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Deuterium isotope effect on gas phase ion–molecule hydrogen-bonding interactions: multiply solvated fluoride, chloride, and alkoxide ions

F.E. Wilkinson, T.B. McMahon*

Department of Chemistry, University of Waterloo, Waterloo, Ont. N2L 3G1, Canada

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Abstract

Fourier transform ion cyclotron resonance (FTICR) measurements of solvent exchange equilibria, where the solvents differ only by a single deuterium substitution at the labile hydroxylic site, have been used to study the deuterium isotope effect on ion–molecule hydrogen-bonding interactions. The systems studied include chloride ion, fluoride ion, and alkoxide ions solvated by up to three molecules of alcohol: $(\text{ROH})_n \cdot \text{Cl}^-$, $(\text{ROH})_n \cdot \text{F}^-$, and $(\text{ROH})_n \cdot \text{RO}^-$. Differences in the measured isotope effects are explained on the basis of the differing hydrogen bond strengths in the adducts and by the ability of the chloride ion to partake in multiple site interactions. (Int J Mass Spectrom 199 (2000) 127–139) © 2000 Elsevier Science B.V.

Keywords: Kinetic isotope effect; Hydrogen bonding; Fourier transform ion cyclotron resonance (FTICR); Ion–molecule reactions

1. Introduction

There has been a heightened interest very recently in so-called “low barrier hydrogen bonds” [1]. Such hydrogen bonds are said to be characterised by their significant bond strengths, short bond distances between the heteroatoms participating in the hydrogen bond, and low intermediate barriers for proton motion between these atoms [2]. The renewed interest in hydrogen bonds of this type is associated with the significant role that they may play in catalysis involving enzyme bound intermediates or transition states [3]. The properties attributed to these low barrier

hydrogen bonds are exactly those found for the class of gas phase entities known as proton bound dimers. These charged species, involving two bases, either anionic (I) or neutral (II), bound together by a proton can have hydrogen bond strengths [4] on the order of 30 kcal mol^{-1} , heteroatom bond distances [5] as short as $\sim 2.4 \text{ \AA}$, and may frequently have barriers to proton motion between the two heteroatoms [6] less than 1 kcal mol^{-1}



Many studies of the energetics of solvation of gaseous ions by a single molecule of common solvent species have been carried out [7] that aid significantly in the understanding of the role that solvent effects

* Corresponding author. E-mail: mcMahon@sciborg.uwaterloo.ca
Dedicated to Henri Edouard Audier on the occasion of his 60th birthday.

might play in masking the intrinsic nature of ionic entities. Similarly, the determination of the thermochemistry of selected multiply solvated ions has led to an even greater insight into the nature of solvent effects [8].

Hiraoka and Mizuse [9] studied the gas phase clustering of Cl^- with several alcohols, $(\text{ROH})_n \cdot \text{Cl}^-$, for n up to 11. They suggested, based on small but discernible entropy changes between $n = 6$ and $n = 7$, that for methanol and ethanol the sixth ligand completes the first solvation shell and ligands with $n \geq 7$ belong to the second solvation shell. The bond energies were found to increase in the order $\text{H}_2\text{O} < \text{CH}_3\text{OH} < \text{C}_2\text{H}_5\text{OH} < i\text{-C}_3\text{H}_7\text{OH} < t\text{-C}_4\text{H}_9\text{OH} < n\text{-C}_3\text{H}_7\text{OH}$. The stronger bond observed for $n\text{-C}_3\text{H}_7\text{OH} \cdots \text{Cl}^-$ was explained by the fact that both the acidic hydrogen atoms in the $-\text{OH}$ and in the terminal $-\text{CH}_3$ interact with Cl^- with the most favourable configuration, as illustrated in Fig. 1. These “chelate” or “multiple site” interactions may also occur for the other alcohols, however, in these cases the C-H-Cl distance is greater, or the Cl^- can only interact with one of the methyl hydrogens for structural reasons. With an increasing number of ligands, the geometry of the ligands interacting with Cl^- may gradually change from the “chelate” mode to the “open” mode in which the $\text{Cl}^- \cdots \text{H-O}$ is more linear in order to reduce the mutual repulsion between ligands. By so changing the mode of interactions, the entropy changes would become more favourable (less negative) owing to the increased degree of freedom of motion. Such chain length effects on chelation are consistent with recent data on the acidity of alcohols as a function of chain length and on the change in binding energies of Cl^- to carboxylic acids as a function of chain length.

Recent measurements from this laboratory [10] have extended the studies of halide ion binding to alcohols, $\text{X}^-(\text{ROH})_n$, to fluoride, bromide, and iodide adducts of methanol, ethanol, *i*-propanol, and *t*-butanol for $n \leq 3$. Data obtained for the chloride adducts were in very good agreement with those of Hiraoka and Mizuse whereas the qualitative trends observed for chloride were, in general, reproduced for the adducts of the other three halide ions. As expected,

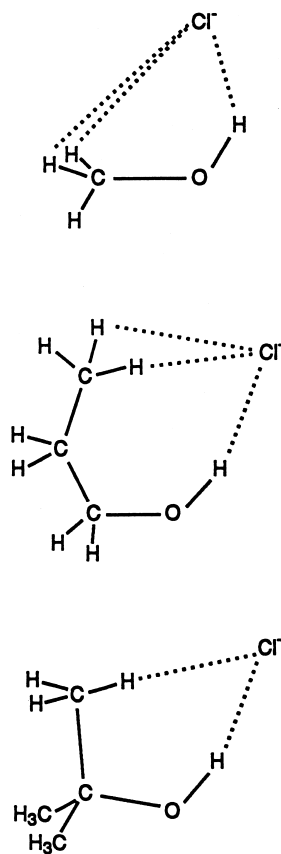


Fig. 1. Illustration of multiple site interactions of Cl^- with alcohols.

the overall bond energies increased in the order $\text{I}^- < \text{Br}^- < \text{Cl}^- < \text{F}^-$.

In contrast to the relatively abundant data available for halide ion–alcohol clusters there is little data for alkoxide–alcohol adducts. The bond energy for methoxide methanol has been independently determined both in this laboratory and by Paul and Kebarle using high pressure mass spectrometry (HPMS) equilibrium measurements with excellent agreement between the three values obtained [11]. In addition, Caldwell et al. [12] have examined alcohol exchange equilibria using ion cyclotron resonance (ICR) techniques to obtain a set of relative free energies of binding in symmetric alkoxide–alcohol dimers. For example, the *t*-butoxide–*t*-butanol dimer is found to be less strongly bound in terms of free energy by $1.5 \text{ kcal mol}^{-1}$ relative to methoxide methanol. No data are available for the

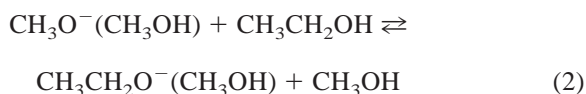
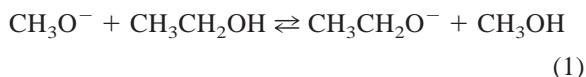
clustering energetics of alkoxide ions with more than one molecule of alcohol.

In addition to these energetics determinations, rate constant measurements for ion–molecule reactions as a function of the number of solvent molecules associated with the ionic reagent also permit an insight into the subtle effects solvent might play in modifying chemical reactivity. Work by MacKay, Rakshit, and Bohme [13] measured the rate constants for the reactions of several acids with methoxide ion solvated with up to three molecules of methanol. These experiments provided insight into the perturbation of the intrinsic reactivity and basicity of the methoxide ions by stepwise methanol solvation. For some reagent acids, the addition of one molecule of methanol to the methoxide ion essentially stopped the reaction. For other acids, the addition of three methanol molecules did not reduce the rate by more than a factor of ten. For yet other acids, an intermediate behaviour was observed, in which the sharp drop in rate was delayed until the addition of two molecules of methanol to the methoxide ion. This divergence of observed rate constants can be accounted for by a consideration of the degree of stabilisation of the reactant and product ions by solvation, and their influence on overall reaction energetics. The rate of proton transfer can be expected to remain high upon solvation if the reaction remains exoergic. Conversely, a sharp drop in rate can be anticipated if solvation renders the reaction endoergic. The solvent-free reactions are all exoergic, and exoergic is preserved if the free energy of solvation of the conjugate base produced is comparable to or greater than the corresponding free energy of solvation of CH_3O^- , or if a lower free energy of solvation of the product base is offset by the exoergicity of the unsolvated reaction.

Bowie et al. [14] observed that the rates of reaction of $\text{CH}_3\text{O}^-(\text{CH}_3\text{OH})_n$ with acetone decreased dramatically as the extent of solvation of the nucleophile increased. This result is not surprising based on the trends observed by Bohme [13].

In similar work, McIver, Scott, and Riveros demonstrated the effect of a single solvent molecule on the intrinsic relative acidities of methanol and ethanol [15]. They observed, by a comparison of the free

energy changes for reactions (1) and (2), that the reversal of relative acidities is already substantial with the first molecule of solvation



where $\Delta G^0 = -1.9$ and -1.2 kcal mol⁻¹, respectively. Thus, the first molecule of methanol solvent produces a decrease of about 0.7 kcal mol⁻¹ in the apparent relative acidity of methanol and ethanol. Caldwell et al. similarly obtain a value of -1.4 kcal mol⁻¹ for ΔG_2^0 . This is consistent with the expected trend in going from the gas phase to the solution phase, but obviously more than one solvent molecule is required to reverse the relative acidity order.

Because a reversal in reactivity order occurs upon going from the nonsolvated ion to the bulk solution, there must be some point in the stepwise solvation where such a reversal occurs. MacKay and Bohme [16] investigated reactions of the form of Eq. (3), using flowing afterglow, where X^- is OH^- , Y^- is CH_3O^- , and S is H_2O or CH_3OH



The magnitude of the measured equilibrium constant was found to decrease dramatically upon solvation by one molecule, and continue to drop, but at a decreased rate, for higher solvent molecule additions. This means that water becomes more acidic than methanol upon solvation, and more so for excess methanol than excess water. The results implied a higher solvent (H_2O and CH_3OH) affinity for OH^- than for CH_3O^- , and more so for CH_3OH than H_2O . Apparently, solvation by more than approximately two methanol molecules actually results in a reversal of the relative acidity of water and methanol.

Thus, in general, in some cases, the first molecule of solvent makes the behaviour of the ion very solution-like, whereas in others, many solvent molecules are necessary for the reactivity and solvation

thermochemistry to approach that of the bulk-solvated form.

Several other studies have demonstrated the effect of extent of solvation on the rate of reactions, such as the gas phase S_N2 reaction [17]. However, because the focus of the present study is on hydrogen bonding interactions, these systems will not be discussed further.

Baltzer and Bergman [18] determined values of the fractionation factor for the methoxide ion in solutions of methanol and dimethyl sulfoxide (DMSO). The fractionation factor, which is effectively the equilibrium constant defining the preference for deuterium to be found in the ionic species in solution as opposed to being present in the bulk solvent, was found to decrease from 0.74 in pure methanol to 0.38 in 75 mole percent DMSO. A rough extrapolation of this data to pure DMSO gives a fractionation factor in the neighbourhood of 0.3. This drop of fractionation factors seems to be a common type of behaviour for hydrogen-bonded complexes on transfer from hydroxylic solvents to dipolar aprotic ones. It was suggested that in the limit when the mole fraction of DMSO tends to unity, the methoxide ion exists as the monosolvate, and that the trisolvate is a correct representation of the true nature of the solvated methoxide ion in methanol. Baltzer and Bergman also suggested that the gradual desolvation of the ion leads to more symmetric hydrogen bonds for those methanol molecules that are still in a hydrogen-bonded position, possibly through an inductive effect. Thus, in DMSO, the adduct takes the form of a centrosymmetric ion, which changes to an increasingly asymmetric ion as the solvent hydrogen bonding to the anion weakens the hydrogen bond of the proton-bound dimer with increasing methanol content. Larson and McMahon [19] suggested that little additional change occurs upon change from aprotic media to the gas phase.

Recent contributions from this laboratory have discussed the deuterium isotope effect or fractionation factor in mono alcohol solvated fluoride [20] and chloride adducts, as well as symmetrical alkoxide-alcohol adducts [21]. These latter species have also been studied by Dixon and co-workers [22]. In the

present work the deuterium isotope effect for the interaction of the three anions (fluoride, chloride, and alkoxide) with up to three molecules of solvent alcohol are presented. It was possible in a few cases to compare the equilibrium constant measured from ions generated in the external source with that measured from ions created internally. For the systems $\text{CH}_3\text{OH} \cdot \text{F}^-$, $\text{CH}_3\text{OH} \cdot \text{Cl}^-$, $\text{CH}_3\text{OH} \cdot \text{OCH}_3^-$, and $(\text{CH}_3\text{OH})_2 \cdot \text{OCH}_3^-$, the equilibrium constants measured from ions created in both sources matched extremely well. Most of these higher cluster experiments used the multiple ion monitoring mode of operation to determine accurate intensities of the ions for the determination of the equilibrium constant. As we have demonstrated previously, these deuterium isotope effects, also called deuterium fractionation factors in solution, can provide a qualitative view of the nature of the potential in which the hydrogen bonding hydrogen finds itself. Thus, the transition from the isotope effect found for naked gas phase ions to that found in solution can be studied on a solvent molecule-by-molecule basis.

2. Experimental

All experiments were carried out on a Spectrospin CMS 47 Fourier transform ion cyclotron resonance (FTICR) spectrometer that has been modified by the addition of a high pressure external ion source. Multiple exchange reactions and nonreactive collisions in the FTICR cell ensure that ions are at thermal equilibrium with the neutral gas. Details of the design and operation of the basic FTICR apparatus and our modification have been described extensively elsewhere [23,24].

The external high pressure source is differentially pumped and permits nine orders of magnitude pressure differential between the ion source and the ICR cell. This allows the synthesis of extensively solvated ions at high pressure in the external source whose chemistry can then subsequently be examined in detail in the low pressure of the ICR cell. Use of this external high pressure ion source is necessary for the preparation of the multiply solvated anions that can-

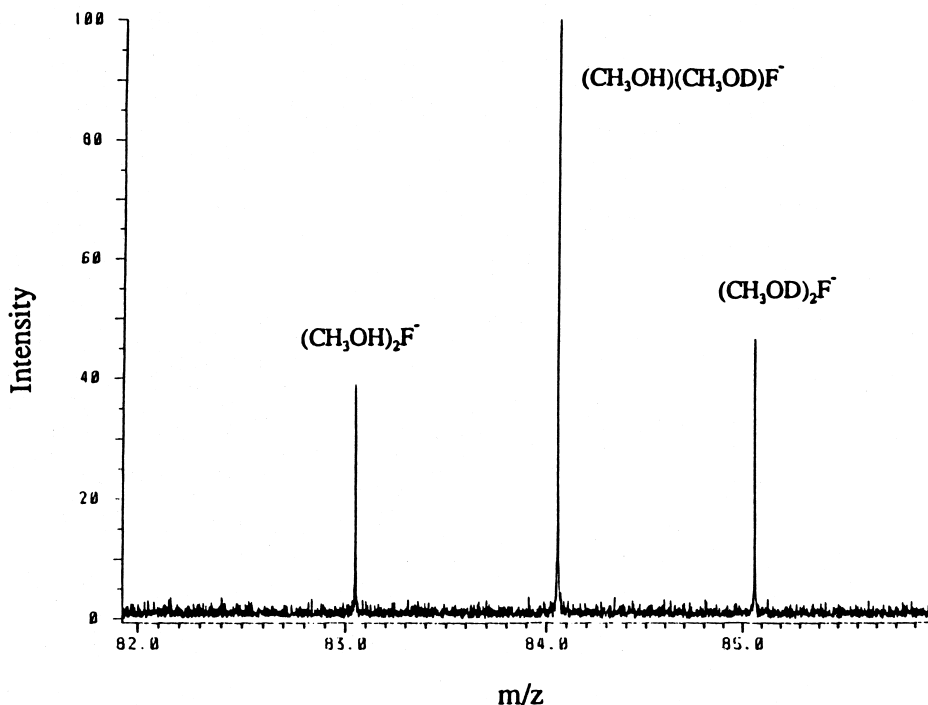


Fig. 2. Illustration of a “multiple ion monitoring” spectrum obtained by single-shot excitation of each of the isotopic peaks in the spectrum. FTICR cell pressure was 2.6×10^{-8} mbar.

not otherwise be generated in the low pressure environment of ICR experiments.

A mixture of normal and deuterated alcohols was prepared and admitted to one of the ICR inlets. Because significant amounts of hydrogen/deuterium (H/D) exchange typically take place in the ICR inlet system, the mixture was allowed to equilibrate with the walls of the vacuum inlet system, and the isotopic ratio of alcohols was determined in situ. High resolution spectra on the molecular ions and fragment ions for which no isotope scrambling should occur provided the intensity ratio. If fragment peaks were used, the spectra were obtained using low ionizing energy and short ionisation pulses to minimise the possibility of isotope scrambling and ion–molecule reactions.

A second mixture, containing known pressures of the alcohol, the compound serving as the source of the desired anion (NF_3 , CCl_4 , or CH_3ONO), and methane was attached to one of the external ion source inlet lines. The ion of interest was then produced by

chemical ionisation, and transferred via ion acceleration and deceleration lenses, and ion optics, into the ICR cell.

Selected ion ejection was used to eliminate all ions except the one of interest from the ICR cell. The intensities of the ionic adducts were then monitored as a function of increasing trapping time. Experiments were performed using the multiple ion monitoring mode of operation, in which accurate intensity data is obtained on all ions observed within a relatively limited frequency range, in a single experiment. This method consists of carrying out a narrow band experiment over a small mass range covering the three (or four) isotopic species of interest and applying three (or four) “shot” excitations to each species. The time domain signal is then acquired for as long a period of time as is warranted by the pressure in the FTICR cell. For example, a representative spectrum obtained for the three isotopic peaks of interest for $\text{F}^-(\text{CH}_3\text{OH})_2$ is shown in Fig. 2. Reactions were monitored for at least

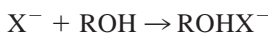
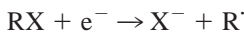
twice the length of time required to establish equilibrium, and the relative abundances of the adduct ions at equilibrium were used in calculating the equilibrium constants.

In order to verify the accuracy of these equilibrium experiments, separate experiments were performed using different partial pressure ratios of the isotopic alcohols. Experiments were also performed with and without the presence of argon leaked in through the second ICR inlet valve. The presence of argon was used to ensure that the ions arriving from the external source were thermalized. Equilibrium constants invariant with both the isotope ratio and presence or absence of argon were obtained.

Most chemicals used in this study were obtained from commercial sources and were used without further purification with the exception of degassing by successive freeze–pump–thaw cycles.

Some deuterated alcohols were prepared by conversion of the normal alcohol into the alkoxide by reaction with sodium metal in anhydrous ether solvent. The solid alkoxide was then dissolved in D₂O to convert it to the deuterated alcohol. Purification of the product was achieved by extraction with ether and distillation.

Experiments were performed on adducts of Cl[−], F[−], and CH₃O[−] with up to three molecules of solvent alcohol attached. Each of multiply solvated adduct ions was produced using the general sequence of reactions shown in Scheme 1

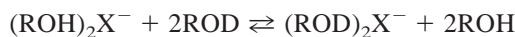
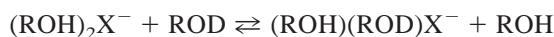


Scheme 1.

All experiments were carried out at an ion source temperature of 25 °C and typical pressures in the high pressure source were 0.05 mbar of alcohol and 2.5 mbar CH₄. The pressure of RX, the negative ion formation reagent, varied from 10^{−4} mbar of CCl₄ to 0.05 mbar for NF₃ and CH₃ONO.

In addition to the clusters formed, as described in Scheme 1, F[−] adducts with up to 5 alcohol molecules and CH₃O[−] adducts with up to 4 methanol molecules were observed to be formed in the high pressure source under the conditions described.

As noted above, after transfer to the FTICR cell, the cluster ion of interest was isolated and allowed to react with a mixture of ROH and ROD of known partial pressure ratio leaked into the FTICR cell to a known pressure. The variation of relative ionic abundances was then followed as a function of time after the isolation of the cluster ion to be studied. In each case the reaction sequence could be described by the general equilibrium equations outlined in Scheme 2 and Scheme 3. *K*₁, *K*₂, and *K*₃ represent the equilibrium constants for the individual replacement reactions and *K*_{eq} is the equilibrium constant for the complete replacement of ROH by ROD in the cluster. From the known partial pressure ratio of ROH and ROD and the equilibrium ion intensities of the appropriate adducts, each of these equilibrium constants could be readily obtained from the plots of ion intensity as a function of reaction time



$$K_{eq} = K_1 K_2 = \frac{[(ROD)_2F^-][ROH]^2}{[(ROH)_2F^-][ROD]^2}$$

Scheme 2.

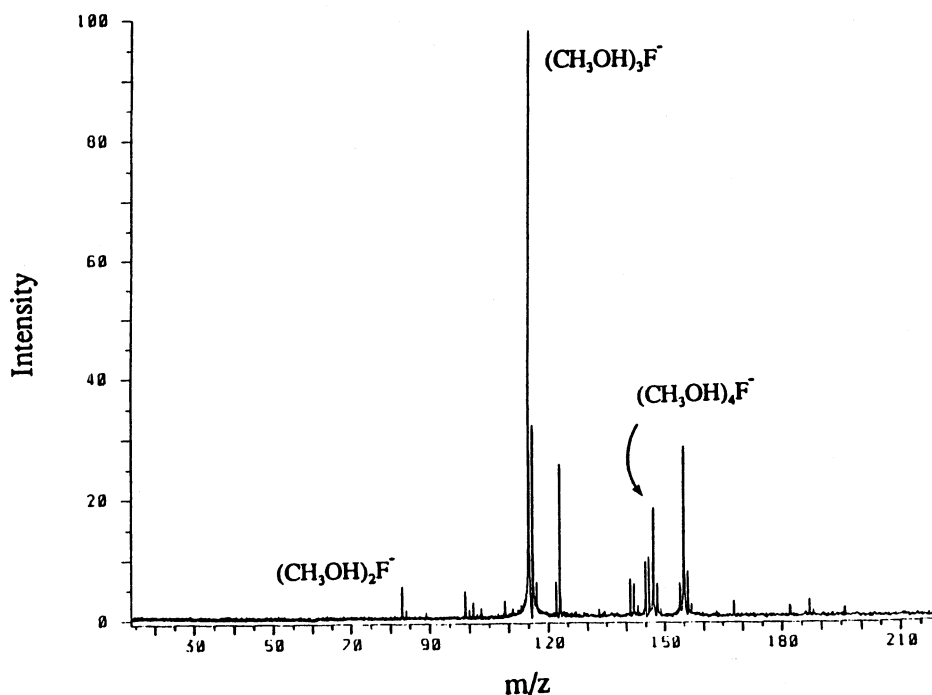
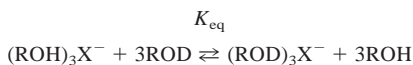
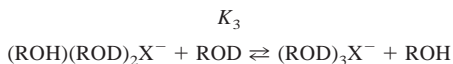
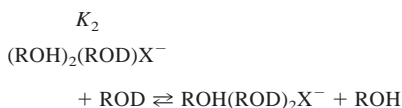
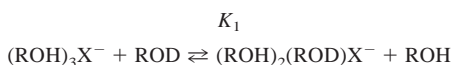


Fig. 3. Broadband spectrum demonstrating the mixture of ions obtained from the external ion source. FTICR cell pressure of the $\text{CH}_3\text{OH}-\text{CH}_3\text{OD}$ mixture is 2.6×10^{-8} mbar. A small amount of H/D exchange is evident.



$$K_{\text{eq}} = K_1 K_2 K_3 = \frac{[(\text{ROD})_3\text{F}^-][\text{ROH}]^3}{[(\text{ROH})_3\text{F}^-][\text{ROD}]^3}$$

Scheme 3.

3. Results and discussion

3.1. $(\text{CH}_3\text{OH})_n \cdot \text{F}^-$ clusters

A typical spectrum showing the distribution of clusters obtained from the external source for F^- and

methanol is shown in Fig. 3. Peaks due to the small amount of deuterium exchange that has already occurred during the ionization pulse and detection cycle are also evident. The $(\text{CH}_3\text{OH})_4 \cdot \text{F}^-$ cluster ion decreases in intensity very rapidly after it is trapped in the FTICR cell and thus no equilibrium experiments could be performed with this species. Similarly, the $(\text{CH}_3\text{OH})_3 \cdot \text{F}^-$ ion was found to undergo unimolecular dissociation in competition with deuterium exchange. These purely unimolecular dissociations have been shown by us previously to be due to the interaction of the ions trapped in the FTICR cell with the ambient black-body radiation emitted by the cell walls [25]. For example, the data shown in Fig. 4 for the disappearance of the $n = 3$ cluster yield a unimolecular dissociation rate constant of 0.006 s^{-1} that is found to be independent of the added pressure of either argon or methanol. In contrast, however, the disappearance of $(\text{CH}_3\text{OH})_3 \cdot \text{F}^-$ is observed to be linearly dependent on the pressure of added acetone to the FTICR cell. This suggests that a chemical reaction

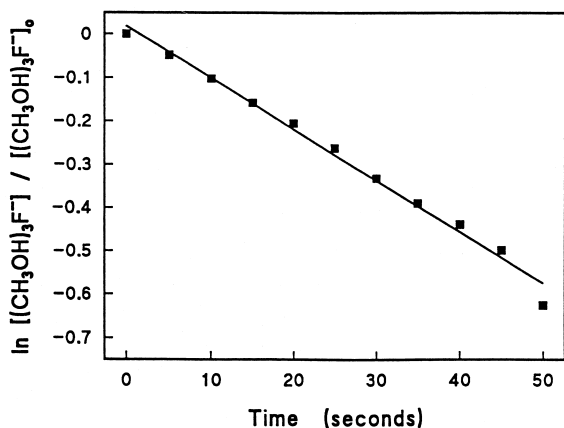
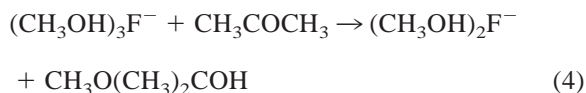


Fig. 4. Kinetics of $(\text{CH}_3\text{OH})_3 \cdot \text{F}^-$ decay in the presence of 7×10^{-8} mbar argon.

is actually taking place that couples acetone to one of the methanol molecules in the cluster. One such possibility is hemi-acetal formation [Eq. (4)] that can be estimated to be roughly 9 kcal mol^{-1} exothermic.

This, and similar reactions, are currently under further study in our laboratory



The unimolecular dissociation of $(\text{CH}_3\text{OH})_3 \cdot \text{F}^-$ is, however, sufficiently slow that exchange equilibrium among the various $n = 3$ species is established simultaneously with that of the $n = 2$ species. For example, the spectrum shown in Fig. 5 was obtained after a reaction time of 5 s following isolation of the $n = 3$ cluster in the FTICR cell. The overall approach to and attainment of equilibrium are shown in Fig. 6 for the $n = 2$ cluster. In this case the isotopic variants of the $n = 3$ cluster have been omitted for clarity.

The equilibrium constants obtained for the $n = 2$ and $n = 3$ clusters of methanol and fluoride ion are summarized in Table 1. Also included for comparison are the data for the $n = 1$ cluster previously pub-

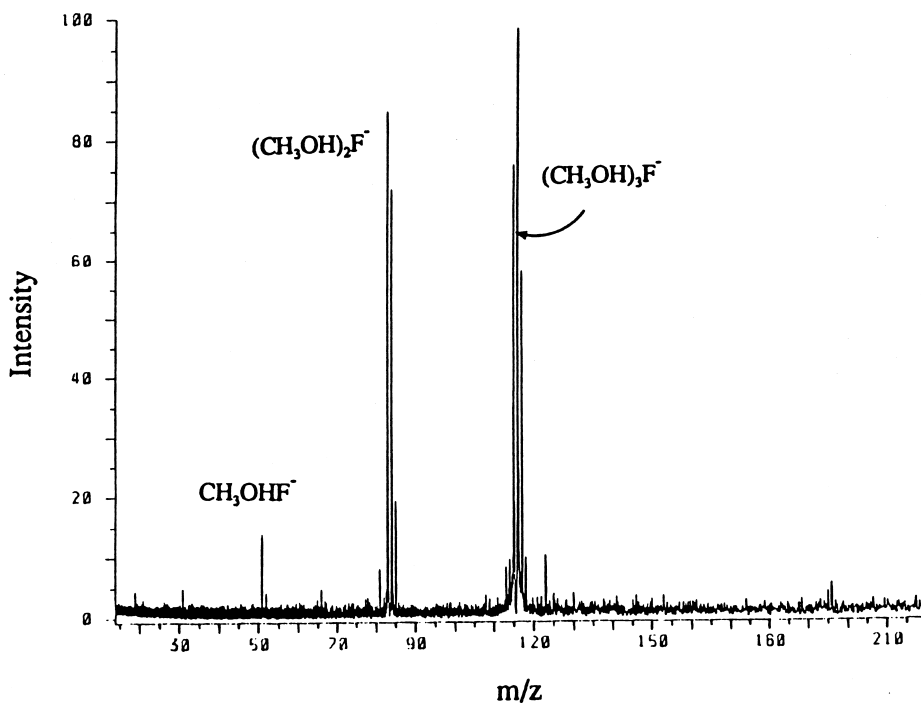


Fig. 5. Broadband spectrum demonstrating attainment of H/D exchange equilibrium for the $(\text{CH}_3\text{OH})_3 \cdot \text{F}^-$ and $(\text{CH}_3\text{OH})_2 \cdot \text{F}^-$ clusters 5s following isolation of $(\text{CH}_3\text{OH})_3 \cdot \text{F}^-$. Pressure of the $\text{CH}_3\text{OH}-\text{CH}_3\text{OD}$ mixture is 2.6×10^{-8} mbar.

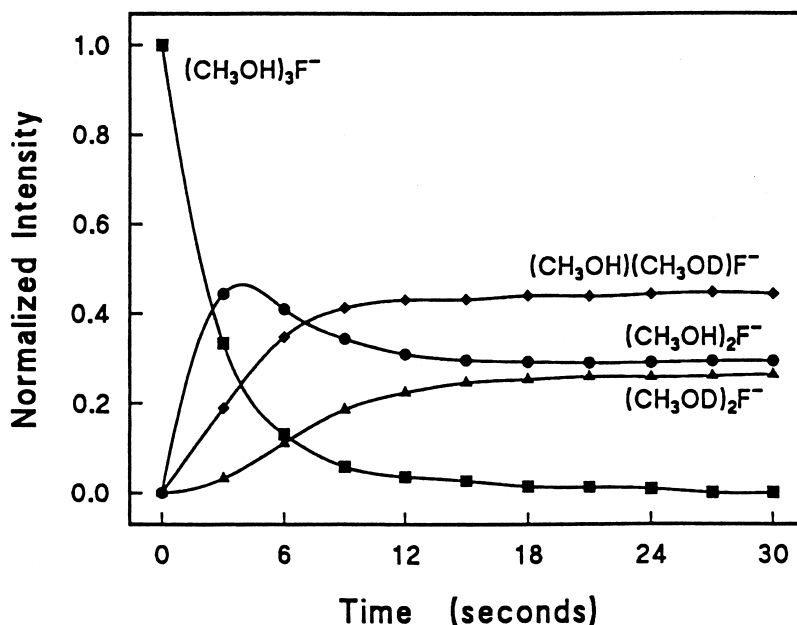
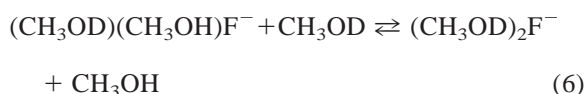
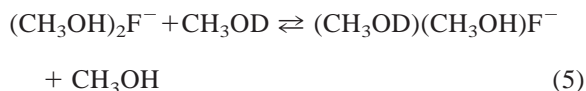


Fig. 6. A plot of the approach to equilibrium for $(\text{CH}_3\text{OH})_2 \cdot \text{F}^-$. Pressure of the $\text{CH}_3\text{OH}-\text{CH}_3\text{OD}$ mixture is 2.6×10^{-8} mbar.

lished. The results for the overall exchange equilibrium constants, K_{eq} are plotted in Fig. 7 as a function of the number of solvent molecules, and an apparently straight line correlation between K_{eq} and n is seen to exist. This linear behaviour would not be expected to continue to the $n = 4$ cluster, however, because a plateau toward the solution phase isotope effect value of close to 1.0 would be anticipated.

HPMS experiments on the temperature dependence of the reactions have been performed previously for the $n = 2$ clusters of methanol with fluoride ion. The results of these experiments from van't Hoff plots on Eqs. (5) and (6) are presented in Table 2 [26]



There seems to be a significantly larger entropy term in the second equilibrium [reaction (6)] than in the first [reaction (5)] and also a reversal in the sign of the entropy change. This is actually simply a result of the symmetry of the reactions; whereas in Eq. (9) the products are less symmetric than the reactants, in Eq. (10), the opposite is true. The overall symmetry can

Table 1
Equilibrium constants for $(\text{CH}_3\text{OH})_n \cdot \text{F}^-$

n	K_1	K_2	K_3	K_{eq}
1	0.48 ± 0.01			0.48 ± 0.01
2	2.10 ± 0.09	0.36 ± 0.02		0.76 ± 0.05
3	3.10 ± 0.18	0.93 ± 0.07	0.34 ± 0.03	0.96 ± 0.12

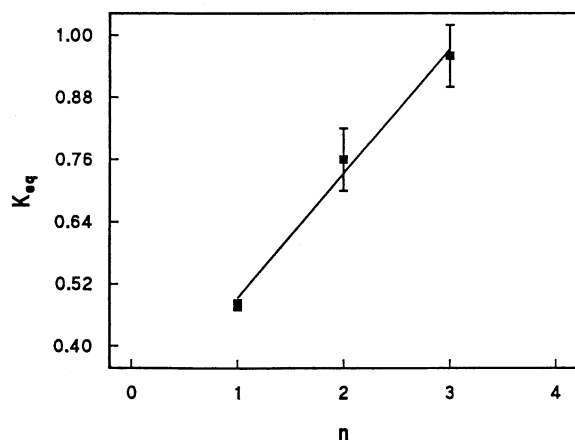


Fig. 7. Variation of K_{eq} for $(\text{CH}_3\text{OH})_n \cdot \text{F}^-$ clusters as a function of n .

be expressed as a combination of the intrinsic entropy and the entropy due to symmetry, Eq. (7):

$$\Delta S_n^\circ = \Delta S_n^{\circ,\text{int}} + \Delta S_n^{\circ,\text{symm}} \quad (7)$$

Because $\Delta S_n^{\circ,\text{symm}}$ is evaluated as $R \ln 2$, it is possible to then calculate the intrinsic entropy contribution to these reactions. Once the symmetry component has been removed, one can see that the intrinsic entropy is negative, and equals $-0.6 \pm 0.2 \text{ cal mol}^{-1} \text{ K}^{-1}$. It is important to note that the FTICR and HPMS determined values of K_{eq} are in excellent agreement.

3.2. $(\text{ROH})_n \cdot \text{Cl}^-$ clusters

The deuterium isotope effect on the hydrogen bonding position was also examined for Cl^- solvated by two molecules of alcohol for methanol, ethanol, and isopropyl alcohol. These data are summarized in Table 3. No equilibrium data could be obtained for the $(t\text{-C}_4\text{H}_9\text{OH})_2 \cdot \text{Cl}^-$ cluster because of the competition from black-body radiation induced dissociation of this cluster. Even though the binding energy of the second alcohol molecule in the cluster is stronger than that for all of the other alcohols, this species dissociates the most rapidly because of the increased number of vibrational modes that gives rise to a more rapid energy exchange with the background infrared radia-

tion. Similarly, no results could be obtained for the $n = 3$ clusters of any alcohols other than methanol.

Fig. 8 is a plot of the equilibrium constant versus the gas phase acidity of the alcohol for the $n = 2$ clusters. A linear relationship with essentially zero slope is observed, about unity. It is thus seen for these clusters that no significant isotope effect is operating, and the results are essentially the statistically predicted ones. Whereas there is only one form in which both $(\text{ROH})_2 \cdot \text{Cl}^-$ and $(\text{ROD})_2 \cdot \text{Cl}^-$ can exist, there are two distinguishable configurations of $(\text{ROH})(\text{ROD}) \cdot \text{Cl}^-$. Thus, statistically these three ions should be present in the proportions 1:2:1. The ensuing equilibrium constants are then statistically predicted to be $K_1 = 2/1 = 2$ and $K_2 = 1/2 = 0.5$. This result is not surprising because the hydrogen bonding to chloride ion is much weaker than the analogous fluoride ion–alcohol bonding, thus the chloride ion does not perturb the alcohol as much, and a much less significant isotope effect is expected.

In Fig. 9, the equilibrium constants for the methanol clusters are plotted versus n , the number of methanol molecules in the cluster. From this plot, it is seen that the isotope effect only operates for the $n = 1$ cluster, and levels off to the statistical prediction for the larger clusters. This can be explained by the further weakening of the hydrogen bond upon addition of the second and third molecules of methanol. For the $n = 1$ case, the hydrogen bond is strong enough that the chloride ion will perturb the alcohol, but for the $n = 2$ and $n = 3$ cases, the average hydrogen bond strength is weak enough that this perturbation does not occur.

3.3. $(\text{ROH})_n \text{OR}^-$ clusters

Equilibrium constants for the $n = 1, 2,$ and 3 clusters of methanol onto methoxide ion were obtained via external source experiments. The results are given in Table 4, and a plot of the results is shown in Fig. 10.

For the $n = 2$ and $n = 3$ clusters, the K_1 values have a greater uncertainty than the others due to lower intensities of the $(\text{CH}_3\text{OH})_n \cdot \text{OCH}_3^-$ ions. The first observation to note is that the value of K_{eq} for the $n =$

1 adduct ion is very similar to that obtained using the internal ion source, 0.35 ± 0.02 . Also, it was possible to examine the equilibrium for the $n = 2$ adduct generated internally, and for these equilibria, the equilibrium constants were found to be $K_1 = 1.40 \pm 0.02$, $K_2 = 0.35 \pm 0.01$, and the overall $K_{\text{eq}} = 0.49 \pm 0.02$. Thus, it is clear that the internal and external methods of producing the ions give the same equilibrium results.

A very interesting aspect of these results is seen if they are compared to the results obtained by Baltzer and Bergman for the solution phase equilibrium of methoxide ion and methanol in pure methanol and in mixtures of methanol and dimethyl sulfoxide [18]. In pure methanol, they obtained a fractionation factor, φ , of 0.74, whereas in solutions with increasing mole percent DMSO, the fractionation factor was observed to drop dramatically: 0.7 in 25% DMSO to 0.38 in 75% DMSO. Extrapolating to 100% DMSO, they give an estimate of 0.3 for the fractionation factor. Baltzer and Bergman explain the drop as a common type of behaviour for hydrogen-bonded complexes upon transfer from hydroxylic solvents to dipolar aprotic ones. Finally, Baltzer and Bergman suggest that the trisolvate is a correct representation of the true nature of the methoxide ion in pure methanol, and as more and more DMSO is added, the form changes to disolvate and then monosolvate. This, then, would give $\varphi_{n=1} = 0.30$, $\varphi_{n=2} = 0.47$, and $\varphi_{n=3} = 0.74$. The equilibrium constants obtained in the present study can be converted to fractionation factors using the values given by Weil and Dixon. This procedure yields fractionation factors of 0.42, 0.57, and 0.96 for the $n = 1, 2,$ and 3 clusters, respectively. This is not in good agreement with the results of Baltzer and Bergman [18], and perhaps suggests that they are incorrect in their conclusion that the

Table 2
High pressure mass spectrometry results for $(\text{CH}_3\text{OH})_2 \cdot \text{F}^-$ [26]

Equation	ΔH^0 (kcal mol ⁻¹)	ΔS^0 (eu)	K_n	K_{eq}
5	-0.1	0.6	1.70	0.75
6	0.0	-1.8	0.44	

Table 3
Equilibrium constants for $(\text{ROH})_n \cdot \text{Cl}^-$ clusters

Alcohol	K_1	K_2	K_3	K_{eq}
$n = 1$				
Methanol	0.84 ± 0.06			0.84 ± 0.06
$n = 2$				
Methanol	2.29 ± 0.14	0.49 ± 0.04		1.13 ± 0.12
Ethanol	2.23 ± 0.20	0.46 ± 0.04		1.02 ± 0.13
Isopropyl alcohol	2.19 ± 0.14	0.52 ± 0.03		1.13 ± 0.10
$n = 3$				
Methanol	3.53 ± 0.37	1.10 ± 0.03	0.28 ± 0.03	1.09 ± 0.15

methoxide ion in solution exists as the triply solvated species. Perhaps what they observed giving a fractionation factor of 0.74 is actually a mixture of the doubly and triply solvated species.

4. Conclusions

It has been clearly demonstrated that the value of the deuterium isotope effect differs significantly for the fluoride ion, chloride ion, and alkoxide ion adducts of aliphatic alcohols. These differences can be directly linked to the hydrogen bond strength in the adduct ions, and the capability of the chloride ion to undergo multiple site interactions.

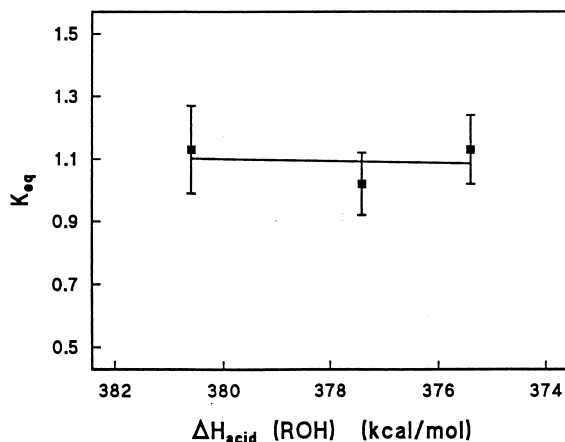


Fig. 8. Variation of K_{eq} for H/D exchange of $\text{ROH}_2 \cdot \text{Cl}^-$ clusters with the gas phase acidity of ROH.

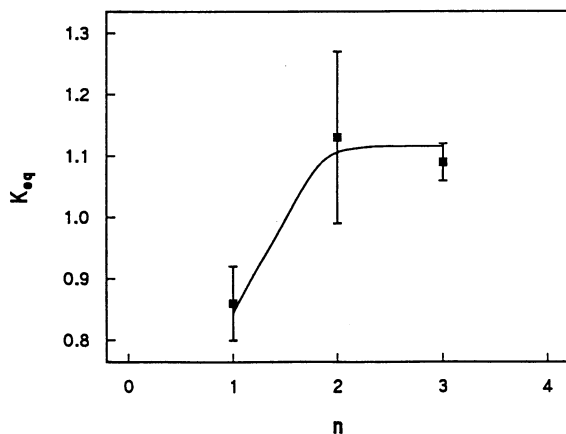


Fig. 9. Variation of K_{eq} for $(\text{CH}_3\text{OH})_n \cdot \text{Cl}^-$ clusters as a function of n .

The hydrogen bond strengths of alkyl alcohols to fluoride and chloride have been shown to differ significantly. This observation is found to be directly related to the fact that the chloride ion is a large, polarizable base, whereas the fluoride ion is a small, hard, highly electronegative base that forms very strong hydrogen bonds.

The capability of the chloride ion to undergo multiple site interactions also contributes to the different isotope effect for the chloride ion systems. Whereas the fluoride ion forms only one very strong bond to the alcohol $-\text{OH}$ moiety, the chloride ion, because of its larger size, can also interact with the acidic hydrogens on the methyl groups. Thus, the chloride ion will possibly form up to two additional hydrogen bonds to the alcohol.

Qualitatively, it is expected that fluoride and alkoxide ions would give similar results based on the similar nature of these two ions. Both are smaller and more basic than the chloride ion, and form hydrogen bonds with a pronounced dependence on the gas

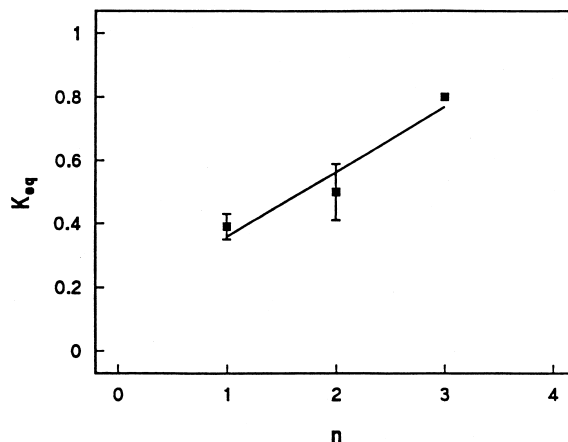


Fig. 10. Variation of K_{eq} for $(\text{CH}_3\text{OH})_n \cdot \text{OCH}_3^-$ clusters as a function of n .

phase acidity of the Brønsted acid substrate. Indeed, both of these anions give significant isotope effects for all clusters formed with aliphatic alcohols. The $n = 1$ adducts yielded very similar equilibrium constants. As n is increased, the equilibrium constant increases for both alkoxide and fluoride adducts, but more so for the fluoride adducts. The $n = 3$ adduct of methanol with fluoride gave an equilibrium constant of almost unity, or an almost nonexistent isotope effect. It is predicted that if it had been possible to examine the $n = 4$ and higher adducts of methanol with a fluoride ion, the measured equilibrium constant would level off after $n = 4$ because four methanol solvent molecules would complete the solvation shell of the fluoride ion.

From this and other work, it has been clearly demonstrated that the strength of the hydrogen-bonded interaction is reflected in the magnitude of the isotope effect [20,21,26].

Table 4

Equilibrium constants for $(\text{CH}_3\text{OH})_n \cdot \text{OCH}_3^-$ clusters

n	K_1	K_2	K_3	K_{eq}
1	0.39 ± 0.04			0.39 ± 0.04
2	1.52 ± 0.18	0.32 ± 0.02		0.50 ± 0.07
3	2.67 ± 0.21	0.88 ± 0.02	0.35 ± 0.03	0.80 ± 0.09

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