



THE NMR INVESTIGATIONS OF D-GLUCOFURANOSIDURONO-6,3-LACTONES CONFORMATIONS

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Despite of their ubiquity in biological structures, furanosides have received much less attention than pyranosides as regards the conformational analysis. This is because different conformations of five-membered rings have quite similar energies, whereas six-membered rings are normally present in a single low-energy chair conformation. Therefore, conformations of pyranosides in solution are easily identified by NMR techniques, which is not the case with furanosides. These are equilibrating rapidly on the NMR scale and averaging of coupling constants occurs. However, when a tetrahydrofuran ring is conformationally restricted by a rigid second skeleton, it is possible to predict its conformation.¹

A fused bicyclic structure of D-glucufuranurono-6,3-lactones and their glycosides forces the C2, C3, C4 and O4 atoms to lie in one plane, whereas only carbon C1 is able to move freely above or below this plane. Thus, the ¹E or ¹E₁ conformations seem to be the preferred for such the compounds. From these two conformations the ¹E form should be preferred by β-anomers, because it allows the anomeric hydroxy or alkoxy groups to be placed pseudoaxially (Fig. 1).² In the case of ¹E₁ form these groups would be oriented pseudoequatorially.

Previously, we found that methyl 2,5-di-O-acetyl-β-D-glucufuranosidurono-6,3-lactone (Fig. 1) and 1,2,5-tri-O-acetyl-β-D-glucufuranurono-6,3-lactone adopt a ¹T₂-like conformation, both in the crystal structure and in solution.² The ¹T₂ conformation is slightly twisted around the C1-C2 bond in comparison with the ¹E form, but both forms are very closed to each other. The ¹H NMR spectra of these two lactones are very characteristic. They consist of two singlets (H1 and H2), two doublets (H3 and H5) and one doublet of doublets (H4) (Fig. 2). The identical conformation of both lac-

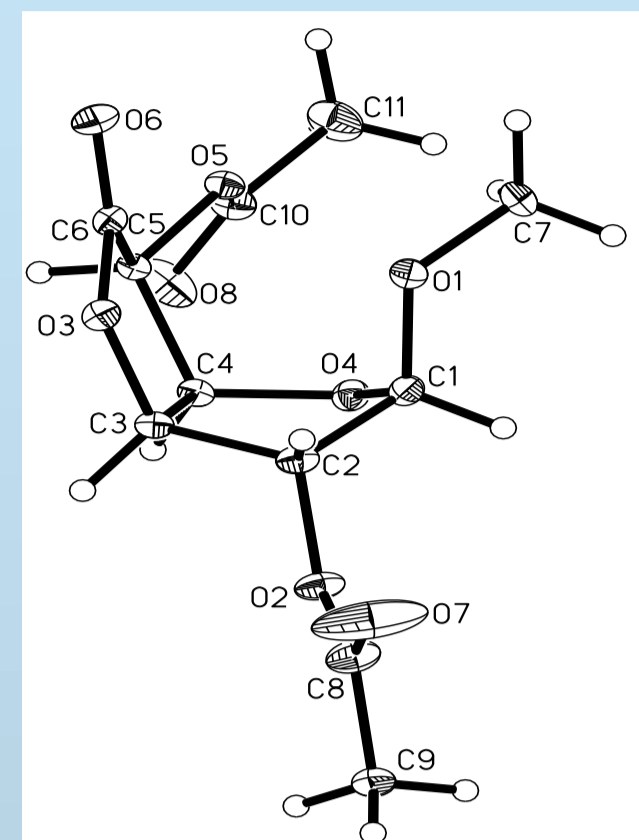


Fig. 1 The ¹T₂-like conformation of methyl 2,5-di-O-acetyl-β-D-glucufuranosidurono-6,3-lactone in a crystal structure.²

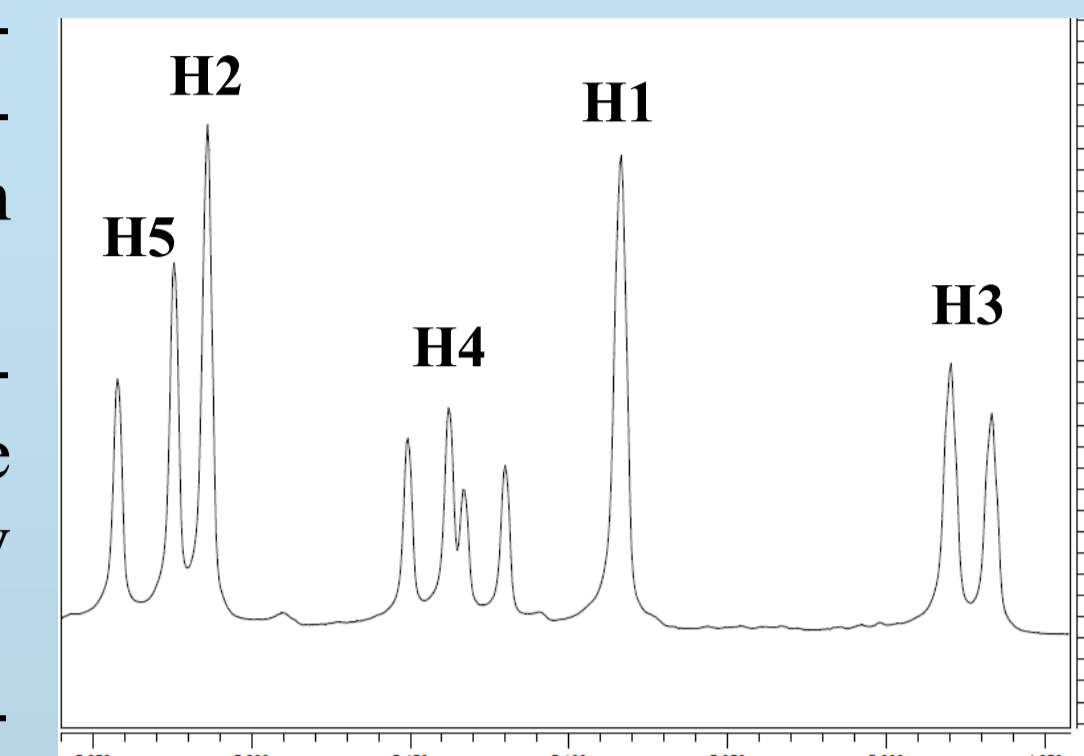


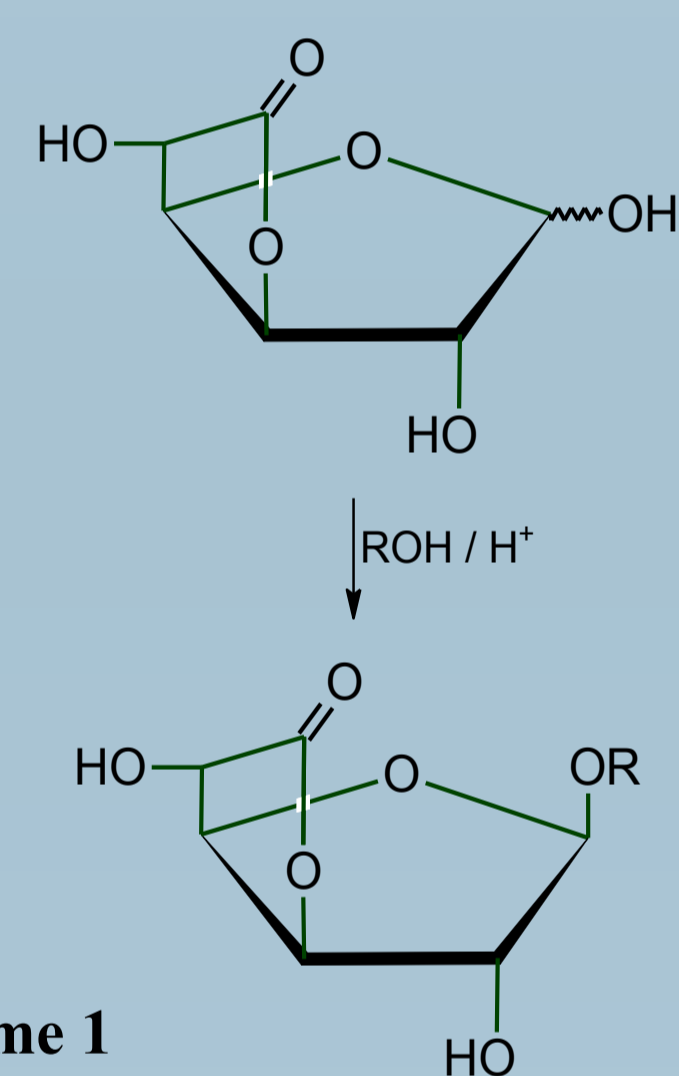
Fig. 2 Characteristic ¹H NMR spectra of per-O-acetylated D-glucufuranosidurono-6,3-lactones.

tones is additionally confirmed by the same ¹H-¹H coupling constants ($J_{3,4}$ and $J_{4,5}$). Typically, there is no coupling between H1 and H2 as well as H2 and H3 protons. It seems to us that the characteristic ¹H NMR spectra of these β-D-glucufuranurono-6,3-lactones may be indicative of a ¹T₂-like conformation. To verify this thesis we synthesized a series of D-glucufuranosidurono-6,3-lactones with different aglycones and different ring substituents.

First group of synthesized β-D-glucufuranosidurono-6,3-lactones was obtained by Fischer glycoside synthesis (Scheme 1). The ¹H NMR spectra of this group of compounds are more complicated since the coupling between the H2 and 2-OH as well as H5 and 5-OH protons in CDCl₃ solvent occurs (Table 1). However, all these spectra are very typical and usually consist of one singlet (H1), two doublets (H2 and H3) and two doublet of doublets (H4 and H5). Importantly there is lack of coupling between H1 and H2 as well as H2 and H3 protons, which is characteristic for the ¹T₂-like conformation.

Second group of β-D-glucufuranosidurono-6,3-lactones was obtained employing respective acetate as glycosyl donor in the presence of BF₃-Et₂O (Scheme 2). The ¹H NMR spectra of this group of compounds are in agreement with our assumptions and indicative for the ¹T₂-like conformation (Table 2).

Third group of D-glucufuranurono-6,3-lactones consists of the partially deprotected O-acetyl furanosides and furanose (Fig. 3). These were obtained as the side products of reaction employing respective acetate or bromoacetate as glycosyl donors. The ¹H NMR spectra of the β-anomers from this group of compounds (Table 3) again indicate the ¹T₂-like conformation with a lack of coupling between H1 and H2 as well as H2 and H3 protons. Unexpectedly, we have obtained the prove that the α-anomers of D-glucufuranurono-6,3-lactones also adopt the ¹T₂-like conformation. The change



Scheme 1

Table 1

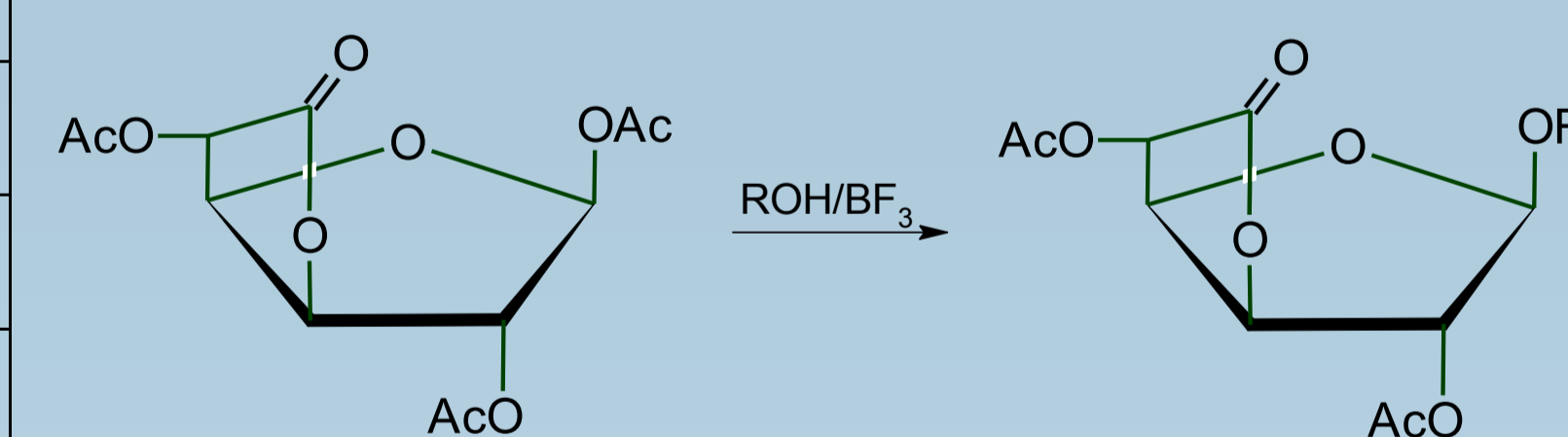
Chemical shifts (ppm) of the protons and ¹H-¹H coupling constants (Hz) in the ¹H NMR spectra of D-glucufuranosidurono-6,3-lactones synthesized by Fisher method.

R=	H-1	H-2	H-3	H-4	H-5	2-OH	5-OH	aglycone						$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	J_{gem}	$J_{CH,CH}$	$J_{2,OH}$	$J_{5,OH}$
								CHA	CHB	CH	CH ₂	CH ₃	C ₆ H ₅								
CH ₂ CH ₃	5,12 (s)	4,45 (bs)	4,87 (d)	5,02 (dd)	4,37 (t)	2,17 (bs)	2,69 (d)	3,76 (dq)	3,52 (dq)	-	-	1,84 (t)	-	-	5,2	6,8	9,2	7,2	*	8,4	
CH ₂ CH ₂ CH ₃	5,11 (s)	4,44 (s)	4,88 (d)	5,02 (dd)	4,38 (bs)	2,49 (bs)	2,80 (bs)	3,66 (dt)	3,40 (dt)	-	1,57 (hx)	0,89 (t)	-	-	5,2	6,8	9,2	6,8	*	*	
CH(CH ₃) ₂	5,22 (s)	4,41 (d)	4,87 (d)	5,00 (dd)	4,36 (dd)	2,19 (d)	2,72 (d)	-	-	3,91 (hp)	-	1,18(d) 1,16(d)	-	-	4,8	7,2	-	6,0	4,0	9,2	
CH ₂ CH ₂ CH ₂ CH ₃	5,10 (s)	4,43 (s)	4,88 (d)	5,02 (dd)	4,38 (bt)	2,46 (bs)	2,80 (bd)	3,70 (dt)	3,44 (dt)	-	1,53(qn) 1,32(hx)	0,90 (t)	-	-	4,8	6,8	9,6	6,8	*	6,4	
C(CH ₃) ₃	5,34 (s)	4,29 (d)	4,89 (d)	4,59 (dd)	4,36 (d)	3,31 (d)	3,00 (d)	-	-	-	-	1,22 (s)	-	-	5,2	7,2	-	-	3,6	10,0	
CH ₂ Ph	5,17 (s)	4,44 (s)	4,82 (d)	4,97 (dd)	4,33 (d)	1,69 (bs)	2,63 (bd)	4,70 (d)	4,55 (d)	-	-	-	7,29-7,38	-	4,8	6,4	12,0	-	*	*	

* not determined

Table 2
Chemical shifts (ppm) of the protons and ¹H-¹H coupling constants (Hz) in the ¹H NMR spectra of D-glucufuranosidurono-6,3-lactones obtained employing respective acetate as glycosyl donor.

R=	H-1	H-2	H-3	H-4	H-5	OAc	aglycone						$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	J_{gem}	$J_{CH,CH}$
							CHA	CHB	CH	CH ₂	CH ₃	C ₆ H ₅						
CH ₂ CH ₃	5,08 (s)	5,21 (s)	4,97 (d)	5,13 (dd)	5,23 (d)	2,22(s) 2,10(s)	3,80 (dq)	3,45 (dq)	-	-	1,18 (t)	-	-	5,2	6,8	8,8	7,2	
CH ₂ CH ₂ CH ₃	5,07 (s)	5,21 (s)	4,96 (d)	5,13 (dd)	5,23 (d)	2,21(s) 2,10(s)	3,71 (dt)	3,31 (dt)	-	1,57 (hx)	0,88 (t)	-	-	5,2	7,2	8,8	6,8	
CH(CH ₃) ₂	5,16 (s)	5,20 (s)	4,96 (d)	5,11 (dd)	5,23 (d)	2,20(s) 2,09(s)	-	-	3,92 (hp)	-	1,17(d) 1,12(d)	-	-	5,2	6,8	-	6,4	
CH ₂ CH ₂ CH ₂ CH ₃	5,07 (s)	5,21 (s)	4,96 (d)	5,13 (dd)	5,23 (d)	2,22(s) 2,10(s)	3,76 (dt)	3,35 (dt)	-	1,54(dqn) 1,33(dhx)	0,90 (t)	-	-	5,2	7,2	9,2	6,8	
CH ₂ Ph	5,16 (s)	5,29 (s)	5,00 (d)	5,18 (dd)	5,30 (d)	2,25(s) 2,08(s)	4,84 (d)	4,45 (d)	-	-	-	7,29-7,37	-	4,8	7,2	11,6	-	



Scheme 2

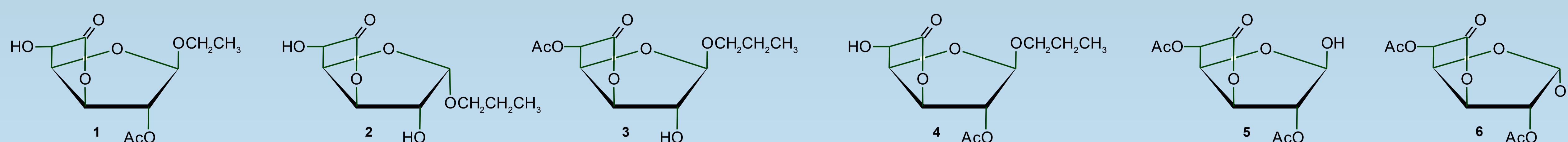


Fig. 3 D-Glucufuranosidurono-6,3-lactones with different aglycones and different ring substituents.

Table 3

Chemical shifts (ppm) of the protons and ¹H-¹H coupling constants (Hz) in the ¹H NMR spectra of 1-6.

Comp.	H-1	H-2	H-3	H-4	H-5	1-OH	2-OH	5-OH	OAc	aglycone				$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	J_{gem}	$J_{CH,CH}$	$J_{1,OH}$	$J_{2,OH}$	$J_{5,OH}$
										CHA	CHB	CH ₂	CH ₃									
1	5,14 (s)	5,23 (s)	4,94 (d)	4,99 (dd)	4,36 (t)	-	-	2,69 (d)	2,13 (s)	3,75 (dt)	3,57 (dt)	-	1,20 (t)	-	-	5,2	7,2	9,6	6,8	-	-	8,4
2	5,28 (d)	4,40 (t)	4,77 (d)	4,84 (dd)	4,47 (dd)	-	2,62 (d)	3,07 (d)	-	3,86 (dt)	3,58 (dt)	1,67 (hx)	0,95 (t)	4,8	-	3,6	4,8	9,2	6,8	-	5,6	8,4
3	5,05 (s)	4,43 (d)	4,91 (d)	5,16 (dd)	5,24 (d)	-	2,03 (d)	-	2,22 (s)	3,73 (dt)	3,31 (dt)	1,58 (hx)	0,89 (t)	-	-	5,2	7,2	9,2	6,8	-	4,8	-
4	5,13 (s)	5,23 (s)	4,94 (d)	4,99 (dd)	4,36 (dd)	-	-	2,68 (d)	2,13 (s)	3,65 (dt)	3,46 (dt)	1,58 (hx)	0,90 (t)	-	-	5,2	6,8	9,2	6,8	-	-	9,2
5	5,50 (d)	5,26 (s)	5,01 (d)	5,16 (dd)	5,31 (d)	3,12 (d)	-	-	2,12(s) 2,24(s)	-	-	-	-	-	-	5,2	7,2	-	-	3,2	-	-
6	5,76 (dd)	5,14 (d)	5,03 (d)	5,08 (t)	5,44 (d)	3,23 (d)	-	-	2,17(s) 2,23(s)	-	-	-	-	4,4	-	5,2	4,8	-	-	6,0	-	-

s	singlet
bs	broad singlet
d	doublet
bd	broad doublet
dd	doublet of doublets
t	triplet
dt	doublet of triplets
dq	doublet of quartets
qn	quintet
dqn	doublet of quintets
hx	sextet
dhx	doublet of sextets
hp	heptet
dhp	doublet of heptets

References:

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- Liberek, B.; Tuwalska, D.; do Santos-Zounon, I.; Konitz, A.; Sikorski, A.; Smiatacz, Z. *Carbohydr. Res.* **2006**, *341*, 2275-2285.

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