The Applicability of Nuclear Magnetic Resonance for the Determination of Anomeric Configuration of Purine Nucleosides

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CUSHLEY *et. al.*[1] have previously proposed a general method for determining the anomeric configuration of pyrimidine nucleosides based on the anisotropic effect of the 5,6-double bond of the aglycone on the resonance signal of the C-2′ acetoxy-group.

It was noted [1b] that hydrogenation of the 5,6-double bond of acetylated pyranosyl pyrimidine nucleosides caused a diamagnetic (up-field) shift in the resonance signal of the C-2′ acetoxy-group when this group and the pyrimidine were *cis*, whereas a paramagnetic (down-field) shift of the

C-2′ acetoxy-group signal occurred when they were *trans*.

In the case of acetylated furanosyl pyrimidine nucleosides, it was shown [1a] that saturation of the 5,6-double bond produced a paramagnetic shift in the resonance signal of the C-2′ acetoxy-group when the C-1′ and C-2′ substituents were *cis*. pyranosyl indole–indoline pairs, (I and II) and (III and IV), where a *trans*-diequatorial relationship obtains for the C-1′ and C-2′ substituents, a large paramagnetic shift is found in the resonance signal of the C-2′ acetoxy-group as predicted previously.[1b] The values for the C-2′ acetoxy-group signal of the indole compounds, τ 8·37 (I)

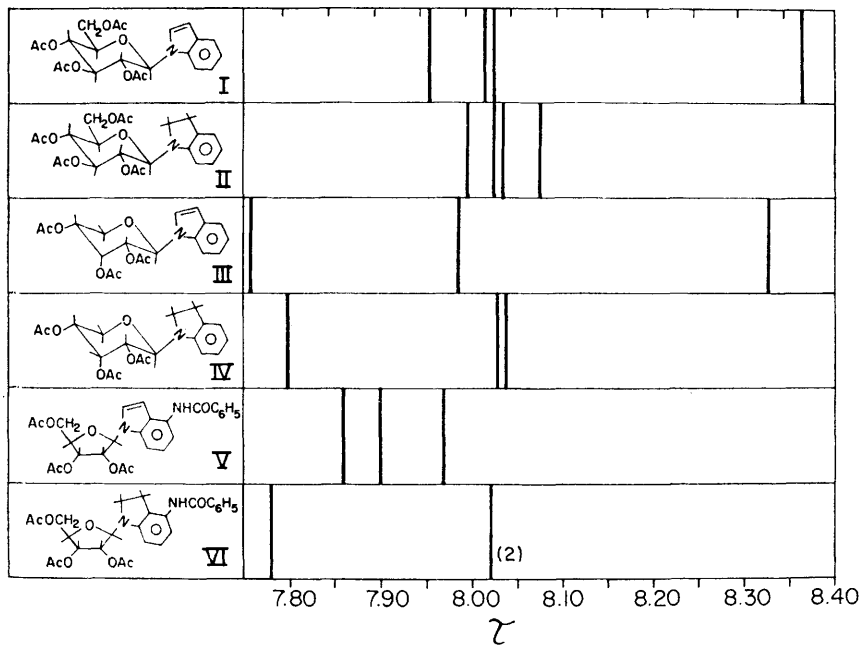

FIGURE. *N.m.r. data for acetylated indole and indoline nucleosides in* [$^2H_6$]*dimethyl sulphoxide.*[a]

[a] Determined with a Bruker HFX-3 spectrometer operating at 90 MHz in the field-frequency lock mode and fitted with a Hewlett–Packard 5216A frequency counter; τ values accurate to $<0{\cdot}01$ p.p.m.

When the C-1′ and C-2′ substituents were *trans* no dramatic shift in the resonance signal of the C-2′ acetoxy-group was observed, but the average value of the three acetyl resonances, in all cases, showed a small but significant diamagnetic shift upon removal of the anisotropy of the 5,6-double bond.

The general rule should have much wider appeal if it can be applied to both purine and pyrimidine nucleosides. Models show that the 7,8-double bond of the purine occupies about the same position as the 5,6-double bond of the pyrimidine in the preferred conformation.

Recent publications [2,3] have reported the synthesis of several indole and indoline nucleosides which are analogues of purine and 7,8-dihydropurine. The acetyl resonance data for two pairs of pyranosyl compounds and one pair of furanosyl compounds are shown in the Figure. For the two and 8·33 (III), are at much higher field than the other *O*-acetyl signals because of the anisotropic effect of the aglycone.[1b,4] For both pairs of pyranosyl compounds a large downfield shift of at least 0·29 p.p.m. is found in the resonance signal of the C-2′ acetoxy-group owing to removal of anisotropy of the 2,3-double bond of the indole. The magnitude of this paramagnetic shift is six times that found previously[1b] in the pyrimidine series and is probably due to two factors. First, the anisotropy of the 5-membered ring is greatly enhanced by ring current effects. Second, since the indole aglycone is more bulky than the pyrimidine aglycone, a greater preponderance of conformers in which the indole 2,3-double bond "sits over" the plane of the sugar ring will probably occur.

The furanosyl compounds were prepared from the corresponding benzoyl analogues and were

shown to be essentially pure by n.m.r. and mass spectra [M^+: (V) **494**, (VI) **496**]. No high field acetyl signal is found for the benzamidoindole compound. Also, the average position of the three acetyl signals of the benzamidoindoline compound (VI) is 0·03 p.p.m. to higher field than that of the benzamidoindole compound (V). Hence, the two compounds must be of the β-D-*ribo*-configuration, as suggested by Walton.[2]

In conclusion, the general rule proposed[1] for determining the anomeric configuration of pyrimidine nucleosides seems equally applicable to glycosylindoles. Application of this general method to the purine nucleosides must await a method of removing the anisotropic effect of the 7,8-double bond of purines.

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