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Interaction of potassium fluoride with α-D-glucose

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Abstract

Addition of KF to solutions of α-D-glucose (αDG) in DMSO-d_6 and D_2O alters the ^1H NMR spectra, which is attributed to an interaction of the hydrogen atoms of the –OH groups with the basic F^- anions of the salt. It is shown that K^+ cations do not interact with the oxygen atoms of the –OH groups of the αDG. Mutarotation rates of αDG in D_2O in the presence of potassium halides and alkaline chlorides were measured from the integrated ^{13}C NMR signal of the anomeric protons. The mutarotation rates were higher with KF than other potassium halides. In order to shed light on the interactions of KF with the αDG, the mutarotation of αDG in the presence of KF and KOH were also studied using polarimetric measurements. At similar pH values, the effect of KF on the mutarotation rate is about five times that observed for KOH, indicating a major affinity for the F^- anion by the anomeric proton as compared with OH^-. The acceleration of the mutarotation process of αDG is evidence for KF–αDG interactions, since NMR spectra of β conformer are also altered by the presence of KF.

Keywords: Potassium fluoride (KF); α-D-Glucose; Proton NMR; Mutarotation

1. Introduction

The interaction of metallic cations with carbohydrates is a subject of growing interest in recent years due to the importance of the complexes in chemistry [1–3] and biology [4–8]. Most of the work has been carried out in aqueous solutions. The models used for the analysis of the interaction are based in the structure of the sugars and the properties of the cations (charge, size, polarizability) with practically no reference to the role of the anions [9].

Recently, it has been reported on the interaction in the solid state of alkali fluorides with acidic substances where the stability of the acid fluoride anion, HF_2^-, determines the course of the mechanochemical reactions [10]. A strong interaction is also observed between KF and D-xylose, both in solid state and from methanolic solutions, with formation of a KF–xylose complex [11]. According to IR and NMR spectra, the driving force of the complex formation is the interaction of F^- with the –OH protons.

Mutarotation of all reducing sugars are catalyzed by acids and bases [12], with a same value of the mutarotation constant for α- and β-D-glucose over a wide temperature range, from 0 to 40°C [13]. Also, the reaction constant is independent of the concentration of sugar over a wide range. Later work revealed that catalysis of mutarotation is not an exclusive property of hydrogen and hydroxyl ions [13]. It has been reported [14] that the determination of the catalytic activity of anions of weak acids requires adjustment of the pH of the solution in order to keep the concentration of hydroxyl ion low, because the catalytic activity of the hydroxyl ions resulting from hydrolysis of the salt is so great that it masks the smaller catalytic effect of the anion. Evaluation of the catalytic activity of the hydroxyl ion is difficult, because the mutarotation becomes too rapid to allow an accurate measurement. Small variations in the hydroxyl ion concentration cause large differences in the reaction rates. It has been reported that the mutarotation process of αDG follows kinetics of pseudo-first-order [13].

The aim of the present paper is to shed light on the nature of αDG–KF interactions using NMR spectroscopy and polarimetric measurements. According to the obtained evidence, the main role is played by the F^- ion and not by the K^+ ion. In order to discard the effect of the salt hydrolysis in the observed interactions, parallel polarimetric experiments were carried out adding KOH to the αDG aqueous solution instead of KF.

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2. Experimental

2.1. Reagents

The KF, KOH and αDG used in this study were analytical grade commercial products (Merck, Sigma). Water was doubly distilled.

2.2. Measurements

2.2.1. Spectroscopic data

The KF–αDG interactions both in DMSO-d_6 and D_2O were measured in a JEOL ECLIPSE 270 FT NMR pulse spectrometer, using 270 MHz for the ^1H NMR and 67.5 MHz for the ^{13}C NMR spectra. For NMR kinetic experiments, solutions of KF and αDG in D_2O were prepared at $T = 20°C$ and the spectra were taken at different times up to 48 h (taken as infinite time). The ratio of αDG to βDG in the solution was determined by means of anomeric signal integration in each ^{13}C NMR spectrum. The salts were dissolved until saturation.

2.2.2. Optical rotation

Given amounts of KF or KOH and αDG were dissolved in water, quickly poured into a 20-cm cell, and the optical rotation measured at 18°C at certain time intervals with a polarimeter Polax Atago Kagaku Co. instrument. In order to minimize the time required for dissolution, the αDG should be ground.

2.2.3. Kinetic

In all cases (from NMR and optical rotation data), mutarotation rate was determined by the expression

$$k = \frac{1}{t_2 - t_1} \log\left(\frac{\beta_1 - \phi}{\beta_2 - \phi}\right)$$

where β_1 and β_2 are the values at the end of the corresponding times t_1 and t_2, and ϕ the constant final and was measured at 48 h. From the slope of each straight line obtained in the first-order plot of the data, a pseudo-first-order rate constant, k', was estimated. The mutarotation constant is expressed by use of logarithmic base 10 and the time in minutes, because this custom has been largely maintained by carbohydrate chemists [15].

3. Results and discussion

3.1. Interactions of KF with α-D-glucose in DMSO-d_6

In order to study the mechanism of KF–αDG interactions, DMSO-d_6 was selected because in this solvent, the equilibrium processes for monosaccharides are slow on the NMR time scale (ion sugar equilibrium, mutarotation) [16,17]. The ^1H NMR spectra of αDG in DMSO-d_6 in the 4.10–6.80 ppm region are shown in Fig. 1. The assignment of the signals was based on the work of Perlin [18]. When KF is added to a solution of αDG in DMSO-d_6, the ^1H NMR spectrum shows significant changes (see Fig. 2). All the OH proton signals are broadened. The signals of the anomeric protons $H_{1\alpha}$ and $H_{1\beta}$ can now be clearly seen. The coupling $^3J_{H_1-H_2}$ excludes the possibility that these protons could be involved in some dynamic process due to conformational change in the sugar molecule. Therefore, the broadening of the signals is not due to the influence of the other proton linked to the same carbon atom. We interpreted the observed broadening as a result of the interactions of the basic F^- anions with protons of OH groups of the αDG. To test the validity of this hypothesis, experiments with other potassium salts including KCl, KBr and KI instead of KF added to αDG solutions in DMSO-d_6 instead of KF were carried out. The corresponding ^1H NMR spectra do not show significant modifications when compared with that of pure αDG (Fig. 1). Also, this proves that K^+ cations do not interact with the oxygen atoms of the OH groups of the αDG, and therefore, the observed changes in the NMR signals when KF is added to αDG solutions must be only due to F^- and OH^- groups interactions.

3.2. Mutarotation kinetic from NMR spectra in D_2O

The mutarotation kinetics from NMR spectra were determined in D_2O because the water is one of the most common solvents used in the study of interactions of carbohydrates with other species. The results of the kinetic study are shown in Table 1. In all runs, the regression coefficient was >0.9980. Mutarotation of αDG in the presence of KF is very fast, so it is impossible to obtain reliable data on the percent conversion of αDG versus time. The calculated values of the pseudo-first-order constant k' for the mutarotation of αDG in the presence of KCl, KBr and KI or in absence of these salts were similar (see Table 1). It seems that only KF shows a pronounced interaction with αDG. In order to study the cation effect on the mutarotation rate of αDG in D_2O, NMR spectra were recorded adding LiCl, NaCl and CsCl. No significant role of the cation on the mutarotation rate of αDG was observed since the calculated k' values were similar in the presence of these last salts and also similar to the k' value in water without a catalyst (see Table 1). The observed increase in the mutarotation rate when KF is added to a αDG solution in D_2O is assumed to be due to an interaction between αDG and the F^- ion. These results are in accordance with the above-discussed experiments in DMSO-d_6. When compared in water, the obtained k' values in D_2O was slightly smaller because of an isotopic effect [12].

3.3. Mutarotation rate of α-D-glucose in water in the presence of KF

Mutarotation of αDG in the presence of KF was too fast and it was not possible to obtain the mutarotation rate data in

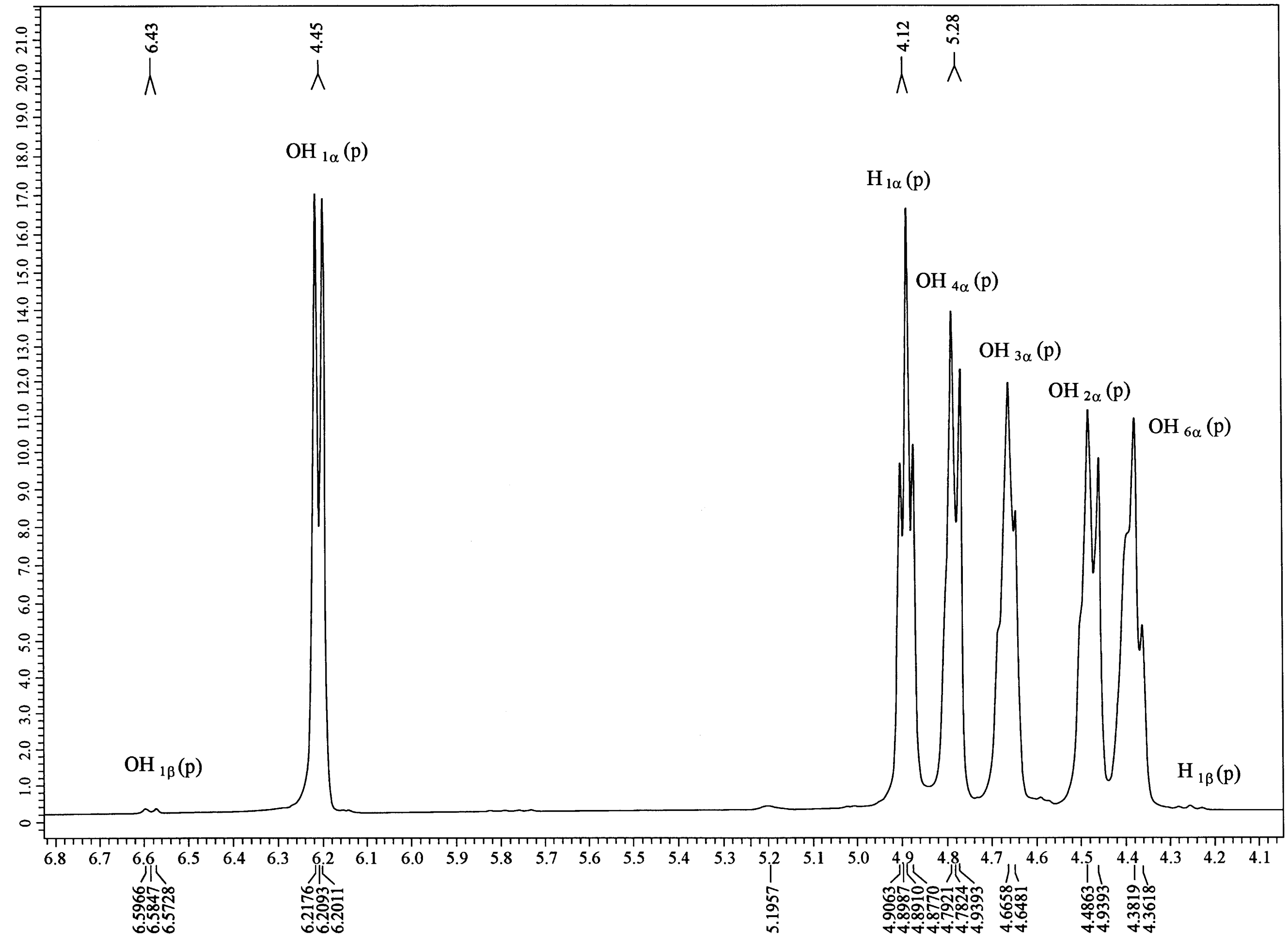

Fig. 1. ^{1}H NMR spectrum of α-D-glucose in DMSO-d$_6$. Indicated are the assignments of the observed signals.

the time from ^{13}C NMR spectra, so it was necessary to make polarimetric measurements.

Mutarotation rate of αDG in the presence of KF was measured and compared with those obtained in water with and without addition of KOH as catalyst. Fig. 3 shows how the mutarotation of αDG evolves in water when KF or KOH is added. In Table 2 are collected the pseudo-first-order rate constants calculated for different concentrations of KF or KOH. The equilibrium values in water and KF were similar and smaller than that observed with KOH, which was attributed to the formation of gluconate ion when KOH is added. As expected, any of these two substances (KF or KOH) accelerates the evolution of the sugar to the equilibrium of its conformers in the solution. The effect of a base, like KOH, on the mutarotation is well-known [12]. KF is a salt, which undergoes hydrolysis in aqueous solution. One could think that the observed effect of KF on the mutarotation of αDG is associated to hydrolysis of this salt. However, at similar pH value, the effect of KF (measured through the value of k') is about five times that observed for KOH (Table 2), indicating a major interaction of F$^-$ anion with the protons, when compared with KOH. However, the interaction of KF with αDG is not limited to an increase in the mutarotation rate to reach equilibrium of conformers. The ^{1}H NMR signals of the OH protons of the β conformer also show a pronounced broadening when KF is present

Table 1
Values of pseudo-first-order constant (k') derived from NMR spectra for the mutarotation of the α-D-glucose, in deuterium oxide, in the presence of potassium halides and alkaline chloride

Salt	Only D$_2$O	Only D$_2$O	KF	KCl	KBr	KI	LiCl	NaCl	CsCl
k' ($\times$ 10^3 min^{-1})[a]	2.62	2.60	–[b]	3.0	2.10	2.00	1.97	2.31	2.00

[a] All measurements were carried out at $T = 20°$C.

[b] The mutarotation was too fast to allow the acquisition of a representative NMR spectrum.

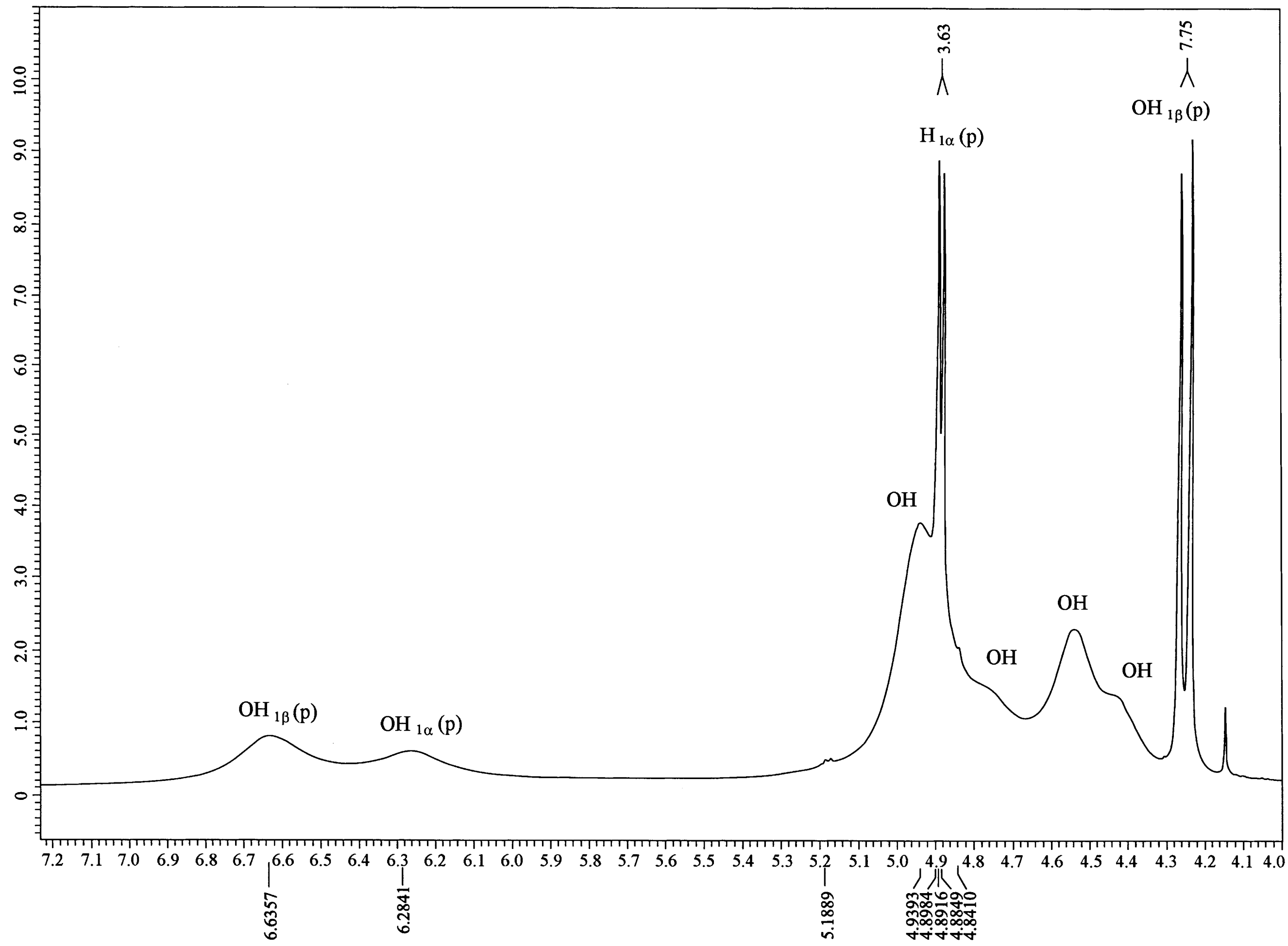

Fig. 2. ^{1}H NMR spectrum of α-D-glucose in DMSO-d_6 when KF is added. The broadening of the OH proton signals can be observed. Now the signals of anomeric protons in α-D-glucose are well resolved.

(see Fig. 2). The increase in the mutarotation rate is only a way to reveal the KF–αDG interactions.

From the kinetical point of view, there are some points that deserve comment. The mutarotation rate in the presence of KF follows a pseudo-first-order behavior (see Fig. 4). The calculated pseudo-first-order constant k', shows a linear dependence of the KF concentration (see Fig. 5). From the slope of Fig. 5, the following pseudo-second-order constant was derived: $k' = 0.00735\ \mathrm{l\,mol^{-1}\,min^{-1}}$. Therefore, k' can be expressed as

$$k' = k_{\mathrm{H_2O}}[\mathrm{F^-}]$$

where the term $k_{\mathrm{H_2O}}$ represents the contribution of the water molecules. Since $[\mathrm{H_2O}]$ varies only slightly in aqueous systems, its effect is usually included in the $k_{\mathrm{H_2O}}$ term. Thus, the mutarotation rate of αDG in the presence of KF is given by

$$\frac{-\mathrm{d}[\alpha\mathrm{DG}]}{\mathrm{d}t} = k_{\mathrm{H_2O}}[\alpha\mathrm{DG}][\mathrm{F^-}]$$

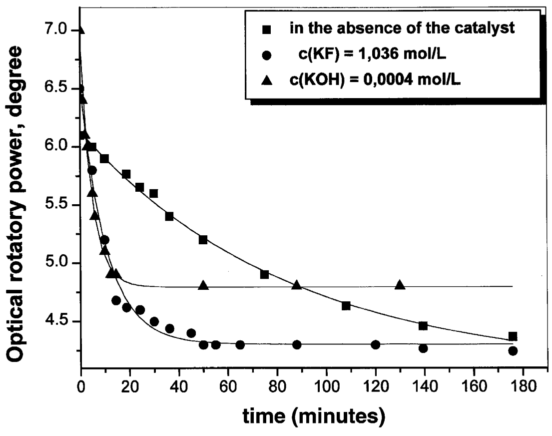

Fig. 3. Rotation power of α-D-glucose in water with and without KF and KOH added as catalyst.

The most acidic protons of the sugar are those of the anomeric OH^- groups. The major KF–αDG interactions must proceed through these protons, catalyzing the opening of the sugar ring at that site to favor the mutarotation process. The mutarotation begins with the ionization of

Table 2

Experimental conditions and the values of pseudo-first-order constant for the mutarotation of α-D-glucose in water, in the presence of KF and KOH[a]

Experiment	[α-D-Glucose] (mol l^{-1})	[KF] (mol l^{-1})	[KOH] (mol l^{-1})	k' (× 10^3 min^{-1})[a]	pH1[b]	pH2[b]
G1	0.2001[c]	–	–	6.4	7.01	6.85
G2	0.2003	0.0356	–[d]	7.5	7.80	6.90
G3	0.2262	0.2363	–[d]	24.5	8.01	7.00
G4	0.2262	0.4750	–[d]	28.0	8.32	7.25
G5	0.2438	0.4774	–[d]	27.9	8.31	7.14
G6	0.2330	0.6166	–[d]	39.0	8.35	7.20
G7	0.2614	0.7155	–[d]	55.0	8.42	7.65
G8	0.2335	1.0361	–[d]	67.0	8.53	7.70
G9	0.2334	–[e]	0.000001	8.7	7.98	5.71
G10	0.2455	–[e]	0.000013	8.7	9.12	6.78
G11	0.2453	–[e]	0.000150	31.5	10.10	8.85
G12	0.2450	–[e]	0.000240	58.1	10.38	9.20
G13	0.2457	–[e]	0.000370	93.0	10.57	9.35
G14	0.2310	–[e]	0.003500	–[f]	11.54	11.50

[a] All measurements were carried out at $T = 18°C$.

[b] pH1 and pH2 are the pH values at $t = 0$ min and at the end of the mutarotation process, respectively.

[c] Mutarotation of α-D-glucose in absence of a catalyst.

[d] With KF as catalyst.

[e] With KOH as catalyst.

[f] The mutarotation was very fast to allow a reliable measurement.

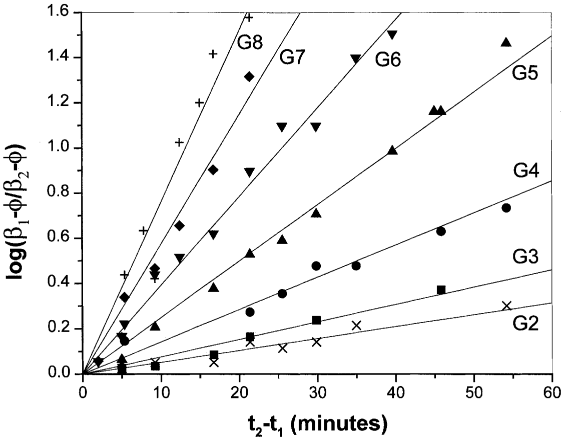

Fig. 4. Pseudo-first-order plots of the mutarotation process of α-D-glucose in water in the presence of KF.

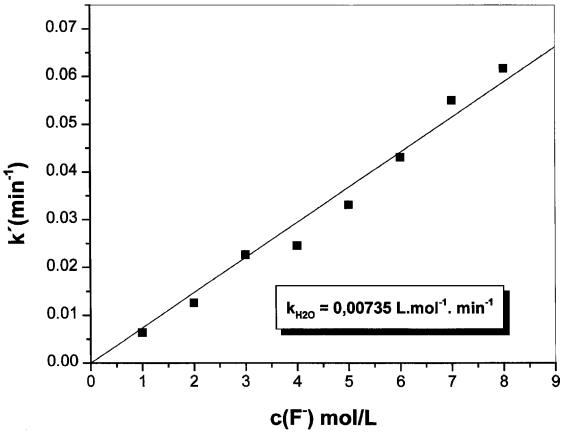

Fig. 5. Dependence of the pseudo-first-order rate constant, k', on the initial concentration of KF.

the sugar. The mutarotation mechanism involves mobile and reversible addition of a catalyst to the sugar anion, followed by slow rupture of the ring, as in the base-catalyzed mechanism suggested in [12].

KF is a salt, which shows a pronounced interaction with acidic protons [11]. In solid state reactions with acidic substances, F^- anions collect protons to form the acidic salt KHF_2 [11]. For weakly acidic substances, the presence of water can hinder the occurrence of the proton transfer reactions due to the solvation effect of water [19]. The protons of sugar are not too acidic to be removed by interaction with KF, however, at least in the solid state that interaction is very pronounced shifting the O–H stretching bands (in the IR spectra) toward the lower frequency. The interaction in solution (DMSO, D_2O or H_2O) are weaker, but sufficient to explain the observed broadening in the ^1H NMR signals of the OH groups of the sugar when KF is added. In addition, they are also sufficient to accelerate the mutarotation process.

4. Conclusions

When KF is added to solutions of αDG in DMSO-d_6, the ^1H NMR signals of the OH groups of the sugar are significantly broadened. When the NMR experiments are carried out in D_2O, a pronounced increase in the mutarotation rate of the sugar is observed. The observed changes can be ascribed to the F^- anion since no effects are observed for other potassium halides or alkali chlorides. When the mutarotation process is studied by a polarimetric method in parallel experiments by adding KF or KOH to the αDG aqueous solutions at similar OH concentration, KF shows an activity five times that observed for KOH suggesting that the observed effect of KF is not directly related with its hydrolysis in water. From these observations, then appears to be a direct interaction of KF with αDG.

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