

Hydrogen Isotope Exchange between Fluoroform (CF₃H) and Water. 2. Catalysis by Hydroxide Ion in the Presence of Added Dimethyl Sulfoxide¹

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Abstract: Hydroxide ion catalyzed isotope exchange between CF₃D or CF₃T and Me₂SO/water has been studied as a function of solvent composition and temperature in a stirred reactor. The solubility of CF₃H gas in the catalyst solutions has been measured over a range of temperatures to enable conversion of the experimental exchange rate constants to in-solution values. The resultant $k_{\text{obsd}}(\text{CF}_3\text{D})$ for 0.011 mol·L⁻¹ OH⁻ at 49.1 °C increases by a factor of 10⁶ on changing from water to 70 mol % Me₂SO. The heat of solution of CF₃H at 50 °C passes through a minimum in the region of 30–35 mol % Me₂SO; the “salting-out” effect on CF₃H solubility is also strongest in this region of greatest Me₂SO/H₂O association. Hydrolysis of CF₃H is a factor of ca. 600 slower than isotope exchange at 50 °C in 30 mol % Me₂SO. The slopes of linear plots of log $k_{\text{obsd}}(\text{CF}_3\text{D})$ vs. H_- and vs. Cox and Stewart's excess basicity function are 0.80 and 0.99, respectively; their significance is discussed. The Arrhenius activation parameters (CF₃D) determined as a function of solvent composition have been broken down to enthalpy, entropy, and free energy of transfer functions for the reactants and transition state. Comparisons are made with similar data available for chloroform and molecular hydrogen. The primary kinetic isotope effect $k_{\text{D}}/k_{\text{T}}$, calculated from rate constant data for CF₃D and CF₃T exchange, increases smoothly from an inverse value in 20 mol % Me₂SO (ca. 0.4) to ca. 1.5 in 70 mol % Me₂SO. The above results are consistent with a product-like transition state for CF₃D isotope exchange.

It was shown in part 1² that, although reactivity is practically zero at ambient temperature,³ gaseous CF₃H will undergo hydrogen isotope exchange in NaOD/D₂O solution at elevated temperature. Because of our interest in developing an effective catalyst system for CF₃H/HOD isotope exchange,² we have studied the effect of added dimethyl sulfoxide (Me₂SO) on this hydroxide ion catalyzed reaction. It is well-known that many carbon acid reactivities are greatly enhanced under such conditions,⁴ including that for the similar compound CCl₃H.⁵

It was found that this reaction with fluoroform gains the full advantage of the great increase in hydroxide ion basicity known for the alkaline aqueous Me₂SO system.^{6,7} For CF₃D at 50 °C and 0.011 mol·L⁻¹ hydroxide ion, the rate acceleration on changing from water to 70 mol % Me₂SO is a factor of 10⁶. Reported below are the kinetic results of this study, including the solvent dependence of the in-solution exchange rate constant, kinetic isotope effects, and activation parameters, with the latter broken down to thermodynamic transfer functions for reactants and transition state.

Experimental Section

Reagents. CF₃H was used as received from Matheson.²

Initially, a batch of CF₃D was prepared by reacting CF₃I (PCR Research Chemicals, Inc.) with solid NaOD in anhydrous CH₃CH₂OD (cf. ref 8); however, the yield was less than 50%. Following discovery of the large activation energy for NaOD-catalyzed exchange of CF₃H with D₂O,² this reaction was adapted to the facile production of CF₃D. Half mole batches of CF₃H were contacted with 200 mL of 1 mol·L⁻¹ NaOD/D₂O in a 1-L stainless-steel tank heated to ca. 105 °C. Gentle agitation of the tank for 7 h was sufficient to produce complete equilibration of deuterium, yielding 97.6 mol % CF₃D as determined by mass spectrometry.

Similarly, tritium was introduced into fluoroform at the tracer level by using 1 mol·L⁻¹ NaOH/HTO (23.5 mCi·L⁻¹) as the catalyst solution. About 6000 counts per minute (cpm) were obtained for 1-mL product gas samples dissolved in 20 mL of Omnifluor in toluene (New England

Nuclear, 4 g·L⁻¹), using a Beckman LS250 scintillation counter.

Me₂SO (Fisher Scientific) was stored over activated 4A molecular sieves and then vacuum distilled, the central fraction being retained. Karl Fischer analysis on selected samples indicated an average 0.2 wt % water. Solid Me₄NOH·5H₂O (Fisher Scientific) was used to make up stock aqueous Me₄NOH solutions. The OH⁻/H₂O/Me₂SO solvent mixtures were prepared by weight.

CF₃H Gas Solubility. Measurements were carried out by using the gas chromatographic procedure described earlier.² Net CF₃H pressure was maintained at 0.10 MPa; estimates of water/Me₂SO mixture vapor pressures were made from literature⁹ data at 80 °C and the vapor pressures of pure Me₂SO and water between 25 and 80 °C.

Reproducibility of solubilities was generally ±1–2% for the 4–7 liquid samples taken from each solution over a period of 1 h or more after the CF₃H pressure had stabilized.

CF₃H Hydrolysis. As for the aqueous solution studies,² the formation of F⁻ ion was monitored by specific ion electrode. It was necessary to prepare NaF calibration solutions in the Me₂SO/water mixture of interest, since the absolute millivolt readings were quite dependent on solvent composition; however, the concentration–millivolt slope remained constant within experimental error.

Deuterium-Exchange Runs. The experimental procedure and data workup were as before.² CF₂H⁺ and CF₂D⁺ ion response factors were identical within 1%.

The vapor/solution conversion factor² decreased with increasing Me₂SO content in the solvent, as a result of the rise in fluoroform solubility. For example, at 49 °C the factor changed from 25 in water (0.94 mol·L⁻¹ OH⁻) to 4.9 in 40 and 2.0 in 70 mol % Me₂SO (0.011 mol·L⁻¹ OH⁻).

Tritium-Exchange Runs. The same reaction vessel was used as for the deuterium-exchange runs, with one modification. An Ace Glass threaded septum holder was glass blown horizontally to the side of the vessel top. One milliliter fluoroform gas samples could then be removed during a kinetic run by syringe. Each sample was immediately transferred to a “20-mL” scintillation vial (hole drilled in cap, fitted with a Teflon/silicone rubber septum) containing 20 mL of the fluid described above.

Plots of ln (net cpm) vs. time were linear for the period measured, up to several half-lives, with some scatter due partly, presumably, to non-uniformity of vial volumes. The solubility of CF₃H in toluene at 0.10 MPa was determined at 25 °C (see Results); calculations indicated that under the above sampling conditions more than 90% of the fluoroform in each vial would be in solution.

Results

CF₃H Gas Solubility. Shown in Figure 1 is the dependence of CF₃H solubility on mol % Me₂SO at 50.0 °C and 0.10 MPa

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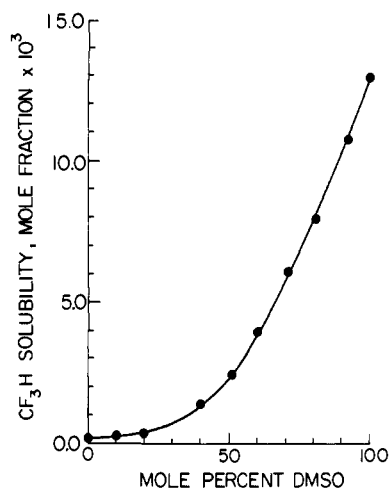


Figure 1. Solubility of fluoroform in Me_2SO /water mixtures at 50 °C and 0.10 MPa of CF_3H . Data points from smooth plots of solubility vs. temperature for each solvent composition (raw data in supplementary material).

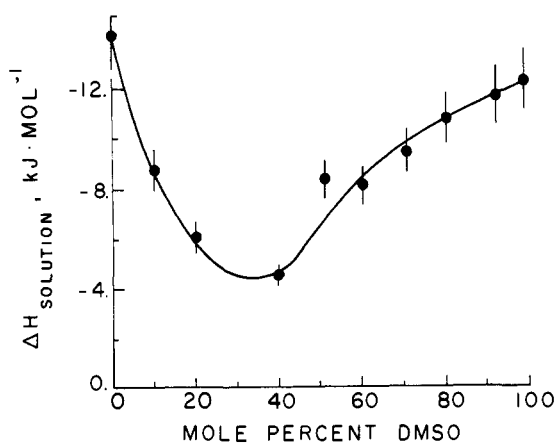


Figure 2. Dependence of heat of solution of fluoroform at 50 °C on solvent composition. Vertical bars represent $\pm 10\%$.

partial pressure of CF_3H . The solubility increase with added Me_2SO becomes quite marked above 40 mol % Me_2SO . The points for this plot were obtained from smooth curves through arrays of data measured as a function of temperature for each solvent (see Supplementary Material). Although the solvent mixtures contained low (for most, 0.01 mol·L⁻¹) concentrations of hydroxide ion, the effect on CF_3H solubility would be minimal at this level.² The solubility data are believed to be accurate within $\pm 2\%$.

These data were calculated on a mole fraction basis. Where mol·L⁻¹ values were required, the mole fraction data were converted by using the appropriate solvent mixture densities; the latter were interpolated from literature data at several temperatures.¹⁰

The effect of CF_3H partial pressure on its solubility was examined for 79.4 mol % Me_2SO at 30.0 °C. Henry's law was clearly obeyed over the range 0–120 kPa.

In Figure 2 is shown the change in heat of solution of CF_3H with solvent composition. The ΔH values were calculated from the slopes of tangents at 50 °C to plots of \ln (mole fraction solubility) vs. reciprocal absolute temperature;¹¹ these plots were prepared from smooth curves drawn through solubility data at the various temperatures.

The solubility of CF_3H in toluene at 24.9 °C was found to be 1.06×10^{-2} mole fraction.

CF_3H Hydrolysis. The hydrolysis reaction was studied for only one Me_2SO /water mixture, 30.2 mol % Me_2SO containing 0.011

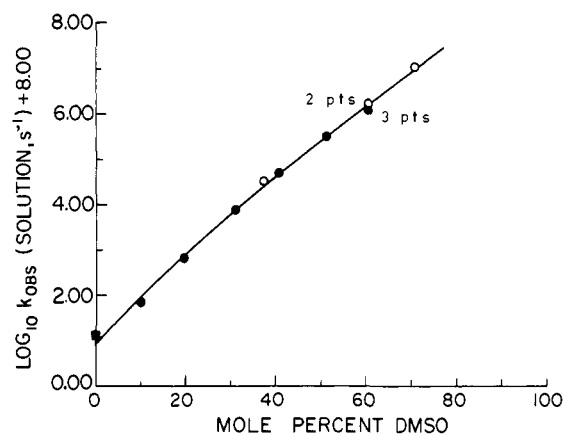


Figure 3. Dependence of in-solution rate constant for CF_3D exchange at 49.1 °C on solvent composition, with 0.011 mol·L⁻¹ hydroxide ion: closed symbols, NaOH; open symbols, Me_4NOH . Value for water is from extrapolation of higher temperature and $[\text{NaOD}/\text{D}_2\text{O}]$ data and the 70.7 % Me_2SO value from data at lower temperature.

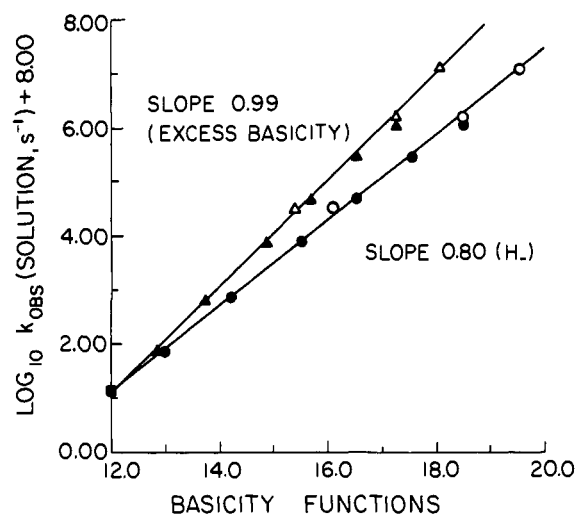


Figure 4. Dependence of in-solution rate constant for CF_3D exchange at 49.1 °C on basicity functions for the Me_2SO /water system. Symbols are defined in the Figure 3 caption; excess basicity + 12.0.

mol·L⁻¹ NaOH at 50 °C. Hydrolysis is still quite slow, but the initial rate,² 3×10^{-9} mol·L⁻¹·s⁻¹, is about 3000× faster than that expected for pure water (based on the value measured with 1.0 mol·L⁻¹ NaOH²). For this system, isotope exchange is still a factor of almost 600× faster than hydrolysis.

CF_3D Isotope Exchange. The effect of added Me_2SO on catalytic reactivity of the $\text{OH}^-/\text{H}_2\text{O}$ solution for CF_3D isotope exchange is shown in Figure 3 for 0.011 mol·L⁻¹ hydroxide ion at 49.1 °C. The $k_{\text{obsd}}(\text{soln})^2$ increases by a factor of 10^6 on changing from pure water to 70 mol % Me_2SO . The point at the latter composition was obtained by extrapolation of data at lower temperatures (1–30 °C), while the point for water was estimated from data at higher deuteroxide ion concentration and temperature (runs with CF_3H). Because reaction in solution is so rapid above about 70 mol % Me_2SO , no measurements were made beyond this point; suitably lower temperatures were not possible because of the relatively high freezing points of such solutions.

The correlation of rate constant with effective basicity of the solvent system is better shown in Figure 4, where $\log k_{\text{obsd}}$ is plotted against both the normal H_- function for the Me_2SO /water system with 0.011 mol·L⁻¹ hydroxide ion⁶ and the refined "excess basicity" function suggested by Cox and Stewart.⁷

The Arrhenius activation parameter functions given in Figure 5 were calculated¹² from rate constant data (CF_3D) obtained at

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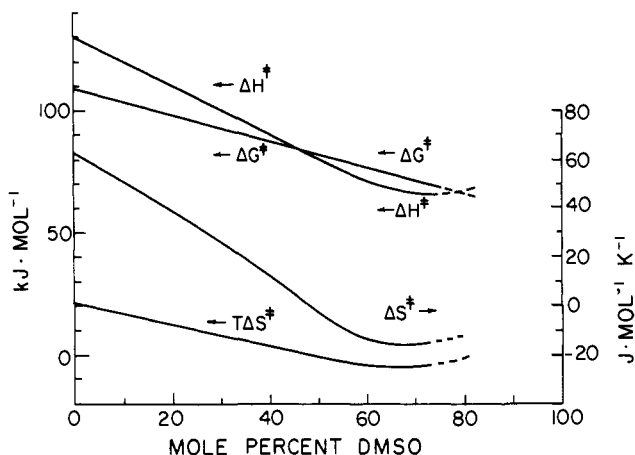


Figure 5. Dependence of activation parameters for CF₃D exchange at 49.1 °C on solvent composition.

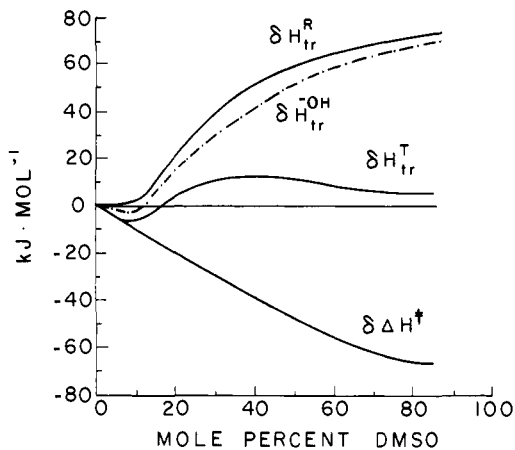
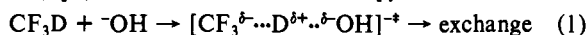


Figure 6. Enthalpy of transfer functions for ⁻OH-catalyzed exchange of CF₃D in the Me₂SO/water system at 50 °C.

two or three temperatures over a range of at least 19 °C at each of the seven solvent compositions. These plots were derived from smooth curves drawn through the E_a and $\log k_{\text{obsd}}$ vs. mol % Me₂SO data. The E_a points fell within ± 5 kJ of their curve. The value for water was measured with CF₃H at 0.94 mol·L⁻¹ NaOD.

Where sufficient data are available, it is possible to determine for a given reaction the effect of solvent change on the enthalpy, entropy, and free energy of the transition state.¹³ For the present reaction (eq 1), literature data for the enthalpy of transfer function



for hydroxide ion in Me₂SO/water,¹⁴ $\delta H_{\text{tr}}^{\text{OH}}$, were combined with $\delta H_{\text{tr}}^{\text{CF}_3\text{D}}$ values derived from the change in heat of solution of CF₃H with solvent composition to obtain $\delta H_{\text{tr}}^{\text{R}}$ for reactants.¹³ Differences between the CF₃H and CF₃D functions were assumed to be negligible. The function $\delta H_{\text{tr}}^{\text{T}}$, for the transition state, was then calculated via eq 2.¹³ These enthalpy functions are plotted

$$\delta H_{\text{tr}}^{\text{T}} = \delta H_{\text{tr}}^{\text{R}} + \delta \Delta H^{\ddagger} \quad (2)$$

in Figure 6. The corresponding free energy function $\delta G_{\text{tr}}^{\text{T}}$ was obtained in a similar manner, by using $\delta G_{\text{tr}}^{\text{OH}}$ literature data¹⁵ (interpolation/extrapolation) and $\delta G_{\text{tr}}^{\text{CF}_3\text{D}}$ values derived from the CF₃H solubility data according to ref 16. Finally the entropy function $\delta TS_{\text{tr}}^{\text{T}}$ was determined via eq 3.¹³ The δG , δH , and δTS transition-state functions representing CF₃D isotope exchange are

$$\delta G_{\text{tr}}^{\text{T}} = \delta H_{\text{tr}}^{\text{T}} - \delta TS_{\text{tr}}^{\text{T}} \quad (3)$$

given in Figure 7.

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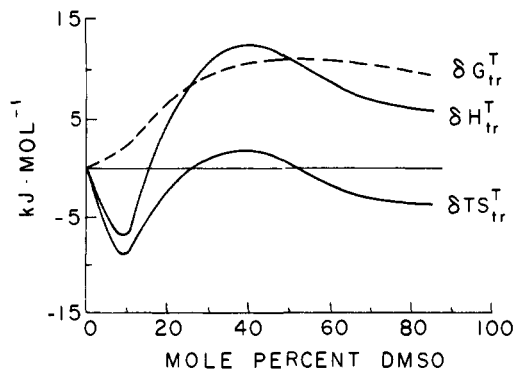


Figure 7. Enthalpy, entropy, and free energy of transfer functions for ⁻OH-catalyzed exchange of CF₃D in the Me₂SO/water system at 50 °C.

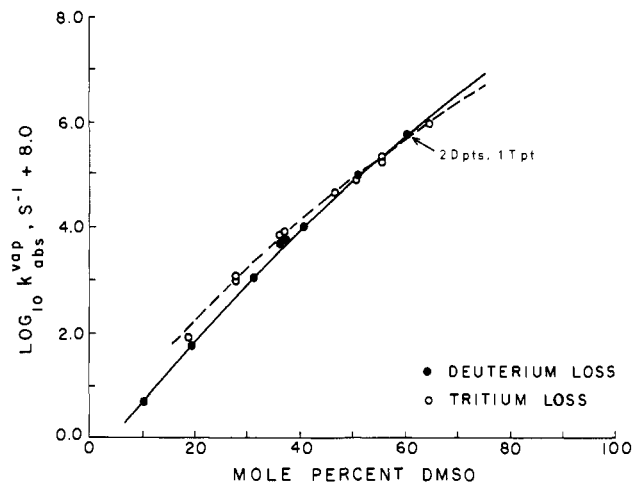


Figure 8. Dependence of the vapor-phase² rate constants for deuterium and tritium loss from fluoroform on solvent composition at 49.1 °C and 0.011 mol·L⁻¹ hydroxide ion.

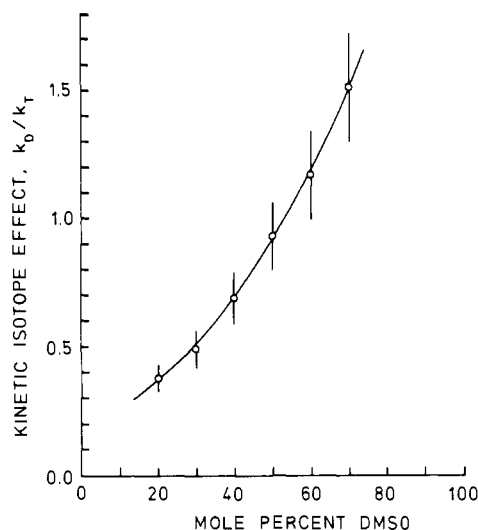


Figure 9. Dependence of the primary kinetic isotope effect for ⁻OH-catalyzed CF₃D/CF₃T exchange at 49.1 °C on solvent composition.

The primary kinetic isotope effect $k_{\text{D}}/k_{\text{T}}$ was determined by using data taken at 10 mol % Me₂SO intervals from smoothed plots of $\log k_{\text{D}}(\text{vap})$ and $\log k_{\text{T}}(\text{vap})$ ($k_{\text{obsd}}(\text{vap})$) defined in ref 2) for fluoroform exchange vs. solvent composition (Figure 8). Although $k_{\text{H}}/k_{\text{D}}$ could be calculated via the equation¹⁷ $k_{\text{H}}/k_{\text{D}} = (k_{\text{D}}/k_{\text{T}})^{2.344}$, the $k_{\text{D}}/k_{\text{T}}$ values are plotted as a function of solvent composition in Figure 9.

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Discussion

CF₃H Gas Solubility. The shapes of the solubility and heat of solution curves in Figures 1 and 2, respectively, are consistent with other physical property data (e.g., ref 18 and references therein) that demonstrate the strong interaction between Me₂SO and water molecules in these mixtures. The 1:2 Me₂SO/H₂O complex formation manifests itself in the minimum observed for the CF₃H heat of solution in the region 30–35 mol % Me₂SO.

For a given solvent composition the "ideal"¹⁸ CF₃H solubility at any temperature can be estimated from the amount of CF₃H that would dissolve independently in the two solvent components at that temperature. The calculated *difference* between a curve based on such values and the measured solubility as a function of solvent composition goes through a maximum, at e.g., 30 °C, near 35–40 mol % Me₂SO. The same behavior was seen for another inert gas, hydrogen.¹⁸ In effect the CF₃H is "salted out" of the mixed solvents, with the effect being maximized in the region of strongest Me₂SO/water association.

CF₃D, CF₃H(T) Isotope Exchange. (A) Acidity Function Correlations. The big increase in k_{obsd} for hydroxide ion catalyzed CF₃D exchange with water when Me₂SO is added as cosolvent is demonstrated in Figure 3. A more quantitative indication of the effect is given by the slope of 0.80 for the log k_{obsd} vs. H_- plot in Figure 4. This value compares with the range of smaller slopes, 0.23–0.36, seen for exchange of D₂ in the same solvent system.¹⁹ The detritiation of Me₂SO itself produced a slope of 0.94.²⁰ For detritiation of another haloform, chloroform, log k was plotted against $H_- + \log ([\text{H}_2\text{O}]/[\text{OH}^-])^5$; the slope of the resultant straight line was 0.98. Cox and Stewart have suggested⁷ that the "excess basicity" function $H_- - pK_w - \log [\text{OH}^-] + \log a_{\text{H}_2\text{O}}$ better represents the real change in solution basicity. This function is roughly parallel to, but offset from, that employed for the chloroform plot, so that the slopes of plots against either will be quite similar. For CF₃D exchange the plot against "excess basicity" (Figure 4) yields a slope of 0.99, in close agreement with the value above for the similar acid CCl₃H(T). Note that the H_- data were determined at 25 °C, while the kinetic data were obtained at various temperatures (e.g., 50 °C for CF₃D).

If one makes the standard assumption that the slope of such basicity function plots can be equated with Brønsted β values for degree of proton transfer (e.g., ref 21–23), then the transition state for both fluoroform and chloroform exchange should be quite product-like, $[\text{CF}_3^{\delta-} \cdots \text{D}^{\delta+} \cdots \text{OH}]^{\ddagger}$.

The slope of 0.8 for the H_- plot for CF₃D changes to 1.0 when the excess basicity function is used. For cases such as Me₂SO detritiation where the H_- slope is already close to 1.0, the slope of the excess basicity plot becomes greater than one.²⁴ The significance of β greater than unity for the Me₂SO exchange case has not been explained,²⁴ although it has been suggested²¹ that such values are possible for situations where the rate of the reverse reaction, i.e., reprotonation of the carbanion, is strongly dependent on change in the medium.

(B) Activation Parameters/Transfer Functions. The behavior of the activation parameters with change in solvent composition, shown in Figure 5, is similar to that seen for D₂ exchange in the same system.²⁵ However, the decline in ΔG^\ddagger is much greater for CF₃D exchange. In both cases the decreases in ΔH^\ddagger and $T\Delta S^\ddagger$ are complementary.

The results for chloroform detritiation are also similar to those for CF₃D over the solvent composition range available for comparison (0–24 mol % Me₂SO);⁵ however, E_a for chloroform is

always about 25 kJ·mol⁻¹ lower than E_a for fluoroform. The deactivating effect of the fluorine atom relative to the chlorine atom on hydrocarbon acidity²⁶ is clearly demonstrated in this case. Chloroform is estimated² to be a factor of $\sim 3 \times 10^6$ more reactive than fluoroform for ⁻OH-catalyzed proton exchange in water at 0 °C. In 23.6 mol % Me₂SO at 25 °C the factor is almost the same, $\sim 2 \times 10^6$, on the basis of data in Table III of ref 5 and on the E_a and 49 °C rate constant interpolated for CF₃D at this solvent composition.

A better indication of the general structure of the CF₃D-exchange transition state can be obtained from interpretation of the transfer functions shown in Figures 6 and 7. The distinct minimum seen near 10 mol % Me₂SO for the $\delta H_{\text{tr}}^\ddagger$ and $\delta TS_{\text{tr}}^\ddagger$ functions is a direct result of the dip measured for the $\delta H_{\text{tr}}^{\text{-OH}}$ function in this region;¹⁴ the hydroxide ion undergoes a maximum in solvation at this point.¹⁴ The magnitude of the $\delta H_{\text{tr}}^\ddagger$ function is close to that for $\delta H_{\text{tr}}^{\text{CF}_3\text{D}}$ (difference between two top curves in Figure 6), which suggests that solvation of the transition state is very similar to that of CF₃D, on an enthalpy basis. Thus the proton must be very close to the hydroxide ion, and the negative charge on the CF₃⁻ carbanion is dispersed onto the strongly electronegative fluorine atoms.²⁷ In fact, a comparison of $\delta H_{\text{tr}}^\ddagger$ with enthalpy of transfer data for halide ions²⁸ indicates solvation comparable to that for Cl⁻ up to 40 mol % Me₂SO but closer to that for Br⁻ above 50 mol %, again on an enthalpy basis.

As in the case of chloroform exchange,²⁹ over the region 0–10 mol % Me₂SO it appears to be increased solvation of the transition state that is responsible for the rate acceleration with added Me₂SO. Above 10 mol %, however, progressive desolvation of the hydroxide ion is the major contributor. For the D₂-exchange system, a localized charge was largely retained near oxygen in the transition state; there the $\delta H_{\text{tr}}^\ddagger$ function was only somewhat below the $\delta H_{\text{tr}}^{\text{-OH}}$ function.²⁵

In Figure 7 the complementary behavior of the $\delta H_{\text{tr}}^\ddagger$ and $\delta TS_{\text{tr}}^\ddagger$ functions is reflected in the almost constant value of 10 ± 1 kJ·mol⁻¹ seen for $\delta G_{\text{tr}}^\ddagger$ above ca. 30 mol % Me₂SO. By comparison, $\delta G_{\text{tr}}^{\text{-OH}}$ at 50 mol % is ca. 45 kJ·mol⁻¹ and rising.

(C) Primary Kinetic Isotope Effect (KIE). The rather unusual dependence of the KIE on solvent composition (sharp rise from inverse to normal with added Me₂SO, Figure 9) raises an obvious question—is the effect real or does it arise from some error(s) in the data? Consistent $k_{\text{p}}(\text{vap})$ and $k_{\text{T}}(\text{vap})$ rate constant data (Figure 8) were obtained with different batches of reagents over a period of more than eight months. Therefore it is felt that the KIE results are valid. The indicated experimental error in the plotted points was derived from an assigned error of $\pm 10\%$ in the k values taken from the smooth curves in Figure 8.

What then is a reasonable explanation for the KIE results? When proton transfer to base is rate limiting, a "normal" kinetic isotope effect would be expected, with its magnitude dependent on the position of the proton in the transition state. The range of possible values, on changing from reactant-like to product-like transition state, is $1.0 \rightarrow (k_{\text{H}}/k_{\text{D}})_{\text{sym}} \rightarrow K_{\text{H}}/K_{\text{D}}$,^{30,31} the latter being the equilibrium isotope effect. In the present system the slopes of the basicity function plots and the behavior of the enthalpy of transfer functions (see above) strongly suggest that the proton is almost fully transferred over most of the solvent composition range. Thus it seems plausible that in water-rich solutions, where the hydroxide ion basicity is weakest (relative to in Me₂SO-rich solutions), the observed KIE is equal to $K_{\text{D}}/K_{\text{T}}$ and that therefore the latter must be inverse. This is possible; for example, the corresponding equilibria involving D and T distribution between

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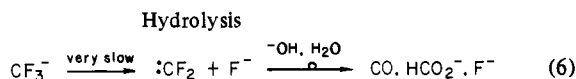
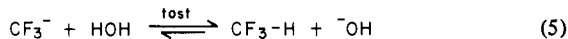
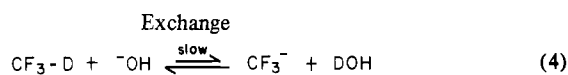
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Scheme I



molecular hydrogen and water are inverse, with $K_D/K_T = 0.54$ at 25 °C.³²

As the Me_2SO content of the solvent is increased, the hydroxide ion basicity also increases (cf. the H_- and excess basicity functions^{6,7}), and the proton should move progressively away from ^-OH in the transition state.³³ This change would produce the observed smooth increase in KIE from the inverse value seen for water-rich solutions (Figure 9).

A problem with the above argument is that there is, for example, no corresponding decrease in the slopes of the basicity function plots as Me_2SO is added to the solvent (Figure 4). The reason may be that there is a difference in sensitivity of the two probes to changes in transition-state structure.³⁴ A similar situation arose for ionization of ethyl nitroacetate with a series of bases; while the $\log k$ vs. pK_a plot was essentially linear, the k_H/k_D ratio passed through a distinct maximum.³⁶ In the present case it would be valuable to have KIE and basicity function dependence data to beyond 90 mol % Me_2SO . An alternate means of sample recovery or gas/solution contact would be necessary because the in-solution reaction becomes so fast.

Margolin and Long reported⁵ a value of $k_H/k_D = 1.42$ for hydroxide-catalyzed exchange of chloroform with water at 25 °C. However, the experimental method involved relative rates of tritium uptake from the solvent by CCl_3H and CCl_3D ; there is

(32) From $K_D = 3.806$: Rolston, J. H.; den Hartog, J.; Butler, J. P. *J. Phys. Chem.* **1976**, *80*, 1064–1067. $K_T = 6.996$: Butler, J. P., private communication.

(33) Bordwell, F. G.; Boyle, W. J., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 3907–3911.

(34) It has been suggested that (a) from studies involving deprotonation of several types of carbon acids by a series of bases, "... the absolute size of β for carbon acids can provide, therefore, little or no information concerning the nature of the transition state of the deprotonation",³³ (b) from studies of several base-catalyzed proton-transfer reactions in different types of solvent mixtures, "... the use of solvent variation to alter the total free-energy change occurring during proton-transfer reactions does not lead to normal Brønsted β values..."³⁵

(35) Cox, B. G.; Gibson, A. *J. Chem. Soc., Chem. Commun.* **1974**, 638–639.

(36) More O'Ferrall, R. A. In "Proton Transfer Reactions"; Caldin, E., Gold, V., Ed.; Chapman and Hall: London 1976; Chapter 8, pp 230–231.

some concern about the validity of such an approach,³⁷ and values nearer to 1.0 might always be expected under such conditions.³⁷

(D) Fluoroform Exchange/Hydrolysis Mechanism. Both hydrolysis and hydrogen isotope exchange of fluoroform, catalyzed by hydroxide ion, should proceed via the same initial stage, i.e., proton transfer, as indicated in Scheme I. For hydrolysis of most trihalomethanes, the faster step is considered to be reversible formation of the trihalomethyl anion, with halide ion loss from the latter being rate limiting.³⁸ While the fluorine atom is the best (relative to the other halogens) for stabilizing $:CX_2$, it is the least effective in stabilizing the CX_3^- ion.³⁸ The latter observation is counter to that predicted from a simple inductive effect argument²⁶ (i.e., CF_3H is much less, not more, reactive than CCl_3H for hydrolysis and exchange). Hine et al.²⁶ considered qualitatively several possible reasons for this reversal in ability of halogen atoms to activate haloforms for carbanion formation; factors included were d orbital resonance, steric strain among the three halogen atoms in the tetrahedral haloform, and polarizability. They favored a combination of polarizability and the inductive effect. In addition, destabilization of the CF_3^- ion arising from repulsion between the free-electron pair on carbon and the electron pairs in the p orbitals of the fluorine atoms may be involved³⁹ (the " α effect").

The structure of the transition state for the slow proton-exchange step, eq 4, is quite product-like, i.e., $[CF_3^{\delta-} \cdots D^{\delta+} \cdots OH]^\ddagger$, on the basis of our results as discussed earlier. The final products suggested for the hydrolysis step, eq 6, are analogous with those observed for the more rapid chloroform hydrolysis reaction.⁴⁰

Acknowledgment. We wish to thank Mr. M. F. Powell and Drs. R. V. Osborne and H. C. Birnboim for advice on analysis of tritium in gases and Dr. P. Unrau for access to the Beckman scintillation counter. Discussions on some of the data interpretation with Drs. E. Buncl, J. H. Rolston, D. J. McLennan, and J. Lessard, and especially Mr. Powell, are gratefully acknowledged. Comments on the manuscript by Dr. Rolston and the two reviewers were much appreciated.

Supplementary Material Available: A table of CF_3H solubilities as a function of solvent composition and temperature and the figure showing CF_3H solubility dependence on CF_3H pressure at 30 °C, 79.4 mol % Me_2SO (2 pages). Ordering information is given on any current masthead page.

(37) Powell, M. F.; Kresge, A. J., Chemistry Department, University of Toronto, private communication.

(38) Hine, J. "Physical Organic Chemistry", 2nd ed.; McGraw-Hill, New York, 1962; pp 484–488.

(39) Edwards, J. O.; Pearson, R. G. *J. Am. Chem. Soc.* **1962**, *84*, 16–24. Faid, R.; McMahan, T. B. *Can. J. Chem.* **1980**, *58*, 2307–2311.

(40) Hine, J. *J. Am. Chem. Soc.* **1950**, *72*, 2438–2445.