The Standardization of Aromatic and Heteroaromatic Nitration Rates †

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Methods for extrapolating rates for nitrations in aqueous sulphuric acid to different temperatures and acidities are discussed. A standard procedure to obtain k_0 values at 25° and H_0 −6.6 is applied to literature data for 131 nitration rates. Allowance is made where necessary for minority species concentrations.

NITRATION is perhaps the most common of the electrophilic substitution reactions of aromatic rings. It is widely used preparatively, and has been extensively studied kinetically in this[2] and in other laboratories.[3-5] Comparison of nitration rates of different compounds is complicated by their variation with solvent and acidity. Because of the considerable acidity dependence, kinetic rates can be obtained for compounds of widely differing reactivity in aqueous sulphuric acid of appropriate concentration. In this respect nitration kinetics resemble those for acid-catalysed hydrogen exchange: in previous work, we have given reasons for choosing pH = 0 and

100° as standard conditions for comparing hydrogen exchange rates,[6] and have defined a procedure for extrapolating measured rates at various temperatures and

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acidities to these standard conditions.[7] The present paper suggests standard conditions for nitration rates, outlines a procedure to obtain such standard rates, and lists the standard rates so obtained. The availability of such standard nitration rates enables a test[8] of the general applicability of the reactivities of the various ring positions of the different heterocyclic rings towards electrophilic substitution as measured by the standard k_0 obtained from the hydrogen exchange data.[7,9,10] Individual standard nitration rate constants are usually more accurate than those for hydrogen exchange, since the nitration kinetics were followed in dilute solution by u.v., instead of in more concentrated solution by n.m.r., thus obviating salt effects on activities.

Variation of Rate Constants with Acidity.*—The variation of nitration rate constants with acidity is well known.[5] Plots of log k_2 against acidity (rate profiles) are widely used as mechanistic criteria for determining the species undergoing reaction, especially in the form of (a) ' high acidity rate profiles ' with the H_0 acidity function as abscissa,[2a,4a] (b) ' Moodie–Schofield plots ', in which $(H_R + \log a_{H_2O})$ is used as a measure of the acidity,[3a] (c) ' modified rate profiles ', (Tarhan plots) in which the rate constants are first corrected for the [$NO_2{}^+$] concentration and then plotted against H_0.[2e] The theoretical values for the slopes are approached when the acidity functions are corrected for their variation with temperature [5,10] (*cf.* also ref. 11).

Unusual behaviour is exhibited by benzene: at 25°, the slope of the Moodie–Schofield plot is 1.0 in the range 63—68% H_2SO_4, but the slope increases at greater acidities to 1.2. The non-linearity for benzene may be due to the closeness to the encounter rate. However, it is noteworthy that plots for many substituted benzenes, including compounds more reactive than benzene (toluene, biphenyl, xylenes, mesitylene) and also naphthalene remain linear over a range 56—80% H_2SO_4.[3e] The variation of H_R with wt. % H_2SO_4 at 25° was recently redetermined; [12] its variation with temperature [equation (1)] is similar to that [equation (2)] [10] for H_0, although

$$H_0(T) = K/T + L \qquad (1)$$

$$H_R(T) = A/T + B \qquad (2)$$

the proportionality coefficient A is smaller than K at each wt. % H_2SO_4. The a_{H_2O} values for aqueous H_2SO_4 were derived [13,14] from vapour pressure measurements from plots of log a_{H_2O} against wt. % H_2SO_4, using the values of Shankman and Gordon [15] below 69% and of

Deno and Taft [16] above 69% H_2SO_4. This provides values of $-(H_R + \log a_{H_2O})$ for each wt. % H_2SO_4.

The variation of the a_{H_2O} with temperature is known for sulphuric acid below 40 wt. % from e.m.f. measurements.[17] At acidity up to 40% H_2SO_4 log a_{H_2O} increases in a linear fashion with temperature according to equation (3).[18] B is a constant at a given wt. % H_2SO_4; a plot of B against wt. % H_2SO_4 (or H_0) is a smooth curve, and in the region 0—40% H_2SO_4 log B can be fitted to a polynomial of third degree [equation (4)]. However, this implies that B reaches a maximum at H_0 -2.8 (*i.e.* 44.5% H_2SO_4 at 25°) and thereafter decreases with increasing $-H_0$. This would imply that at high acidities a_{H_2O} decreases with temperature in contrast to its behaviour at low acidities. Such a conclusion is unlikely; it is unfortunate that no experimental data are available for ⩾40 wt. % H_2SO_4. Therefore Moodie–Schofield plots cannot presently be accurately corrected for temperature, and are thus unsuitable for extrapolating rate constants.

$$\log a_{H_2O}(T°) = \log a_{H_2O}(25°) + (T - 298.15)\,B \qquad (3)$$

$$\log B = a(H_0)^3 + b(H_0)^2 + c(H_0) + d \qquad (4)$$

A proper application of the modified rate profile requires knowledge of both the acidity function followed by nitric acid and of the variation of the pK_a of nitric acid with temperature: these are not available and unsuccessful attempts of their evaluation will be reported elsewhere.[19]

In view of the difficulties in applying the other methods, we consider that rate profiles at elevated temperatures are best plotted using $H_0(T)$.

Temperature Variation of Rate Constants at Constant wt. % H_2SO_4.—The temperature variations previously studied [2-4] refer to constant wt. % H_2SO_4. Values for $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, recalculated (where possible) from these literature data, are recorded in Table 1.

A large spread in the distribution of the activation entropies is observed (the mean value is -16 cal mol^{-1} K^{-1} with a standard deviation of 9), whereas the heats of activation lie within a smaller range (17.6 ± 4.0 kcal mol^{-1}). The average value of $\Delta H^{\ddagger}$ is larger for reactions taking place on a minority species (21.7 ± 4.0 kcal mol^{-1}) than for those on a majority species (16.1 ± 2.8 kcal mol^{-1}).

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* The following symbols are used in this paper: k_0, standard rate for H/D; k_2, observed nitration rate; $k_2{}^0$ standard nitration rate; H_0, H_R, acidity functions; a_{H_2O}, activity of water; K, proportionality coefficient between H_0 and T; T, temperature in Kelvins; $T°$, temperature in degrees Celsius; $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, activation parameters at constant wt. % H_2SO_4; $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, activation parameters at constant H_0; m, slope of the rate profiles.

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Temperature Variation at Constant H_0.—As previously pointed out for hydrogen exchange,[7] the variation of acidity with temperature renders the activation parameters determined from solutions of identical wt. %

H_2SO_4 at different temperatures ' apparent values '. We now consider $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ which refer to constant H_0 values. The simplest method for measuring $\Delta \bar{H}^{\ddagger}$ and $\Delta \bar{S}^{\ddagger}$ is by the construction of two or more rate profiles

TABLE 1

Activation parameters at constant wt. % H_2SO_4 ($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$) and at constant H_0 ($\Delta \bar{H}^{\ddagger}$, $\Delta \bar{S}^{\ddagger}$)

Compound	Wt. % H_2SO_4	$-H_0$ (25°)	m^a	$\Delta H^{\ddagger\,b}$ (kcal mol⁻¹)	$\Delta S^{\ddagger\,b}$ (cal mol⁻¹ K⁻¹)	$\Delta \bar{H}^{\ddagger\,c}$ (kcal mol⁻¹)	$\Delta \bar{S}^{\ddagger\,d}$ (cal mol⁻¹ K⁻¹)	Ref.
(i) Majority species reactions								
Benzene	67.1	5.35	2.31 ^{e}	17.4 ^{f}	-8^f	32.4	42	3e
	73.2	6.45		13.3 ^{f}	-17^f	31.5	44	
Fluorobenzene	67.5	5.43	2.34	16.5	-14	31.9	38	3g
	73.2	6.45		13.4 ^{f}	-15^f	31.8	46	
Chlorobenzene	67.5	5.43	2.35	18.7	-8	34.2	44	3g
Bromobenzene	67.5	5.43	2.50	17.7	-12	34.1	43	3g
Benzamide	81.2	7.69	2.28	14.8	-24	36.9	51	3f
Trimethylbenzylammonium cation	70.0	5.82	2.36	18.3	-18	35.1	38	4d
p-Dichlorobenzene	73.2	6.45	2.61	15.4	-19	35.9	50	3g
	80.5	7.57		10.6	-21	35.6	63	
Thiophen	66.4	5.25	2.04	17.8	-2	30.6	41	4g
	69.2	5.72		16.1	-4	30.3	44	
3,5-Dimethylisothiazole	81.7	7.71	1.74	17.2	-32	34.2	24	2h
2,3,5-Trimethylisothiazolium cation	81.4	7.68	1.89	16.1	-35	34.6	27	2h
2-Dimethylaminopyridine	76.2	6.83	2.01	16.8	-9	34.1	49	2i
3,5-Dimethoxypyridine 1-oxide	82.3	7.82	1.97 ^{g}	19.5	-13	39.1	53	2c
2,6-Dimethoxypyridine 1-oxide	84.8	8.24	2.50	13.8	-26	40.1	62	2c
2,4,6-Trimethoxypyridine 1-oxide	81.0	7.60	2.75	16.1	-18	42.6	71	2c
Isoquinoline	81.3	7.69	1.88	13.5 ^{f}	-25^f	31.8	36	3c
2-Methylisoquinolinium cation	81.3	7.69	1.94	14.3 ^{f}	-22^f	33.2	41	3c
2-Hydroxyisoquinolinium cation	83.1	7.97	2.19	14.0	-23	36.3	52	3b
2-Methoxyisoquinolinium cation	83.1	7.97	2.22	14.9	-22	37.5	54	3b
Cinnoline	76.1	6.82	2.17	23.7	-19	42.4	44	3c
	81.1	7.63		19.5	-24	40.5	46	
2-Methylcinnolinium cation	81.2	7.64	2.26	18.4	-25	40.3	48	3c
4-Quinolone	81.4	7.71	2.45	13.3	-23	37.3	58	3i
1-Methyl-4-quinolone	81.4	7.71	2.28	12.9	-26	35.2	49	3i
4-Methoxyquinoline	81.4	7.71	2.50	13.2	-24	37.7	58	3i
4-Cinnolone	81.2	7.69	2.07	19.7	-13	40.0	55	3i
(ii) Minority species reactions								
Acetophenone	81.4	7.71	1.63	16.9	-10	32.9	44	3f
2,3-Dimethyl-4-nitro-1-phenyl-Δ^3-pyrazolin-5-one	84.1	8.12	0.82	15.8	-15	24.4	14	2l
2,3-Dimethyl-4-nitro-1-p-nitrophenyl-Δ^3-pyrazolin-5-one	84.1	8.12	1.22	17.2	-11	31.6	30	2l
2-Dimethylamino-5-nitropyridine	79.8	7.42	1.59	24.6	8	39.4	58	2i
2-Dimethylamino-3-nitropyridine	79.6	7.35	1.67	20.4	-9	35.9	43	2i
2,6-Dimethylpyridine 1-oxide	78.2	7.15	0.73	25.8	-7	32.4	15	3b
	81.4	7.71		23.2	-12	30.3	12	
	84.3	8.14		22.6	-12	30.2	14	
2,6-Dichloropyridine 1-oxide	82.4	8.16	0.98 ^{g}	26.2	-7	35.9	26	2c
3,5-Dimethoxy-2-nitropyridine 1-oxide	82.0	7.77	1.12	19.5	-13	30.6	24	2c
1-p-Nitrophenylpyrazole	81.0	7.60	1.27	26.6	-6	35.9	35	2m

^{a} Rate profile slope. ^{b} Recalculated from literature data by the Eyring equation, unless otherwise stated. ^{c} Calculated by equation (15). ^{d} Calculated by equation (17). ^{e} Rate profile up to 70.6% H_2SO_4. ^{f} Calculated from E_a and log A values reported in the quoted reference. ^{g} N. Shakir, Ph.D. Thesis, University of East Anglia, 1966.

TABLE 2

Thermodynamic parameters at constant H_0 calculated from rate profiles at various temperatures

Compound	$T/°C$	Slope	$-\log k_2{}^a$	$\Delta \bar{H}^{\ddagger\,a}$ (kcal mol⁻¹)	$\Delta \bar{S}^{\ddagger\,a}$ (cal mol⁻¹ K⁻¹)	Ref.
4-Pyridone	86	1.53	4.65	34.2	15.4	2e
	110	1.39	3.22			
	133.5	1.59	1.99			
	157.5	1.36	1.15			
2-Pyridone (at C-3)	25	1.04	5.45	36.7	35.8	2k
	40	0.91	4.17			
2-Pyridone (at C-5)	25	1.20	5.91	34.4	29.9	2k
	40	1.08	4.68			

^{a} At $H_0 = -6.6$.

at different temperatures: such data are available for a few cases and are recorded in Table 2.

A less accurate procedure for determining $\Delta \bar{H}^{\ddagger}$ values requires just a rate profile and an individual point at a different temperature. The activation parameters are then calculated by the Eyring equation, at the particular acidity of the individual run, from that rate constant and the interpolated value on the rate profile corresponding to the same H_0. Relevant examples are shown in Table 3.

We have sought an alternative procedure for the many cases where the data available consist of a rate profile at one temperature together with values of individual rates for one wt. % H_2SO_4 over a temperature range (Figure). We now deduce general relations between $\Delta H^{\ddagger}$ and $\Delta \bar{H}^{\ddagger}$ and between $\Delta S^{\ddagger}$ and $\Delta \bar{S}^{\ddagger}$ as follows. Over the limited temperature range t—u, the rate is found experimentally to vary as a linear function of the inverse temperature [equations (5)—(8)] when the wt. % H_2SO_4 is kept con-

$$RT \ln k = -\Delta H^{\ddagger} + T\Delta S^{\ddagger} \qquad (5)$$

$$2.3Rtf = -\Delta H^{\ddagger} + t\Delta S^{\ddagger} \qquad (6)$$

$$2.3Rug = -\Delta H^{\ddagger} + u\Delta S^{\ddagger} \qquad (7)$$

$$2.3R(g-f) = \Delta H^{\ddagger}(1/t - 1/u) \qquad (8)$$

stant at c. Assuming that, over the same limited temperature range, the rate at the constant H_0 value of a also varies as a linear function of the inverse temperature giving the similar equations (9) and (10), hence we find (11).

$$RT\ln k = -\Delta \bar{H}^{\ddagger} + T\Delta \bar{S}^{\ddagger} \qquad (9)$$

$$2.3R(g-e) = \Delta \bar{H}^{\ddagger} (1/t - 1/u) \qquad (10)$$

find (11). From the slope m of the rate profile at the temperature of t and relation (12) we deduce (13). Equations of type (1) hold for the variation of H_0 for a particular wt. % H_2SO_4 where K is a constant for each wt. % H_2SO_4[10] [equation (14)].

$$2.3R(f-e) = (\Delta \bar{H}^{\ddagger} - \Delta H^{\ddagger})(1/t - 1/u) \qquad (11)$$

$$f-e = m(a-b) \qquad (12)$$

$$\Delta \bar{H}^{\ddagger} - \Delta H^{\ddagger} = 2.3Rm(a-b)/(1/t-1/u) \qquad (13)$$

$$a-b = K(1/t - 1/u) \qquad (14)$$

$$\Delta \bar{H}^{\ddagger} - \Delta H^{\ddagger} = 2.3RmK \qquad (15)$$

Provided that the rate profile is not curved, a consequence of equation (15) is the non-variance of $(\Delta \bar{H}^{\ddagger} - \Delta H^{\ddagger})$ with acidity. Thus if $\Delta H^{\ddagger}$ is a true constant for a certain wt. % H_2SO_4 which at different temperatures spans a range of H_0 values, then $\Delta \bar{H}^{\ddagger}$ does not vary over this H_0 range. We show later that, at acidities below H_0 —8.5, $\Delta \bar{H}^{\ddagger}$ varies little with H_0.

The corresponding relation connecting $\Delta S^{\ddagger}$ and $\Delta \bar{S}^{\ddagger}$ follows similarly. We deduce (16) from (5) and (9). Substituting (12) and (14) gives (17). The difference in the entropy terms is seen to vary as the inverse of the unique temperature u at which the H_0 and the wt. %

H_2SO_4 under consideration are identical. When quoting $\Delta \bar{S}^{\ddagger}$, we take u as the standard temperature of 25°.

$$\Delta \bar{S}^{\ddagger} - \Delta S^{\ddagger} = 2.3Ru(f-e)/(u-t) \qquad (16)$$

$$\Delta \bar{S}^{\ddagger} - \Delta S^{\ddagger} = 2.3RmK/u \qquad (17)$$

Heats of Activation $\Delta \bar{H}^{\ddagger}$ *at Constant* H_0.—Thermodynamic parameters obtained by equations (15) and (17) from
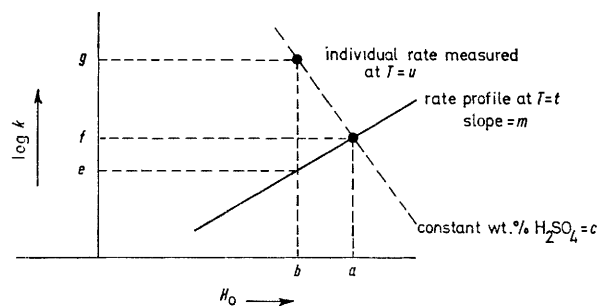
Relation between rates at constant wt. % H_2SO_4 and constant H_0. In this figure and in equations (5)—(17), the following symbols are used: t, u, experimental temperatures in Kelvins ($u > t$; the whole rate profile is available at t; only an individual rate is available at u); e, f, g, log k values (see Figure); a, b, H_0 values (see Figure); c, wt. % H_2SO_4 (corresponding to $H_0 = a$ at $T = t$, and $H_0 = b$ at $T = u$.

literature results in the range H_0 —5 to —8.5 are summarised in Table 1. Because of the curvatures of the rate profiles at higher acidities such data are excluded.

There is no significant correlation of $\Delta \bar{H}^{\ddagger}$ with acidity within the range H_0 —5 to —8.5 (correlation coefficient 0.20, slope 0.85). Since the rate profile slopes vary little with temperature,[7] we consider the mean value of 34.9 kcal mol^{-1} (standard deviation 3.9) for $\Delta \bar{H}^{\ddagger}$ to be more

TABLE 3

Thermodynamic parameters at constant H_0 calculated from a rate profile and an individual run at a different temperature

Compound	Wt. % H_2SO_4[a]	T (°C)[a]	H_0 (T)[b]	Slope[c]	T (°C)[d]	$-\log k_2$[e]	$\Delta \bar{H}^{\ddagger}$ (kcal mol^{-1})	$\Delta \bar{S}^{\ddagger}$ (cal mol^{-1} K^{-1})	Ref.
Fluorobenzene	73.2	2.3	6.84	2.35	25	—0.85	32.7	55	3g
p-Dichlorobenzene	73.2	45.1	6.00	2.61	25	3.60	36.6	48	3g
p-Dichlorobenzene	80.5	45.1	7.10				0.73	36.0	59	
Thiophen	69.2	9.2	5.99	1.98	25	—0.74	30.0	45	4g
2-Dimethylaminopyridine	76.2	50.0	6.36	2.01	30	1.78	29.5	31	2i
4-Methoxyquinoline	81.4	45.0	7.24	2.50	25	3.35	38.2	54	3i

[a] Experimental conditions for the individual run. [b] At the temperature of the preceding column. [c] Slope of the available rate profile. [d] Temperature of the rate profile. [e] Interpolated value of log k_2 on the rate profile at H_0 reported in the third column.

significant than interpolated value of $\Delta \bar{H}^{\ddagger}$ 34.4 kcal mol^{-1} at the standard (see later) acidity of H_0 —6.6. The mean value for minority species reactions (33.5 kcal mol^{-1}) is close to the overall average.

A comparison of the thermodynamic parameters of Table 1 with those reported in Table 3 shows minor discrepancies between the two procedures, which are ascribed to the fact that the Eyring equation is applied to two points only to obtain the activation parameters of Table

The standard acidity of H_0 —6.6 minimises the extrapolations needed for the rate profiles of many substrates and is not far from the range of ' normal ' behaviour found for benzene.

The procedure for the determination of standard rates from the experimentally measured rates requires four consecutive steps. (A) Determination of k_2 (obs) at the individual acidity and temperature, involving knowledge of the acidity function followed and its

TABLE 4

Slopes and correlation coefficients of plots of log k_2 (obs) against H_0, H_R, and $(H_R + \log a_{H_2O})$ [a]

Compound	T (°C)	$\dfrac{d[\log k_2]}{d[-H_0]}$	r [b]	$\dfrac{d[\log k_2]}{d[-H_R]}$	r [b]	$\dfrac{d[\log k_2]}{d[-(H_R + \log a_{H_2O})]}$	r [b]	Ref.
Benzene	25	2.31	0.9995	1.26	0.9975	1.18	0.9995	3e
Naphthalene	25	2.20	0.9997	1.15	0.9983	1.00	0.9993	3e
p-Dichlorobenzene	25	2.61	0.9981	1.59	0.9974	1.12	0.9975	3g
Thiophen	25	2.04	0.9999	1.06	0.9956	0.94	0.9994	4g
2-Phenylpyridine	25	2.47	0.9854	1.49	0.9789	1.02	0.9734	2d
Acetophenone	25	1.63	0.9998	0.94	0.9960	0.66	0.9965	3f
3,5-Dimethylisothiazole	80	1.74	0.9967	1.10	0.9959	0.72	0.9970	2h
2-Pyridone (at C-3)	40	0.91	0.9995	0.57	0.9984	0.39	0.9991	2k
2-Pyridone (at C-5)	40	1.08	0.9989	0.67	0.9996	0.46	0.9998	2k
1,5-Dimethyl-2-pyridone	40	1.21	0.9981	1.07	0.9997	0.71	0.9999	2e
Uracil	60	1.15	0.9992	0.67	0.9990	0.46	0.9993	2g
1,3-Dimethyluracil	60	1.25	0.9962	0.73	0.9976	0.50	0.9977	2g

[a] H_0 and H_R are corrected for their variation with temperature as in refs. 10 and 12, respectively, whereas log a_{H_2O} values are always at 25°. [b] Correlation coefficient.

TABLE 5

Difference (Δ log k_2) between log k_2 at H_0 —9.66 (94% H_2SO_4 at 25°) and log k_2 at H_0 —6.60 (75% H_2SO_4 at 25°) for majority species reactions at 25°

Compound	Range % H_2SO_4	Range $-H_0$	m [a]	$-\log k_2$ [b]	Range % H_2SO_4	Range $-H_0$	m [c]	$-\log k_2$ [d]	Δ log k_2	Ref.
p-Dichlorobenzene	73—85	6.4—8.4	2.61	2.00	93—98	9.4—10.5	−0.21	−4.11	6.11	3g
p-Chloronitrobenzene	80—88	7.5—8.7	2.25	5.60	91—98	9.2—10.5	−0.48	0.57	5.03	4h
p-Nitrotoluene	71—88	6.0—8.8	2.36	2.95	91—98	9.2—10.2	−0.61	−1.88	4.83	4h
o-Chloronitrobenzene	80—88	7.4—8.7	2.24	3.79	90—98	9.1—10.4	−0.42	−0.97	4.76	4h
2-Methoxy-4-methylthiazole	74—88	6.5—8.8	2.22	4.56	93—98	9.4—10.3	−0.27	−0.52	5.08	e
1,2,3,5-Tetramethylpyrazolium cation	76—88	6.7—8.6	2.31	5.02	92—98	9.3—10.4	−0.68	0.34	4.68	2h
1,3,5-Trimethylpyrazole [f]	73—88	6.4—8.6	2.35	5.14	92—98	9.3—10.4	−0.84	0.47	4.61	2h
1-Phenylpyrazole	78—88	7.1—8.7	1.64	3.13	90—97	9.1—10.3	−0.19	−0.60	3.73	2m
5-Methoxy-3-methyl-4-nitro-1-phenylpyrazole	81—88	7.7—8.7	1.51	3.63	90—96	8.9—9.9	−0.21	0.44	3.19	2l

[a] Rate profile slope in the low acidity range. [b] At H_0 —6.60. [c] Rate profile slope in the high acidity range. [d] At H_0 —9.66. [e] C. Ogretir, unpublished results. [f] At 20.9°.

3, but to all the available temperatures for those of Table 1.

The activation entropies cover a much larger range than the corresponding $\Delta \bar{H}^{\ddagger}$. The average $\Delta \bar{S}^{\ddagger}$ is highly positive (42 ± 14 cal mol^{-1} K^{-1}); the transition state structure is presumably less solvated than the ground state.

Definition of Standard Conditions.—The definition of standard conditions is more difficult for nitration than for hydrogen exchange because of uncertainty in the NO_2^+ activity variation and the peculiar behaviour of benzene itself. We have selected $T = 25°$ and $H_0 = -6.6$ (75% H_2SO_4 at 25°) as the standard conditions. We chose 25° because many nitration kinetics have been followed at this temperature, and most in the range 0—100°.

variation with temperature. (B) Determination of k_2 (T) at H_0 —6.6, involving construction of the rate profile and its extrapolation to the proper acidity. (C) Determination of k_2 (25°) at the standard acidity, involving evaluation or estimate of the thermodynamic parameters at that acidity. (D) Determination of $k_2°$, involving correction for minority species reaction, which requires knowledge of the pK_a of the substrate at the standard temperature.

PROCEDURE

(A) *Determination of* k_2 (obs) *at a particular* T *and* H_0.—This is obtained from individual experimental runs. The standardisation of acid is often done by titration.[2] The low substrate concentration required for u.v. analyses obviates acidity corrections for the protonation of the substrate or salt effects.

The variation [10] of H_0 with wt. % H_2SO_4 at 25° is used to obtain H_0 values corresponding to the experimental percentages of sulphuric acid. The variation of H_0 with temperature at any particular wt. % H_2SO_4 is given by equation (18); H_0 is a linear function of the inverse of the absolute temperature.[10] The appropriate values of K are requires the construction and the extrapolation of a rate profile. We have given above reasons for using a plot of log k_2 (obs) $(T°)$ against $-H_0$. Such plots always show good straight lines with positive slopes in the range 65—86% H_2SO_4; at higher acidities the plot curves until the slope becomes negative.

TABLE 6

Difference between log k_2 at 94% H_2SO_4 and log k_2 at 75% H_2SO_4 for majority species reactions at temperatures $> 25°$

Compound	T (°C)	Range % H_2SO_4	Range $-H_0$	m [a]	$-\log k_2$ $(-H_0)$ [b]	Range % H_2SO_4	Range $-H_0$	m [c]	$-\log k_2$ $(-H_0)$ [d]	$\Delta \log k_2$	Ref.
5-Methoxy-3-methyl-1-p-nitrophenyl-pyrazole	40	81—88	7.1—8.4	1.73	4.82 (6.31)	90—98	8.6—10.3	−0.39	1.22 (9.24)	3.60	2l
1,3-Dimethylpyrazole	40	75—87	6.4—8.2	2.23	5.35 (6.31)	89—97	8.6—9.9	−0.67	0.99 (9.24)	4.36	e
1,5-Dimethylpyrazole	40	75—87	6.4—8.2	2.21	5.57 (6.31)	89—96	8.6—9.5	−0.87	1.33 (9.24)	4.24	e
3,5-Dimethylisothiazole	80	78—88	6.1—7.6	1.74	6.69 (5.65)	92—97	8.2—9.1	−0.38	3.21 (8.30)	3.48	2h
2,3,5-Trimethyliso-thiazolium	80	78—88	6.1—7.5	1.89	6.86 (5.65)	92—97	8.1—9.0	−0.45	3.15 (8.30)	3.71	2h
1-Methylpyrazole	80	80—88	6.4—7.8	1.59	5.12 (5.65)	90—98	7.8—9.3	−0.45	1.80 (8.30)	3.32	e
2,4-Dimethylthiazole	90	81—87	6.3—7.1	3.08	5.95 (5.50)	90—98	7.5—8.9	−0.34	1.33 (8.01)	4.62	f
3,5-Dimethyliso-thiazole	130	74—84	4.9—6.6	1.76	4.72 (5.07)	92—96	7.1—7.7	−0.42	1.95 (7.39)	2.77	g

[a] Rate profile slope in the low acidity region. [b] At 75% H_2SO_4; the corresponding H_0 (T) values are given in parentheses. [c] Rate profile slope in the high acidity region. [d] At 94% H_2SO_4; the corresponding H_0 (T) values are given in parentheses. [e] H. O. Tarhan, unpublished results. [f] S. Ilkay and H. O. Tarhan, *Chimica Acta Turcica*, 1973, **1**, 123. [g] B. Terem, unpublished results.

TABLE 7

Experimental thermodynamic parameters (at constant wt. % H_2SO_4) in the high acidity region [a]

Compound	Wt. % H_2SO_4	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (cal mol^{-1} K^{-1})	Ref.
Acetophenone	98.1	17.1	−9	3f
p-Nitroaniline	90.1	18.4	−6	4f
	98.0	17.7	−13	
2-Chloro-4-nitroaniline	93.8	19.0	2	4f
	98.0	18.5	−4	
Pyrazole	98.6	16.5	−26	4c
4-Nitro-1-phenylpyrazole	95.9	15.6	−13	2m
2,3-Dimethyl-4-nitro-1-phenyl-Δ^3-pyrazolin-5-one	91.2	12.6	−24	2l
4-Pyridone	92.2	19.3	−20	2e
3-Methyl-2-pyridone	94.2	17.1	−9	2e
2-Methoxy-3-methylpyridine	95.3	15.7	−24	2e
2,4-Dimethoxypyridine	89.5	14.8	−17	2a
3,5-Dimethoxypyridine	90.0	11.9	−19	2b
3,5-Dimethoxy-2-nitropyridine	89.8	22.2	−7	2b
2,6-Dichloropyridine	98.3	16.9	−8	2a
2,4,6-Trimethylpyridine	90.4	12.6	−18	2a
	90.7	17.5	−26	
	98.1	19.6	−23	
2-Dimethylaminopyridine	97.4	13.3	−4	2i
2,6-Dichloropyridine 1-oxide	94.9	23.5	−8	2c
3,5-Dimethylpyridine 1-oxide	91.8	25.3	−9	2c
2,6-Dimethylpyridine 1-oxide	92.5	21.4	−14	3b
	97.8	23.8	−10	
2-Dimethylamino-3-nitropyridine	97.5	14.1	−22	2i
4-Dimethylamino-3-nitropyridine	90.3	17.6	−14	2i
2,4-Dimethoxypyrimidine	97.5	15.8	−24	2g
Uracil	91.2	22.6	1	2g
6-Methyluracil	90.2	23.5	9	2g
1,3-Dimethyluracil	91.2	23.4	6	2g
Quinoline	98.0	13.6	−22	4a

[a] All figures were recalculated from literature data by the Eyring equation.

found from a graph, constructed [10] from the acidity variation.

$$H_0(T°) = H_0(25°) + K(298.15 - T)/298.15\,T \quad (18)$$

(B) *Determination of* k_2 (obs) *at* T = T *and* H_0 −6.6.— The determination of a rate constant at a given acidity for a reaction investigated only in a different range of acidities

Data recorded in Table 4 show that the correlation coefficients of these plots are slightly higher (mean value is 0.998) than those of the plots against H_R (mean value 0.996) and of the Moodie–Schofield plots (mean value 0.997). The log k_2 (obs) $(T°)$ values at H_0 −6.6 are taken from a regression analysis on the region $-H_0$ 5.5—8.5 of the plots.

(C) *Determination of* k_2 (obs) *at* T = 25° *and* H_0 = −6.6.—

When experimental data are recorded at temperatures higher than 25° the rate constants at standard conditions are calculated by equation (19) from the extrapolated k_2 (obs) at T° and H_0 −6.6.

$$\log k_2(T^{\circ}) = \log k_2(25^{\circ}) - \frac{\Delta H^{\ddagger}}{2.3\ R}\left(\frac{1}{273.15 + T} - \frac{1}{298\cdot 15}\right)$$
(19)

We need therefore the $\Delta H^{\ddagger}$ value, since we are referring to a constant acidity. As we have just pointed out in the introduction most of the variation appears to be included in the $\Delta S^{\ddagger}$ term, whereas the activation enthalpies do not vary significantly with the individual compounds. Henceforth we use $\Delta H^{\ddagger}$ 35 kcal mol⁻¹ at H_0 −6.6 which is the statistical average value for all compounds.

(D) *Determination of Standard Rates* (k_2^0 *at* 25° *and* H_0 −6.6).—For reactions proceeding on a majority species k_2 (obs) = k_2^0. For reactions proceeding on a minority species (*e.g.* on a free base below the pK_a value) a correction must be made [equation (21)] easily derived from equation (20), where $H_0^{\frac{1}{2}}$ is the half-protonation value of the particular substrate and m is the slope of log [BH⁺]/[B] against H_0.[2k]

$$\log k_2^0 = \log k_2(\text{obs}) - m(H_0^{\frac{1}{2}} - H_0)$$
(20)

$$\log k_2^0 = \log k_2(\text{obs}) + pK_a + 6.6m$$
(21)

Alternative Procedure.—If insufficient experimental data are available for rates at acidities below H_0 −8.5 extrapolated rates are obtained from the high acidity region of the rate profiles by a different procedure. This same procedure is also used for the extrapolation of compounds which show a mechanistic changeover, *i.e.* where the nitration proceeds *via* a minority species (free base) mechanism at low acidities but a majority species (conjugate acid) mechanism at higher acidities. For majority species reactions in which no such change in mechanism occurs, the difference in the log k_2 (obs) (25°) values at H_0 −6.60 (75% H_2SO_4) and −9.66 (94% H_2SO_4) lies within a narrow range (Table 5). The average difference for homocyclic substrates (5.2 ± 0.6 log units) is higher than that for heteroaromatic compounds (4.3 ± 0.8 log units) presumably because of systematic differences in the activity coefficients in the two classes of compounds, which are known to affect significantly the rate profile slopes in the high acidity region.[4h]

It is an experimental fact that rate profiles at temperatures higher than 25° continue to show a maximum near 88% H_2SO_4; *i.e.* at progressively less negative H_0 values as the temperature increases.[4h] In Table 6 we report log k_2 (obs) values for 75—94% H_2SO_4 for compounds measured at higher temperatures. The data in Table 6 are arranged in order of the temperature, little variation and no clear trend are found between $\Delta\log k_2$ and the temperature, and for all these values $\Delta\log k_2$ = 3.8 ± 0.6. This value is close to that found for 25°, implying that $\Delta H^{\ddagger}$ does not change significantly with % H_2SO_4. Table 7 records $\Delta H^{\ddagger}$ values for higher % H_2SO_4 recalculated by the Eyring equation from literature data:[2-4] we find $\Delta H^{\ddagger}$ = 18.0 ± 3.8, close to the values found for lower % H_2SO_4 values. Taken together, the data of Tables 5 and 6 provide an average of 4.0 ± 0.7 for $\Delta\log k_2$.

This result allows use of the following procedure to calculate extrapolated rates at H_0 − 6.6 even when a mechanistic changeover has occurred. log k_2 (obs) Values at T° are obtained from the rate profile at H_0 (T) corresponding to 94%

H_2SO_4. Subtraction of 4.0 from this value gives an estimate for log k_2(obs) at H_0 (T) corresponding to 75% H_2SO_4.

log k_2 (obs) (T_0) values are then converted to 25°, by equation (19), using the average $\Delta H^{\ddagger}$ value (17.6 kcal mol⁻¹), *i.e.* by a temperature extrapolation at constant % H_2SO_4: in this way log k_2 (obs) for a conjugate acid reaction at 25° and H_0 −6.6 is obtained.

RESULTS

Typical examples of the application of the procedure just mentioned are given in Table 8, which gives details of calcu-

TABLE 8

Examples of application of the standardisation procedure

(1) Free base reaction: 4-pyridone at 133.5°
(A)   (a) Wt. % H_2SO_4 = 80.5
      (b) H_0 (25°) = −7.54 from data of ref. 10
      (c) H_0 (133.5°) = −5.68 using equation (1) with K = 2080
(B)   log k_2(obs) at H_0 −6.6 is −1.99 by least square extrapolation of the rate profile
(C)   Using an $\Delta H^{\ddagger}$ of 35 kcal mol⁻¹ gives log k_2(obs) (25°) at H_0 −6.6 as −8.84
(D)   (a) pK_a (25°) = 3.27; m = 0.65
      (b) Hence log k_2^0 (calc) is −1.28 using equation (21)
      (c) Since nitration occurs at two equivalent positions log k_2^0(corr) is −1.58

(2) Conjugate acid reaction: 3,5-dimethylisothiazole at 80°
(A)   (a) Wt. % H_2SO_4 = 81.7
      (b) H_0 (25°) = −7.72 from data of ref. 10
      (c) H_0 (80°) = −6.70 using equation (1) with K = 2150
(B)   log k_2(obs) at H_0 −6.6 is −6.69 by least square interpolation of the rate profile
(C)   Using an $\Delta H^{\ddagger}$ of 35 kcal mol⁻¹ gives log k_2(obs) (25°) at H_0 −6.6 as −9.03
(D)   No correction for majority species. Hence log k_2^0 is −9.03

(3) Alternative procedure: pyrazole at 80°
(A)   (a) Wt. % H_2SO_4 = 95.0
      (b) H_0 (25°) = −9.81 from data of ref. 10
      (c) H_0 (80°) = −8.44 using equation (1) with K = 2600
(B′)   (a) log k_2(obs) at $H_0(T)$ corresponding to 94% H_2SO_4 (−8.30) is −2.39 by least square interpolation of the rate profile at acidities higher than 90% H_2SO_4
      (b) log k_2(obs) at $H_0(T)$ corresponding to 75% H_2SO_4 (−5.65) is −6.39 by subtraction of the constant 4.0
(C′)   log k_2(obs) at H_0 = −6.6 and 25° is −8.43, by a temperature extrapolation at constant % H_2SO_4, using $\Delta H^{\ddagger}$ 17.6 kcal mol⁻¹
(D)   No correction for majority species. Hence log k_2^0 is −8.43

lations for 4-pyridone (free base reaction), 3,5-dimethylisothiazole (majority species reaction), and pyrazole (from data in the high acidity range).

Available data from previous work are summarised in Table 9, and the procedures already outlined have been applied to this data to yield the results given in the same table.

For benzene and a few halogenobenzenes we report the more recent data of Moodie, Schofield, *et al.*[3e,g] and not the older ones by Deno and Stein,[4j] although the standard rates obtained from the two data sets show good agreement: for example log k_2^0 for benzene is 0.21 from data of ref. 4j and 0.45 from data of ref. 3e.

When nitration occurs at more than one position the slope refers to the overall reaction. Standard rates for nitration at the individual positions are obtained using the isomer distribution at the nearest measured acidity to 75% H_2SO_4.

When nitration occurs at two or more equivalent positions,

TABLE 9

Standard rate constants

Substituent	Range % H_2SO_4	T (°C)	Range $-H_0$	$\dfrac{d[\log k_2]}{d[-H_0]}$	$-\log k_2$ at H_0 -6.6 $T = T°$	$-\log k_2$ at H_0 -6.6 $T = 25°$	Species charge	For minority species pK$_a$	m	$-\log k_2°$ (calc.)	Position (%)	$-\log k_2°$ (corr.) a	Ref.
(i) Substituted benzenes
None	63—71	25	4.8—5.9	2.31	−1.23	−1.23	0			−1.23	Any	−0.45	3e
1-Me	63—79	25	4.8—7.4	2.18	−2.26	−2.26	0			−2.26	2,6(60)	−1.73	3e
											3,5(2)	−0.26	
											4(37)	−1.82	
1-F	68—77	25	5.4—7.0	2.34	−0.30	−0.30	0			−0.30	2,6(13)	0.89	3g
											3,5(0.6)	2.22	
											4(86)	−0.23	
1-Cl	68—77	25	5.4—7.1	2.35	−0.05	−0.05	0			−0.05	2,6(36)	0.69	3g
											3,5(0.9)	2.29	
											4(63)	0.15	
1-Br	68—75	25	5.4—6.6	2.50	−0.10	−0.10	0			−0.10	2,6(43)	0.57	3g
											3,5(0.8)	2.30	
											4(56)	0.15	
1-I	68—75	25	5.4—6.6	2.29	−0.47	−0.47	0			−0.47	2,6(45)	0.18	3g
											4(55)	−0.21	
1-COMe	75—85	25	6.7—8.3	1.63	3.46	3.46	0	−4.58 b	0.73 b	3.22	2,6(26)	3.80	3f
											3,5(72)	3.35	
1-CONH₂	81—85	25	7.7—8.3	2.28	5.64	5.64	0			5.64	2,6(27) c	6.51	3f
											3,5(70) c	6.09	
1-CO₂H	78—81	25	7.1—7.7	2.15	3.03	3.03	0	−5.30 d	0.73 e	3.51	2,6(17)	4.28	3f
											3,5(82)	3.60	
1-NHCOMe	66—81	25	5.2—7.6	1.91	1.00	1.00	+			1.00	2,6(28)	1.85	3j
											4(72)	1.14	
1-CH₂NMe₃⁺	75—82	25	6.6—7.7	2.36	3.20	3.20	+			3.20	3,5(85)	3.57	4d
					2.21	6.14	6.14				6.14	2,6	6.44	
1-NH₂	82—87	25	7.8—8.5	2.44	5.59	5.59	+			5.59	3,5	5.89	4e
					2.36	4.95	4.95				4.95	4	4.95	
1-NH₂	92—98	25	9.4—10.4	0.49	0.31 f	5.51 g	+			5.51	3,5	5.81	4b
				0.63	0.10 f	5.30 g					5.30	4	5.30	
1-OCH₃	41—63	25	2.5—4.7	2.19	−2.54	−2.54	0			−2.54	2,6(31) h	−1.73	4j
											4(67) h	−2.37	
1-CN	80—85	25	7.4—8.3	2.36	6.06	6.06	0			6.06	3,5	6.36	4j
1-NO₂	80—85	25	7.5—8.3	2.86	7.16	7.16	0			7.16	3,5	7.46	4l
1-CH₂OMe	67—73	25	5.4—6.3	2.10	−0.12	−0.12	0			−0.12	2,6(19)	0.90	3j
											3,5(21)	0.86	
											4(60)	0.10	
1-CH₂CH₂OMe	68—81	25	5.4—7.6	2.21	−1.34	−1.34	0			−1.34	2,6(35)	−0.58	3j
											3,5(9)	0.01	
											4(56)	−1.19	
1,4-Me₂	61—68	25	4.5—5.5	1.80	−2.25	−2.25	0			−2.25	2,3,5,6	−1.65	3e
1,4-Cl₂	73—85	25	6.3—8.4	2.61	2.00	2.00	0			2.00	2,3,5,6	2.60	3g
1,2-Cl₂	77—81	25	7.1—7.6	2.87	1.92	1.92	0			1.92	3(11)	2.86	3g
											4(89)	2.27	
1,3-Cl₂	75—79	25	6.7—7.3	2.79	1.33	1.33	0			1.33	2(4)	2.73	3g
											4,6(96)	1.65	
1-Me-2,4-(NO₂)₂	92—99	90	7.7—9.3	−0.28	1.67 f	9.18 g	0			9.18	6	9.18	4k
1,3-(OMe)₂	58—64	22.7	4.1—4.9	2.05	−2.34	−2.54	0			−2.54	4,6	−2.24	2a
1-Me-4-NO₂	71—88	25	6.0—8.8	2.36	1.88	1.88	0			1.88	2,6	2.18	4h
1-NO₂-2-Cl	80—88	25	7.4—8.7	2.24	3.79	3.79	0			3.79	5	3.79	4h
1-NO₂-4-Cl	80—88	25	7.4—8.7	2.25	5.30	5.30	0			5.30	3,5	5.60	4h
1-NH₂-4-NO₂	84—88	25	8.1—8.7	1.48	6.17	6.17	0	0.99	1	−1.42	2,6	−1.12	4f
1,3,5-Me₃	67—79	25	5.3—7.4	1.99	−2.47	−2.47	0			−2.47	2,4,6	−1.99	3e
1-NH₂-2-Cl-4-NO₂	85—88	25	8.3—8.7	1.54	3.34	3.34	0	0.85	1	−4.11	6	−4.11	4f
1-NO₂-2,4-(OMe)₂	67—73	31	5.3—6.2	1.92	−0.78	0.27	0			0.27	5	0.27	2a
1,3,5-Me₃-2,4-(NO₂)₂	90—96	25	9.3—9.9	−0.41	1.99 f	7.19 g	0			7.19	6	7.19	4l
(ii) Substituted pyridines
4-OMe	90—96	110	7.4—8.5	−0.34	3.04 f	9.90	+			9.90	3,5	10.20	2e
3-OMe	90—96	60	8.1—9.3	−0.41	2.73 f	8.09	+			8.09	2	8.09	2f
3-OH	90—96	40	9.0—10.0	−0.79	3.04 f	7.66	+			7.66	2	7.66	2f
2-NMe₂	76—86	30	6.7—8.2	2.01	1.30	1.72	+			1.72	3(11)	2.68	2i
											5(89)	1.77	
4-NMe₂	72—86	50	5.7—7.8	1.49	0.69	2.68	+			2.68	3,5	2.98	2i
2-NMe₂-5-NO₂	77—84	30	6.9—8.0	1.59	4.43	4.85	0	3.11 i	1 j	−4.86	3	−4.86	2i
2-NMe₂-3-NO₂	79—86	30	7.2—8.2	1.67	4.97	5.39	0	2.50 i	1 j	−3.71	5	−3.71	2i
4-NMe₂-3-NO₂	82—89	50	7.2—8.2	1.61	4.79	6.78	0	5.23 i	1 j	−5.05	5	−5.05	2i
3,5-(OMe)₂-2-NO₂	82—85	51	7.3—7.7	1.12	4.94	7.00	0	−2.52	1.10	2.26	6	2.26	2b
2,4,6-Me₃	92—98	101	7.6—8.7	−0.51	3.11 f	9.73	+			9.73	3,5	10.05	2a
2,6-(OMe)₂	74—81	58.5	5.7—6.8	2.17	1.84	4.43	+			4.43	3,5	4.73	2f
3,5-(OMe)₂	82—88	25	7.8—8.7	2.00	4.45	4.45	+			4.45	2,6	4.75	2b
2-OMe-3-Me	91—96	25	9.1—10.0	−0.58	3.98 f	7.98	+			7.98	5	7.98	2e
2-Ph	77—81	25	7.0—7.6	2.47	3.80	3.80	+			3.80	2′,6′(9)	5.15	2d
											3′,5′(45)	4.45	
											4′(46)	4.14	
(iii) Pyridones
2-Pyridone	75—87	25	6.6—8.6	1.04	5.45	5.45	0	0.77	0.65 k	0.39	3	0.37	2k
		40	6.4—8.4	0.91	4.17	5.40	0			0.34	3		
		25	6.6—8.6	1.20	5.91	5.91	0			0.85	5	0.85	
		40	6.4—8.4	1.08	4.68	5.91	0			0.85	5		
4-Pyridone	85—89	86	7.0—7.6	1.53	4.65	9.01	0	3.27	0.65 k	1.45	3,5		
	85—89	110	6.6—7.2	1.39	3.22	8.91	0			1.35	3,5	1.69	2e
	79—85	133.5	5.5—6.3	1.59	1.99	8.84	0			1.28	3,5		
	73—81	157.5	4.5—5.4	1.36	1.15	9.05	0			1.49	3,5		
	93—98	86	8.0—9.2	−0.53	3.31 f	9.50	+			9.50	3,5	9.76	
	92—98	110	7.4—8.7	−0.53	2.56 f	9.42	+			9.42	3,5		
3-Me-2-pyridone	78—87	31	7.1—8.4	1.04	2.23	2.74	0	0.25	0.65 k	−1.80		−1.80	
	75—81	34.5	6.4—7.4	0.85	2.04	2.83	0			−1.71	5	−1.70	2e
	62—77	44.2	4.8—6.5	1.12	1.41	2.96	0			−1.58	5		
5-Me-2-pyridone	74—81	35	6.3—7.4	1.03	2.76	3.59	0	1.13	0.65 k	−1.83	3	−1.83	2e
1,5-Me₂-2-pyridone	76—84	29	6.7—8.1	0.98	2.37	2.71	0	0.79	0.65 k	−2.37	3	−2.08	2e
	71—78	39.5	5.8—6.9	1.21	2.11	3.30				−1.78	3		
6-OH-2-pyridone	70—77	27.5	5.7—7.0	1.19	1.84	2.05	0	1.19	0.65 k	−3.43	3	−3.43	2f
6-OH-1-Me-2-pyridone	70—77	27.5	5.8—6.9	1.23	1.90	2.11	0	0.61	0.65 k	−2.79	3	−2.79	2f
6-OMe-2-pyridone	71—80	27.5	6.0—7.4	1.29	2.30	2.51	0	1.14	0.65 k	−2.92	3	−2.92	2f
3-NO₂-4-pyridone	83—86	157	5.0—5.3	1.30	1.85	9.73	0	−0.82	0.65 k	6.26	5	6.26	2e
(iv) Pyridine 1-oxides
2,6-Me₂	78—88	80	5.9—7.6	0.73	4.05	8.05	l	1.38 m	0.65 k	2.38	4	2.38	3b
2,6-(OMe)₂	80—86 n	25	7.5—8.4	2.50 n	7.18	7.18	+			7.18	3,5	7.48	2c
2,4,6-(OMe)₃	80—85 n	25	7.5—8.3	2.75 n	5.81	5.81	+			5.81	3,5	6.11	2c

TABLE 9 (Continued)

Substituent	Range % H_2SO_4	T (°C)	Range $-H_0$	$\dfrac{d[\log k_2]}{d[-H_0]}$	$-\log k_2$ at H_0 -6.6 $T = T°$	$-\log k_2$ at H_0 -6.6 $T = 25°$	Species charge	For minority species pK_a	m	$-\log k_2°$ (calc.)	Position (%)	$-\log k_2°$ (corr.) [a]	Ref.
2-Ph	75—79	25	6.6—7.3	2.41	3.77	3.77	+			3.77	2',6'(3)	5.59	2d
											3',5'(79)	4.17	
											4'(18)	4.51	
(v) Pyridinium cations													
1-Me-2-NHMe	78—89	25	7.2—8.8	2.46	5.44	5.44	+			5.44	3(31)	5.95	2j
											5(69)	5.60	
1-Me-4-NMe₂	76—80	25	6.8—7.4	1.08 o	1.88 o	1.88	+			1.88	3,5	2.18	2j
(vi) Pyrimidine derivatives													
2-Pyrimidone	86—89	115	6.6—7.3	1.89	0.50	6.45	0	2.24	0.65 k	-0.08	5	-0.08	2g
Uracil	76—85	60	6.1—7.5	1.15	3.33	6.03	0	-1.85	0.53	4.38	5	4.38	2g
1,3-Me₂-uracil	76—85	60	6.1—7.5	1.25	2.99	5.69	0	-1.85	0.56	3.84	5	3.84	2g
6-Me-uracil	76—85	60	6.1—7.5	1.05	3.23	5.93	0	-1.42	0.56	3.65	5	3.65	2g
(vii) Substituted pyrazoles													
None	90—99	81	7.8—9.4	-0.47	2.39 f	8.43	+			8.43	4	8.43	4c
1,3,5-Me₃	73—87	21	6.4—8.6	2.35	5.14	4.79	+			4.79	4	4.79	2h
1-Ph	70—82	40	5.5—7.4	2.03	1.87	3.10	+			3.10	4'⎫	3.11	2m
	78—87	25	7.1—8.6	1.64	3.13	3.13				3.13	4'⎬		2m, 3l
1-Ph-4-NO₂	68—79	40	5.2—6.9	1.13	3.24	4.47	0	-2.65	0.73	2.30	4'⎫		
	80—87	25	7.5—8.6	1.61	4.16	4.16				1.99	4'⎬	2.15	2m
1-p-NO₂C₆H₄	75—79	75	5.8—6.3	1.27	3.64	7.33	0	-0.84	1 j	1.57	4⎫		
	81—87	60	6.8—7.8	1.15	4.80	7.50				1.74	4⎬	1.66	2m
1-Ph-3-Me	79—80	25	7.3—7.5	2.21	2.76	2.76	+			2.76	4'	2.76	3l
1-Ph-5-Me	82—88	25	7.8—8.7	2.31	4.68	4.68	+			4.68	4'	4.68	3l
1-Ph-3,5-Me₂	79—85	25	7.3—8.3	2.33	3.66	3.66	+			3.66	4'	3.66	3l
1-(o-Tolyl)	79—84	25	7.3—8.1	2.37	3.41	3.41	+			3.41	4'	3.41	3l
1-(2,6-Me₂)-Ph	75—79	25	6.6—7.3	2.37	1.62	1.62	+			1.62	4'	1.62	3l
1-Ph-3-Me-5-OMe-4-NO₂	76—82	50	6.3—7.2	2.64	2.37	4.36	+			4.36	4'	4.36	2l
1-p-NO₂C₆H₄-3-Me-5-OMe	81—88	40	7.1—8.4	1.73	4.32	5.55	+			5.55	4	5.55	2l
(viii) Pyrazolinones													
1-Ph-3-Me-4-NO₂-5-one	72—78	25	6.1—7.0	1.99	0.32	0.32	+			0.32	4'	0.32	2l
1-Ph-2,3-Me₂-4-NO₂-5-one	78—86	25	7.0—8.4	0.82	3.37	3.37	0	-1.90	0.62	1.18	4'	1.18⎫	2l
	89—98	25	8.8—10.4	-0.41	1.94 f	5.94	+			5.94	4'	5.94⎬	
1-p-NO₂C₆H₄-3-Me-5-one	74—87	40	6.1—8.3	0.99	1.21	2.44	0	0.25	0.50	-1.11	4	-1.11⎫	2l
	89—96	40	8.5—9.7	-0.44	0.22 f	4.84	+			4.84	4	4.84⎬	
1-p-NO₂C₆H₄-2,3-Me₂-5-one	77—86	25	6.9—8.5	1.22	4.38	4.38	0	0.25	0.50	0.83	4	0.83⎫	2l
	88—95	25	8.7—9.8	-0.34	1.79 f	5.79	+			5.79	4	5.79⎬	
(ix) Pyrazolium cations													
1-Ph-2-Me	82—88	25	7.8—8.7	1.95	5.17	5.17	+			5.17	4'	5.17	3l
1,2,3,5-Me₄	76—87	24	6.7—8.6	2.31	5.02	4.93	+			4.93	4	4.93	2h
1-Me-2-Ph	75—81	50	6.2—7.2	1.99	3.57	5.56	+			5.56	4'	5.56	2m
1-Me-4-NO₂-2-Ph	75—81	80	5.7—6.7	2.19	3.51	7.51	+			7.51	4'⎫	7.40	2m
	83—88	60	7.2—7.9	1.92	4.60	7.30				7.80	4'⎬		
1-Me-2-p-NO₂C₆H₄	77—82	140	5.1—5.7	2.13	1.57	8.71	+			7.81	4	7.81	2m
(x) Other five-membered rings													
Thiophen	64—72	25	4.9—6.1	2.04	-1.98	-1.98	0			-1.98	2,5	-1.68	4g
2-Me-thiophen	64—72	25	4.9—6.1	1.67	-1.87	-1.87	0			-1.87	5	-1.87	4g
2-Cl-thiophen	66—73	25	5.2—6.3	2.05	-1.55	-1.55	0			-1.55	5	-1.55	4g
3,5-Me₂-isoxazole	77—87	80	5.9—8.5	1.05	4.04	8.04	0	-1.61 p	1.05 p	2.72	4	2.72	2h
3,5-Me₂-isothiazole	78—88	80	6.1—7.6	1.74	5.04	9.03	+			9.03	4	9.03	2h
2,3,5-Me₃-isothiazolium	77—87	80	6.1—7.5	1.89	5.04	9.03	+			9.03	4	9.03	2h
Imidazole	91—96	25	9.2—10.0	-0.70	2.91 f	6.91	+			6.91	4,5	7.21	4c
1-Ph-imidazole	69—80	25	5.6—7.6	2.11	3.41	3.41	+			3.41	4'	3.41	3l
(xi) Bicyclic compounds													
Naphthalene	61—71	25	4.5—5.9	2.20	-2.49	-2.49	0			-2.49	1,4,5,8(91)	-1.85⎫	3e
											2,3,6,7(9)	-0.85⎬	
1-NHCOMe-naphthalene	66—76	25	5.2—6.7	1.97	-0.70	-0.70	+			-0.70	2(40)	-0.31⎫	3k
											4(60)	-0.48⎬	
Quinoline	77—87	25	7.1—8.7	2.19	5.98	5.98	+			5.98	5(50) q	6.28⎫	
											8(42) q	6.36⎬	
	92—98	25	9.3—10.4	-0.60	1.56 f	5.56	+			5.56	5(50)	5.86⎫	4a
											8(42)	5.94⎬	
4-Quinolone	81—85	25	7.6—8.4	2.45	4.60	4.60	+			4.60	6(81)	4.69⎫	3i
											8(19)	5.32⎬	
1-Me-4-quinolone	77—86	25	7.1—8.4	2.28	4.81	4.81	+			4.81	3(14)	5.67⎫	3i
											6(86)	4.88⎬	
4-OMe-quinoline	81—85	25	7.7—8.3	2.50	4.96	4.96	+			4.96	6(72)	5.10⎫	3i
											8(28)	5.51⎬	
Isoquinoline	68—73	80	4.7—5.4	1.88	1.16	5.16	+			5.16	5(50)	5.46⎫	3c
											8(50)	5.46⎬	
2-Me-isoquinolinium	64—73	80	4.3—5.5	1.94	0.93	4.93	+			4.93	5(50)	5.23⎫	3c
											8(50)	5.23⎬	
2-OH-isoquinolinium	76—83	25	6.9—8.0	2.19	5.58	5.58	+			5.58	5(90)	5.53⎫	3b
											8(10)	6.58⎬	
2-OMe-isoquinolinium	76—83	25	6.9—8.0	2.22	6.13	6.13	+			6.13	5(90)	6.08⎫	3b
											8(10)	7.13⎬	
Cinnoline	76—83	80	5.9—6.8	2.17	3.34	7.34	+			7.34	5(48)	7.66⎫	3c
											8(51)	7.63⎬	
2-Me-cinnolinium	77—81	80	6.0—6.5	2.26	2.98	6.98	+			6.98	5(50)	7.28⎫	3c
											8(50)	7.28⎬	
4-Cinnolone	81—87	25	7.7—8.4	2.07	6.67	6.67	+			6.67	6(58)	6.91⎫	3i
											8(40)	7.07⎬	
							+				5(14)	7.55⎫	
Cinnoline-2-oxide	70—81	80	5.1—6.6	1.35	2.70	6.70	+			6.70	8(52)	6.98⎬	3d
							0	Unknown			6(35)		
1,2,3-Me₃-benzimidazolium	70—76	25	5.9—6.7	2.99	2.32	2.32	+			2.32	5	2.62	4i

a Corrected for isomer distribution and, (where necessary) for the statistical facto-. b C. C. Greig, Ph.D. Thesis, University of East Anglia, 1970. c K. E. Cooper and C. K. Ingold, J. Chem. Soc., 1927, CXXIV, 836. d $H_0\frac{1}{2}$ -7.26 from D. D. Perrin 'Dissociation Constants of Organic Bases in Aqueous Solution,' Butterworths, London, 1965, p. 422. e Estimated as in b. f log k_2 At the H_0 corresponding to 94% H_2SO_4 as the alternative procedure is used (see text). g Δ log k_2 is taken as 5.2 since the substrate is benzenoid. h P. H. Griffiths, W. A. Walkey, and H. B. Watson, J. Chem. Soc., 1934, 631. i Ref. 2j. j m = 1, Since protonation takes place on nitrogen, cf. M. J. Cook, N. L. Dassanayake, C. D. Johnson, A. R. Katritzky, and T. W. Toone, J.C.S. Perkin II, 1974, 1069. k Estimated value see ref. 2h. l The mechanism is in doubt: see original reference and ref. 3d. m Ref. 3d. n N. Shakir, Ph.D. Thesis, University of East Anglia, 1966. o Approximate value: see original reference. p S. Clementi, P. P. Forsythe, C. D. Johnson, A. R. Katritzky, and B. Terem, J.C.S. Perkin II, 1974, 399. q Ref. 3h.

the log $k_2{}^0$ (calc) values reported refer to overall reactivity whereas in the log $k_2{}^0$ (corr) values the statistical factor has been allowed for by division of the rate by 2(or 3 *etc.*).

The alternative procedure, by which the standard rate is obtained from that part of the rate profile at acidities higher than 90% H_2SO_4, has been applied to 16 compounds. Fair agreement is found for the standard rates derived applying both the standard and the alternative procedure to the data for quinolinium and anilinium ions. Nevertheless we realise that the error involved in this method is much larger than that involved in the standard procedure. The standard procedure error is estimated as 0.2 log units, on the basis of standard rates obtained from different data sets for the same compound.

Analysis of the *ca.* 130 rate profiles examined shows that the magnitude of the slope $d[\log k_2]/d[-H_0]$ provides a mechanistic criterion. All majority species reactions with only three exceptions (4-dimethylaminopyridine, 1-phenyl-pyrazole, and 2-methylthiophen) exhibit slopes higher than 1.7 (mean value 2.24 ± 0.27) whereas the slope for all minority species reactions is less than 1.7 (mean value 1.23 ± 0.24); 2-pyrimidone is an apparent exception, whereas benzoic acid has a pK_a value which lies within the relevant H_0 region. Compounds undergoing reaction with rate profile slopes close to 1.7 must be investigated by other mechanistic criteria.[2-5]

It is planned in a later paper [8] to attempt to correlate the standard rates of Table 9 with analogous hydrogen-exchange data and by the Hammett equation.