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STEREOSPECIFIC LONG-RANGE COUPLINGS OF HYDROXYL PROTONS OF PYRANOSES

J.C.Jochims, G.Taigel, A.Seeliger, P.Lutz and H.E.Driesen

Max-Planck-Institut für Medizinische Forschung
Institut für Chemie, Heidelberg, Germany.

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The hydroxyl groups of carbohydrates give well resolved proton magnetic resonances if exchange reactions can be suppressed. Usually this is the fact when the pure sugar is dissolved in dry dimethyl sulfoxide-d_6 (DMSO) or better in mixtures of DMSO and acetone-d_6 [1,2].

Under these conditions the high resolution resonance *) of the anomeric hydroxyl proton OH^1 of α-D-glucose I is not a doublet as sometimes reported [3,4,5] but a doublet of doublets (6.18 ppm [a]) as shown in Fig. 1. In a frequency swept spin decoupling experiment irradiating at 3.25 ppm reduces the OH^1 signal to a sharp doublet with 4,5 c/s splitting. At the same time the triplet of H^1 (5.02 ppm) collapses to a doublet. Thus H^2 must absorbe at

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*) All spectra were recorded with a Varian HA-100 spectrometer. The chemical shift are reported in ppm from tetramethyl silane as intern reference signal.

a) In 0,2 ccm DMSO + 0,2 ccm acetone-d_6.

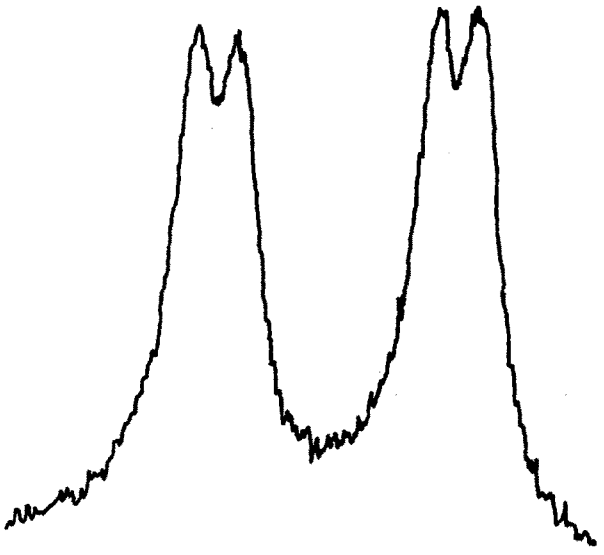
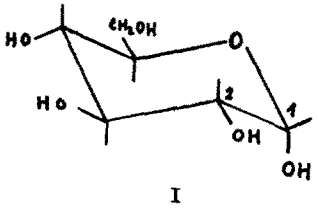
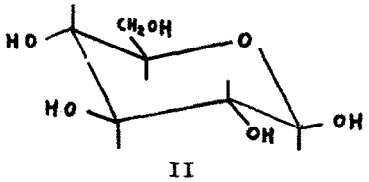


FIG.1.: The proton magnetic resonance of the anomeric hydroxyl OH^1 of α-D-glucose I [a].



I



II

3.25 ppm and is coupled to H^1 with ~4 c/s and to OH^1 with 0.7 c/s. The long-range coupling of OH^1 to H^2 is not virtual [6] because OH^1 (6.18 ppm), H^1 (5.02 ppm), H^2 (3.25 ppm) and H^3 (3.60 ppm) are all sufficiently shifted from one another. The hydroxyls OH^2, OH^3 and OH^4 do not show any long-range coupling.

In ß-D-glucose II, differing from I by an inverted configuration at C-atom 1 the hydroxyl OH^1 gives rise to a sharp doublet (6.54 ppm [b]) with 6.4 c/s spacing. No long-range coupling can be detected.

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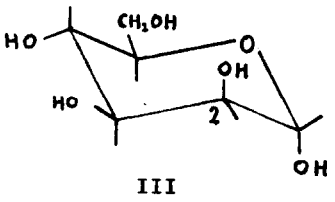
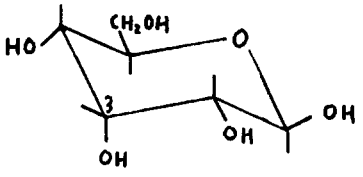
b) In DMSO.



III

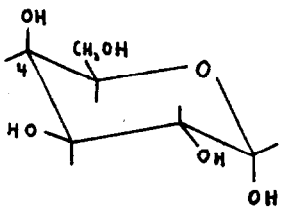
The same holds for α-D-mannose III, differing from I by changing the configuration at C-atom 2. III shows a sharp doublet for OH^1 (6.17 ppm, 0.8 c/s line width at half length [a]). Inversion of the configuration at C-atom 3 of II leads to β-D-allose IV.

While the C-1-conformation [7] for the molecules I - III in solution is well established [4,8,9], this is not the case for IV. The signals of H^1 (4.72 ppm [c]), H^2 (3.16 ppm), H^3 (3.95 ppm) and H^4 ($\sim$ 3.4 ppm) are so much shifted that their splittings can be taken very approximately as the coupling constants. Thus $J_{H1,H2}$ = 7.6 c/s, $J_{H2,H3}$ = 3.1 c/s and $J_{H3,H4} \approx$ 3 c/s is found according to a diaxial and two gauche arrangements. The hydroxyl groups OH^1 (6.33 ppm; J_{OH^1,H^1} = 6.7 c/s), OH^2 (4.48 ppm; J_{OH^2,H^2} = 6.5 c/s), OH^3 (4.60 ppm; J_{OH^3,H^3} = 3.1 c/s), OH^4 (4.29 ppm; $J_{OH^4,H^4} \approx 7$ c/s) and OH^6 (4.27 ppm) form four doublets and one triplet.



IV

Thus β-D-allose is in solution a pyranose in the C-1-conformation IV. From all the hydroxyl protons only the axial OH^3 shows small long-range couplings to both H^2 ($\sim$ 0.35 c/s) and H^4 ($\sim$ 0.3 c/s). These couplings were not resolved but secured by spin decoupling.



V

Finally α-D-galactose V, differing from I by the inverted configuration at C-atom 4, and also dissolved as pyranose with C-1-conformation, again shows a 0.8 c/s long-range coupling from OH^1 (6.07 ppm, J_{OH^1,H^1} = 4.5 c/s [b]) to H^2 (3.53 ppm; J_{H^1,H^2} = 2.7 c/s) as found by spin decoupling. This coupling again is absent in β-D-galactose VI.

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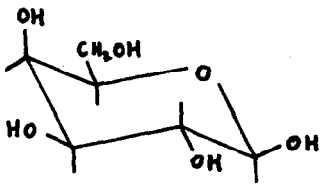
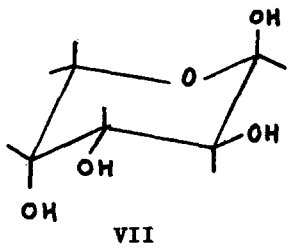
c) In 0.2 ccm DMSO + 0.15 ccm acetone-d_6.

The remainder of the spectra of III, V and VI was not further analyzed. It can be concluded from these observations that OH long-range couplings of pyranoses in chair conformations appear between, and only between, the protons of an axial hydroxyl group vicinal to an axial proton.

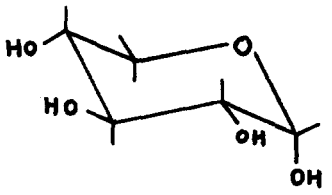


VI

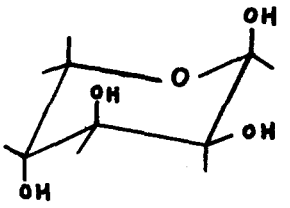
This rule applies to all examples so far examined. Thus, OH^1 is further coupled to H^2 with 0.4 - 0.6 c/s in ß-D-arabinose VII, in α-D-xylose VIII and in ß-D-lyxose IX but neither in



VII

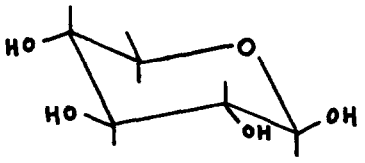


VIII

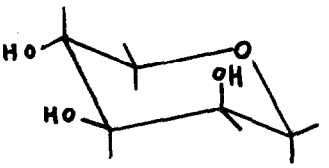


IX

ß-D-xylose X nor in α-D-lyxose XI.



X



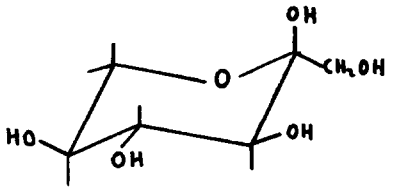
XI

The spectra of these compounds will be discussed more intensively elsewhere.

Hydroxyl long-range couplings should be of special value in determining the configuration of ketoses , for these sugars have no proton attached at the anomeric C-atom the vicinal coupling constant of the former depends on the configuration as in the case for the aldoses.

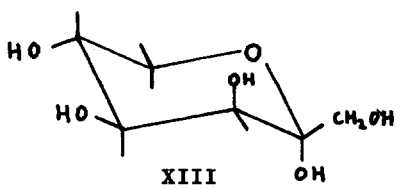
Thus, L-sorbose shows a broad and poorly resolved signal for the CH-protons from which nothing can be said either about conformation or configuration. But the hydroxyls give rise to three doublets (4.76 ppm; 4.0 c/s splitting. 4.60 ppm; 3.8 c/s splitting. 4.28 ppm; 6.6 c/s splitting [a]), a quartet (4.48 ppm; 6.1 c/s spacing between first and second line, 7.0 c/s distance between first and third line) and a doublet at lowest field (5.16 ppm) with the small spacing of 0.8 c/s.

Because there is only one primary hydroxyl group L-sorbose must be a pyranose. The small coupling of the anomeric hydroxyl group OH^2 (5.16 ppm) disappears on irradiating at 3.42 ppm. At the same time the hydroxyl doublet (4.76 ppm) collapses thus showing diaxial orientation of OH^2 (5.16 ppm) and H^3 (3.42 ppm). This leads to a 1-C-conformation and α-configuration of L-sorbose XII.

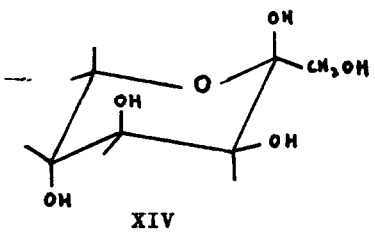


XII

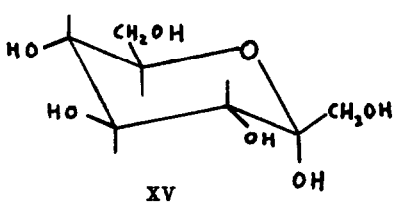
D-Tagatose (m.p. 136 - 138°) remains a mixture of at least four stereoisomers even after several recrystallisations. The anomeric hydroxyl of the main product (about 80 %) appears as a sharp, not long-range coupled singlet at 5.33 ppm [b]. Very likely this is α-D-tagatose with C-1-conformation XIII. One of the side products (about 15 %) shows an OH^2-signal with 0.8 c/s splitting at 5.25 ppm giving a sharp singlet on irradiating at 3.30 ppm. If the above conclusions are right this substance has to be ß-D-tagatose with 1-C-conformation XIV. Finally, the resonance of the anomeric hydroxyl OH^2 of D-glucoheptulose at 5.25 ppm [a] is a doublet with 0.9 c/s splitting collapsing to a sharp singlet on irradiating at 3.35 ppm. Discarding the possibility of a furanose form - a septanose is impossible because three secondary and two primary hydroxyl groups are observed - D-glucoheptulose must therefore have C-1-conformation and α-configuration XV. The compound is stereochemically pure and does not show any noticable change of the spectrum within a week.



XIII



XIV

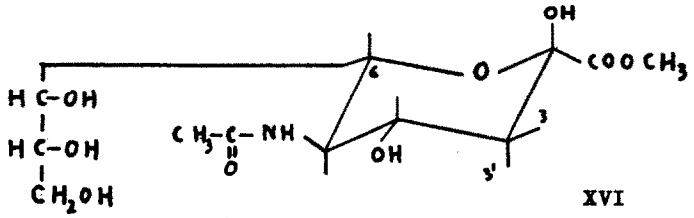


XV

A very large OH long-range coupling was found for the anomeric hydroxyl proton OH^2 of the methyl ester of N-acetyl-neuraminic acid XVI. The 1-C-conformation of this compound is well established [10]. The anomeric hydroxyl proton OH^2 appears at 6.60 ppm [d] as a well resolved doublet

d) In 0.4 ccm DMSO + 0.15 ccm C_6D_6.

of 2.1 c/s splitting. This resonance becomes a sharp singlet on decoupling from the axial $H^{3'}$ (1.94 ppm). But the OH^2 signal is not affected in any way on irradiating the equatorial H^3 (2.32 ppm). The protons H^3 and $H^{3'}$ are shifted enough from one another and are far away from the signal of H^4(~ 3.7 ppm) to



XVI

exclude virtual coupling. Thus, the question as to the configuration of XVI can now be answered: the methylester of N-acetyl-neuraminic acid is dissolved in DMSO in the 1-C-conformation and shows α-configuration *) (axial OH^2) XVI and no mutarotation within a week. The same applies to the 4,7,8,9-tetraacetyl-derivate [13] of XVI with a long-range coupling of OH^2 to axial $H^{3'}$ of 1.5 c/s.

The splitting of the long-range coupled hydroxyls depends markedly on the solvent and on preparation of the sample and is probably affected by proton exchange reactions. Therefore in most cases the splitting will be smaller than the real coupling constants are.

We think a coplanar arrangement of the coupling protons and the connecting atoms (W-mechanism; but see for instance [11,12]) is necessary for the OH long-range couplings. Following that, the size of the coupling constant must depend on the statistical weight of the rotational isomer of the hydroxyl properly sterically orientated for a long-range coupling. This will be fully discussed elsewhere.

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*) α, because the substitution at C-atom 6 of the pyranose ring is that of an L-sugar.

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