

Two- and Three-bond $^{13}\text{C}-^1\text{H}$ Couplings in Some Carbohydrates

KLAUS BOCK and CHRISTIAN PEDERSEN

Institute of Organic Chemistry, The Technical University of Denmark, DK-2800 Lyngby, Denmark

From the proton coupled ^{13}C NMR spectrum of 1,6-anhydro- β -D-galactopyranose, measured at 67.89 MHz, the two and three bond C–H coupling constants with values larger than ± 2 Hz were obtained. Some long-range C–H couplings of a few other hexose derivatives were also measured. The three bond couplings show a Karplus type of dependence. The two bond couplings have values which are determined by the orientation of the oxygen atoms directly connected to the coupling path.

With modern pulsed Fourier NMR spectrometers proton coupled ^{13}C NMR spectra of carbohydrates are readily obtained. The numerically large one-bond $^{13}\text{C}-^1\text{H}$ couplings can in most cases be measured directly from these spectra.^{1–3} The much smaller two- and three-bond $^{13}\text{C}-^1\text{H}$ couplings have, on the other hand, mostly been obtained from proton NMR spectra of ^{13}C -enriched carbohydrates.^{4–11} Lately, however, a few long-range $J(^{13}\text{C}-^1\text{H})$ values have been measured from natural abundance ^{13}C NMR spectra of carbohydrates;^{9,10} but in no case has a proton coupled ^{13}C NMR spectrum of a carbohydrate been completely analysed.

In the proton coupled ^{13}C NMR spectra measured previously at 22.63 MHz^{1–3} a large number of long-range couplings were observed, but the assignment of these couplings was difficult. We have now measured some carbohydrates at 67.89 MHz; under these conditions it was possible to obtain two- and three-bond $^{13}\text{C}-^1\text{H}$ couplings for virtually all carbon atoms in a number of cases. In the present paper we report the analysis of the spectrum of 1,6-anhydro- β -D-galactopyranose (*I*). In addition some spectral data of a few other hexose derivatives are reported. Chemical shifts and some coupling constants of *I* and

of other 1,6-anhydro-hexopyranoses have been reported recently.^{10,12}

The two galactose derivatives *1* and *2* were chosen because their ^{13}C as well as their ^1H NMR spectra are rather well dispersed at 63.4 kG, and second order effects are therefore less likely.

In Table 1 the $^2J(^{13}\text{C}-^1\text{H})$ and $^3J(^{13}\text{C}-^1\text{H})$ values of 1,6-anhydro- β -D-galactopyranose (*I*) are presented. The signs of these coupling constants were not determined, but are assumed to be in agreement with those measured by Perlin *et al.*⁹ Coupling constants not shown are not necessarily zero, but may have values between ± 2 Hz. Almost all assignments could be made through selective proton decoupling. Some selectively deuterated derivatives of *I* were, however, also studied in order to confirm the assignments.

In Fig. 1A is shown the signal of C1 in the proton coupled spectrum of *I*. Selective irradiation of H5 or H6_{endo} produced the spectra shown in Fig. 1B and C, respectively; it is seen that C1 couples with H5 and H6_{endo}. Other decoupling experiments showed that C1 couples with H3, but not with H2, H4, or H6_{exo}.

Fig. 2B shows the signals of C2, C3, and C5 in the proton coupled spectrum of *I*. Selective decoupling of H1 produced the spectrum depicted in Fig. 2A, showing that the signals of all three carbons were simplified and, hence, that they couple to H1. The same result was obtained from a proton coupled spectrum of the 1-deuterio analogue of *I* (Fig. 2C).

Similar decoupling experiments confirmed the assignments shown in Table 1. In addition the 4-deuterated and the 6,6-dideuterated analogues of *I* were prepared and their proton coupled ^{13}C NMR spectra were studied.

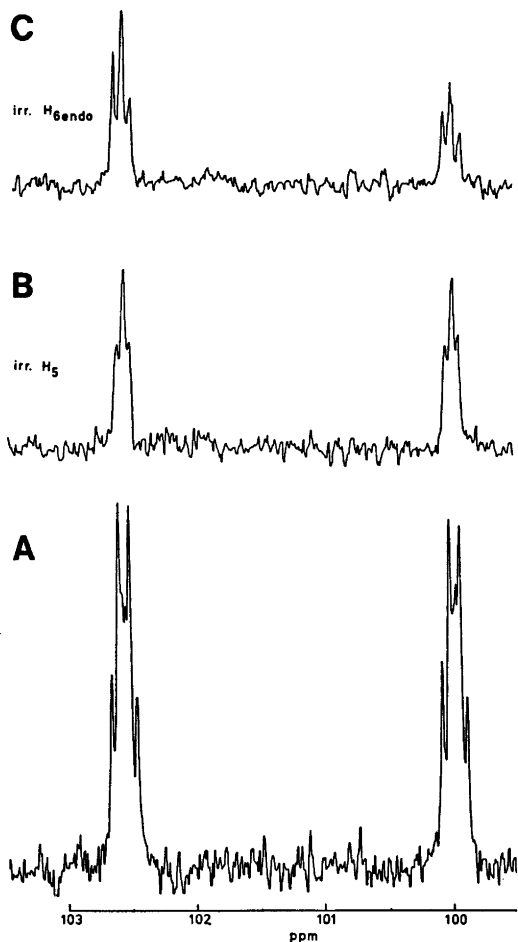
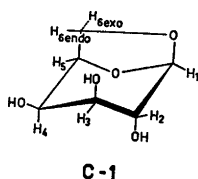


Fig. 1. The ^{13}C NMR signal of C1 of 1,6-anhydro- β -D-galactopyranose (A) Fully proton coupled signal; (B) and (C) selective decoupling of H5 and H6_{endo}, respectively.

It may be seen from Table 1 that $^3J(\text{C}-\text{C}-\text{C}-\text{H})$ values of ca. 4–5 Hz are found in the cases where the dihedral angle is close to 180° . When the dihedral angle is close to 60° (or 120°) no coupling is observed. This is similar

to previous results in carbohydrates^{5,7,10,11} and in other compounds.¹³ A somewhat larger $^3J(\text{C}1-\text{H}5)$ values (6.1 Hz) was found, possibly because an oxygen atom is part of the coupling path in this case.⁵

The three bond couplings observed in methyl α -D-galactopyranoside (2) and in 3-O-acetyl-1,2-5,6-di-O-isopropylidene- α -D-glucopyranose (4) seem to show the same dependence of the dihedral angle. In the glucopyranose derivative (4) $J_{\text{C}1\text{H}3}$ was found to be 4.6 Hz, slightly lower than the values found for the pyranoses. In agreement herewith the C1–C2–C3–H3 angle of 4 was ca. 140° , measured from a model. In 3-O-acetyl-1,2-5,6-di-O-isopropylidene- α -D-allofuranose no coupling was observed between C1 and H3, corresponding to a dihedral angle of 100° , measured on a model of this compound.^{5,7}

In addition to the three bond couplings discussed above a number of two bond couplings were also found (Table 1). Two bond $^{13}\text{C}-\text{H}$ couplings have been measured in some carbohydrates^{7–11} and in a few cases their signs have been determined. For $^2J_{\text{CH}}$ values angular dependence is probably not important; but orientation of oxygen atoms around the coupling path will affect the coupling constant. Thus $J_{\text{C}1\text{H}3}$ values varied from -6 to $+5.5$ Hz, depending on the orientation of the two oxygen atoms at C1 relative to the C2–H2 bond.^{7,9} When the “resultant” of the C1–O1 and C1–O5 bonds is pointing away from the C2–H2 bond the coupling constant becomes more positive.⁹

We find that the rules of Perlin *et al.*^{7–11} explain the two bond couplings of C3, C4, C5, and C6 in 1 and 2. However, the $J_{\text{C}1\text{H}3}$ and $J_{\text{C}2\text{H}1}$ values are not in agreement with these rules. Thus C2 of methyl α -D-galactopyranoside (2) couples to H3 (-5.0 Hz), but not to H1 although O2 is *gauche* to both H3 and H1.¹⁰ Similarly, C2 of methyl tri-O-acetyl- α -D-rhamnopyranoside (α -3) does not couple to H1 in spite of the fact that O2 is *gauche* to H1. The β -anomer (β -3), on the other hand, has a $J_{\text{C}2\text{H}1}$ value of $+9.0$ Hz (the sign of this coupling constant was determined by selective proton decoupling).

The $J_{\text{C}1\text{H}3}$ and $J_{\text{C}2\text{H}1}$ values may be related to the orientation of the oxygen atoms, which are connected to the coupling path, if all three

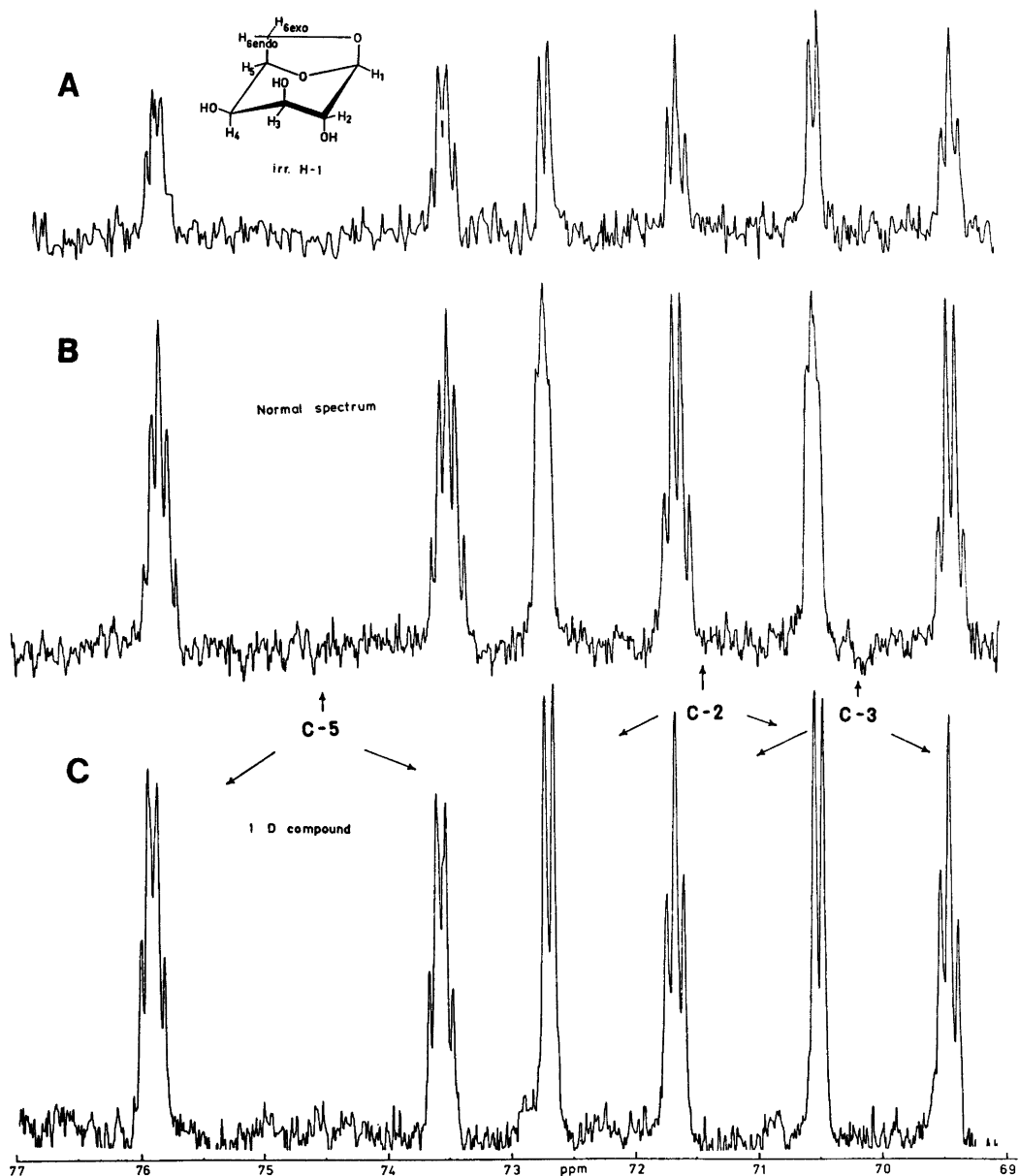


Fig. 2. The ^{13}C NMR signals of C2, C3, and C5 of 1,6-anhydro- β -D-galactopyranose. (B) Fully proton coupled spectrum; (A) Selective decoupling of H1; (C) The 1-deuterio analogue.

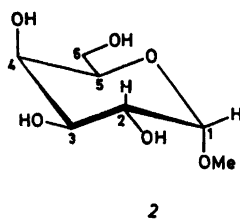
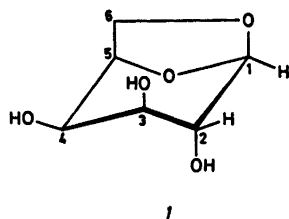
oxygens (O1, O5, and O2) are considered. In a Newman projection, viewed from ^{13}C to ^{12}C , the C–O bonds are projected on an axis *trans* to the ^{12}C –H bond and the sum of the three projections are then related to the coupling constant.

In 5 is shown a Newman projection of β -3, viewed from C2 to C1. If the projection of the C2–OAc bond on an axis *trans* to the C1–H1 bond is given the value +1, then the projections of C1–O1 and C1–O5 will each be +0.5 (cosine of 60°) and the sum will be +2. This

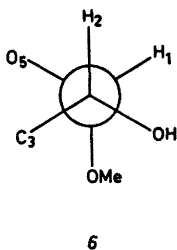
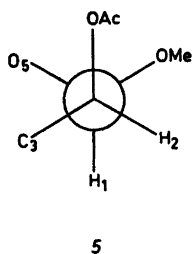
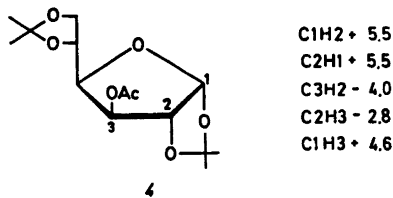
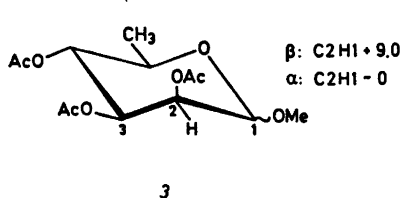
Table 1. ²J(¹³C—¹H) and ³J(¹³C—¹H) values of 1,6-anhydro-β-D-galactopyranose (1) in deuterium oxide solution. Couplings not shown are not observable.

Carbon	² JCH values		³ JCH values and dihedral angles ^d		
C1			+3.7 ^a H3 170°	+3.7 ^{a,b} H6 _{endo} 120°	+6.1 ^a H5 170°
C2	-3.2 ^{a,b} H1	-4.1 ^{a,b} H3			
C3	-4.6 ^a H2		+4.6 ^{a,b} H1 180°	+4.6 ^a H5 180°	
C4	-3 ^c H5	-3 ^c H3	+4 ^c H2 180°	+3 ^c H6 _{exo} 170°	
C5	-4.5 ^b H4	-4.5 ^c H6 _{exo}	+5 ^{a,b} H1 180	+4.5 ^a H3 180	
C6	-2.8 H5		+5.2 ^{a,b} H1 160°	+5.2 ^{a,b} H4 180°	

^a By selective decoupling. ^b By deuteration. ^c From line width. ^d Measured from Dreiding models.



C2H1 - 0 C2H4 + 5.0
 C2H3 - 5.0 C3H1 + 5.0
 C3H2 - 5.0 C5H1 + 6.0
 C3H4 - 5.0
 C6H5 - 5.0



corresponds to a $J_{C_2H_1}$ value of +9.0 Hz. A similar projection (6) of methyl α-D-galactopyranoside (2) gives a sum of +0.5 (+0.5 from C1—O5 and C1—OMe and -0.5 from C2—O2),

corresponding to a $J_{C_2H_1}$ value of ca. 0 Hz. The same values are found for α-3.

These projection sums and similar sums corresponding to the $J_{C_1H_3}$ data of Perlin *et al.*⁹ are plotted against the coupling constants in Fig. 3. The plot indicates that a sum of +0.5 corresponds to a coupling of ca. 0 Hz; a sum of +1 should give a small positive coupling, in many cases probably too small to observe. A sum of +1.5 is found for $J_{C_2H_1}$ and $J_{C_1H_3}$ of the furanose 4, corresponding to couplings of +5.5 Hz.

3-O-Acetyl-1,2,5,6-di-O-isopropylidene-α-D-allofuranose has the same sum and $J_{C_2H_1} = 5.1$ Hz and $J_{C_1H_3} = +4.5$ Hz.

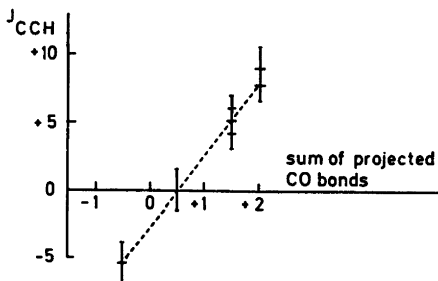


Fig. 3.

One point, representing $J_{C_{2}H_1} = -3.2$ Hz of **1**, is apparently falling outside in Fig. 3. The sum plotted for this coupling is $+0.5$ assuming a regular chair conformation for **1**. The conformation may, however, be distorted and this would result in a different sum.

The projection sum corresponding to $J_{C_{2}H_1}$ will be $+0.5$ for all α -pyranoses or pyranosides in the 4C_1 conformation, irrespective of the configuration at C2; a $J_{C_{2}H_1}$ value of ca. 0 Hz may therefore be expected. The same value is found for β -pyranoses (4C_1 conformation) with the *R*-(*D*-) configuration at C2. Those β -pyranoses which have the *S*-(*L*-) configuration at C2 will have a projection sum of $+2$ and a large positive $J_{C_{2}H_1}$ value is found for β -3 and also for β -*D*-mannopyranose ($J_{C_{2}H_1} = +8.0$ Hz).

The projection sum corresponding to $J_{C_1H_2}$ is $+1$ for α - and β -*D*-pyranoses and pyranosides (4C_1) with C2 in the *S*-(*L*-) configuration (e.g. *D*-mannose and *D*-rhamnose) and α -*D*-pyranoses with *R*-(*D*-) configuration at C2. Walter *et al.*¹² observed a small (~ 1.6 Hz) coupling in β -*D*-[^{13}C]-mannopyranose whereas C1 of the α -anomer only coupled to H1. No coupling was observed between C1 and H2 in α -*D*-glucopyranose.⁹ In β -*D*-pyranoses with *R*-(*D*-) configuration at C2 the projection sum is -0.5 and in agreement herewith $J_{C_1H_2}$ values of ca. -5 Hz are found for β -*D*-gluco- and β -*D*-allopyranose.⁹

Similar sums were also calculated for the two bond C-H couplings involving only two oxygen atoms. In most of the compounds discussed above, the sum is zero, corresponding to a coupling constant of -3 to -5 Hz. In a few cases the sum is $+1.5$ which corresponds to a coupling of ~ 0 Hz. The data are insufficient to document a relation equivalent to that of

Fig. 3; the rules of Perlin *et al.*⁷⁻¹¹ are, however, applicable when only two oxygen atoms are connected to the coupling path.

EXPERIMENTAL

Spectra were measured at 67.89 MHz on a Bruker HX-270S instrument. Compounds **1** and **2** were measured in deuterium oxide solution, **3** and **4** in deuteriochloroform. Spectra were measured with a spectral width of 6000 Hz using 32 K of computer memory for spectrum accumulation, corresponding to a digital resolution of 0.4 Hz. Gated decoupling was used for fully proton coupled spectra, decoupling time 3 s, pulse width 13 μ s ($\alpha = 90^\circ$). For selective proton decoupling a weak, continuous field was applied at the appropriate proton frequency. The latter frequency was found by measuring a 1H spectrum of the same sample (10 mm sample tube) using the proton decoupler coil of the ${}^{13}C$ -probe head as transmitter-receiver coil.

Preparation of the selectively deuterated derivatives of **1** will be described elsewhere.

The Bruker HX-270S instrument was provided by the Danish National Science Research Council.

REFERENCES

- Bock, K., Lundt, I. and Pedersen, C. *Tetrahedron Lett.* (1973) 1037.
- Bock, K. and Pedersen, C. *J. Chem. Soc. Perkin Trans. 2* (1974) 293.
- Bock, K. and Pedersen, C. *Acta Chem. Scand. B* 29 (1975) 258.
- Lemieux, R. U., Nagabhushan, T. L. and Paul, B. *Can J. Chem.* 50 (1972) 773.
- Lemieux, R. U. *Ann. N.Y. Acad. Sci.* 222 (1973) 915.
- Perlin, A. S. and Casu, B. *Tetrahedron Lett.* (1969) 2921.
- Schwarz, J. A. and Perlin, A. S. *Can. J. Chem.* 50 (1972) 3667.
- Perlin, A. S., Natsuko Cyr, Ritchie, R. G. S. and Parfondry, A. *Carbohydr. Res.* 37 (1974) C1-C4.
- Schwarz, J. A., Natsuko Cyr and Perlin, A. S. *Can. J. Chem.* 53 (1975) 1872.
- Ritchie, R. G. S., Natsuko Cyr and Perlin, A. S. *Can. J. Chem.* 54 (1976) 2301.
- Walker, T. E., London, R. E., Whaley, T. W., Barker, R. and Matwiyoff, N. A. *J. Am. Chem. Soc.* 98 (1976) 5807.
- Paulsen, H., Sinnvill, V. and Greve, W. *Carbohydr. Res.* 49 (1976) 27.
- Marshall, J. L., Miiller, D. E., Conn, S. A., Seiwel, R. and Ikrig, A. M. *Acc. Chem. Res.* 7 (1974) 333.

Received December 8, 1976.