The Protonation of Nitroalkane Anions by Acetic Acid in Mixed H_2O–D_2O Solvents[1]

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Abstract: The rates of protonation of the anions of nitromethane and nitroethane by acetic acid have been measured in mixed H_2O–D_2O solvents at 25°. These are combined with earlier results of Reitz for the reverse reaction and analyzed using generalized Gross–Butler equations. Use of such equations with neglect of the medium effect cannot account for the data. Most of the contributions to this isotope effect on solvation can be measured independently. The ratio of degenerate activity coefficients for transfer of chloride and acetate ions from light to heavy water is needed, and the value $\gamma_{Cl^-}/\gamma_{Ac^-} = 1.19$ was found *via* emf measurements on the silver salts. The influence of chloride, acetate, and nitroalkane anions on the structure of water is discussed. Fractionation factors for the transition states are in good agreement with those calculated from isotope effects in the reverse reactions. A transition state involving direct proton transfer between acid and base is consistent with all the data, whereas one with transfer *via* a water bridge is incompatible.

Two effects must be considered when comparing reactions in light and heavy water and their mixtures. When the reaction or equilibrium involves large force constant changes in bonds to labile protons, the *exchange effect* predominates. This derives its name because it covers primary and secondary isotope effects arising from exchange of protons for deuterons in reactants and products (or transition states). Interest in the Gross-Butler theory for exchange[3–6] involving the hydronium ion was renewed following a paper by Purlee;[7] in 1963 Salomaa, Schaleger, and Long[8] developed a simple, generalized theory for exchange effects with labile hydrogens from any acid or base. This theory and its assumptions are reviewed by Kresge.[9]

Secondly there is the *transfer*, or *medium effect*, which is essentially an isotope effect on solvation. Kingerley and La Mer[10] were the first to attempt to separate the exchange and medium effects, and their approach is a model for the present study. In a formal treatment of the medium effect Halevi, Long, and Paul[11] showed that this could often account for H_2O–D_2O mixture results as adequately as the exchange effect, and, of course, there were many combinations of the two which could do better than either alone.

Medium isotope effects arise from differences in bulk solvent and solvation shell structures in light and heavy water.[12–14] Swain and Bader[14a] used Bernal's model for tetrahedral coordination of water around ions and some experimental values to develop entropies of transfer of simple ions. Their methods have been criticized,[15] and Salomaa's[16] recent determination of the transfer free energy of potassium chloride demonstrates that Swain's approximate method considerably overestimates this value. Thus there is little information on which to base quantitative estimates of the medium effect.

In principle, the form of the rate dependence on H_2O–D_2O mixture composition can yield information about the participation of solvent bridges in proton-transfer reactions because the generalized Gross–Butler equations for exchange contain a term for every proton involved in a reaction. Huang, Robinson, and Long[17] recently analyzed experimental results for the mutarotation of glucose, catalyzed by various acids and bases, in terms of mechanisms involving varying numbers of water molecules; they were unable to make a clear distinction among all the possibilities.

It is now agreed that no distinction between the proton formulations H_3O^+ and higher hydrates (*e.g.*, $H_9O_4^+$) can be made from solvent mixture theory;[8,18] thus it is meaningless to speculate on water bridges in proton transfers from the hydronium ion. Kreevoy suggested that a different situation would result if a weak acid were used as a proton donor[19] and has interpreted recent preliminary data for solvent and product isotope effects in the reaction between bisulfate ion and allylmercuric iodide as evidence for a water-bridge mechanism.[20]

It is worth noting that in all of these studies the medium effect was neglected. The validity of this assumption has never been established.

As part of a continuing attempt to evaluate the use of the generalized Gross–Butler theory in the elucida-

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tion of mechanisms, this paper presents data on one of the simplest protonation reactions which can be studied using a weak acid—the formation of a nitroalkane from its anion. Specifically, data are reported for the reactions of the anions of nitromethane and nitroethane with acetic acid in mixtures of light and heavy water. The role of the medium effect in these reactions is also considered.

Both steps in the reaction scheme shown below are slow and were used by Junell and Pedersen as early tests of the Brønsted catalysis law. Maron and La Mer have given a comprehensive summary of this early work[21] and point out that the measured Brønsted exponents for forward and reverse reactions sum to unity as expected. Primary isotope effects[22,23] and solvent isotope effects[22] have been separately measured for the reverse reaction.

$$\mathrm{RR'CNO_2^-} + \mathrm{HA} \rightleftharpoons \mathrm{RR'CHNO_2} + \mathrm{A^-}$$

Experimental Section

(a) Kinetics. Save for nitroethane, from which the fraction bp 114.0° was taken after drying, all materials were of analytical grade and used without further purification. Doubly distilled water and heavy water of 99.7% stated isotopic purity were the solvents for all stock solutions, and solutions in water mixtures were made up by appropriate dilution and mixing of these. The difference in molar volume of H_2O and D_2O is only 0.4% at 25°;[24] thus the mole fraction of D_2O in a mixture never differs from the volume fraction by more than one part in the third decimal place, and we have used the two synonomously. To reduce mensuration errors, the same pipets and syringes were used to prepare parallel solutions in the water mixtures and when standardizing the acid stock solutions. Molar deuterioacetic acid was prepared by hydrolyzing the theoretical amount of acetic anhydride in boiling heavy water. Molar acid stock solutions were standardized with 0.2% reproducibility against standard sodium hydroxide solution and the results used to calculate the acid normalities in the buffer solutions with 0.20 *N* sodium acetate used in nitroethane anion runs. The 4×10^{-3} and 2×10^{-2} *N* acid solutions in 0.10 *N* sodium acetate, stock solutions for the nitromethane anion runs, were standardized (0.5% reproducibility) by titration using a Radiometer Model 4 pH meter.

A fresh solution of the sodium salt of nitroethane was made up each day by neutralization of an H_2O solution of the nitroalkane with a slight excess of hydroxide solution. (Sodium deuteroxide and D_2O were used for the series of runs in 99.7% D_2O.) To commence a run, this was diluted 200-fold (to $\approx 2 \times 10^{-4}$ *N*) into the acetic acid solution in a 1-cm spectrophotometer cell, held in a block thermostated by circulating water at 25.0°. With the same buffer in the standard cell, the decrease in absorbance at the 228-mμ nitroethane anion peak was followed as a function of time on a Carey Model 14 recording instrument.

Nitromethane anion solution becomes yellow on standing; since the color develops faster the higher the pH, half-neutralized 4×10^{-2} *N* nitromethane was diluted 100-fold into the acid in the spectrophotometer cell to start the run. The sodium salt of nitromethane was always prepared in light water; the α hydrogens exchange fairly quickly in D_2O,[25] and one must guard against unwanted secondary isotope effects. The absorption maximum here is at 232 mμ. Dexterity in injection and mixing of the reactants was needed, as reaction half-lives were as short as 7.5 sec.

Small corrections were necessary for consumption of acid during the run; for the most dilute acetic acid used (4×10^{-3} *N*), the starting concentration was corrected by 5% to its value at $t_{1/2}$.

In each run the complete optical density range available (OD 2 to 0) was covered, and the observed first-order plots were analyzed graphically using the usual log $[(\mathrm{OD})_t - (\mathrm{OD})_\infty]$ *vs. t* method; final optical densities ($8t_{1/2}$ to $10t_{1/2}$) were constant. The graphs were accurately linear, and the pseudo-first-order rate coefficients derived from them were treated on the basis of the known reactions.

$$\begin{tikzcd} \mathrm{S^-} + \underset{\text{acetic acid}}{\mathrm{LAc}} \arrow[r, "k_{\mathrm{LAc}}"] \arrow[d, shift right, "K_{\mathrm{LS}}"'] & \underset{\text{nitroalkane}}{\mathrm{SL}} + \mathrm{Ac^-} \\ \underset{aci\text{-nitroalkane}}{\mathrm{LS} + \mathrm{Ac^-}} \arrow[u, shift right] & \end{tikzcd}$$

$$[\mathrm{LAc}] = [\mathrm{HAc}] + [\mathrm{DAc}]$$

Protonation of the nitroalkane anion proceeds to completion at the pH's used. A preequilibrium precedes the rate-determining step, so we have

$$\frac{d[\mathrm{SL}]}{dt} = \frac{-d([\mathrm{LS}] + [\mathrm{S^-}])}{dt} = k_{\mathrm{LAc}} \frac{[\mathrm{LAc}]}{\left(1 + \dfrac{[\mathrm{LS}]}{[\mathrm{S^-}]}\right)} ([\mathrm{S^-}] + [\mathrm{LS}]) \quad (1)$$

The observed rate coefficient is converted to k_{LAc} knowing [LAc] and [LS]/[S⁻] The latter is a small term, better expressed as

$$\frac{[\mathrm{LS}]}{[\mathrm{S^-}]} = \frac{[\mathrm{LAc}]}{[\mathrm{Ac^-}]} \frac{K_{\mathrm{LAc}}}{K_{\mathrm{LS}}} \quad (2)$$

which assumes cancellation of the activity coefficients for the closely similar oxygen acids, acetic acid, and *aci*-nitromethane (or -ethane) and their anions. Knowing the p*K* values in water for acetic acid, *aci*-nitromethane, and *aci*-nitroethane (4.75, 3.3, and 4.4 respectively), one calculates that this term is negligible for nitromethane; for nitroethane it ranges in value from 0.02 to 0.11 for the buffer ratios used in our runs. The values of the p*K* of *aci*-nitromethane are not known in H_2O–D_2O mixtures, and we have to assume that $K_{\mathrm{LAc}}/K_{\mathrm{LS}} = K_{\mathrm{HAc}}/K_{\mathrm{HS}}$. No trend was observed in K_{LAc} after making this assumption, which is concordant with the similar p*K*'s of acetic acid and *aci*-nitroethane.

In the formation of nitroethane, it can be shown that all acids present, apart from acetic acid, give negligible contributions to the observed rate. Data are available for *aci*-nitroethane and the hydronium ion,[26] and the water rate follows from the p*K* of the substrate and the rate of deprotonation by hydroxide ion.[23]

For nitromethane anion as reactant, all data for H_2O–D_2O mixtures were obtained using 4×10^{-3} *N* acetic acid solutions. Here a minor correction is necessary since the rate of protonation by water in H_2O[27] is calculated to be 5% of the observed first-order rate, while in D_2O it is found to be about 3%. This represents an isotope effect of around 8 in the protonation of nitromethane anion by water.[28] The rates of protonation by solvent in H_2O–D_2O mixtures were then estimated using a generalized Gross-Butler equation.[29] These small contributions to the over-all rates have been taken into account in calculating the rate constants for protonation by acetic acid.

The acids H_3O^+ and D_3O^+ contribute 0.8 and ~1.5% to the observed rates in the pure waters, and no corrections were made for this.

The results in Table I check the dependence of the rate of protonation of nitromethane anion on acetic acid concentration in 98.7% D_2O. The water rate, $\approx 5 \times 10^{-4}$ sec⁻¹, was found from a plot of k_{obsd} against [DAc]. Results are satisfactory over a fivefold range in acid concentration. Table II summarizes the data for nitromethane anion in H_2O–D_2O mixtures. Probable errors are tabulated with the results.

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[28] This high value is concordant with the isotope effect in the reverse reaction, measured by Bell and Goodall with ⁻OH as the base.

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Table I. Acetic Acid and Nitromethane Anion at 25°[a]

[DAc], $M \times 10^3$	k_{obsd}, $\text{sec}^{-1} \times 10^2$	$(k_{\text{obsd}} - k_{D_2O})$ $= k_1$, $\text{sec}^{-1} \times 10^2$	k_{DAc}, $M^{-1}\ \text{sec}^{-1}$
3.62	1.64	1.59	4.39
3.84	1.78	1.73	4.50
3.84	1.77	1.72	4.47
7.57	3.36	3.31	4.37
7.81	3.56	3.51	4.49
11.60	5.10	5.05	4.35
11.82	5.25	5.20	4.39
19.47	8.95	8.90	4.57
19.49	8.82	8.77	4.50
19.69	8.55	8.50	4.32
19.71	8.93	8.88	4.50
		Mean =	4.44 ± 0.05

[a] k_{DAc} as a function of acetic acid concentration in 98.7% D_2O.

Table II. Acetic Acid + Nitromethane Anion at 25°[a]

n, atom fraction of D	No. of expts	L_2O, k_{LAc}, $M^{-1}\ \text{sec}^{-1}$
0	6	23.4 ± 0.3
0.247	3	18.9 ± 0.2
0.494	3	14.4 ± 0.1
0.740	3	9.74 ± 0.13
0.987	3	4.42 ± 0.09

[a] k_{LAc} as a function of atom fraction of deuterium in solvent; [acetic acid] = 3.80×10^{-3} N.

Table III. Acetic Acid + Nitroethane Anion at 25°[a]

Atom fraction of D	[LAc] (to first significant figure) 0.01	0.02	0.02	0.05	0.05	Mean k_{LAc}
0	17.45	17.40	17.52	17.55	17.77	17.54 ± 0.09
0.248		14.35	14.27	14.53	14.41	14.39 ± 0.07
0.496	10.63	10.68	10.61	10.65	10.60	10.63 ± 0.02
0.744		6.84		6.88	6.84	6.85 ± 0.02
0.997	2.780	2.779		2.762	2.737	2.76 ± 0.01

[a] k_{LAc} ($M^{-1}\ \text{sec}^{-1} \times 10^2$) as a function of acetic acid concentration and atom fraction of deuterium in solvent.

The observations for nitroethane anion are all listed in Table III. Again, good second-order rate constants are obtained.

(b) Free Energies of Transfer. The ratio of degenerate activity coefficients for chloride and acetate ions was evaluated at 25° using the cell shown.

$$\begin{array}{l|l||l|l} & \text{KCl} & \text{NaAc} & \\ \text{Ag, AgCl} & \text{AgCl}_{(\text{satd})} & \text{AgAc}_{(\text{satd})} & \text{AgCl, Ag} \end{array}$$

The emf E^{H_2O} is found with solvent H_2O throughout the cell, and the emf E^{D_2O} is measured on changing the solvent to D_2O.

$$E^{D_2O} - E^{H_2O} = \frac{RT}{\mathfrak{F}} \ln \frac{(K_S{}^{H_2O}/K_S{}^{D_2O})_{\text{AgCl}}}{(K_S{}^{H_2O}/K_S{}^{D_2O})_{\text{AgAc}}} \frac{(a^{H_2O}/a^{D_2O})_{\text{Ac}^-}}{(a^{H_2O}/a^{D_2O})_{\text{Cl}^-}} \quad (3)$$

K_S is the solubility product $a_{\text{Ag}^+}a_{\text{X}^-}$.

The concentrations of acetate ion and chloride ion were made the same in both cells. Since deviations from ideality due to interionic effects are the same for both solvents (see Discussion), the anion activity ratios are then unity. The measured emf difference thus gives the difference between the free energies of transfer of the silver salts, and, since these free energies are separable into terms for the individual ions

$$E^{D_2O} - E^{H_2O} = \frac{RT}{\mathfrak{F}} \ln \frac{\gamma_{\text{AgCl}}}{\gamma_{\text{AgAc}}} = \frac{RT}{\mathfrak{F}} \ln \frac{\gamma_{\text{Cl}^-}}{\gamma_{\text{Ac}^-}} \quad (4)$$

Transfer free energies for the individual silver salts were found by using silver nitrate solution of known normality in one of the half-cells.

Silver electrodes did not give stable and reproducible potentials, so electrolytic silver–silver chloride electrodes were prepared on platinum wire by a standard method.[30] Two electrodes were used in each solution, and the same electrodes used in parallel solutions in the two solvents; constant bias potentials can thus be accepted (such bias potentials were observed, though they did not exceed 0.2 mv). Emf's were read on a Radiometer Model 4 pH meter. The cells were suspended in a thermostated tank at 25.0 ± 0.05°.

All solutions were prepared by weight from AR grade chemicals, and silver nitrate solutions were checked by Volhard thiocyanate titration. In different sets of measurements the AgCl half-cell contained (a) 0.0667 N KCl with 0.40 N KNO_3, (b) 0.400 N KCl. The normality of KNO_3 in the bridge was also varied, 0.40 N KNO_3 and 1.00 N KNO_3 being used. The high concentration of sodium acetate was chosen to minimize uncertainties in the acetate ion concentration in D_2O. From the stability constants obtained by MacDougall and Peterson,[31] one calculates that dissolved silver acetate and the complex ions AgAc and $AgAc_2^-$ cause $[Ac^-]^{H_2O}$ to differ from stoichiometric sodium acetate by only 1.7% in 0.40 N solution. The error introduced by assumption of the same figure for $[Ac^-]^{D_2O}$ will not be greater than 1%.

No variation in the emf difference was noted with the concentration changes made, implying that the assumptions of identity of interionic effects and liquid junction potentials in the two solvents are valid.

From four sets of measurements on the cell with silver chloride and silver acetate, $E^{D_2O} - E^{H_2O} = 4.5 \pm 0.3$ mv, giving $\gamma_{\text{Cl}^-}/\gamma_{\text{Ac}^-} = 1.19 \pm 0.01$. Two measurements at the different chloride concentrations gave for silver chloride alone, $E^{D_2O} - E^{H_2O} = 11.6 \pm 0.1$ mv, and one measurement for silver acetate gave $E^{D_2O} - E^{H_2O} = 6.9$ mv; $\gamma_{\text{AgCl}} = 1.53$, $\gamma_{\text{AgAc}} = 1.28$. These lead to the ratio for the anions which has already been presented.[32]

Discussion

Since a consideration of medium effects is necessary to explain the experimental results, we shall begin by giving an outline of a convenient medium effect correction to the equations of the generalized Gross–Butler theory.

For transfer of an electrolyte from a solution of molarity M in H_2O to a solution of the same molarity in D_2O, we define the degenerate activity coefficient of transfer γ by the equation

$$(\mu_{\text{MX}}{}^{D_2O})^M = (\mu_{\text{MX}}{}^{H_2O})^M + RT \ln (\gamma_{\text{MX}})^M \quad (5)$$

Experimentally it is found that $(\gamma_{\text{MX}})^M$ shows little deviation from $(\gamma_{\text{MX}})^0$ over the concentration range 0–1 M.[37,38] This can be rationalized knowing that deviations from ideality caused by electrostatic effects

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(32) An independent estimate of this activity coefficient ratio can be obtained as follows. Differences in solubility between the two waters have been reported for $AgMnO_4$,[33] $KMnO_4$,[34] $AgClO_3$,[35] and $KClO_3$.[34] γ_{KCl} is known[16] and γ_{AgCl} can thus be calculated. We measured $\gamma_{\text{AgAc}} = 1.32$ by thiocyanate titration of saturated silver acetate solutions in H_2O and D_2O, and all the data together suggest $\gamma_{\text{Cl}^-}/\gamma_{\text{Ac}^-} = 1.22$. The drawback to this method is that these titrimetric or gravimetric solubility measurements do not distinguish between simple and complex ions, and the latter often predominate.[36] It is perhaps fortuitous in this case that fairly good agreement is obtained with the emf method, where the true cation activity is measured; in other cases the estimates are seriously in error.[10]

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are the same in H_2O and D_2O, which have dielectric constants differing by only 0.3%.[24] The effect on γ from the overlap of solvation shells of neighboring ions does not become important until the solution is concentrated. Since all our comparisons between H_2O and D_2O are carried out at constant molarity in the range 0–0.4 *M*, we shall drop the superscripts from eq 5.

The values $\gamma_{\mathrm{LiF}} = 0.77$[39] and $\gamma_{\mathrm{CaF_2}} = 2.0$[40] at 25° indicate the range of magnitude of degenerate activity coefficients of transfer.

Experimental data for transfer from H_2O–D_2O mixtures[14b,37] are fitted well by eq 6, in which n is the deuterium atom fraction of the solvent mixture L_2O, and γ refers to transfer between the pure solvents.

$$\mu_{\mathrm{MX}}{}^{\mathrm{L_2O}} = \mu_{\mathrm{MX}}{}^{\mathrm{H_2O}} + nRT\ln\gamma_{\mathrm{MX}} \tag{6}$$

Since H_2O–D_2O mixtures are ideal, $\gamma_{\mathrm{H_2O}} = \gamma_{\mathrm{D_2O}} = \gamma_{\mathrm{HDO}} = 1$.

We shall define the fractionation factor ϕ as the equilibrium constant for eq 7. This has no medium effect contribution and should therefore be relevant to the generalized Gross–Butler equations, where a constant fractionation factor is assumed over the full H_2O–D_2O mixture range. The fractionation factor normally quoted is defined by eq 8 and will be termed ϕ'; this is more accessible to experimental determination and is related to ϕ by the degenerate activity coefficient of transfer (eq 10).

$$\mathrm{HA^{H_2O}} + 0.5\mathrm{D_2O^{H_2O}} \rightleftharpoons \mathrm{DA^{H_2O}} + 0.5\mathrm{H_2O^{H_2O}} \qquad \phi \tag{7}$$

$$\mathrm{HA^{H_2O}} + 0.5\mathrm{D_2O^{D_2O}} \rightleftharpoons \mathrm{DA^{D_2O}} + 0.5\mathrm{H_2O^{H_2O}} \qquad \phi' \tag{8}$$

$$\mathrm{DA^{D_2O}} \rightleftharpoons \mathrm{DA^{H_2O}} \qquad \gamma \tag{9}$$

$$\phi = \phi'\gamma \tag{10}$$

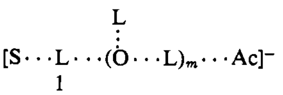
Equilibrium constants for the general equilibrium 11 are related to the equilibrium constant in H_2O by eq 12.[41] Kinetics are treated in a similar fashion,

$$\mathrm{L}_i\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{L}_{i-1}\mathrm{A}^- + \mathrm{BL}^+ \tag{11}$$

$$\frac{K^{\mathrm{L_2O}}}{K^{\mathrm{H_2O}}} = \frac{(1 - n + n\phi_{\mathrm{L}_{i-1}\mathrm{A}^-})^{i-1}(1 - n + n\phi_{\mathrm{BL}^+})}{(1 - n + n\phi_{\mathrm{L}_i\mathrm{A}})^{i}} \times \left(\frac{\gamma_{\mathrm{L}_i\mathrm{A}}\gamma_{\mathrm{B}}}{\gamma_{\mathrm{L}_{i-1}\mathrm{A}^-}\gamma_{\mathrm{BL}^+}}\right)^n \tag{12}$$

fractionation factors for transition state protons replacing thoese for products in eq 12.

From the general eq 12 we now turn to the specific reaction of a nitroalkane anion (S^-) with acetic acid (LAc). Equation 13 gives the theoretical expression for the ratio of rate coefficients in a solvent mixture and pure water, and refers to the very general transition state I.

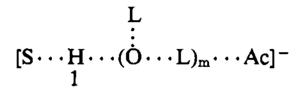


$$[\mathrm{S}\cdots\underset{1}{\mathrm{L}}\cdots(\overset{\overset{\mathrm{L}}{\vdots}}{\mathrm{O}}\cdots\mathrm{L})_m\cdots\mathrm{Ac}]^-$$

I

$$\frac{k_{\mathrm{LAc}}{}^{\mathrm{L_2O}}}{k_{\mathrm{HAc}}{}^{\mathrm{H_2O}}} = \frac{(1 - n + n\phi_1{}^{\ddagger})\prod_i^{2m}(1 - n + n\phi_i{}^{\ddagger})}{(1 - n + n\phi_{\mathrm{LAc}})}\left(\frac{\gamma_{\mathrm{LAc}}\gamma_{\mathrm{S}^-}}{\gamma^{\ddagger}}\right)^n \tag{13}$$

This allows for proton transfer through a bridge of *m* water molecules; there is a product of terms for each of the 2*m* protons such waters contribute to the transition state. Fortunately these unknowns can be eliminated with the help of data obtained by Reitz[22] for the reverse reaction, specifically, the reaction of nitromethane with acetate ion in light and heavy water. In the reverse reaction the proton numbered 1 does not exchange with the solvent, so we have the transition state II.



$$[\mathrm{S}\cdots\underset{1}{\mathrm{H}}\cdots(\overset{\overset{\mathrm{L}}{\vdots}}{\mathrm{O}}\cdots\mathrm{L})_{\mathrm{m}}\cdots\mathrm{Ac}]^-$$

II

and

$$\frac{k_{\mathrm{Ac^-}}{}^{\mathrm{D_2O}}}{k_{\mathrm{Ac^-}}{}^{\mathrm{H_2O}}} = \prod_i^{2m}\phi_i{}^{\ddagger}\left(\frac{\gamma_{\mathrm{SH}}\gamma_{\mathrm{Ac^-}}}{\gamma^{\ddagger}}\right) = \frac{1}{1.14} = 0.88 \tag{14}$$

For strict identity of terms in eq 13 and 14 we shall concentrate on the case where $\mathrm{S} = -\mathrm{CH_2NO_2}$. The two equations are combined with the help of the approximation

$$\phi^n = 1 - n + n\phi \tag{15}$$

(ϕ^n is given within 1% by the leading term of the expansion, when $0.7 < \phi < 1.3$ and n is in the range 0–1).

$$\frac{k_{\mathrm{LAc}}{}^{\mathrm{L_2O}}}{k_{\mathrm{HAc}}{}^{\mathrm{H_2O}}} = \frac{(1 - n + n\phi_1{}^{\ddagger})}{(1 - n + n\phi_{\mathrm{LAc}})}\left(\frac{\gamma_{\mathrm{LAc}}\gamma_{\mathrm{S^-}}}{\gamma_{\mathrm{SH}}\gamma_{\mathrm{Ac^-}}}0.88\right)^n \tag{16}$$

Analysis of Data with Neglect of Medium Effects. As a first approach to eliminating unknowns from eq 16 we adopt the common practice of ignoring the medium effect; *i.e.*, we set the ratio of γ's equal to unity. The same approximation is inherent in the fractionation factor for acetic acid which is quoted normally.[42] Under this approximation the only parameters are ϕ_{LAc} and ϕ_1. The value of the first of these is calculable from the known value of $K_{\mathrm{HAc}}{}^{\mathrm{H_2O}}/K_{\mathrm{DAc}}{}^{\mathrm{D_2O}}$ although there is a possible range in the value of ϕ_{LAc} of from 1.17 to 0.99, corresponding to the uncertainty in L of from 8.0 to 11.0.[15] Fixing $\phi_1{}^{\ddagger}$ from the results for the pure waters, eq 15 would then suggest a curve in the cross-hatched region of Figure 1.

This analysis is quite inadequate to account for the experimental data, and medium effects clearly have to be considered. This also suggests that neglect of medium effects when fitting data to generalized Gross–Butler equations is not justifiable, particularly when mechanistic conclusions are to be drawn from such treatments.

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[39] H. W. Birnthaler and E. Lange, *Z. Elektrochem.*, **43**, 649 (1937).

[40] E. C. Noonan, *J. Am. Chem. Soc.*, **71**, 102 (1949).

[41] We make the usual assumption (*cf.* ref 14b) that $\gamma_{\mathrm{BH}^+} = \gamma_{\mathrm{BD}^+}$; *i.e.*, that γ is determined by the electronic properties of the substrate.

[42] Based on the ratio of dissociation constants of acetic acid in water and D_2O. Values have been reported by S. Korman and V. K. La Mer, *J. Am. Chem. Soc.*, **58**, 1396 (1936); J. P. Chittum and V. K. La Mer, *ibid.*, **58**, 1642 (1936); P. K. Glasoe and F. A. Long, *J. Phys. Chem.*, **64**, 188 (1960); R. A. Robinson, National Bureau of Standards, Technical Note No. 271, U. S. Government Printing Office, Washington, D. C., 1965 (this figure has had to be corrected to the molarity scale). They are respectively 3.33, 3.33, 3.3, and 3.255. We have taken 3.30 as the mean.

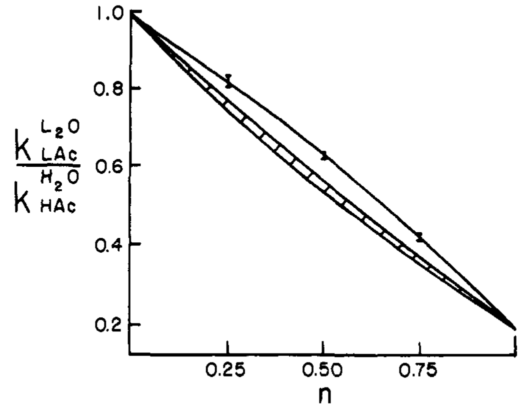

Figure 1. Relative rate of reaction between nitromethane anion and acetic acid *vs.* atom fraction *n* of deuterium in mixed H_2O–D_2O solvents. Experimental points are fitted to eq 22 with $\gamma_{s^-}/\gamma_{Ac^-} = 1.27$. Curves in the cross-hatched region are predicted if the medium effect is neglected, *i.e.*, eq 16 with all $\gamma_S = 1$ and ϕ_{LAc} between 1.17 and 0.99.

Combination of Exchange and Transfer. Experiments were designed toward measurement of the degenerate activity coefficients in eq 16. The emf of the cell

$$M\,|MX^{H_2O}\,|X\text{-}X\,|MX^{D_2O}\,|M$$

with the salt at the same molarity in the two solvents gives directly the free energy of transfer of the electrolyte.

Salomaa[16] used such a cell in his work on potassium chloride. La Mer and co-workers[10,43] combined exhange with transfer in their measurements on hydrochloric acid, from which they found

$$\frac{[H_3O^+]^2[D_2O]^3}{[D_3O^+]^2[H_2O]^3}(\gamma_{D_3O} + \gamma_{Cl^-})^2 = 18.0 \qquad (17)$$

This may be combined with the well-documented ratio of equilibrium constants of acetic acid in water and heavy water[42] (eq 18), giving (19). The ratio of degenerate activity coefficients for the anions was found by emf measurement of silver ion concentrations in saturated solutions of silver chloride and silver acetate in water and heavy water. Since the solid phases are unhydrated, the solubility product differences are measured at constant chemical potential for each solute. The method is described in the Experimental Section and yields the result

$$\frac{[H_3O^+][D_2O][DAc]}{[D_3O^+][H_2O][HAc]}\,\frac{\gamma_{Ac^-}\gamma_{D_3O^+}}{\gamma_{DAc}} = 3.30 \qquad (18)$$

$$\frac{[DAc][H_2O]^{1/2}}{[HAc][D_2O]^{1/2}} = \phi_{LAc} = \gamma_{DAc}\frac{\gamma_{Cl^-}}{\gamma_{Ac^-}}0.78 \qquad (19)$$

$$\gamma_{Cl^-}/\gamma_{Ac^-} = 1.19 \pm 0.01 \qquad (20)$$

From the solubility difference of CH_3NO_2 in light and heavy water,[44] $\gamma_{SH} = 1.06$.

Equations 19 and 20 give

$$\gamma_{LAc}/\phi_{LAc} = 1.08 \qquad (21)$$

and with both terms presumably close enough to unity for the exponential approximation (15) to hold, eq 16 reduces to

$$k_{LAc}^{L_2O}/k_{HAc}^{H_2O} = (1 - n + n\phi_1^{\ddagger})\left(0.89\frac{\gamma_{S^-}}{\gamma_{Ac^-}}\right)^n \qquad (22)$$

It is unfortunately difficult to determine the degenerate activity coefficient ratio remaining in eq 22 using our emf method, as the silver salts of nitroalkane anions are very unstable. We have to accept this treatment of solvent isotope effects[45] to deduce the unknowns

$$\gamma_{S^-}/\gamma_{Ac^-} = 1.27 \qquad (23)$$

from the kinetic data in H_2O–D_2O mixtures. The value gives the best fit for both nitroethane and nitromethane anions and is used in Table IV and Figure 1.

Table IV. Comparison between Observed Solvent Isotope Effects and Calculated Values from Eq 22 with $\gamma_{S^-}/\gamma_{Ac^-} = 1.27$[a]

Nitromethane anion			Nitroethane anion		
	$k_{LAc}^{L_2O}/k_{HAc}^{H_2O}$			$k_{LAc}^{L_2O}/k_{HAc}^{H_2O}$	
n	Obsd	Calcd	*n*	Obsd	Calcd
0	1.000		0	1.000	
0.247	0.805 ± 0.014	0.816	0.248	0.820 ± 0.006	0.810
0.494	0.616 ± 0.009	0.620	0.496	0.606 ± 0.003	0.608
0.740	0.415 ± 0.008	0.412	0.744	0.391 ± 0.002	0.392
0.987	0.189 ± 0.005		0.997	0.157 ± 0.001	
(1.00	0.178	0.178)	(1.00	0.154	0.154)

[a] Recent experimental measurements by L. Friedman and V. J. Shiner, *J. Chem. Phys.*, **44**, 4639 (1966), and independently by J. W. Pyper, R. S. Newbury, and G. W. Barton, Jr., *ibid.*, **46**, 2253 (1967), lead to a value of 3.75 for the disproportionation constant of water at room temperature; previous evidence suggested the statistical value of 4.0, used in the generalized Gross-Butler theory. The effect of the new constant on the ratio [DAc]/[HAc] of eq 19 was established, assuming constancy of ϕ_{LAc}. Then, using the equation

$$k_{LA} = k_{HA}\frac{[HA]}{[HA] + [DA]} + k_{DA}\frac{[DA]}{[HA] + [DA]}$$

the predicted rate is decreased by 0.5% for solvent containing 25% D, increased by 1.0% for 75% D, and, of course, unaffected at 50% D. As these corrections are small, they are not considered further in the Discussion.

Variation of Transfer Effect with the Nature of the Anion. Transfer terms at 25° for the silver salts studied may be compared with those of lithium fluoride[39] and potassium chloride.[16]

Salt	LiF	KCl	AgAc	AgCl
γ_{MX}	0.77	1.46	1.28	1.53

Since O–D···O bonds are stronger than the corresponding hydrogen bonds, small, structure-ordering ions (Li^+ and F^-) have low γ values (transfer of solvent from the bulk into the cosphere is more favorable in D_2O); larger ions (K^+, Cl^-), where the charge is more diffuse, are structure disordering: they have $\gamma > 1$.

The fact that γ_{Ac^-} is much smaller than γ_{Cl^-} is consistent with the findings of Gurney,[46] who compared

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(43) E. C. Noonan and V. L. La Mer, *J. Phys. Chem.*, **43**, 247 (1939).

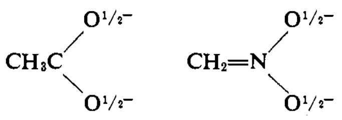
(44) I. B. Rabinovitch, V. D. Fedorov, N. P. Pashkin, M. A. Avdesnyak, and N. Y. Pimenov, *Dokl. Akad. Nauk SSSR*, **105**, 108 (1955).

(45) The errors cumulative in this figure of $\gamma_{S^-}/\gamma_{Ac^-} = 1.27$ will not be greater than 10%, most of this arising from an uncertainty of approximately 5% in Reitz's value for $k_{Ac^-}^{D_2O}/k_{Ac^-}^{H_2O}$ (eq 14). We now have preliminary results of electromeric titrations of the sodium salts of phenylacetic acid and phenylnitromethane with silver nitrate, in water and heavy water. These are consistent with a value $\gamma_{RCHNO_2^-}/\gamma_{RCH_2COO^-}$ appreciably greater than unity, as we have deduced here.

(46) R. W. Gurney, "Ionic Processes in Solution," McGraw-Hill Book Co., Inc., New York, N. Y., 1953, pp 259, 169.

deviations from Debye–Huckel behavior of the alkali halides and acetates and also reviewed the effect of the anions on the viscosity of water. He concluded that acetate ion structured the water around it. As further evidence for this, the isotope effect on the heat of solution of sodium acetate has been measured[47] and is considerably smaller than that for sodium chloride.[48]

What is more surprising is that the acetate ion is not a good model for the nitroalkane anion.



These are formally very similar, yet $\gamma_{S^-}/\gamma_{Ac^-} = 1.27$. The greater charge delocalization permitted in the nitroalkane anion is presumably responsible for the lesser ordering of the solvent around this anion. Transfer effects for other silver salts are currently being investigated.

Fractionation Factors and Primary Isotope Effects. From eq 22 and Table IV, the values of $\phi_1^{\ddagger}$ for the transition states involving nitromethane anion and nitroethane anion are 0.157 and 0.136, respectively. Independent estimates of these quantities can be made from primary isotope effects measured in the reverse reactions

$$SH + Ac^- \xrightarrow{H_2O} S^- + HAc$$

$$SD + Ac^- \xrightarrow{H_2O} S^- + DAc$$

The primary isotope effect is related to the fractionation factors for the proton in the nitroalkane and its transition state, thus

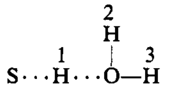
$$k^H/k^D = \phi_{SL}/\phi^{\ddagger}$$

Since ϕ for a proton in a stable bond is always close to unity, a large primary isotope effect corresponds to a low value of $\phi^{\ddagger}$. For nitroisopropane, $k^H/k^D = 7.6$, and $\phi_{SL} \approx 0.97$.[23] (This value can be computed from analyses of the deuterated substrate during various stages of its preparation by exchange with heavy water.) For nitromethane, where the comparison is, in fact, for reaction of CH_3NO_2 *vs.* CD_3NO_2, $k^H/k^D = 6.5$ and $\phi_{SL} = 0.91$ per proton[22] (from the value $\phi_{Cl_3NO_2} = 0.78$ obtained by Reitz).

It follows that values of $\phi_1^{\ddagger}$ for the transition states involving nitromethane and nitroisopropane are 0.14 and 0.13, respectively. Both values are free from medium effect uncertainties. Exact correspondence between the two estimates of $\phi_1^{\ddagger}$ for nitromethane is not to be expected, because a secondary isotope effect is present in the deprotonation reaction (CH_3NO_2 *vs.* CD_3NO_2), but absent in the protonation reaction.

The correlation between these large primary isotope effects and the degree of proton transfer in the transition state has been discussed elsewhere. The present study confirms that the primary isotope effect increases with increasing substitution of alkyl groups in nitromethane.

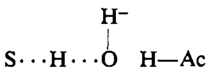
Magnitudes of the Fractionation Factors and Their Bearing on Reaction Mechanism. It is apparent from eq 13 and 14 that the relative weights given to the water-bridge term ($\Pi_i{}^{2m}\phi_i{}^{\ddagger}$) and the term for solvation of the transition state ($\gamma^{\ddagger}$) cannot be resolved by experiment. If no water bridge is assumed ($m = 0$, and the product $= 1$), a physically reasonable value of $\gamma^{\ddagger}$ emerges. Here $\gamma_{S^-} > \gamma^{\ddagger} > \gamma_{Ac^-}$, suggesting that the solvation characteristics of the transition state are intermediate between those of reactants and products. With a water bridge, $\Pi_i{}^{2m}\phi_i{}^{\ddagger}$ and its individual fractionation factors would have to be close to unity if a value of $\gamma^{\ddagger}$ in keeping with data on other degenerate activity coefficients were to be retained. But $\phi_1^{\ddagger}$ is 0.14 for nitromethane anion, and such a gross difference between this and $\phi_i \approx 1$ could only be accommodated in a transition state such as III or IV. Here the force constants governing the motions of protons 2 and 3 are little changed from their values in water or acetic acid, and the transition state modes are effectively described by the three atoms centered on proton 1.



$$S\cdots\overset{1}{H}\cdots\overset{\overset{2}{H}}{O}\!-\!\overset{3}{H}\quad Ac^-$$

(acetate ion assisting transfer from a hydronium ion)

III



$$S\cdots H\cdots\overset{H^-}{O}\quad H\!-\!Ac$$

(acetic acid assisting transfer from water)

IV

These transition states offer no explanation for the Brønsted plots in forward and reverse reactions of nitroalkane–nitroalkane anion equilibration and cannot account for large differences in the isotope effects for the reactions of nitromethane with acetate ion, water, and hydroxide.[22,23,49]

Another factor weighing against the intermediacy of a water bridge is that this would considerably decrease the probability of steric interactions,[50] which have been demonstrated for reaction of nitroalkanes with α-substituted pyridines.[51]

All the evidence is therefore in favor of the traditional "direct" mechanism for proton transfer to carbon.

Bell mentions other proton or deuteron transfers which take place 20–40% more slowly in D_2O than in H_2O,[52] when no isotopic change is made in the reactants. These figures we would again attribute entirely to isotope effects on solvation, though it is not possible to estimate the contribution of nonequilibrium solvation discussed in Bell's paper.

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(47) $\Delta H^{D_2O} - \Delta H^{H_2O} = 380$ cal mole^{-1} at 8×10^{-3} *N*. We are grateful to Miss Evelyn Stimson for performing this measurement.

(48) $\Delta H^{D_2O} - \Delta H^{H_2O} = 550$ cal mole^{-1} between standard states: E. Lange and W. Martin, *Z. Physik. Chem.*, **180A**, 233 (1937); Y. Wu and H. L. Friedman, *J. Phys. Chem.*, 70, 166 (1966).

(49) This may be contrasted with the stepwise mechanism invoked by C. G. Swain, D. A. Kuhn, and R. L. Schowen, *J. Am. Chem. Soc.*, **87**, 1552 (1965), for a different type of reaction.

(50) *Cf.* V. Gold, *Chimia* (Aarau), 19, 508 (1965).

(51) R. G. Pearson and F. V. Williams, *J. Am. Chem. Soc.*, **75**, 3073 (1953).

(52) R. P. Bell, *Discussions Faraday Soc.*, **39**, 16 (1965).