CHEMICAL SHIFTS OF CARBOHYDRATES

By L. D. Hall

Department of Chemistry, The University of British Columbia,

Vancouver 8, B. C., Canada.

In their study of six-membered ring compounds by nuclear magnetic

resonance (N.M.R.) spectroscopy, Lemieux, Kullnig, Schneider and Bernstein[1]

reported the first observation of chemical shifts which could be attributed

solely to changes in molecular geometry. Evidence from fully acetylated

pyranose carbohydrates lead to the conclusion that axial protons resonate

at higher field (τ-value) than their equatorial counterparts. Since then

comparatively few attempts[2,3,4] have been made within carbohydrate chemistry

to place this observation on a theoretical basis.

We have now measured the N.M.R. spectra of free pentoses and hexoses

in D_2O and remeasured the spectra of fully acetylated sugars in $CHCl_3$ solu-

tion. The anomeric protons gave the only resolved multiplets and inspection

of their chemical shifts shown in the Table indicates that these shifts are

largely dependent on the configuration at C_2 and are only slightly, although

1. R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider,
    J. Amer. Chem. Soc., 1958, 80, 6098.

2. L. M. Jackman, Applications of Nuclear Magnetic Resonance Spectroscopy
    in Organic Chemistry, Pergamon Press, New York, (1959).

3. R. W. Lenz and J. P. Heeschen, J. Polymer Sci., 1961, 51, 247.

4. R. J. Ferrier and M. F. Singleton, Tetrahedron, 1962, 18, 1143.

Table

Anomeric Chemical Shifts (τ-values) for

Pyranose Carbohydrates.

Sugars in D_2O Solution [†]

Group A	Xylose	Glucose	Galactose	6-Deoxy-Galactose	Mean Value
H_{1a}	5.44	5.45	5.43	5.45	5.44 ($\pm$ 0.01)
H_{1e}	4.82	4.87	4.76	4.76	4.82 ($\pm$ 0.04)
δ_{ae}	0.62	0.58	0.67	0.67	0.64

Group B	Mannose	6-Deoxy-Mannose	Talose		
H_{1a}	5.15	5.15	5.21		5.17 ($\pm$ 0.02)
H_{1e}	4.85	4.89	4.76		4.83 ($\pm$ 0.05)
δ_{ae}	0.30	0.26	0.45		0.30

Sugar Acetates in $CHCl_3$ Solution.[*]

Group A	Xylose	Glucose	Galactose	6-Deoxy-Galactose	Mean Value
H_{1a}	4.25	4.24	4.24	4.29	4.25 ($\pm$ 0.01)
H_{1e}	3.73	3.69	3.61	3.67	3.69 ($\pm$ 0.04)
δ_{ae}	0.52	0.55	0.63	0.62	0.58

Group B	Mannose	6-Deoxy-Mannose	Talose		
H_{1a}	4.11	4.15	4.11		4.12 ($\pm$ 0.01)
H_{1e}	3.90	3.98	3.82		3.90 ($\pm$ 0.05)
δ_{ae}	0.21	0.17	0.29		0.23

[†] With reference to external tetramethylsilane

[*] With reference to internal tetramethylsilane

All spectra measured on a Varian A60 Spectrometer

regularly, dependent on the configuration at C_4 or on the substituent at C_5: the compounds in Group A have C_2-O equatorial and those in Group B have C_2-O axial. Thus a change in the configuration at C_2 produces a definite and regular change in the chemical shift of the anomeric protons and although the magnitude of the effect is not the same for the sugars as for their acetates the directions of the shifts are the same.

McConnell[5] derived the expression

$$\Delta\sigma = \frac{(3\cos^2\theta-1)}{3R^3} \cdot \Delta\chi$$

which can be used to calculate the shielding contribution $\Delta\sigma$ at a particular proton due to a bond situated at distance "R" from that proton and having an angle "θ" between the longitudinal axis of the bond and R; $\Delta\chi$ is the diamagnetic anisotropy of the bond under consideration. We have now used the known chemical shifts between the axial and equatorial protons (δ_{ae}) of cyclohexane[6] (0.48 p.p.m.) and of 5,5-dimethyl-1,3-dioxane[7] (0.47 p.p.m.) to estimate with the above equation, values for $\Delta\chi^{C-C}$ = -6.5 x 10^{-30} cm^3/ molecule and $\Delta\chi^{C-O}$ -6.6 x 10^{-30} cm^3/molecule. The value for $\Delta\chi^{C-C}$ is very close to the average of previous values obtained from cyclic alkanes ([8], -5.5 x 10^{-30} and [9], -8.3 x 10^{-30}) which serves to support the validity of the present method of estimation. Using the above value of $\Delta\chi^{C-O}$ together with distances and angles obtained by measurements of Cenco-Peterson Molecular models, the calculated anomeric chemical shift difference

5.   H. M. McConnell, J. Chem. Phys., 1957, 27, 226.

6.   M. Ahmad, F. A. L. Anet and L. D. Hall, unpublished results.

7.   H. Friebolin, S. Kabuss, W. Maier and U. Luttringhaus, Tet. Letters, 1962, 683.

8.   A. A. Bothner-By and C. Naar-Colin, J. Amer. Chem. Soc., 1958, 80, 1728.

9.   J. I. Musher, J. Chem. Phys., 1961, 35, 1159.

between Groups A and B of the free sugars is -0.25 p.p.m. for H_{1a} and -0.01 p.p.m. for H_{1e}. Furthermore, the calculated δ_{ae} values for the free sugars are 0.38 p.p.m. for Group A and 0.17 p.p.m. for Group B which are of the correct order of magnitude and, more importantly, of sign. The fact that these estimates are consistently low by ca 20% suggests that $\Delta\chi^{C-OH}$ is larger than the value used which is strictly a value for $\Delta\chi^{C-O-C}$ and this would be consistent with the findings of Lenz and Heeschen[3]. The difference in δ_{ae} values between Groups A and B of the acetates has previously been commented on by Jackman[2]. It is noteworthy, and indeed expected, that the magnitude of the shifts associated with configurational changes of the acetoxy substituent are different from those of the hydroxyl substituent. It should be possible to use these evidently characteristic shifts to aid spectral assignments in series of configurationally related compounds and this approach is being applied to the 1,6-anhydro-hexoses.

The above points will be dealt with in greater detail when this work is reported in full. At the same time further details will be given of the other compounds which have been measured in this investigation (the three remaining pentoses, D-allose, D-altrose and D-gulose, all as free sugars and acetates). Their anomeric chemical shifts can also be estimated and for some of the pentoses this evidence can be used to support preferred conformations.