[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND THE LABORATORY FOR NUCLEAR SCIENCES, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Mechanism of Exchange of Hydrogen between Ammonium and Hydroxyl Groups. I[1-3]

BY C. GARDNER SWAIN AND MORTIMER M. LABES

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The rate of deuterium exchange between ammonium bromide and methanol in dimethylformamide solution containing hydrogen bromide at 0° is first order in methanol and inversely first order in hydrogen bromide. A mechanism is proposed involving termolecular formation of a hydrogen-bonded ammonia–alcohol complex, dissociation of this intermediate to free ammonia and alcohol and return through the reverse of these two steps.

Although transfers or exchanges of protons between nitrogen and oxygen atoms ordinarily have half-lives of less than a minute, two exceptions with much slower rates were known when the work reported in this paper was begun.[4] Anderson, Briscoe and Spoor[5] showed that deuterium exchange between hexamminocobaltic chloride and water in aqueous buffers at 20° is inversely first order in hydrogen ion, with a half-life of an hour at *p*H 4.7. They suggested the mechanism

$$Co(NH_3)_6^{+++} + OH^- \rightleftarrows Co(NH_3)_5NH_2^{++} + H_2O$$

Brodskii and Sulima[6] found that deuterium exchange in a very concentrated solution of ammonium nitrate in heavy water at 0° can be stopped short of completion by precipitation with acetone after one to ten minutes and that the presence of added nitric acid slows down the exchange. Although the data were rough, Brodskii considered them additional evidence for his theory that ability to exchange hydrogen rapidly is dependent primarily on the presence of an unshared electron pair on the atom bearing the hydrogen, because this permits an easy one-step mechanism with a four-center transition state.

We have now studied the exchange between ammonium-*d* bromide and methanol and between ammonium bromide and methanol-*d* in much more dilute solutions in a non-exchanging solvent, dimethylformamide, containing hydrogen bromide at 0° to determine the kinetic order and mechanism.

Kinetics of Isotope Exchange.—In a system containing ND, NH, OD and OH bonds there are four kinds of hydrogen exchange occurring[7]

$$ND + OH \longrightarrow NH + OD \qquad (1)$$

$$NH + OD \longrightarrow ND + OH \qquad (2)$$

$$ND + OD \longrightarrow ND + OD \qquad (3)$$

$$NH + OH \longrightarrow NH + OH \qquad (4)$$

We shall refer to the first two kinds of exchange as D–H exchange, to the third kind as D–D exchange and to the fourth kind as H–H exchange; and to the rates of the four kinds as R_1, R_2, R_3 and R_4, respectively. Let a, b, c and d be constant molarities such that

$$\begin{aligned} a &= [ND] + [NH] \\ b &= [OD] + [OH] \\ c &= [ND] \text{ at } t = 0 \\ d &= [OD] \text{ at } t = 0 \end{aligned}$$

If the measured exchange is $-\Delta(ND) = +\Delta(OD) = x$, then the actual concentrations at any time are

$$\begin{aligned} [ND] &= c - x \\ [NH] &= a - c + x \\ [OD] &= d + x \\ [OH] &= b - d - x \end{aligned}$$

Let Q be the total rate of hydrogen exchange that would occur if all deuterium were replaced by pro-

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(1) *Cf.* C. G. Swain, J. T. McKnight, M. M. Labes and V. P. Kreiter, THIS JOURNAL, **76**, 4243 (1954); for further details, *cf.* M. M. Labes Ph.D. thesis, M.I.T., February, 1954.

(2) Part II, C. G. Swain, J. T. McKnight and V. P. Kreiter, *ibid.*, **79**, 1088 (1957).

(3) This work was supported in part by the research program of the Atomic Energy Commission. Reproduction permitted for any purpose of the United States Government.

(4) A third exception can be cited but is subject to some doubt. A. G. Ogston reported that conductivity increased slowly for ten minutes when ammonia was added to methyl alcohol and attributed this to slow ionization (*J. Chem. Soc.*, 1023 (1936)). However, other workers found only fast ionization in similar systems (C. W. Hoerr, M. R. McCorkle and A. W. Ralston, THIS JOURNAL, **65**, 328 (1943); R. P. Bell and R. G. Pearson, *J. Chem. Soc.*, 3443 (1953)).

Proton transfers or exchanges between two oxygen atoms also have been studied. W. J. C. Orr reported that deuterium exchange between ethanol and water required many hours at 25° (*Trans. Faraday Soc.*, **32**, 1033 (1936)), but this was not confirmed by four groups of workers (J. C. Jungers and K. F. Bonhoeffer, *Z. physik. Chem.*, **A177**, 460 (1936); H. Kwart, L. P. Kuhn and E. L. Bannister, THIS JOURNAL, **76**, 5998 (1954); J. Hine and C. H. Thomas, *ibid.*, **75**, 739 (1953); **76**, 612 (1954); M. M. Labes, Ph.D. thesis, M.I.T., February, 1954).

A slow proton transfer from one oxygen to another which was discovered recently is the slow protonation of hypochlorous acid in water solution at 25° in the presence of *t*-butyl alcohol, with which the hypochlorous acidium ion reacts as fast as it forms (M. Anbar and I. Dostrovsky, *J. Chem. Soc.*, 1094 (1954)). The rate constant for protonation is about 2 M^{-1} sec.$^{-1}$, although its determination is complicated slightly by other mechanisms for chlorination which occur concurrently in buffer solutions.

Recently some rates of much faster ionizations and exchanges, with half-lives of less than a second, have been determined by the techniques of polarography (P. Delahay and W. Vielstich, THIS JOURNAL, **77**, 4955 (1955); K. Wiesner, *Anal. Chem.*, **27**, 1712 (1955)), sound absorption (M. Eigen, *Disc. Faraday Soc.*, **17**, 194 (1954); M. Eigen and J. Schoen, *Z. Elektrochem.*, **59**, 483 (1955), *C. A.*, **49**, 15396 (1955)) and nuclear magnetic resonance (I. Weinberg and J. R. Zimmerman, *J. Chem. Phys.*, **23**, 748 (1955); H. S. Gutowsky and A. Saika, *ibid.*, **21**, 1688 (1953); R. A. Ogg, Jr., *ibid.*, **22**, 560 (1954); *Disc. Faraday Soc.*, **17**, 215 (1954)). However, each of these methods has limitations which have deterred detailed studies of mechanism.

(5) J. S. Anderson, H. V. A. Briscoe and N. L. Spoor, *J. Chem. Soc.*, 361 (1943).

(6) A. I. Brodskii and L. V. Sulima, *Doklady Akad Nauk S.S.S.R.*, **74**, 513 (1950); *C. A.*, **45**, 424 (1951); A. I. Brodskii, *Zhur. Obshchei Khim.*, **24**, 413 (1954); *C. A.*, **48**, 8621 (1954).

(7) The statistical problem arising from four equivalent exchangeable hydrogens on the ammonium ion is thus taken care of in practice simply by using the concentrations of nitrogen-bound deuterium and nitrogen-bound protium rather than considering the concentrations of all five varieties of ammonium ion. The assumption that substitution of deuterium for one of the protiums on nitrogen does not change the reactivity of the nitrogen unshared pair or of the other bonds or hydrogens is supported by the fact that the rate of reaction of N-deuteropiperidine is within 3% of that of piperidine with either *o*- or *p*-nitrochlorobenzene in xylene at 116° (M. F. Hawthorne, THIS JOURNAL, **76**, 6358 (1954)) and the fact that substitution or elimination rates with ethanolic sodium ethoxide at 25° are the same for α-deuteroisopropyl bromide as for isopropyl bromide within 5% (V. J. Shiner, Jr., *ibid.*, **74**, 5285 (1952)).

tium so that $[\mathrm{NH}] = a$, $[\mathrm{OH}] = b$, $[\mathrm{ND}] = [\mathrm{OD}] = c = d = x = 0$. Q is the most significant rate physically, since it is the rate of H–H exchange that would occur at the same total concentrations (a and b) without a tracer. In attempting to measure this rate Q by using a tracer, the concentrations of NH and OH bonds are necessarily less at the same total concentrations because some of these bonds are labeled, *i.e.*, ND or OD instead. In the actual deuterated system used, the rate of H–H exchange is therefore less than Q and is given by

$$R_4 = Q\left(\frac{[\mathrm{NH}]}{[\mathrm{ND}] + [\mathrm{NH}]}\right)\left(\frac{[\mathrm{OH}]}{[\mathrm{OD}] + [\mathrm{OH}]}\right) = \frac{Q[\mathrm{NH}][\mathrm{OH}]}{ab}$$

This expression for R_4 is correct regardless of the mechanism or kinetic order of the exchange process. Note that Q is not a rate constant but instead a rate; the factors multiplying Q represent not concentrations but instead the probability that colliding nitrogen and oxygen bonds will both have protium rather than deuterium. If we neglect isotope effects, the rates of the other kinds of hydrogen exchange are

$$R_1 = Q[\mathrm{ND}][\mathrm{OH}]/ab$$
$$R_2 = Q[\mathrm{NH}][\mathrm{OD}]/ab$$
$$R_3 = Q[\mathrm{ND}][\mathrm{OD}]/ab$$

and the measured rate is

$$-\mathrm{d(ND)}/\mathrm{d}t = R_1 - R_2 = (Q/ab)([\mathrm{ND}][\mathrm{OH}] - [\mathrm{NH}][\mathrm{OD}])$$

The total rate, $S = R_1 + R_2 + R_3 + R_4$, equals Q, as can be shown by combining the four expressions and substituting a for $[\mathrm{ND}] + [\mathrm{NH}]$ and b for $[\mathrm{OD}] + [\mathrm{OH}]$.

If there are significant isotope effects the equations should be modified. Let the isotope rate effect for nitrogen bonds (NH/ND) be f and that for oxygen bonds (OH/OD) be g. Then the first two rates will be

$$R_1 = Q[\mathrm{ND}][\mathrm{OH}]/fab$$
$$R_2 = Q[\mathrm{NH}][\mathrm{OD}]/gab$$

However, fractionation of isotopes at equilibrium is negligible in this reaction. Evidence for this is the agreement within experimental error (±5%) of measured infinite time points in kinetic runs with ones calculated assuming random distribution of deuterium between NH and OH bonds, shown by some examples in Table I.

TABLE I

EQUILIBRIUM DISTRIBUTION OF DEUTERIUM IN EXCHANGES BETWEEN 0.30 *M* AMMONIUM BROMIDE AND METHANOL IN DIMETHYLFORMAMIDE AT 0°

Run	[MeOH],[a] *M*	[HBr], *M*	Reaction at $t = \infty$ found[b]/calcd.,[c] %
118	1.2	0.00	100
122	1.8	.13	97[b]
134	1.2	.013	100
135	1.2	.0013	100
147	0.10	.013	99
48	0.10	.010[d]	99[d]

[a] Entries in this column are actually total methanol = $[\mathrm{MeOH}] + [\mathrm{MeOD}] = b$. [b] After more than ten half-lives, except only five half-lives in run 122 and eight in run 147. [c] Assuming $K = 1$. [d] Triethylammonium picrate and hydrogen chloride in toluene used instead of ammonium bromide and hydrogen bromide in dimethylformamide.

Hence the equilibrium constant

$$K = \frac{[\mathrm{NH}][\mathrm{OD}]}{[\mathrm{ND}][\mathrm{OH}]} = \frac{g}{f}$$

is unity and $g = f$. The other rates are therefore

$$R_3 = Q[\mathrm{ND}][\mathrm{OD}]/f^2ab$$
$$R_4 = Q[\mathrm{NH}][\mathrm{OH}]/ab$$

Then the total rate, $S = R_1 + R_2 + R_3 + R_4$, is

$$S = Q\left(\frac{[\mathrm{ND}] + f[\mathrm{NH}]}{fa}\right)\left(\frac{[\mathrm{OD}] + f[\mathrm{OH}]}{fb}\right)$$

If tritium had been used instead of deuterium, the first concentration inside each factor would have been negligible relative to the second, and S would still equal Q. Since this is not the case in the work described in the present paper, the total rate S changes with time during the course of a kinetic run and is not a very useful quantity.

In spite of this variation, the calculated kinetics is first order, and a simple expression for Q/f can be obtained.

$$-\frac{\mathrm{d(ND)}}{\mathrm{d}t} = R_1 - R_2 = \frac{Q}{fab}([\mathrm{ND}][\mathrm{OH}] - [\mathrm{NH}][\mathrm{OD}])$$

$$+\frac{\mathrm{d}x}{\mathrm{d}t} = \frac{Q}{fab}(bc - ad - (a + b)x)$$

Integrating and noting that $x = 0$ at $t = 0$ gives

$$+\ln\left[1 - \frac{(a + b)x}{bc - ad}\right] = -\frac{Qt(a + b)}{fab}$$

Since $R_1 = R_2$ at equilibrium

$$[\mathrm{ND}]_\infty[\mathrm{OH}]_\infty = [\mathrm{NH}]_\infty[\mathrm{OD}]_\infty$$
$$(c - x_\infty)(b - d - x_\infty) = (a - c + x_\infty)(d + x_\infty)$$
$$x_\infty = \frac{bc - ad}{a + b}$$

Thus if k_e is the experimental first-order rate constant from any kinetic run

$$k_e = \frac{-2.303}{t}\log[1 - (x/x_\infty)]$$

and if we define the rate R as Q/f, then

$$R = \left(\frac{ab}{a + b}\right)k_e \qquad (1)$$

Since the expression for the rate R in equation 1 is the same as in the simpler case where $f = 1$,[8] the kinetics of D–H exchange gives no indication that f differs from unity unless independent rate measurements are made on one of the other exchanges, T–H or T–D. In the following paper[2] an isotope effect determined in a similar ammonium salt–methanol exchange reaction will be shown to differ significantly from unity by comparing rates of D–H and T–H exchanges. For the present purpose, *i.e.*, for determining the kinetic order with respect to each of the reactants, it is not necessary to determine the value of f since f is a constant from one run to another. Therefore the kinetic order of R with respect to a, b, acid, etc., must be the same as that of Q, since R is defined as Q/f. The rate Q is the physically significant rate of H–H exchange of NH_4^+ with CH_3OH when $[\mathrm{NH}] = a$ and $[\mathrm{OH}] = b$. Since R, Q, f and k_e are each constant within a kinetic run, it is the variation in R from one run to another which is diagnostic of mechanism.

[8] H. A. C. McKay, *Nature*, **142**, 997 (1938).

Results

Runs 131 and 120 in Table III show that the first-order rate constant, k_e (and hence also R), is independent of whether the label is in the ammonium bromide or in the methanol. This is as predicted, because equation 1 is symmetrical with respect to a and b; hence interchanging N with O does not change the measured rate.

Table II shows that the exchange is first order in total methanol. Table III shows that it is inverse first order in total hydrogen ion. Along with the mean R for each run is given the average deviation from the mean for all points of the run.

TABLE II

EXCHANGE OF 0.30 M AMMONIUM BROMIDE WITH METHANOL AND 0.013 M HYDROGEN BROMIDE IN DIMETHYLFORMAMIDE AT 0°

Run	[MeOH],[a] M	R,[b] M sec.$^{-1}$ × 10^4	R/[MeOH], sec.$^{-1}$ × 10^4
147	0.10[c]	0.63 ± 0.1	6.3
149	.20[c]	1.24 ± .1	6.2
148	.40[c]	2.4 ± .2	6.0
134	1.20[c]	4.4 ± .6	3.7

[a] Total methanol = b. [b] This rate is the R in equation 1. [c] Deuterium initially in the methanol.

TABLE III

EXCHANGE OF 0.30 M AMMONIUM BROMIDE WITH 1.2 M METHANOL IN DIMETHYLFORMAMIDE AT 0°

Run	[HBr],[a] M	R,[b] M sec.$^{-1}$ × 10^4	R[HBr] M^2sec.$^{-1}$ × 10^7
135	0.0013[c]	46 ± 2	6.0
137	.0026[c]	23 ± 4	6.0
134	.013[c]	4.4 ± 0.6	5.7
133	.033[c]	1.7 ± .2	5.6
132	.065[c]	1.0 ± .2	6.5
131	.13[c]	0.5 ± .1	6.5
120	.13[d]	.5 ± .1	6.5

[a] [HBr] = h = stoichiometric concentration of hydrogen bromide. [b] This rate is the R in equation 1. [c] Deuterium initially in the methanol. [d] Deuterium initially in the ammonium bromide.

Thus the rate R is

$$R = kab/h \qquad (2)$$

where k is independent of a, b and h, a is four times the total concentration of ammonium ion, b is total methanol and h is total hydrogen ion, probably present in the solution predominantly in the form of conjugate acid of the solvent, $OHCNH(CH_3)_2^+$ + $OHCND(CH_3)_2^+$, *i.e.*, as solvated protons.

To be sure that added methanol was not decreasing the acidity of the solution, its effect on an acid–base indicator equilibrium was examined. The absorption maximum for the acid form of methyl orange in dimethylformamide containing hydrogen bromide is at 520 mμ. The percentage transmittance at this wave length was found to be inversely proportional to the concentration of hydrogen bromide but did not change when 0.30 M methanol was added to a solution 0.12 M in hydrogen bromide. Therefore adding methanol does not significantly change the acidity of hydrogen bromide in dimethylformamide.

Mechanism.—The kinetic expression (equation 2) demonstrates that the transition state contains ammonium ion plus methanol *minus a proton.* Since the proton is completely gone at the transition state, it is very probable that it is lost to the solvent in a prior step. It could be a proton originally on the ammonium ion or one originally on the alcohol.

If the proton were removed from the ammonium ion, the mechanism would be

$$\text{Solvent} + NH_4^+ \underset{k_b}{\overset{k_a}{\rightleftarrows}} \text{solvent H}^+ + NH_3$$

$$CH_3OH + NH_3 \xrightarrow{k_c} \text{interchange of protons}$$

with k_b[solvent H$^+$] >> k_c[CH_3OH] over the range of acidity that we have studied. The transition state could be a four-center cyclic one in the k_c step. However the k_c step of such a mechanism would not be possible for tertiary ammonium ions. The fact that they exhibit similar rates and kinetic dependence on acidity (see following paper[2]) suggests that they have a similar mechanism. Hence we conclude that the proton is probably removed not from the ammonium ion but from the alcohol.

A *bimolecular* removal of the proton from the alcohol would give an alkoxide ion intermediate

$$\text{Solvent} + CH_3OH \underset{k_b}{\overset{k_a}{\rightleftarrows}} \text{solvent H}^+ + CH_3O^-$$

$$CH_3O^- + NH_4^+ \underset{k_d}{\overset{k_c}{\rightleftarrows}} CH_3OH + NH_3$$

However, the concentration of alkoxide ion in such a strongly acid solution would be extremely low. The exchange with ethanol in ethanol solution exhibits similar rates and kinetic dependence on acidity (see following paper[2]) suggesting a similar mechanism, and in that case the concentration of ethoxide ion can be calculated to be three powers of ten lower than that of the transition state (see Experimental section of present paper for details of calculation). Hence it is unlikely that a free alkoxide ion is an intermediate.

We conclude that the loss of the proton from the alcohol is probably a *termolecular* process and that the mechanism is

$$\text{Solvent} + CH_3OH + NH_4^+ \underset{k_b}{\overset{k_a}{\rightleftarrows}} \text{solvent H}^+ + \text{I}$$

$$\text{I} \underset{k_d}{\overset{k_c}{\rightleftarrows}} CH_3OH + NH_3$$

where intermediate I is a hydrogen-bonded methanol–ammonia complex ($CH_3OH{-}{-}{-}NH_3$ or $CH_3O^-{-}{-}{-}HNH_3^+$ or a structure intermediate between these extremes) and k_b[solvent H$^+$] >> k_c over the range of acidity that we have studied. The transition state (point of highest free energy) should then be in the proton exchange (k_c) process. However, k_a may be either larger or smaller numerically than k_c and is probably smaller, considering the chemistry involved. The k of equation 2 is $k_a k_c/k_b$.

The proton exchange reaction k_c may itself be multistep. For example, if the intermediate is $CH_3O^-{-}{-}{-}HNH_3^+$, $CH_3OH{-}{-}{-}NH_3$ may be a second intermediate preceding $CH_3OH + NH_3$. However, since our experiments do not require process k_c to be more than one step, we have written the simplest possibility. Even this involves four steps (k_a, k_c, k_d and k_b) and three intermediates between ammonium ion and exchanged ammonium ion.

An unusual consequence of this mechanism is that k_d, one of the rate constants for the step involving the transition state, does not appear in the rate expression. This result is calculated simply from the usual steady state assumptions, *i.e.*, that rate of formation of each intermediate equals its rate of removal.

Experimental

The ammonium bromide was Mallinckrodt analytical reagent dried before use at 110° for at least 12 hr. Ammonium-*d* bromide was prepared by successive equilibrations with 99.8% deuterium oxide from the Stuart Oxygen Co., until an appreciable deuterium enrichment existed. Methanol-*d* was prepared by the hydrolysis of pure methyl borate with 99.8% deuterium oxide.[9] The methanol-*d* so obtained was refluxed over dry magnesium methoxide and distilled. Hydrogen bromide and hydrogen chloride gas were obtained from the Matheson Chemical Co. Solutions in dimethylformamide were prepared by passing the gas through a Dry Ice trap before bubbling the gas into solution. Dimethylformamide, du Pont technical grade, was purified by fractional distillation through a 6-foot Podbielniak column at reduced pressure or by fractionation at atmospheric pressure after treatment with solid potassium hydroxide and calcium oxide.[10] The *o*-fluorotoluene was Eastman Kodak Co. white label grade redistilled, b.p. 113–114°. Other materials are described in the following paper.[2]

In all the work reported, samples of ammonium bromide were isolated from the reaction mixture and equilibrated with water; the deuterium concentration of the resulting water was a measure of the amount of exchange which had occurred. Prior to starting a kinetic run, the required amount of a stock solution of salt in dimethylformamide was placed in a glass-stoppered test-tube. The required amounts of stock solutions of hydrogen bromide and methanol in dimethylformamide and additional pure solvent were combined in a volumetric flask. After keeping the volumetric flask and the glass-stoppered test-tube in a stirred ice-water thermostat for 30 minutes, the reaction was started by pouring the contents of the volumetric flask into the test-tube and shaking the solution in the ice-bath for about one minute. The acid and salt concentrations in the reacting solution were determined by titrating an aliquot first with 0.1 *M* sodium hydroxide and brom thymol blue, then with 0.1 *N* mercuric nitrate and diphenylcarbazide. To follow the rate, 1-ml. aliquot samples were added to the quenching solution of 60 ml. of diethyl ether in a separatory funnel fitted with a glass wool plug and porcelain filter plate. The reaction time was taken as the interval between mixing the reactants and adding the aliquot to the ether. The separatory funnel was shaken immediately and the salt precipitated quickly. The separatory funnel was connected to a vacuum line and the quenching solution drawn off leaving the precipitated salt on the porcelain plate and glass wool plug. The funnel was then connected to a vacuum distillation train consisting of three traps. The system was evacuated to 1 mm. and heated with a microburner to remove traces of organic vapors and water. It was then opened to the atmosphere through a protective trap in a Dry Ice–acetone mixture. The stopcock of the separatory funnel was closed and 0.5 to 1 ml. of distilled water was added to dissolve the ammonium bromide. The water was then allowed to enter the first trap of the distillation train, the system again evacuated and the water distilled to the second trap of the train, which contained potassium permanganate and calcium oxide. Dry air was admitted to the system and the second trap heated to boiling. The system was then evacuated again, and the water was distilled to the third trap of the distillation train through a glass wool plug designed to stop permanganate spray. Six duplicate apparatus for running six simultaneous distillations were employed. Mercurometric titrations of the salt remaining in the separatory funnel and first trap after distillation showed that the precipitations were close to quantitative. After use, the traps containing potassiun permanganate and calcium oxide were rinsed with water, then with an oxalic acid–nitric acid solution and finally with distilled water. All other traps were washed four to six times with distilled water. Silicone grease was used on all ground-glass connections. The apparatus was dried in an oven at 110° overnight, and the assembled distillation trains were evacuated to 1 mm. and heated with a microburner to remove traces of moisture.

The apparatus used to determine the deuterium concentration of the water samples was a falling-drop apparatus similar in design to that of Schloerb and co-workers.[11] It consisted of a graduated dropping tube containing *o*-fluorotoluene, a micropipet to deliver droplets of uniform size (0.022 ml.) into the dropping tube, and a thermostat to maintain the temperature of the dropping tube at about 27° and constant to ±0.001°. At least four droplets of each sample to be analyzed were allowed to fall through the dropping tube and their drop times between two lines 15 cm. apart were recorded on stopwatches. A standard of conductivity water was dropped with each series of samples. The conductivity water was prepared in a metal still, collected under nitrogen, and stored in a Pyrex bottle fitted with an all-glass siphon and protected from the atmosphere with a drying tower containing ascarite, activated charcoal and layers of paraffin.

A calibration curve relating the difference in reciprocals of dropping times for sample and standard (conductivity water) to % deuterium was constructed, using known dilutions of 99.8% deuterium oxide with conductivity water. The calibration curve is linear in the region 0.0 to 2.0 atom % deuterium.

$$\frac{1}{T_d} - \frac{1}{T_d^0} = K(\%\ \mathrm{D})$$

where % D means the excess above that in conductivity water. The reciprocal of dropping time for conductivity water ($1/T_d^0$) varied slightly from day to day, due to a continuous slow upward drift in the temperature of the thermostat, but there was no noticeable drift during the hour required to determine the deuterium concentrations of all the samples from a given kinetic run. A sample containing 1.0% deuterium could be analyzed to ±0.01% deuterium, or 1% accuracy.

All calculations of % exchange between ammonium bromide and methanol were made neglecting exchange with hydrogen bromide. This introduces less than 2% error except in the runs with 0.13 *M* hydrogen bromide, where the possible error is about 5%.

Acidity of Hydrogen Bromide in Dimethylformamide.—Table IV gives transmittances (final intensity/initial intensity) measured with a Beckman model DU spectrophotometer at room temperature.

TABLE IV

TRANSMITTANCE AT 520 mμ OF 5.1×10^{-5} *M* METHYL ORANGE IN DIMETHYLFORMAMIDE SOLUTION

[HBr], *M*	[CH_3OH], *M*	Transmittance, %
0.000	0.00	86
.058	.00	29
.117	.00	15
.117	.30	15

Calculation to Prove that Free Alkoxide Ion Is Not an Intermediate.—The exchange of 0.098 *M* triethylammonium chloride with ethanol in ethanol solution containing 0.77 *M* hydrogen chloride at 0° has a k_e of 7.7×10^{-3} sec.$^{-1}$ and hence a calculated R of 7.5×10^{-4} and a transition state

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[9] T. Charnley, H. A. Skinner and N. B. Smith, *J. Chem. Soc.*, 2288 (1952).

[10] G. R. Leader and J. F. Gormley, THIS JOURNAL, **73**, 5731 (1951).

[11] P. R. Schloerb, B. J. Friis-Hansen, I. S. Edelman, D. B. Sheldon and F. D. Moore, *J. Lab. Clin. Med.*, **37**, 653 (1951).

concentration of $R/5.7 \times 10^{12} = 1.3 \times 10^{-16}$ M.[12] Alkoxide ion cannot be an intermediate in this case at least because its concentration, calculated from the autoprotolysis constant[13] of ethanol (4×10^{-20}), is on a thousandth as large as this, *viz.*, 5×10^{-20}.

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[12] 5.7×10^{12} is the Boltzmann constant times absolute temperature divided by the Planck constant.

[13] B. Gutbezahl and E. Grunwald, THIS JOURNAL, **75**, 571 (1953).

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The Mechanism of Exchange of Hydrogen between Ammonium and Hydroxyl Groups. II[1-3]

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The rate of exchange of hydrogen between substituted ammonium salts and alcohols has been studied as a function of the following variables: isotope used as tracer; concentration and structure of acid, substituted ammonium salt, alcohol and solvent; and temperature. The results are consistent with the mechanism proposed in part I.

In part I, the kinetics of exchange of ammonium bromide with methanol was examined in an inert solvent (dimethylformamide) and found to be consistent with the mechanism

$$\text{Solvent} + \text{ROH} + \text{R}_3\text{NH}^+ \underset{k_b}{\overset{k_a}{\rightleftharpoons}} \text{solvent H}^+ + \text{I}$$

$$\text{I} \underset{k_d}{\overset{k_c}{\rightleftharpoons}} \text{ROH} + \text{R}_3\text{N}$$

where I is a hydrogen-bonded alcohol–amine complex ($\text{ROH}\cdots\text{NR}_3$ or $\text{RO}^-\cdots\text{HNR}_3^+$).

$$\text{Rate} = \frac{k_a[\text{ROH}][\text{R}_3\text{NH}^+]}{1 + (k_b/k_c)[\text{H}^+]} \qquad (1)$$

In this part, structural influences of the substituted ammonium salt, hydroxyl compound and solvent are examined in the light of this mechanism.

The substituted ammonium salts were always deuterated and the alcohol undeuterated at the start of a run, unless otherwise noted. Triethylammonium chloride ("triethylamine hydrochloride" in "Chemical Abstracts") and the solvent methanol were used unless otherwise noted. We use substituted "ammonium" names for simplicity and uniformity with the "ammonium bromide" ("*Chemical Abstracts*" name) of the previous paper, although we recognize that primary, secondary and tertiary ammonium halides are all weaker electrolytes than quaternary ammonium halides as a result of hydrogen bonding.

Reproducibility of the Kinetic Results.—A typical kinetic run is presented in detail in the Experimental section (Table VII) to illustrate the constancy of the experimental first-order rate constants (k_e) within runs. The reproducibility of these rate constants is also good from one run to another considering the speed of many of the runs and the difficulty in quenching the reaction. Table I is a representative sampling of the check runs that were done and shows that the average deviation is under ±5%.

Factors Not Affecting the Rate.—The following variables had little or no effect on the rate (*cf.* Table I): the procedures used for preparing deuterated salt or for drying the alcohol (*cf.* runs 67, 80); the initial locus of the deuterium, whether in the salt or the alcoholic hydroxyl (Part I)[2] or its percentage of the total hydrogen (58, 56); the amount of surface (84, 89); the concentration of more rapidly exchanging ammonium ions, either stronger or weaker acids (119, 89, see Discussion in section 3 below); and the choice of anion (runs 34, 40, 41, 30 in Table IV).

Factors Affecting the Rate. 1. Isotope Used as Tracer.—Comparison of Table II with Tables III and IV shows that tritium exchanges approximately 0.8 as fast as deuterium (*cf.* runs 3 and 106, 4 and 49). If one assumes statistical distribution of deuterium between salt and methanol at equilibrium, as was found to be the case with ammonium bromide and methanol in dimethylformamide solution,[2] the same isotope effect (k_D/k_T = 1.2) must hold for both forward and reverse rate constants.

2. Acid.—Exchange of triethylammonium chloride with methanol was complete in less than 34 sec. at 0° when no acids were added to the methanol solution.

The reaction was studied in basic media since the suggestion was made by Ogston[5] that the net proton transfer from ethanol to diethylamine at 25° is a slow process. It was found that isotope exchange between deuterated diethylamine and either methanol or ethanol as solvent at 0° under comparable experimental conditions was complete in less than 30 sec. Thus hydrogen atoms bound to a free amine are exchanged rapidly in these hydroxylic solvents. A reasonable mechanism might involve either an ammonium ion as an intermediate or a four-center transition state with no intermediate. Higher-speed kinetic methods will have to be used to distinguish these alternatives.

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[1] *Cf.* C. G. Swain, J. T. McKnight, M. M. Labes and V. P. Kreiter, THIS JOURNAL, **76**, 4243 (1954). For further details on deuterium exchanges, *cf.* J. T. McKnight, Ph.D. Thesis, M.I.T., September, 1953; all work with tritium was carried out by V. P. K.

[2] Part I, C. G. Swain and M. M. Labes, THIS JOURNAL, **79**, 1084 (1957).

[3] This work was supported in part by the research program of the Atomic Energy Commission. Reproduction permitted for any purpose of the United States Government.

[4] Atomic Energy Commission Fellow, 1951–1953.

[5] A. G. Ogston, *J. Chem. Soc.*, 1023 (1936).