

Mechanism of the Spontaneous Dehydration of Bicarbonate Ion

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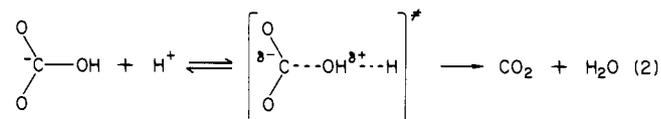
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Abstract: ¹³C kinetic isotope effects on the dehydration of HCO₃⁻ in aqueous solution have been measured in D₂O at 24 °C ($k^{12}/k^{13} = 1.0178 \pm 0.0005$) and in H₂O at 1 and 24 °C (1.0171 ± 0.0006 and 1.0151 ± 0.0008 , respectively) by measuring the isotopic composition of CO₂ formed at 10% and 100% conversion of HCO₃⁻. Expected kinetic isotope effects were calculated by means of the BEBOVIB-IV program. Comparison of observed with predicted carbon and solvent isotope effects indicates that the mechanism of HCO₃⁻ dehydration is stepwise, rather than concerted. The first step is the protonation of bicarbonate by hydronium ion, forming the zwitterionic intermediate H₂O⁺-CO₂⁻, which then decomposes to give products. The rates of the protonation and decomposition steps are similar.

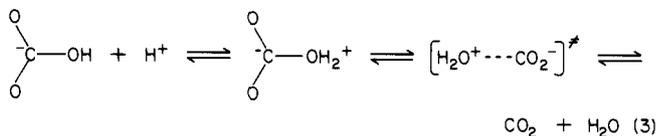
Although the dehydration of bicarbonate ion and its reverse, the hydration of carbon dioxide, are among the simplest and most fundamental of chemical reactions, the detailed reaction mechanisms of both spontaneous and enzyme-catalyzed reactions remain obscure.¹⁻³ The stoichiometry of the dehydration of bicarbonate ion requires proton transfer



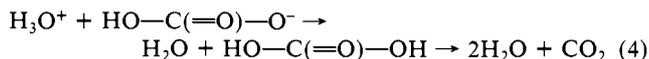
Two types of mechanisms have been suggested for this process.¹ They differ according to the timing of the proton-transfer and carbon-oxygen bond cleavage steps. In the concerted mechanism, the proton transfer from hydronium ion to bicarbonate is simultaneous with carbon-oxygen bond breaking, and there is no intermediate (eq 2). In the stepwise mechanism, the proton



transfer occurs first, forming either carbonic acid or the zwitterion of carbonic acid. Decomposition of the protonated intermediate occurs in a separate step. If the intermediate is a zwitterion, it is expected to be highly reactive both toward proton transfer and toward carbon-oxygen bond cleavage, and it is not immediately obvious which step should be rate-determining (eq 3).



Alternatively, the first proton transfer might form carbonic acid. This step should be rapid.⁴ Decomposition of carbonic acid to form products would occur in a following step, perhaps with participation of one or more waters as proton transfer (eq 4). It



is also possible that decomposition of carbonic acid might involve more than a single step.

We have recently reported that the dehydration of HCO₃⁻ and the hydration of CO₂ show small carbon kinetic isotope effects.⁵ The ratio of the two effects gives, as expected, the equilibrium isotope effect on the process. In that work, we were unable to distinguish convincingly between the concerted and stepwise mechanisms. In this paper, we report additional isotope effect evidence supporting a stepwise mechanism.

Table I. Carbon Isotope Effects^a (k^{12}/k^{13}) on the Dehydration of HCO₃⁻ at pH 8.2, in Aqueous Solution

	H ₂ O		D ₂ O
	1 °C	22 °C	24 °C
	1.0166	1.0143	1.0170
	1.0178	1.0150	1.0183
	1.0168	1.0159	1.0184
	1.0165		1.0178
	1.0169		1.0176
	1.0171		1.0174
	1.0173		
	1.0181		
mean	1.0171 ± 0.0006	1.0151 ± 0.0008	1.0178 ± 0.0005

^aThe value for 24 °C reported earlier⁵ equals $k_{12}/k_{13} = 1.0147 \pm 0.0007$.

Experimental Section

N-(2-Hydroxyethyl)piperazine-*N'*-2-ethanesulfonic acid (HEPES) was obtained from Sigma Chemical Co. NaHCO₃ was obtained from Columbus Chemical Industries, Inc., and the same bottle was used throughout, for isotopic consistency. D₂O was obtained from Stohler Chemical Co. H₂¹⁸O (97% ¹⁸O) was obtained from Mound Laboratories, Miamisburg, OH. Water was purified with a Millipore Super-Q water purification system.

Isotope Effects. The previously published⁵ procedure was applied; 10 mL of 0.5 M HEPES, pH 8.2, was placed in a 50-mL two-necked, round-bottom flask equipped with a magnetic stirring bar. The buffer was freed of dissolved CO₂ by purging with CO₂-free N₂ for at least 4 h. After the degassing was completed, the reaction was initiated by adding 1.0 mL of 1.0 M NaHCO₃ to the solution through a septum, following which the system was evacuated through a set of two 2-propanol-dry ice traps and one liquid nitrogen trap for a period of time sufficient to allow dehydration of about 10% of the HCO₃⁻. The CO₂ in the liquid nitrogen trap was then purified, measured manometrically, and analyzed for isotopic composition.

Isotope ratios were measured on a Finnigan Delta-E isotope ratio mass spectrometer. All ratios were corrected for oxygen-17. Individual isotope ratios are estimated to be reproducible to ±0.05%.

The D₂O used in these experiments was enriched in ¹⁷O and ¹⁸O. In order to eliminate any errors in the isotope ratios resulting from the presence of ¹⁷O in the samples, the CO₂ produced in the experiments with D₂O was equilibrated with normal water prior to isotopic analysis.

Results

Carbon isotope effects on the dehydration of HCO₃⁻ were obtained by the comparison of the isotopic composition of CO₂

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formed at low (ca. 10%) conversion (R_f) with that produced at 100% conversion (R_{100}). Reactions were carried out under vacuum so that CO_2 was removed from the solution as rapidly as it was formed. Isotope effects were calculated by using the equation

$$k^{12}/k^{13} = \{\ln(1-f)\}/\{\ln(1-fR_f/R_{100})\} \quad (5)$$

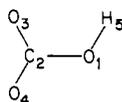
where f is the extent of reaction and was calculated from the yield of CO_2 compared to the initial quantity of bicarbonate in the sample. Usually 50–100 μL of CO_2 was produced for mass spectrometric analysis. Experiments were designed so that the same volumes of CO_2 were obtained at both conversion levels. The isotope effect was measured at 22 °C under the same conditions used previously,⁵ at 1 °C under otherwise identical conditions, and at 24 °C in D_2O . The results obtained are summarized in Table I. The solvent isotope effect on this reaction has been measured by Pocker and Bjorquist.¹

The key to the success of these experiments is that removal of CO_2 from the solution must be rapid compared to hydration of CO_2 to form HCO_3^- . We have previously demonstrated by means of studies in H_2^{18}O that this criterion is met.⁶ In experiments with ^{18}O -labeled water, we find that only 3% of the CO_2 formed has exchanged one oxygen atom with water. Therefore, no correction for reverse reaction was necessary.

Theoretical Calculations

The BEBOVIB-IV program^{7,8} was used in order to find transition-state structures consistent with the carbon isotope effects in H_2O at 1 and 24 °C and in D_2O at 24 °C. We did not attempt to replicate the solvent isotope effect.

As a starting point, we used ground-state data for aqueous HCO_3^- obtained by George et al.⁹ Initially, the ground state was modeled by using a planar five-atom model with no interaction between hydrogen H_5 and either of the nonbridging oxygens (O_3 or O_4):



Bond lengths and force constants for C–O stretches for both oxygen atoms were, therefore, equal. For diagonal force constants, the standard⁸ values were used, and these were adjusted by the program according to assumed bond orders. We used the off-diagonal force constant to couple these stretches. The off-diagonal force constants were adjusted by the equation

$$f = 0.084(F_{23}F_{24})^{1/2} \quad (6)$$

where F_{23} and F_{24} (which are equal in the present case) are stretching force constants for $\text{C}_2\text{--O}_3$ and $\text{C}_2\text{--O}_4$ bonds. The factor 0.084 is the ratio of the force constants $f/F_{\text{C=O}}$ for CO_2 .¹⁰ The normal vibration frequencies calculated from our model are in good agreement with the experimental values.

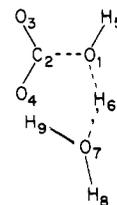
Various models for the transition state were tried with the goal, first, of reproducing the magnitude of the isotope effect in H_2O , second, reproducing the temperature dependence of the observed isotope effect, and finally, reproducing (with the same force constants) the isotope effect in D_2O . For each set of calculations, we first identified transition-state structures which would fit the observed carbon isotope effect at 22 °C (1.0151). We then adjusted the model so that it would also be consistent with the value at 1 °C (1.0171). Provided that consistency could be obtained,

Table II. Bond Orders of Different Transition-State Models

bond	TS1	TS2	TS3	TS4
C2–O1	0.5	0.5	0.4	0.4
O1–H5	1.0	1.0	1.0	1.0
C2–O3	1.75	1.75	1.7	1.7
C2–O4	1.75	1.75	1.7	1.7
O1–H6	0.6	1.0	0.6	0.6
O7–H6	0.4		0.4	0.4
O7–H8	1.0		1.0	1.0
O7–H9	1.0		1.0	1.0
O3–H10			0.12	0.09
O3–H11				0.09
O3–H12				0.09
O4–H13			0.12	0.09
O4–H14				0.09
O4–H15				0.09

we then changed the masses of all hydrogens from 1 to 2 in order to model the isotope effect in D_2O (1.0178).

Our initial model of the transition state for the concerted reaction was the structure which was obtained by Nguyen and Ha from the geometry and energy optimization.¹¹ Once again, the hydrogen bond between H_9 and O_4 was neglected. We also increased the bond orders of the nonbridging oxygens in order to maintain the total bond order to the carbon atom at 4:



The reaction coordinate was chosen to correspond to an asymmetric motion of the $\text{O}_7\text{--H}_6\text{--O}_1\text{--C}_2$ system, leading to fragmentation of the transition state to products. The reaction coordinate was generated by use of two additional interacting (off-diagonal) force constants coupling stretching motions $\text{O}_7\text{--H}_6$ with $\text{H}_6\text{--O}_1$ and $\text{H}_6\text{--O}_1$ with $\text{O}_1\text{--C}_2$. These were adjusted so that the determinant of the force constants matrix for the transition state was always negative and close to -0.2 .¹² The geometry of the transition state was then changed progressively until the model reproduced the experimental carbon isotope effects at 22 and 1 °C (Table II). The best-fit parameters of this model, called TS1, are given in Table II. This model gave a good fit to the observed isotope effects in H_2O at the two temperatures, but it failed to reproduce the carbon isotope effect in D_2O . This model and similar models with slightly changed geometries always predict a decrease in the size of the carbon kinetic isotope effect whenever protons are replaced with deuterons.

Similar results were obtained when we attempted to model the transition state for C–O bond breaking in the stepwise reaction (eq 3). For this purpose, the bond order for forming the $\text{O}_1\text{--H}_6$ bond was set equal to unity (TS2). Again, replacement of H by D always results in a decrease in the calculated isotope effect.

A more realistic model of the ground state and transition state accounts for the fact that both structures have hydrogen bonds to all oxygens. We varied the number of hydrogen bonds and their strengths (e.g., TS3 and TS4 in Table II) assuming that force constants of the hydrogen bonds are in the range 0.15–0.08 of a force constant for a full O–H bond.^{11,13,14} Both the ground state and transition state had the general structure

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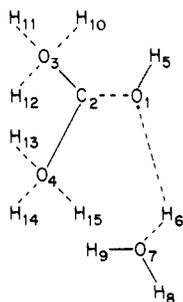
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As with the previous model, a variety of structures were able to reproduce the carbon isotope effects in H_2O at two temperatures, but these models invariably predict that the carbon isotope effect will be smaller in D_2O than in H_2O . In fact, although the introduction of hydrogen bonds should make our model more realistic, the more hydrogen bonds we introduced, the greater the decrease of the isotope effect on substitution of deuterium for hydrogen.

Discussion

The dehydration of HCO_3^- shows a significant carbon kinetic isotope effect. Qualitatively, this indicates that breaking of the carbon-oxygen bond is occurring in the rate-determining step. The size and direction of the temperature effect on the isotope effect are also consistent with this conclusion. As we have noted previously,⁵ the dehydration of HCO_3^- resembles a decarboxylation, and we would expect that carbon isotope effects on decarboxylations should provide a reasonable model for the isotope effect on the dehydration of HCO_3^- . However, decarboxylations shows isotope effects which are substantially larger than that seen in the dehydration of HCO_3^- . Consequently, either the transition state for HCO_3^- dehydration is very reactant-like or else the mechanism involves more than a single kinetically significant step.

Within a single transition state, the isotope effect reflects the amount of bond making or breaking to the isotopic atom and the contribution of the isotopic atom to motion along the reaction coordinate. Other factors held constant, any change which decreases this latter contribution will decrease the isotope effect. This should be the case, for example, for solvent deuterium substitution in the dehydration of HCO_3^- . We expect that substitution of D for H in the transition state should decrease the contribution of carbon motion to the transition state. Thus, we qualitatively expect that the carbon isotope effect should be smaller in D_2O than in H_2O if the reaction occurs by a single-step mechanism.

The same conclusion was reached more quantitatively by use of the BEBOVIB IV program. This program has been used successfully to predict isotope effects for a variety of simple chemical processes.^{8,12} When we attempt to explain our isotope effects by using this approach and considering a concerted one-step reaction mechanism, a variety of transition-state structures can be found which are consistent with the observed isotope effects at 1 and 24 °C in H_2O . However, all such models predict carbon isotope effects in D_2O which are smaller than those in H_2O . Experimentally, the effect of D_2O is in the opposite direction. For this reason, we conclude that the dehydration of HCO_3^- does not proceed by a single-step, concerted mechanism.

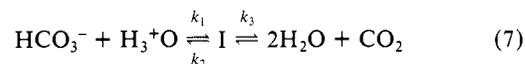
It should be emphasized that this conclusion does not depend on the accuracy of the calculations from the BEBOVIB-IV program or on identification of the optimum structure of the ground state and transition state. The important variable is the relative sizes of isotope effects in H_2O and in D_2O , and this seems to be independent of the precise structures assumed.

The second class of mechanism is stepwise mechanisms in which the first step is a rapid proton transfer (eq 3 and 4). In either of these cases, the isotope effect reflects the structure difference between the starting state (HCO_3^-) and dehydration transition state. As in the case of the totally concerted mechanism, substitution of D_2O for H_2O invariably leads to a predicted reduction in the magnitude of the carbon isotope effect. Thus, we conclude

that these mechanisms are not consistent with the experimental data.

The third possibility is that the dehydration mechanism is stepwise (eq 3, or some more complex scheme) with at least two steps having similar rates. Precedent for an effect of D_2O on a carbon isotope effect in such a complex mechanism is found in studies of the enzymatic decarboxylation of glutamic acid.¹⁵ A mathematical treatment of such "isotope effects on isotope effects" has been presented, but that treatment applies only to cases in which only one step is sensitive to carbon isotope substitution and only one step is sensitive to deuterium substitution.¹⁶

Next we will consider in detail such two-step mechanisms. Such cases can be described as



in which the nature of the intermediate I is yet to be specified. We will assume that the carbon isotope effect on the first step is negligible¹⁷ and that the carbon isotope effect on the second step is the same in H_2O as in D_2O . The experimental carbon and solvent isotope effects at 24 °C are then given by

$$1.0147 = \frac{k_3^{12}/k_3^{13} + k_3/k_2}{1 + k_3/k_2} \quad (8)$$

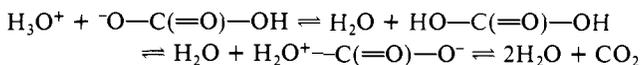
$$1.0178 = \frac{k_3^{12}/k_3^{13} + (k_3/k_2)(k_2^{\text{H}}/k_2^{\text{D}})/(k_3^{\text{H}}/k_3^{\text{D}})}{1 + (k_3/k_2)(k_2^{\text{H}}/k_2^{\text{D}})/(k_3^{\text{H}}/k_3^{\text{D}})} \quad (9)$$

$$0.56 = \frac{k_1^{\text{H}}/k_1^{\text{D}} k_3^{\text{H}}/k_3^{\text{D}} + (k_3/k_2)(k_2^{\text{H}}/k_2^{\text{D}})}{k_2^{\text{H}}/k_2^{\text{D}} + k_3/k_2} \quad (10)$$

The value 0.56 is taken from ref 1. Because there are five unknowns (four intrinsic isotope effects and the ratio k_3/k_2) and only three equations, it is not possible to derive a unique solution. However, two important results can be obtained from these equations: Combining eq 8 with eq 9 leads to the conclusion that $k_3^{\text{H}}/k_3^{\text{D}} > k_2^{\text{H}}/k_2^{\text{D}}$. Substitution of this result into eq 10 leads to the conclusion that $k_1^{\text{H}}/k_1^{\text{D}} < 0.56$. These conclusions apply to any mechanisms which can be summarized by eq 7.

The simplest two-step mechanism is the stepwise mechanism (eq 3) in which the first step is formation of a zwitterionic intermediate. Considerations outlined in the preceding paragraph require that the first step be partially rate-determining and that the solvent isotope effect on this step be less than 0.56. The zwitterionic intermediate should be very high in energy; thus, we expect that the transition state will resemble the intermediate. Four solvent hydrogens should contribute to the isotope effect: the hydrogen in transit, the two remaining protons in the hydronium ion, and the bicarbonate proton. If the transition state resembles the intermediate, then we expect that each would have a fractionation factor near 0.69 (ref 18). The bicarbonate proton will have a fractionation factor near 1/0.69. If the isotope effect for the proton in transition state being very asymmetric), then the predicted isotope effect might fall near the required upper limit of 0.56. The second step, decomposition of the zwitterion, might also show a small solvent isotope effect. The carbon isotope effect should be small both because of the early transition state and because of the two-step mechanism.

Another reasonable model is a three-step model related to eq 4 involving carbonic acid as an intermediate:



The first step will be at equilibrium⁴ and will show an equilibrium isotope effect¹⁹ of 0.69,³ or 0.33. The second step is a cyclic proton

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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 ketones²⁰ 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.

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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.

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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 deuterium, 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

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