Chemical Shift Changes in the ^{1}H Nuclear Magnetic Resonance Spectrum of β-D-Arabinose induced by Boron(III) Oxide

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The ^{1}H n.m.r. spectrum of β-D-arabinose was measured at 89.6 MHz in the presence of boron(III) oxide. The boron(III) oxide produces remarkable chemical shift changes in hydroxy proton signals and the signals of all methine and methylene groups in the β-D-arabinose dissolved in $(CD_3)_2SO$. The assignments of the spectrum of β-D-arabinose with 2 mol. equiv. of boron(III) oxide were determined by spin-decoupling experiments.

The structures of organic compounds are of considerable importance in explaining their chemical and physical properties but until recently no method has existed by which the configurations of the compounds could be determined in solution. It has now been shown that ^{1}H n.m.r., which is well established as a powerful method for determining the detailed structure and stereochemistry of molecules, can also yield precise information on conformations. For this purpose, and for characterizing the molecule, a full analysis of the ^{1}H n.m.r. spectrum is essential. However, one of the inherent shortcomings of ^{1}H n.m.r. spectroscopy as a method for studying the structure of complex organic substances is associated with the intrinsically low sensitivity of proton chemical shifts to changes in chemical environment. In the past the complexity of carbohydrate spectra has resulted in the detailed assignment and interpretation of comparatively few examples.

The effects of paramagnetism on n.m.r. are well known.[1] Despite large observed frequency shifts caused by several paramagnetic complexes, much work beginning in 1969 [2] has been concerned with the question of which metal will permit the observation of high-resolution n.m.r. spectra of complexes with acceptable levels of signal broadening. However, because induced shifts are dependent on changes in the concentration of complex, it may prove difficult to obtain reproducible chemical shift data, and for substrates which are insufficiently soluble in non-polar solvents, lanthanide salts can be used to effect small induced shifts in $(CD_3)_2SO$ and other polar solvents.

This investigation is concerned with the ability of boron(III) oxide (B_2O_3) to produce remarkable shift changes in hydroxy proton signals and the signals of all methine and methylene groups in β-D-arabinose.

Experimental

The following compounds were obtained from commercial sources: β-D-arabinose and B_2O_3 from Nakarai Chemicals Ltd., Kyoto and $(CD_3)_2SO$ from Aldrich. β-D-Arabinose was recrystallized twice from methanol–tetrahydrofuran (4 : 1). It had m.p. 178 °C and $[\alpha]_D^{15}$ -173.3 to $-101.2°$.

The spectra were recorded at 89.6 MHz with a JEOL model FX-90Q spectrometer. Tetramethylsilane was used as an internal standard. B_2O_3 was finely pulverized in an alumina mortar with a pestle in a dry atmosphere and was dried over P_2O_5 under vacuum for 48 h at 115 °C. A calculated amount of anhydrous B_2O_3 was weighed into a vial containing 0.66M-β-D-arabinose dissolved in $(CD_3)_2SO$. The air in a reaction mixture was replaced with N_2 through a stopper and stopcock connected to a vacuum pump and also to a source of H_2O-free nitrogen. The vial was placed on an effective vibrator at 50 °C for 5 h. The resulting clear solution was transferred to an n.m.r. measuring tube.

Results and Discussion

Because of the overlap of several signals in the spectra, few ^{1}H n.m.r. data for arabinose and its derivatives have thus far been reported, except for those of some benzoylated derivatives of the D-enantiomorphs,[3,4] 1,2:3,4-di-*O*-isopropylidene-β-L-arabinose,[5] and peracetylated derivatives of methyl L-arabinofuranosides in the presence of europium shift-reagent.[6]

The normal n.m.r. spectrum of 0.66M-β-D-arabinose in $(CD_3)_2SO$ is shown in Figure 1A. Up to a molar ratio of $X = 3$ ($X = [B_2O_3]/[\text{sugar}]$), B_2O_3 was dissolved in a 0.66M solution of β-D-arabinose in $(CD_3)_2SO$ and the spectra obtained from experiments with $X = \frac{1}{4}, \frac{1}{2}, 1, 2$, and 3 are shown in Figures 1 B—F, respectively.

It is well known that increased strength of hydrogen bonding leads to a more downfield shift of the proton involved. Addition of a trace of acid also simplifies the spectra by shifting the hydroxy proton peaks and removing any coupling between these and adjacent ring protons.[7]

In the normal spectrum of β-D-arabinose, hydroxy proton resonances occur in the range δ 4.3—4.5, except for O(1)H, and ring protons in the range δ 3.3—3.7 with the exception of 1-H which appears as a doublet of doublets at δ 4.8 p.p.m. Comparison of the spectra in Figures 1A and B shows that the doublet of O(1)H in Figure 1A shifts slightly upfield (0.16 p.p.m.) and the signal for 1-H in Figure 1A is converted to a somewhat irregular feature by the addition of B_2O_3. The signals in the region δ 4.0—5.0 (Figure 1B) were superimposed with a broad peak, and 1-H which is coupled only to a vicinal proton, resonates at δ 5.64 and 5.57 as a small doublet having a coupling constant of *J* 5.91 Hz. When the value of X was increased by further addition of B_2O_3, the O(1)H doublet was gradually reduced, whereas the 1-H doublet was increased in intensity. It should be pointed out that the *J* value and the chemical shift of the 1-H doublet in the spectra remain unchanged during a series of experiments from $X = \frac{1}{4}$ to $X = 3$.

For $X = 2$, all the hydroxy proton signals in β-D-arabinose (Figure 1A) were found to be together as a broad peak at the most downfield region (δ 7.2) in the spectrum as shown in Figure 1E. An integral curve in Figure 1E shows the presence of four protons from hydroxy groups and six protons from methine and methylene groups. A new broad signal of the hydroxy proton at δ 7.2 moves more downfield and sharpens upon increasing the value of X from 2 to 3. The features of some signals from the ring protons in the spectrum in $X = 3$ were slightly blurred due to an increase in the viscosity of the solu-

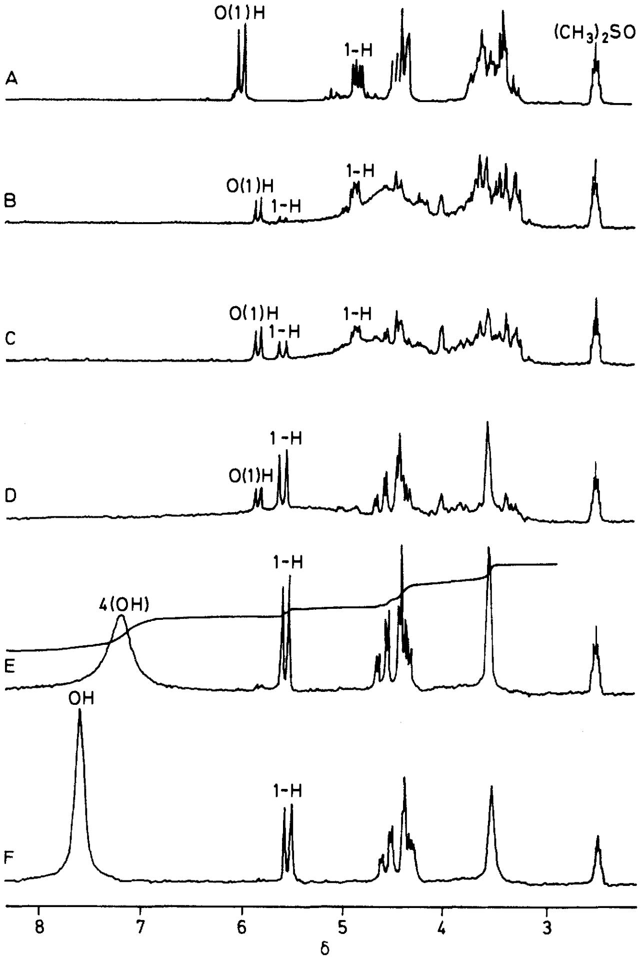

Figure 1. The chemical shift changes induced by incremental additions of B_2O_3. A, Normal spectrum of β-D-arabinose in $(CD_3)_2SO$; B, spectrum obtained from the experiment with $X = \frac{1}{4}$; C, with $X = \frac{1}{2}$; D, with $X = 1$; E, with $X = 2$; F, with $X = 3$

tion. However, the chemical shifts of the methine and methylene groups remained unchanged.

It was observed that a new signal for the hydroxy proton accompanying the well dispersed ring protons occurs in other experiments on some pentoses and hexoses with the appropriate molar ratio X. The chemical shifts of the hydroxy proton signals of these sugars induced by B_2O_3 are given in the Table. It can be seen from the data that the chemical shifts of the hydroxy proton signals from various sugars exist in the narrow range δ 7.1—7.3.

When measurements were carried out on samples which was obtained by two-fold dilution of a 0.66M solution of β-D-arabinose in the presence of 2 mol equiv. of B_2O_3, the peak of the hydroxy proton signal becomes broader as shown in Figure 2. However, such a dilution did not cause any noticeable shifts in the remaining signals.

The doublet due to 1-H occurs at a lower field than any of other ring hydrogens because of the proximity of this atom to two oxygen atoms. From the splitting of this doublet, the 2-H to which 1-H coupled is identified. The assignments shown in Figure 2 were determined by spin-decoupling experiments. The signals of 2- and 3-H appear as two doublets of doublets, with coupling constants of $J_{2,3}$ 2.31 and $J_{3,4}$ 8.34 Hz, respectively. The signal for 4-H appears as a multiplet which was partly superposed with the 2-H signals and was well shifted from 5- and 5′-H.

Chemical shifts (δ) of hydroxy proton of some sugars in the presence of B_2O_3. Data were obtained from 0.66M solutions of the sugar in $(CD_3)_2SO$

Sugar	OH chemical shift	$X = [B_2O_3]/[sugar]$
α-D-Xylose	7.2	2
β-D-Ribose	7.3	2
α-D-Glucose	7.1	2.5
α-D-Mannose	7.3	2.5
α-D-Galactose	7.2	2.5

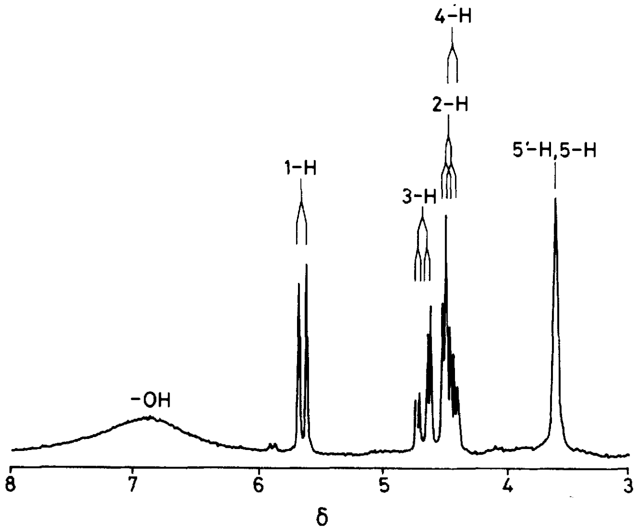

Figure 2. N.m.r. spectrum of a 0.33M solution of β-D-arabinose in the presence of 2 mol equiv. of B_2O_3

The value of $J_{1,2}$ and the chemical shift of 1-H are constant throughout the series of experiments from $X = \frac{1}{4}$ to $X = 3$ (Figure 1 B—F), which implies that the ring atoms C-1 and C-2 are in fixed positions and that the valency angle between 1- and 2-H will remain unaltered in the presence of different amounts of B_2O_3. The dihedral angles (φ) between the vicinal hydrogens of $\varphi_{1,2}$ 35, $\varphi_{2,3}$ 120, and $\varphi_{3,4}$ 156° for β-D-arabinose with B_2O_3 at $X = 2$, can be calculated from the values of $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ by applying the Karplus equation as modified by Abraham *et al.*[7] However, the application of the single set of parameters of Abraham *et al.* to a cyclic compound is an approximation along the way to a more precise approach.

Angyal *et al.*[8] showed the conformational effect of *cis*-fused isopropylidene rings on five- and six-membered rings. The *cis*-fusion of one isopropylidene ring to a pyranose ring does not distort the initial chair conformation. They also showed from hydrogen bonding studies that *cis*-fusion of two isopropylidene rings forces the ring structure to adopt a non-chair conformation, generally of the skew type. The persistence of the valency angles between vicinal protons of β-D-arabinose in the presence of various amounts of B_2O_3 indicates that B_2O_3 causes little distortion from the initial conformation of sugar in $(CD_3)_2SO$.

For 1,2:3,4-di-isopropylidene-β-L-arabinose in $CDCl_3$, Cone and Hough[5] found that the signals for 5- and 5′-H appeared at δ 3.86 and 3.67 with $J_{5,5'}$ 13.0 Hz. The presence of splittings between 5- and 5′-H provides important support for the pyranose ring form. The chemical shifts for a variety of closely related pentofuranose derivatives are given by Stevens *et al.*[3] For those cases in which 4- and 5-, 5′-H are clearly separated, the shift of 5-, 5′-H is reported as a single value. The absence of detectable splittings between 5- and 5′-H in Figure 2 suggests that the structure of β-D-arabinose in this experiment favours a furanose ring form.

In conclusion, it has been shown that boron(III) oxide does indeed produce useful chemical shift changes in the ^{1}H n.m.r. spectra of carbohydrates and the reagent can be used effectively by a simple procedure to obtain reproducible data.

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