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Preliminary communication

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^{13}C–^{1}H coupling in natural-abundance ^{13}C spectra: applications to branched sugars, disaccharides, and alcohol groups

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For technical reasons, most data on ^{13}C–^{1}H coupling in carbohydrates have been obtained from ^{13}C satellite signals in the p.m.r. spectra of ^{13}C-enriched compounds[1–4]. However, the measurement of J_{C-H} from natural-abundance ^{13}C spectra is becoming much more feasible through improvements in instrumentation[5,6]. This is well illustrated by the spectrum of α,β-D-glucose-*5,6,6-d*$_3$ (see Fig. 1A), which furnishes examples of several features of proton-coupled, ^{13}C spectra: *e.g.*, C-3 of α-glucose exhibits coupling with H-3 (^{1}J 147 Hz), H-2 (^{2}J 5.5 Hz), and H-1 (^{3}J 5.5 Hz), and C-1 of β-glucose, with H-1 (^{1}J 161 Hz) and H-2 (J 5.5 Hz), but not with H-3 ($^{3}J < 1$ Hz), whereas C-1 of α-glucose is affected, visibly, only through direct coupling with H-1 (^{1}J 169 Hz). Some of these values were obtained earlier with ^{13}C-enriched α,β-D-glucose[1,3], but otherwise, most of the coupling data derivable from Fig. 1A would involve highly complex labelling procedures.

Measurement of J_{C-H} from natural-abundance spectra is facilitated when the carbon atom considered can couple with relatively few protons, and, hence, produces a simple signal. This can be especially fortuitous, because p.m.r. spectroscopy is less helpful in precisely such circumstances, as is illustrated with the branched-chain sugar derivative 1,2-*O*-isopropylidene-3-*C*-ethynyl-β-D-psicopyranose (**1**). In the synthesis of **1**, *via* nucleophilic addition of lithium acetylide to the appropriate 2,3-hexodiulose[7], the configuration of the branch point could be surmised by analogy with related addition reactions, but was not amenable to confirmation by p.m.r. spectroscopy. Now, the signal of C-3^{1} of **1** would be expected to show a vicinal splitting[1–4] of <3 Hz due to *gauche* H-4 and, from the only other spin interaction possible, a typical splitting of about 50 Hz due to H-3^{2}. For the alternative configuration at C-3 (**2**) and the same conformation (see later), a $^{3}J_{C\text{-}3^1-H\text{-}4}$ value of 5–6 Hz or more was to be expected[1–4], because C-3^{1} and H-4 would be *anti-periplanar.* As may be seen in Fig. 1B, the C-3^{1} signal appears essentially as a doublet ($^{2}J_{C\text{-}3^1-H\text{-}3^2}$ 49.2 Hz) the line width of which is only 1.5–2 Hz greater than that of the C-3^{2} doublet. Hence, this small coupling is consistent with the branching orientation shown in **1**. Equally important, however, is the fact that the C-6 signal (especially its clearly visible, upfield portion of the main triplet) shows that there can be only weak coupling (<2Hz) with the vicinal H-4. Analogously, this is indicative of a *gauche* arrangement* of C-6 and H-4 (as in **1** or **2**), whereas these nuclei would be *anti* (and a large,

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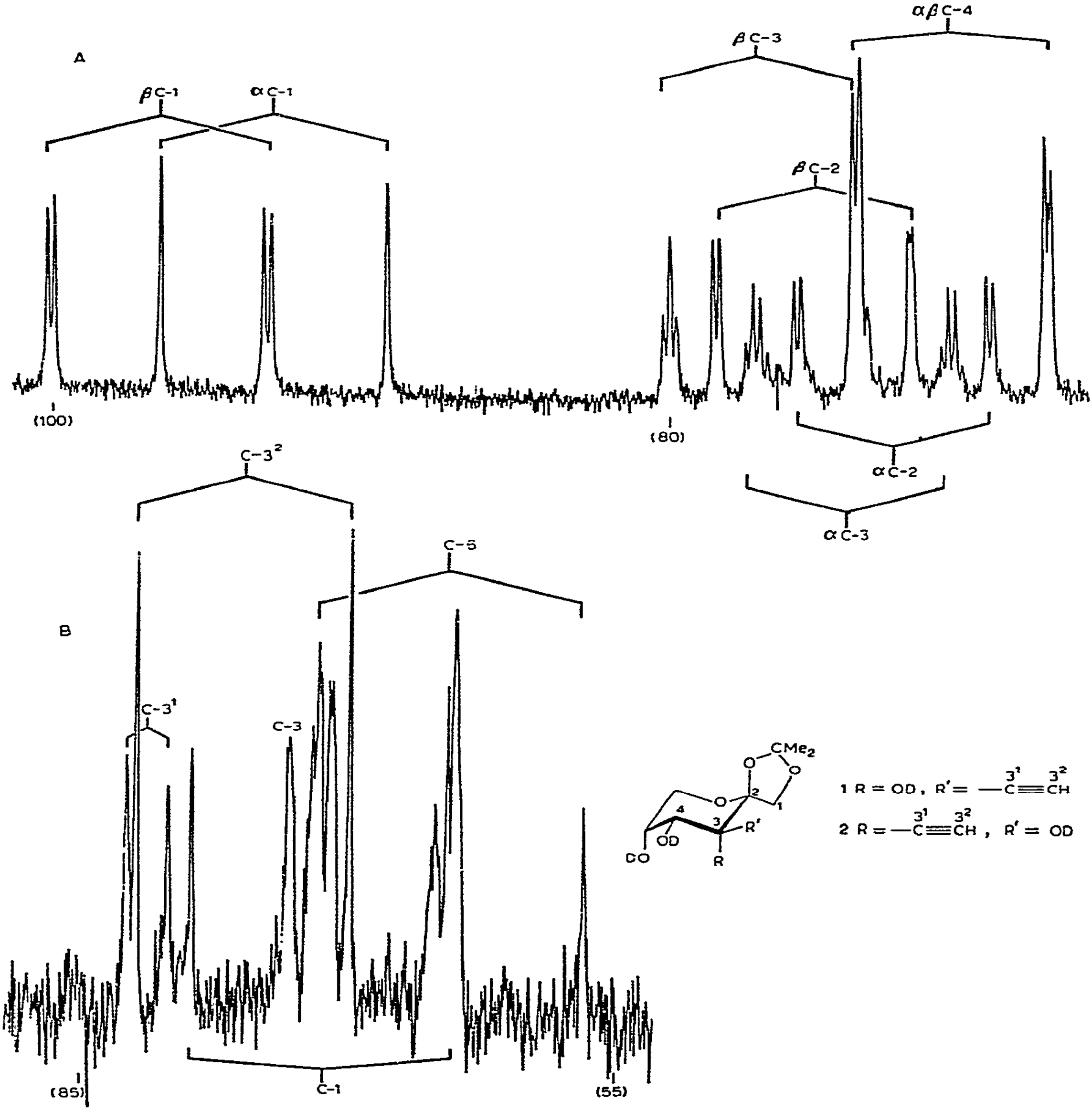
*In this arrangement of the nuclei, also, there is no detectable geminal coupling between C-6 and H-5, possibly because the latter is *anti*[3] to O-6.

vicinal splitting produced[1–4]) were the compound to exist in the alternative [*C1*(D)] conformation. Therefore, both the configuration at the branch and the conformation of the compound are specified by these $^{13}C-^{1}H$ coupling data.

Vicinal $^{13}C-^{1}H$ coupling across the glycosidic linkage of cellobiose or maltose may be advanced as evidence that, in aqueous solution, each of these disaccharides adopts a conformation similar to that in the solid state. According to X-ray diffraction data, the inter-residue angles H-1–C-1–O-4′–C-4′ and H-4′–C-4′–O-4′–C-1 (corresponding[8] to ϕ



$\mathbf{1}$ R = OD, R′ = $-\overset{3^1}{C}\equiv\overset{3^2}{C}H$

$\mathbf{2}$ R = $-\overset{3^1}{C}\equiv\overset{3^2}{C}H$, R′ = OD

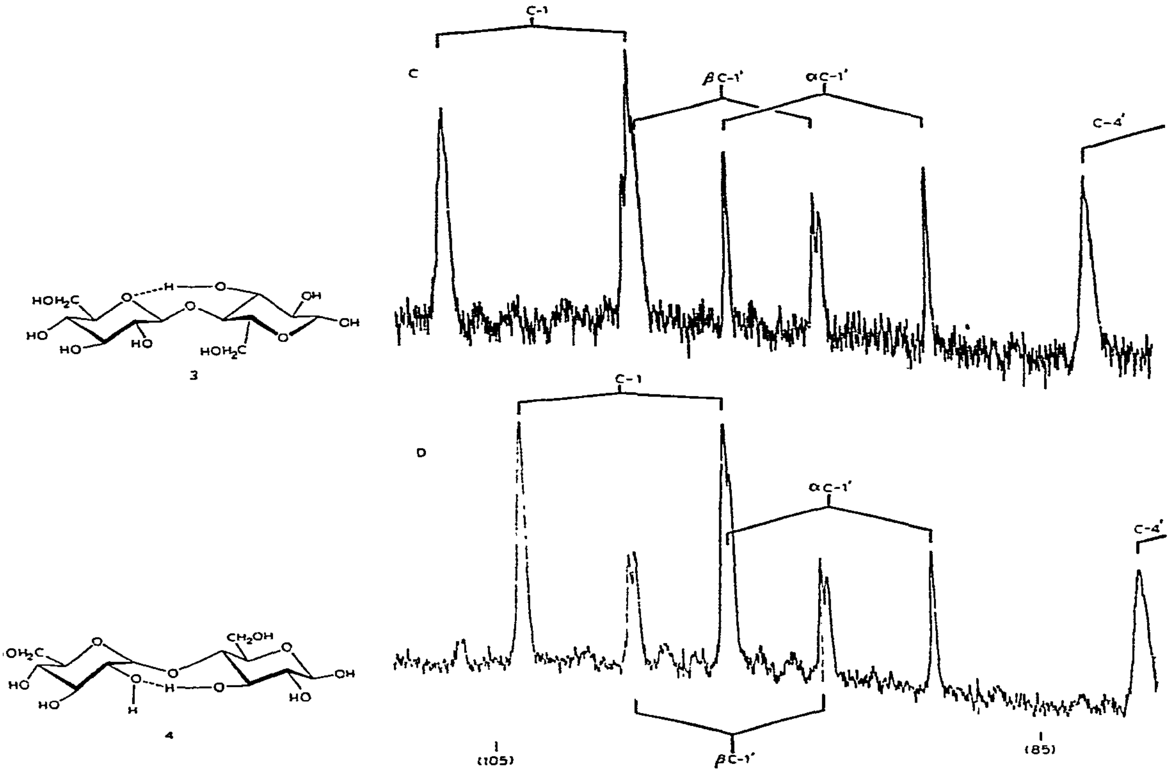


Fig.1. ^{1}H-coupled, F.T., natural-abundance ^{13}C n.m.r. spectra (22.63 MHz) obtained at 30° by "gated" decoupling. A, α,β-D-glucose-*5,6,6-d*$_3$ in D_2O; B, partial spectrum of branched-chain derivative 1 or 2; C and D, low-field regions of the spectra of cellobiose (3) and maltose (4), respectively (the formulas illustrate hydrogen bonding found for the crystalline compounds[8,9] and for solutions of these compounds in methyl sulfoxide[10]). The numbers in brackets are p.p.m. relative to tetramethylsilane.

and ψ, respectively) are substantially larger in α-cellobiose (30–40°)[8] than in methyl β-maltoside (~10°)[9]. By comparison, the inter-residue, vicinal couplings given by the line widths of the C-1 and C-4' signals (see Figs. 1C and 1D) are estimated to be 1–2 Hz for cellobiose (3), and 3–4 Hz for maltose (4). These values are clearly consistent with a more staggered orientation of the ^{13}C and ^{1}H nuclei in rotamers representing the glycosidic linkage in cellobiose than in those for maltose*.

A related application deals with the favored orientation of hydroxyl groups. As an example, OH-1 of 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (5) in $CDCl_3$ exhibits a large coupling (9.2 Hz) with C-2, indicative of an *antiperiplanar* orientation of these

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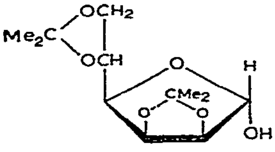
*Because of the wide scatter that has been observed[3,11] for ${}^3J_{C-H}$ values involving sp^3 carbon atoms, only rough approximations of average dihedral angles may be ventured at present: ~60° for cellobiose, and <30° for maltose. However, due to the "Karplus curve" nature of the ${}^3J_{C-H}$-dihedral angle relationship[2–4,11], angles of ~120° or >150° are possible alternatives. The latter would correspond to gross departures from the conformations in the crystals, and such a conclusion would certainly be less attractive in terms of general precedence than the possibility suggested.

two nuclei[1-4]. (The *syn* arrangement is assumed to be improbable.) The coupling observed between OH-1 and H-1 (2.6 Hz) is in good agreement with this possibility, because the corresponding dihedral angle relating these protons should be close to the value[12] of 60° anticipated for conformer **6**.



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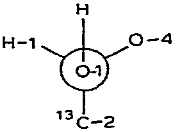

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