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Considerations on the Nuclear Magnetic Resonance Spectra of Some Anomeric Tetra-*O*-acetyl-D-glucopyranosides

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We have measured the nuclear magnetic resonance spectra (NMR) of some anomers of aryl 2, 3, 4, 6-tetra-*O*-acetyl-D-glucopyranosides and found that the signal of the anomeric proton in the α-anomers could be separated from the signals due to the other protons, and that the chemical shift in fact distinctly appeared in a lower mangetic field ($\delta=5.95$ ppm, $J=3.0$ to 3.5 cps) than those in alkyl 2, 3, 4, 6-tetra-*O*-acetyl-D-glucopyranosides. Lower field shifts have also been observed in β-anomers, but it was impossible to determine the chemical shift exactly possibly because of the overlapping with the signals due to the other protons attached to the pyranose ring.

Recently, stereochemical studies have been carried out by means of high-resolution NMR spectra in the field of carbohydrates, *e. g.*, the anomeric penta-*O*-acetates of monosaccharides[1] and anomeric 2, 3, 4, 6-tetra-*O*-acetyl-D-glucopyranosides.[2] The signal of the anomeric proton is particularly important, since both the chemical shift and the spin-spin coupling constant (J-value) definitely reveal a type of glycoside linkage and the steric environments around the anomeric proton (H_1). However, no NMR studies of anomeric aryl tetra-*O*-acetyl-D-glucopyranosides have ever been reported.

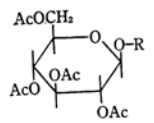
In the present work the NMR spectra of some anomeric aryl tetra-*O*-acetyl-D-glucopyranosides will be measured to get information on the chemical shift and the J-value of the anomeric proton.

Results and Discussion

The compounds (tetraacetyl β-aryl-D-glucosides) studied are listed in Table 1. Their NMR spectra are shown in Fig. 1.

Comparing all the β-anomers with methyl tetra-*O*-acetyl-D-glucopyranoside, whose chemical shift is $\delta=4.32$ ppm and $J=7$ cps, the chemical shift of the H_1 proton was found to appear in a lower magnetic field than that of the methyl glucoside.

TABLE 1. β-ARYL-D-GLUCOSIDES 2, 3, 4, 6-TETRA-*O*-ACETYL DERIVATIVES



Compound	Aglycone (R)	$[\alpha]_D^{20}$ in $CHCl_3$	Mp°C
I[3]	*o*-Nitrophenyl	+43.5	150—152
II[3]	*p*-Nitrophenyl	−41.5	174—175
III[3]	2, 4-Dinitrophenyl	+34.9	176—177
IV[4]	*o*-Methylphenyl	−24.9	144—146
V[4]	*m*-Methylphenyl	−18.4	109—110
VI[4]	*p*-Methylphenyl	−17.3	113—115
VII[4]	Phenyl	−22.6	125—126
VIII[5]	α-Naphthyl	−72.0	178—179

1) R. U. Remieux, R. K. Kulling, H. G. Bernstein and W. G. Schneider, *J. Am. Chem. Soc.*, **79**, 1005 (1957); *ibid.*, **80**, 6098 (1958).

2) N. Mori, S. Omura, O. Yamamoto, T. Suzuki and Y. Tsuzuki, This Bulletin, **36**, 1047 (1963).

3) H. G. Latham, E. May and E. Mosettig, *J. Org. Chem.*, **15**, 884 (1950).

4) E. M. Montgomery, N. K. Richtmeyer and C. S. Hudson, *J. Am. Chem. Soc.*, **64**, 690 (1942).

5) B. Helferich and E. Schmitz-Hillebrecht, *Ber.*, **66**, 378 (1933).

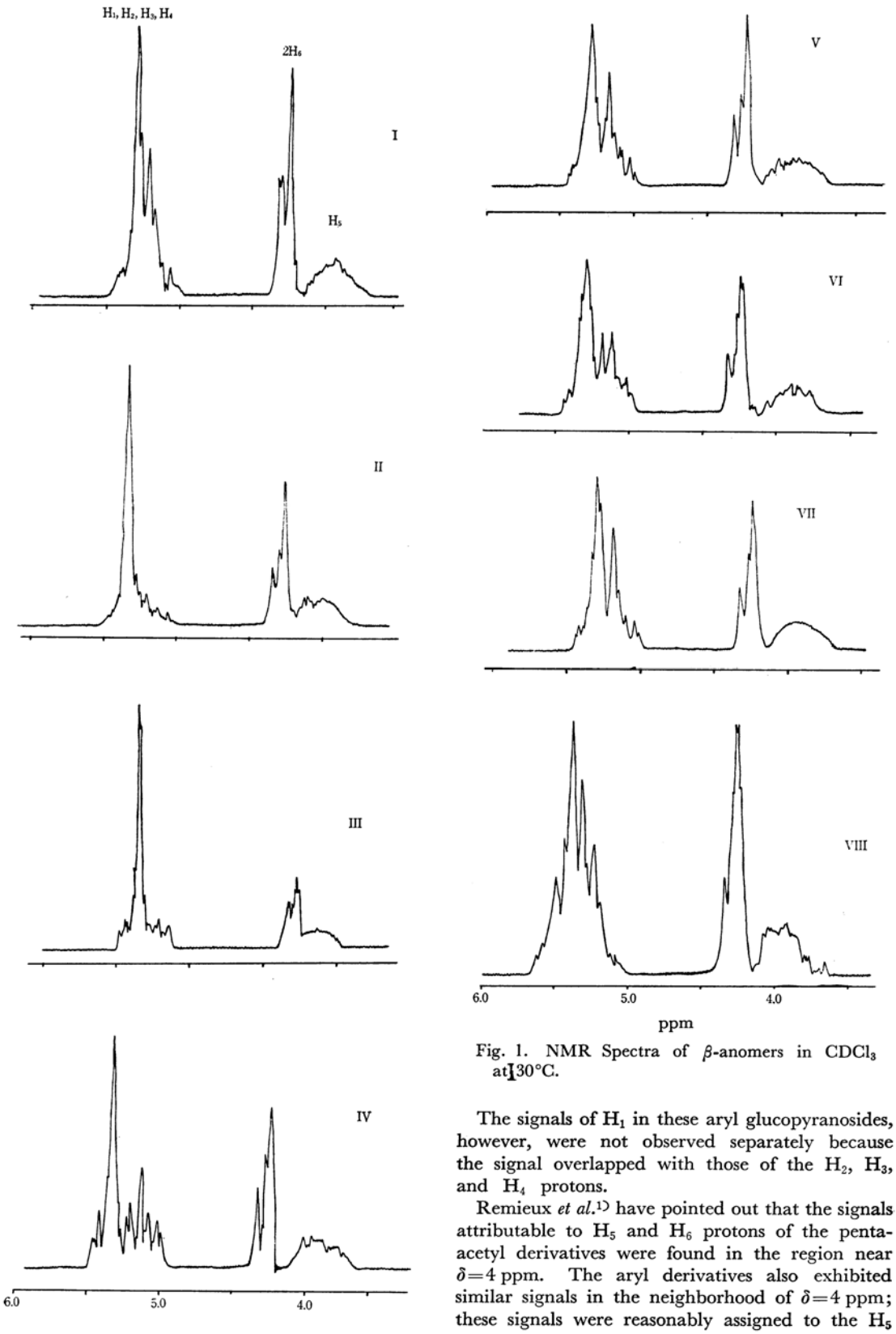


Fig. 1. NMR Spectra of β-anomers in $CDCl_3$ at 30°C.

The signals of H_1 in these aryl glucopyranosides, however, were not observed separately because the signal overlapped with those of the H_2, H_3, and H_4 protons.

Remieux *et al.*[1] have pointed out that the signals attributable to H_5 and H_6 protons of the penta-acetyl derivatives were found in the region near $\delta=4$ ppm. The aryl derivatives also exhibited similar signals in the neighborhood of $\delta=4$ ppm; these signals were reasonably assigned to the H_5

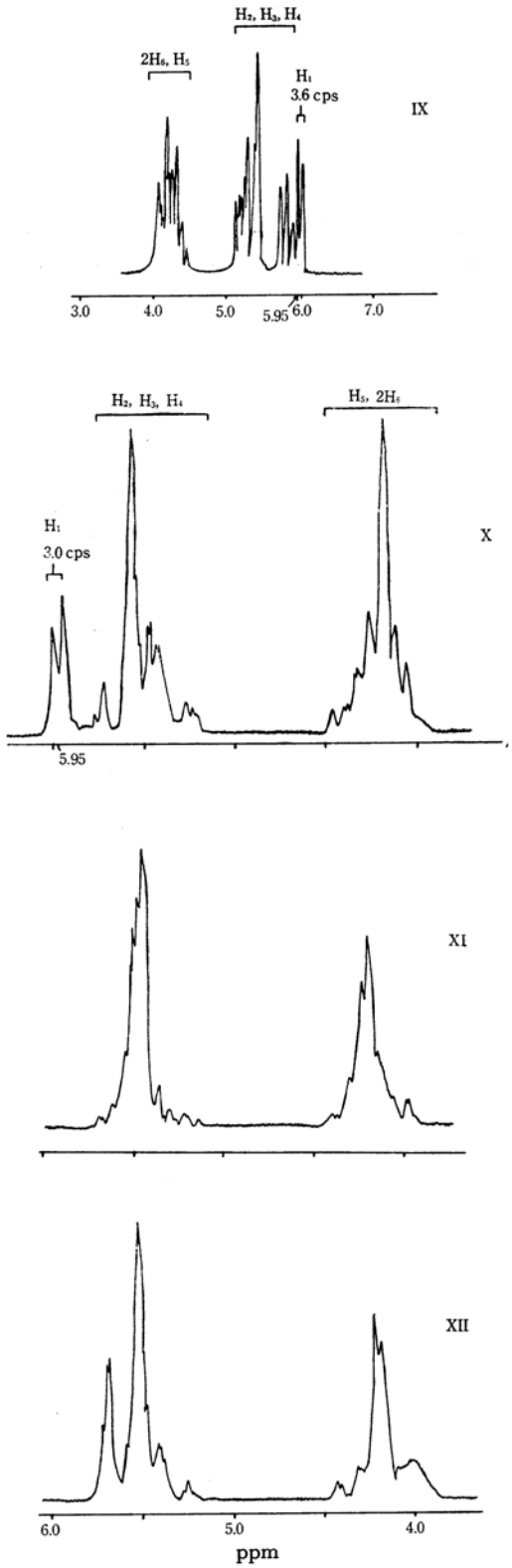


Fig. 2. NMR Spectra of α-anomers in $CDCl_3$ at 30°C.

and H_6 protons. In addition, the ratio of the absorption intensities of the signals which appeared $\delta=4$ ppm and near $\delta=5.00$ to 5.45 ppm were found to be three-to-four, indicating that the signal of the anomeric proton is incorporated in the region of $\delta=5.00$ to 5.45 ppm in these compounds. As a reason for the shift of the signal to a lower field, it is considered that the shifts are not only based on the magnetic anisotropy of the benzene ring, but also on a different electronic effect, namely, the inductive effect, between the aryl and the methyl groups.

On the contrary, the anomeric proton of the α-anomers (see Table 2) has the equatorial orientation. In general, the signal of the equatorial proton appears in a lower magnetic field than that of the axial proton. Therefore, the appearance of the signal in the region of $\delta=5.00$ to 5.45 ppm is quite reasonable. As is shown in Fig. 2, the H_1 signal of compound IX appears near $\delta=5.9$ ppm and the coupling constant has a spacing of 3.6 cps. The H_1 signal of compound X has a similar chemical shift, as is shown in Fig. 2 ($\delta=5.95$ ppm, $J=3.0$ cps).

In general, the $2B$-value of the specific rotations of anomers in alkyl D-glycopyranosides follows the

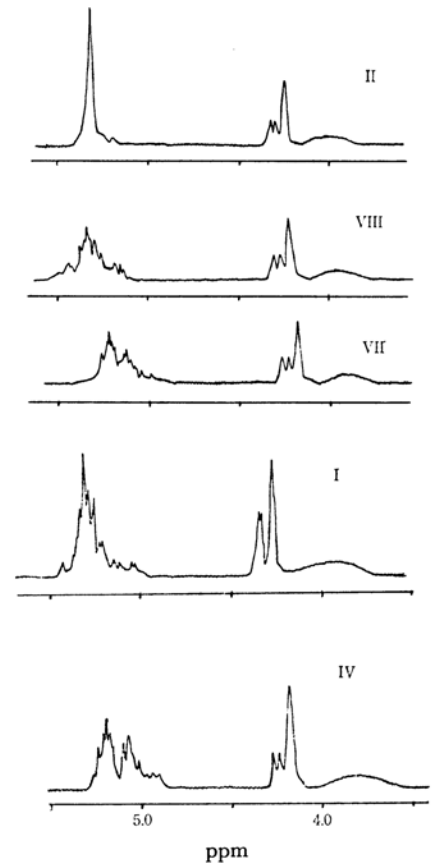


Fig. 3. NMR Spectra of β-anomers in $CDCl_3$ at 70°C.

TABLE 2. 2,3,4,6-TETRA-*O*-ACETYL DERIVATIVES OF α-ARYL-D-GLYCOPYRANOSIDES

Compound	Glycoside	Aglycone	$[\alpha]_D^{20}$ in $CHCl_3$	Mp °C
IX[4]	D-Glucoside	*p*-Nitrophenyl	200.0	113
X[6]	D-Galactoside	*p*-Nitrophenyl	207.7	133—134.5
XI[7]	D-Mannoside	*p*-Methoxyphenyl	68.4	100—101
XII[7]	D-Mannoside	*p*-Nitrophenyl	103.0	151—152

second isorotation rule of Hudson. However, the 2*B*-value obtained from the specific rotations of *o*-nitrophenyl 2, 3, 4, 6-tetra-*O*-acetyl-D-glucopyranosides is particularly high due to the anomalous positive rotation of the β-anomer.

To interpret this anomaly, Pigman[8] and Overend[9] assumed that steric interactions exist between the ortho nitro group and the substituent at C_2 on the pyranose ring, that the interactions are so strong at room temperature that a special conformation is formed with the aglycone, and that a particular conformation introduces further asymmetry into the molecule.

Moreover, Overend *et al.* have pointed out that the anomaly is not only based on the particular conformation but also on the interaction between the N–O dipole on the nitro group and the C–O dipole on the acetyl group in the sugar moiety.

Thus, it may be expected, according to their assumption, that the chemical shift of the anomeric proton in the compound I would be different from those of the other β-anomers because of the particular conformation of the aryl group.

However, no notable difference really appears in the chemical shift of the anomeric proton. Some of the β-anomers show, at 70°C, the same signal of the anomeric proton in NMR spectra as at an ordinary temperature. The signals of the anomeric proton of β-anomers were so overlapped on those of H_2, H_3, and H_4, as is shown in Fig. 3, that their chemical shifts could not be discriminated. Therefore, it may be concluded that the substituted phenyl groups of the aglycone rotate freely.

The anomalous optical rotatory power should thus not be attributed to the particular conformation of the aryl group, as in the literature already cited; the anomalous optical behavior of *o*-nitrophenyl glucosides seem rather to be attributable to some property of the nitro group, such as the field effect of the group exerted upon the anomeric center through space.

6) B. Helferich and K.-H. Jung, *Ann.*, **589**, 77 (1954).

7) The anomeric proton of the α-anomers of D-mannose derivatives, XI, and XII is in the axial position. Therefore, the signal does not distinctly appear in a region similar to that of glucosides IX and X because of overlapping with the signals due to the H_2, H_3, and H_4 protons.

8) W. Pigman, *J. Res. Nat. Bur. Stand.*, **33**, 129 (1944).

9) B. Capon, W. G. Overend and M. Sobell, *J. Chem. Soc.*, **1961**, 5172.

Experimental

NMR Spectra. The NMR spectra were measured by means of a Varian A-60 spectrometer operating at a fixed radio frequency of 60 Mc/sec, with the exception of Compound IX, which was measured at 100 Mc/sec. The measurements were carried out with 15%(w/v) solutions in deutrochloroform at 30 and 70°C respectively. Tetramethylsilane was used as the internal standard.