



CONFORMATIONAL STUDIES OF THE FURANOSIDES - IMPORTANT BIOLOGICAL COMPONENTS



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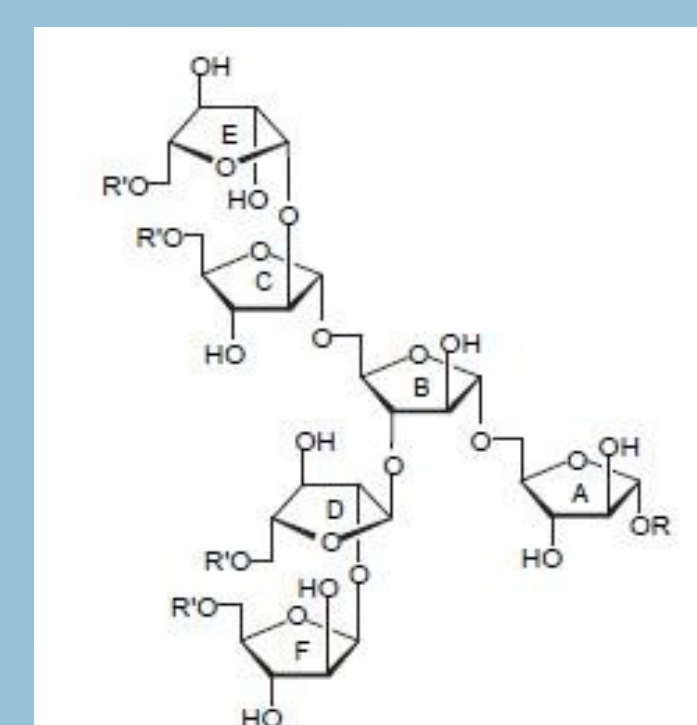
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Many of biological compounds, e.g. polysaccharides and oligosaccharides, which are important components of number of microorganisms, fungi and plants, contain furanose ring in their structure (Fig. 1). What is more, furanoses are extremely important constituents of nucleic acids, by attaching a phosphate group into a backbone and constituting a place to attach the appropriate bases. Change in conformation of these five-membered rings may have significant effect on the final conformations of DNA and RNA molecules. Thus, the knowledge of conformational freedom of the furanose ring is vital for the estimation of biological activity and chemical reactivity of the compounds consisting of furanosides.

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 [2-4].

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



LAM: R=arabinomannan; R'=H
AG: R=arabinogalactan; R'=mycolic acids

Fig. 1 Arabinofuranoside-based hexasaccharide in *mycobacteria* [1].

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

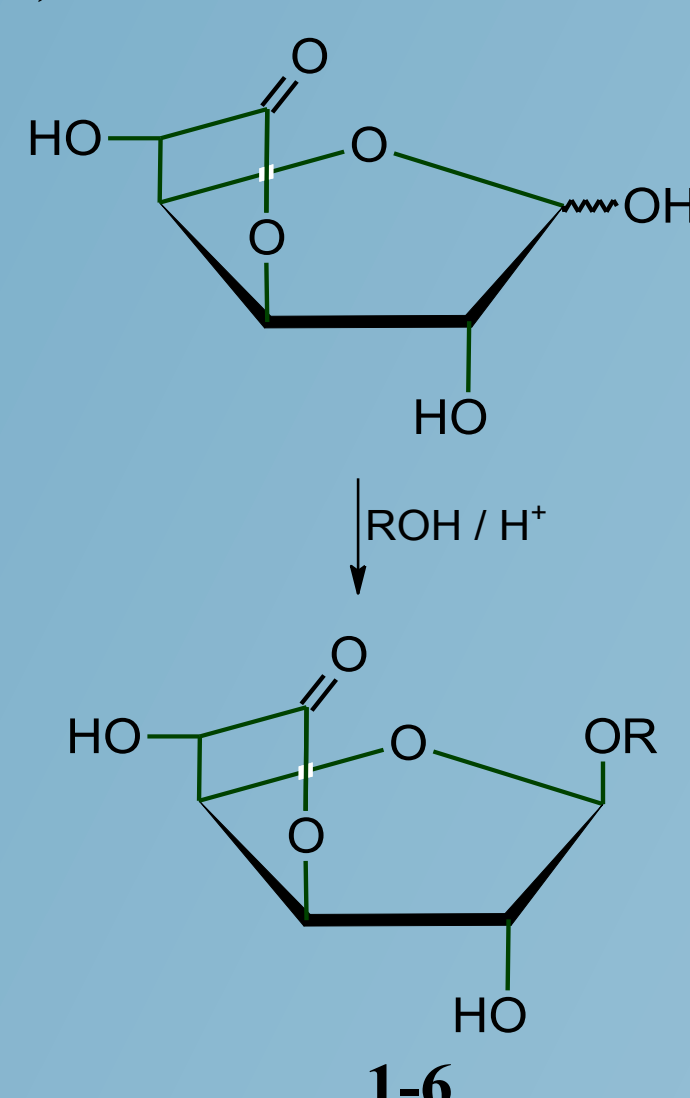


Table 1

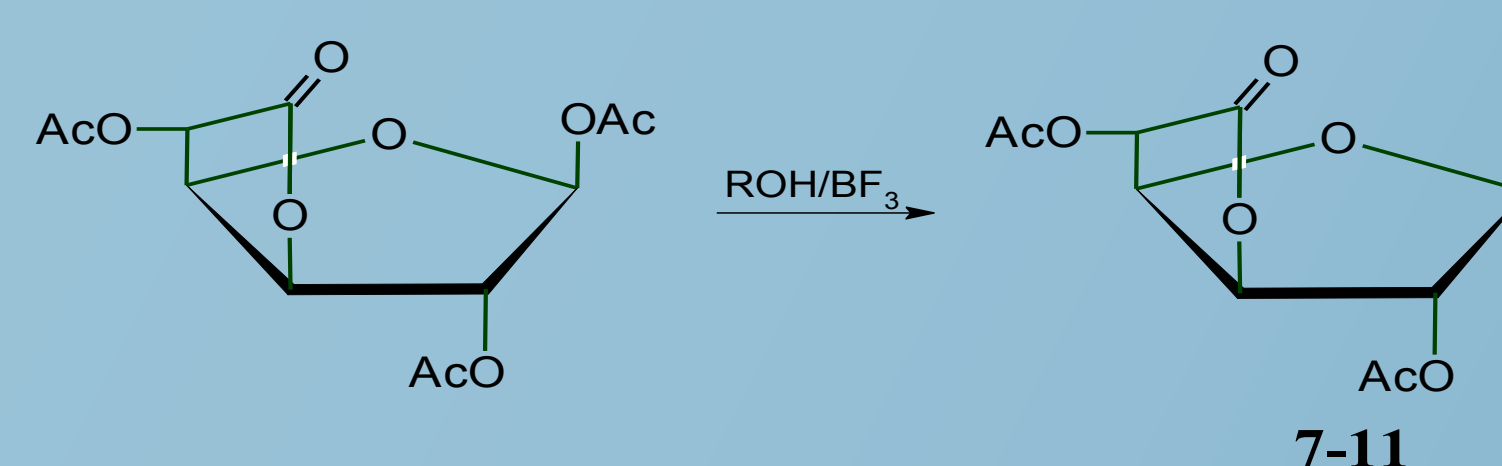
Chemical shifts (ppm) and ¹H-¹H coupling constants (Hz) in the ¹H NMR spectra (CDCl₃) of D-glucofuranosidurono-6,3-lactones (1-6).

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,OH}	J _{5,OH}
1	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)	-	-	5,2	6,8	-	8,4
2	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)	-	-	5,2	6,8	-	-
3	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)	-	-	4,8	7,2	4,0	9,2
4	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)	-	-	4,8	6,8	-	6,4
5	C(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 ₂ Ph	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	-	-

Table 2

Chemical shifts (ppm) and ¹H-¹H coupling constants (Hz) in the ¹H NMR spectra (CDCl₃) of 2,5-di-O-acetyl-D-glucofuranosidurono-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 ₂ CH ₃	5,08 (s)	5,21 (s)	4,97 (d)	5,13 (dd)	5,23 (d)	-	-	5,2	6,8
8	CH ₂ CH ₂ CH ₃	5,07 (s)	5,21 (s)	4,96 (d)	5,13 (dd)	5,23 (d)	-	-	5,2	7,2
9	CH(CH ₃) ₂	5,16 (s)	5,20 (s)	4,96 (d)	5,11 (dd)	5,23 (d)	-	-	5,2	6,8
10	CH ₂ CH ₂ CH ₂ CH ₃	5,07 (s)	5,21 (s)	4,96 (d)	5,13 (dd)	5,23 (d)	-	-	5,2	7,2
11	CH ₂ Ph	5,16 (s)	5,29 (s)	5,00 (d)	5,18 (dd)	5,30 (d)	-	-	4,8	7,2



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

conformation ¹T₂

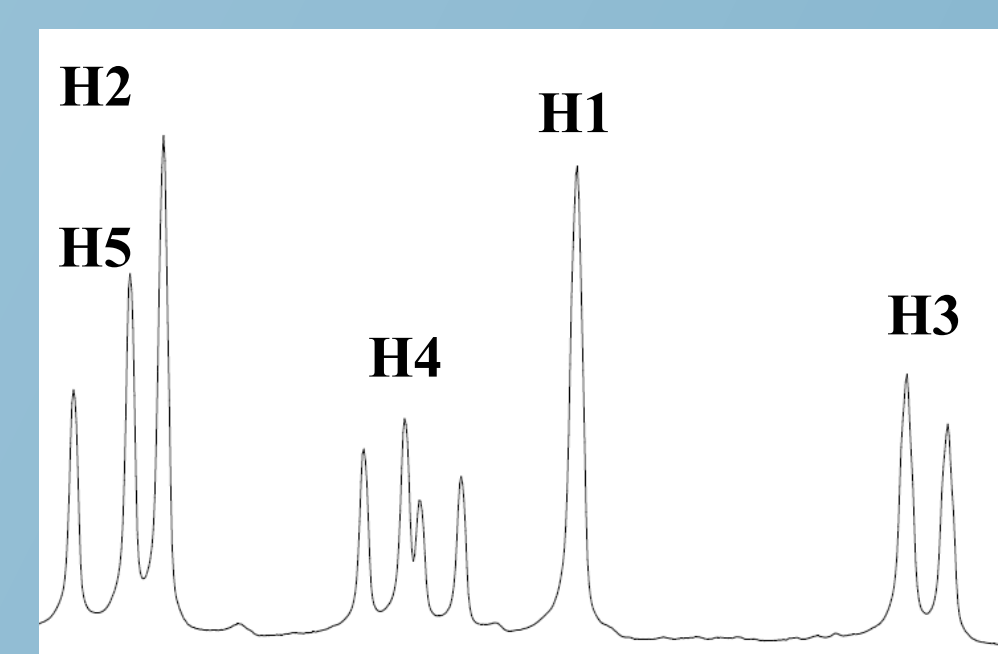


Fig. 2 Characteristic ¹H NMR spectra of furanosides 7-11.

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. 2). 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 ¹T₂-like conformation [5]. ¹H NMR spectra of furanosides 1-6 also indicate the ¹T₂ conformation.

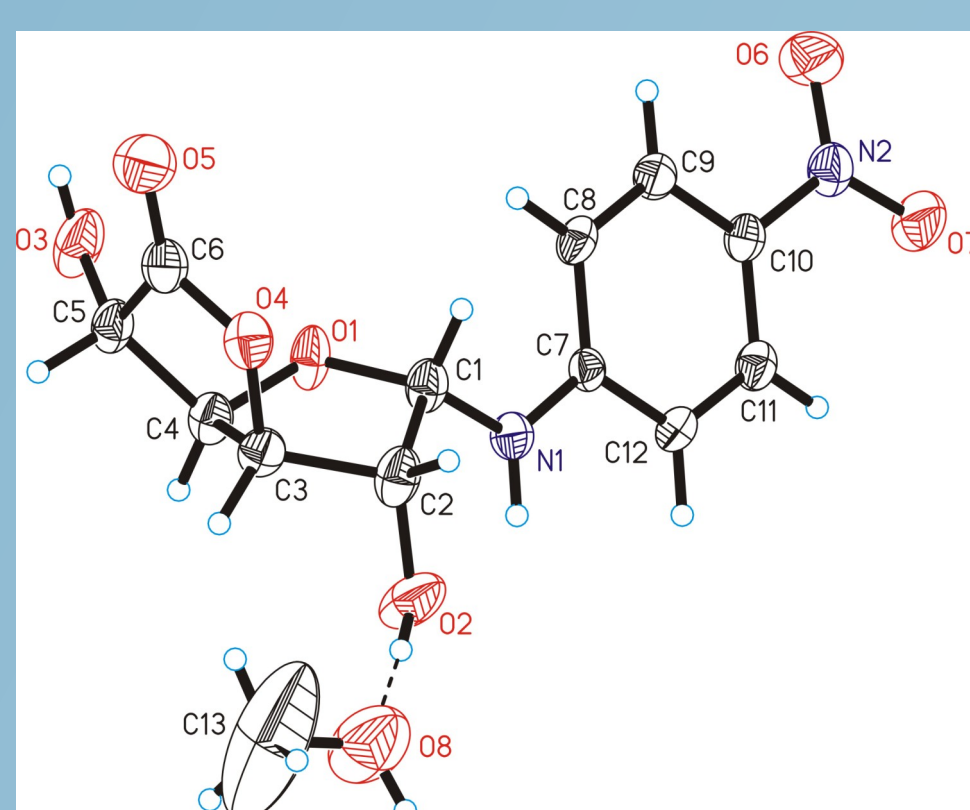


Fig. 3 Structure of 12 showing 25% probability displacements for ellipsoids. Compound 12 crystallines with one molecule of methanol. The O-H...O hydrogen bond, represented by a dashed line, is created between MeOH and 2-OH.

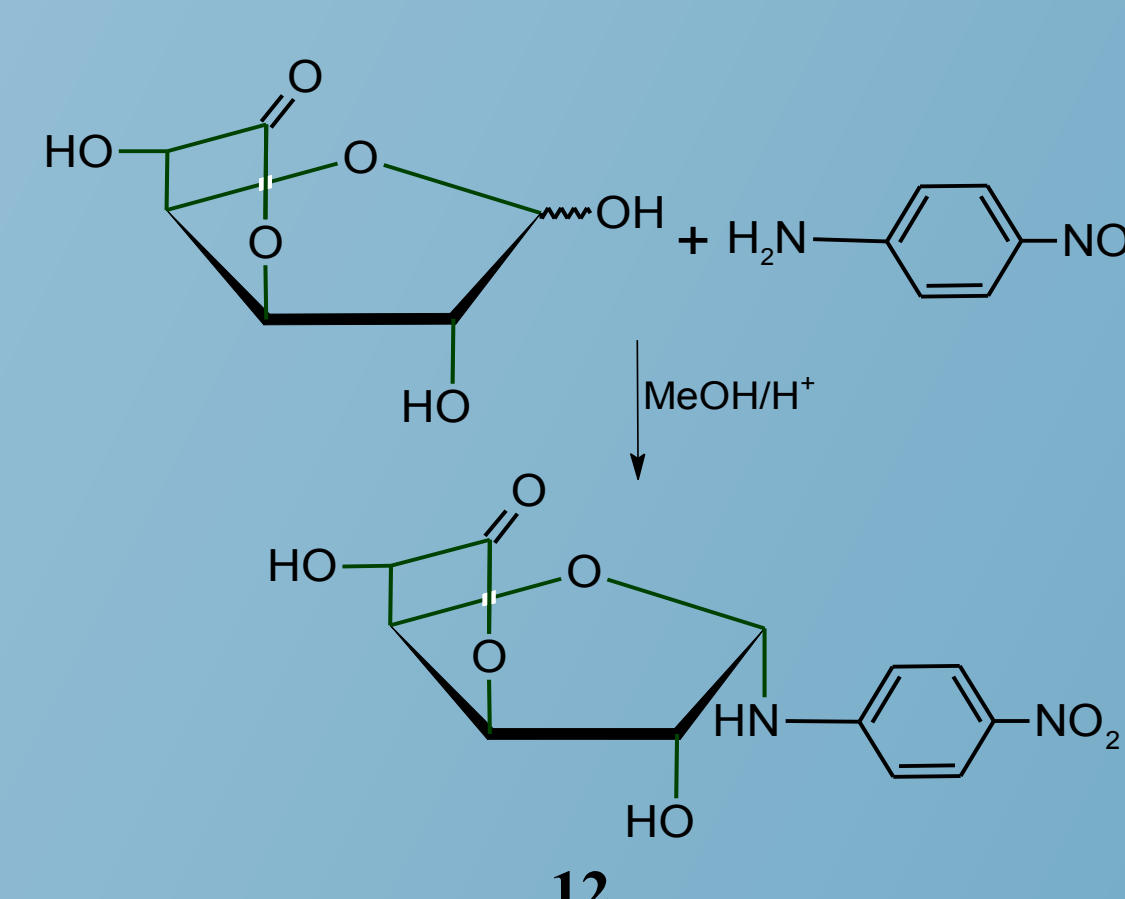
Table 3

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

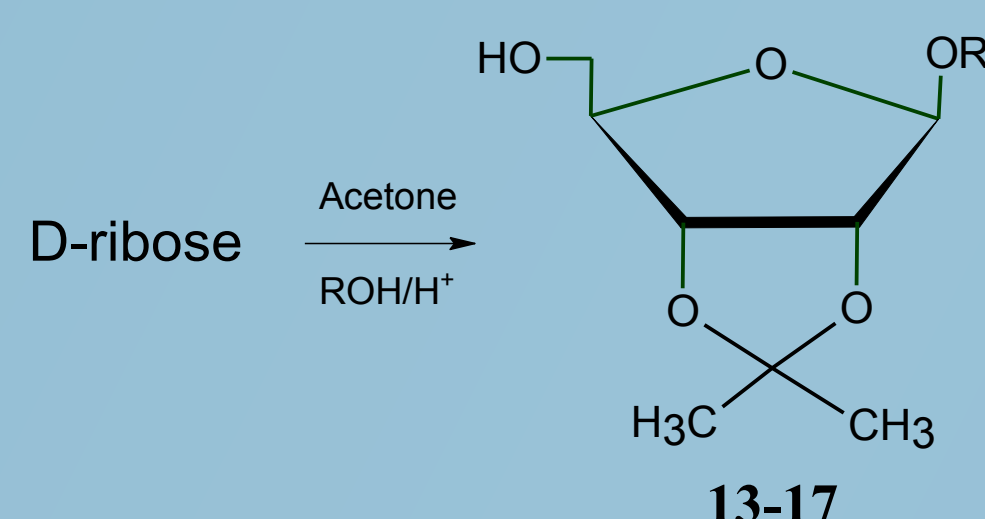
H-1	H-2	H-3	H-4	H-5	2-OH	5-OH	J _{1,2}	J _{2,3}	J _{3,4}	J _{4,5}
5,44 (d)	5,31 (d)	4,89 (d)	4,65 (dd)	4,48 (t)	6,29 (bs)	5,93 (d)	4,0	-	3,6	4,8

conformation ³E

The ¹H NMR spectra of N-(α-D-glucofuranourono-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 3). In the crystal lattice, 12 adopts the ³E conformation (Fig. 3). It is possible that the same conformation is adopted by 12 in solution.



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



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

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 (CH₂OH) (Table 4). In this case, there is lack of coupling between H1 and H2 as well as H3 and H4 protons (Fig. 4).

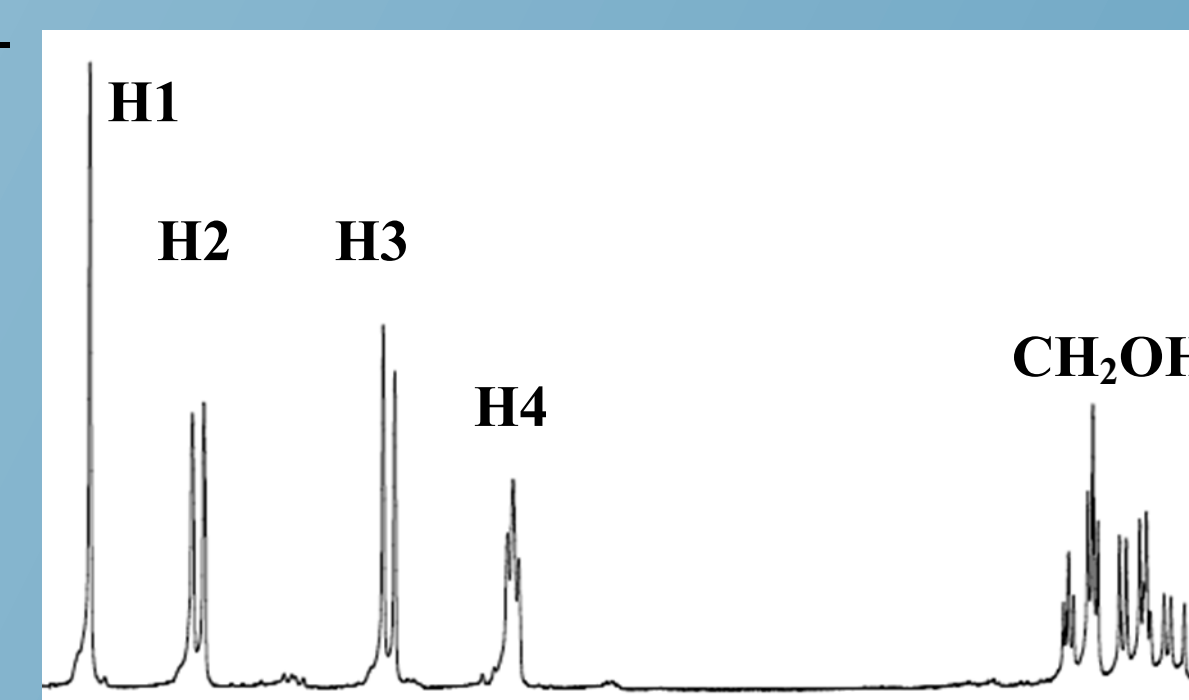


Fig. 4 Characteristic ¹H NMR spectra of furanosides 13-17.

Table 4

Chemical shifts (ppm) and ¹H-¹H coupling constants (Hz) in the ¹H NMR spectra (CDCl₃) of 2,3-O-isopropylidene-D-ribofuranosides (13-17).

no.	R=	H-1	H-2	H-3	H-4	CH ₂ OH	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 ₂ CH ₃	5,07 (s)	4,84 (d)	4,59 (d)	4,41 (t)	3,68 (m)	-	6,4	-	2,8
15	CH ₂ CH ₂ CH ₃	5,06 (s)	4,84 (d)	4,60 (d)	4,41 (t)	3,68 (m)	-	6,0	-	2,8
16	CH(CH ₃) ₂	5,17 (s)	4,85 (d)	4,56 (d)	4,40 (t)	3,67 (m)	-	6,0	-	2,4
17	CH ₂ CH ₂ CH ₂ CH ₃	5,05 (s)	4,83 (d)	4,59 (d)	4,40 (t)	3,73 (m)	-	6,4	-	2,4

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Acknowledgements

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