transfer involving one or more molecules. This step should show a small, normal solvent isotope effect, similar to those observed in proton transfers in addition of water to aldehydes and ketones[20] and in decomposition of carbamates. The last step, decomposition of the zwitterionic intermediate, should have an early transition state and may show a small normal solvent isotope effect.

Thus, we conclude that the dehydration of the bicarbonate ion occurs via a stepwise mechanism involving a zwitterionic intermediate. Whether formation of the zwitterionic intermediate occurs by way of carbonic acid or directly by reaction of hydronium ion with bicarbonate cannot be determined from the present data. One-step mechanisms and two-step mechanisms involving a preequilibrium proton transfer are not consistent with these data.

(18) Schowen, K. B.; Schowen, R. L. *Methods Enzymol.* **1982**, *87*, 551.
(19) Bell, R. P.; Critchlow, J. E. *Proc. R. Soc. London, Ser. A* **1971**, *325A*, 35. Funderbunk, L. H.; Aldwin, L.; Jencks, W. P. *J. Am. Chem. Soc.* **1978**, *100*, 5444.
(20) Ewing, S. P.; Lockshon, D.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 3072.

Gas-Phase Hydrogen–Deuterium Exchange Reactions of Anions: Kinetics and Detailed Mechanism

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Abstract: Rate coefficients and branching ratios for anionic hydrogen–deuterium exchange reactions between isotopically labeled hydroxide, amide, hydrogen sulfide, and methoxide ions and their corresponding neutral compounds have been measured in the gas phase by using the selected ion flow tube (SIFT) technique. The kinetic data for the methoxide–methanol systems lead to a determination of the relative base strength of CD_3O^- and CH_3O^-. The reaction efficiencies and branching ratios of hydroxide–water, amide–ammonia, and amide–water systems are discussed in terms of the mechanism by which exchange occurs; the multiply labeled systems reveal that more proton transfers occur than one might expect upon initial inspection of the data. The product distributions are discussed in terms of relative ion–molecule complex lifetimes and dissociation of the complex in competition with scrambling. Efficient H/D exchange was also observed to occur between compounds containing second-row elements and the implications of this are discussed.

The study of multiple proton transfer within an ion–dipole complex has been demonstrated by a number of workers as useful in examining potential energy surfaces.[2–8] For example, in a recent study hydrogen/deuterium (H/D) scrambling was observed to occur in the initial encounter complex of hydroxide with a series of substituted propenes, even in the cases where direct proton transfer is exothermic.[8] The considerable amount of exchange observed in those systems led us to speculate about the extent of multiple proton transfer occurring in similar, but simpler systems (i.e., those containing a smaller number of degrees of freedom). In an earlier study, we reported H/D exchange in systems in which the reactant ion contains only one exchangeable proton or deuteron, reactions such as DO^- with NH_3 and HO^- with C_6D_6.[5] Similar studies on H/D scrambling in positive ion reactions have been carried out[3,4,6] and analogous conclusions have been reached

for both positive and negative ion systems.

In the study reported here we have taken advantage of several unique features of the selected ion flow tube (SIFT) technique to extend these investigations in several new directions. First we have examined isotope effects in reactions of CH_3O^- and CD_3O^- with CH_3OH, CH_3OD, CD_3OH, and CD_3OD. Then, using the appropriate double label, we have examined in detail the extent of exchange in the reactions of HO^- with H_2O, H_2N^- with NH_3, and H_2N^- with H_2O. Finally, we have examined rates of H/D exchange for an ion containing a second-row element, namely HS^-. Taken together, these studies shed new light on gas-phase reactions in which protons are transferred to and from heteroatoms and suggest numerous other studies which bear on one of the most fundamental of all chemical reactions.

Experimental Section

These studies were performed in Boulder, using primarily a SIFT apparatus in which the reactant ion is formed in a low pressure ion source and is mass selected and injected into the flow tube.[5,9] The reactant ions were generated by direct electron impact on the appropriate source gas: H_2N^- from NH_3, D_2N^- from ND_3, $D^{18}O^-$ from $D_2^{18}O$, DO^- from D_2O, CH_3O^- from CH_3OH, and CD_3O^- from CD_3OD. DS^- was produced in a bimolecular reaction in the flow tube by allowing injected DO^- to react with CS_2 (eq 1).[10] Typical helium pressures and flow rates were 0.3 to

(1) (a) Harvard University. (b) University of Colorado.
(2) Squires, R. R.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1981**, *103*, 4256–4258.
(3) Ausloos, P.; Lias, S. G. *J. Am. Chem. Soc.* **1981**, *103*, 3641–3647.
(4) Hunter, E. P.; Lias, S. G. *J. Phys. Chem.* **1982**, *86*, 2769–2775.
(5) Grabowski, J. J.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1983**, *105*, 2565–2571.
(6) Lias, S. G. *J. Phys. Chem.* **1984**, *88*, 4401–4407.
(7) Adams, N. G.; Smith, D.; Henchman, M. J. *Int. J. Mass Spectrom. Ion Phys.* **1982**, *42*, 11–23.
(8) Squires, R. R.; Bierbaum, V. M.; Grabowski, J. J.; DePuy, C. H. *J. Am. Chem. Soc.* **1983**, *105*, 5185–5192.

(9) (a) Adams, N. G.; Smith, D. *Int. J. Mass Spectrom. Ion Phys.* **1976**, *21*, 349–359. (b) Smith, D.; Adams, N. G. In "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 1, pp 1–44.

Table I. Branching Ratios, Rate Coefficients, and Reaction Enthalpies at 300 ± 2 K

reaction[a]	k_{obsd}[b]	eff[c]	ΔH_{rxn}[d]
$H_2N^- + ND_3 \rightarrow$ 44% $D_2N^- + H_2ND$	$5.2\ (\pm 0.4) \times 10^{-10}$	0.24	+0.8
$\rightarrow$ 56% $DHN^- + D_2NH$			+0.4
$D_2N^- + NH_3 \rightarrow$ 73% $H_2N^- + D_2NH$	$9.0\ (\pm 0.8) \times 10^{-10}$	0.41	−0.8
$\rightarrow$ 27% $DHN^- + H_2ND$			−0.4
$H_2N^- + D_2O \rightarrow$ 83% $DO^- + H_2ND$	$2.6\ (\pm 0.2) \times 10^{-9}$	1.1	−13.3
$\rightarrow$ 17% $HO^- + D_2NH$			−13.8
$D^{18}O^- + H_2O \rightarrow$ 60% $HO^- + D^{18}OH$	$1.7\ (\pm 0.1) \times 10^{-9}$	0.76	−0.3
$\rightarrow$ 30% $H^{18}O^- + HOD$			−0.3
$\rightarrow$ 10% $DO^- + H_2{}^{18}O$			0.0
$DO^- + H_2S \rightarrow HS^- + DOH$	fast		−40.5
$CH_3O^- + CD_3OD \rightarrow CD_3O^- + CH_3OD$	$4.5\ (\pm 0.2) \times 10^{-10}$	0.24	+0.5
$CD_3O^- + CH_3OD \rightarrow CH_3O^- + CD_3OD$	$1.0\ (\pm 0.1) \times 10^{-9}$	0.55	−0.5
$CD_3O^- + CH_3OH \rightarrow CH_3O^- + CD_3OH$	$1.1\ (\pm 0.1) \times 10^{-9}$	0.60	−0.5
$CH_3O^- + CD_3OH \rightarrow CD_3O^- + CH_3OH$	$5.3\ (\pm 0.3) \times 10^{-10}$[e]	0.28	+0.5
$DS^- + H_2S \rightarrow HS^- + DSH$	$9.0\ (\pm 0.5) \times 10^{-10}$	0.62	−0.3
$DS^- + (CH_3)_3CSH \rightarrow$ 96% $HS^- + (CH_3)_3CSD$	$7.2\ (\pm 0.9) \times 10^{-10}$	0.35	−0.2[f]
$\rightarrow$ 4% $(CH_3)_3CS^- + HSD$			+0.9[g]
$DS^- + CH_3SH \rightarrow HS^- + CH_3SD$	$1.9\ (\pm 0.1) \times 10^{-10}$	0.11	−0.2[f]

[a] With the exception of the H_2N^-/D_2O reaction (two experiments) and the $D^{18}O^- + H_2O$ reaction (six experiments) the branching ratios were determined from a single experiment; the absolute errors in the branching ratios are estimated to be less than 15% of the percentage reported. [b] Units are cm³ particle⁻¹ s⁻¹. The observed rate coefficient is the average of 5 or 6 independent measurements during which concentrations were varied to ensure that the kinetics are bimolecular; the indicated error bars represent one standard deviation of the experimental value. The absolute errors are estimated to be ±20%. [c] k_{obsd}/k_{ADO}, k_{ADO} calculated according to ref 12. [d] Reaction enthalpy, units are kcal mol⁻¹. Unless otherwise stated, reaction enthalpies were calculated from the heats of formation of neutral species obtained from ref 13 and electron affinities from ref 14. The electron affinities of H_2N, D_2N, and HDN were assumed to be equal. The heat of formation of the partially deuterated ammonias was assumed to be that of the weighted average of ND_3 and NH_3. HSD was treated in a similar fashion. The heat of formation of H_2O was obtained from ref 15. [e] Compare to $k = 9.5 \times 10^{-10}$ as obtained by pulsed ion cyclotron resonance spectroscopy in ref 16. [f] Estimated by assuming that the difference in heats of formation between RSD and RSH could be approximated as that between HSD and HSH. [g] Calculated in part by using the gas-phase acidities of hydrogen sulfide and 2-methane-2-propanethiol obtained from ref 17.

0.6 torr and 120 to 200 STP cm³ s⁻¹, respectively; the temperature was 300 ± 2 K.

$$DO^- + CS_2 \rightarrow DS^- + OCS + 45\ \text{kcal mol}^{-1} \tag{1}$$
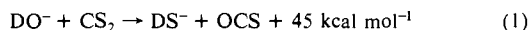
The reagent gas purities were as follows: ammonia (Air Products, 99.997%), ammonia-d_3 (Merck, 99%), water-d_2 (Merck, 99.7%), hydrogen sulfide (Matheson, 99.6%), methanol-d_4 (Aldrich, 99.5%), methanol-O-d (Stohler, 99%), methanol-d_3 (99%, prepared by exchanging CD_3OD with H_2O (1:1 mixture) and distillation; repeated five consecutive times), tert-butyl mercaptan (Aldrich, 99%), and methyl mercaptan (Matheson, 99.5%). The neutral reagent flow rates were determined by monitoring the pressure increase with time in a calibrated volume. Rate coefficients were measured by following reactant ion counts as a function of reaction distance which is directly proportional to time.

Results

The branching ratios reported are the initial product distributions (those obtained by extrapolation to zero neutral flow, determined at a fixed reaction time) as determined by the standard procedure.[11] To obtain a branching ratio for reactions involving amide or labeled hydroxide, a correction for the small amount of contaminating initial HO^- was always performed. The rate coefficients are the average of at least five independent measurements; each measurement of a rate coefficient was made with different concentrations of the various reagents to ensure that the exchange reactions were pseudo-first-order. The standard deviation of a set of rate coefficient measurements was typically ±10% or better, while we estimate the absolute accuracy of the rate coefficients to be ±20%. We estimate the errors in the branching ratios to be less than 15% of the percentages reported.

The results for the exchange reactions are collected in Table I. The first column gives the observed product distribution, the second column is the average of the observed two-body rate coefficients, the third column is the observed reaction efficiency
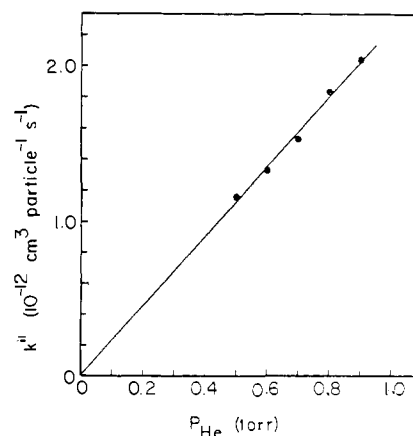
Figure 1. A plot of the apparent bimolecular rate coefficient vs. helium pressure for the three-body reaction of hydroxide with water in helium.

(k_{obsd}/k_{ADO}),[12] while the last column is the best estimate of the reaction enthalpy. Since the efficiencies of the isotope exchange reactions are high, only low flow rates of the neutral reactants were employed, and association reactions were not normally ob-

(10) DePuy, C. H.; Grabowski, J. J.; Bierbaum, V. M. *J. Phys. Chem.* **1984**, *88*, 1389–1393.

(11) Adams, N. G.; Smith, D. *J. Phys. B: Atom. Mol. Phys.* **1976**, *9*, 1439–1451.

(12) Su, T.; Bowers, M. T. *Int. J. Mass Spectrom. Ion Phys.* **1973**, *12*, 347–356.

(13) Chase, M. W., Jr.; Curnutt, J. L.; Downey, J. R.; McDonald, R. A.; Syverud, A. N.; Valenzuela, E. A. *J. Phys. Chem. Ref. Data* **1982**, *11*, 695–940.

(14) Drzaic, P. S.; Marks, J.; Brauman, J. I. In "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1984; Vol. 3, pp 167–211.
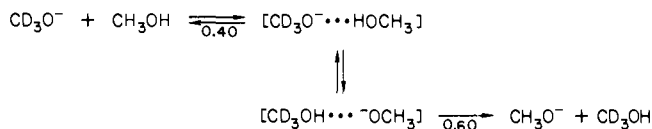
(15) Benson, S. W. "Thermochemical Kinetics"; John Wiley and Sons: New York, 1976; p 292.

(16) Farneth, W. E.; Brauman, J. I. *J. Am. Chem. Soc.* **1976**, *98*, 7891–7898.

(17) Bartmess, J. E.; McIver, R. T., Jr. In "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 2, pp 87–121.

Scheme I

$$CD_3O^- + CH_3OH \underset{0.40}{\rightleftharpoons} [CD_3O^-\cdots HOCH_3]$$

$$\updownarrow$$

$$[CD_3OH\cdots {}^-OCH_3] \xrightarrow{0.60} CH_3O^- + CD_3OH$$

served. To study the slow three-body clustering reaction of HO⁻ with H_2O, the flow rates of H_2O were increased by 2 to 3 orders of magnitude. The conventional flowing afterglow (FA) in Boulder was used for these studies.[18] Figure 1 gives a plot of the apparent two-body rate coefficient as a function of helium pressure. A linear least-squares regression analysis 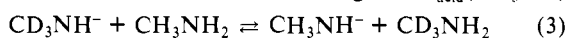of the five data points and the origin gives a correlation coefficient of 0.999 and the three-body rate coefficient of 7.0×10^{-29} cm⁶ particle⁻² s⁻¹.

Discussion

Methoxide/Methanol. We begin by considering the isotope-labeled reactions of methoxide ion with methanol (eq 2). All four of these reactions are reasonably fast as indicated by the data in Table I. From these kinetic data the equilibrium constants and $\Delta G°$ values for the following equilibria can be calculate . For

$$CD_3O^- + CH_3OD \rightleftharpoons CH_3O^- + CD_3OD \qquad (2a)$$

$$CD_3O^- + CH_3OH \rightleftharpoons CH_3O^- + CD_3OH \qquad (2b)$$
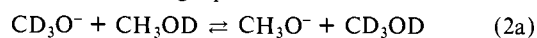
reaction 2a the equilibrium constant calculated from the observed forward and reverse rate coefficients is 2.3 which yields $\Delta G°_{300}$(eq 2a) = −0.49 kcal mol⁻¹. Similarly, for reaction 2b, the derived equilibrium constant is 2.1 and $\Delta G°_{300}$(eq 2b) = −0.44 kcal mol⁻¹. Thus, we conclude that CD_3O^- is a stronger base than CH_3O^- by 0.47 ± 0.06 kcal mol⁻¹ where the error limits include systematic errors. This result is in excellent agreement with that obtained by pulsed ion cyclotron resonance spectroscopy for the free energy of proton transfer for reaction 2b, in which it was determined[19] that $\Delta G°$(eq 2b) = −0.50 ± 0.10 kcal mol⁻¹. The observation that CD_3O^- is a stronger base than CH_3O^- is also in agreement with the generalization that the deuterated species would rather be uncharged, i.e., deuterated methoxide is less stable than methoxide and hence a stronger base. For example, in the liquid phase, pK_D − pK_H at 298 K for DCOOH and HCOOH is 0.030 ± 0.004 and for CD_3COOH and CH_3COOH it is 0.014 ± 0.002 (i.e., the protio compounds are stronger acids).[20] Likewise, in the gas phase, CD_3NH^- has been demonstrated to be a stronger base than CH_3NH^- by $\Delta G°$(eq 3) = −0.37 ± 0.08 kcal mol⁻¹ and CD_3S^- has been observed to be a stronger base than CH_3S^- by $\Delta G°$(eq 4) = −0.30 ± 0.08 kcal mol⁻¹.[19] Assuming[21] $\Delta H°_{acid}(CH_3OH)$

$$CD_3NH^- + CH_3NH_2 \rightleftharpoons CH_3NH^- + CD_3NH_2 \qquad (3)$$

$$CD_3S^- + CH_3SH \rightleftharpoons CH_3S^- + CD_3SH \qquad (4)$$

= 381.4 kcal mol⁻¹ and ΔH(eq 2a) $\simeq$ ΔG(eq 2a), then $\Delta H°_{acid}(CD_3OH)$ = 381.9 kcal mol⁻¹. Furthermore, assuming no difference in the O–D bond strength in CH_3OD vs. CD_3OD or the O–H bond strength in CH_3OH vs. CD_3OH, one concludes that $CH_3O\cdot$ has a higher electron affinity than $CD_3O\cdot$ by 0.47 kcal mol⁻¹ (0.020 eV). This same difference in electron affinities has been measured experimentally by negative ion photodetachment spectroscopy (ΔEA = 0.018 ± 0.006 eV).[22]

The mechanism that we envision for exchange is simple since there is only one exchangeable proton. The collision of methoxide with 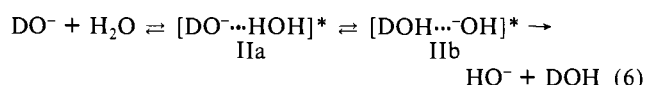methanol leads to a fairly long-lived complex, bound by ion–dipole and ion–induced dipole forces of ~22 kcal mol⁻¹.[23] While the equilibrium geometry is probably that of an asym-

metrical hydrogen-bonded species, the energy necessary to attain the symmetrical species is undoubtedly a small fraction of the available energy of the system. Thus as is shown in Scheme I, the collision of methoxide-d_3 with methanol leads to what can be considered to be two ion–molecule complexes in equilibrium, which will then fragment both in the exothermic direction producing CH_3O^-, and with a slower relative rate in the thermoneutral direction (back to reactants). The relative rates for the two dissociation channels shown in Scheme I are those derived from the observed two-body rate coefficient and the calculated collision-rate coefficient (Table I). The ratio of the product distribution indicates that the exothermic channel predominates over the thermoneutral channel by a factor of 1.5 to 1 when exothermic by 0.5 kcal mol⁻¹. Likewise, the reaction of CH_3O^- and CD_3OH indicates that the endothermic channel is disfavored with respect to the thermoneutral channel by a factor of 28/72 or 1 to 2.6 when endothermic by 0.5 kcal mol⁻¹. An analogous mechanism is discussed in more detail in the next section.

Hydroxide/Water. We next consider the reaction of hydroxide ion with water (eq 5). In common with all gas-phase ion–molecule

$$HO^- + H_2O \underset{k_b}{\overset{k_c}{\rightleftharpoons}} [HO^-\cdot H_2O]^* \xrightarrow{\beta k_s[He]} HO^-\cdot H_2O \qquad (5)$$
$$\text{I}$$
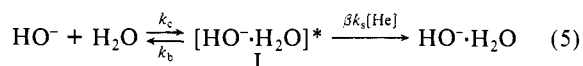
reactions, the ion and neutral will be attracted to one another by ion–dipole and ion–induced dipole forces, until they enter an ion–dipole complex, I. Unless the complex has a sufficiently long lifetime to allow it to lose energy by one or more collisions with the helium buffer gas, it will dissociate. However, within the complex, proton transfers between the two oxygens can occur. Depending upon the lifetime of the complex and the rates of proton transfer, one may see complete scrambling of the hydrogens at one extreme, or at the other extreme proton transfer may be slow compared to back dissociation. In our earlier study,[4] we allowed DO⁻ to react with H_2O; HO⁻ was produced with a rate coefficient of $k = 1.8 \times 10^{-9}$ cm³ particle⁻¹ s⁻¹. The encounter rate of DO⁻ and H_2O can be calculated by using the average dipole orientation theory of Su and Bowers.[12] Thus the observed reaction efficiency of eq 6 is k_{obsd}/k_{ADO} = 0.74. From this result we conclude that

$$DO^- + H_2O \rightleftharpoons [DO^-\cdots HOH]^* \rightleftharpoons [DOH\cdots {}^-OH]^* \rightarrow$$
$$\text{IIa} \qquad \qquad \text{IIb}$$
$$HO^- + DOH \qquad (6)$$

proton transfer is at least as fast as dissociation of the complex. However, an observed reaction efficiency of greater than 50% (the value expected if complex II would dissociate to products and reactants with equal ease) does not distinguish among other possibilities (vide infra).

In the first place, the reaction as written is slightly exothermic (ΔH_{rxn}(eq 6) = −0.3 kcal mol⁻¹) since DO⁻ is a stronger base than HO⁻. Thus one might expect the complex to dissociate more often in the exothermic forward direction than in the thermoneutral reverse direction. Superimposed upon this effect could be scrambling among the H's and D which would favor the forward direction by a factor of 2 to 1, to give an efficiency of 0.67, which is smaller than the value found. For these reasons, we decided to look at this reaction in greater detail.

The most straightforward experiment was to obtain an estimate of the lifetime of the complex. Kebarle has determined the dissociation energy of $HO^-\cdot H_2O$ to be 25 kcal mol⁻¹, so it is a quite stable species.[24] However, its formation from HO⁻ and H_2O in the flowing afterglow is a slow three-body process. The apparent two-body rate coefficients for this clustering reaction are given at five helium pressures in Figure 1. From the slope of this line, one can calculate the three-body rate coefficient for this process ($k^{III} = 7.0 \times 10^{-29}$ cm⁶ particle⁻² s⁻¹).

From the model of the reaction in eq 5, in the [He] → 0 limit:

$$k^{III} = k_c \beta k_s / k_b \qquad (7)$$

where k_c can be estimated by ADO theory to be 2.4×10^{-9} cm³

(18) Stewart, J. H.; Shapiro, R. H.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* 1977, *99*, 7650–7653.

(19) DeFrees, D. J.; Bartmess, J. E.; Kim, J. K.; McIver, R. T., Jr.; Hehre, W. J. *J. Am. Chem. Soc.* 1977, *99*, 6451–6452.

(20) Melander, L.; Saunders, W. H., Jr. In "Reaction Rates of Isotopic Molecules"; John Wiley & Sons: New York, 1980; pp 198–199.
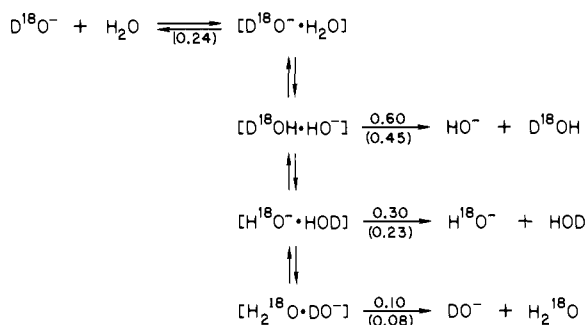
(21) Moylan, C. R.; Brauman, J. I. *J. Phys. Chem.* 1984, *88*, 3175–3176.

(22) Engelking, P. C.; Ellison, G. B.; Lineberger, W. C. *J. Chem. Phys.* 1978, *69*, 1826–1832.

(23) Caldwell, G.; Rozeboom, M. D.; Kiplinger, J. P.; Bartmess, J. E. *J. Am. Chem. Soc.* 1984, *106*, 4660–4667.

(24) Kebarle, P. *Annu. Rev. Phys. Chem.* 1977, *28*, 445–476.

Scheme II

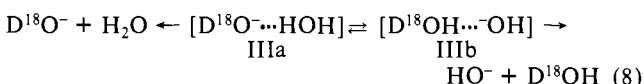$$D^{18}O^- + H_2O \underset{(0.24)}{\rightleftharpoons} [D^{18}O^- \cdot H_2O]$$

$$\updownarrow$$

$$[D^{18}OH \cdot HO^-] \xrightarrow[(0.45)]{0.60} HO^- + D^{18}OH$$

$$\updownarrow$$

$$[H^{18}O^- \cdot HOD] \xrightarrow[(0.23)]{0.30} H^{18}O^- + HOD$$

$$\updownarrow$$

$$[H_2^{18}O \cdot DO^-] \xrightarrow[(0.08)]{0.10} DO^- + H_2^{18}O$$

particle^{-1} s^{-1}. The stabilization rate coefficient for helium as third body, k_s, is calculated by ADO theory to be 5.6 × 10^{-10} cm^3 particle^{-1} s^{-1} and β, the stabilization efficiency factor, is estimated to be 14%.[25] In eq 7 the lifetime of the complex to dissociation is $\tau_b = 1/k_b$. Our results indicate that the hydroxide–water complex formed by association at 300 K lives on the average ~400 ps (~4 × 10^{-10} s) before dissociation.

Our next step was to determine more precisely how many proton transfers occur during this time period. To do this, we prepared D^{18}O$^-$ by electron impact on D$_2^{18}$O, injected it into our flow tube, and allowed it to react with H$_2$O. We examined the product ions as a function of H$_2$O concentration and extrapolated to zero H$_2$O flow, thus obtaining the products from the primary ion–neutral encounter. The results are summarized in Scheme II.
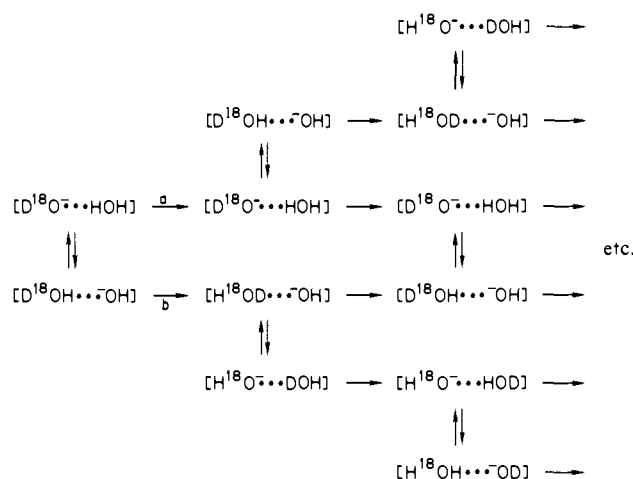
From these equations, it is clear that the double label can be used to reveal the extent of proton scrambling. Two sets of reaction efficiencies are included in these equations. We inject D^{18}O$^-$ (m/z 20) and measure the appearance of HO$^-$ (m/z 17), H^{18}O$^-$ (m/z 19), and DO$^-$ (m/z 18). The relative efficiencies for the appearance of these ions (0.60, 0.30, and 0.10, respectively) are given in Table I and above the arrows in Scheme II. However, the overall reaction efficiency is only 0.76 as determined by monitoring the disappearance of D^{18}O$^-$ (in excellent agreement with the value of 0.74 found earlier, vide supra); 24% of the complexes dissociate to reactants. More meaningful branching ratios which take this into consideration are given in parentheses below the arrows.

In a completely random reaction in which equilibration occurred · before dissociation, and ignoring any energy effects, the resultant branching ratios would be 0.17 for D^{18}O$^-$ (found 0.24), 0.33 for HO$^-$ (found 0.45), 0.33 for H^{18}O$^-$ (found 0.23), and 0.17 for DO$^-$ (found 0.08). It is important to note that HO$^-$ and H^{18}O$^-$ are not observed to be produced in equal intensities. In addition, there is indeed an energy effect, the protio-hydroxide channels are 0.3 kcal mol^{-1} exothermic with respect to reactants. Since equilibrium is not attained, kinetics and mechanism must be considered if we are to understand the product distribution, that is, scrambling occurs, but in competition with dissociation. The major ion is that which appears to result from the transfer of a single proton. However, more proton transfers occur than might be obvious at first glance. The reaction proceeds by formation of a very energetic hydrogen-bonded complex (III). Dissociation in the exothermic
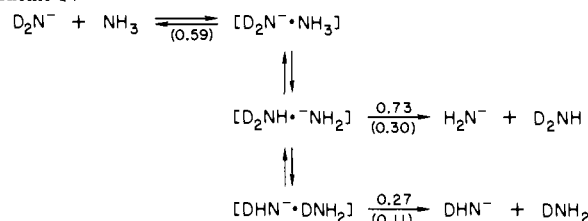
$$D^{18}O^- + H_2O \leftarrow \underset{IIIa}{[D^{18}O^- \cdots HOH]} \rightleftharpoons \underset{IIIb}{[D^{18}OH \cdots {}^-OH]} \rightarrow$$
$$HO^- + D^{18}OH \quad (8)$$

direction to form HO$^-$ is slightly favored. Of course, the proton can be transferred between the two oxygens very rapidly. In order for further exchange to occur, there must be rotation of a water molecule, breaking the hydrogen bond and forming a new hydrogen or deuterium bond. If the H$_2$O molecule rotates (path a, Scheme III), a new complex forms which is identical with the old. However, if D^{18}OH rotates (path b, Scheme III) a new complex forms which can dissociate equally easily to H^{18}O$^-$ and HO$^-$. This analysis can be extended to include subsequent ro-

(25) Van Koppen, P. A. M.; Jarrold, M. F.; Bowers, M. T.; Bass, L. M.; Jennings, K. R. *J. Chem. Phys.* **1984**, *81*, 288–297. See also: Smith, D.; Adams, N. G.; Alge, E. *Chem. Phys. Lett.* **1984**, *105*, 317–321.

Scheme III

$$[H^{18}O^- \cdots DOH] \longrightarrow$$

$$\updownarrow$$

$$[D^{18}OH \cdots {}^-OH] \longrightarrow [H^{18}OD \cdots {}^-OH] \longrightarrow$$

$$\updownarrow$$

$$[D^{18}O^- \cdots HOH] \xrightarrow{a} [D^{18}O^- \cdots HOH] \longrightarrow [D^{18}O^- \cdots HOH] \longrightarrow$$

$$\updownarrow \qquad\qquad \updownarrow \qquad\qquad etc.$$

$$[D^{18}OH \cdots {}^-OH] \xrightarrow{b} [H^{18}OD \cdots {}^-OH] \longrightarrow [D^{18}OH \cdots {}^-OH] \longrightarrow$$

$$\updownarrow$$

$$[H^{18}O^- \cdots DOH] \longrightarrow [H^{18}O^- \cdots HOD] \longrightarrow$$

$$\updownarrow$$

$$[H^{18}OH \cdots {}^-OD] \longrightarrow$$

Scheme IV

$$D_2N^- + NH_3 \underset{(0.59)}{\rightleftharpoons} [D_2N^- \cdot NH_3]$$

$$\updownarrow$$

$$[D_2NH \cdot {}^-NH_2] \xrightarrow[(0.30)]{0.73} H_2N^- + D_2NH$$

$$\updownarrow$$

$$[DHN^- \cdot DNH_2] \xrightarrow[(0.11)]{0.27} DHN^- + DNH_2$$

tations as shown. (Note, the dissociation channels are not shown in Scheme III.)

As Scheme III shows, then, rotation of a water molecule within the initially formed complex will lead to the formation of H^{18}O$^-$ only about one-fourth of the time; the rest of the time D^{18}O$^-$ or HO$^-$ will be formed. Thus the observed 30% (23% if one accounts for a 0.76 reaction efficiency) of H^{18}O$^-$ actually indicates much further progress toward eventual equilibration than might be obvious on the surface. Similarly the 10% (8%) formation of DO$^-$ can arise only after several rotations, since back reactions to give D^{18}O$^-$, HO$^-$, or H^{18}O$^-$ are much more numerous than the single reaction which can lead to this product.
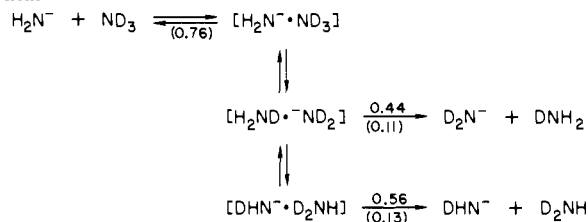
The data do not justify exact quantitative analysis at this stage, primarily because they are quite sensitive to a value which cannot be measured directly, namely the amount of D^{18}O$^-$ formed. Our estimate for this value must come from a comparison of our rate coefficient with that calculated by ADO theory. Nevertheless, one can easily see from the data that a considerable fraction of any complex undergoes rotation of a water molecule without dissociation while the remainder dissociates before such rotation.

In order to fit the observed data to the model depicted in Scheme III, an estimate of the effect of the enthalpy constraints on the branching among the possible pathways available to each complex is required. Recall the CD$_3$O$^-$ + CH$_3$OH reaction in which we observed that the fractionation was 1.5 to 1, favoring the 0.5 kcal mol^{-1} exothermic channel over the thermoneutral channel. If there were no energy difference among the possible pathways, the fractionation would be 1 to 1. Linear interpolation then indicates that for competition between a 0.3 kcal mol^{-1} exothermic channel and a thermoneutral channel, the fractionation will be about 1.3 to 1. The model in Scheme III is used in conjunction with this fractionation factor for both dissociation and rotation, i.e., in [D^{18}O$^-$···HOH] ⇌ [D^{18}OH···$^-$OH], dissociation to HO$^-$ is favored over dissociation to D^{18}O$^-$ and rotation of D^{18}OH is favored over rotation of HOH. A product distribution and reaction efficiency in agreement with the experimental values is obtained when four-fifths of the complexes are assumed to undergo rotation before dissociation.

This is not a unique fit to the data. A variety of relative rates of dissociation to rotation as well as a small range of isotope effects both on dissociation and/or rotation give similar predictions. The important conclusion is that while somewhere in the neighborhood

Scheme V

$$H_2N^- + ND_3 \underset{(0.76)}{\overset{}{\rightleftharpoons}} [H_2N^- \cdot ND_3]$$

$$\updownarrow$$

$$[H_2ND \cdot {}^-ND_2] \xrightarrow[(0.11)]{0.44} D_2N^- + DNH_2$$

$$\updownarrow$$

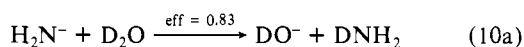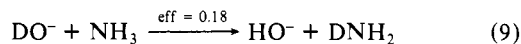$$[DHN^- \cdot D_2NH] \xrightarrow[(0.13)]{0.56} DHN^- + D_2NH$$

of one-fifth of the complexes dissociate before rotation, much more is occurring within the complex before dissociation than is initially obvious.

Amide/Ammonia. We next examined H/D exchange in the reaction of amide ion with ammonia. In this case, the two deuteron atoms in D_2N^- can serve as the necessary double label. We also examined the reaction in both directions, namely $D_2N^- + NH_3$ and $H_2N^- + ND_3$ (Schemes IV and V). At first glance, the data are surprising, showing rather low efficiencies and, in the case of $H_2N^- + ND_3$, more double exchange (formation of DHN^-) than single (formation of D_2N^-). However, they can be interpreted in a manner analogous to that for water. The overall reaction efficiencies are low, presumably because the binding energy of the $[H_2N^-\cdots NH_3]^*$ complex is low. Indeed we are unable to measure a three-body rate coefficient for this clustering reaction at attainable helium pressures in our FA, though we are able to observe formation of a small amount of the adduct. The lifetime of the complex is probably shorter than that for the hydroxide–water complex discussed above. The bond energy in the amide–ammonia complex has not been experimentally determined in the gas phase but is probably only about 13 kcal mol^{-1}.[26] Thus the transition state for isotope exchange is closer to the total available energy of the system and the reaction is slowed. A second factor to consider is that, because of the presence of two deuterium atoms in D_2N^-, equilibrium isotope effects are greater than in the case for DO^-.

Let us first examine D_2N^- reacting with NH_3. Proton transfer to form H_2N^- is reasonably exothermic, so that most complexes should break up to give H_2N^-; the fact that 59% D_2N^- is formed suggests that many of the complexes dissociate before any proton transfer can occur (i.e., the majority of the initial encounters result in no reaction even though there are two exothermic channels available).

For reaction in the opposite direction ($H_2N^- + ND_3$), exchange is endothermic and the overall reaction efficiency is lower than that for the exothermic $D_2N^- + NH_3$ reaction. The first exchange is quite endothermic, leading to a longer lifetime and reduced rate of dissociation. We thus see more of the multiple exchange product DHN^-. Thus, for both Schemes IV and V, the more thermodynamically favored exchange product is dominant.

Hydroxide/Ammonia and Amide/Water. Interesting supplements to the above experiments are those we have carried out for exchange on the one hand between $DO^- + NH_3$ (see ref 4) and on the other between H_2N^- and D_2O (see Table I). It seems

$$DO^- + NH_3 \xrightarrow{\text{eff} = 0.18} HO^- + DNH_2 \tag{9}$$

$$H_2N^- + D_2O \xrightarrow{\text{eff} = 0.83} DO^- + DNH_2 \tag{10a}$$

$$\xrightarrow{\text{eff} = 0.17} HO^- + D_2NH \tag{10b}$$

surprising that there should be more of the multiply exchanged ion product in the highly exothermic reaction of H_2N^- with D_2O (17%) than there is in either of the nearly thermoneutral reactions of amide ion with ammonia (branching ratio times reaction efficiency equals 13% for $H_2N^- + ND_3$ and 11% for $D_2N^- + NH_3$). However, a longer-lived complex in the former case, due to a stronger hydrogen bond, must account for the observed results.

Even more surprising is the similar amount of exchange in the thermoneutral $DO^- + NH_3$ and exothermic $H_2N^- + D_2O$ systems (e.g., compare eq 9 and 10b). In these two cases, the ion–dipole complex is the same, but contains 13 kcal mol^{-1} more energy in the latter than in the former reaction. This implies that the two processes, exchange and dissociation, are accelerated by comparable amounts by the additional energy.

Exchange in Sulfur-Containing Systems. With this general picture of H/D exchange in mind, we can use exchange to probe other ion–molecule complexes and the importance of hydrogen bonding in them. For example, while DO^- exchanges readily with NH_3 (eff = 0.18) which is 13 kcal mol^{-1} less acidic than H_2O, we note that HS^- and H_2P^- do not exchange with deuterated alcohols which are closer than that in relative acidity to H_2S or PH_3. In earlier work,[18] it had been noted that HS^- does not exchange with trifluoroethanol-*O-d* which is only 11.0 kcal mol^{-1} less acidic than H_2S ($\Delta H^\circ_{acid}(CF_3CH_2OD) = 364.4$ kcal mol^{-1}; $\Delta H^\circ_{acid}(H_2S) = 353.4$ kcal mol^{-1}).[27] This result was particularly

$$HS^- + CF_3CH_2OD \nrightarrow DS^- + CF_3CH_2OH \tag{11}$$

perplexing in light of the observation that $^-CH_2CN$ undergoes rapid exchange with D_2O, a system in which the gas-phase acidity difference is ~ 19 kcal mol^{-1}.

To provide additional insight into this question, we examined exchange reactions of DS^- with other sulfur acids. The essentially thermoneutral proton transfer with H_2S occurs rapidly (eq 12), and its reaction efficiency is very close to the statistical value of $^2/_3$; the reaction is expected to be only slightly exothermic, ΔH_{rxn} (eq 12) = -0.3 kcal mol^{-1}. However, exchange with CH_3SH, which involves a 5.6 kcal mol^{-1} endothermic proton transfer, is more than 5 times less efficient (eq 13). The exchange reaction

$$DS^- + H_2S \xrightarrow{\text{eff} = 0.62} HS^- + DSH \tag{12}$$

$$DS^- + CH_3SH \xrightarrow{\text{eff} = 0.11} HS^- + CH_3SD \tag{13}$$

$$DS^- + (CH_3)_3CSH \xrightarrow{\text{eff} = 0.34} HS^- + (CH_3)_3CSD \tag{14}$$

with 2-methyl-2-propanethiol for which the acidity difference is only 1.3 kcal mol^{-1} (eq 14) is intermediate, exhibiting an exchange efficiency of 34%. Indeed, in this latter reaction, 1–2% of the $DS^-/(CH_3)_3CSH$ encounters lead to $(CH_3)_3CS^-$ formation.

These data are readily understood in terms of the ion–dipole, ion–induced dipole forces available to drive the exchange. These processes for sulfur anions are significantly less efficient than for oxygen anions due undoubtedly to the smaller ion–dipole energy in the former systems. Water has a larger dipole moment than H_2S, and while H_2S is more polarizable, it is also larger. The result is that weaker hydrogen-bonded complexes are formed with the sulfur-containing species (e.g., compare a bond strength[24] of 25 kcal mol^{-1} for $HO^- \cdot H_2O$ to that[28] of 13.5 kcal mol^{-1} for $HS^- \cdot H_2S$) and hence less efficient exchange is observed.

The data for these exchange reactions are in line with the conclusions arrived at in the earlier studies,[2–8] namely that the closer the species in acidity and the stronger the solvation interactions the more efficient is the exchange. The reaction of DO^- with H_2S is a check on the extent that these factors control the amount of H/D exchange that does occur. For this reaction the direct proton transfer is quite exothermic (eq 15) and HS^- is the only ion that emerges from the encounter complex.

$$DO^- + H_2S \rightarrow HS^- + DOH + 4.05 \text{ kcal mol}^{-1} \tag{15a}$$

$$\nrightarrow HO^- + HSD - 0.1 \text{ kcal mol}^{-1} \tag{15b}$$

$$\nrightarrow DS^- + H_2O + 39.8 \text{ kcal mol}^{-1} \tag{15c}$$

Conclusion

By examining the rate coefficients for proton abstraction, CD_3O^- was determined to be a stronger gas-phase base than

(26) The $H_2N^- \cdot NH_3$ bond energy has been calculated to be 12 kcal mol^{-1}. Squires, R. R. In "Ionic Processes in the Gas Phase", Almoster Ferreira, M. A., Ed.; D. Reidel: Boston, 1984; pp 337–340.
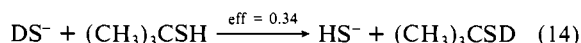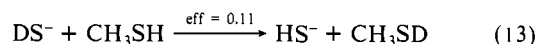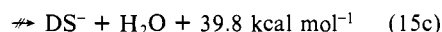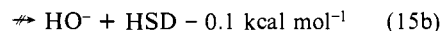
(27) Unless specified otherwise, the gas-phase acidities used in this work are taken from ref 17.
(28) McMahon, T. B., private communication.

CH_3O^- by 0.5 kcal mol^{-1}, a fact which can be entirely explained by electron affinity differences between $CH_3O\cdot$ and $CD_3O\cdot$. The exchange reactions of hydroxide with water, first reported in an earlier publication, were extended by making use of a doubly labeled system. The $D^{18}O^- + H_2O$ reaction was found to proceed with a high overall reaction efficiency to form products which at first sight appear to be dominated by a single proton transfer when compared to a simple statistical model. However, closer examination suggests that only about one-fifth of the initially formed complexes dissociate immediately, while the remainder undergo one or more rotations of a water molecule to form a new complex. The amide–ammonia systems were studied for both combinations of isotopic reactants ($H_2N^- + ND_3$ and $D_2N^- + NH_3$). While significant multiple exchange was observed in both cases, the overall efficiencies are considerably lower than in the hydroxide–water systems. The product distributions can be understood in terms of relative ion-molecule complex lifetimes and dissociation of the complex in competition with scrambling. Finally, the exothermic proton abstraction reaction of amide with D_2O was observed to give 17% HO^- while the more highly exothermic reaction of DO^- with H_2S gives only HS^-.

We also demonstrated that hydrogen/deuterium exchange in acid–base systems containing second-row elements is observed to proceed in the gas phase with exchange reagents of the same type, i.e., DS^- undergoes efficient exchange with methanethiol, 2-methyl-2-propanethiol, and hydrogen sulfide. The relative efficiencies of exchange correlate well with the relative acidities and relative ion–dipole binding energies. The lack of exchange reported earlier for HS^- with CF_3CH_2OD is not unexpected when the relative acidities and relative ion–dipole energies are considered. It is expected that HS^- will exchange with a first-row acid closer in acidity to H_2S than CF_3CH_2OD, perhaps, for example, $CF_3C(CH_3)_2OD$.

Finally, these systems are ideal candidates for modeling by phase space/RRKM theory. Such studies would provide valuable insight into the detailed pathways involved, including the barriers to rotation discussed above. Further investigations, both in the lab and by theory, will continue to contribute to our understanding of this fundamental process.

Mechanism of Cytochrome *c* Oxidase-Catalyzed Dioxygen Reduction at Low Temperatures. Evidence for Two Intermediates at the Three-Electron Level and Entropic Promotion of the Bond-Breaking Step

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Abstract: The reaction of cytochrome *c* oxidase with dioxygen has been examined by using a modification of the triple-trapping technique (Chance, B.; Saronio, C.; Leigh, J. S., Jr. *J. Biol. Chem.* **1975**, *250*, 9226–9237) in conjunction with EPR spectroscopy. The investigation has been extended to a broader temperature range than previous studies, and several new reaction steps have been resolved. Where possible, the temperature dependences of the rates of individual steps have been measured, enabling estimation of enthalpies of activation. Both the low potential sites (Fe_a and Cu_A) and the dioxygen reduction site (Fe_{a_3}/Cu_B) have been monitored simultaneously, enabling clarification of the relationship between the electron transfers to the dioxygen reduction site and the events which occur there. The evidence indicates that there are two intermediates at the three-electron level of dioxygen reduction, only the first of which is EPR-detectable. The conversion between these two intermediates, which probably corresponds to the breaking of the dioxygen bond, exhibits a distribution of activation enthalpies which peaks at 18.1 ± 1.6 kcal mol^{-1}. Assuming a preexponential factor of 10^{13}, the corresponding activation entropy is 21.4 ± 8.2 cal mol^{-1} K^{-1}, indicating that this process is promoted by entropic factors. Experiments using enzyme reduced by only three electrons confirm the existence of the two different three-electron intermediates proposed. These experiments also indicate that the rate of electron transfer from Fe_a to the Fe_{a_3}/Cu_B site depends upon which intermediate of dioxygen reduction is present at the latter site. Finally, we have obtained evidence that one of the three-electron intermediates of dioxygen reduction, probably a ferryl ion, can react with carbon monoxide at low temperature (211 K) to produce CO_2 and a partially reduced enzyme species which exhibits EPR signals characteristic of a magnetically isolated Cu_B center. These results are discussed in terms of the electron-transfer pathways within the enzyme and its mechanisms of dioxygen reduction and energy conservation.

Cytochrome *c* oxidase is the terminal component in the mitochondrial respiratory chain of eukaryotic organisms. In this role, the enzyme catalyzes the rapid reduction of dioxygen to water, using electrons derived from ferrocytochrome *c* (eq 1) and con-

$$4H^+ + O_2 + 4\text{ferrocytochrome } c \rightarrow$$
$$2H_2O + 4\text{ferricytochrome } c \quad (1)$$
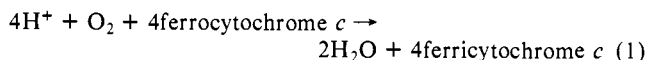
serves part of the free energy released in this reaction by con-

tributing to the generation of the proton electrochemical potential across the inner mitochondrial membrane.[1] The turnover rate of the enzyme is as high as 400 electrons transferred per second.[2]

Mitochondrial cytochrome *c* oxidase is a large (M_r 170 000) multisubunit protein.[3] The functional monomer contains four metal ions: two coppers, designated Cu_A and Cu_B, and two irons

(1) Wikström, M. *Curr. Top. Membr. Transp.* **1982**, *16*, 303–321.
(2) Vik, S. B.; Capaldi, R. A. *Biochem. Biophys. Res. Commun.* **1980**, *94* (1), 348–354.
(3) Merle, P.; Kadenbach, B. *Eur. J. Biochem.* **1980**, *105*, 499–507.

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