Carbohydrate Research, 47 (1976) 311—314

Note

Conformation of the C-5/C-6 fragment of aldohexopyranoses

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(Received July 21st, 1975; accepted for publication, October 19th, 1975)

The assignment of the n.m.r. signals of the anisochronous protons of a methylene group adjacent to a chiral center remains a controversial problem[1]. Data on the C-5/C-6 fragment of aldohexopyranose derivatives have been reported by several authors[2–5]. Following mono-deuteration at C-6 in D-glucose derivatives, Gagnaire, Horton, and Taravel concluded[1] that 6(*S*) and 6(*R*) forms were present in a ratio of 3:2, thereby allowing a stereochemical assignment to the primary acetoxymethylene grouping in α-D-glucopyranose penta-acetate. We have now interpreted the coupling constants on the basis of considerations of the C-5–C-6 rotamer population, and the results are in agreement with the relative chemical shifts of the methylene protons interpreted on the basis of the so-called "syn-up" rule[6].

The chemical shifts and coupling constants[7] of the protons in the C-5/C-6 fragment in both anomeric pyranoses of D-glucose, D-mannose, and D-galactose, and the corresponding methyl glycosides are shown in Table I. The coding A refers to the signal at lower field.

TABLE I

CHEMICAL SHIFTS AND COUPLING CONSTANTS[7] OF H-5,6A,6B OF ALDOHEXOPYRANOSES IN D_2O

	H-5	*H-6A*	*H-6B*	$^3J(5,6A)$	$^3J(5,6B)$	$^3J(6A,6B)$
β-D-Glucopyranose	3.42	3.89	3.72	2.0	5.8	−12.0
α-D-Glucopyranose	3.82	3.83	3.77	2.0	5.8	−12.0
β-D-Galactopyranose	3.71	~3.75	~3.75	—	—	—
α-D-Galactopyranose	4.09	~3.74	~3.74	—	—	—
β-D-Mannopyranose	3.37	3.91	3.73	2.3	5.7	−12.0
α-D-Mannopyranose	3.82	3.88	3.76	2.0	5.6	−12.0
Methyl β-D-glucopyranoside	3.47	3.93	3.73	2.1	5.8	−12.3
Methyl α-D-glucopyranoside	3.65	3.85	3.75	2.2	5.4	−12.3
Methyl β-D-galactopyranoside	3.70	3.83	3.76	8.5	3.5	−11.4
Methyl α-D-galactopyranoside	3.90	~3.69	~3.69	~6.4	~5.3	—
Methyl α-D-mannopyranoside	3.62	3.91	3.76	1.9	5.8	−12.0

The separation of the signals of the hydroxymethylene protons in the D-glucose and D-mannose series is 0.17–0.20 p.p.m. for the β and 0.06–0.15 p.p.m. for the α isomers. These values are <0.07 p.p.m. in the galactose series. For the glucose and mannose compounds, $J_{5,6A}$ is 1.9–2.3 Hz and $J_{5,6B}$ 5.4–5.8 Hz. For α-D-galactoses, these values are ~ 6 Hz, whereas for methyl β-D-galactoside, $J_{5,6A}$ is 8.5 Hz and $J_{5,6B}$ is only 3.5 Hz.

The rotamers for D-glucose and D-mannose (and their methyl glycosides) are represented in Fig. 1. Using the Karplus relationship qualitatively, the following conclusions are drawn. Rotamer AOB may be excluded as a major contributor

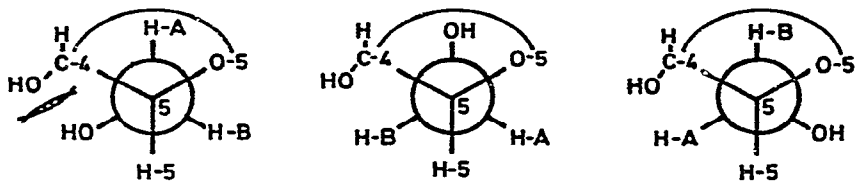

Fig. 1.

because we would then expect (*a*) $J_{5,6A} > J_{5,6B}$, (*b*) HO-4 and HO-6 to stay quasi-*syn*-axial, and (*c*) the signal for H-A to be found at higher field (see below). For methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside, Gagnaire *et al.*[1] found $J_{5,6A}$ 11, and $J_{5,6B}$ 5 Hz (with H-6A axial and H-6B equatorial, *cf.* Fig. 1, AOB). In our compounds, the location of H-6A and H-6B is interchanged. It follows that $J_{5,6B}$ is lower in magnitude because of the presence of both AHB and ACB rotamers.

Also, $J_{5,6A}$ is expected to be <5 Hz, because H-5 in AHB and H-6A in ACB are antiperiplanar to an electronegative substituent, a configuration that is known[14] to cause a maximal decrease of J.

Another, different rotamer population occurs in the D-galactose derivatives (Fig. 2). Because HO-4 stays axial, the quasi-*syn*-axial nature of HO-6 in the AHB form will prevent this form from making a major contribution. In the α anomer, rotamers AOB and ACB are presumably equally populated, resulting in $J_{5,6A} = J_{5,6B}$ and causing almost identical shifts for H-6A and H-6B. In the β anomer, the ACB

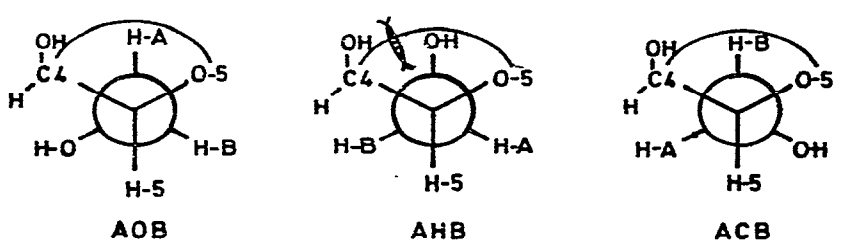

Fig. 2.

form seems to be disfavoured, possibly because of a mutual repulsion between dipoles associated with C-6–O-6 and C-1–O-1 bonds as is shown by molecular models. The contribution of AOB is estimated as ~80% from the following considerations. In the D-glucose and D-mannose series, H-6A remains *syn* to H-5 in AHB and ACB, and either H-6A or H-5 is antiperiplanar to an oxygen-bearing substituent. Therefore, the value of 2.2 Hz for $J_{5,6A}$ must be typical for this kind of inter-proton coupling. On the other hand, the value 6.4 Hz observed for $J_{5,6A}$ in the α-D-galactose series is the result of two nearly equally populated forms, namely AOB and ACB (Fig. 2), and it is thus the average of *J* (antiperiplanar) and *J* (syn) values. Since *J* (syn) is 2.2 Hz, *J* (antiperiplanar) must be 10.6 Hz (*cf.* 11 Hz cited in Ref. 1). A value of 8.5 Hz indicates the presence of ~80% of an AOB rotamer.

The signals for protons which are *syn* to a substituent are shifted upfield[8–12]. A decrease of the induced shift occurs when passing from an eclipsed to an antiperiplanar conformation[6]. In both the staggered and the eclipsed conformations, the *syn* proton will be shielded relative to the *anti* proton[13]. Thus, the syn-upfield rule was introduced for cyclic and acyclic systems. Also, an additivity seems to be valid. Predictions based on this rule are summarized in Table II. It is clear that, in the D-glucose and D-mannose series, there is little contribution from AOB. In the β-D-galactose series, the proton signal at the higher-field side should display the largest coupling. However, the conflict is only apparent, and a superimposed deshielding effect[27] by quasi-*syn*-axial HO-4 readily explains the findings.

TABLE II

EXPECTED, RELATIVE SHIFT POSITION OF H-6A AND H-6B IN THE C-5/C-6 FRAGMENT

Rotamer	syn-*Atoms*		*Conclusion*
	H-6A	*H-6B*	
AOB	O-5, C-4	O-5	H-6A at higher field than H-6B
AHB	O-5	C-4	H-6A and H-6B collapse
ACB	C-4	C-4, O-5	H-6A at lower field than H-6B

The simultaneous use[15] of ^3J (H,H) and ^3J (^{13}C,H) values enables the correct assignments in CH–CH$_2$ fragments of rotamers.

REFERENCES

1 D. GAGNAIRE, D. HORTON, AND F. R. TARAVEL, *Carbohyd. Res.*, 27 (1973) 363–372.
2 R. U. LEMIEUX AND J. D. STEVENS, *Can. J. Chem.*, 43 (1963) 2059–2070.
3 C. V. HOLLAND, D. HORTON, M. J. MILLER, AND N. S. BHACCA, *J. Org. Chem.*, 32 (1967) 3077–3084.
4 L. D. HALL, J. F. MANVILLE, AND J. G. DALTON, *Can. J. Chem.*, 47 (1969) 1–17.
5 G. DESCOTES, F. CHIZAT, AND J. C. MARTIN, *Bull. Soc. Chim. Fr.*, (1970) 2304–2309.
6 D. DANNEELS AND M. ANTEUNIS, *Org. Magn. Res.*, 6 (1974) 617–621.
7 A. DE BRUYN, M. ANTEUNIS, AND G. VERHEGGE, *J. Acta Ciencia Indica*, 1 (1975) 83–87.
8 C. K. FAY, J. B. GRUTZNER, L. F. JOHNSON, S. STERNHELL, AND P. WESTERMAN, *J. Org. Chem.*, 38 (1973) 3122–3155.

9 P. LASZLO AND P. v. R. SCHLEYER, *J. Amer. Chem. Soc.*, 35 (1963) 2709–2712.
10 K. L. WILLIAMSON, C. A. LANFORD, AND C. R. NICHOLSON, *J. Amer. Chem. Soc.*, 86 (1964) 762–765.
11 K. M. CRECELY, V. S. WATTS, AND J. H. GOLDSTEIN, *J. Mol. Spectrosc.*, 30 (1969) 184–191.
12 Y. ROMMELAERE AND M. ANTEUNIS, *Bull. Soc. Chim. Belg.*, 79 (1970) 523–530.
13 D. DANNEELS, Ph.D. Thesis, State University of Ghent, 1975.
14 H. BOOTH, *Tetrahedron*, 22 (1966) 615–620.
15 J. FEENEY, *J. Magn. Res.*, 17 (1975) 249–261.