Chemical Studies by ^{13}C Nuclear Magnetic Resonance Spectroscopy: Some Chemical Shift Dependencies of Oxygenated Derivatives

By L. D. HALL*

(*Department of Chemistry, The University of British Columbia, Vancouver 8, British Columbia, Canada*)

and L. F. JOHNSON

(*N.M.R. Applications Laboratory, Varian Associates, Palo Alto, California*)

WE present some preliminary studies of pyranose carbohydrate derivatives which establish some of the influences which oxygen containing substituents have on ^{13}C-chemical shifts.

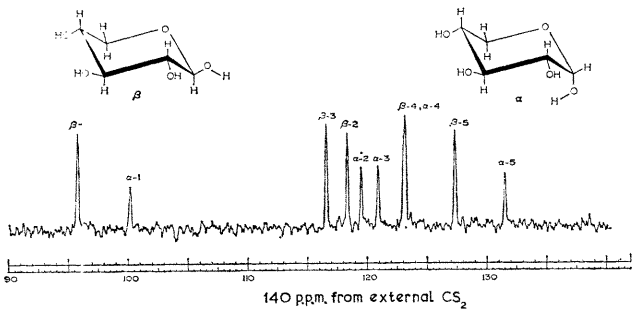

FIGURE. *Natural abundance ^{13}C n.m.r. spectrum of* D-*xylose* (0·4 g.) *in* H_2O *solution* (1·0 ml.). *The spectrum shown is the resultant of time-averaging* 100 *scans, each at* 100 *sec. scan-time; the proton couplings were removed by noise-modulated spin-decoupling. The assignments of peaks to the* α- *and* β-*anomers follows the known* (*ref.* 2) *proportions of these anomers in a fully equilibrated solution. The assignments of the other ring carbon resonances are tentative; however, they are consistent with several sets of configurational dependencies.*

The Figure shows a typical ^{13}C n.m.r. spectrum, obtained from a solution of D-xylose (0·4 g.) in water (1 ml.);† noise-modulated[1] proton decoupling was used to simplify the measurement‡ and the half-height width of the resonances is *ca.* 5Hz. Figure shows the resultant of time-averaging the spectrum 100 times, each scan taking 100 sec.; thus the total time required was only 167 mins.§

Although we have tentatively assigned all of the ^{13}C resonances of derivatives (1)—(12), only the anomeric (C-1) resonances (Table 1) will be discussed in any detail here. For the free sugars, the anomeric assignments are based on the known[2] composition of the fully mutarotated aqueous solutions. It is significant that there is good agreement between the shifts of each hexose and its configurationally related pentose counterpart.

The shift of any individual C-1 resonance is dependent on the nature of the C-1 substituent and on the configuration both of C-1 and at other carbons in the ring. Taking the anomeric shifts of the free-sugars (1) and (4) as references, conversion to the methyl glycosides deshields C-1 by 7·1 ±0·1 p.p.m. for both the α- and β-configuration.

The separation between the C-1 chemical shifts of the two anomers of any particular sugar ($C\text{-}1_\alpha - C\text{-}1_\beta$) appears to be independent of the substituent attached to C-1; for the D-glucose derivatives (1), (9) it is +3·7 ± 0·2 p.p.m.[3]

TABLE 1. *Anomeric ^{13}C-chemical shifts for pyranose derivatives*

Derivative	Chemical shifts[a] α-Anomer	β-Anomer
Free sugar[b]		
D-Glucose (1)	100·2	96·4
D-Galactose (2)	100·1	96·0
D-Mannose (3)	98·4	98·7
D-Xylose (4)	100·2	95·8
D-Arabinose (5)	95·6	99·8
D-Lyxose (6)	98·5	98·5
D-Ribose (7)	98·9	98·6
2-Deoxy-D-glucose (8)[c]	101·2	99·1
Methyl glycoside[b]		
D-Glucose (9)	93·2	89·3
D-Xylose (10)	93·1	88·6
Methyl glycoside peracetate[d]		
D-Glucose (11)	95·8	
D-Xylose (12)		91·2

[a] In p.p.m. from external $^{13}CS_2$, all shifts are positive.
[b] In aqueous solution.
[c] Strictly, this should be referred to as 2-deoxy-D-*arabino*-hexopyranose.
[d] In dimethyl sulphoxide solution.

The effect on the shift of a neighbouring carbon, of inverting a hydroxyl group from an equatorial to an axial orientation, follows from a comparison of the C-1-shifts of D-glucose (1) and D-mannose (3). When C-1 itself bears an axially oriented hydroxyl group, as in the α-anomers, the induced shift is −1·8 p.p.m., whereas for the β-anomers where the C-1 substituent is equatorially oriented, the shift is +2·3 p.p.m. If the shifts of the anomers of 2-deoxy-D-glucose (8) are included, it is possible to attribute values to the induced shifts following the replacement of a C–H bond by a C–OH bond. The replacement of the $C\text{-}2\text{–}H_{ax}$ substituent by a hydroxyl group shifts $C\text{-}1_\alpha$ by −2·8 and $C\text{-}1_\beta$ by −0·4 p.p.m.; replacement of $C\text{-}2\text{–}H_{eq}$ by hydroxyl shifts $C\text{-}1_\alpha$ by −1·0 and $C\text{-}1_\beta$ by −2·7 p.p.m.

Evidently anomeric shifts are not sensitive to changes in configuration at C-4 [compare (1) and (2)],¶ nor are they particularly susceptible to the presence of a hydroxymethyl substituent at C-5 [compare (1) with (4) or (3) with (6)].

The chemical shifts of the methoxyl groups attached to C-1 appear to be characteristic of the anomeric configuration. These data are summarised in Table 2.

Most important from the viewpoint of structure-determination is our observation that a ^{13}C-shift is indicative of

† Varian HA-100 spectrometer operating at 25·15 MHz with a V-3530 RF/AF sweep unit and a V-4335-1 8 mm. probe.
‡ Proton decoupling was effected by a Varian V-3512-1 Heteronuclear Noise decoupler.
§ Time-averaging was done with a Varian C-1024 computer. When a solution of a single species is used, adequate spectra can be obtained in less than 40 min.
¶ Comparisons not detailed here suggested that the inversion $C\text{–}3\text{–}OH_{eq} \rightarrow C\text{–}3\text{–}OH_{ax}$ should shift $C\text{–}1_\beta$ by *ca.* +4 p.p.m.

the general position of that carbon in, or on, a carbohydrate ring system. Thus the anomeric carbons, which bear two oxygen substituents, resonate between +88 and +102 p.p.m. The shifts of the other ring carbons (C-2, C-3, C-4, and C-5 of hexoses) which bear only one oxygen, are +116—+126 p.p.m. The C-6 resonance of a normal hexose occurs between +131 and +132 p.p.m. Acetoxy groups give resonances at +22·0 to +23·0 p.p.m. (carbonyl) and at *ca.* +171·7 p.p.m. (methyl).

TABLE 2. ^{13}C-*Chemical shifts of anomeric methoxyl groups*

Derivative	Chemical shifts[a] α-Anomer	β-Anomer
Methyl D glucoside (9)[b]	137·5	135·3
Methyl D-glucoside tetra-acetate (11)[c]	137·3	—
Methyl D-xyloside (10)[b]	137·3	135·3
Methyl D-xyloside triacetate (12)[c] ..	—	136·0

[a] In p.p.m. from external $^{13}CS_2$, all shifts are positive.
[b] In aqueous solution.
[c] In dimethyl sulphoxide solution.

Deoxy-sugars, many of which are biochemically important, may be studied by ^{13}C n.m.r. Thus the C-6 resonances of α,β-L-rhamnose are observed at +175·6 p.p.m., while the C-2 resonances of α- and β- 2-deoxy-D-glucose (8) come at +155·2 and at +152·9 p.p.m. respectively. It also appears likely that the technique will provide a simple distinction between pyranose and furanose systems since the ^{13}C-spectrum of D-ribose, which is known to exist to a significant extent in the furanose forms, showed two additional resonances (+91·4, +96·1 p.p.m.) to low field of the pyranose C-1 resonances.

Two important points may be concluded from this preliminary study. Firstly, carbohydrate derivatives appear to be excellent model systems for studying the configurational dependencies of ^{13}C n.m.r. parameters. Secondly, ^{13}C n.m.r. spectroscopy appears to have considerable potential in elucidating the structures of many carbohydrate derivatives.

One of us (L.D.H.) thanks the National Research Council of Canada for financial support.

(*Received, March 24th,* 1969; *Com.* 410.)

[1] R. R. Ernst, *J. Chem. Phys.*, 1966, **45**, 3845.
[2] S. J. Angyal, *Austral. J. Chem.*, 1968, **21**, 2737, and references cited therein.
[3] This is comparable with the value obtained for cyclohexanols: see G. W. Buchanan, D. A. Ross, and J. Stothers, *J. Amer. Chem. Soc.*, 1966, **88**, 4301.