anomeric effect in a series of *N*-, *C*-, *S*-, and *O*-'furanosides' were obtained when a tetrahydrofuran ring was conformationally restricted by a rigid norbornane skeleton attached at carbons C-3 and C-4.[9] The norbornane skeleton maintains the 'furanoside' ring carbons in one plane, allowing only the ring oxygen to move above or below the plane. Such norbornyl 'furanosides' can exist in two conformations only—^0E and E_0—and the anomeric effect is a major factor influencing the $^0E \leftrightharpoons E_0$ conformational equilibrium.

Investigation of furanosides and their derivatives by X-ray crystallography is a precise way of determining their structures and conformations. However, in the case of the furanoid ring, this analysis is restricted to the crystal structure. Since the energies of furanose ring conformations are similar, the conformation of a furanoside enclosed in a crystal lattice may differ significantly from that adopted in solution.

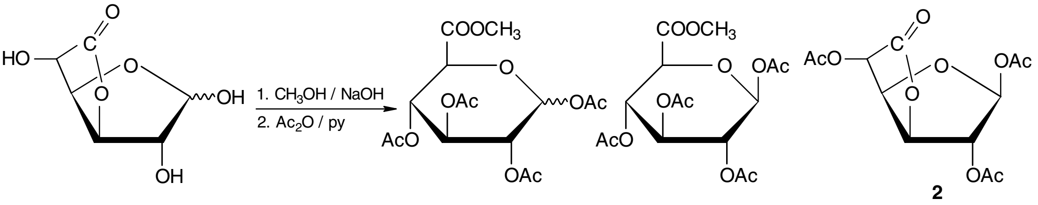
Methyl 2,5-di-*O*-acetyl-β-D-glucofuranosidurono-6,3-lactone (**1**) and 1,2,5-tri-*O*-acetyl-β-D-glucofuranurono-6,3-lactone (**2**) were obtained as byproducts of two independent procedures, which were examined in order to obtain methyl 1,2,3,4-tetra-*O*-acetyl-D-glucopyranuronate, the versatile intermediate in the synthesis of glucopyranuronates modified at the anomeric carbon. We found the conformational studies of these lactones interesting. The present paper reports on their 3D molecular structures as determined by X-ray crystallography, and compares their conformations in the crystal with those in solution as revealed by high-resolution NMR spectroscopy.

2. Results and discussion

The first procedure that we examined to obtain methyl 1,2,3,4-tetra-*O*-acetyl-D-glucopyranuronate involved the acid-catalyzed esterification of glucuronic acid with methanol,[10] followed by acetylation of the hydroxyl groups. This yielded five products, among them being methyl 2,5-di-*O*-acetyl-β-D-glucofuranosidurono-6,3-lactone (**1**) (Scheme 1). But since this procedure was not very effective, we tested another one using D-glucurono-6,3-lactone as the starting compound. This was transesterified with methanol in the presence of basic catalysts to produce a mixture of methyl D-glucopyranuronates,[11] which when acetylated, yielded good quantities of methyl 1,2,3,4-tetra-*O*-acetyl-D-glucopyranuronates



Scheme 1.



Scheme 2.

(Scheme 2). We and others have used this method with success.[12,13] However, in one preparative run we obtained 1,2,5-tri-*O*-acetyl-β-D-glucofuranurono-6,3-lactone (**2**) as a byproduct; this was probably because the duration of the first reaction step was too short.

Both lactones reported here can be readily synthesized directly from D-glucurono-6,3-lactone by methyl glycosidation,[14] followed by acetylation (**1**) and by straightforward acetylation (**2**).

2.1. Structures of 1 and 2 in crystal lattices: discussion

Examination of the molecular structure of methyl 2,5-di-*O*-acetyl-β-D-glucofuranosidurono-6,3-lactone (**1**) and 1,2,5-tri-*O*-acetyl-β-D-glucofuranurono-6,3-lactone (**2**) has revealed that in the crystalline state both molecules have bicyclic structures, consisting of fused furanose (O-4/C-1/C-2/C-3/C-4) and five-membered lactone (O-3/C-3/C-4/C-5/C-6) rings (Fig. 3). Both furanoid

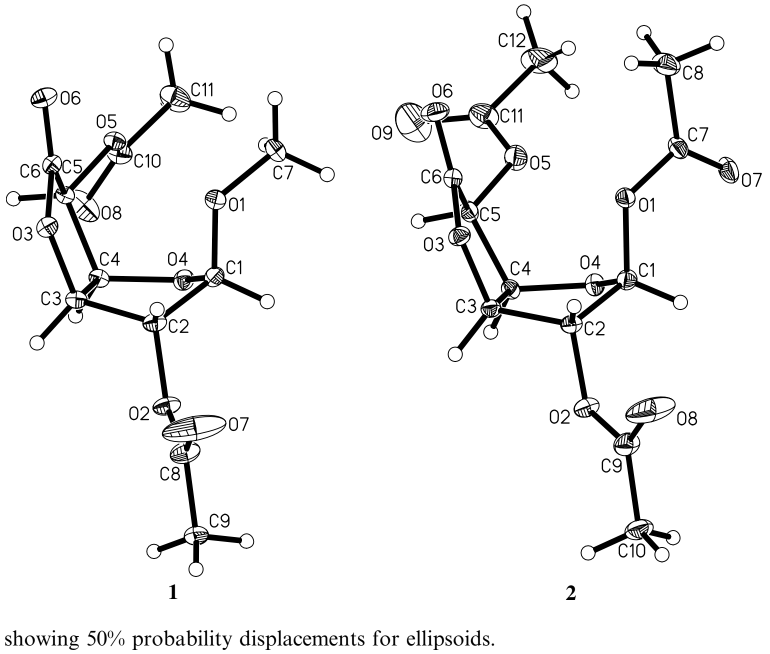


Figure 3. Structures of **1** and **2** showing 50% probability displacements for ellipsoids.

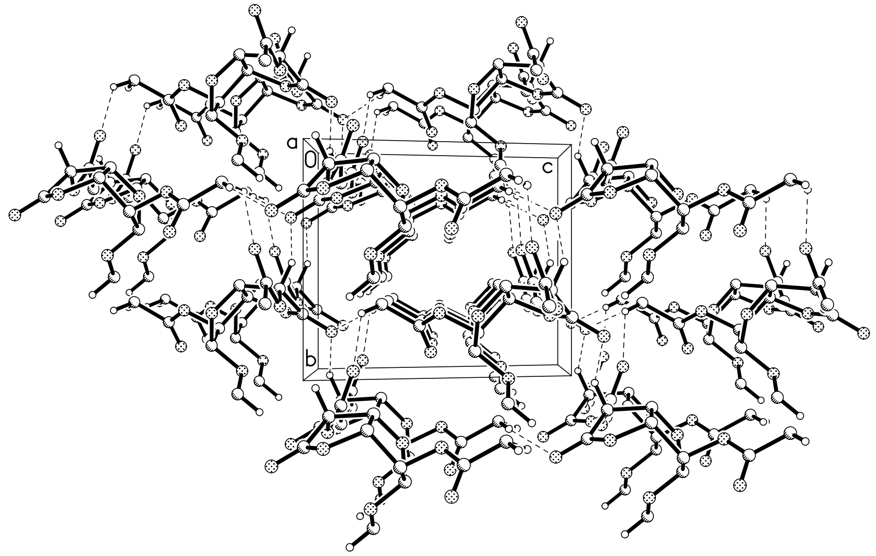


Figure 4. Molecular packing of **1** (view along *b*-axis). The hydrogen atoms not involved in C–H· · ·O interactions have been omitted.

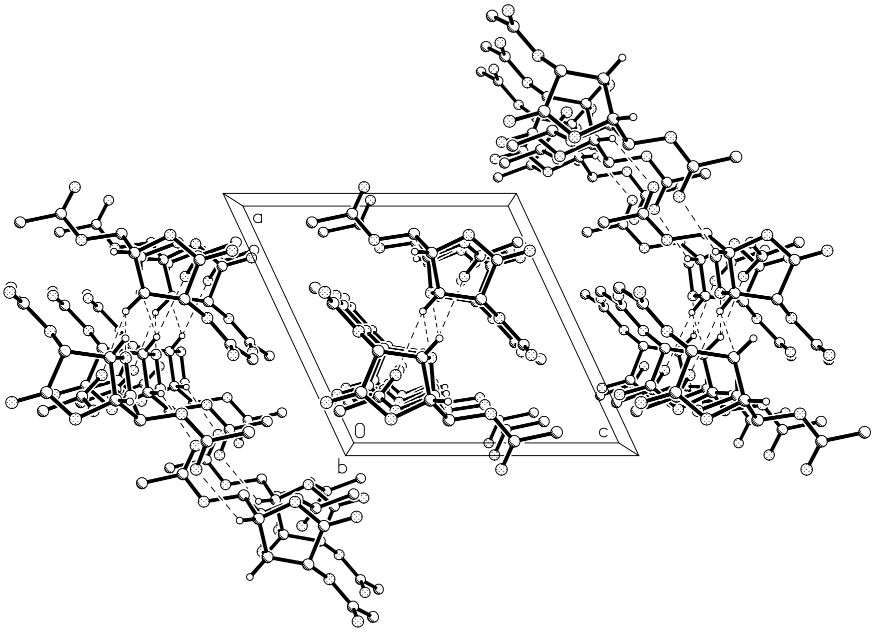


Figure 5. Molecular packing of **2** (view along *b*-axis). The hydrogen atoms not involved in C–H· · ·O interactions have been omitted.

rings adopt conformations close to the $^{1}T_{2}$ form[15,16] with ring-puckering parameters[17,18] $\theta = 0.348(4)$ Å and $\phi = 227.8(7)°$ for compound **1** and $\theta = 0.309(5)$ Å and $\phi = 230.0(9)°$ for compound **2**, pseudorotation parameters[3] $P = 315.1(4)°$ and $\tau_{\mathrm{m}} = 37.7(3)°$ for the C-2–C-3 reference bond in **1** and $P = 316.7(4)°$ and $\tau_{\mathrm{m}} = 33.8(2)°$ for the C-2–C-3 reference bond in **2**, and delta parameter[19] $\Delta = 630.2°$ for **1** and $\Delta = 633.5°$ for **2**.

Small differences are visible in the lactone ring conformations of **1** and **2**. The lactone ring in **1** exhibits an almost envelope conformation with carbon C-5 shifted from the four-atom plane (^{5}E) with ring-puckering parameters[17,18] $\theta = 0.202(4)$ Å and $\phi = 291.6(12)°$, pseudorotation parameters[3] $P = 25.3(8)°$ and $\tau_{\mathrm{m}} = 21.6(3)°$ for the C-4–C-5 reference bond, and delta parameter[19] $\Delta = 50.5°$. The lactone ring in **2** is twisted around the C-4–C-5 bond and adopts an almost $^{5}T_{4}$ conformation with ring-puckering parameters[17,18] $\theta = 0.184(5)$ Å and $\phi = 274.9(14)°$, pseudorotation parameters[3] $P = 7.2(9)°$ and $\tau_{\mathrm{m}} = 19.3(3)°$ for the C-4–C-5 reference bond, and delta parameter[19] $\Delta = 14.4°$. These conformations of lactones **1** and **2**, respectively, correspond to forms ${}^{3}E$ and ${}^{3}T_2$ on the pseudorotational itinerary.

The furanose ring conformations found in the crystal structures of **1** and **2** seem to be typical for β-D-furanurono-6,3-lactones and their derivatives. To our knowledge, β-D-mannofuranurono-6,3-lactone,[20] β-D-glucofuranurono-6,3-lactone[21] and 5-*O*-pivaloyl-β-D-glucofuranurono-6,3-lactone[22] all adopt ${}^{1}T_2$-like forms in the crystal lattice. Methyl β-D-glucofuranosidurono-6,3-lactone,[14,21] one of the two conformers of methyl 2-*O*-acetyl-5-*O*-pivaloyl-β-D-glucofuranosidurono-6,3-lactone[21] and methyl 2-acetamido-2-deoxy-β-D-glucofuranosidurono-6,3-lactone,[23] adopted identical or at least very similar conformations in their crystal structures. Even though all the above-mentioned furanurono-6,3-lactones differ significantly in the substituents and their (gluco/manno) orientation, all of them prefer a ${}^{1}T_2$-like form in the crystal state. Why, then, is the ${}^{1}T_2$ geometry so advantageous for these compounds? Furanurono-6,3-lactones have a bicyclic structure with two five-membered rings fused at carbons C-3 and C-4; therefore, they are not as flexible as free furanoses or furanosides. Such a system of fused rings forces atoms C-2, C-3, C-4, and O-4 to lie in one plane, whereas only carbon C-1 is able to move freely above or below this plane. Carbons C-3 and C-4 are the most restricted in this structure, whereas atoms C-2 and O-4 have some freedom of movement. Although the bicyclic structure of furanurono-6,3-lactones is not quite rigid, the ${}^{1}E$ or E_1 forms seem to be the preferred ones. From these two conformations, the ${}^{1}E$ form should be strongly preferred by β-D-furanurono-6,3-lactones, because it allows the anomeric hydroxy, methoxy, or acetoxy groups to be placed pseudoaxially. In the case of the E_1 form, these groups are oriented pseudoequatorially. This criterion arises from the *endo* anomeric effect, an important factor influencing both pyranose and furanose ring conformations. The ${}^{1}T_2$ conformation observed in the crystal structure of β-D-furanurono-6,3-lactones is slightly twisted around the C-1–C-2 bond in comparison with the ${}^{1}E$ form, but still allows the anomeric O-substituted groups to be oriented pseudoaxially.

Very similar geometries lying within the ${}^{1}T_0 \rightleftharpoons {}^{1}E \rightleftharpoons {}^{1}T_2$ range were found for β-D-galactofuranose structures in the CCDF data file.[5] Although the latter structures are devoid of a lactone ring, this does not significantly change their crystal conformations in comparison with β-D-furanurono-6,3-lactones. Crystallographic analysis of isomeric methyl 3,6-anhydrohexofuranosides showed that the furanoid ring of β anomers adopts a conformation intermediate between the E_2 and ${}^{1}T_2$ forms.[24] Analogous α isomers exhibited a related but opposite geometry intermediate between the ${}^{2}E$ and ${}^{2}T_1$ forms. These results demonstrate that the ${}^{1}T_2$- and ${}^{1}T_2$-like conformations are also advantageous for β-D-furanoses and furanosides in the crystal structure. Additionally, these results confirm that the anomeric effect is the main factor determining the conformation of the furanoid ring.

2.2. Structures of 1 and 2 in solution: discussion

The ^{1}H NMR spectra of lactones **1** and **2** presented in this paper, as well as that of methyl β-D-glucofuranosidurono-6,3-lactone (**3**, Fig. 6) described in the literature,[14] are very characteristic and almost identical. They consist of two singlets, two doublets and one doublet of doublets, which correspond to the five protons of the furanoid ring (Table 1). These three spectra differ in the chemical shifts of the furanoid ring protons, owing to the different substituents attached to the sugar ring. However, their geometries must be similar, because the

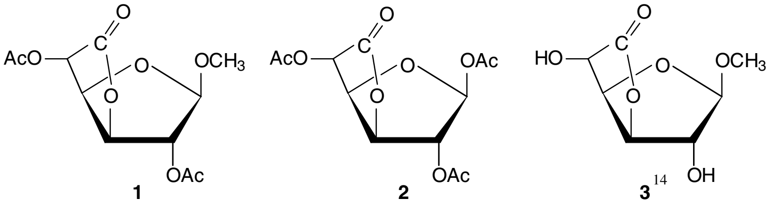


Figure 6. Discussed lactones **1**–**3**.

Table 1. Chemical shifts (ppm) and ^{1}H–^{1}H coupling constants (Hz) of the protons in the ^{1}H NMR spectra (CDCl$_3$) of lactones **1**–**3**

	H-1	H-2	H-3	H-4	H-5	OMe	OAc	$J_{3,4}$	$J_{4,5}$
1	5.02 (s)	5.23 (s)	5.00 (d)	5.17 (dd)	5.26 (d)	3.41 (s)	2.27 (s) 2.13 (s)	4.88	7.33
2	6.19 (s)	5.32 (s)	5.09 (d)	5.26 (dd)	5.24 (d)	—	2.18 (s) 2.15 (s) 2.08 (s)	4.88	7.32
3[14]	4.95 (s)	4.20 (s)	4.83 (d)	4.94 (dd)	4.52 (d)	—	—	4.88	5.49

structures of their proton signals are identical: they have the same ^1H–^1H coupling constants. The basic ^1H NMR and COSY spectra of lactones **1** and **2** do not indicate exactly which proton is responsible for which signal. We therefore produced the heteronuclear single-quantum (gHSQC) and multi-bond correlated spectra (gHMBC) presented in Figures 7 and 8. Analysis of such spectra for lactones **1** and **2** shows that the two singlets correspond to protons H-1 and H-2, the two doublets to protons H-3 and H-5, and the doublet of doublets to proton H-4.

As was mentioned above, the chemical shifts of the furanoid ring protons in **1**–**3** differ, depending on the O-substituent. Thus, the H-1 proton signal is significantly deshielded when lactone **2** is compared with **1** and **3** ($\Delta\delta > 1$ ppm). This is due to the 1-OAc group influencing the H-1 proton. Inversely, the same 1-OAc group moves the C-1 carbon signal to higher field in

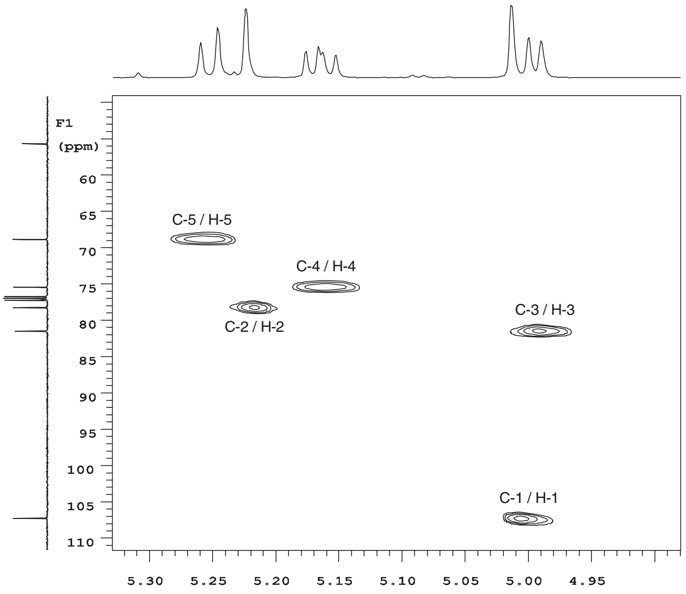


Figure 7. The heteronuclear single-quantum correlated spectrum (gHSQC) for lactone **1**.

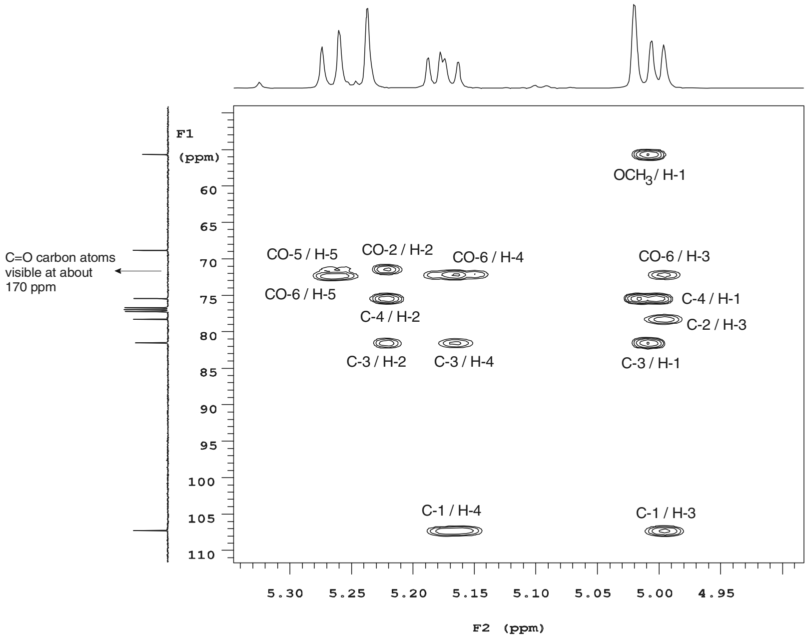


Figure 8. The heteronuclear multi-bond correlated spectrum (gHMBC) for lactone **1**.

Table 2. Chemical shifts (ppm) of the carbon atoms in the ^{13}C NMR spectra ($CDCl_3$) of lactones **1**–**3**

	C-1	C-2	C-3	C-4	C-5	C=O	CH_3(OMe)	CH_3(OAc)
1	107.29	78.29	81.54	75.46	68.90	169.94 (C_6) 169.48 169.20	55.74	20.60 20.21
2	98.55	78.03	81.58	76.13	68.03	170.02 (C_6) 169.32 (C_5) 169.04 (C_2) 168.70 (C_1)	—	20.73 20.51 19.87
3[14]	110.59	77.59	83.24	77.05	69.05	175.67	—	—

Table 3. Crystal data and structure refinement for **1** and **2**

	1	**2**
Empirical formula	$C_{11}H_{14}O_8$	$C_{12}H_{14}O_9$
Formula weight	274.22	302.23
Temperature (K)	293(2)	293(2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1$	$P2_1$
Unit cell dimensions		
a (Å)	9.318(2)	10.267(2)
b (Å)	7.906(2)	7.4740(10)
c (Å)	9.688(2)	10.387(2)
β (°)	112.10(3)	115.01(3)
V (Å^3)	661.3(3)	722.3(2)
Z	2	2
D_{calcd} (Mg m^{-3})	1.377	1.390
Absorption coefficient (mm^{-1})	0.120	0.122
$F(000)$	288	316
Crystal size (mm)	0.5 × 0.4 × 0.3	0.5 × 0.5 × 0.3
Θ Range for data collection (°)	2.27–25.00	2.16–25.00
Limiting indices	$-10 \leqslant h \leqslant 10$, $0 \leqslant k \leqslant 9$, $-11 \leqslant l \leqslant 0$	$-12 \leqslant h \leqslant 11$, $0 \leqslant k \leqslant 8$, $0 \leqslant l \leqslant 12$
Reflections collected/unique	1331/1255 [$R_{int} = 0.0293$]	1452/1375 [$R_{int} = 0.0468$]
Completeness $2\Theta = 50.00°$ (%)	99.7	99.8
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	1255/1/176	1375/1/191
Goodness-of-fit on F^2	1.028	0.884
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0438$ $wR_2 = 0.1051$	$R_1 = 0.0419$ $wR_2 = 0.0972$
R indices (all data)	$R_1 = 0.0732$ $wR_2 = 0.1175$	$R_1 = 0.0862$ $wR_2 = 0.1081$
Absolute structure parameter	0(2)	1(2)
Extinction coefficient	0.034(9)	0.051(7)
Largest diff. peak and hole (e Å^{-3})	0.349 and −0.234	0.178 and −0.196

comparison with **1** and **3** ($\Delta\delta > 8$ ppm, Table 2). The lack of *O*-acetyl substituents on carbons C-2 and C-5 in **3** causes the signals of the respective protons to be shielded in comparison with **1** and **2** ($\Delta\delta \sim 1$ ppm for H-2 and $\Delta\delta \sim 0.7$ ppm for H-5). We observed the same deshielding effect of the OAc group for pyranosides.[25] There are no significant differences in the chemical shifts of protons H-3 and H-4 in lactones **1**–**3**, because their chemical surroundings are comparable.

The lack of coupling between protons H-1 and H-2, and between H-2 and H-3 in the ^1H NMR spectra of **1**–**3** gives us important information concerning the H-1–C-1–C-2–H-2 and H-2–C-2–C-3–H-3 torsion angles in the furanoid ring of the lactones discussed by us. These should come within the 80–90° range, as required by the Karplus curve.[26] The respective torsion angles of lactones **1** and **2**, gleaned from the crystallographic data, do in fact lie within this range (Table 5). We can conclude from this agreement that the furanoid ring conformations of lactones **1** and **2** in the crystal and in solution are the same. This appears to be possible because, as we demonstrated earlier, the $^1T_2$-like conformation is advantageous and strongly preferred in the crystal lattice of the β-D-furanurono-6,3-lactones, irrespective of their protective groups and the configuration at carbon C-2. Since the lactones are structurally somewhat restricted, it is most likely that the same form of the furanoid ring found in the crystal is dominant in

Table 4. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **1** and **2**; U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor

1					**2**				
Atom	*x*	*y*	*z*	*U*(eq)	Atom	*x*	*y*	*z*	*U*(eq)
C-1	−5799(5)	−3711(6)	−3776(4)	54(1)	C-1	−2370(5)	−3163(6)	−3999(4)	51(1)
C-2	−7240(4)	−3006(7)	−3639(4)	53(1)	C-2	−1533(4)	−4732(7)	−4134(3)	50(1)
C-3	−6607(4)	−1604(6)	−2514(4)	45(1)	C-3	−2306(4)	−6318(7)	−3848(4)	45(1)
C-4	−5093(4)	−1094(5)	−2680(5)	43(1)	C-4	−3813(5)	−5610(6)	−4217(4)	45(1)
C-5	−3897(4)	−1238(5)	−1106(4)	40(1)	C-5	−4051(4)	−6036(6)	−2919(4)	51(1)
C-6	−4648(4)	−2346(6)	−301(4)	44(1)	C-6	−2576(5)	−6351(6)	−1764(5)	54(1)
O-1	−5149(4)	−4812(4)	−2586(3)	62(1)	O-1	−1806(3)	−2776(4)	−2499(3)	51(1)
O-2	−8133(3)	−2215(4)	−5036(3)	63(1)	O-2	−1768(3)	−4868(6)	−5586(2)	61(1)
O-3	−6187(3)	−2298(4)	−1031(3)	48(1)	O-3	−1649(3)	−6650(4)	−2334(3)	53(1)
O-4	−4855(3)	−2282(4)	−3675(3)	52(1)	O-4	−3779(3)	−3746(4)	−4487(3)	49(1)
O-5	−2467(3)	−1963(4)	−992(3)	47(1)	O-5	−4751(3)	−4620(6)	−2552(3)	75(1)
O-6	−4051(4)	−3111(5)	822(3)	62(1)	O-6	−2227(4)	−6391(6)	−521(3)	82(1)
O-7	−10022(8)	−3886(13)	−5364(8)	216(5)	O-7	−3071(4)	−222(4)	−2992(4)	74(1)
O-8	−1931(5)	445(5)	−1861(6)	96(2)	O-8	310(6)	−3708(11)	−5091(5)	186(4)
C-7	−3846(6)	−5727(7)	−2640(6)	80(2)	O-9	−6143(7)	−6504(12)	−2109(8)	172(3)
C-8	−9524(6)	−2769(9)	−5774(6)	74(2)	C-7	−2287(5)	−1272(7)	−2129(5)	56(1)
C-9	−10306(5)	−1872(7)	−7174(5)	72(2)	C-8	−1737(6)	−1104(10)	−564(5)	87(2)
C-10	−1552(5)	−968(8)	−1417(6)	60(1)	C-9	−749(6)	−4314(8)	−5933(5)	73(2)
C-11	−133(6)	−1818(9)	−1359(7)	91(2)	C-10	−1084(6)	−4511(10)	−7445(5)	84(2)
H-1A	−6043	−4296	−4729	64	C-11	−5767(6)	−4969(11)	−2159(6)	86(2)
H-2A	−7827	−3853	−3330	63	C-12	−6348(9)	−3361(12)	−1754(8)	124(3)
H-3A	−7330	−654	−2694	54	H-1A	−2292	−2135	−4547	61
H-4A	−5150	63	−3060	52	H-2A	−514	−4677	−3475	60
H-5A	−3708	−114	−645	48	H-3A	−2291	−7370	−4404	54
H-7A	−3475	−6495	−1812	120	H-4A	−4504	−6223	−5065	54
H-7B	−3037	−4948	−2588	120	H-5A	−4609	−7142	−3074	61
H-7C	−4151	−6353	−3554	120	H-8A	−2491	−1321	−268	130
H-9A	−11394	−2120	−7542	108	H-8B	−1383	93	−312	130
H-9B	−9885	−2230	−7892	108	H-8C	−969	−1939	−102	130
H-9C	−10153	−677	−7011	108	H-10A	−251	−4247	−7608	125
H-11A	581	−994	−1453	136	H-10B	−1857	−3731	−8013	125
H-11B	−380	−2617	−2161	136	H-10C	−1365	−5732	−7701	125
H-11C	328	−2399	−425	136	H-12A	−6967	−2757	−2611	185
					H-12B	−5441	−2752	−1333	185
					H-12C	−6786	−3367	−1100	185

Table 5. Selected bond lengths (Å), valence angles (°) and torsion angles (°) for **1** and **2**

1		**2**	
Bond lengths	(Å)	Bond lengths	(Å)
C-1–O-1	1.388(5)	C-1–O-1	1.443(5)
C-1–O-4	1.413(6)	C-1–O-4	1.385(6)
C-1–C-2	1.504(6)	C-1–C-2	1.495(6)
C-2–O-2	1.438(5)	C-2–O-2	1.427(4)
C-2–C-3	1.510(6)	C-2–C-3	1.523(7)
C-3–O-3	1.448(4)	C-3–O-3	1.447(5)
C-3–C-4	1.533(6)	C-3–C-4	1.523(6)
C-4–O-4	1.421(5)	C-4–O-4	1.425(5)
C-4–C-5	1.517(5)	C-4–C-5	1.502(6)
C-5–O-5	1.416(4)	C-5–O-5	1.419(5)
C-5–C-6	1.509(6)	C-5–C-6	1.501(6)
C-6–O-6	1.186(5)	C-6–O-6	1.185(5)
C-6–O-3	1.339(4)	C-6–O-3	1.335(5)
Valence angles	(°)	Valence angles	(°)
O-1–C-1–O-4	112.2(3)	O-1–C-1–O-4	109.8(3)
O-1–C-1–C-2	106.5(3)	O-1–C-1–C-2	105.9(3)
O-4–C-1–C-2	104.5(3)	O-4–C-1–C-2	105.8(4)
O-2–C-2–C-1	107.4(3)	O-2–C-2–C-1	107.9(4)
O-2–C-2–C-3	106.9(4)	O-2–C-2–C-3	106.4(4)

Table 5 (*continued*)

1		**2**	
Bond lengths	(Å)	Bond lengths	(Å)
Valence angles	(°)	Valence angles	(°)
C-1–C-2–C-3	102.5(3)	C-1–C-2–C-3	103.0(3)
O-3–C-3–C-2	108.9(4)	O-3–C-3–C-2	107.7(3)
O-3–C-3–C-4	106.8(3)	O-3–C-3–C-4	106.9(3)
C-2–C-3–C-4	104.0(3)	C-2–C-3–C-4	103.8(4)
O-4–C-4–C-5	112.9(3)	O-4–C-4–C-5	114.3(3)
O-4–C-4–C-3	106.4(3)	O-4–C-4–C-3	106.4(4)
C-5–C-4–C-3	103.4(3)	C-5–C-4–C-3	103.5(3)
O-5–C-5–C-6	109.3(3)	O-5–C-5–C-6	110.9(4)
O-5–C-5–C-4	115.0(3)	O-5–C-5–C-4	112.1(4)
C-6–C-5–C-4	104.8(3)	C-6–C-5–C-4	105.0(3)
O-6–C-6–O-3	122.6(4)	O-6–C-6–O-3	122.3(4)
O-6–C-6–C-5	128.5(3)	O-6–C-6–C-5	127.8(4)
O-3–C-6–C-5	108.9(3)	O-3–C-6–C-5	109.8(3)
C-6–O-3–C-3	111.7(3)	C-6–O-3–C-3	111.2(3)
C-1–O-4–C-4	108.9(3)	C-1–O-4–C-4	110.1(4)
Torsion angles	(°)	Torsion angles	(°)
O-1–C-1–C-2–O-2	−165.6(4)	O-1–C-1–C-2–O-2	−164.6(3)
O-4–C-1–C-2–O-2	75.4(4)	O-4–C-1–C-2–O-2	78.8(4)
O-1–C-1–C-2–C-3	82.0(4)	O-1–C-1–C-2–C-3	83.2(3)
O-4–C-1–C-2–C-3	−37.0(4)	O-4–C-1–C-2–C-3	−33.4(3)
O-2–C-2–C-3–O-3	159.7(3)	O-2–C-2–C-3–O-3	157.5(3)
C-1–C-2–C-3–O-3	−87.5(4)	C-1–C-2–C-3–O-3	−89.2(3)
O-2–C-2–C-3–C-4	−86.7(4)	O-2–C-2–C-3–C-4	−89.5(4)
C-1–C-2–C-3–C-4	26.1(4)	C-1–C-2–C-3–C-4	23.9(3)
O-3–C-3–C-4–O-4	108.3(3)	O-3–C-3–C-4–O-4	106.5(4)
C-2–C-3–C-4–O-4	−6.8(4)	C-2–C-3–C-4–O-4	−7.1(4)
O-3–C-3–C-4–C-5	−10.9(4)	O-3–C-3–C-4–C-5	−14.2(5)
C-2–C-3–C-4–C-5	−126.0(3)	C-2–C-3–C-4–C-5	−127.9(3)
O-4–C-4–C-5–O-5	24.3(4)	O-4–C-4–C-5–O-5	23.7(5)
C-3–C-4–C-5–O-5	138.8(3)	C-3–C-4–C-5–O-5	139.0(4)
O-4–C-4–C-5–C-6	−95.7(4)	O-4–C-4–C-5–C-6	−96.8(4)
C-3–C-4–C-5–C-6	18.8(4)	C-3–C-4–C-5–C-6	18.5(4)
O-5–C-5–C-6–O-6	37.3(6)	O-5–C-5–C-6–O-6	43.1(7)
C-4–C-5–C-6–O-6	161.1(4)	C-4–C-5–C-6–O-6	164.4(5)
O-5–C-5–C-6–O-3	−145.4(3)	O-5–C-5–C-6–O-3	−138.7(4)
C-4–C-5–C-6–O-3	−21.6(4)	C-4–C-5–C-6–O-3	−17.4(5)
O-6–C-6–O-3–C-3	−167.3(4)	O-6–C-6–O-3–C-3	−173.3(5)
C-5–C-6–O-3–C-3	15.2(5)	C-5–C-6–O-3–C-3	8.4(5)
C-2–C-3–O-3–C-6	109.3(4)	C-2–C-3–O-3–C-6	114.9(4)
C-4–C-3–O-3–C-6	−2.5(5)	C-4–C-3–O-3–C-6	3.9(5)
O-1–C-1–O-4–C-4	−80.8(4)	O-1–C-1–O-4–C-4	−83.4(4)
C-2–C-1–O-4–C-4	34.3(4)	C-2–C-1–O-4–C-4	30.5(4)
C-5–C-4–O-4–C-1	95.7(4)	C-5–C-4–O-4–C-1	99.2(4)
C-3–C-4–O-4–C-1	−17.0(4)	C-3–C-4–O-4–C-1	−14.4(4)
H-1A–C-1–C-2—H-2A	81.0	H-1A–C-1–C-2—H-2A	83.6
H-2A–C-2–C-3—H-3A	−90.3	H-2A–C-2–C-3—H-3A	−91.6
H-3A–C-3–C-4—H-4A	−7.1	H-3A–C-3–C-4—H-4A	−9.2
H-4A–C-4–C-5—H-5A	21.5	H-4A–C-4–C-5—H-5A	19.9

Table 6. Hydrogen bonds for **1** with distances (*d*): $d(\mathrm{D}\cdots\mathrm{A}) < R(\mathrm{D}) + R(\mathrm{A}) + 0.50$ Å; $d(\mathrm{H}\cdots\mathrm{A}) < R(\mathrm{H}) + R(\mathrm{A}) - 0.12$ Å and angle $(<) < \mathrm{D{-}H}\cdots\mathrm{A} > 100.0°$

D–H	A	d(D–H)	d(H···A)	d(D···A)	<D–H···A
C-5–H-5A	O-6$^{\mathrm{i}}$	0.98	2.57	3.200(6)	122
C-7–H-7A	O-4$^{\mathrm{ii}}$	0.96	2.59	3.531(6)	165
C-9–H-9A	O-7$^{\mathrm{iii}}$	0.96	2.51	3.436(6)	162
C-9–H-9B	O-7$^{\mathrm{i}}$	0.96	2.57	3.343(7)	138

Symmetry codes: (i) $-1-x$, $1/2+y$, $-z$; (ii) $-1-x$, $-1/2+y$, $-1-z$; (iii) $-1+x$, y, $-1+z$.

Table 7. Hydrogen bonds for **2** with distances (d): $d(\mathrm{D}\cdots\mathrm{A}) < R(\mathrm{D}) + R(\mathrm{A}) + 0.50$ Å; $d(\mathrm{H}\cdots\mathrm{A}) < R(\mathrm{H}) + R(\mathrm{A}) - 0.12$ Å and angle (<) < D–H···A > 100.0°

D–H	A	d(D–H)	d(H···A)	d(D···A)	<D–H···A
C-3–H-3A	O-8^{i}	0.98	2.51	3.243(8)	131
C-4–H-4A	O-4^{ii}	0.98	2.49	3.256(6)	135
C-4–H-4A	O-7^{ii}	0.98	2.57	3.299(6)	132

Symmetry codes: (i) $-x$, $-1/2+y$, $-1-z$; (ii) $-1-x$, $-1/2+y$, $-1-z$.

the conformational equilibrium of the β-D-furanurono-6,3-lactones in solution.

Our findings are in accordance with the results of NMR investigations for 3,6-anhydrohexofuranose derivatives with β-D-gluco and α-L-ido configurations.[27]

3. Conclusions

The crystal and NMR data of the β-D-furanurono-6,3-lactones **1** and **2** we have been discussing show that a $^{1}T_{2}$-like conformation of the furanoid ring is the preferred form for these compounds, both in the crystal and in solution. This preference is probably due to certain restrictions resulting from the fused bicyclic structure of furanurono-6,3-lactones as well as to the anomeric effect. The characteristic ^{1}H NMR spectra of lactones **1** and **2** may be indicative of a $^{1}T_{2}$-like conformation.

4. Experimental

4.1. Characterization of 1

Mp 82–84 °C; $[\alpha]_{D}^{20}$ +32.9 (*c* 0.9, CHCl$_3$); IR: *ν* 1804 (lactone C=O), 1752 (acetyl C=O), 1374 (acetyl CH$_3$), 1225 (acetyl CO–O) cm^{-1}. Anal. Calcd for $C_{11}H_{14}O_{8}$: C, 48.18; H, 5.15. Found: C, 48.13; H, 5.13.

4.2. Characterization of 2

Mp 193–194 °C; $[\alpha]_{D}^{20}$ +89.9 (*c* 1.0, CHCl$_3$); IR: *ν* 1803 (lactone C=O), 1751 (acetyl C=O), 1376 (acetyl CH$_3$), 1220 (acetyl CO–O) cm^{-1}. Anal. Calcd for $C_{12}H_{14}O_{9}$: C, 47.69; H, 4.67. Found: C, 47.37; H, 4.56.

4.3. X-ray crystallography

Diffraction data were collected at room temperature (293 K) on a KUMA KM-4 four circle diffractometer[28] with Mo Kα radiation ($\lambda = 0.71073$ Å) using the $2\Theta/\omega$ scan mode. The initial phase angle determination was performed by SHELXS.[29] All H atoms were placed geometrically and refined using a riding model with C–H = 0.97–0.98 Å, and $U_{\mathrm{iso}}(\mathrm{H}) = 1.2U_{\mathrm{eq}}(\mathrm{C})$ (C–H = 0.96 Å and $U_{\mathrm{iso}}(\mathrm{H}) = 1.5U_{\mathrm{eq}}(\mathrm{C})$ in the case of the methyl H atoms). The crystallographic data, data collection, and structure refinement are summarized in Table 3. The coordinates of atoms and their isotropic temperature factors are set out in Table 4, selection of the crystal's important geometric parameters is given in Table 5 and short contacts are summarized in Tables 6 and 7.

The crystal structure was refined to $R_1 = 0.1849$ (2413 reflections, all unique reflections) and $R_1 = 0.0589$ (1023 reflections with $F_0 > 2\sigma(F_0)$) by full-matrix least-squares method using the program SHELXL-97[30] based on 150 parameters. The compound structures showing the conformations and atom numbering system are illustrated in Figure 3.[31] Molecular packing in the crystals, illustrated in Figures 4 and 5, were prepared by PLUTO-78.[32] The computational material for publication was prepared using the PLATON program.[17]

4.4. NMR spectroscopy

NMR spectra were recorded on a Unity Plus 500 MHz spectrometer. ^{1}H NMR spectra were measured at 500 MHz and ^{13}C spectra at 125 MHz in CDCl$_3$ solution, using the standard pulse sequence and procedures. 2D COSY ^{1}H NMR spectra were recorded using 1024 $(t_2) \times 256$ (t_1) data points and eight scans per acquisition with Fourier transformation performed into 2048 × 1024 matrix. 2D ^{1}H–^{13}C heteronuclear single-quantum correlated spectra (gHSQC) were acquired by the use of 1024 $(t_2) \times 122$ (t_1) point data sets and 1 scan per acquisition with Fourier transformation performed into 1024 × 1024 matrix. 2D ^{1}H–^{13}C heteronuclear multi-bond correlated spectra (gHMBC) were measured by the use of 1536 $(t_2) \times 140$ (t_1) point data sets and eight scans per acquisition with Fourier transformation performed into 2048 × 1024 matrix.

4.5. Supplementary materials

Full crystallographic details, excluding structures features, have been deposited (deposition No. CCDC 600463 for methyl 2,5-di-*O*-acetyl-β-D-glucofuranosidurono-6,3-lactone and deposition No. CCDC 600464 for 1,2,5-tri-*O*-acetyl-β-D-glucofuranurono-6,3-lactone) 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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