The Kinetics and Mechanism of the Electrophilic Substitution of Heteroaromatic Compounds. Part XXXI.[1] The Standardisation of Acid Catalysed Hydrogen Exchange Rates

By **Ali El-Anani, John Banger, Giorgio Bianchi, Sergio Clementi, C. David Johnson,*** and **Alan R. Katritzky,*** School of Chemical Sciences, University of East Anglia, Norwich NOR 88C

It is suggested that k_0 (100°) at pH = 0 should be used for correlations of hydrogen exchange rates. A procedure for obtaining these k_0 values is given involving successive determination of (A) k(stoich) T°; (B) k(stoich) T° at pH = 0; (C) k(stoich) (100°) at pH = 0; (D) correction for minority species reaction; and (E) correction for isotope effects. This procedure is applied to available data.

A MAJOR aim of the kinetic determination of reaction rates is their quantitative comparison and correlation with predictions from theories of reactivity. Acid catalysed hydrogen exchange is a suitable reaction for such work as it is undergone by a very wide range of heteroaromatic compounds of differing reactivity. Many previous papers in this series, and from other laboratories, have recorded kinetic rates for reactions of this class; the present paper attempts to define the most satisfactory method for obtaining comparable rate constants for such data (we hope later to report a similar procedure for nitration studies).

We have previously[2] given reasons for choosing to compare rate constants measured at pH 0 and 100°: measuring at pH 0 is the best available means of converting pseudo first-order rate constants into second-order rate constants, and 100° is chosen to minimise temperature extrapolation as most rates have been measured in the range 20—180°.

The procedure for the determination of k_0 (100°) at

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[1] Part XXX, A. G. Burton, P. J. Halls, and A. R. Katritzky, *J.C.S. Perkin II*, 1972, 1953.

[2] P. Bellingham, C. D. Johnson, and A. R. Katritzky, *J. Chem. Soc. (B)*, 1968, 866.

pH = 0 is a complex one and requires the following steps: (A) determination of k(stoich) ($T°$), involving knowledge of the acidity function at $T°$, of the effect of dissolved substrate on the acidity function, and of the effect of using D_2SO_4 instead of H_2SO_4; (B) determination of k(stoich) ($T°$) at pH = 0, involving construction of the rate profile and extrapolation to pH = 0; (C) determination of k(stoich) (100°) at pH = 0, involving assumptions about or measurement of rate variation with temperature; (D) determination of k_0 (100°) at pH = 0, involving correction for minority species, assumptions being required regarding protonation behaviour of substrate pK with temperature; and (E) correction for isotope effects when comparing exchange rates involving different hydrogen isotopes.

Each of these steps will be discussed in detail, and then the results of the application of this procedure to available results will be presented and discussed.

PROCEDURE

A. *Determination of* k(stoich) *at a Particular Acidity and Temperature*.—(a) *Standardisation of acid.* This is achieved by the titration of 1 g of acid against N-sodium hydroxide, using screened Methyl Orange indicator. If y ml is required, wt% acid = $5{\cdot}004y$ for D_2SO_4 and $4{\cdot}904y$ for H_2SO_4. Subsequent acid solutions are made up directly by weight.

(b) *Acidity correction to allow for protonation of the substrate.* If y g of a substrate S of equivalent weight E are taken in z g of acid of w wt%, then the new wt% of acid is given by $(Ewz - 5004y)/(Ez - 50{\cdot}04y)$ for D_2SO_4 or $(Ewz - 4904y)/(Ez - 49{\cdot}04y)$ for H_2SO_4.

(c) *Determination of* H_0 *for solutions of* D_2SO_4 *at* 25°. Wyatt[3] has listed values for D_0 for wt% D_2SO_4 at 25° and has shown that at equal molarities of D_2SO_4 and H_2SO_4 experimental values of D_0 are not significantly different from those for H_0 (determined by ref. 4) at least up to 90% D_2SO_4. Hence the graph provided by Wyatt[3] of D_0 *vs.* wt% D_2SO_4 may be used to obtain values of H_0.

(d) *Temperature correction of* H_0. From published data,[4] the variation of the acidity for a particular wt% H_2SO_4 solution is given by equation (1). The appropriate value of K is found from a graph (constructed from ref. 4) of its variation with H_0 (25°).

$$H_0(T°) = H_0(25°) + K(298{\cdot}15 - T)/298{\cdot}15T \quad (1)$$

(e) *Correction for salt effects.* Previously we have corrected for the salt effect of dissolved substrate in deuterium exchange reactions by adding 0·35 H_0 units to the calculated H_0 value.[5] This procedure was based on the average effect of dissolved substrates on the acidity as measured by Hammett indicators[5] and was recognised as approximate. We are now investigating in detail the effect of substrate and inert solute concentration on rates: however, until detailed results are available we prefer to make no corrections for this factor.

B. *Determination of* k(stoich) ($T°$) *at* pH = 0.—The determination of a rate constant at pH = 0 for a reaction which has been investigated only at higher acidities requires the construction and extrapolation of a rate profile. The majority of acid catalysed hydrogen exchange reactions appear to give straight line plots against H_0; extrapolation is then straightforward, and where alternative data are available is carried out independently on each set of data. Of the rate profiles against H_0 considered in this paper, those which are curved were approximated to straight lines: the errors thereby involved are not large.

C. *Determination of* k(stoich) (100°) *at* pH = 0.—(a) *Determination of activation parameters at a given acidity.* Because of the variation of acidity with temperature, activation parameters determined using solutions of the same wt% sulphuric acid at different temperatures give only 'apparent values'. To find true activation parameters referring to a definite H_0 value, the most satisfactory procedure is to construct two or more rate profiles at different temperatures, and then to use interpolated rates which refer to the same H_0 value.

To find activation parameters from literature data where only one (or no) complete rate profile has been determined, together with the rates at different temperatures for a single wt% sulphuric acid, the following procedure is adopted: (i) the corrected H_0 values are calculated for the individual rates at the various temperatures but constant wt% sulphuric acid; (ii) an average H_0, *e.g.* x, is selected from those just determined; (iii) assuming that the rate profile slope does not change with temperature, the rates at the H_0 values of x at the various temperatures are calculated; (iv) the activation parameters at H_0 of x are calculated using these rates.

(b) *Temperature extrapolation at* pH = 0. The value of E_a or $\Delta H^‡$ at pH = 0 is required. We have chosen to use $\Delta H^‡$ in this work in preference to E_a; the justification is that the $\Delta H^‡$–$\Delta S^‡$ treatment has a sounder theoretical basis than the treatment in terms of E_a and A.[6]

Table 1 summarises the 'uncorrected' and 'corrected' activation parameters for the available compounds for which two rate profiles are available (published work or in Appendix). The uncorrected parameters refer to rate determinations using solutions of the same % sulphuric acid at different temperatures, and the H_0 quoted is the H_0 at 25° for this concentration of sulphuric acid. The corrected parameters refer to measurements using at the different temperatures solutions of the same $(H_0)_T$ value. In all cases rates at integral and half-integral H_0 values were obtained from least square plots of the available data at the particular temperature. $\Delta H^‡$ and $\Delta S^‡$ were obtained from these rates using equation (2), the appropriate thermodynamic formulation of reaction rates.[7]

$$\log k/T = 10{\cdot}319 + \Delta S^‡/4{\cdot}574 - \Delta H^‡/4{\cdot}574T \quad (2)\,†$$

Since log k depends on H_0 by a quantity given by the slope of the rate profiles, it follows that $\Delta H^‡$ will be acidity invariant only if the same slope is found at different temperatures. Generally such variations of $\Delta H^‡$ with acidity are related to the difference between the slopes, which are

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† A sign is wrongly reported in the cited reference.

[3] J. Sierra, M. Ojeda, and P. A. H. Wyatt, *J. Chem. Soc.* (*B*), 1970, 1570.

[4] C. D. Johnson, A. R. Katritzky, and S. A. Shapiro, *J. Amer. Chem. Soc.*, 1969, **91**, 6654.

[5] P. Bellingham, Ph.D. Thesis, University of East Anglia, 1967.

[6] L. P. Hammett, 'Physical Organic Chemistry: Reaction Rates, Equilibria and Mechanisms,' McGraw-Hill, New York, 1970, 2nd edn., p. 105.

[7] F. W. Cagle, jun. and H. Eyring, *J. Amer. Chem. Soc.*, 1951, **73**, 5628.

TABLE 1

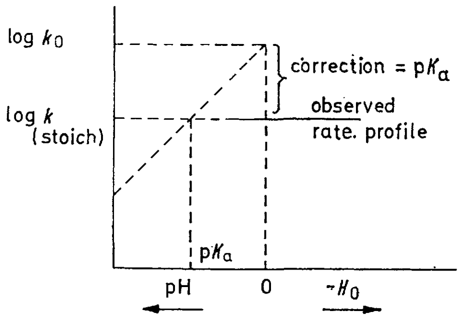
Activation parameters for rate profiles uncorrected and corrected for variation of acidity with temperature

Compound and species	T/°C	Ref.	Profile slopes		$-H_0$	Uncorrected[a]		Corrected[a]	
			Uncorrected[a]	Corrected[a]		$\Delta H^{\ddagger}$ kcal mol^{-1}	$\Delta S^{\ddagger}$ cal mol^{-1} K^{-1}	$\Delta H^{\ddagger}$ kcal mol^{-1}	$\Delta S^{\ddagger}$ cal mol^{-1} K^{-1}
2,4,6-Trimethylpyridine (cation)	180	*b*	0·42	0·66	0	31·8	−29·1	31·2	−30·1
	204	*c*	0·54	0·88	4	33·6	−17·2	40·2	1·6
	209	*b*	0·37	0·63	5	34·0	−14·3	42·4	9·7
					6	34·5	−11·3	44·7	17·8
4-Aminopyridine (monocation)	107	*d*	0·55	0·66	0	23·5	−29·4	23·9	−28·3
	146	*b*	0·45	0·54	1·5	21·2	−31·7	21·5	−30·0
	170	*b*	0·43	0·54	2·5	19·7	−33·3	19·9	−31·2
					3·5	18·1	−34·8	18·4	−32·3
2-Amino-5-chloropyridine (free base)	158	*e*	0·00	0·00	0	32·5	−10·8	32·5	−10·8
	179	*b*	0·00	0·00	1	32·5	−10·8	32·5	−10·8
					2	32·5	−10·8	32·5	−10·8
					3	32·5	−10·8	32·5	−10·8
2-Amino-5-chloropyridine (monocation)	158	*e*	0·40	0·56	0	55·6	35·4	45·7	12·6
	179	*b*	0·31	0·50	4	40·2	7·1	35·5	−1·0
					5	36·3	0·0	32·9	−4·3
					6	32·5	−7·1	30·1	−7·7
4-Amino-2,6-dichloropyridine (free base)	107	*d*	−0·20	−0·23	0	22·2	−18·7	21·7	−19·9
	122	*b*	−0·11	−0·12	1	26·3	−8·6	26·8	−7·6
					2	30·5	1·4	31·9	4·7
					3	34·7	11·4	37·0	17·0
4-Amino-2,6-dichloropyridine (monocation)	107	*d*	0·70	0·98	0	18·9	−47·1	23·1	−38·1
	122	*b*	0·74	1·05	4	26·3	−14·9	36·0	13·8
					5	28·1	−6·8	39·3	26·8
					6	30·0	1·2	42·5	39·8
2,4,6-Trimethylpyridine 1-oxide (cation)	185	*b*	0·37	0·46	0	30·4	−32·7	15·1	−64·5
	202	*f*	0·40	0·75	4	32·0	−22·4	31·9	−18·3
	216	*b*	0·38	0·57	5	32·4	−19·9	36·1	−6·7
					6	32·7	−17·3	40·3	4·9
2-Amino-5-bromopyridine 1-oxide (monocation)	158	*e*	0·28	0·46	0	29·6	−23·3	32·6	−17·6
	182	*b*	0·29	0·45	2·5	30·4	−18·4	31·5	−15·0
					3·5	30·7	−16·2	31·1	−13·7
					4·5	31·1	−14·1	30·7	−12·5
4-Pyridone (free base)	170	*g*	−0·09	−0·12	0	32·8	−7·4	32·8	−7·5
	187	*g*	−0·10	−0·13	1	32·2	−9·1	32·2	−9·4
					2	31·6	−10·8	31·6	−11·2
					3	31·1	−12·5	31·1	−13·0
Quinoline (cation, at C-8)	180	*h*	0·51	0·83	0	33·2	−24·9	40·3	−10·5
	245	*h*	0·58	0·78	1	34·3	−20·0	39·5	−8·5
					3	36·7	−10·3	37·8	−4·6
					5	39·0	−0·4	36·2	−0·6
Isoquinoline (cation, at C-5)	180	*h*	0·59	0·93	0	28·6	−35·4	33·2	−25·9
	245	*h*	0·72	1·00	1	30·7	−28·0	34·3	−19·1
					3	35·0	−13·1	36·7	−5·4
					5	39·3	1·8	39·0	8·2
4-Quinolone (free base)	90	*g*	−0·11	−0·13	0	16·0	−35·7	16·2	−35·2
	124	*b*	0·00	0·00	2	20·3	−24·8	21·3	−22·4
					3	22·5	−19·4	23·8	−16·0
					4	24·6	−14·0	26·4	−9·6
6-Aminoquinoline (monocation)	35	*i*	0·53	0·53	0	23·8	2·6	23·8	2·6
	50	*i*	0·56	0·56	−2	22·0	−8·2	22·0	−8·2
					−3	21·0	−13·5	21·0	−13·5
					−4	20·1	−18·9	20·1	−18·9
7-Aminoquinoline (monocation)	35	*i*	0·74	0·74	0	39·6	54·3	39·6	54·3
	50	*i*	0·88	0·88	−1	35·4	37·0	35·4	37·0
					−2	31·1	19·8	31·1	19·8
					−3	26·8	2·6	26·8	2·6
6-Methoxyquinoline (cation)	50	*i*	0·69	1·14	0	23·4	−24·6	25·5	−19·9
	180	*i*	0·76	0·76	1	23·7	−20·4	23·6	−20·7
					2	24·1	−16·1	21·6	−21·5
					3	24·5	−11·8	19·7	−22·4

[a] See text. [b] Present work; for details see Appendix. [c] A. R. Katritzky and B. J. Ridgewell, *J. Chem. Soc.*, 1963, 3753. [d] G. P. Bean, C. D. Johnson, A. R. Katritzky, B. J. Ridgewell, and A. M. White, *J. Chem. Soc.* (*B*), 1967, 1219. [e] A. El-Anani, P. E. Jones, and A. R. Katritzky, *J. Chem. Soc.* (*B*), 1971, 2363. [f] G. P. Bean, P. J. Brignell, C. D. Johnson, A. R. Katritzky, B. J. Ridgewell, H. O. Tarhan, and A. M. White, *J. Chem. Soc.* (*B*), 1967, 1222. [g] P. Bellingham, C. D. Johnson, and A. R. Katritzky, *J. Chem. Soc.* (*B*), 1967, 1226. [h] U. Bressel, A. R. Katritzky, and J. R. Lea, *J. Chem. Soc.* (*B*), 1971, 4. [i] U. Bressel, A. R. Katritzky, and J. R. Lea, *J. Chem. Soc.* (*B*), 1971, 11.

unpredictable because of the unknown behaviour of the activity coefficient of the transition states: in fact we found them to be random. Nevertheless it is clear from Table 1 that the major variations occur in $\Delta S^{\ddagger}$. The $\Delta H^{\ddagger}$ values, both uncorrected and corrected, are relatively constant. For the fifteen compounds measured, the average uncorrected $\Delta H^{\ddagger}$ is 30 ± 6 kcal mol^{-1} (mean and standard deviation) and the average corrected $\Delta H^{\ddagger}$ is 31 ± 7 kcal mol^{-1}. Furthermore it is possible to extrapolate all the $\Delta H^{\ddagger}$ values to pH = 0 obtaining uncorrected $\Delta H^{\ddagger}$ 30 ± 9 kcal mol^{-1}, corrected $\Delta H^{\ddagger}$ 29 ± 9 kcal mol^{-1}. Henceforth we take as a corrected $\Delta H^{\ddagger}$ at pH = 0 the standard value of 30 kcal mol^{-1} for all compounds.

(a) Base with pKa $>$ 0



(b) Base with pKa $<$ 0

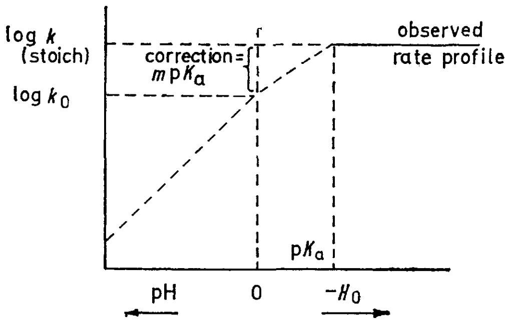


FIGURE 1 Correlation for minority species reaction

D. *Determination of* k_0 (100°) *at* pH = 0.—(a) *Correction for minority species.* For reactions which proceed on a majority species, k(stoich) = k_0, but for reactions which proceed on a minority species (*e.g.*, on a free base below the pK_a value) a correction must be made [equation (3)].*

$$k_0 = k(\text{stoich})\ .\ [\text{stoich}]/[\text{min}] \qquad (3)$$

As is evident from Figure 1, $k_0 > k$(stoich) for a base with p$K_a > 0$, but $k_0 < k$(stoich) for bases with p$K_a < 0$. As all bases in the pH region show Hammett behaviour, the correction in the first case is +pK log units to k(stoich). In the second case, the algebraic correction is +m pK log units (pK is now negative) where m is the slope of log{[BH$^+$]/[B]}/$-H_0$ and depends on the acidity function followed: 1·0 for H_0, *ca.* 0·65 for H_A, *ca.* 1·9 for H_R, *etc.*

(b) *Correction of* pK_a *for deuteriated solvent.* Bases are stronger in deuteriated media than in the analogous protic acid media. For primary amine protonation in the pH range ΔpK is *ca.* 0·55 unit: for weaker bases *ca.* 0·35 unit.[8] We have taken a standard value of 0·4 unit for ΔpK_a.

(c) *Temperature correction of* pK_a. The pK_a values to be used above should be corrected to 100°. For the protonation of primary aromatic amines, equations (4) and (5) have been shown to apply,[9,10] with $x = (T - 298{\cdot}15)/298{\cdot}15$. Combining these equations we find equation (6).

$$R\ln K_a = \frac{-\Delta G^{\circ}_{25}}{298{\cdot}15} + \frac{\Delta H_{25}}{298{\cdot}15}\cdot\left(\frac{x}{1+x}\right) \qquad (4)$$

$$\text{p}K_a\,(25^{\circ}) = 0{\cdot}88\Delta H_{25} - 1{\cdot}97 \qquad (5)\,\dagger$$

$$\text{p}K_a\,(100^{\circ}) = 0{\cdot}83\text{p}K_a\,(25^{\circ}) - 0{\cdot}33 \qquad (6)$$

Equation (6) is applicable only to primary aromatic amines, whereas equation (4) should apply to all Hammett bases. Recently, we have found that the analogous relations to (5) for protonation at the pyridine nitrogen

TABLE 2

Extrapolation procedure applied to 2-amino-5-chloropyridine

(1) Free base

A. (b) Corrected acidity 19·02%
Wt. substrate y = 0·0876 g; wt. acid z = 0·5620 g; wt. % of acid w = 24·01.
(c) H_0 (25°) −1·09 from data of ref. 3.
(d) H_0 (158°) −0·79 using equation (1) with K = 290.

B. log k(stoich) at pH 0 is −5·88 by least squares extrapolation of corrected rate profile.

C. (a) Two rate profiles available. For $\Delta H^{\ddagger}$ values at different H_0 values see Table 1.
(b) Using $\Delta H^{\ddagger}$ = 30 kcal mol^{-1} gives k(stoich) (100°) at pH 0 as −8·25.

D. (a) pK_a (25°) = 4·71.
(b) Corrected for deuteriated solvent: pK_a (25°) = 5·11.
(c) pK_a (100°) = 4·38 using equation (8).
(d) Hence k_0 (100°) at pH 0 is −3·87.

(2) Conjugate acid

A. (b) Corrected acidity 75·43%.
Wt. substrate y = 0·0821 g; wt. acid z = 0·9037 g; wt. % of acid w = 76·3.
(c) H_0 (25°) −6·99 from data of ref. 3.
(d) H_0 (179°) −4·77 using K = 1940.

B. log k(stoich) at pH 0 is −6·39 by least square extrapolation of the corrected rate profile.

C. (a) Two rate profiles available. For $\Delta H^{\ddagger}$ values at different H_0 values see Table 1.
(b) Using $\Delta H^{\ddagger}$ as 30 kcal mol^{-1} gives k(stoich) (100°) at pH 0 as −9·46.

D. No correction for majority species.
Hence k_0 (100°) at pH 0 is −9·46.

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* *Added in proof.* The assumption of a constant E_a (or $\Delta H^{\ddagger}$) has recently been criticised (B. N. McMaster, M. C. A. Opie, and G. J. Wright, *Tetrahedron Letters*, 1972, 2191). However, their work illustrates that a variation of 10 kcal mol^{-1} in our estimate of 30 kcal mol^{-1} for $\Delta H^{\ddagger}$ would lead only to a variation of *ca.* 0·4 in log f for a temperature extrapolation of 40 °C.

† See footnote on p. 1066.

[8] E. Högfeldt and J. Bigeleisen, *J. Amer. Chem. Soc.*, 1960, **82**, 15.

[9] P. D. Bolton and F. M. Hall, *Austral. J. Chem.*, 1967, **20**, 1797; 1968, **21**, 939.

[10] P. D. Bolton, C. D. Johnson, A. R. Katritzky, and S. A. Shapiro, *J. Amer. Chem. Soc.*, 1970, **92**, 1567.

atom [11] and at the N-oxide oxygen atom [12] are (7) and (9) respectively. Combination of (4) and (7) gives equation (8); combination of (4) and (9) gives equation (10), which has been used for all compounds protonated at an oxygen atom.[13]

$$\mathrm{p}K_\mathrm{a}\,(25^\circ) = 0{\cdot}90\Delta H_{25} + 0{\cdot}57 \qquad (7)$$

$$\mathrm{p}K_\mathrm{a}\,(100^\circ) = 0{\cdot}82\mathrm{p}K_\mathrm{a}\,(25^\circ) + 0{\cdot}09 \qquad (8)$$

$$\mathrm{p}K_\mathrm{a}\,(25^\circ) = 0{\cdot}62\Delta H_{25} + 0{\cdot}03 \qquad (9)$$

$$\mathrm{p}K_\mathrm{a}\,(100^\circ) = 0{\cdot}76\mathrm{p}K_\mathrm{a}\,(25^\circ) + 0{\cdot}01 \qquad (10)$$

E. *Correction for Isotope Effects.*—Much of the heterocyclic data on hydrogen exchange is concerned with deuteriation in D_2SO_4, whereas other rate data, *e.g.* for 2,6-di- and 2,4,6-tri-methylpyridine, have been measured using detritiation in H_2SO_4. It is therefore necessary to

TABLE 3

Standardised reactivities data

Substituent	Ref.	T/°C	Position(s)	Species charge	Range % H_2SO_4	Range $-H_0$ (T)	Range −log k(stoich)	$\frac{d[\log k(\text{stoich})]}{d(-H_0)}$	−log k(stoich) at $H_0 = 0$	−log k(stoich) at $H_0 = 0$, T = 100 °C	pK_a at 25°	pK_a at 100°	m	−log k_0 calc.	−log k_0 average
(i) Substituted benzenes															
1-NH_2, 4-Cl	*a*	107	2,6	0	10—16	0·3—0·7	5·4—5·4	0·00	5·36	5·69	4·38	3·31	1	2·38	2·4
1-NH_2, 4-NO_2	*a*	107	2,6	0	12—24	0·5—1·2	4·1—4·1	0·00	4·07	4·40	1·40	0·83	1	3·57	3·6
1-NH_2, 4-Me	*a*	107	2,6	0	21—26	1·0—1·3	5·0—5·0	0·00	4·98	5·31	5·47	4·21	1	1·10	1·1
1-NH_2, 4-OMe	*a*	107	2,6	0	2—39	−0·6—2·2	5·4—5·6	0·00	5·47	5·80	5·74	4·43	1	1·37	1·4
1-NH_2, 4-OMe	*a*	107	3,5	+	2—39	−0·6—2·2	6·9—4·2	0·94	6·42	6·75				6·75	6·8
1-OH	*b*	128	2,4,6	0		−2·0 → −0·8	4·6—3·5	0·89	2·77	3·99				3·99	4·0
1-OH	*b*	128	2,4,6	−		−4·5 → −4·0	5·7—5·7	0·00	5·73	6·95	10·38	7·90	1	−0·95	−1·0
1-OH, 3,5-Me_2	*c*	100	2,4,6	0		−2·2 → −1·0	4·7—3·7	0·89	2·77	2·77				2·77	2·8
1-OH, 3,5-Me_2	*c*	100	2,4,6	−		−4·8 → −3·7	5·4—5·4	0·00	5·42	5·42	10·55	8·03	1	−2·61	−2·6
2-Naphthol	*d*	50	1	−		−12·6 → −11·7	4·6—3·5	1·15	−10·01	−12·73				−12·73	−12·7
(ii) Substituted pyridines															
2-NH_2, 3-Me	*e*	158	5	+	4—78	−0·4—5·2	5·7—3·0	0·47	5·58	7·95				7·95	8·0
2-NH_2, 5-Me	*f*	107	3	+	14—61	0·5—4·0	7·4—4·8	0·67	7·72	8·05				8·05	8·1
2-NH_2, 4-Me	*g*	148	3	+	17—43	0·6—2·4	5·3—3·7	0·93	5·83	7·84				7·84	7·8
2-NH_2, 4-Me	*g*	148	3	0	2—10	−0·7—0·3	5·2—5·4	−0·21	5·36	7·37	7·88 [h]	6·56	1	0·81	0·8
2-NH_2, 4-Me	*g*	148	5	+	17—43	0·6—2·4	5·3—4·2	0·63	5·61	7·62				7·62	7·6
2-NH_2, 4-Me	*g*	148	5	0	2—10	−0·7—0·3	4·8—5·2	−0·39	5·09	7·10	7·88 [h]	6·56	1	0·54	0·5
2-NH_2, 6-Me	*g*	158	3	+	19—36	0·8—1·6	4·4—3·8	0·78	5·03	7·40				7·40	7·4
2-NH_2, 6-Me	*g*	158	3	0	2—8	−0·7—0·1	4·5—4·6	−0·14	4·61	6·98	7·81 [h]	6·50	1	0·48	0·5
2-NH_2, 6-Me	*g*	158	5	+	8—36	0·1—1·6	4·4—3·5	0·66	4·53	6·90				6·90	6·9
2-NH_2, 6-Me	*g*	158	5	0	2—8	−0·7—0·1	4·1—4·4	−0·37	4·41	6·78	7·81 [h]	6·50	1	0·28	0·3
2-NH_2, 5-Cl	*e*	158	3	+	71—96	4·6—6·9	4·9—3·6	0·56	7·49	9·86				9·86	9·7
2-NH_2, 5-Cl	*i*	179	3	+	71—90	4·4—6·2	4·1—3·3	0·50	6·39	9·46				9·46	
2-NH_2, 5-Cl	*e*	158	3	0	19—33	0·8—1·6	5·9—5·9	0·00	5·88	8·25	5·11	4·38	1	3·87	3·8
2-NH_2, 5-Cl	*i*	179	3	0	14—28	0·5—1·3	5·1—5·1	0·00	5·09	8·16	5·11	4·38	1	3·78	
2-NMe_2, 5-Cl	*e*	158	3	+	66—88	4·0—6·3	4·4—2·9	0·62	6·85	9·22				9·22	9·2
2-NMe_2, 5-Cl	*e*	158	3	0	54—66	3·1—4·0	4·5—4·4	0·00	4·51	6·88	5·51	4·72	1	2·16	2·2
3-NH_2	*g*	176	2	+ (min.)	20—40	0·8—2·0	4·7—4·8	0·00	4·79	7·77	−1·03 [h]	−1·18	1	8·95	8·7
3-NH_2	*g*	176	2	+ (maj.)	9—20	0·2—0·8	5·4—4·7	1·06	5·56	8·54				8·54	
3-NH_2	*g*	176	2	0	1—4	−1·1 → −0·4	5·5—5·4	0·00	5·43	8·41	6·38 [h]	5·33	1	3·08	3·1 [j]
4-NH_2	*f*	107	3,5	+	3—69	−0·5—4·8	7·0—3·7	0·66	6·95	7·28				7·28	7·6
4-NH_2	*i*	146	3,5	+	4—51	0·1—3·0	5·8—4·3	0·54	5·83	7·76				7·76	
4-NH_2	*i*	170	3,5	+	4—51	0·1—2·9	4·9—3·4	0·54	4·89	7·66				7·66	
4-NH_2, 2,6-Cl_2	*f*	107	3,5	+	62—68	4·0—4·6	4·7—4·1	0·98	8·72	9·05				9·05	9·1
4-NH_2, 2,6-Cl_2	*i*	122	3,5	+	65—69	4·1—4·6	3·9—3·4	1·05	8·20	9·18				9·18	
4-NH_2, 2,6-Cl_2	*f*	107	3,5	0	17—58	0·8—3·7	4·1—4·7	−0·23	3·94	4·27	1·57 [h]	1·39	1	2·88	3·0
4-NH_2, 2,6-Cl_2	*i*	122	3,5	0	2—57	−0·7—3·5	3·4—3·9	−0·12	3·45	4·43	1·57 [h]	1·39	1	3·04	
2,6-Me_2	*k*	204	3,5	+	89—95	5·5—6·2	5·7—5·0 [l]	0·99	12·02 [l]	15·85 [l]				15·59	15·6 [j]
2,4,6-Me_3	*k*	204	3,5	+	73—86	4·1—5·3	5·2—4·1 [l]	0·88	8·83 [l]	12·66 [l]				12·40	12·4 [j]
2,4,6-Me_3	*i*	180	3,5	+	71—91	4·2—6·0	5·9—4·7	0·66	8·70	11·80				11·80	11·6
2,4,6-Me_3	*i*	209	3,5	+	66—91	3·5—5·6	5·1—3·8	0·63	7·40	11·37				11·37	
4-OMe, 2,6-Me_2	*c*	100	3,5	+	60—91	4·0—8·4	7·1—4·1	0·69	9·80	9·80				9·80	9·8
4-OMe, 2,6-Me_2	*c*	100	3,5	0	22—42	1·1—2·5	7·8—7·8	0·00	7·83	7·83	8·26 [h]	6·87	1	0·96	1·0
2-Pyridone	*b*	128	3,5	0	40—93	2·2—7·1	4·7—5·5	−0·16	4·37	5·58	1·10 [h]	0·84	1	4·75	4·8
3-Me-2-pyridone	*b*	103	5	0	32—89	1·7—7·0	4·9—5·7	−0·15 [m]	4·63 [m]	4·76	0·65 [h]	0·50	1	4·26	4·3
5-Me-2-pyridone	*b*	120	3	0	32—89	1·6—6·7	5·2—5·8	−0·12	4·97	5·88	1·52 [h]	1·15	1	4·73	4·7
4-Pyridone	*b*	170	3,5	0	<98	−4·3—7·1	4·1—4·7	−0·12 [m]	4·84 [m]	7·61	3·67 [h]	2·76	1	4·85	4·8
4-Pyridone	*b*	187	3,5	0	<98	−4·3—6·9	4·7—5·3	−0·13 [m]	4·25 [m]	7·56	3·67 [h]	2·76	1	4·80	
1-Me-4-pyridone	*b*	170	3,5	0	<98	−3·0—7·2	4·6—5·2	−0·08 [m]	4·81 [m]	7·58	3·73 [h]	2·81	1	4·77	4·8
2,6-Me_2-4-pyridone	*c*	108	3,5	+	62—99	4·0—8·6	5·9—3·6	0·50	8·10	8·46				8·46	8·5
2,6-Me_2-4-pyridone	*c*	108	3,5	0	<40	−2·2—2·3	5·5—6·1	−0·15	5·86	6·22	4·53 [h]	3·41	1	2·81	2·8
1,2,6-Me_3-4-pyridone	*c*	100	3,5	+	52—96	3·3—8·1	6·4—4·1	0·56	8·64	8·64				8·64	8·6
1,2,6-Me_3-4-pyridone	*c*	100	3,5	0	22—41	1·1—2·4	6·6—6·6	0·00	6·62	6·62	4·52 [h]	3·40	1	3·22	3·2
(iii) Substituted pyridine N-oxides															
4-OH, 2,6-Me_2	*c*	100	3,5	+	73—93	5·4—7·8	5·9—4·7	0·52	8·74	8·74				8·74	8·7
4-OH, 2,6-Me_2	*c*	100	3,5	0	25—51	1·3—3·2	6·6—6·5	0·00	6·55	6·55	3·40	2·59	1	3·96	4·0
4-OH, 2,6-Me_2	*c*	100	3,5	−	<2	−3·2 → −1·1	5·4—6·5	−0·55	7·07	7·07	10·44 [n]	7·94 [n]	1	−0·87	−0·7
4-OH, 2,6-Me_2	*c*	100	3,5	−		−6·3 → −4·9	4·7—4·9	0·00	4·82	4·82	7·04	5·36	1	−0·54	
4-NH_2	*a*	107	3,5	+	13—67	0·5—4·6	7·3—4·2	0·76	7·59	7·92				7·92	7·9
2-NH_2, 5-Br	*e*	158	3	+	50—79	2·7—5·1	6·2—5·1	0·46	7·44	9·81				9·81	9·8
2-NH_2, 5-Br	*i*	182	3	+	48—80	2·6—5·2	5·4—4·2	0·45	6·54	9·71				9·71	
2-NH_2, 5-Br	*e*	158	3	0	4—17	−0·4—0·6	6·6—6·5	0·00	6·55	8·92	2·35	1·80	1	7·12	7·1
2-NH_2, 5-Br	*i*	182	3	0	16—28	0·6—1·3	5·7—5·7	0·00	5·71	8·88	2·35	1·80	1	7·08	
3,5-Me_2	*o*	230	2,6	0	8—85	0·1—4·9	4·8—5·8	−0·21	4·76	9·31	1·56 [h]	1·18	1	8·13	8·1
3,5-Me_2	*o*	230	4	0	8—85	0·1—4·9	5·0—5·7	−0·13	5·01	9·56	1·56 [h]	1·18	1	8·38	8·4
2,4,6-Me_3	*i*	185	3,5	+	85—97	5·4—6·7	5·7—5·1	0·46	8·17	11·43				11·43	11·8
2,4,6-Me_3	*o*	202	3,5	+	55—82	2·8—5·0	6·1—4·6	0·75	8·31	12·08				12·08	
2,4,6-Me_3	*i*	216	3,5	+	71—97	3·8—6·3	5·4—4·1	0·57	7·70	11·87				11·87	
3,5-OMe_2	*o*	119	2,6	+	39—78	2·2—5·6	4·7—3·2	0·43	5·65	6·48				6·48	6·5
3,5-OMe_2	*o*	119	2,6	0	<39	−3·1—2·2	4·3—4·7	−0·21 [m]	4·24 [m]	5·07	1·30 [h]	0·99	1	4·09	4·1
4-OMe, 2,6-Me_2	*c*	100	3,5	+	61—99	4·1—8·8	7·2—4·3	0·62	9·68	9·68				9·68	9·7

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[11] M. J. Cook, N. L. Dassanayake, and A. R. Katritzky, *J.C.S. Perkin II*, to be submitted.

[12] N. L. Dassanayake and T. W. Toone, personal communication.

[13] R. B. Homer and C. D. Johnson, in 'The Chemistry of Amides,' ed. J. Zabicky, Interscience, London, 1970, p. 187.

TABLE 3 (*Continued*)

Substituent	Ref.	T/°C	Position(s)	Species charge	Range % H$_2$SO$_4$	Range $-H_0$ (T)	Range −log k(stoich)	$\frac{d[\log k(\text{stoich})]}{d(-H_0)}$	−log k(stoich) at $H_0 = 0$	−log k(stoich) at $H_0 = 0$, T = 100 °C	pK_a at 25°	pK_a at 100°	m	−log k_0 calc.	−log k_0 average
(iv) Substituted quinolines and isoquinolines															
Unsubstituted	*p*	180	5,6	+	80—94	5·0—6·4	6·0—4·5	1·16	11·86	14·96				14·96 [j]	
Unsubstituted	*p*	245	5	+	6—48	−0·3—2·3	6·9—5·8	0·45	6·76	11·68				11·68	11·7
Unsubstituted	*p*	245	6	+	6—48	−0·3—2·3	7·2—5·9	0·52	7·17	12·09				12·09	12·1
Unsubstituted	*p*	245	7	+	37—66	1·0—3·3	7·4—6·1	0·83	8·80	13·72				13·72	13·7
Unsubstituted	*p*	180	8	+	61—90	3·4—5·9	6·0—3·9	0·83	8·76	11·86				11·86	11·5
Unsubstituted	*p*	245	8	+	6—48	−0·3—2·3	6·5—4·5	0·78	6·27	11·19				11·19	
Unsubstituted	*p*	245	3	+	48—66	2·3—3·3	6·6—5·9	0·68	8·14	13·06				13·06	13·1
4-OMe	*b*	90	3	+	73—99	5·4—9·0	6·3—3·6	0·72	9·99	9·52				9·52	9·5
6-OH	*d*	50	5	+	26—56	1·5—3·9	6·4—4·5	0·81	7·69	4·97				4·97	5·0
6-OH	*d*	50	5	0		−2·7 → −0·6	6·2—6·3	−0·06	6·31	3·59	5·57 [h]	4·19	1	−0·60	−0·6
6-OH	*d*	50	5	−		−12·7 → −10·8	5·9—3·4	1·34	−11·14	−13·86				−13·86	−13·9
6-OMe	*d*	50	5	+	32—68	1·7—3·9	6·9—4·5	1·14	8·80	6·08				6·08	6·4
6-OMe	*d*	180	5	+	2—10	−0·8 → −0·3	4·3—3·9	0·76	3·69	6·79				6·79	
6-OMe	*d*	180	5	0		−4·5 → −1·4	4·5—4·5	0·00	4·50	7·60	5·46 [h]	4·11	1	3·50	3·5
6-OH, 1-Me	*d*	50	5	+	22—42	1·1—2·5	6·8—5·9	0·65	7·48	4·76				4·76	4·8
6-OH, 1-Me	*d*	50	5	0		−9·2—1·1	4·8—6·8	−0·06 [m]	6·72 [m]	4·00	7·55 [h]	5·67	1	−1·67	−1·7
6-NH$_2$	*d*	35	5	+ (min.)	<22	−1·7—1·1	4·4—4·7	−0·13	4·58	0·87	1·68 [q]	1·10	1	−0·23	−0·2
6-NH$_2$	*d*	35	5	+(maj.)		−3·2 → −1·7	5·2—4·4	0·53	3·49	−0·22				−0·22	
6-NH$_2$	*d*	50	5	+		−4·0 → −1·9	5·0—3·8	0·56	2·69	−0·03				−0·03	
6-NH$_2$	*d*	50	5	0		−7·0 → −4·5	4·6—5·1	−0·33	6·59	3·87	6·03 [h]	5·16	1	−1·29	−1·3
7-NH$_2$	*d*	35	8	+ (min.)	6—22	0·0—1·2	3·5—3·5	0·00	3·48	−0·23	0·15 [q]	−0·18	1	−0·41	−0·4
7-NH$_2$	*d*	35	8	+ (maj.)	1—6	−1·2—0·0	4·4—3·5	0·74	3·45	−0·26				−0·26	
7-NH$_2$	*d*	50	8	+		−3·4 → −1·9	5·0—3·7	0·88	2·13	−0·59				−0·59	
7-NH$_2$	*d*	50	8	0		−7·5 → −4·5	5·5—5·5	0·00	5·47	2·75	7·05 [h]	6·01	1	−3·26	−3·3
1-Oxide	*p*	180	5,6	+	77—86	4·7—5·5	5·7—5·2	0·58	8·43	11·53				11·53	11·5
1-Oxide	*p*	180	8	+	64—86	3·5—5·5	5·2—4·0	0·56	7·17	10·27				10·27	10·3
2-Quinolone	*r*	110	3	+	71—86	4·9—6·6	5·8—5·0	0·51	8·44	8·90				8·90	8·9
2-Quinolone	*r*	110	5	+	71—86	4·9—6·6	6·1—4·9	0·76	9·95	10·41				10·41	10·4
2-Quinolone	*r*	110	6	+	71—86	4·9—6·6	5·3—4·0	0·75	9·03	9·49				9·49	9·5
2-Quinolone	*r*	110	8	+	71—86	4·9—6·6	4·4—3·4	0·60	7·40	7·86				7·86	7·9
4-Quinolone	*b*	90	3	+	77—99	5·9—9·0	4·8—3·2	0·54	8·08	7·61				7·61	7·6
4-Quinolone	*b*	90	3	0	5—64	−0·2—4·4	4·6—5·1	−0·13	4·57	4·10	2·67 [h]	2·01	1	2·09	2·4
4-Quinolone	*i*	124	3	0	16—67	0·6—4·3	3·6—6·7	0·00	3·70	4·76	2·67 [h]	2·01	1	2·75	
Isoquinoline	*p*	180	5	+	70—87	4·1—5·7	4·9—3·4	0·93	8·69	11·79				11·79	11·7
Isoquinoline	*p*	245	5	+	11—37	0·2—1·7	6·4—5·0	1·00	6·63	11·55				11·55	
Isoquinoline	*p*	180	8	+	70—94	4·1—6·3	6·1—4·1	0·90	9·92	13·02				13·02	13·0
Isoquinoline 2-oxide	*p*	180	5	+	63—88	3·5—5·7	5·0—3·5	0·64	7·15	10·25				10·25	10·3
Isoquinoline 2-oxide	*p*	180	8	+	77—88	4·7—5·7	6·0—5·2	0·69	9·22	12·32				12·32	12·3
(v) Substituted azines															
4-NH$_2$-pyridazine	*s*	186	5	+	8—53	0·1—2·8	6·0—4·0	0·76	6·14	9·43				9·43	9·4
Pyridazin-4-one	*s*	186	5	0 (min.)	12—80	0·3—4·9	3·8—4·8	−0·21	3·69	6·98	1·47 [h]	1·11	1	5·87	5·9
Pyridazin-4-one	*s*	186	5	0 (maj.)		−2·4 → −1·3	5·4—4·2	1·12	2·65	5·94				5·94	
2-NH$_2$-pyrimidine	*t*	107	5	0 (min.)		−3·0 → −1·2	5·7—5·7	0·00	5·70	6·03	3·85 [h]	3·32	1	2·71	2·7
2-NH$_2$-pyrimidine	*t*	107	5	0 (maj.)		−4·8 → −4·0	6·6—6·0	0·89	2·40	2·73				2·73	
6-NH$_2$-2,4-Me$_2$-pyrimidine	*t*	107	5	+		−1·9 → −0·3	5·7—4·4	0·76	4·21	4·54				4·54	4·5
6-NH$_2$-2,4-Me$_2$-pyrimidine		107	5	0		−7·4 → −3·7	6·5—6·4	0·00	6·47	6·80	7·30 [h]	6·09	1	0·71	0·7
(vi) Pyrones and thiopyrones															
2,6-Me$_2$-4-pyrone	*c*	148	3,5	0	25—98	1·1—7·4	4·2—5·5	−0·21 [m]	3·99 [m]	6·00	0·17 [h]	0·14	1	5·86	5·9
2,6-Me$_2$-1-thio-4-pyrone	*c*	148	3,5	0	22—99	1·0—8·1	5·5—5·9	−0·10	5·38	7·39	0·96 [h]	0·73	1	6·66	6·7
Chromone	*d*	180	3	0	40—84	1·9—5·4	2·6—2·9	0·00	2·83	5·93	−1·60	−1·21	0·65	6·71	6·7
Chromone	*d*	180	6	0	40—84	1·9—5·4	4·3—3·9	0·00	4·06	7·16	−1·60	−1·21	0·65	7·94	7·9
Chromone	*d*	180	8	0	53—84	2·8—5·4	4·8—4·4	0·00	4·62	7·72	−1·60	−1·21	0·65	8·50	8·5
1-Thiochromone	*d*	180	3	0	39—84	1·8—5·4	3·2—3·4	0·00	3·31	6·41	−0·72	−0·54	0·65	6·95	7.0
1-Thiochromone	*d*	180	6,8	0	39—84	1·8—5·4	5·5—5·1	0·00	5·25	8·35	−0·72	−0·54	0·65	8·89	8·9

[a] G. P. Bean and A. R. Katritzky, *J. Chem. Soc.* (*B*), 1968, 864. [b] P. Bellingham, C. D. Johnson, and A. R. Katritzky, *J. Chem. Soc.* (*B*), 1967, 1226. [c] Ref. 2. [d] U. Bressel, A. R. Katritzky, and J. R. Lea, *J. Chem. Soc.* (*B*), 1971, 11. [e] A. El-Anani, P. E. Jones, and A. R. Katritzky, *J. Chem. Soc.* (*B*), 1971, 2363. [f] G. P. Bean, C. D. Johnson, A. R. Katritzky, B. J. Ridgewell, and A. M. White, *J. Chem. Soc.* (*B*), 1967, 1219. [g] A. El-Anani, S. Clementi, A. R. Katritzky, and L. Yakhontov, following paper. [h] At 20 °C. [i] Present work; for details see Appendix. [j] Uncertain value; see the appropriate ref. [k] A. R. Katritzky and B. J. Ridgewell, *J. Chem. Soc.*, 1963, 3753. [l] Detritiation. [m] Interpolated values: the experimental region includes $H_0 = 0$. [n] The sum of both first and second pK_a must be used, since the reaction occurs on the minority species of a minority species (*i.e.* the anion in presence of the conjugate acid). [o] G. P. Bean, P. J. Brignell, C. D. Johnson, A. R. Katritzky, B. J. Ridgewell, H. O. Tarhan, and A. M. White, *J. Chem. Soc.* (*B*), 1967, 1222. [p] U. Bressel, A. R. Katritzky, and J. R. Lea, *J. Chem. Soc.* (*B*), 1971, 4. [q] At 30 °C. [r] G. P. Bean, A. R. Katritzky, and A. Marzec, *Bull. Acad. polon. Sci., Ser. Sci. chim.*, 1967, **16**, 453. [s] A. R. Katritzky and I. Pojarlieff, *J. Chem. Soc.* (*B*), 1968, 873. [t] A. R. Katritzky, M. Kingsland, and O. S. Tee. *J. Chem. Soc.* (*B*), 1968, 1484.

consider isotope effects on the rate of the generalised reactions (11) and (12). Since the energy profile for hydrogen exchange is approximately symmetrical, the observed rate constants for the forward and back reactions will be equal, to a first approximation. This problem has been recently discussed by Liler,[14] assuming the validity of the Swain equation (13),[15] which has also been supported by experimental evidence.[16,17]

$$\mathrm{ArD} + \mathrm{H}^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{ArDH}^+ \xrightarrow{k_2} \mathrm{ArH} + \mathrm{D}^+ \qquad (11)$$

$$\mathrm{ArT} + \mathrm{H}^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{ArTH}^+ \xrightarrow{k_2} \mathrm{ArH} + \mathrm{T}^+ \qquad (12)$$

$$(k_{-1}/k_2)_\mathrm{T} = (k_{-1}/k_2)_\mathrm{D}{}^{1\cdot442} \qquad (13)$$

Gold[18] measured the rates of loss of tritium and deuterium from 1,3,5-trimethoxybenzene in aqueous perchloric acid solution and acetate buffers and found that the ratio $(k_\mathrm{T})_\mathrm{obs}/(k_\mathrm{D})_\mathrm{obs}$ did not vary greatly with acidity. Values ranging from 0·45 to 0·55 were reported.

Olsson[19] measured the ratio $(k_\mathrm{T})_\mathrm{obs}/(k_\mathrm{D})_\mathrm{obs}$ for several substituted benzenes in aqueous sulphuric acid solutions and concluded that it did not change very much with acidity or temperature but was fairly sensitive to substrate reactivity, increased reactivity of the aromatic substrate

[14] M. Liler, 'Reaction Mechanisms in Sulphuric Acid and other Strong Acid Solutions,' Academic Press, London, 1971, p. 263.

[15] C. G. Swain, E. C. Stivers, J. F. Reuwer, jun., and L. J. Schaad, *J. Amer. Chem. Soc.*, 1958, **80**, 5885.

[16] S. Olsson, *Arkiv Kemi*, 1961, **16**, 489

[17] E. S. Lewis and J. K. Robinson, *J. Amer. Chem. Soc.*, 1968, **90**, 4337.

[18] B. D. Batts and V. Gold, *J. Chem. Soc.*, 1964, 4284.

[19] S. Olsson, *Arkiv Kemi*, 1970, **32**, 105, and previous papers in the series.

leading to a stronger isotope effect. Values ranging from 0·45 to 0·64 were reported. For present purposes, a value of $(k_T)_{obs}/(k_D)_{obs}$ of 0·55 has been used.

RESULTS

A typical example of the application of the procedure just mentioned is given in Table 2 for 2-amino-5-chloropyridine; two calculations are made, for reaction as the free base species, and for reaction as the cation.

Available data from previous work is summarised in Table 3; and the procedure already outlined has been applied to this data to yield the results given in the same table.

The pK_a values reported in the Table are corrected for deuteriated media. Where values were available at 20° the proper equations (6′), (8′), and (10′), easily derived

$$\text{p}K_a\,(100°) = 0{\cdot}82\text{p}K_a\,(20°) - 0{\cdot}35 \qquad (6')$$

$$\text{p}K_a\,(100°) = 0{\cdot}82\text{p}K_a\,(20°) + 0{\cdot}10 \qquad (8')$$

$$\text{p}K_a\,(100°) = 0{\cdot}75\text{p}K_a\,(20°) + 0{\cdot}01 \qquad (10')$$

from equations (4), (5), (7), and (9) have been used. Because of the kinetic procedure involved,[2] where more than one proton exchanges at the same rate, the obtained reactivity refers to one position only.

It is planned in a later paper of this series to attempt to correlate the k_0 values of Table 3 by the Hammett equation and by the application of MO methods.

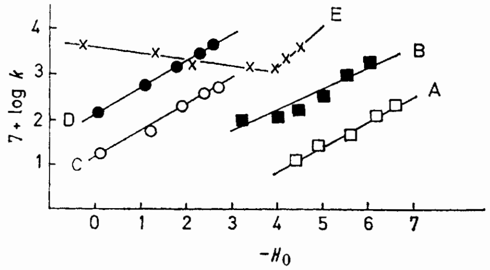

FIGURE 2 Rate profiles for 2,4,6-trimethylpyridine at A, 180° and B, 209°; for 4-aminopyridine at C, 146° and D, 170°; and for 4-amino-2,6-dichloropyridine at E, 122°

APPENDIX

Table 4 records the hydrogen exchange data needed to construct the rate profiles in Figures 2 and 3 from which some activation parameter data of Table 1 were calculated. All the compounds of Table 4 have been studied previously, and the new results did not disclose any surprising features.

TABLE 4

Pseudo-first-order rate constants (s^{-1}) for hydrogen–deuterium exchange

(i) 2,4,6-Trimethylpyridine at 180 and 209°

% D_2SO_4	$-H_0$ (180)	$-\log k$	$-H_0$ (209)	$-\log k$
91	6·00	4·71	5·63	3·76
87	5·64	4·92	5·30	3·97
82	5·20	5·29	4·88	4·42
77	4·71	5·60	4·42	4·77
71	4·17	5·90	3·92	4·96
66	—	—	3·48	5·05

(ii) 4-Aminopyridine at 146 and 170°

% D_2SO_4	$-H_0$ (146)	$-\log k$	$-H_0$ (170)	$-\log k$
51	2·95	4·28	2·86	3·37
46	2·58	4·40	2·49	3·57
38	2·02	4·67	1·95	3·83
26	1·22	5·24	1·17	4·25
4	0·10	5·76	0·09	4·86

TABLE 4 (*Continued*)

(iii) 2-Amino-5-chloropyridine at 179°

% D_2SO_4	$-H_0$ (179)	$-\log k$
90	6·18	3·31
88	6·00	3·46
83	5·59	3·60
79	5·12	3·75
75	4·77	4·01
71	4·38	4·10
28	1·27	5·09
19	0·71	5·08
14	0·48	5·09

(iv) 4-Amino-2,6-dichloropyridine at 122°

% D_2SO_4	$-H_0$ (122)	$-\log k$
69	4·55	3·43
67	4·33	3·67
65	4·12	3·88
57	3·45	3·85
40	2·20	3·82
28	1·36	3·56
2	−0·71	3·37

(v) 2,4,6-Trimethylpyridine 1-oxide at 185 and 216°

% D_2SO_4	$-H_0$ (185)	$-\log k$	$-H_0$ (216)	$-\log k$
97	6·70	5·08	6·32	4·10
95	6·42	5·21		
91	5·93	5·42	5·54	4·50
85	5·41	5·68	5·06	4·69
78			4·45	5·22
76			4·26	5·30
71			3·85	5·44

(vi) 2-Amino-5-bromopyridine 1-oxide at 182°

% D_2SO_4	$-H_0$ (182)	$-\log k$
80	5·22	4·23
66	3·84	4·72
56	3·13	4·92
48	2·59	5·43
28	1·26	5·72
16	0·58	5·70

(vii) 4-Quinolone at 124°

% D_2SO_4	$-H_0$ (124)	$-\log k$
67	4·31	3·70
60	3·67	3·70
54	3·20	3·70
44	2·48	3·70
19	0·83	3·60
16	0·64	3·63

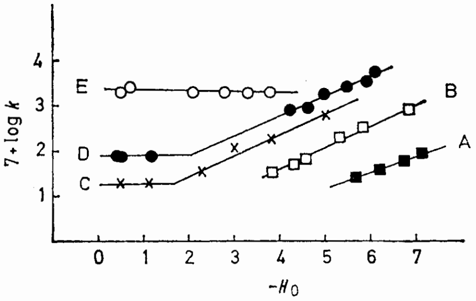

FIGURE 3 Rate profiles for 2,4,6-trimethylpyridine 1-oxide at A, 185°; and B, 216°; for 2-amino-5-bromopyridine 1-oxide at C, 182°; for 2-amino-5-chloropyridine at D, 179°; and for 4-quinolone at E, 124°

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