Conformation of 1,2-isopropylidene derivatives of α -D-glucopyranose

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The conformation of 1,2-O-isopropylidene-3,4,6-tri-O-methyl- α -D-glucopyranose and 1,2-O-isopropylidene-4,6-di-O-methyl- α -D-glucopyranose in solution were investigated by p.m.r. spectroscopy. The above-mentioned substances adopt essentially the skew-boat conformation under the given conditions of measurement.

As known, pyranoses of sugar derivatives preferentially possess the energetically favourable chair conformation. The attachment of a five-membered acetal ring to the pyranoid one results in the deformation of the latter. This is in agreement with some p.m.r. studies [1-3] reporting the acetal rings, attached to those of pyranoses, to adopt a nonplanar conformation in solution.

Of great interest are papers by Coxon [4-6] referring to the p.m.r. conformational studies of saccharides. His statement that 1,2-O-alkylidene-pyranose derivatives display skew-boat conformation does not agree with other papers [7-9] of which mainly *Trotter* and *Fawcett* [7] favoured the flattened chair conformation.

The goal of this paper is to throw more light on the conformation of derivatives of saccharides with a five-membered acetal ring.

Experimental

The p.m.r. spectra of 1,2-O-isopropylidene-3,4,6-tri-O-methyl- α -D-glucopyranose (I) and 1,2-O-isopropylidene-4,6-di-O-methyl- α -D-glucopyranose (II) were measured at 80 MHz with a Tesla (Brno) 487 B spectrometer, tetramethylsilane being the internal reference substance. Deuteriochloroform was used to dissolve both the compound I and the deuteriated substance II; concentration was approximately 30 mg in 0.3 ml of the solvent. Protons in the spectra were ascribed using double resonance INDOR technique.

Substances I and II characterized by $[\alpha]_D^{24}$ 42.5° (c 1.0, ethanol) and m.p. 70-71°C, $[\alpha]_D^{24}$ 33.8° (c 1.0, ethanol), respectively, were prepared according to [10].

Chemical shift values are seen in Fig. 1; coupling constants of the first-order part of the spectra are listed in Table 1.

Discussion

To determine the conformation of saccharides by means of p.m.r. spectroscopy the *Karplus*' equation [11, 12] has been applied, according to which the coupling constant (J) of two protons attached to neighbouring carbon atoms is a function of the dihedral angle $[\Phi]$ they contain. In this paper we applied the Karplus' equation, modified by *Abraham* and co-workers [13], to calculate the proper angles from coupling constants.



Fig. 1. The p.m.r. spectrum.
a) 1,2-O-isopropylidene-3,4,6-tri-O-methyl-α-D-glucopyranose;
b) 1,2-O-isopropylidene-4,6-di-O-methyl-α-D-glucopyranose. Sweep width 250 Hz; sweep offset 200 Hz.

As seen from the calculated dihedral angles listed in Table 2, there is no doubt that any of the two substances exists in the chair form (Scheme 1). Protons H-2, H-3, H-4, and H-5 in this conformation are axially oriented and for this reason $J_{2,3} \simeq J_{3,4} \simeq$ $\simeq J_{4,5} > 9$ cps.

Only the coupling constants $J_{1,2}$ and $J_{4,5}$ and the dihedral angles corresponding to them are consistent with the conformation shown in Scheme 1. The other angles for H-2,



H-3 and H-3, H-4 calculated from the coupling constants have too low values, particularly in the case when the parameter J_0 for an angle less than 90° is taken into consideration. At first sight, the low values of coupling constants $J_{2,3}$ and $J_{3,4}$ seem to be quite substantiated.

Table 1

First-order coupling constants (cps)

Compound	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	
I	5.0	3.4	3.4	9.2	
II	4.6	4.1	3.8	9.0	

Table 2

Approximate values of proton-proton dihedral angles for substances I and II

Compound	Conformation	Dihedral angles (in degrees)							
		$\mathrm{H_{1},H_{2}}$		$\rm H_2, \rm H_3$		H_3, H_4		H_4, H_5	
		М	С	М	С	М	С	м	С
	skew-boat	40	38	50	49	115	127	170	176
I	flattened chair	42	38	162	127	176	127	170	176
	skew-boat	40	41	50	44	115	129	170	170
II	flattened chair	42	41	162	131	176	129	170	170

M – Measured on Dreiding models (measurement deviation $\pm 5^{\circ}$).

C - Calculated from J constants.

The low values of coupling constants for H-2, H-3 and H-3, H-4 let us suggest the mentioned hydrogen atoms to be rather gauche than diaxially oriented. This would mean that the attachment of the five-membered acetal ring to the molecule altered the fundamental chair conformation.

The appearance of a long-range coupling, which is reported to be stereospecific in a planar arrangement of atoms in a "W" shape [14] is an important factor when studying the conformation of pyranoid rings. *Coxon*, who examined [15] the p.m.r. spectra of 1,2:4,6-di-O-benzylidene derivatives of glucopyranose and ascribed a flattened chair conformation to them, found no measurable value for $J_{2,4}$. The $J_{2,4}$ value = 2.5 cps of 3-O-benzyli-1,2,4-O-benzylidene- α -D-ribopyranose, a model substance, which can exist

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in a skew-boat conformation only, was found by the same author [6]. We estimated the $J_{2,4}$ value for both substances I and II to be 0.85 cps.



Regarding what has been said, it is reasonable to consider the skew-boat conformation as shown in Scheme 2. This assumption is supported by examination of Dreiding models of substances I and II in skew-boat conformation; when taking the calculated angle H-1, H-2 as being 38-41° and that between H-4, H-5 170-176°, it follows that the angle formed by H-3, H-4 equals approximately 115°. This value is greater than 90° what entitles to use the parameter $J_0 = 10.4$.

The calculated angle for H-3, H-4 is almost consistent with that measured on the Dreiding models; the angle for H-2, H-3 50° remained unchanged and satisfies the skew-boat conformation. Dihedral angles for substances I and II calculated in this way are in good accordance with those measured with Dreiding models and fit the skew-boat conformation.

Basing upon our results as listed in Table 2 we conclude that substances I and II measured in deuteriochloroform satisfy the parameters for the skew-boat conformation drawn in Scheme 2.

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