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Study of the interaction of KF with carbohydrates in DMSO-d_6 by ^{1}H and ^{13}C NMR spectroscopy

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Abstract

The interaction of KF with sugars (D-glucose, D-xylose, D-galactose, D-ribose, D-mannose, D-lyxose, cellobiose, maltose, maltotriose, amylose, saccharose and γ-cyclodextrin) were studied by ^{1}H and ^{13}C NMR spectroscopies in DMSO-d_6. The main interactions are of the hydrogen bonding type between the sugar hydroxyl protons and the F^- anions of KF. The shifts in mutarotation toward the β anomers are due to the breaking of the $(OH)_1\cdots(OH)_2$ intramolecular hydrogen bonds by F^-, which destabilizes the α form in glucose, xylose, galactose and ribose. KF also attacks and breaks intermolecular hydrogen bond bridges as those observed between $(OH)_2$ and $(OH)_{3'}$ groups of neighboring hexose units in amylose. © 2002 Published by Elsevier Science B.V.

Keywords: Potassium fluoride; Sugars; Mutarotation; Hydrogen bonding; ^{1}H and ^{13}C NMR

1. Introduction

The interactions of sugars and salts is a field of active interest due to the role of carbohydrate-cation complexes in chemistry and biology [1–4]. The formation of the complexes is explained in terms of the interactions of the cations with the hydroxyl oxygens in the sugar [2,5]. The stability of the complexes increases with: (a) increase of the charge Z^{n+} of the cation and the decrease of its ionic radii; (b) the configuration of the sugar, the most effective being that which has three vicinal OH groups in axial–equatorial–axial positions in pyranose rings.

The role of the anion has always been disregarded. We have recently studied the interactions of KF with D-glucose in DMSO-d_6 and found a large broadening of the ^{1}H hydroxyl signals and a large acceleration of the mutarotation of the α and β pyranose forms [6]. We have interpreted the D-glucose–KF interactions as due to the formation of strong hydrogen bonds between the hydroxyl protons and the fluoride anions. To test this hypothesis in other sugars we now present a study by ^{1}H and ^{13}C NMR of 12 sugars in DMSO-d_6 solutions with KF. This solvent has been selected since in it the mutarotation process is slow compared to the NMR time scale [7,8].

The effect of KF on the ^{1}H and ^{13}C NMR spectra together with the calculation of the population of the molecular species α-pyranose (αp), β-pyranose (βp), α-furanose (αf) and β-furanose (βf) give clear evidence of the existence of the hydroxyl protons interactions with the F^- anions, which leads to a destabilization of the α forms.

2. Experimental

The sugars employed were analytical grade reagents from Sigma, and the KF and the DMSO-d_6 (99.5% deuteration) were from Merck. The solvent came in sealed capsules of 1 ml and the dissolution of KF and sugars was done immediately after breaking the bulb, to minimize the adsorption of atmospheric water. The NMR experiments were run in a pulse Fourier Transform spectrometer Jeol Eclipse$^+$ 270 operated at 270 MHz (^{1}H) and at 67.5 MHz (^{13}C). All the experiments were run at 293 K.

The IR spectra of the sugar samples and of sugars milled with KF, KCl and KBr were run in a Fourier Transform spectrophometer model Equinox (from Bruker) using the KBr pressed disks technique.

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Table 1
Chemical shifts (δ ppm) of the most acidic protons of some sugars in DMSO-d_6 and in DMSO-d_6 + KF

Sugar	In DMSO-d_6	In DMSO-d_6 + KF
D-Glucose	$(OH)_1$ αp: 6.21, $(OH)_1$ βp: 6.58	$(OH)_1$ αp: 6.28, $(OH)_1$ βp: 6.64
D-Galactose	$(OH)_1$ αp: 6.45, $(OH)_1$ βp: 6.10	$(OH)_1$ αp: 6.53, $(OH)_1$ βp: 6.17
D-Ribose	$(OH)_1$ αp: 6.32, $(OH)_1$ βp: 6.06	$(OH)_1$ αp: 6.43, $(OH)_1$ βp: 6.25
D-Xylose	$(OH)_1$ αp: 6.17, $(OH)_1$ βp: 6.58	$(OH)_1$ αp: 6.22, $(OH)_1$ βp: 6.63
Amylose	$(OH)_2$: 5.41, $(OH)_{3'}$: 5.52; $(OH)_6$: 4.60	$(OH)_2$=$(OH)_{3'}$: 5.71, $(OH)_6$: 4.74
γ-Cyclodextrin	$(OH)_2$=$(OH)_{3'}$: 5.75, $(OH)_6$: 4.54	$(OH)_2$=$(OH)_{3'}$: 5.89, $(OH)_6$: 4.58

3. Results and discussion

3.1. ^1H NMR spectra of sugars in DMSO-d_6 and in DMSO-d_6 saturated in KF

In all the spectra of the 12 sugars employed, the δ (ppm) values of the hydroxyl protons in DMSO-d_6 were slightly deshielded on passing to a saturated KF solution in DMSO-d_6 (see Table 1). The CH signals remained narrow as in the pure solvent but the OH signals were broadened in the KF solution, see Fig. 1. The observed deshielding in the proton OH signals suggests the occurrence of a hydrogen bonding $OH\cdots F^-$ interaction.

Using KCI and KBr solutions instead of KF did not produce any change in the sugar spectra. For this reason one can conclude that K^+ cation is not responsible for the

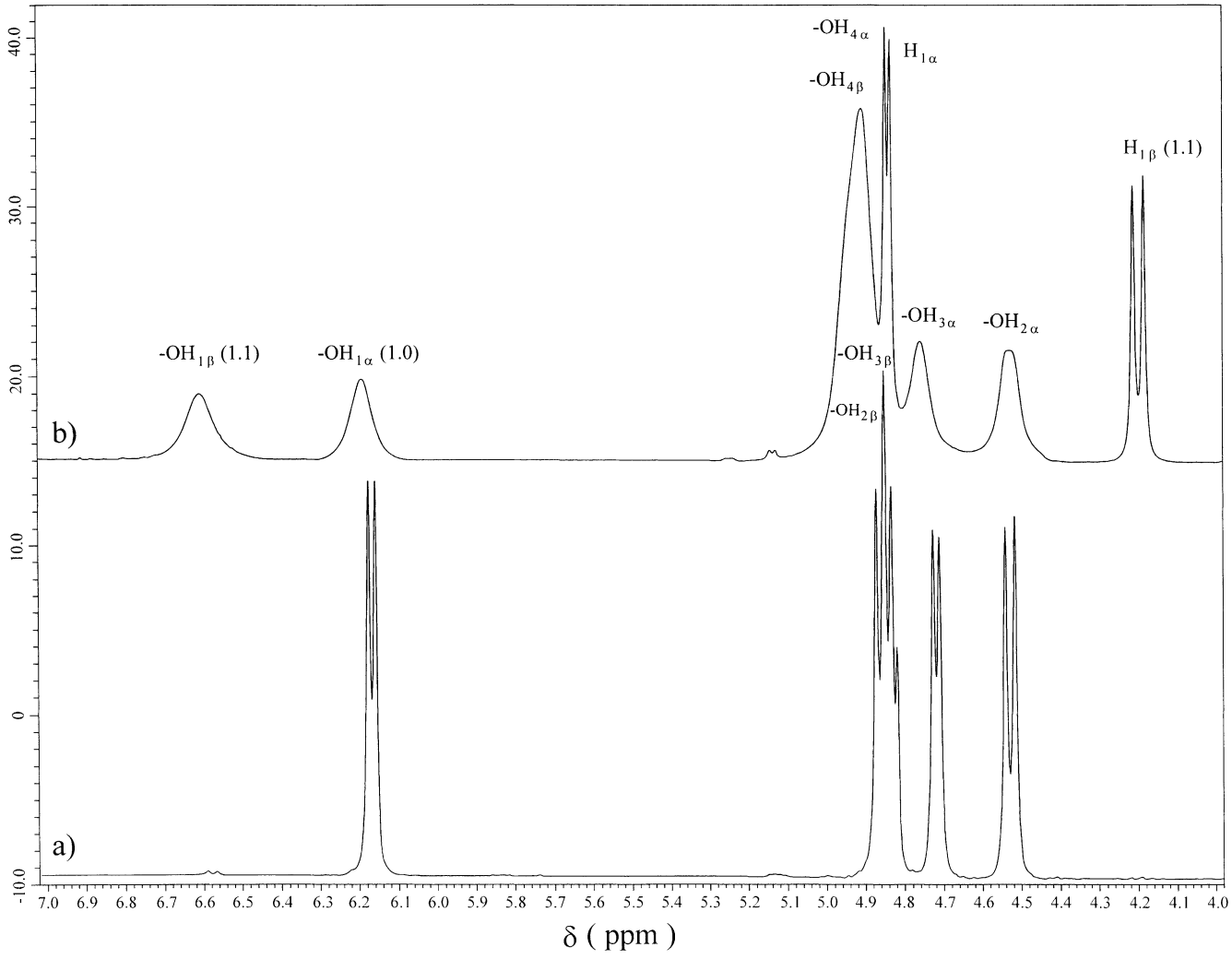

Fig. 1. ^1H NMR spectra of: (a) D-xylose in DMSO-d_6; (b) D-xylose in DMSO-d_6 saturated in KF. All the proton signals of hydroxyl groups of the sugar are broadened in presence of KF while the signals from CH remain narrow as in the pure solvent. The occurrence of a mutarotation process from αp → βp can also be observed in the spectrum (b).

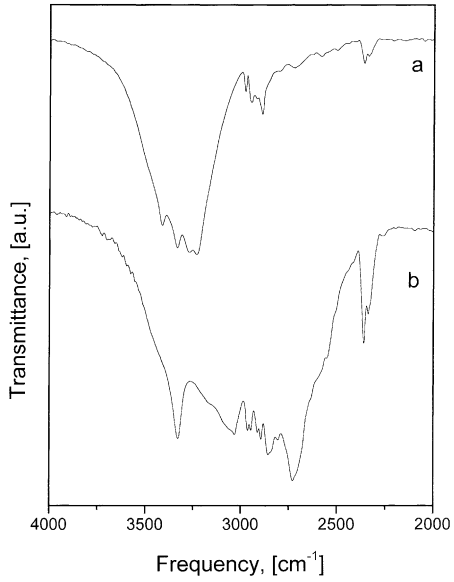

Fig. 2. IR spectra (4000–2000 cm^{-1} region) of: (a) D-xylose; (b) D-xylose milled with KF. In presence of KF the OH stretching vibrations of the sugar shift to low frequency suggesting the presence of a strong $OH\cdots F^-$ hydrogen bonding interaction.

spectral changes. The Cl^- and Br^- anions do not interact strongly with the OH protons, therefore, the observed effect in KF solutions can be only due to hydrogen bonding of the hydroxyl proton with the highly polarizing F^- anion. To test this hypothesis we milled several sugars with KF and KBr in an agate mortar. The IR spectra of the milled samples of sugar with KF show a very strong shift of the OH stretching of the sugars to lower vibration frequencies, see Fig. 2. These strong vibration shift can be easily done due to $OH\cdots F^-$ interactions.

3.2. ^{13}C NMR spectra in DMSO-d_6

The ^{13}C experiments were used to determine the relative abundance of the sugar forms αp, βp, αf and βf in DMSO-d_6 and in DMSO-d_6 saturated in KF. Since the dipolar contribution to the spin–lattice relaxation time (T_1) is fundamental in carbohydrates [9,10], it is possible to integrate the spectral signals even when using the broad band proton decoupling technique. In this case, it is necessary to use protonated carbon atoms. This procedure was validated measuring the isomer composition in D-mannose in D_2O, obtaining the following populations: ^1H NMR (αp = 72%); ^{13}C $\{^1H\}$ NMR (αp = 71%) and ^{13}C NMR (without nOe) (αp = 79%). These results indicate that the relative population of one isomer in a sugar sample can be obtained from ^{13}C NMR spectra in wide band proton decoupling conditions. The calculated relative abundance of the sugar forms is collected in Table 2.

3.3. ^{13}C NMR spectra of monosaccharides

In Fig. 3 we present the ^{13}C NMR spectra of D-xylose in KF solution in DMSO-d_6. In Table 2 the population (in %) of the different forms of the sugar molecule in DMSO-d_6 and in KF saturated DMSO-d_6 is collected. It can be observed that in some sugars there is large shifts of population of the αp → βp forms (D-glucose, D-xylose, D-galactose and D-ribose) while others are not affected (D-mannose and D-lyxose).

In Figs. 4 and 5 are shown the conformations αp and βp of these sugars. It can be observed that all the mutarotating sugars have the same C_1–C_2 conformation of the hydroxyl groups in which $(OH)_2$ is equatorial. This allows an intramolecular hydrogen bond in the αp forms between $(OH)_1$ axial and $(OH)_2$ equatorial, see Fig. 4. In Fig. 5, it can be seen that the sugars that were not affected in population have a C_1–C_2 structure in which $(OH)_2$ is axial. The rest of the sugar moieties are different in OH disposition and in size of the molecule (pentoses and hexoses), see Figs. 4 and 5.

For this reason we postulate as a working hypothesis that the crucial effect on accelerating the mutarotation of D-glucose, D-xylose, D-galactose and D-ribose is the attack of the F^- anion to the C_1–C_2 hydroxyl groups with the breaking of the $(OH)_1\cdots(OH)_2$ hydrogen bond bridge. This effect on C_1 increases the negative charge and accelerates the etheric oxygen bridge breaking which leads to mutarotation.

An additional evidence of the role of KF as accelerator of the mutarotation process in sugars is obtained by recording

Table 2
Relative populations (%) of isomers of sugars at 293 K in DMSO-d_6 and in KF-DMSO-d_6 solutions calculated from ^{13}C NMR spectra

Sugar	Isomers (%) in DMSO-d_6				Isomers (%) in DMSO-d_6 + KF			
	αp	βp	αf	βf	αp	βp	αf	βf
D-Glucose	99	1	–	–	39	61	–	–
D-Xylose	98	2	–	–	39	61	–	–
D-Mannose	86	14	–	–	86	14	–	–
D-Lyxose	86	16	–	–	86	14	–	–
D-Galactose	89	11	–	–	31	39	10	20
D-Ribose	25	53	6	16	13	66	3	10
Maltose	–	100	–	–	30	70	–	–
Maltotriose	40	60	–	–	40	60	–	–
Cellobiose	11	89	–	–	11	89	–	–

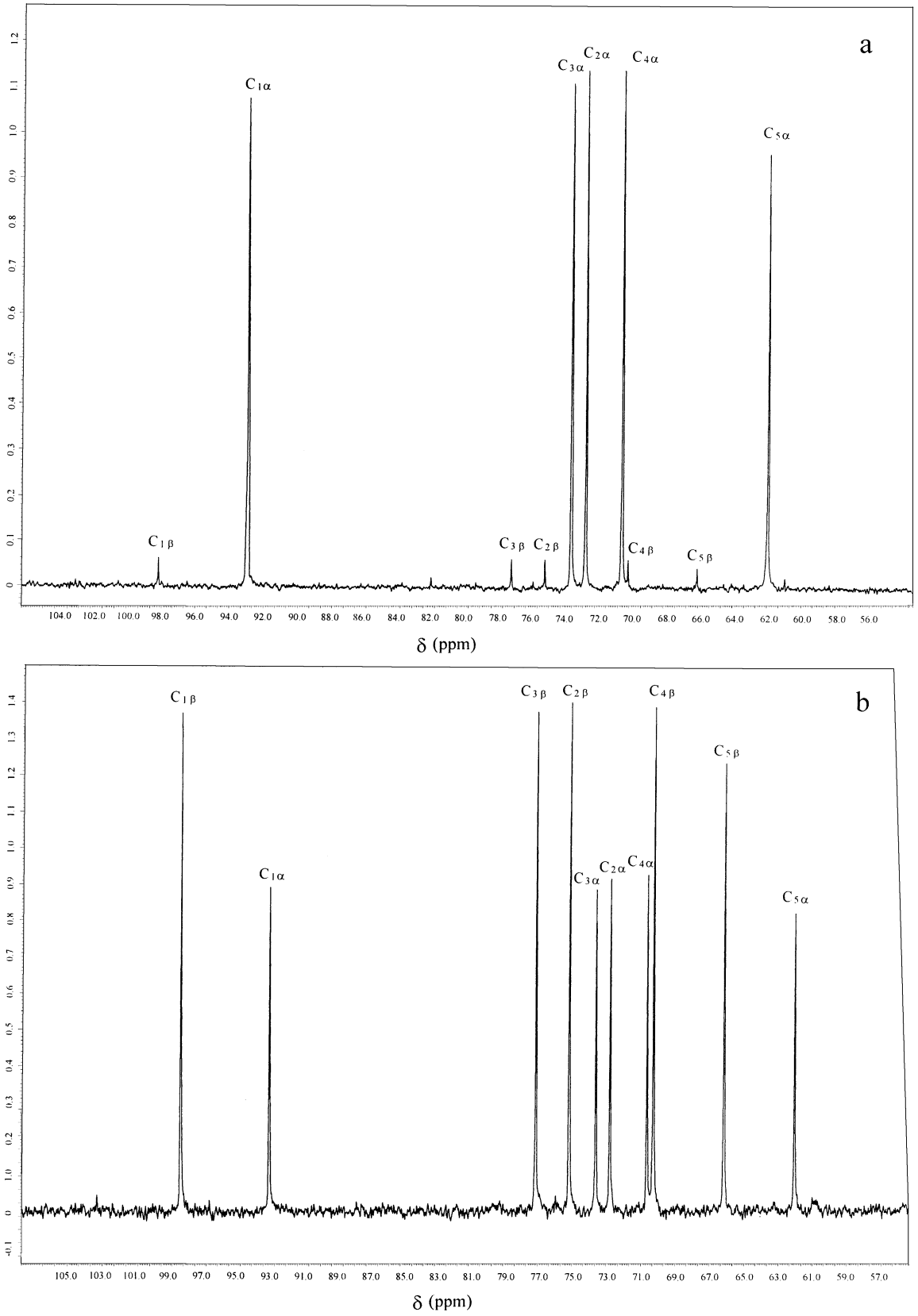

Fig. 3. ^{13}C NMR spectra of: (a) D-xylose in DMSO-d_6; (b) D-xylose in DMSO-d_6 saturated in KF. A pronounced mutarotation process takes place in presence of KF in favor of the β form, which is also observed in Fig. 1.

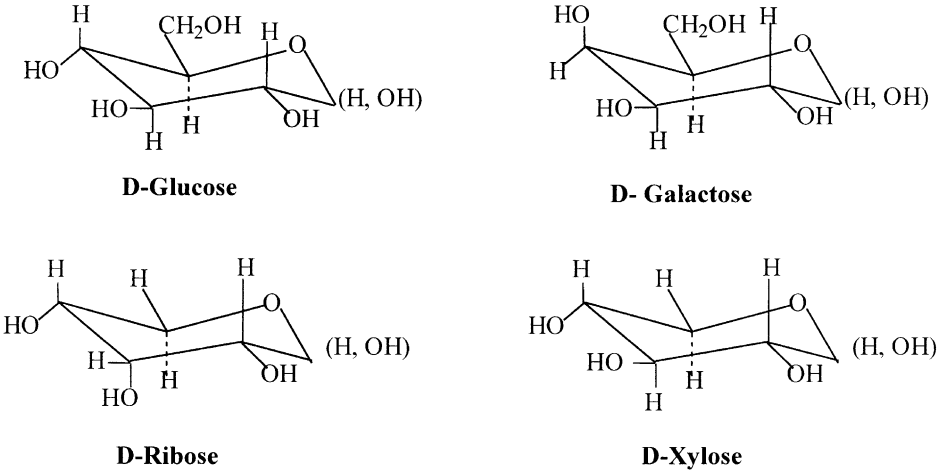

Fig. 4. Conformations of pyranose forms of monosaccharides which isomers population is affected by the presence of KF. These sugars have a C_1–C_2 conformation of the hydroxyl groups in which the $(OH)_2$ is equatorial and interacts with $(OH)_1$ group through a hydrogen bond.

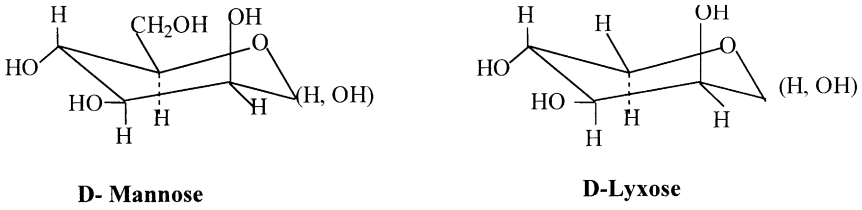

Fig. 5. Conformations of monosaccharides which population of isomers is not affected by the presence of KF. These sugars have a C_1–C_2 structure in which the $(OH)_2$ is axial.

the ^{1}H NMR spectra of sugar in DMSO-d_6 at different temperatures and comparing their behavior with that observed when KF is added. When this experiment is carried out with α-glucopyranose in the range 20–70 °C no mutarotation is observed in the absence of KF but if KF is present the sugar mutarotates even at 20 °C.

3.4. Effects of KF on ^{13}C NMR spectra of di, tri and polysaccharides

In Table 2 are collected the population changes of maltose, cellobiose and maltotriose. Maltose, originally in pure βp form, mutarotates to an anomeric equilibrium analogous but not equal to D-glucose. This indicates an effect of the first glucose ring linked $1 \rightarrow 4$ to the second unit of glucose. Maltotriose has a similar behavior but with equilibrium concentration of anomers as in D-glucose. Cellobiose does not mutarotate, being also in equilibrium, but with larger population of the β form in the second glucose unit. Amylose has such a long chain of $1 \rightarrow 4$-*o*-α-D-glucopyranose units that mutarotation effects can not be noticed.

The attack of F^- to protons of hydroxyl groups of the sugar is well observed in ^{1}H NMR spectra of amylose in DMSO-d_6 and in DMSO-d_6 + KF. In amylose the $(OH)_2$ group of a hexose molecule forms a hydrogen bond bridge with the $(OH)_{3'}$ group of a neighbor molecule of the chain. Since one of this (OH) group behaves as donor ($(OH)_2$) and the other ones as acceptor ($(OH)_{3'}$) they appear in the ^{1}H NMR spectra as two separated signals. However, the interaction with F^- anion breaks that intermolecular hydrogen bonding bridge and the $(OH)_2$ and $(OH)_{3'}$ are now equivalent with only one slightly deshielded proton signal (see Table 1).

3.5. Effect of KF on non-mutarotating sugars

Two non-mutarotating sugars were studied, saccharose and γ-cyclodextrin. The signals of hydroxyl protons in these sugars result broadened and slightly deshielded when KF is added indicating that the $OH\cdots F^-$ interaction is always present but the lack of a hydroxyl group in C_1 forbids mutarotation.

4. Conclusions

The main interaction of KF and sugars is through the attack of the protons of hydroxyl groups by the F^- anions with formation of $OH\cdots F^-$ hydrogen bond. Those sugars that initially are in α forms undergo mutarotation to β forms due to the breaking of $(OH)_1\cdots(OH)_2$ intramolecular hydrogen bond bridge. In non-mutarotating sugars and even in

polysaccharides the $OH\cdots F^-$ interaction is also present but is detected only through a broadening and a deshielding of the proton (^1H) OH signals. The $OH\cdots F^-$ interaction can also disrupt intermolecular hydrogen bond bridges as those formed between neighbor molecules of a polysaccharide like amylose.

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