Kinetic Electron Spin Resonance Spectroscopy. Part III.† Proton Exchange Rates for Ketyl Radicals in Organic Solvents

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Measurements of linewidths and hyperfine splittings in the e.s.r. spectra of some photochemically generated ketyl radicals have been used to determine the rates of acid-catalysed carboxy-proton exchange reactions in these species. For $CH_3\dot{C}(OH)CO_2H$ radicals in chloroform, ethanol, and propan-2-ol the second-order rate constants k are 1·7, 2·0, and 2·8 × 10^7 l mol^{-1} s^{-1} respectively at 298 K and for $HO_2CCH_2\dot{C}(OH)CO_2H$ radicals in ethanol k = 2·8 × 10^7 l mol^{-1} s^{-1}. Measured activation energies are *ca.* 30 kJ mol^{-1}.

EXCHANGE processes of various kinds have been extensively studied using magnetic resonance techniques and a variety of theories, differing in the level of sophistication, has been employed.[1] The simplest system is a two-site system and in e.s.r. the effect of the exchange process is to cause an alternation in the distribution of the unpaired electron spin in the free radical with a consequent alternation in the nuclear hyperfine splittings. If the resonance frequencies of the unpaired electron in the two different sites are ω_1 and ω_2 and if τ is the mean lifetime between exchanges, the relation between linewidth and lifetime is particularly simple in the two limits defined by $|(\omega_1 - \omega_2)| \gg \tau^{-1}$ (slow exchange) and $|(\omega_1 - \omega_2)| \ll \tau^{-1}$ (fast exchange).

Near the slow exchange limit the observed linewidth $1/T_2{}^*$ is related to the linewidth in the absence of exchange $1/T_2$ by the relationship $1/T_2{}^* = 1/T_2 + 1/\tau$. In the fast exchange limit line narrowing is observed and $1/T_2{}^* = 1/T_2 + \tau a^2$ where a is the peak separation in the absence of exchange, equal to $|\omega_1 - \omega_2|$ in frequency units.

Most experimental studies have been confined to measurements close to one limit or the other because of experimental limitations.[2-9] However we found that the changes in the e.s.r. spectrum of the radical derived from pyruvic acid $CH_3\dot{C}(OH)CO_2H$ (a doubling of all lines at low concentrations of acid and exchange narrowing of the coalesced lines at high concentration) could be followed from one limit to the other by suitable choice of solvent and temperature.[10] Our preliminary results showed reasonably good agreement between values of τ obtained close to the two limits and we attributed the effects to exchange of the carboxy-proton on the radical with the carboxy-proton of the parent acid.

Since there appears to be very little information about the rates of exchange of carboxy-protons we have made a more detailed investigation of this system in a variety of solvents and over a range of temperature. In order to make use of as much as possible of the line shape data available from our experiments we have compared the experimental line shapes with those computed by means of the modified Bloch equations over the entire accessible range of exchange frequencies.

EXPERIMENTAL

Pyruvic acid was obtained from B.D.H. and 2-oxobutyric acid from Emmanuel. Solvents were of AnalaR quality and were not further purified. All examples were degassed

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† Part II, P. B. Ayscough and R. C. Sealy, *J.C.S. Perkin II*, 1973, 543.

[1] See *e.g.* C. S. Johnson, jun., *Adv. Magnetic Resonance*, 1965, **1**, 33.

[2] M. T. Jones, *J. Chem. Phys.*, 1963, **38**, 2892.

[3] T. Layloff, T. Miller, R. N. Adams, H. Fäh, A. Horsfield, and N. Proctor, *Nature*, 1965, **205**, 382.

[4] R. Chang and C. S. Johnson, jun., *J. Amer. Chem. Soc.*, 1966, **88**, 2338.

[5] T. A. Miller, R. N. Adams, and P. M. Richards, *J. Chem. Phys.*, 1966, **44**, 4022.

[6] C. L. Malinowski and W. H. Bruning, *J. Amer. Chem. Soc.*, 1967, **89**, 5063.

[7] R. Chang and S. I. Weissman, *J. Amer. Chem. Soc.*, 1967, **89**, 5968.

[8] R. Chang and C. S. Johnson, jun., *J. Chem. Phys.*, 1967, **46**, 2314.

[9] N. Hirota, R. Carraway, and W. Schook, *J. Amer. Chem. Soc.*, 1968, **90**, 3611.

[10] P. B. Ayscough and M. C. Brice, *J. Chem. Soc.* (*B*), 1971, 491.

before use. Thin-walled Pyrex sample tubes were used. For variable temperature studies these were supported within a double-walled outer jacket through which dry gaseous nitrogen was passed. The Decca e.s.r. spectrometer and optical system, together with the procedures for measuring hyperfine splittings and radical concentrations, have been described earlier.[10]

RESULTS

The Bloch equations relating the rate of change of overall magnetisation of a system of free radicals to the static and oscillating magnetic fields H_0 and H_1, the resonance frequency ω_0, and the transverse and longitudinal relaxation times T_1 and T_2, can be modified to include the effect of the exchange rate τ^{-1}.[11,12] For a two-site system the total magnetisation $G(= u + \mathrm{i}v$ where u and v are components in phase and 90° out of phase with H_1 respectively) is given by equation (1). Here M_0 is the equilibrium magnetisation,

$$G = \frac{\mathrm{i}\omega_1 M_0 \sum_j P_j/(1 + \alpha_j\tau)}{\sum_j P_j\alpha_j/(1 + \alpha_j\tau)} \qquad (1)$$

ω_1 is the angular frequency of the microwave radiation, τ is the mean lifetime between exchanges, and P_j is the fraction of unpaired spins in site j.

For a spectrum which consists of two equally intense hyperfine lines at $\omega_0 \pm a/2$ in the absence of exchange, the values of α_A and α_B are given by equations (2) and (3)

$$\alpha_A = 1/T_2 - \mathrm{i}(\Delta\omega + a/2) \qquad (2)$$

$$\alpha_B = 1/T_2 - \mathrm{i}(\Delta\omega - a/2) \qquad (3)$$

where $\Delta\omega = \omega_0 - \omega$ and ω is the microwave frequency. In general for a two-site system $P_A = P_B = 1/2$.

Under these conditions expansion of equation (1), retaining only the imaginary part v which is proportional to the energy absorption in the system, gives, following the procedure adopted by Jones,[2] equation (4) where $W =$

$$v = \omega_1 M_0(PZ + RW)/(R^2 + P^2) \qquad (4)$$

$1 + \tau/T_2$, $Z = \tau\Delta\omega$, $R = 1/T_2 + \tau/T_2{}^2 + \tau a^2/4 - \tau\Delta\omega^2$, and $P = (1 + 2\tau/T_2)\Delta\omega$. The derivative of equation (4) $\mathrm{d}v/\mathrm{d}(\Delta\omega)$ yields the usual first derivative e.s.r. curve as a function of T_2, τ, and a.

A computer programme to calculate the line shape was constructed in such a manner that the functions $r' = a'/h'$ and $r'' = a/h''$ could be calculated. The significance of the terms a', h', and h'' is best illustrated diagramatically (see Figure 1). Clearly for spectra observed with slow rates of exchange the appropriate comparison to make is between theoretical and experimental values of r': for fast exchange where the lines have coalesced r'' is the appropriate function to employ.

Computation of v requires values for the hyperfine splitting a and line width $1/T_2$ which must be determined experimentally from spectra observed under conditions of essentially negligible exchange. With this information the ratios r' and r'' can be calculated for a series of values of τ and from the computed plots of r' and r'' we can estimate τ from any other spectrum.

The Radical $CH_3\dot{C}(OH)CO_2H$.—The exchange process occurring in this radical was investigated in three solvents, propan-2-ol, ethanol, and chloroform.

Solutions of pyruvic acid in the appropriate solvent were rigorously degassed and then photolysed using u.v. light from a 1 kW high-pressure mercury lamp. The e.s.r. spectrum of the radical $CH_3\dot{C}(OH)CO_2H$ has been described earlier.[10] For acid concentrations $>$*ca.* 0·4M the spectrum consists of four doublets ($a^{H}_{CH_3} = 1·660 \pm 0·002$, $a^{H}_{OH} = 0·233 \pm 0·003$ mT at 293 K). At concentrations *ca.* 0·05M each line is further split into two (a' *ca.* 0·100 mT). With increasing concentration a' decreases and h' increases until the lines merge at *ca.* 0·5M: above this concentration the single line narrows, h'' decreasing from *ca.* 0·100 to 0·050 mT at 1·8M.

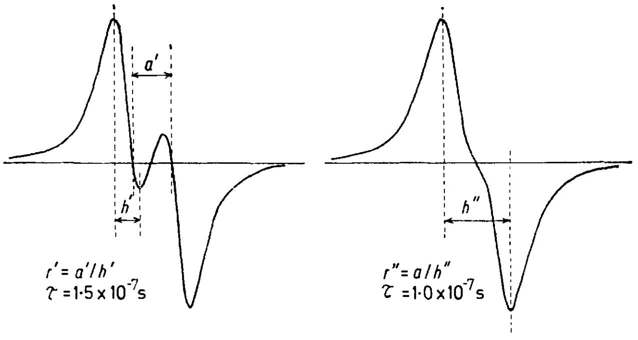

FIGURE 1 Line shape parameters r' and r'' for slow and fast exchange respectively

During the recording of the spectra care was taken to avoid instrumental distortion of the line shape: spectra were measured with low modulation amplitude and low microwave power levels. Values of a', h', and h'' are given in Table 1.

Limiting values a and h $(= 1/T_2)$ were derived by extrapolation of measurements for very dilute solutions. The values $a = 0·102$ mT and $h = 0·031$ mT were used in the computation of line shapes. The spectra shown in Figure 1 were computed for $\tau = 1·5 \times 10^{-7}$ and $1·0 \times 10^{-7}$ s. The parameters r' and r'' calculated for various values of τ are shown in Figure 2. It will be seen that there is considerable overlap in the values of τ though of course we can derive from any given spectrum only a value for either r' or r''.

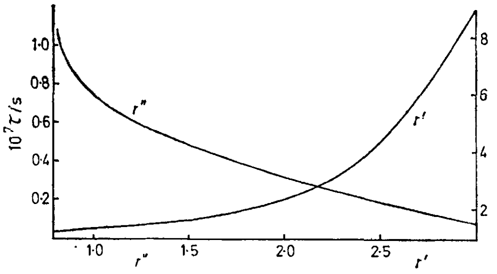

FIGURE 2 Computed line shape data for the radical $CH_3\dot{C}(OH)CO_2H$ in propan-2-ol. The left-hand ordinate scale refers to values of r'' applicable to fast exchange: the right-hand ordinate scale refers to values of r' applicable to slow exchange

Comparison of experimental values of r' and r'' with the data shown in Figure 2 gives us values of the mean lifetime between exchanges τ as a function of acid concentration as shown in Figure 3. Note that the first six points are derived from measurements at slow rates of exchange (r') and the

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[11] H. S. Gutowksy, D. W. McCall, and C. P. Slichter, *J. Chem. Phys.*, 1953, **21**, 279.

[12] C. P. Slichter, 'Principles of Magnetic Resonance,' Harper and Row, New York, 1963.

remainder are from measurements on exchange-narrowed lines (r''). The best straight lines through the two different sets of lines do not exactly coincide, but the difference is barely significant and the line shown in Figure 3 is the best straight line through all points.

TABLE 1

Experimental line shape data for ' slow ' and ' fast ' exchange in $CH_3\dot{C}(OH)CO_2H$ radicals

Solvent	[Pyruvic acid]/M	$a'/\mu T$ *	$h'/\mu T$ *	$h''/\mu T$ *
Me_2CHOH	0·05	100 ± 4	32 ± 2	
	0·10	97 ± 4	34 ± 2	
	0·15	97 ± 4	36 ± 2	
	0·25	87 ± 4	38 ± 2	
	0·30	90 ± 4	45 ± 2	
	0·35	88 ± 4	45 ± 2	
	0·40	70 ± 3	47 ± 2	
	0·76			113 ± 6
	0·88			121 ± 6
	1·00			113 ± 6
	1·06			106 ± 6
	1·12			70 ± 4
	1·22			70 ± 4
	1·31			57 ± 4
	1·50			68 ± 4
	1·60			57 ± 4
	1·75			53 ± 4
	1·86			51 ± 4
EtOH	0·10	97 ± 6	34 ± 2	
	0·15	97 ± 6	34 ± 2	
	0·20	97 ± 6	38 ± 2	
	0·30	87 ± 6	36 ± 2	
	0·35	87 ± 6	36 ± 2	
	0·45	76 ± 6	39 ± 2	
	0·50	77 ± 6	40 ± 2	
$CHCl_3$	0·04			118 ± 5
	0·05			108 ± 5
	0·08			112 ± 5
	0·13			74 ± 4
	0·20			62 ± 4
	0·25			57 ± 4
	0·30			49 ± 3
	0·35			42 ± 3
	0·40			42 ± 3

* The parameters a' and h' refer to slow exchange: h'' refers to fast exchange (see Figure 1).

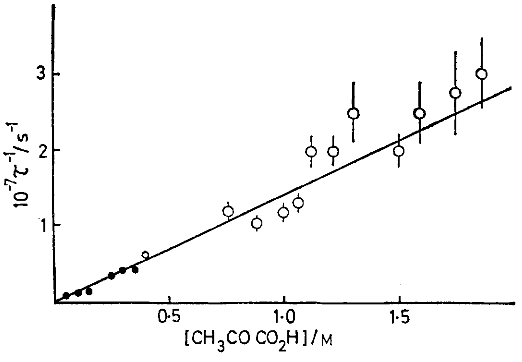


FIGURE 3 Exchange rate τ^{-1}/s^{-1} as a function of pyruvic acid concentration for $CH_3\dot{C}(OH)CO_2H$ radicals in propan-2-ol. The lowest six points are derived from slow exchange data (r') and the remainder from fast exchange data (r'')

The near-linearity of the plot over the whole range is itself a vindication of the use of the modified Bloch equations. The fact that the best straight lines passes through the origin shows that the exchange reaction is first order in keto-acid concentration [A].

Furthermore since the spin lifetime of the ketyl radical R• is defined by equation (5) and $\tau^{-1}_{R\cdot} = k[A]$, it follows that

$$\tau^{-1}_{R\cdot} = \frac{1}{[R\cdot]}\frac{d[R\cdot]}{dt} \qquad (5)$$

$d[R\cdot]/dt = k[R\cdot][A]$ and the gradient of the line gives the second-order rate constant k. Since only half the exchanges lead to a change of spin the rate constant for proton exchanges is $2k$.

Similar experiments were carried out using ethanol and chloroform as solvents. The plots of τ^{-1} against acid concentration are shown in Figures 4 and 5.

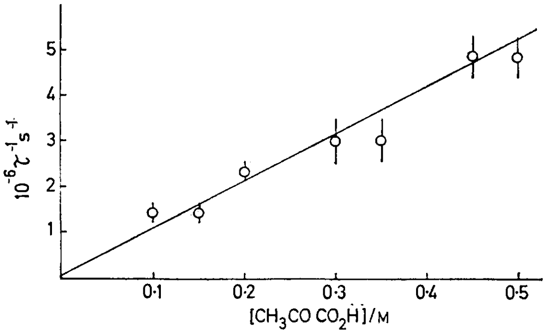


FIGURE 4 Exchange rate τ^{-1}/s^{-1} as a function of pyruvic acid concentration for $CH_3\dot{C}(OH)CO_2H$ radicals in ethanol (derived from slow exchange data)

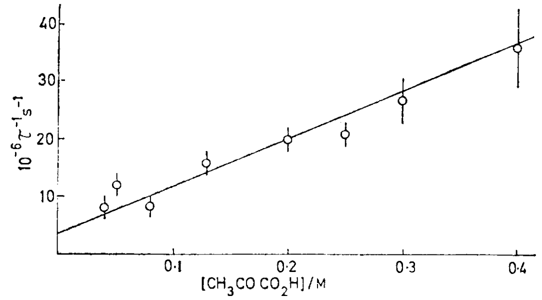


FIGURE 5 Exchange rate τ^{-1}/s^{-1} as a function of pyruvic acid concentration for $CH_3\dot{C}(OH)CO_2H$ radicals in chloroform (derived from fast exchange data)

The data derived from measurements in chloroform are less reliable than the others because we were unable to obtain the necessary parameters for computation from the slow exchange limit at room temperature, though we were able to approach the limit closely by cooling the sample to 245 K. The estimated value for linewidth of 0·032 ± 0·003 mT is the same as that observed at the fast exchange limit at 293 K. From the value of hyperfine splitting at 245 K, assuming a linear relationship between the hydroxy-proton splitting and temperature,[13] we estimated a = 0·097 mT in this solvent. Our overall estimates of error in the exchange rates in chloroform reflect this additional source of error.

For chloroform and propan-2-ol we carried out a series of measurements of line shape over a range of temperature (295—360 K for propan-2-ol, 269—352 K for chloroform). Because of the variation of a^{H}_{OH} with temperature the

[13] P. B. Ayscough and R. E. D. McClung, *Mol. Phys.*, 1971, **20**, 35.

exchange was studied over a smaller temperature range than we would have wished. The estimated values of log (τ^{-1}) are plotted against T^{-1} in Figure 6, and the observed activation energies are given in Table 2.

The Radical $\mathrm{HO_2CCH_2\dot{C}(OH)CO_2H}$.—The kind of exchange reaction observed in the radical derived from pyruvic acid appears to apply to other radicals of the type $\mathrm{R\dot{C}(OH)CO_2H}$ in organic solvents. For instance similar line shape changes were observed for the radical $\mathrm{CH_3CH_2\dot{C}(OH)CO_2H}$. When we photolysed solutions of oxaloacetic acid in propan-2-ol an e.s.r. signal was observed corresponding to the radical $\mathrm{HO_2CCH_2\dot{C}(OH)CO_2H}$, which again displays behaviour characteristic of an acid-catalysed proton exchange.

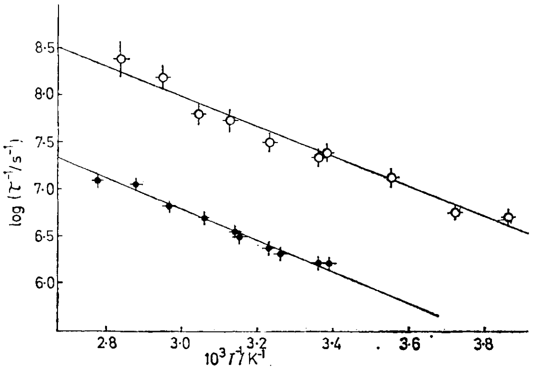


FIGURE 6 Arrhenius plot of $\log_{10}$ (τ^{-1}) against T^{-1} for exchange reaction of $\mathrm{CH_3\dot{C}(OH)CO_2H}$ radicals in propan-2-ol and chloroform: ● propan-2-ol; ○ chloroform

At high concentrations of the acid the spectrum consists of a 1 : 2 : 1 triplet of doublets with $a^{\mathrm{H}}_{\mathrm{CH_2}} = 1{\cdot}020 \pm 0{\cdot}003$ and $a^{\mathrm{H}}_{\mathrm{OH}} = 0{\cdot}250 \pm 0{\cdot}003$ mT. On decreasing the keto-acid concentration a further splitting of *ca.* 0·1 mT is observed, which we attribute to hyperfine interaction with the carboxy-proton.

TABLE 2

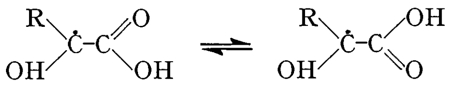
Termination rates for $\mathrm{CH_3\dot{C}(OH)CO_2H}$ and $\mathrm{HO_2CCH_2\dot{C}(OH)CO_2H}$ radicals

Radical	Solvent	10^7k/ l mol^{-1} s^{-1}	E_a/ kJ mol^{-1}	log (A/ l mol^{-1} s^{-1})
$\mathrm{CH_3\dot{C}(OH)CO_2H}$	$\mathrm{CHCl_3}$	1·7 ± 0·4	26·5 ± 2·9	12·3 ± 0·5
	$\mathrm{Me_2CHOH}$	2·8 ± 0·3	30·9 ± 3·4	12·6 ± 0·6
	EtOH	2·0 ± 0·2		
$\mathrm{HO_2CCH_2\dot{C}\text{-}(OH)CO_2H}$	$\mathrm{Me_2CHOH}$	2·0 ± 0·2		

We made a series of measurements of exchange rate as a function of acid concentration as in the case of pyruvic acid, though the concentration range was limited by the low solubility of oxaloacetic acid in propan-2-ol. We used the values $a = 99 \pm 6$ and $h = 44 \pm 2$ mT from measurements at the slow exchange limit and obtained a linear plot of τ^{-1} against acid concentration. The second-order rate constant for exchange was found to be $(2{\cdot}0 \pm 0{\cdot}1) \times 10^7$ l mol^{-1} s^{-1} (*i.e.* twice the rate constant for spin exchange).

DISCUSSION

Our measurements of linewidths and lifetimes have been interpreted in terms of an acid-catalysed exchange of the carboxy-protons in $\mathrm{R\dot{C}(OH)CO_2H}$ radicals, but alternative interpretations are in principle possible. For example the exchange may be inter- or intra-molecular or it could correspond to an intramolecular *cis–trans* isomerisation (6). We can rule out this particular interpretation since a recent report has shown that the hyperfine splittings $a^{\mathrm{H}}_{\mathrm{CH_3}}$ and $a^{\mathrm{H}}_{\mathrm{OH}}$ for the two isomers differ[14] whereas we find these parameters essentially invariant at acid concentrations from 0·3 to 3·7M: this implies that the differences in $a^{\mathrm{H}}_{\mathrm{CH_3}}$ and $a^{\mathrm{H}}_{\mathrm{OH}}$ for the two isomers are small compared with the proton exchange rate under these conditions (*i.e.* $<10^6$ Hz). We can also be certain that the exchange does not involve the OH protons since we can identify this hyperfine splitting by its characteristic value of *ca.* 0·2 mT in species $\mathrm{R^1\dot{C}(OH)COR^2}$[10] and this is also essentially invariant throughout the concentration range studied. Only the hyperfine splitting which we have to attribute to the carboxy-protons is affected by changes in acid concentration or temperature. Intramolecular exchange of the OH and $\mathrm{CO_2H}$ protons would cause changes in both hyperfine splittings, contrary to our observations.


(6)

We therefore conclude that the process we are observing is intermolecular exchange of the carboxy-protons according to equation (7). As far as we know other data

$$\mathrm{R\dot{C}(OH)CO_2H_A + H_BO_2CCOR \rightleftharpoons R\dot{C}(OH)CO_2H_B + H_AO_2CCOR} \quad (7)$$

are not available for exchange reactions of this type involving free radicals, and there are also very little data available for the exchange of carboxy-protons in carboxylic acids. Grunwald *et al.*[15] have shown by an n.m.r. method that the second-order rate constant for proton transfer between benzoic acid and the benzoate ion involving one molecule of methanol is $1{\cdot}52 \times 10^8$ l mol^{-1} s^{-1} which is quite similar to our values. Proton exchange reactions between $\mathrm{NH_4^+}$, $\mathrm{CH_3NH_3^+}$, $\mathrm{(CH_3)_2NH_2^+}$, and $\mathrm{(CH_3)_3NH^+}$ and their conjugate bases in water have rate constants between $0{\cdot}9 \times 10^8$ and $9{\cdot}0 \times 10^8$ l mol^{-1} s^{-1}.[16] Proton exchange processes between $\mathrm{OH^-}$ and $\mathrm{RNH_3^+}$ groups in amino-acids are much faster, with rate constants *ca.* 2×10^{10} l mol^{-1} s^{-1},[17] and these are much faster than exchanges involving the carboxy-protons in these species, so that again the rate constants for these latter processes are likely to be in the range 10^8—10^9 l mol^{-1} s^{-1}.

The observed difference between the exchange rates for the radicals $\mathrm{CH_3\dot{C}(OH)CO_2H}$ and $\mathrm{HO_2CCH_2\dot{C}(OH)CO_2H}$ ($2{\cdot}8 \times 10^7$ and $2{\cdot}0 \times 10^7$ l mol^{-1} s^{-1} respectively at 298 K) is barely significant but is in the correct direction for a reaction involving a transition state with an

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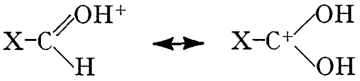
[14] A. Samuni, personal communication.

[15] E. Grunwald, L. Jumper, and L. Meilboom, *J. Amer. Chem. Soc.*, 1963, **85**, 522.

[16] E. Grunwald and M. Cocivera, *Discuss. Faraday Soc.*, 1965, **39**, 105.

[17] R. D. White, L. J. Sluksky, and S. Pattison, *J. Phys. Chem.*, 1971, **75**, 161.

incipient positive charge, *i.e.* process (8). In such a case increasing electron-withdrawing character of X will tend



(8)

to destabilise the transition state and reduce the exchange rate, as observed. Furthermore, if we are dealing with a transition state which is more polar than the initial species, the observed solvent effect, though small, is readily rationalised. If the solvent is of low polarity we would not expect a large change in solvation in forming the transition state; however, for a polar solvent, increased solvation in the transition state should effect a negative contribution to the activation entropy ΔS^* which will reduce the rate constant for proton exchange in solvents of higher dielectric constant if the activation energy is unchanged. In addition, as has been pointed out by North,[18] differences in the temperature coefficient of viscosity for the solvents used may influence the measured activation energy. Unfortunately the experimental errors in our observed activation energies are such that we cannot establish whether the solvent effect is primarily on the activation energy or entropy.

[3/603 *Received, 22nd March,* 1973]

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[18] A. M. North, ' The Collision Theory of Chemical Reactions in Liquids,' Methuen, London, 1964, p. 84.