

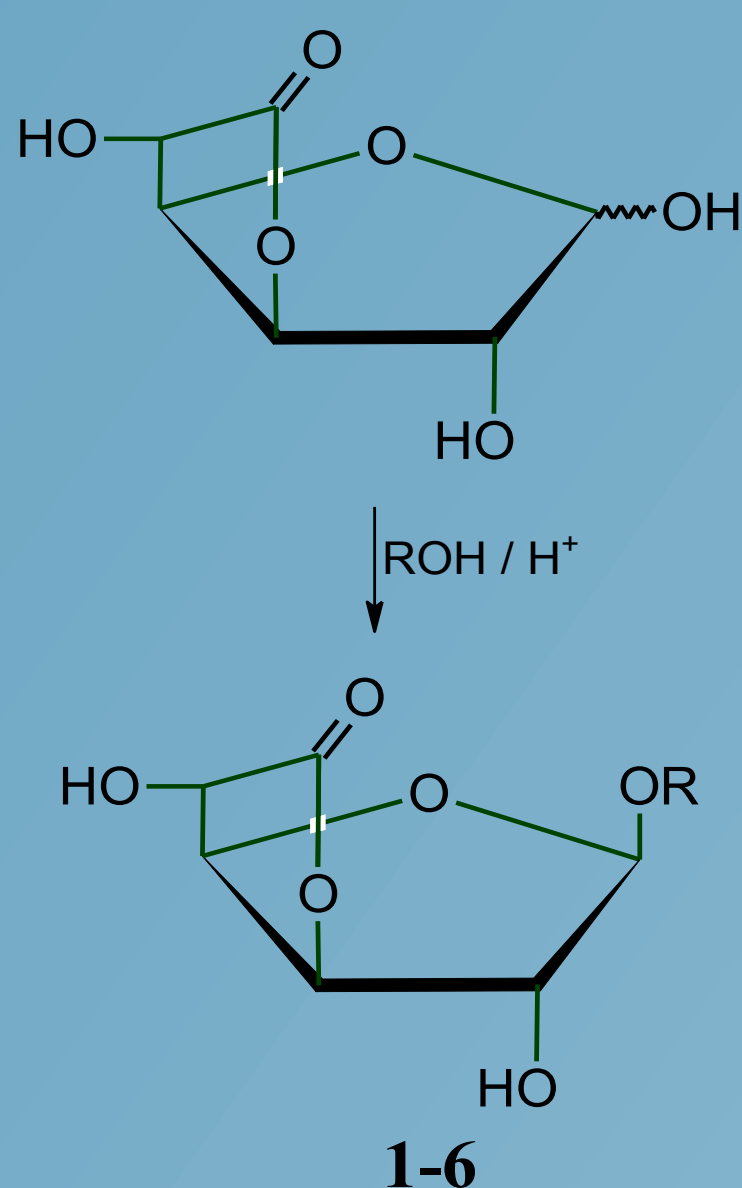
Despite of their ubiquity in biological structures, furanosides have received much less attention than pyranosides as regards the conformational analysis. This is because different conformations of five-membered rings have quite similar energies, whereas six-membered rings are normally present in a single 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 [1-3].

To study conformations of a furanose ring we synthesized two series of the conformationally restricted furanosides. The first one consists of D-glucofuranosiduro-6,3-lactones (compounds **1-12**). The second one consists of 2,3-*O*-isopropylidene-D-ribofuranosides (compounds **13-17**).

Table 1

Chemical shifts (ppm) and ^1H - ^1H coupling constants (Hz) in the ^1H NMR spectra (CDCl_3) of β -D-glucofuranosiduro-6,3-lactones (**1-6**).

no.	R=	H-1	H-2	H-3	H-4	H-5	2-OH	5-OH	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{2,\text{OH}}$	$J_{5,\text{OH}}$
1	CH_2CH_3	5,12 (s)	4,45 (bs)	4,87 (d)	5,02 (dd)	4,37 (t)	2,17 (bs)	2,69 (d)	-	-	5,2	6,8	-	8,4
2	$\text{CH}_2\text{CH}_2\text{CH}_3$	5,11 (s)	4,44 (bs)	4,88 (d)	5,02 (dd)	4,38 (bs)	2,49 (bs)	2,80 (bs)	-	-	5,2	6,8	-	-
3	$\text{CH}(\text{CH}_3)_2$	5,22 (s)	4,41 (d)	4,87 (d)	5,00 (dd)	4,36 (dd)	2,19 (d)	2,72 (d)	-	-	4,8	7,2	4,0	9,2
4	$\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$	5,10 (s)	4,43 (s)	4,88 (d)	5,02 (dd)	4,38 (bt)	2,46 (bs)	2,80 (bd)	-	-	4,8	6,8	-	6,4
5	$\text{C}(\text{CH}_3)_3$	5,34 (s)	4,29 (d)	4,89 (d)	4,59 (dd)	4,36 (dd)	3,31 (d)	3,00 (d)	-	-	5,2	7,2	3,6	10,0
6	CH_2Ph	5,17 (s)	4,44 (s)	4,82 (d)	4,97 (dd)	4,33 (d)	1,69 (bs)	2,63 (bd)	-	-	4,8	6,4	-	-



Scheme 1 Synthesis of alkyl β -D-glucofuranosiduro-6,3-lactones (**1-6**).

conformation 1T_2

Characteristic ^1H NMR spectra of furanosides **7-11** consist of two singlets (H1 and H2), two doublets (H3 and H5) and doublet of doublets (H4) (Fig. 1). Really important is that there is lack of coupling between H1 and H2 as well as H2 and H3 protons, which is characteristic for the 1T_2 -like conformation [4]. The ^1H NMR spectra of furanosides **1-6** are slightly more complicated because of the coupling with the hydroxyl protons. However, these are also characteristic by the lack of coupling between H1 and H2 as well as H2 and H3 protons, indicating the 1T_2 conformation.

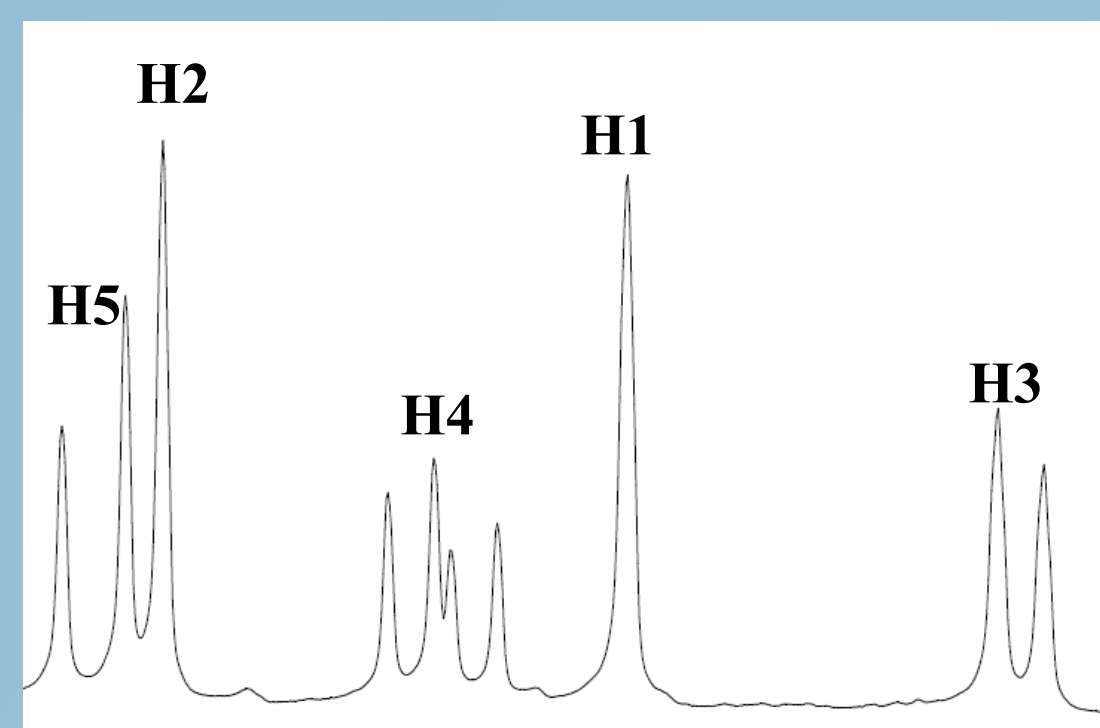
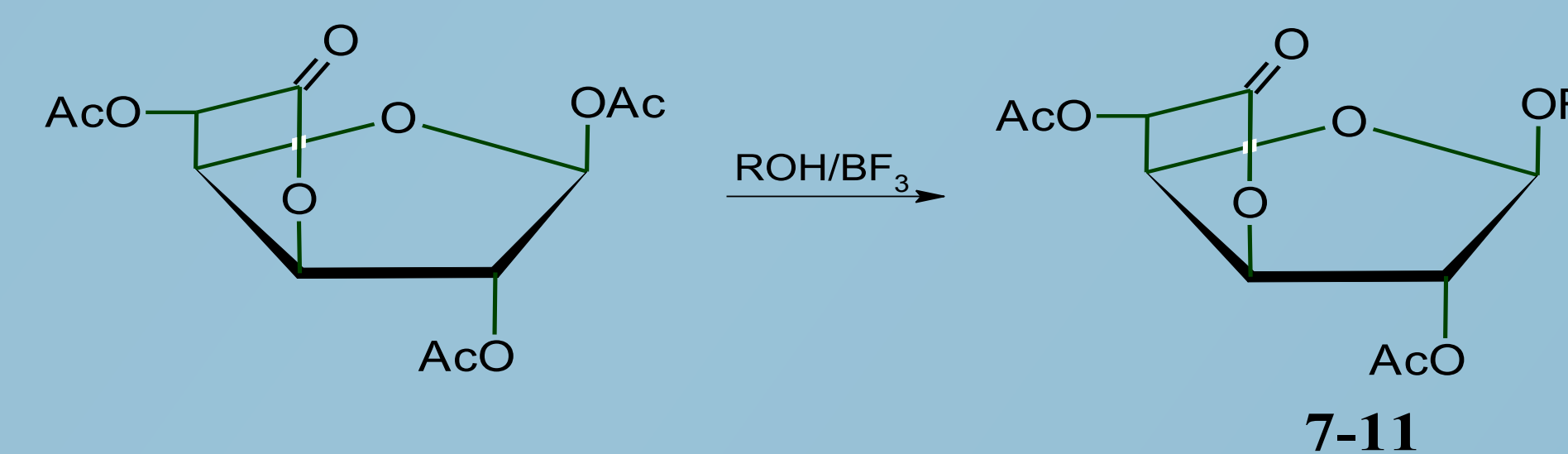


Fig. 1 Characteristic ^1H NMR spectra of furanosides **7-11**.



Scheme 2 Synthesis of alkyl 2,5-di-*O*-acetyl- β -D-glucofuranosiduro-6,3-lactones (**7-11**).

Table 2

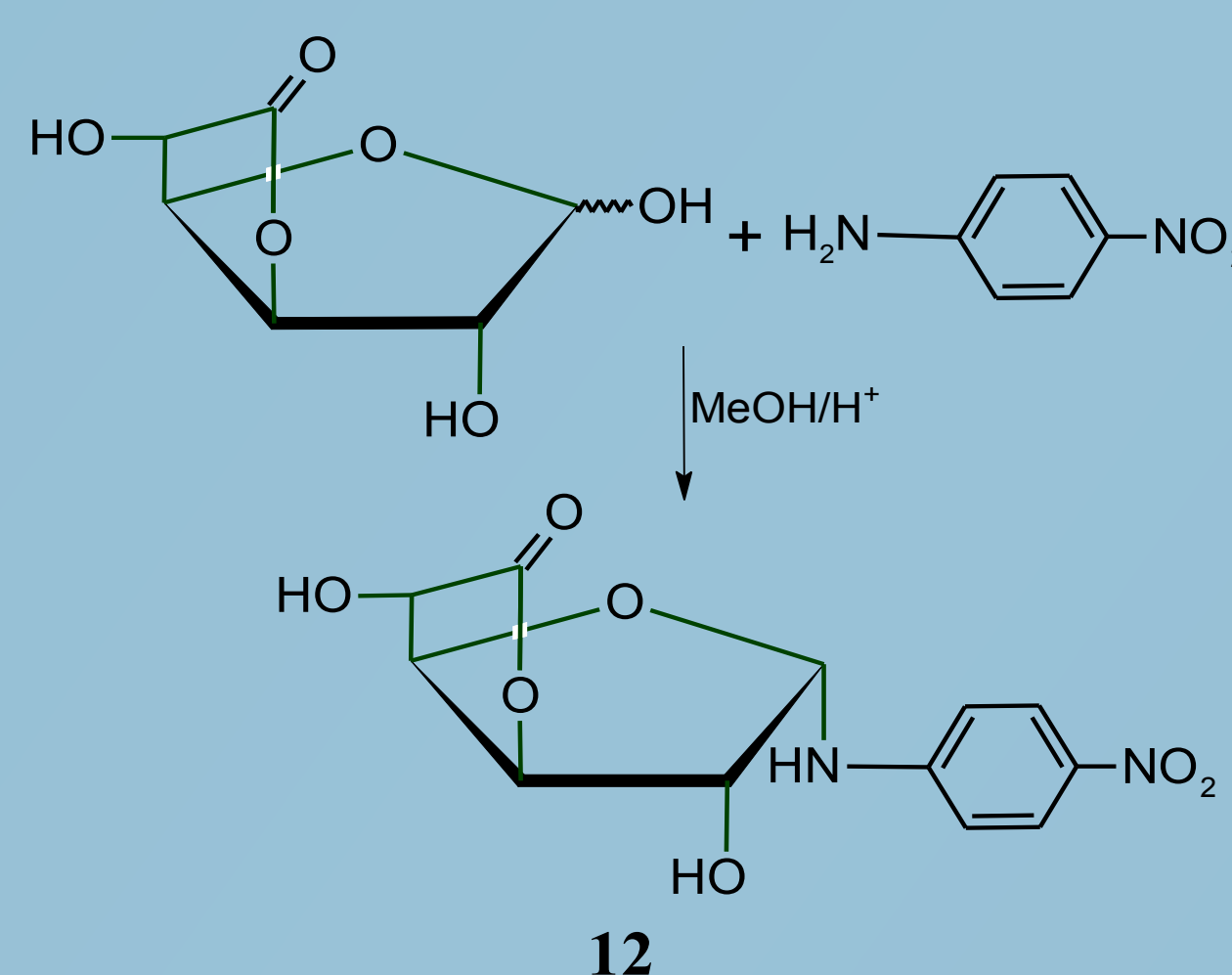
Chemical shifts (ppm) and ^1H - ^1H coupling constants (Hz) in the ^1H NMR spectra (CDCl_3) of 2,5-di-*O*-acetyl-D-glucofuranosiduro-6,3-lactones (**7-11**).

no.	R=	H-1	H-2	H-3	H-4	H-5	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
7	CH_2CH_3	5,08 (s)	5,21 (s)	4,97 (d)	5,13 (dd)	5,23 (d)	-	-	5,2	6,8
8	$\text{CH}_2\text{CH}_2\text{CH}_3$	5,07 (s)	5,21 (s)	4,96 (d)	5,13 (dd)	5,23 (d)	-	-	5,2	7,2
9	$\text{CH}(\text{CH}_3)_2$	5,16 (s)	5,20 (s)	4,96 (d)	5,11 (dd)	5,23 (d)	-	-	5,2	6,8
10	$\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$	5,07 (s)	5,21 (s)	4,96 (d)	5,13 (dd)	5,23 (d)	-	-	5,2	7,2
11	CH_2Ph	5,16 (s)	5,29 (s)	5,00 (d)	5,18 (dd)	5,30 (d)	-	-	4,8	7,2

Table 3

Crystal data and structure refinement for **12**.

Empirical formula	$\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_7, \text{CH}_4\text{O}$
Formula weight	328,28
Temperature (K)	295
Wavelength (Å)	0,71073
Crystal system	orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	a = 5,5455(8) Å b = 7,8178(8) Å c = 32,251(4) Å
V (Å ³)	1398,2(3)
Z	4
D_{calc} (Mg m ⁻³)	1,560
Absorption coefficient (mm ⁻¹)	0,131
$F(000)$	688
θ Range for data collection (°)	3,63 – 25,05
Limiting indices	-6 ≤ h ≤ 6 -9 ≤ k ≤ 9 -38 ≤ l ≤ 26
Reflections collected/unique	1486 / 917 [$R_{\text{int}} = 0,0985$]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	1486/0/209
Completeness $2\theta = 24,99^\circ$ (%)	99,7
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0,0584$ $wR_2 = 0,1318$
R indices (all data)	$R_1 = 0,1064$ $wR_2 = 0,1549$
Goodness-of-fit on F^2	1,123
Largest diff. peak and hole (e Å ⁻³)	0,202 and -0,270



Scheme 3 Synthesis of *N*-(α -D-glucofuranuro-6,3-lactonyl)-*p*-nitroaniline (**12**).

The ^1H NMR spectra of *N*-(α -D-glucofuranuro-6,3-lactonyl)-*p*-nitroaniline (**12**) show, that the change of an aglycone and an anomeric carbon atom configuration results in a coupling between the H1 and H2 protons, but there is still lack of coupling between the H2 and H3 protons (Table 4). In the crystal lattice **12** adopts the 3E conformation (Fig. 2). It is possible that the same conformation is adopted by **12** in solution.

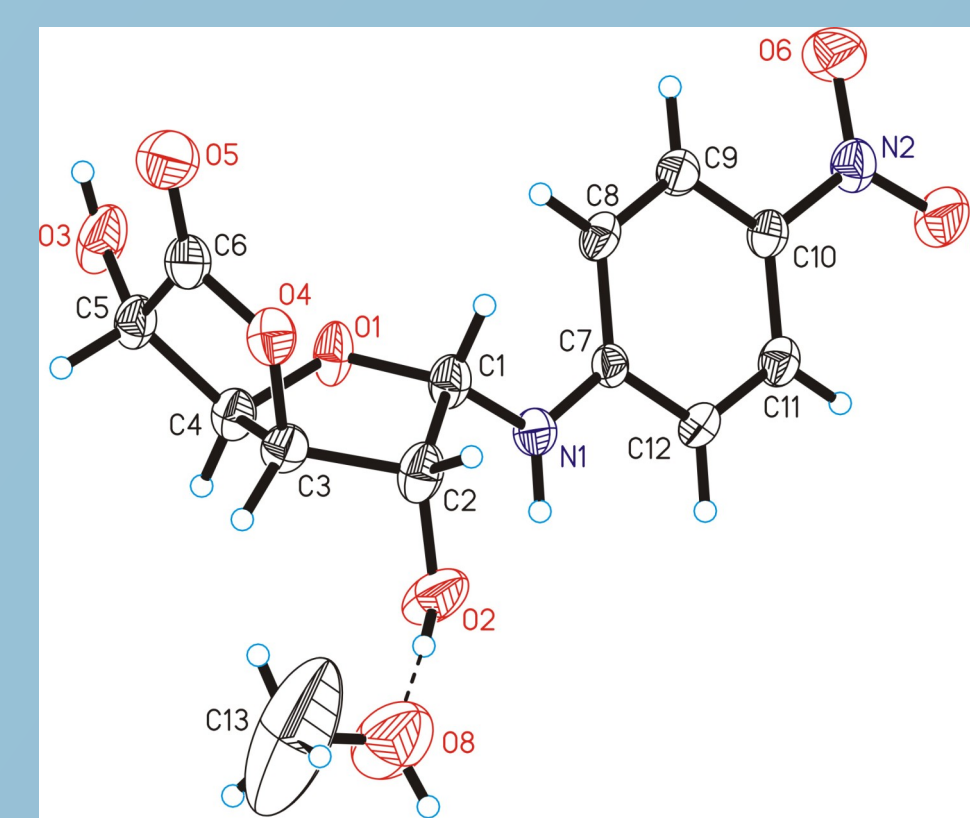


Fig. 2 Structure of **12** showing 25% probability displacements for ellipsoids. Compound **12** crystallines with one molecule of methanol. The $\text{O}\cdots\text{H}\cdots\text{O}$ hydrogen bond, represented by a dashed line, is created between MeOH and 2-OH.

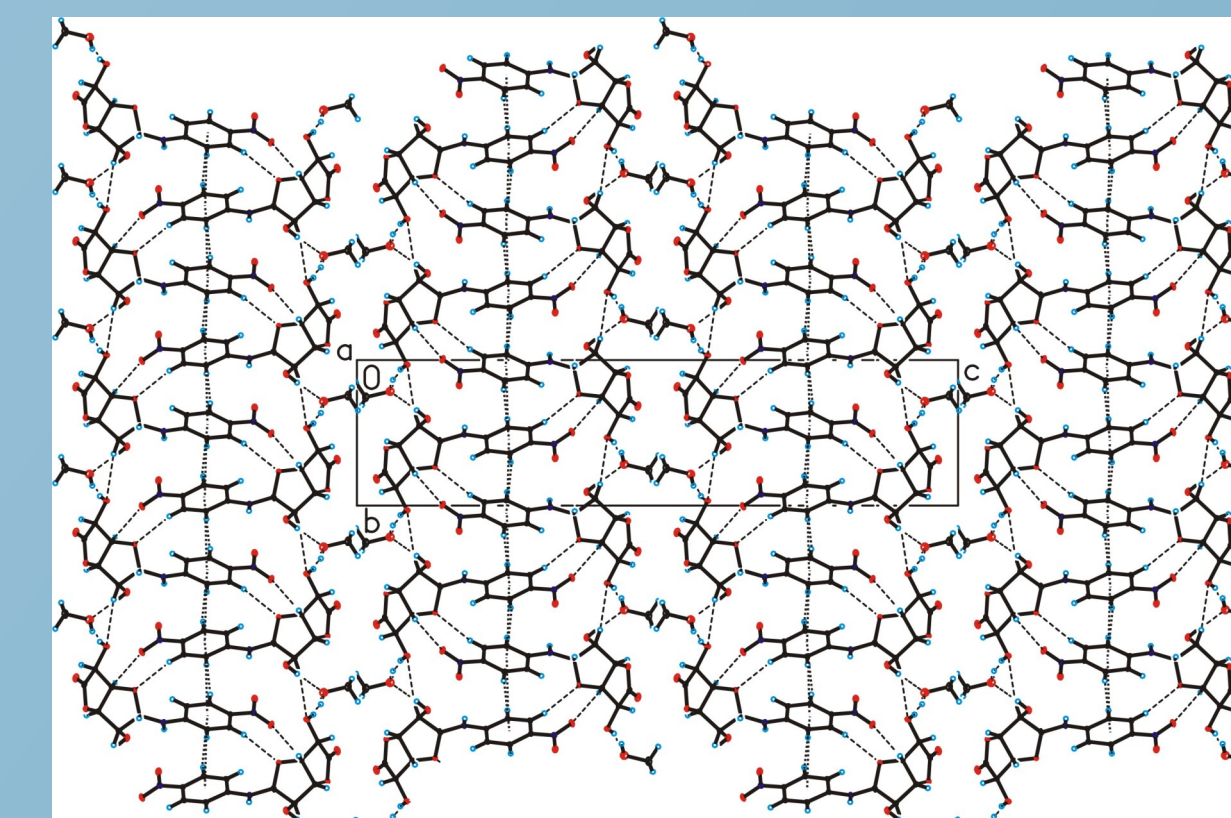


Fig. 3 Molecular packing of **12** (view along a -direction). The $\text{O}\cdots\text{H}\cdots\text{O}$ and $\text{C}\cdots\text{H}\cdots\text{O}$ intermolecular interactions are represented by dashed lines, and $\text{C}\cdots\text{H}\cdots\pi$ by dotted lines.

conformation 3E

Table 4

Chemical shifts (ppm) and ^1H - ^1H coupling constants (Hz) in the ^1H NMR spectra (DMSO) of *N*-(α -D-glucofuranuro-6,3-lactonyl)-*p*-nitroaniline (**12**).

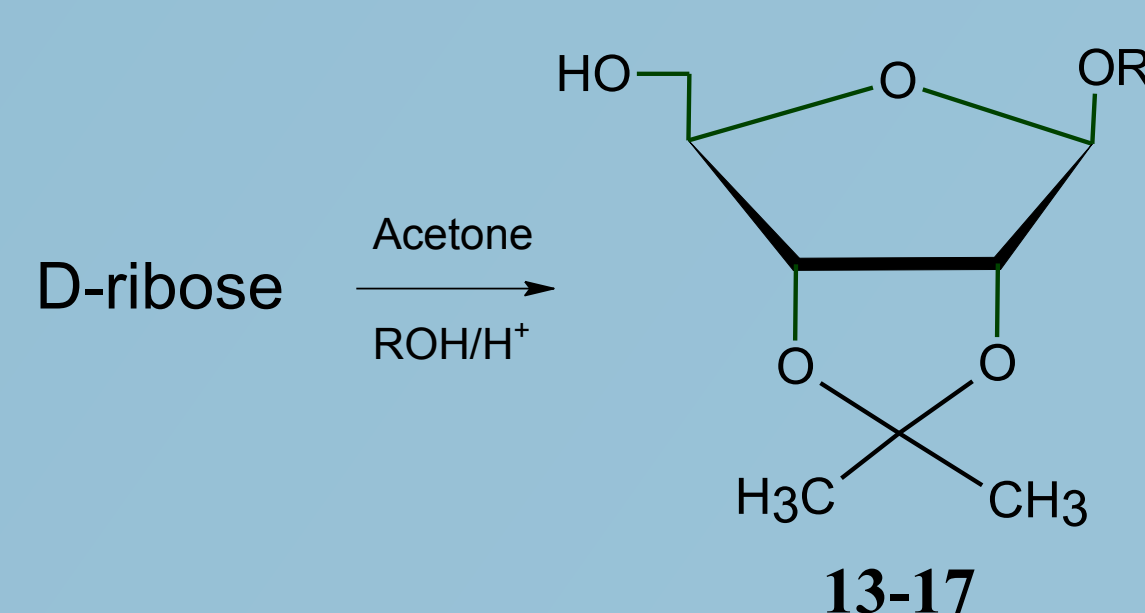
H-1	H-2	H-3	H-4	H-5	2-OH	5-OH	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
5,44 (d)	5,31 (d)	4,89 (d)	4,65 (dd)	4,48 (t)	6,29 (bs)	5,93 (d)	4,0	-	3,6	4,8

Table 5

Chemical shifts (ppm) and ^1H - ^1H coupling constants (Hz) in the ^1H NMR spectra (CDCl_3) of 2,3-*O*-isopropylidene-D-ribofuranosides (**13-17**).

no.	R=	H-1	H-2	H-3	H-4	CH_2OH	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
13	CH_3	4,97 (s)	4,83 (d)	4,58 (d)	4,42 (t)	3,65 (m)	-	6,4	-	2,8
14	CH_2CH_3	5,07 (s)	4,84 (d)	4,59 (d)	4,41 (t)	3,68 (m)	-	6,4	-	2,8
15	$\text{CH}_2\text{CH}_2\text{CH}_3$	5,06 (s)	4,84 (d)	4,60 (d)	4,41 (t)	3,68 (m)	-	6,0	-	2,8
16	$\text{CH}(\text{CH}_3)_2$	5,17 (s)	4,85 (d)	4,56 (d)	4,40 (t)	3,67 (m)	-	6,0	-	2,4
17	$\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$	5,05 (s)	4,83 (d)	4,59 (d)	4,40 (t)	3,73 (m)	-	6,4	-	2,4

The ^1H NMR spectra of 2,3-*O*-isopropylidene-D-ribofuranosides are also typical and consist of one singlet (H1), two doublets (H2 and H3), one triplet (H4) and one multiplet (CH_2OH) (Table 5). In this case, there is lack of coupling between H1 and H2 as well as H3 and H4 protons (Fig. 4).



Scheme 4 Synthesis of alkyl 2,3-*O*-isopropylidene-D-ribofuranosides (**13-17**).

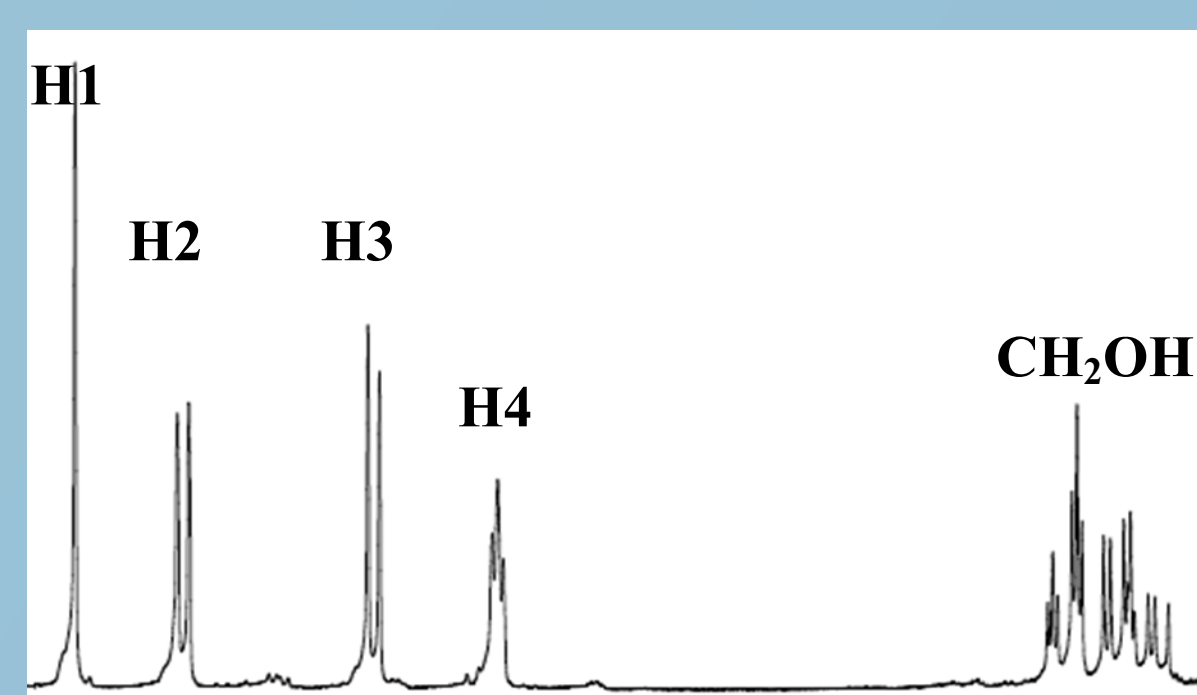


Fig. 4 Characteristic ^1H NMR spectra of furanosides **13-17**.

conformation ?

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