^{1}H Nuclear Magnetic Resonance Studies of Solutions of Aromatic Bases. Part I. Proton Exchange in Ethanol Solutions of Pyridines

By **R. Large** and **M. R. Willis,*** Chemistry Department, University of Nottingham, Nottingham NG7 2RD

The overall rate of proton exchange in ethanol solutions of pyridine, γ-picoline, and 2,6-lutidine was measured by observation of the methylene proton lineshape as a function of concentration. The process obeys the empirical rate equation (i) where $k_1 = 2{\cdot}8 \times 10^9$ l mol^{-1} s^{-1} for pyridine, $4{\cdot}3 \times 10^8$ for γ-picoline, and $0{\cdot}7 \times 10^8$ for 2,6-lutidine and k_2 is approximately constant at 6×10^8 s^{-1}. The first term refers to the symmetrical exchange reaction (ii).

$$\text{Rate} = k_1[\text{BH}^+][\text{B}] + k_2[\text{BH}^+] \text{ mol l}^{-1}\text{ s}^{-1} \tag{i}$$

$$\text{BH}^+ + \text{EtOH}^* + \text{B} \rightleftharpoons \text{B} + \text{HOEt} + \text{H}^*\text{B}^+ \tag{ii}$$

The second term may reflect exchange catalysed by EtO$^-$.

HYDROXY-PROTON exchange in alcohol solutions is catalysed by both acid and base.[1] The kinetics of the rapid proton exchange in ethanol catalysed by hydroxide and hydrogen ions has been studied in detail[2] by observing the collapse of spin multiplets in the n.m.r. spectrum. Proton exchanges in alcohols catalysed by aliphatic nitrogen bases have been studied by Swain *et al.*[3] using isotopic exchange procedures, and by Grunwald and Cocivera[4] using the n.m.r. method.

In that proton exchange processes involve either single solvent molecules or groups of solvent molecules, the study of proton exchange may provide a means of investigating solution structure in hydroxylic solvents. However, a clear understanding of the kinetics and mechanisms of the process is required. The study of exchange catalysed by weak bases may be particularly interesting as more concentrated solutions, in which solvent structure has been significantly disturbed,[5] can be studied. In this paper the kinetics of proton exchange in ethanolic solutions of pyridine, γ-picoline, and 2,6-lutidine are reported and the mechanism is discussed.

EXPERIMENTAL

Ethyl Alcohol.—Traces of acid, base, and water influence the exchange rate in ethanol.[1] Of the drying agents tried it was found that Hi-Drite (anhydrous calcium sulphate) was the most satisfactory. Absolute alcohol, which contains *ca.* 0·5% water, was dried by standing over an excess of Hi-Drite granules (3/16 in) for not less than a week, decanted, and fractionated. The criteria of purity were the refractive index at 25 °C, the spin–spin splitting of the n.m.r. hydroxy and methylene peaks, and the area under the n.m.r. water peak. The latter was detectable only at very high gain and was compared with a standard sample of known water content, determined by Karl Fischer titration. The ethanol purified by this method had $n_D^{25} = 1{\cdot}3594 \pm 0{\cdot}0001$ and a water content not in excess of 0·02%.

Pyridine Bases.—Pyridine (AnalaR), γ-picoline (B.D.H. Laboratory reagent grade), and 2,6-lutidine (B.D.H. laboratory reagent grade) were purified by methods similar to that used for ethanol. Each base was dried with Hi-Drite, decanted, and fractionated. For pyridine the fraction boiling at 115·5 ± 0·5 °C was collected and fractions with b.p. 143·0 ± 0·5 °C and 142·5 ± 0·5 °C were collected for γ-picoline and 2,6-lutidine. For γ-picoline and 2,6-lutidine this purification procedure will not remove other isomers. However, n.m.r. spectra of the bases showed that the concentrations of other isomers was negligible.

Glassware.—The fact that hydroxy-proton exchange in ethanol is catalysed by very low concentrations of acid or base makes the removal of chance impurities from the glassware important. Varian Pyrex glass sample tubes produced less contamination than those of soda-glass. Even so it proved necessary to condition all glassware carefully. The method was developed from that used by Patterson.[6] All glassware was soaked for 30 min in acetone, then dilute hydrochloric acid, then dilute ammonia solution, and then absolute alcohol. Between each soaking the glassware was steamed for 30 min, and the conditioning was completed by steaming for a further 2 h, followed by drying at 100 °C overnight. Finally the sample tubes were washed two or three times with the ethanolic solution of base to be studied, before a spectrum was run.

N.m.r. Measurements.—Solutions of known concentration of base in alcohol were prepared by weighing, sealed in an n.m.r. tube with a plastic cap, and their spectra run on an AEI RS2 spectrometer operating at 60 MHz. The absorption mode spectra were recorded at an H_1 attenuation of 60 dB, a sweep rate of 60—100 Hz min^{-1} (over which range the lineshape is independent of sweep rate), a constant field homogeneity of approximately 1 part in 10^8, and a sample temperature controlled at 26·5 ± 0·2 °C. At least 5 determinations were made at each concentration, in at least two sample tubes.

The spin–spin splittings of multiplets in the absence of exchange were measured for each sample of pure dry ethanol by use of sideband calibration. They were in the range 4·86 ± 0·1 Hz for the hydroxy-triplet and 4·96 ± 0·1 Hz for the methylene doublets.

Values of the effective transverse relaxation time in the absence of exchange, T_2^* (which includes contribution from magnetic field inhomogeneity), were determined from the line-width of the components of the ethanol methyl resonance, following the practice of Feldbauer and Weller.[7] By careful tuning it was possible to obtain consistent values of 0·32 s.

Measurement of Exchange Rate.—Hydroxy-proton ex-

---

[1] W. Anderson and J. T. Arnold, *Discuss. Faraday Soc.*, 1955, **19**, 226.

[2] Z. Luz, D. Gill, and S. Meiboom, *J. Chem. Phys.*, 1959, **30**, 1540.

[3] C. E. Swain, J. T. McKnight, and V. P. Kreiter, *J. Amer. Chem. Soc.*, 1957, **79**, 1088.

[4] E. Gunwald and M. Cocivera, *Discuss. Faraday Soc.*, 1965, **39**, 105.

[5] M. Martin, *J. Chim. phys.*, 1962, **59**, 736.

[6] W. G. Patterson, *Canad. J. Chem.*, 1963, **41**, 714.

[7] H. Feldbauer and A. Weller, *Z. phys. Chem.*, 1962, **32**, 263.

change rates were determined by comparing the observed shapes of the exchange-broadened multiplets with those calculated by Meiboom and his co-workers[8,9]. The tables[9] give relative values of signal amplitude for specific values of three dimensionless parameters, r (the exchange parameter), s (the frequency parameter), and t (the natural linewidth parameter). The parameters are defined as $r = 2\tau\delta\omega$, $s = \Delta\omega/\delta\omega$, and $t = 1/(T_2\delta\omega)$. $\delta\omega$ Is half the frequency spacing between the multiplet components in the absence of exchange, τ is the mean time interval between successive exchanges, $\Delta\omega$ is the distance (in radian s^{-1}) from the multiplet centre, and T_2 the transverse relaxation time. In practice it is necessary to use the effective transverse relaxation time T_2^*, which includes contributions from magnetic field inhomogeneity.

In principle it should be possible to determine exchange parameters from both the methylene resonance (treating it as four doublets) and the hydroxy-resonance ranging from conditions where the multiplets are exchange-broadened to conditions where the multiplets have collapsed to a broadened single line. In practice satisfactory results were only obtainable for exchange-broadened multiplets as measurements on broadened single lines require higher stability than could be achieved with the spectrometer used.

Comparison with theoretical curves was based on the peak-to-valley intensity ratio of the exchange-broadened multiplet. Exchange rates were obtained from both the methylene and the hydroxy-resonances, and the results agreed within experimental error. The results from the methylene resonances were chosen for kinetic analysis.

RESULTS

Values of τ, the mean lifetime between successive exchanges, were obtained for the hydroxy-proton in ethanol as a function of base concentration. The specific proton exchange rate (R) was obtained from relation (1).[2] The results are in Table 1.

$$1/\tau = (1/[\mathrm{EtOH}])R \qquad (1)$$

TABLE 1

Kinetic measurements on ethanol–base solutions

Pyridine			γ-Picoline			2,6-Lutidine		
[B]	[EtOH]	[EtOH]/τ	[B]	[EtOH]	[EtOH]/τ	[B]	[EtOH]	[EtOH]/τ
0·163	16·91	42·4	0·061	16·99	59·6	0·123	16·74	80·2
0·171	17·06	40·9	0·084	16·89	91·9	0·248	16·81	120·0
0·296	16·71	54·3	0·177	16·84	111·0	0·273	16·57	121·5
0·368	16·61	69·6	0·253	16·72	138·6	0·299	16·47	121·5
0·383	16·69	78·3	0·256	16·61	157·0	0·387	16·24	175·9
0·431	16·54	94·4	0·310	16·54	166·2	0·412	16·43	172·4
0·485	16·45	89·5	0·475	16·36	196·6	0·516	15·89	193·4
0·490	16·45	97·5	0·484	16·31	204·5	0·608	15·90	187·5
0·522	16·41	110·1	0·507	16·45	213·4	0·664	15·95	211·0
0·583	16·32	148·7	0·541	16·23	226·6	0·691	15·78	217·9
0·661	16·08	170·1	0·555	16·22	229·7	0·749	15·67	234·7
0·692	16·03	179·5	0·688	15·93	267·0	0·753	15·67	237·4
0·715	16·13	183·7	0·718	15·93	277·8	0·829	15·44	243·3
0·729	16·11	211·7	0·826	15·76	268·4	0·873	15·41	243·0
0·855	15·96	195·7				0·922	15·39	249·2
0·863	15·95	232·1				0·943	15·31	267·2
1·002	15·71	266·8						

Concentrations are quoted in mol l^{-1} and τ in s.

DISCUSSION

The kinetic measurements show a steady increase in proton exchange rate with base concentration [B]. To interpret the effect in terms of one of the various possible rate equations requires a knowledge of the concentration of the conjugate acid [BH$^+$]. A value of pK_a for pyridine in ethanol of 4·72 has been reported by Larsson,[10] but no value for the other bases used here is available. However, it is possible to make reliable estimates. Rochester[11] has measured pK_a for a number of methylpyridines in methanol. He found that the increase in pK_a (ΔpK_a) on going from pyridine to γ-picoline is 0·79, and that on going from pyridine to 2,6-lutidine is 1·49. These values are within experimental error of those found in water, suggesting that they are independent of the hydroxylic solvent. The ΔpK_a values for α-picoline and 2,4,6-collidine in ethanol of 0·82 and 2·31 respectively, obtained from Larsson's data, tend to support this view. On this basis, therefore, the pK_a values for pyridine, γ-picoline, and 2,6-lutidine in ethanol are taken as 4·72, 5·52, and 6·21 respectively.

The calculation of [BH$^+$] from pK_a demands a knowledge of the ionic product for ethanol in terms of molarities. From published data[12] at 20 °C and 25 °C a value of $1{\cdot}62 \times 10^{-19}$ at 26·5 °C was obtained by extrapolation.

In attempting to fit the observed rates of exchange to empirical rate equations it is assumed that the same rate law applies for each base. Various simple rate expressions used by other workers were tried but none produced a straight-line plot for all three bases. However, a plot of [EtOH]/τ against [B][BH$^+$] did produce a good straight line for the pyridine solutions, but not for those of the other two bases. On the other hand a plot of [EtOH]/τ against [BH$^+$] was linear in all three cases for

---

[8] A. Loewenstein and S. Meiboom, *J. Chem. Phys.*, 1957, **27**, 1067.

[9] 'Tables of Exchange Broadened N.m.r. Multiplets,' The Weizmann Institute of Science, Rehovot, Israel.

[10] E. Larsson, *Z. phys. Chem.*, 1931, **169**, *A*, 207.

[11] C. H. Rochester, *J. Chem. Soc.* (*B*), 1967, 33.

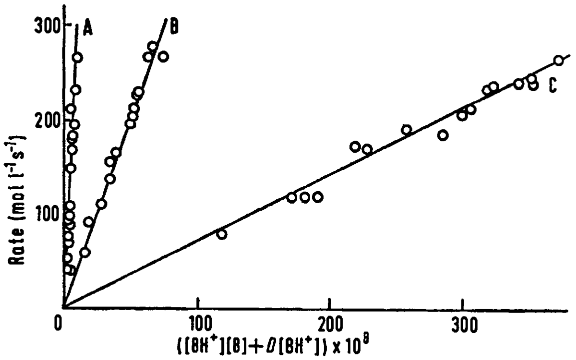
[12] R. Schaal and A. Teze, *Bull. Soc. chim. France*, 1961, 1783.

$[BH^+]$ in excess of $0{\cdot}5 \times 10^{-7}$M, but curved at lower concentration. However by assuming that both terms are involved we were able to produce good straight-line plots for all three bases (Figure). The rate expression (2) was plotted as (3), where C = slope = k_1 and D =

$$\text{Rate} = [\text{EtOH}]/\tau = k_1[BH^+][B] + k_2[BH^+] \quad (2)$$

$$\text{Rate} = C\{[BH^+][B] + D[BH^+]\} \quad (3)$$

k_2/k_1 and is chosen to give the best straight lines. The values of k_1 and k_2 are in Table 2. The probable errors are estimated on the basis of the scatter of points, sensitivity of the linearity of the graphs to changes in the rate constants, and uncertainties in the pK_a values. k_1 For pyridine is much more accurate than the other rate constants since it relates to the dominant kinetic term and the pK_a has been determined experimentally.



Plot of the observed rate of proton exchange (R/mol l^{-1} s^{-1}) against the suggested rate function; A, pyridine; B, γ-picoline; C, 2,6-lutidine

TABLE 2

Base	k_1/l mol^{-1} s^{-1}	k_2/s^{-1}
Pyridine	$2{\cdot}8 \pm 0{\cdot}3 \times 10^9$	$3{\cdot}5 \pm 2 \times 10^8$
γ-Picoline	$4{\cdot}3 \pm 2 \times 10^8$	$11 \pm 6 \times 10^8$
2,6-Lutidine	$0{\cdot}7 \pm 0{\cdot}3 \times 10^8$	$4{\cdot}6 \pm 2 \times 10^8$

The empirical rate equation (3) is comparable with that observed by Cocivera *et al*[13] for proton exchange in solutions of *p*-toluidinium ions in methanol. The first term can be associated with the symmetrical exchange reaction (4) which is likely to involve only one alcohol

$$BH^+ + EtOH^* + B \overset{k_1}{\rightleftharpoons} B + HOEt + H^*B^+ \quad (4)$$

molecule.[14] On this assumption the values may be compared with those reported[14] for γ-picoline in methanol ($3{\cdot}4 \times 10^8$ l mol^{-1} s^{-1}) and 2,6-lutidine in methanol ($0{\cdot}8 \times 10^8$ l mol^{-1} s^{-1}).

The formal similarity of the empirical rate equation to that observed by Cocivera[13] suggests that the second term is associated with the rate of acid dissociation of BH^+. However the rate constant for this process has been established by Cocivera[14] for various methylpyridines in methanol as *ca.* 10^3 s^{-1}. Since rate constants in the two solvents tend to be similar, the term $k_2[BH^+]$ must be associated with some other process. Now the concentration of BH^+ is identical with that of EtO^-. Thus the term could be equally well written as $k_2[EtO^-]$ and be associated with the exchange reaction (5).

$$EtOH + EtO^- \rightleftharpoons EtO^- + EtOH \quad (5)$$

The fact that the rate constants from all three sets of solutions agree within experimental error supports this mechanism although the rate constants are significantly greater than the value of $2{\cdot}4 \times 10^7$ s^{-1} (ref. 2). Now the same paper contained a value for the corresponding process in methanol, determined in the same way. Subsequent measurements in buffer solutions showed that the value of k_2 for methanol was too low by a factor of 80, and it is reasonable to assume that the ethanol value is also too low. The evidence therefore points to the conclusion that the second term in the rate equation can be associated with exchange between ethoxide and ethanol and that the rate constant is *ca.* 6×10^8 s^{-1}.

The support of the S.R.C. is gratefully acknowledged.

[1/1620 *Received, 6th September*, 1971]

---

[13] M. Cocivera, E. Grunwald, and C. Jumper, *J. Phys. Chem.*, 1964, **68**, 3234.

[14] M. Cocivera, *J. Phys. Chem.*, 1968, **72**, 2515.