[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Rates of Ionization of Pseudo Acids.[1] V. Steric Effects in the Base-catalyzed Ionization of Nitroethane

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RECEIVED FEBRUARY 5, 1953

The rates of ionization of nitroethane catalyzed by pyridine, the methylpyridines, quinoline, isoquinoline and 2-methylquinoline have been measured. A linear relationship exists between the logs of the rate constants and the logs of the basic ionization constants except for 2,6-dimethylpyridine and 2-methylquinoline. These two bases react more slowly, an effect which is attributed to steric strain in the transition state. This appears to be a rare example of steric inhibition in a proton removal. One ortho substituent does not give any steric effect.

The conversion of nitroethane into the aci- form is subject to general base catalysis[2] and therefore provides a convenient tool for an investigation of the effect of structure on the reactivity of various bases.

$$CH_3CH_2NO_2 + B \underset{k_2}{\overset{k_1}{\rightleftarrows}} CH_3CHNO_2^- + BH^+ \quad (1)$$

While there are many examples of the rate of ionization of an acid being less than one would expect on the basis of its acidity (see reference 1), these can usually be explained[3] by the structural and electronic changes in the anion which give rise to pseudo acid character. There seems to be no example, in particular, of the presence of bulky substituents in the base slowing down the rate of proton removal from an acid. In fact, in cases where it might have been expected, the reverse has been found to be true. Thus tertiary aliphatic amines, dialkylanilines and bulky carboxylate ions have been found to be better catalysts for proton removals than their basicities would predict.[4] This has been attributed to solvation effects.

Accordingly, a study has been made of the rates of neutralization of nitroethane with pyridine, 2-, 3- and 4-methylpyridine, 2,6-lutidine, quinoline, isoquinoline and 2-methylquinoline in 30% ethanol at 25.0°. The geometry and properties of these molecules provide a favorable test of the steric requirements involved in a proton transfer.

Experimental

Preparation of Materials.—Commercial solvents nitroethane was dried and fractionated through a 10-plate column. Small middle portions boiling within a 0.1° range were collected. Reagent grade pyridine was dried over barium oxide and distilled through a 12" Vigreux column. Eastman Kodak Co. white label synthetic quinoline was distilled from zinc dust. A practical grade of isoquinoline was purified by freezing and then distilled from zinc dust. Quinaldine was vacuum distilled from zinc dust. The picolines and 2,6-lutidine were obtained from the Reilly Tar and Chemical Co. These chemicals were dried over barium oxide and fractionated through a 12" Vigreux column. The first half of the distillate was rejected and half of the remaining material collected for use. The purity of the 4-picoline was checked by conversion of a freshly distilled sample to *p*-phenylphenacyl-4-picolinium bromide, the reaction being run in benzene solution. After recrystallization from water, the salt melted at 261–262°, with decomposition. The only likely contaminant, the 3-picolinium salt, melts at 210°.

Solutions of nitroethane were made up by direct weighing. Solutions of the bases were prepared using CO_2-free water and standardized according to conventional methods. Selected volumes of the base and iodine were mixed to give the desired concentration. These bases undergo a slow irreversible reaction with iodine, hence these solutions were prepared fresh for each run. In addition a rapid reversible reaction occurs with the formation of a complex only slightly soluble in water. This fact, along with the insolubility of several of the bases, dictated the choice of 30% ethanol as a solvent.

Methods.—Resistances were measured with a Jones–Josephs bridge using an oscilloscope for a null-point indicator. The pK_b's were determined in water by measuring the pH of a solution of the base that had been 50% neutralized. Neglecting activity coefficients $pK_b = pK_w - p\mathrm{H}$.

For kinetic runs a sample of the base–iodine solution was introduced directly into the conductance cell which was thermostated in a bath controlled at 25.0°. The quantity of nitroethane needed to react with this sample of base and iodine was added with a pipet from a separately thermostated nitroethane solution. The conductance cell was stoppered and inverted several times to ensure mixing. A calibrated stopwatch was started during the course of the addition of the nitroethane.

Calculations and Results.—The kinetics are complicated by the simultaneous reaction of nitroethane with the amine and hydroxyl ion and by the reversal of reaction (1).

$$CH_3CH_2NO_2 + OH^- \xrightarrow{k_3} CH_3CHNO_2^- + H_2O \quad (2)$$

However, reaction (1) may be driven to completion by the addition of iodine.

$$CH_3CHNO_2^- + I_2 \longrightarrow CH_3CHINO_2 + I^- \quad (3)$$

If reaction (3) is assumed to be instantaneous, the rate expression is

$$\frac{-d[CH_3CH_2NO_2]}{dt} = k_1[CH_3CH_2NO_2][B] + k_3[CH_3CH_2NO_2][OH^-] \quad (4)$$

Now if the equilibrium

$$B + H_2O = BH^+ + OH^- \quad (5)$$

is always maintained, the rate expression then becomes

$$\frac{dx}{dt} = k_1(a - x)(b - x) + k_3K_b\frac{(a - x)(b - x)}{x} \quad (6)$$

where $x = [BH^+] = [I^-]$, $a = [CH_3CH_2NO_2]_0$, $b = [B]_0$.

The assumption that a and $b >> x$ is valid if the concentration of I_2 is chosen much smaller than the initial concentration of nitroethane and base

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(1) For previous papers see R. G. Pearson and R. L. Dillon, THIS JOURNAL, **75**, 2439 (1953).

(2) (a) R. Junell, Dissertation, Uppsala, 1935; (b) S. H. Maron and V. K. La Mer, THIS JOURNAL, **60**, 2588 (1938); (c) R. G. Pearson, *ibid.*, **70**, 204 (1948).

(3) A purely steric retardation seems to be operating in the case of the base-catalyzed ionization of ortho-substituted aldchlorimines, C. R. Hauser, J. W. Le Maistre and A. E. Rainsford, THIS JOURNAL, **57**, 1056 (1935).

(4) (a) Reference 2c; R. P. Bell and A. F. Trotman-Dickenson, *J. Chem. Soc.*, 1288 (1949); (c) R. P. Bell, D. Gelles and E. Moller, *Proc. Roy. Soc.* (*London*), **A198**, 308 (1949).

The reaction essentially ceases when all the I_2 is consumed. Under these conditions

$$dx/dt = k_1ab + k_3K_b(ab/x) \qquad (7)$$

The rate constant, k_3, for hydroxyl ion is known.[5] The accuracy of the available data in the literature for the basic ionization constants of the amines leaves much to be desired. These data, along with some measurements from this Laboratory, are compiled in Table I. Preliminary experiments indicated that k_1 was approximately 10^{-2}. Since K_b for the amines is around 10^{-9} and k_3 is 350 we see that the second factor in equation (7) is small compared with the first term as soon as x has become appreciable. Putting in a drop of strong acid so that $[BH^+]_0$ is $\simeq 2 \times 10^{-3}$ M allows the second term to be neglected from the start of the reaction. The rate should be independent of the exact value of $[BH^+]_0$ as was found experimentally. The rate expression becomes $\frac{dx}{dt} = k_1ab$ which integrates to $x = k_1abt + x_0$. Neglecting the change of equivalent conductance with ionic strength, the reciprocal of the resistance was assumed to be proportional to the extent of reaction. It was found that a plot $1/R$ *versus* time gave a straight line until the reaction was about 80% complete. This is shown in Fig. 1. Extrapolation of the straight line portions of the curves to the equilibrium resistances gave the hypothetical times to complete the reactions if the reaction rate remained constant throughout.

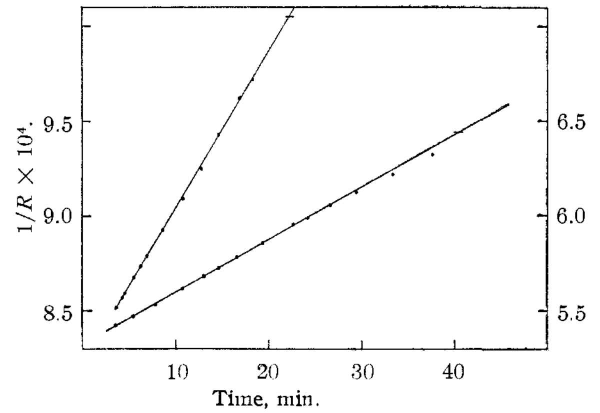

Fig. 1.—Left curve, 2,6-lutidine; right curve, pyridine; vertical line = $1/R_e$.

These times, together with the initial concentrations of iodine, nitroethane and amine, enable a calculation of the rate constant k_1. Table II is a tabulation of the rate constants obtained at 25.0°. The units of all rate constants are liters per mole-minute.

The reaction

$$C_5H_5N + CH_3CH_2NO_2 \xrightarrow{k_1} C_5H_5NH^+ + CH_3CHNO_2^- \qquad (8)$$

was studied at several temperatures and in solvents of various alcohol concentrations. From the variation of k_1 with temperature the activation energy, E_{act}, can be found. Also using the transition state theory of reaction velocity the entropy of activation was calculated for reaction (8). These data are tabulated in Table III.

TABLE I

BASE DISSOCIATION CONSTANTS AT 25°

Base	pK_b
Pyridine	8.79,[a] 8.65,[b] 8.77[c]
2-Methylpyridine	7.98,[b] 8.08,[d] 8.04,[c] 7.90[e]
3-Methylpyridine	8.34,[d] 8.20,[e] 8.00[f]
4-Methylpyridine	8.00,[d] 7.95,[c] 7.90,[e] 8.00[f]
2,6-Dimethylpyridine	7.36,[d] 7.38,[c] 7.10[e]
Quinoline	9.00,[e] 9.06,[g] 9.11,[h] 9.20[i]
Isoquinoline	8.60,[e] 8.64[f]
2-Methylquinoline	8.35,[d] 8.20,[e] 8.40[j]

[a] N. F. Hall, THIS JOURNAL, **52**, 5124 (1930). [b] E. S. Guzman-Barron, *J. Biol. Chem.*, 121, 313 (1937). [c] A. Gero and J. J. Markham, *J. Org. Chem.*, 16, 1835 (1951) [d] This investigation. [e] C. Golumbic and M. Orchin, THIS JOURNAL, **72**, 4145 (1950). [f] E. J. Constam and J. White, *Am. Chem. J.*, **29**, 36 (1903). [g] A. Albert and R. Goldacre, *Nature*, **153**, 467 (1944). [h] P. Karrer and H. Schmidt, *Helv. Chim. Acta*, **29**, 1853 (1946). [i] W. A. Felsing and P. S. Biggs, THIS JOURNAL, **55**, 3624 (1933). [j] H. Goldschmidt and R. M. Salcher, *Z. physik. Chem.*, **29**, 89 (1899).

TABLE II

KINETICS OF B + $CH_3CH_2NO_2 \rightarrow BH^+ + CH_3CHNO_2^-$ IN 30% ETHANOL AT 25°

No.	Base[a]	pK_b	$k_1 \times 10^{3b}$
1	2,6-Dimethylpyridine	7.36	20.8 ± 0.6
2	2-Methylpyridine	7.98	24.5 ± .9
3	4-Methylpyridine	8.00	18.2 ± .3
4	3-Methylpyridine	8.34	13.2 ± .2
5	2-Methylquinoline	8.30	7.7 ± .0
6	Isoquinoline	8.64	7.6 ± .1
7	Pyridine	8.75	6.5 ± .2
8	Quinoline	9.06	4.5 ± .1

[a] Concentrations were 0.1–0.2 M for base and nitroethane and 0.002 to 0.004 M for iodine. [b] At least three runs for each compound except 2-methylquinoline for which only two runs were made. Units are liters/mole-minute.

TABLE III

KINETICS OF $C_5H_5N + CH_3CH_2NO_2 \rightarrow C_5H_5NH^+ + CH_3CHNO_2^-$

% Ethanol by volume	Temp., °C.	$k_1 \times 10^3$	E_{act}, kcal.	$\Delta S\ddagger$, e.u.
0	17.0	3.64		
	25.0	8.92		
	34.85	21.4	16.6	−25.0
30	0.0	0.516		
	25.0	6.50		
	34.85	13.9	15.8	−28.3
70	0.0	0.028		
	25.0	0.352		
	34.85	0.973	17.1	−29.7

Discussion

In general, it is recognized that a linear free energy relationship between rates and equilibria should exist for a reaction that is subject to general acid or base catalysis. It is evident from Fig. 2 that these bases, excepting 2,6-dimethylpyridine and 2-methylquinoline, fulfill this requirement. The straight line has a slope of 0.65. An examination of molecular models shows that there is definite interference between the methyl group of nitroethane

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(5) R. P. Bell and J. C. Clunie, *Proc. Roy. Soc.* (London), **A212**, 16 (1952).

and one of the two substituents on the 2- and 6-positions in pyridine if the nitrogen atom is brought up to the acidic methylene hydrogen atom. When there is only a single substituent on 2 or 6, then the interference can easily be avoided. Thus we appear to have a type of steric hindrance which has been called F-strain by Brown and his associates.[6]

The strain is not associated with the proton being added to the nitrogen, but rather to the methyl group of the reference acid. Thus Bell[7] has studied the base-catalyzed decomposition of nitramide in both water and anisole.

$$HN = NO_2H + B \longrightarrow BH^+ + N_2O + OH^- \quad (9)$$

A linear relation between log k and pK_a (measured in water) was found for pyridine, the methylpyridines, quinoline, isoquinoline and collidine. This latter compound being substituted on the 2- and 6-positions should have steric requirements equal to 2,6-lutidine. Its failure to show a deviation means that at least one bulky substituent on the atom holding the acidic hydrogen is necessary.

On the other hand, Brown[8] has measured the dissociation constants of the addition compounds of pyridine and the methyl pyridines with trimethylboron and has found that 2-methylpyridine forms the least stable derivative. The concept of F-strain was invoked to explain this instability. Also in the reaction of alkyl halides with substituted pyridines[9] it has been noted that a single substituent in the 2-position markedly reduces the rate and 2,6-substitution nearly stops formation of quaternary ammonium salt. Thus it appears that the steric requirements of nitroethane are intermediate between those of nitramide and of trimethylboron and alkyl halides.

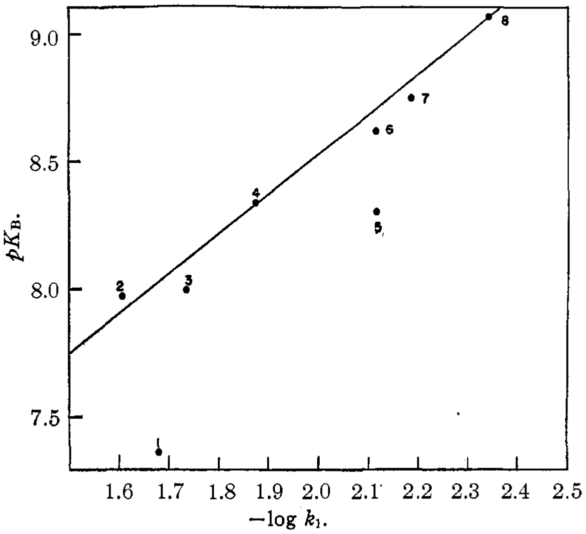

Fig. 2.—Compounds numbered as in Table II.

It may be objected that a rate process determined in 30% ethanol is being compared with an equilibrium in water. While no complete data are available for this system, ionization constants of five of the bases used here have been determined in 100% ethanol.[10] Using the method of Grunwald and Gutbezahl[11] it is possible to estimate the ionization constants in 30% ethanol. In no case do the changes in pK_a differ from each other by more than 0.1 unit. The estimated value is in excellent agreement with the experimental value in the one case where it is known, for pyridine.[12]

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(6) H. C. Brown, H. Bartholomay and M. D. Taylor, THIS JOURNAL, **66**, 435 (1944).

(7) Reference 1b; R. P. Bell and G. L. Wilson, *Trans. Faraday Soc.*, **46**, 407 (1950).

(8) H. C. Brown and G. K. Barbaras, THIS JOURNAL, **69**, 1137 (1947); 2,6-lutidine does not form an addition compound with trimethylboron.

(9) N. Menschutkin, *Chem. Zentr.*, **73**, II, 86 (1902); L. C. King and D. Brebner, THIS JOURNAL, **75**, 2330 (1953).

(10) H. Goldschmidt and E. Mathieson, *Z. physik. Chem.*, **119**, 439 (1926).

(11) B. Gutbezahl and E. Grunwald, THIS JOURNAL, **75**, 559 (1953).

(12) M. Mizutani, *Z. physik. Chem.*, **116**, 350 (1925).