Differentiation between the Protons of the -CO-CH_2- System in Six-membered Rings

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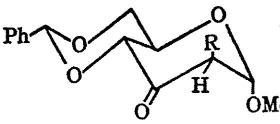
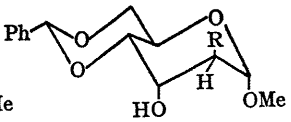
RECENTLY we have shown[1] that the axial proton at C(2) in methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose (I) resonates at lower field in the n.m.r. spectrum than the one at C(2) which is orientated equatorial. This is the reverse of what is normally observed for the protons at α-positions to a substituent in cyclohexane.[2] The reverse effect we observed has been reported before[3,4] but is said not to be the rule.[5]



(I) R=H
(IV) R=D



(II) R=D
(III) R=H

In our earlier work we identified the axial proton at C(2) in the ulose (I) by an indirect method involving the oxime derived from compound (I). Now we have confirmed our previous assignment by a direct method since it has been possible to examine the n.m.r. spectrum of compound (I) specifically monodeuteriated at C(2). Measurements have been made in three solvents.[6]

Treatment of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-alloside with lithium aluminium deuteride afforded compound (II)† by *trans*-diaxial opening[7] of the epoxide. This

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† All deuteriated compounds gave i.r. and mass spectral results consistent with a high percentage of monodeuteriation.

stereochemistry was confirmed by comparing the methylene regions in the n.m.r. spectra of compounds (II) and (III) (Figure 1). As expected, by analogy with a cyclohexyl derivative,[2] the equatorial proton appears at lower field.

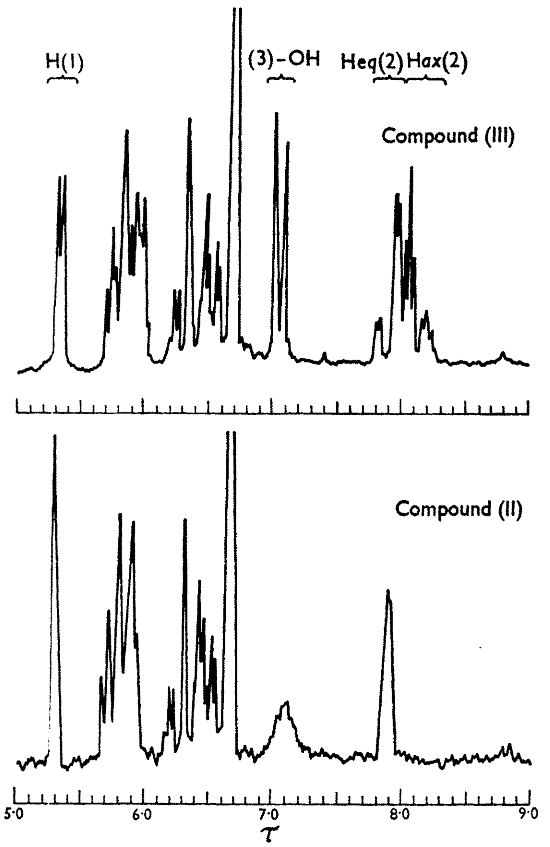

FIGURE 1. *100 MHz spectra of methyl 4,6-O-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside* (III) *and its 2-[^{2}H]-analogue* (II) *in $CDCl_3$ solution.*

By oxidation with ruthenium tetroxide,[8] compound (II) was converted, without isomerisation at C(2),‡ into the ulose (IV). The methylene regions of the n.m.r. spectra of uloses (I) and (IV) in deuteriopyridine are shown in Figure 2. In each case it is clear that the axial proton appears at lower field. By treating the methylene and anomeric protons as an ABX system gives τ 7·06 for H_{ax} (2) and 7·40 for H_{eq} (2) and J_{gem} 14 c./sec. This coupling constant is within the expected range.[9]

For compound (I) in deuteriochloroform the chemical shifts of the methylene protons at C(2) change but the axial proton still remains downfield from the equatorial proton as shown in Figure 3. However, benzene as solvent brings about the dramatic shift reported by Bhacca and Williams.[10] The axial proton now appears at higher field than the equatorial one with $\Delta = 0{\cdot}62$ and $0{\cdot}24$ for, respectively, the axial and equatorial protons at C(2) [$\Delta = \delta(CDCl_3)$ $\delta(C_6D_6)$ p.p.m.].

Compound (I) is a useful model for studying the differentiation of axial and equatorial protons because the axial proton at C(2) suffers no 1,3-diaxial interaction from substituents of the kind that have been present in some earlier work.[4] However, the method appears to be general and

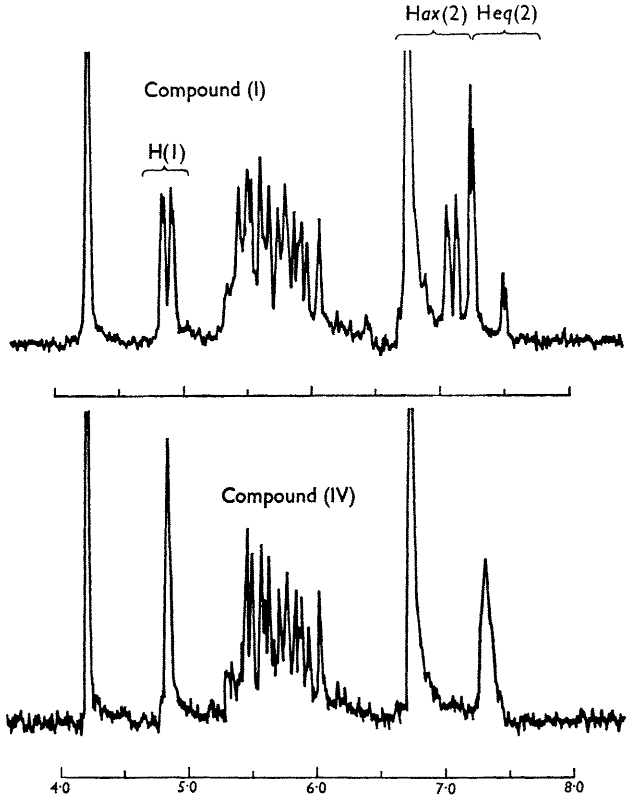

FIGURE 2. *60 MHz spectra of methyl 4,6-O-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose* (I) *and its 2-[^{2}H]-analogue* (IV) *in deuteriopyridine solution.*

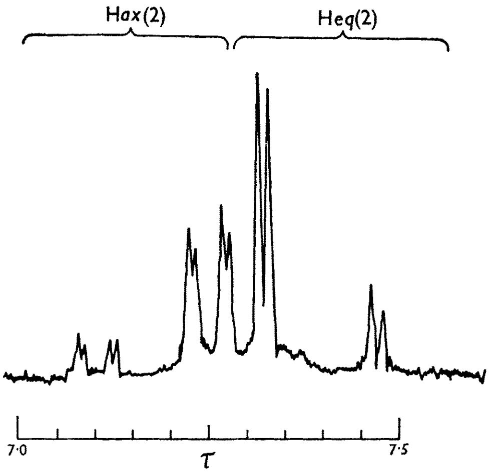

FIGURE 3. *100 MHz spectrum of compound* (I) *in $CDCl_3$ solution.*

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‡ Results obtained in this laboratory.

we have obtained results which lead to the same conclusions with methyl 4,6-*O*-benzylidene-α-D-*threo*-hexopyranosid-3-ulose [the C(4) isomer of compound (I) and its monodeuteriated derivative analogous to compound (IV)].

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