Proton Exchange between Ammonium Ion, Trimethylammonium Ion, and Water. Speed of the Dehydration Step That Precedes Bimolecular Proton Transfer[1]

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Abstract: Rates of proton transfer between trimethylammonium ion and ammonia have been measured at dynamic equilibrium by nuclear magnetic resonance techniques in dilute aqueous acid. Proton transfer with participation by a water molecule is fast ($k_{+7} = [1.65 \pm 0.08] \times 10^8$ sec^{-1} M^{-1} at 30°) while direct bimolecular proton transfer, $Me_3NH^+ + NH_3 \rightleftarrows Me_3N + NH_4$, is too slow to be measured ($k_{+6} < 0.2 \times 10^8$ sec^{-1} M^{-1}). These rate constants are compared with known rate constants for symmetrical proton exchange. It is concluded that the formation of a solvent-separated complex, $BH^+ \cdot OH_2 \cdot B'$, is normally fast while the dehydration of this complex to form a nearest neighbor pair, $BH^+ \cdot B'$, is slowed down markedly by N-alkyl substituents. Rate constants for the dehydration step are estimated from the rate constants for bimolecular proton transfer.

The experiment we report in this paper helps to elucidate the speed at which solvent-separated pairs of solute molecules become nearest neighbors in aqueous solution. It has been known for some time that proton transfer from ammonium ion or a methyl-substituted ammonium ion (BH^+) to its conjugate base (B) can proceed by two distinct processes, with and without participation by a water molecule, as shown in eq 1 and 2.[2]

$$\overset{+}{\mathrm{BH}} + \overset{\mathrm{H}}{\mathrm{O}}H + B \xrightarrow{k_7} \mathrm{B} + \overset{\mathrm{H}}{\mathrm{HO}} + H\overset{+}{B} \qquad (1)$$

$$\overset{+}{\mathrm{BH}} + B \xrightarrow{k_6} \mathrm{B} + \mathrm{H}\overset{+}{B} \qquad (2)$$

"Best values" for the rate constants at 30° are listed in Table I. It is seen that the effects of methyl substitution are quite different: changes in k_7 are relatively small (even if we include the value for NH_4^+, which is somewhat below the others) and can be correlated with changes in the base dissociation constant; changes in k_6 are much larger, and k_6 decreases progressively with methyl substitution.

Table I. Rate Constants for Proton Transfer[a] According to Reactions 1 and 2 at 30°

BH^+	B	$10^{-8}k_6$, sec^{-1} M^{-1}	$10^{-8}k_7$, sec^{-1} M^{-1}	10^4K_B of B
NH_4^+	NH_3	12.7	0.50 ± 0.04	0.183
$CH_3NH_3^+$	CH_3NH_2	4.4	5.8	4.2
$(CH_3)_2NH_2^+$	$(CH_3)_2NH$	0.5	9.9	6.3
$(CH_3)_3NH^+$	$(CH_3)_3N$	0.0[b]	3.7[b]	0.73
$(CH_3)_3NH^+$	NH_3	0.09 ± 0.12	1.65 ± 0.08	0.183
NH_4^+	$(CH_3)_3N$	0.4 ± 0.5	7.6 ± 0.4	0.73

[a] Rate constants shown with standard deviation were measured in this work. Others were taken from the review by E. Grunwald and M. Cocivera, *Discussions Faraday Soc.*, **39**, 105 (1965), and references cited therein. [b] These measurements were reproduced with somewhat lower accuracy in the present work: $10^{-8}k_7 = 3.4 \pm 0.3$ sec^{-1} M^{-1}; $10^{-8}(k_6 + k_7) = 3.7 \pm 0.3$ sec^{-1} M^{-1}.

The mechanism of the reaction in which water participates is fairly well understood. The small methyl-substituent effect and the substantial deuterium isotope effect[3] on k_7 are consistent with the view that the transfer of the two protons in (1) is concerted.[4]

The mechanism of the direct reaction (eq 2) is less well understood. The outstanding fact that must be explained is the marked reduction in k_6 on methyl substitution. Two possible explanations come to mind. The effect is steric; that is, the methyl groups somehow destabilize those conformations in which direct NH·N proton transfer is possible. Or the effect is diffusion kinetic; that is, the methyl groups somehow reduce the speed at which the ammonium ion and the amine molecule become nearest neighbors. But it is clear from the uniformly high values of k_7 (Table I) that the methyl groups do not impede the formation of a solvent-separated encounter complex. The reduction in diffusion rate, if any, must therefore involve the conversion of the solvent-separated to the nearest-neighbor complex. These ideas are made more precise by dividing the direct reaction 2 into steps, as in eq 3–5, where B (or B) denotes a molecule

$$\mathrm{BH^+(aq)} + B\mathrm{(aq)} \underset{k_{\mathrm{diss}}}{\overset{k_{\mathrm{ass}}}{\rightleftharpoons}} \mathrm{BH^+ \cdot OH_2} \cdot B\mathrm{(aq)} \qquad (3)$$

$$\mathrm{BH^+ \cdot OH_2} \cdot B\mathrm{(aq)} \underset{k_{\mathrm{w}}}{\overset{k_{-\mathrm{w}}}{\rightleftharpoons}} \mathrm{BH^+} \cdot B\mathrm{(aq)} \qquad (4)$$

$$\mathrm{BH^+} \cdot B \overset{k_{\mathrm{p}}}{\rightleftharpoons} \mathrm{B \cdot H}B^+ \qquad (5)$$

of amine. On this basis, the explanation of the effect of methyl substitution as a steric effect would visualize that reaction 5 is rate determining and that k_p depends markedly on structure, while the alternative explanation would have reaction 4 be rate determining and structure sensitive.

We believe our experiment tests these theories and eliminates the hypothesis that reaction 5 is rate determining. We have measured the rate constants for reversible proton transfer with and without solvent participation between trimethylammonium ion and

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(1) Work supported by the National Science Foundation under Grant GP 3921.

(2) E. Grunwald, A. Loewenstein, and S. Meiboom, *J. Chem. Phys.*, **27**, 630 (1957); A. Loewenstein and S. Meiboom, *ibid.*, **27**, 1067 (1957). The present notation for the rate constants follows that of these authors.

(3) R. J. Day and C. N. Reilly, *J. Phys. Chem.*, **71**, 1588 (1967).

(4) T. M. Lowry, *J. Chem. Soc.*, 2554 (1927); C. G. Swain, *J. Am. Chem. Soc.*, **72**, 4578 (1950).

ammonia (k_{+6}, k_{-6}, k_{+7}, k_{-7}; see eq 6). Rates

$$\mathrm{(CH_3)_3NH^+\ (+H_2O) + NH_3} \underset{k_{-6}(k_{-7})}{\overset{k_{+6}(k_{+7})}{\rightleftharpoons}} \mathrm{(CH_3)_3N\ (+H_2O) + HNH_3^+} \quad (6)$$

of proton exchange were measured at 30° and 0.5 M ionic strength, using nuclear magnetic resonance techniques similar to those used in previous studies of symmetrical proton exchange.[2,5] The equilibrium constant for reaction 6 is 0.22 under these conditions, not too different from the value of unity for the analogous constant in symmetricial exchange. The new rate constants are listed in Table I. It can be seen that k_{+7} and k_{-7} are of the same magnitude as, and fit into the pattern established by, k_7 for symmetrical exchange. On the other hand, k_{+6} and k_{-6} are experimentally indistinguishable from zero.

In interpreting these results, we reason as follows. It is clear from the high value of k_7 that the water molecule in $\mathrm{(CH_3)_3NH^+ \cdot OH_2 \cdot N(CH_3)_3}$ causes no adverse steric effect. Because of the close similarity in steric requirements of H_2O and NH_3, we expect, by analogy, that the ammonia molecule in $\mathrm{(CH_3)_3NH^+ \cdot NH_3}$ also offers no adverse steric effect. Reversible proton transfer within the complex should therefore be relatively fast and, if reaction 5 were rate determining, k_{+6} and k_{-6} should be relatively high, certainly high enough to be measured easily. This prediction is contrary to fact.

Another method for ruling out the hypothesis that reaction 5 is rate determining makes use of the Bronsted relationship. Consider a reaction of the proton donor, NH_4^+, with a series of bases. If proton transfer were rate determining, the rate constant would increase fairly regularly with K_B of the base. For reaction 1, such a relationship is in fact observed: NH_4^+ reacts faster with trimethylamine than it does with the weaker base, ammonia (Table I). For reaction 2, the opposite is the case: k_6 for $NH_4^+ + NH_3$ is more than 15 times greater than k_{-6} for $NH_4^+ + N(CH_3)_3$.

If reaction 4 is rate determining, it is useful to represent k_6 as in (7), where g is the probability that the prototropic complex $\mathrm{BH^+ \cdot \mathit{B} \rightleftarrows B \cdot H\mathit{B}^+}$ will dissociate

$$k_6 = gk_{\mathrm{ass}}k_{-\mathrm{w}}/(k_{\mathrm{diss}} + k_{-\mathrm{w}}) \quad (7)$$

to form products. For symmetrical exchange, $g = {}^1/_2$; otherwise, g can be approximated by $K/(1 + K)$, where K is the equilibrium constant for the over-all reaction 2. Since $k_{-\mathrm{w}} < k_{\mathrm{diss}}$ by hypothesis, eq 7 can be further simplified as in (8), where $K_{\mathrm{ass}} = k_{\mathrm{ass}}/k_{\mathrm{diss}}$.

$$k_6 = gK_{\mathrm{ass}}k_{-\mathrm{w}} \quad (8)$$

Analysis of the factors in (8) then leads to the conclusion that the marked reduction in k_6 upon methyl substitution must be attributed primarily to a reduction in $k_{-\mathrm{w}}$. The effect of methyl substitution on K_{ass} should be relatively small and may even be an increase. For example, a statistical model similar to that used by Fuoss[6] in the calculation of ionic association constants would lead us to expect that K_{ass} is on the order of 0.2 M^{-1}, and that it increases slightly upon methyl substitution. If we adopt a uniform value of 0.2 M^{-1} for K_{ass} and estimate g as suggested above, then $k_{-\mathrm{w}} \approx 5k_6(1 + K)/K$ on the premise of eq 8, with a probable accuracy within a factor of 3.

The theory that in ionic reactions work must be done against powerful solvation forces to bring the reactant molecules into contact is, of course, well known and of long standing, and the theory is supported by evidence from many sources. However, our knowledge of rate constants for fast processes like those in eq 4 and involving organic molecules is still very incomplete. The present work suggests that such processes, though very fast, are nevertheless subject to marked substituent effects, in such a direction that $k_{-\mathrm{w}}$ decreases with increasing alkyl substitution, other things being equal.[7] This inference is consistent with rate measurements on the exchange of water molecules between the solvation shell of alkylamines and bulk water, eq 9, where the rate constant k_{H} also decreases markedly with alkyl substitution.[8]

$$\mathrm{HOH(aq) + B \cdot \mathit{HOH} \xrightarrow{k_H} B \cdot HOH + \mathit{HOH}(aq)} \quad (9)$$

A roughly monotonic relationship between k_{H} and $k_{-\mathrm{w}}$ is to be expected, especially if the dehydration step occurs by a dissociative (or SN1) mechanism, as it does in the case of various divalent inorganic cations.[9,10]

Regarding the equilibrium constant for reaction 4, it may be relevant that organic nonelectrolytes in aqueous solution are *salted-in* by salts with large organic ions, and that the extent of salting-in tends to increase with molecular size.[11] Such evidence, and consistent evidence from kinetic salt effects,[12] suggests to us that alkyl substitution probably shifts the equilibrium in eq 4 to the right. Association constants for homoconjugation, $\mathrm{BH^+ + B \rightleftarrows BH^+ \cdot B}$, for ammonia and the three methylamines in acetonitrile are all of the same order of magnitude.[13]

Experimental Section

Proton exchange rates were measured by nuclear magnetic resonance techniques, as described previously.[5] The NH proton exchange rate, R_{NH}, of trimethylammonium ion was obtained from the $(CH_3)_3$ proton resonance, recorded in slow passage, and the NH–OH proton exchange rate, R_{OH}, was obtained from spin–echo measurements of T_1 and T_2 of the water protons under conditions of lifetime broadening.[5] All measurements were made at 30° and at a constant ionic strength of 0.5 M. Reaction mixtures were prepared from pure water, trimethylammonium chloride, ammonium chloride, potassium chloride, and/or constant-boiling HCl. The hydrogen ion concentrations were measured by acid–base titration or with a Beckman research pH-meter. The concentrations of free amine were calculated from $[\mathrm{B}] = K_{\mathrm{A}}[\mathrm{BH^+}]/[\mathrm{H^+}]$.

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(5) E. Grunwald, *J. Phys. Chem.*, 67, 2208 (1963).

(6) R. M. Fuoss, *J. Am. Chem. Soc.*, 80, 5059 (1958).

(7) A more picturesque (though anthropomorphic) description of this phenomenon is that the water molecule in $\mathrm{BH^+ \cdot OH_2 \cdot B}$ is trapped in a cage whose walls consist in part of the N-alkyl groups. For this reason, the present phenomenon is related to the striking encapsulation phenomenon observed recently by H. E. Simmons and C. H. Parks in their work on large bicyclic diamines. Ions such as $\mathrm{N{\equiv}[(CH_2)_{10}]_3{\equiv}NH^+}$ in aqueous solution form hydrates analogous to $\mathrm{BH^+ \cdot OH_2 \cdot B}$, in which the $\mathrm{{\equiv}NH^+ \cdot OH_2 \cdot N{\equiv}}$ grouping is inside the hydrocarbon cage formed by the $(CH_2)_{10}$ groups. The water molecule trapped at such a site exchanges with bulk water relatively slowly; $k_{-\mathrm{w}} \approx 10^6$ sec^{-1}. We thank Dr. Simmons for this private communication. See also *Chem. Eng. News*, **45** (28), 46 (1967).

(8) E. Grunwald and E. K. Ralph, *J. Am. Chem. Soc.*, **89**, 4405 (1967).

(9) T. J. Swift and R. E. Connick, *J. Chem. Phys.*, **37**, 317 (1962).

(10) Z. Luz, *ibid.*, **41**, 1748 (1964).

(11) R. L. Bergen and F. A. Long, *J. Phys. Chem.*, **60**, 1131 (1956).

(12) E. F. J. Duynstee and E. Grunwald, *Tetrahedron*, **21**, 2401 (1965).

(13) J. F. Coetzee, *Progr. Phys. Org. Chem.*, **4**, 76 (1967).

At 30° and in an aqueous solution that is 0.25 *M* in BHCl and 0.25 *M* in KCl, $10^{10}K_A$ = 6.63 for NH_4^+ and 1.46 for Me_3NH^+.[5,14,15] These values were used in all calculations.

Reaction mixtures used in the R_{NH} measurements were 0.25 *M* in Me_3NHCl, (0.25 − *x*) *M* in KCl, *x M* in NH_4Cl, and *N*/417 or *N*/870 in HCl. Kinetic results are shown in Figure 1. The data are represented by the rate law given in the figure caption with a standard error of 2.2%, which is within the experimental error. The intercepts agree to better than 2% with values expected on the basis of previous work.[5] The increased rate upon addition of ammonium chloride permits evaluation of $(k_{+6} + k_{+7})$ at 30°. The result is 1.74×10^8 sec^{-1} M^{-1}; see eq 6.

To obtain k_{+7}, we have measured R_{OH} for (1) 0.25 *M* NH_4Cl and 0.25 *M* KCl at pH 2.8–4.75; (2) 0.25 *M* Me_3NHCl and 0.25 *M* KCl at pH 3.0–4.8; and (3) 0.25 *M* NH_4Cl and 0.25 *M* Me_3NHCl at pH 2.76–3.52. In the interpretation of the nmr data, the following values were used for the NH–OH chemical shift: Me_3NH^+–HOH, 5.48 ppm; NH_4^+–HOH, 2.32 ppm. On the basis of these chemical shifts it could be shown that the water resonance was measured in the region of lifetime broadening; that is, eq 10 applied. The maximum error of eq 10 relative to a more exact equation for NH–OH proton exchange, reported elsewhere,[16] was 2% in series 1, 12% in series 2, and less than 1% in series 3. In the final calculation of R_{OH} for series 1 and 2, the more exact equation[16] was used. Results were

$$T_2^{-1} - T_1^{-1} = R_{OH}/2[HOH] \qquad (10)$$

Series 1

$$R^1_{OH} = 38.8[NH_4^+] + 0.0332[NH_4^+]^2/[H^+]$$

Series 2

$$R^2_{OH} = 4.8[Me_3NH^+] + 0.0496[Me_3NH^+]^2/[H^+]$$

Series 3

$$R^3_{OH} = R^1_{OH} + R^2_{OH} + 0.218[Me_3NH^+][NH_4^+]/[H^+]$$

In series 1, the first-order term, which expresses the rate of acid dissociation, is about 10% higher than expected on the basis of previous work.[14] The discrepancy is within the combined experimental error. The second term evaluates k_7 for reaction of $NH_4^+ + OH_2 + NH_3$ as 0.50×10^8 sec^{-1} M^{-1}, about one-half the value reported for this constant 10 years ago.[17] We regard the new value as accurate to ±8%.

In series 2, the small first-order term was not obtained by adjustment to the data but was taken from the measurements of R_{NH}. The second term evaluates k_7 for reaction of $Me_3NH^+ + OH_2 + NMe_3$ as $(3.4 \pm 0.4) \times 10^6$ sec^{-1} M^{-1}, in agreement with earlier work.[5]

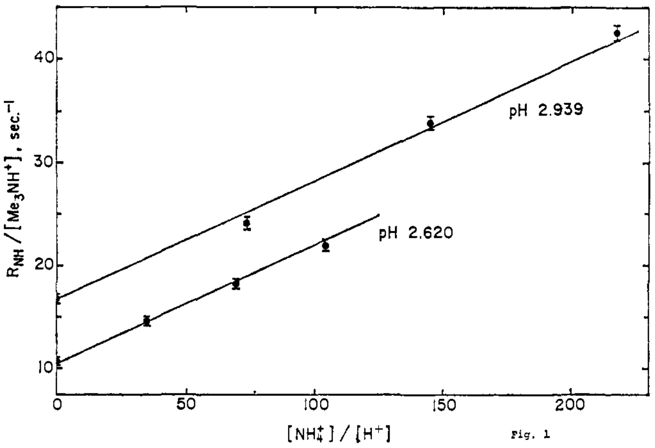

Figure 1. Kinetic plot for the NH proton exchange rate, R_{NH}, of trimethylammonium ion in the presence of ammonium ion at 0.5 *M* ionic strength and 30°. The horizontal bars near each point show the effect of 2% experimental error. The straight lines represent the rate law, $R_{NH}/[Me_3NH^+] = 4.8_5 + 0.054_0[Me_3NH^+]/[H^+] + 0.115_5[NH_4^+]/[H^+]$.

In series 3, the rate in excess of $R^1_{OH} + R^2_{OH}$ has the correct pH dependence for reversible proton exchange according to eq 6, as shown by the data in Table II. In each cycle of exchange, consisting of forward *and* back reaction, *two* water molecules exchange a proton with an NH site. Moreover, because of the existence of dynamic equilibrium, the forward rate R_{+7} is equal to the reverse rate R_{-7}, and either of these rates is evaluated by the results in series 3 as $0.109[Me_3NH^+][NH_4^+]/[H^+]$, with a standard error of ±5%. It then follows, upon use of K_A- values given earlier, that k_{+7} and k_{-7} have values as shown in Table I.

Table II. Analysis of R_{OH} in Series 3

$[H^+]$, m*M*	T_2^{-1}, sec^{-1}	T_1^{-1}, sec^{-1}	R_{OH}^3, *M* sec^{-1}	R_{OH}^1, *M* sec^{-1}	R_{OH}^2, *M* sec^{-1}	$R_{+7}[H^+] \times [NH_4^+]^{-1} \times [Me_3NH^+]^{-1}$
1.74	0.521	0.322	21.7	10.9	3.0	0.108
0.61_2	0.685	0.324	39.3	13.1	6.2	0.098
0.41_8	0.837	0.323	56.0	14.6	8.6	0.110
0.305	0.993	0.326	72.7	16.5	11.4	0.109
					Av	0.109

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(14) M. T. Emerson, E. Grunwald, and R. A. Kromhout, *J. Chem. Phys.*, **33**, 547 (1960).

(15) R. G. Bates and G. D. Pinching, *J. Am. Chem. Soc.*, **72**, 1393 (1950).

(16) E. Grunwald and E. Price, *ibid.*, **86**, 2970 (1964), eq 2.

(17) S. Meiboom, A. Loewenstein, and S. Alexander, *J. Chem. Phys.*, **29**, 969 (1958).