

## The Kinetics and Mechanism of the Electrophilic Substitution of Heteroaromatic Compounds. Part XXX.<sup>1</sup> The Orientation of the Nitration of 2-Pyridones

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The nitration of 2-pyridone yields largely the 3-nitro-derivative in low acidity media and largely the 5-nitro-compound in high acidity media. However, both reactions occur on the free base species. This behaviour is compared with similar phenomena in the literature.

RECENTLY, we studied<sup>2</sup> the kinetics for the nitration of 3-methyl-2-pyridone in the 5-position and for 5-methyl-2-pyridone in the 3-position: the rate constants for these two nitrations showed significantly different dependence on the acidity of the nitration medium. Raising the acidity appeared to increase the relative rate of nitration at the 5-position. In connection with other work,<sup>3</sup> we found that the proportion of the 3- and 5-nitro-derivatives formed in the mono-nitration of 4-methyl-2-pyridone did indeed vary considerably with the condi-

<sup>1</sup> Part XXIX, G. Bianchi, A. G. Burton, C. D. Johnson, and A. R. Katritzky, preceding paper.

<sup>2</sup> P. J. Brignell, A. R. Katritzky, and H. O. Tarhan, *J. Chem. Soc. (B)*, 1968, 1477.

<sup>3</sup> A. J. Boulton, P. J. Halls, and A. R. Katritzky, *J. Chem. Soc. (B)*, 1970, 636.

tions. Continuing our investigations of the mechanism of nitration of pyridones,<sup>2,4</sup> we have further studied this phenomenon, which we now find to occur for 2-pyridone itself, and which is probably responsible for literature discrepancies regarding the preparative nitration of pyridones. Although the nitration of 2-pyridones has been accepted in recent reviews<sup>5</sup> as yielding predominantly 3-nitro-derivatives (at least for the parent compound and its 1- and 6-methyl homologues), which can react further to form 3,5-dinitro-compounds, the original

<sup>4</sup> A. R. Katritzky, H. O. Tarhan, and S. Tarhan, *J. Chem. Soc. (B)*, 1970, 114.

<sup>5</sup> For literature summaries and comment see (a) R. A. Abramovitch and J. G. Saha, *Adv. Heterocyclic Chem.*, 1966, **6**, 254; (b) K. Schofield, 'Heteroaromatic Nitrogen Compounds,' Butterworth, London, 1967, p. 173.

literature is quite confused. 2-Pyridone itself is reported alternatively as giving a mixture of 3-nitro- and 3,5-dinitro-compounds with only a trace of the 5-nitro-derivative<sup>6</sup> or as yielding a mixture of 3- and 5-nitro-derivatives.<sup>7</sup> 1-Methyl-2-pyridone is reported<sup>8,9</sup> as

were obtained under pseudo first-order nitration conditions by following the rise in absorption of the nitro-products as a function of time at 347 nm where both nitro-products have equal extinction and 2-pyridone is transparent (see Figure 2). Isomer ratios were calcu-

TABLE 1  
Preparative nitration

2-Pyridone substituents	Method (see exptl.)	Crude product composition %		Pure product yield %	M.p. (°C)	Lit. m.p. (°C)
		3-NO <sub>2</sub>	5-NO <sub>2</sub>			
None	i	100	0	85 (3-NO <sub>2</sub> )	224—225	224—225 <sup>a</sup>
	ii	17	83	72 (5-NO <sub>2</sub> )	189—190	191 <sup>a</sup>
4-Methyl	i	98	7	82 (3-NO <sub>2</sub> )	234—235	234—235 <sup>b</sup>
	ii	22	78	60 (5-NO <sub>2</sub> )	188—190	189—190 <sup>b</sup>
1-Methyl	i	88	12	75 (3-NO <sub>2</sub> )	174—176	175—176 <sup>c</sup>
	ii	0	100	65 (5-NO <sub>2</sub> )	172—173	172 <sup>c</sup>

<sup>a</sup> Ref. 6. <sup>b</sup> G. R. Lappin and F. B. Slezak, *J. Amer. Chem. Soc.*, 1950, **72**, 2806. <sup>c</sup> Ref. 8.

TABLE 2  
Proton chemical shifts ( $\tau$ ) and coupling constants (Hz) for 2-pyridones

Substituents	Solvent	3-H	4-H	5-H	6-H	1-CH <sub>3</sub>	4-CH <sub>3</sub>	$J_{3,4}$	$J_{3,5}$	$J_{4,5}$	$J_{4,6}$	$J_{5,6}$
None	<i>b</i>	3.40	2.51	3.81	2.59			10.8	1.9	7.5	1.9	7.5
1-Methyl <sup>a</sup>	<i>b</i>	3.48	2.60	3.81	2.53	6.47		9.0	2.0	7.0	2.0	7.0
4-Methyl	<i>b</i>	3.62		3.88	2.68		7.80		2.5			7.0
3-Nitro	<i>c</i>		0.65	2.14	1.32					8.5	1.5	6.3
5-Nitro	<i>c</i>	2.32	0.88		0.84			9.8			2.5	
1-Methyl-3-nitro	<i>c</i>		0.78	2.27	1.39	5.71				8.5	2.0	7.0
1-Methyl-5-nitro	<i>c</i>	2.36	0.99		0.75	5.77		9.5			2.5	9.5
3-Nitro-4-methyl	<i>c</i>			2.33	1.61 <sup>d</sup>		6.96					8.0
4-Methyl-5-nitro	<i>c</i>	2.54			0.86 <sup>d</sup>		7.05					

<sup>a</sup> These chemical shifts are close to literature values: J. A. Elvidge and L. M. Jackman, *J. Chem. Soc.*, 1961, 860. <sup>b</sup> CDCl<sub>3</sub> as solvent; Me<sub>4</sub>Si internal reference. <sup>c</sup> 90% H<sub>2</sub>SO<sub>4</sub> as solvent; TMAS internal reference. <sup>d</sup> Coupled to 1-proton;  $J_{1,6} = 7.3$  Hz (5-nitro), 6.3 Hz (3-nitro).

giving the 3-nitro- or the 5-nitro-derivative, although the latter assignment may be in error.<sup>5a</sup>

As already briefly reported,<sup>10</sup> the use of a high temperature (which decreases the effective acidity of a medium<sup>11,12</sup>), high substrate concentration, and comparatively dilute sulphuric acid, enables the preparation by direct nitration of 3-nitro-2-pyridone and of its 1- and 4-methyl derivatives in 75—85% isolated yields. The use of a low temperature, a low substrate concentration, and a concentrated sulphuric acid medium enables the preparation of the three corresponding 5-nitro-derivatives in 60—75% isolated yields (Table 1). The isomer proportions given for the crude reaction products were obtained by n.m.r. spectroscopic analysis. The spectrum of the mixed 3- and 5-nitro-2-pyridones showed as clearly separated signals the 6-proton of the 3-isomer and the 4- and 6-proton signals of the 5-isomer (see Table 2 and Figure 1), and the isomer ratios were obtained by planimetric integration. For the nitration mixtures derived from 1- and from 4-methyl-2-pyridones the ratios were obtained by integration of the methyl signals.

We now report our detailed study of the nitration kinetics of 2-pyridone. Second-order rate constants

<sup>6</sup> A. Binz and H. Maier-Bode, *Angew. Chem.*, 1936, **49**, 486.

<sup>7</sup> A. E. Tschitschibabin and S. A. Shapiro, *J. Russ. Phys. Chem. Soc.*, 1921, **53**, I, 233.

<sup>8</sup> A. E. Tschitschibabin and R. A. Konowalowa, *Ber.*, 1925, **58B**, 1712.

<sup>9</sup> O. Fischer and M. Chur, *J. prakt. Chem.*, 1916, **93**, 363.

lated for 'infinity' optical densities at 395 nm where only 3-nitro-2-pyridone shows appreciable absorption (see Figure 2).

#### EXPERIMENTAL

M.p.s were recorded on a Kofler hot-stage and are uncorrected. N.m.r. spectra (Table 2) were obtained with

TABLE 3  
U.v. spectra and basicities

Compound	$\lambda_{\max.}$ (log $\epsilon$ ) <sup>a</sup>		$pK_a$ <sup>b</sup>	
	Neutral species <sup>c</sup>	Cation <sup>d</sup>	Proton addition	Proton loss
2-Pyridone	225 (3.89) 295 (3.79)	275 (3.88)	0.77	11.70
3-Nitro-2-pyridone	205 (4.26) 257 (3.42) 363 (3.86)	238 (3.52) 304 (3.90)	-4.00 <sup>e</sup>	8.52
5-Nitro-2-pyridone	212 (3.94) 304 (4.03)	283 (4.05)	-2.45 <sup>e</sup>	7.97

<sup>a</sup> All values are close to literature values.<sup>13</sup> <sup>b</sup> Data from ref. 13. <sup>c</sup> Measured in H<sub>2</sub>O at pH 5. <sup>d</sup> Measured in 98% H<sub>2</sub>SO<sub>4</sub> ( $H_0$  ca. -10.5). <sup>e</sup>  $H_0$  at half-protonation.

a Varian HA 100 spectrometer using H<sub>3</sub>O<sup>+</sup> as lock signal with TMAS as internal reference. Ultraviolet spectra

<sup>10</sup> A. G. Burton, P. J. Halls, and A. R. Katritzky, *Tetrahedron Letters*, 1971, 2211.

<sup>11</sup> C. D. Johnson, A. R. Katritzky, and S. A. Shapiro, *J. Amer. Chem. Soc.*, 1969, **91**, 6654.

<sup>12</sup> C. D. Johnson, A. R. Katritzky, and T. W. Toone, work in progress.

<sup>13</sup> E. Spinner and J. C. B. White, *J. Chem. Soc. (B)*, 1966, 991.

(Table 3) were recorded on a Unicam SP 800 instrument or a Unicam SP 500 for individual optical densities.

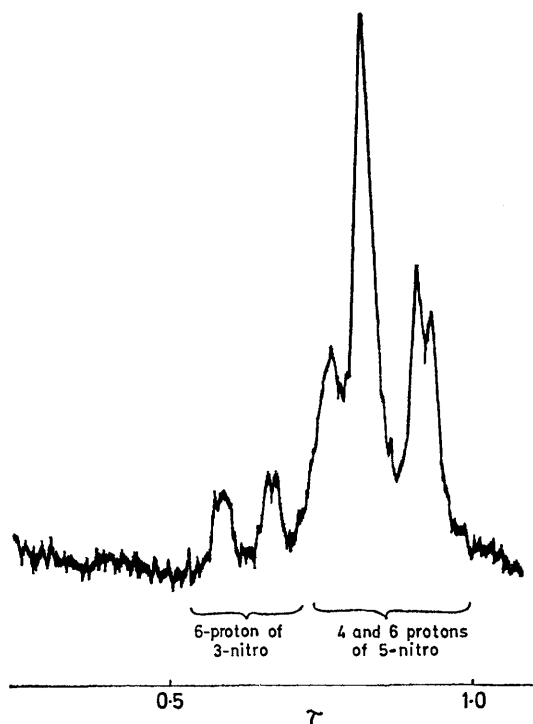


FIGURE 1 Portion of the 100 MHz n.m.r. spectrum (98%  $\text{H}_2\text{SO}_4$ , 250 Hz sweep width) of the crude product from the nitration of 2-pyridone at low acidity

**Materials.**—2-Pyridone had m.p. 107–108° (lit.,<sup>14</sup> 107°) after sublimation at 100°/0.1 mm. 4-Methyl-2-pyridone<sup>15</sup> sublimed at 120°/0.1 mm and had m.p. 129–129.5° (lit.,<sup>15</sup> m.p. 130°). 1-Methyl-2-pyridone<sup>16</sup> had b.p. 105°/0.5 mm (lit.,<sup>16</sup> b.p. 122–124°/11 mm). 3-Nitro-2-pyridone<sup>12</sup> crystallised from aqueous ethanol as needles and had m.p.

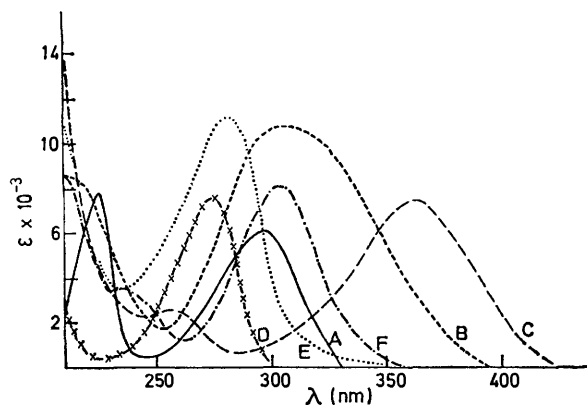


FIGURE 2 (a) U.v. spectra of neutral species in water at pH 5: (A) 2-pyridone; (B) 5-nitro-2-pyridone, and (C) 3-nitro-2-pyridone; (b) U.v. spectra of cations in 98%  $\text{H}_2\text{SO}_4$ : (D) 2-pyridone; (E) 5-nitro-2-pyridone, and (F) 3-nitro-2-pyridone

224–225° (lit.,<sup>12</sup> 224–225°). 5-Nitro-2-pyridone was obtained from diazotisation<sup>10</sup> of 2-amino-5-nitropyridine; it

<sup>14</sup> H. von Pechmann and O. Baltzer, *Chem. Ber.*, 1891, **24**, 3145.

<sup>15</sup> O. Seide, *Ber.*, 1924, **57**, 791.

crystallised from aqueous ethanol as needles and had m.p. 189–190° (lit.,<sup>12</sup> 191°).

**Kinetic Procedures.**—The following are examples of a typical kinetic procedure. 2-Pyridone (16.0 mg) in sulphuric acid (50 ml; 95.92%) was thermostatted in a stoppered flask at 25.0°. Previously thermostatted nitric acid (0.4937 g; 70.54%) was added and the whole shaken. After known time intervals, 1-ml aliquots were withdrawn and diluted to 20 ml with *m*-sodium hydroxide. The absorption of each such solution was measured at 347 nm (Table 4) and the 'infinity' solution was also measured at 395 nm. The isomer proportions were obtained using equation (1). 'Infinity' optical densities were 75–90% of theoretical and were obtained 48–72 h after reaction commenced.

Kinetic data obtained from such runs is recorded in Table 5. In this paper,  $k_2$  (obs) denotes the observed second-order rate constant, and  $k_2^3$  (obs) and  $k_2^5$  (obs) the individual rate constants for reaction at the 3- and 5-position, respectively.  $H_0$  values are from ref. 11 and are corrected for temperature variation.

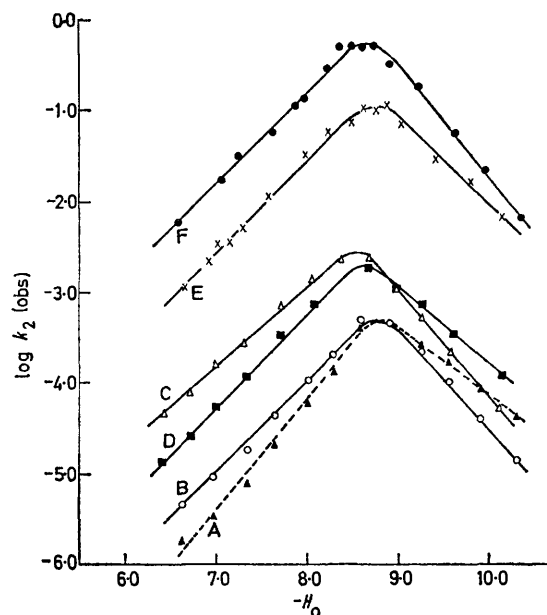


FIGURE 3 Rate profiles for nitration of 2-pyridone: (A) 5-position at 25.0°, (B) 3-position at 25.0°, (C) 3-position at 40° and (D) 5-position at 40°, and for the nitration of (E) 5-methyl-2-pyridone at 31° and (F) 3-methyl-2-pyridone at 31.5°

## RESULTS AND DISCUSSION

Individual rate constants for the nitration of 2-pyridone at the 3- and 5-position are recorded in Table 5, and the rate profiles are plotted in Figure 3. Rate profile slopes are given in Table 6. Figure 3 and Table 6 also contain data for 3-methyl-2-pyridone, 5-methyl-2-

$$\% \text{ 3-nitro} = \frac{\text{OD} (395 \text{ nm})}{\text{OD} (347 \text{ nm})} \cdot \frac{\epsilon (347 \text{ nm})}{\epsilon (395 \text{ nm})} \cdot 100 \quad (1)$$

pyridone, and 1,5-dimethyl-2-pyridone, calculated from ref. 2.

<sup>16</sup> E. A. Prill and S. M. McElvain, *Org. Synth.*, Coll. Vol. II, 1943, 419.

*Confirmation of Nitration as Free Base Species.*— Previous work<sup>2</sup> has shown that the nitrations of 3- and 5-methyl-2-pyridone take place on the free base species;

TABLE 4

Data for a typical kinetic run (see exptl. section)

Time, <i>t</i> (min)	OD <sub><i>t</i></sub> (347 nm)	log (OD <sub>∞</sub> - OD <sub><i>t</i></sub> )
20.0	0.020	0.0069
38.0	0.030	0.0026
59.1	0.050	-0.0061
83.6	0.072	-0.0159
162.0	0.128	-0.0419
213.1	0.164	-0.0595
∞ (calc.)	1.036	

Optical density 0.142 at 395 nm after 48 h = 32% 3-nitro- and 68% 5-nitro-2-pyridone.

Plot of log (OD<sub>∞</sub> - OD<sub>*t*</sub>) vs. *t* gives line of slope  $5.797 \times 10^{-6}$  s<sup>-1</sup> (correlation coefficient 0.9994).

$$k_2(\text{obs}) = 1.203 \times 10^{-4} \text{ l m}^{-1} \text{ s}^{-1}$$

$$k_2^3(\text{obs}) = 3.85 \times 10^{-5} \text{ l m}^{-1} \text{ s}^{-1}$$

$$k_2^5(\text{obs}) = 8.18 \times 10^{-5} \text{ l m}^{-1} \text{ s}^{-1}$$

application of the same criteria confirm that 2-pyridone itself undergoes nitration at both the 3- and 5-positions as the free base. Thus the shapes of the rate profiles

the high acidity region for 2-pyridone and the methyl-2-pyridones are all within the range<sup>17</sup> (0.8—1.5) characteristic for free base nitrations.

$$k_2(\text{fb}) = k_2(\text{obs})/F \quad (2)$$

$$\log k_2(\text{fb}) = \log k_2(\text{obs}) + \text{p}K_a - mH_0 \quad (3)$$

$$\log k_2^3(\text{fb}) = x \log k_2(\text{fb}) \quad (4)$$

$$\log k_2^5(\text{fb}) = (1 - x) \log k_2(\text{fb}) \quad (5)$$

The conclusion that 2-pyridone is nitrated over the entire acidity range *via* the free base is strengthened by further evidence. Correction of rate constants for the concentration of free base gives values of log *k*<sub>2</sub>(fb) (Table 7), defined by equation (2) from which equations (3), (4), and (5) follow. In these equations, F = fraction of substrate in unprotonated form, and *x* = mol fraction of 3-nitro-derivative in the product mixture.

The applicability of the *H*<sub>A</sub> acidity function to the protonation of 2- and 4-pyridones has been previously discussed.<sup>2</sup> Log *k*<sub>2</sub>(fb) values were calculated taking *m* = 0.65.<sup>18</sup> Whereas basic *H*<sub>A</sub> indicators indicate that the *m* value approaches unity as  $-H_0$  nears zero (*cf.* the

TABLE 5

(a) Rate-constants for nitration of 2-pyridone at 25.0°

% H <sub>2</sub> SO <sub>4</sub>	- <i>H</i> <sub>0</sub> (25)	-( <i>H</i> <sub>R</sub> + log <i>a</i> <sub>H<sub>3</sub>O</sub> )	log <sub>10</sub> <i>k</i> <sub>2</sub> (obs)	log <sub>10</sub> <i>k</i> <sub>2</sub> <sup>3</sup> (obs)	log <sub>10</sub> <i>k</i> <sub>2</sub> <sup>5</sup> (obs)
97.48	10.32		-4.28	-4.87	-4.41
95.38	9.91		-3.92	-4.42	-4.09
93.47	9.57		-3.59	-4.01	-3.80
91.60	9.27		-3.32	-3.67	-3.58
89.54	8.92		-3.06	-3.36	-3.38
87.38	8.61		-3.06	-3.31	-3.42
85.19	8.30		-3.49	-3.71	-3.89
83.33	8.02	17.62	-3.78	-3.98	-4.23
81.20	7.64	16.78	-4.20	-4.37	-4.70
79.35	7.35	16.07	-4.59	-4.75	-5.12
77.27	6.98	15.30	-4.91	-5.05	-5.47
75.23	6.64	14.65	-5.20	-5.35	-5.76

(b) Rate-constants for nitration of 2-pyridone at 40.0°

% H <sub>2</sub> SO <sub>4</sub>	- <i>H</i> <sub>0</sub> (40°)	-( <i>H</i> <sub>R</sub> + log <i>a</i> <sub>H<sub>3</sub>O</sub> )	log <sub>10</sub> <i>k</i> <sub>2</sub> (obs)	log <sub>10</sub> <i>k</i> <sub>2</sub> <sup>3</sup> (obs)	log <sub>10</sub> <i>k</i> <sub>2</sub> <sup>5</sup> (obs)
98.48	10.11		-3.76	-4.27	-3.92
95.45	9.56		-3.24	-3.66	-3.45
93.54	9.24		-2.91	-3.26	-3.15
91.67	8.95		-2.65	-2.96	-2.95
89.69	8.65		-2.37	-2.62	-2.73
87.67	8.35		-2.40	-2.62	-2.81
85.60	8.03		-2.67	-2.86	-3.12
83.53	7.68	17.71	-2.98	-3.15	-3.48
81.39	7.30	16.84	-3.40	-3.54	-3.96
79.37	6.98	16.08	-3.69	-3.81	-4.29
77.35	6.69	15.38	-3.99	-4.11	-4.61
75.37	6.39	14.73	-4.24	-4.36	-4.87

(Figure 3) are similar to those<sup>2</sup> for 3- and 5-methyl-2-pyridone as are the rate profile slopes for both the low and high acidity regions (Table 6); 2-methoxy-3-methylpyridine, which nitrates as the conjugate acid, was previously shown to react much more slowly and to show a rate profile typical for a conjugate acid.<sup>2</sup> The decrease in the slope of the Moodie-Schofield plots with increasing temperature is expected from the recently established<sup>12</sup> temperature dependence of *H*<sub>R</sub>.

The slopes of the rate profiles  $[-d \log k_2(\text{obs})/dH_0]$  in

<sup>17</sup> Summarised by E. F. V. Scriven, Ph.D. Thesis, University of East Anglia, 1969.

acidity function behaviour of pyridine 1-oxides<sup>18</sup>, for greater acidities the appropriate value is *m* = 0.65, and the corrected slopes (Table 6) were within the range<sup>17</sup> (0.2—0.6) found for majority species nitrations as expected.<sup>2</sup>

The low acidity rate profile slopes (Table 6) confirm free base reaction in this acidity region. Thus, the Moodie-Schofield plots [log *k*<sub>2</sub>(obs)] have low slopes, and while plots of 'corrected' rate constants [log *k*<sub>2</sub>(fb)]

<sup>18</sup> *m* = *n*<sup>-1</sup>. For definition of *n* see: C. D. Johnson, A. R. Katritzky, B. J. Ridgwell, N. Shakir, and A. M. White, *Tetrahedron*, 1965, **21**, 1055.

TABLE 6

Rate profile slopes <sup>a</sup>

Position of nitration	2-Pyridone substituents	Temp.	Low acidity region				High acidity region			
			$-\text{d} \log k_2$ (obs)		$-\text{d} \log k_2$ (fb) <sup>c</sup>		$-\text{d} \log k_2$ (obs)		$-\text{d} \log k_2$ (fb)	
			$\text{d} [(H_R + \log a_{H_2O})]$	$r^b$	$\text{d} [(H_R + \log a_{H_2O})]$	$r^b$	$\text{d} H_0$	$r^b$	$\text{d} H_0$	$r^b$
3		25°	0.46	0.999	0.76	0.999	1.15	0.999	0.49	0.999
3		40	0.40	0.998	0.68	0.999	1.14	0.999	0.49	0.999
3	5-Methyl	31.5					0.89	0.996	0.26	0.977
3	5-Methyl	35	0.48	0.995	0.73	0.996				
3	1,5-Dimethyl	29					1.23	0.997	0.59	0.985
3	1,5-Dimethyl	39.5	0.60	0.998	0.86	0.999				
5		25	0.52	0.998	0.82	0.999	0.80	0.999	0.16	0.998
5		40	0.45	0.997	0.74	0.999	0.85	0.999	0.23	0.996
5	3-Methyl	31	0.40	0.991	0.66	0.996	1.29	0.999	0.66	0.998
5	3-Methyl	34.5	0.39	0.993	0.65	0.997				
5	3-Methyl	44.2	0.52	0.994	0.71	0.995				
5	<i>d</i>	25.9					0.53	0.998		

<sup>a</sup> Missing figures denote data not available. <sup>b</sup>  $r$  = Correlation coefficient. <sup>c</sup> Calculated using the following  $\text{p}K_a$  values: 2-pyridone, 0.77;<sup>13</sup> 3-methyl-2-pyridone, 0.20;<sup>13</sup> 5-methyl-2-pyridone, 1.13;<sup>13</sup> 1,5-dimethyl-2-pyridone, 0.79;<sup>2</sup> and assuming  $H_A$  behaviour, see discussion. <sup>d</sup> 3-Methyl-2-methoxypyridine.

TABLE 7

## Corrected rate constants

(a) At 25°						
% $H_2SO_4$	$-H_0$	$-(H_R + \log a_{H_2O})$	$\log k_2$ (fb)	$\log k_2^3$ (fb) <sup>a</sup>	$\log k_2^5$ (fb) <sup>a</sup>	$\log k_2^*$
97.48	10.32		3.20	2.62	3.07	-4.28
95.38	9.91		3.29	2.80	3.13	-3.92
93.47	9.57		3.40	2.99	3.19	-3.59
91.60	9.27		3.48	3.13	3.22	-3.32
89.54	8.92		3.51	3.22	3.20	-3.01
87.38	8.61		3.31	3.06	2.95	-2.72
85.19	8.30		2.68	2.46	2.28	-2.59
83.33	8.02	17.62	2.20	2.01	1.76	-2.28
81.20	7.64	16.78	1.54	1.37	1.05	-1.77
79.35	7.35	16.07	0.96	0.81	0.43	-1.42
77.27	6.98	15.30	0.40	0.26	-0.16	-0.89
75.23	6.64	14.65	-0.11	-0.25	-0.66	-0.43
(b) At 40°						
% $H_2SO_4$	$-H_0$	$-(H_R + \log a_{H_2O})$ <sup>b</sup>	$\log k_2$ (fb)	$\log k_2^3$ (fb) <sup>a</sup>	$\log k_2^5$ (fb) <sup>a</sup>	$\log k_2^*$
98.48	10.11		3.58	3.07	3.42	-3.76
95.45	9.56		3.74	3.33	3.53	-3.24
93.54	9.24		3.87	3.51	3.62	-2.91
91.67	8.95		3.94	3.63	3.64	-2.61
89.69	8.65		4.02	3.77	3.66	-2.09
87.67	8.35		3.80	3.58	3.40	-1.60
85.60	8.03		3.32	3.13	2.87	-1.19
83.53	7.68	17.71	2.78	2.62	2.28	-0.66
81.39	7.30	16.84	2.12	1.98	1.56	-0.10
79.37	6.98	16.08	1.62	1.50	1.02	0.33
77.35	6.69	15.38	1.13	1.01	0.51	0.67
75.37	6.39	14.73	0.68	0.56	0.05	1.10

<sup>a</sup> Calculated assuming  $H_A$  behaviour: see text. <sup>b</sup> Calculated from data for 25°.

TABLE 8

## Arrhenius parameters for the nitration of 2-pyridone

$-H_0$	3-Nitration					5-Nitration				
	$E_a$ (kcal mol <sup>-1</sup> )	$\Delta H^\ddagger$ (kcal mol <sup>-1</sup> )	$\Delta S^\ddagger$ (e.u.)	$\Delta G_{25}^\ddagger$ (kcal mol <sup>-1</sup> )	$\log_{10} A$	$E_a$ (kcal mol <sup>-1</sup> )	$\Delta H^\ddagger$ (kcal mol <sup>-1</sup> )	$\Delta S^\ddagger$ (e.u.)	$\Delta G^\ddagger$ (kcal mol <sup>-1</sup> )	$\log_{10} A$
6.5	37.5	36.9	39.9	25.0	22.0	35.5	34.9	31.2	25.7	20.1
7.0	35.0	34.4	33.8	24.3	20.6	33.8	33.2	28.2	24.8	19.4
7.5	33.3	32.7	30.4	23.6	19.9	32.4	31.8	26.1	24.0	18.9
8.0	31.6	31.0	27.1	22.9	19.2	31.0	30.4	24.0	23.2	18.5
8.5	25.0	24.4	7.5	22.2	14.9	26.7	26.1	12.4	22.4	15.9
9.0	10.8	10.2	-39.9	22.1	4.5	11.9	11.3	-36.1	22.1	5.3
9.5	10.0	9.4	-45.2	22.8	3.4	10.2	9.6	-43.4	22.6	3.7
10.0	9.7	9.1	-48.7	23.6	2.6	9.7	9.1	-47.2	23.1	2.9

also have slopes less than unity, the discrepancy is far less. (Rate constants corrected for the concentration of free base assuming that the protonation of 2-pyridones follows  $H_0$  rather than  $H_A$  do give Moodie-Schofield plots with slopes close to unity.)

The use of rate constants corrected for the concentration of nitronium ion as a mechanistic criterion has been discussed previously.<sup>2</sup> Log  $k_2^*$  values, defined from equation (6), were calculated as previously described.<sup>2</sup>

$$\log k_2^* = \log k_2(\text{obs}) \{[\text{HNO}_3]/[\text{NO}_2^+]\} \quad (6)$$

Plots of log  $k_2^*$  against  $H_0$  for overall nitration of 2-pyridone in the region 75–90%  $\text{H}_2\text{SO}_4$  have slopes of 1.33 at 25° ( $r = 0.999$ ) and 1.38 at 40° ( $r = 0.999$ ), again confirming free base nitration.

The calculated<sup>2</sup> rate of encounter log  $k$  (enc) between a nitronium ion and a neutral 2-pyridone molecule is 8.45 in 90–98%  $\text{H}_2\text{SO}_4$  at 25°. The log  $k_2$  (fb) values in Table 7 show that 2-pyridone reacts as the neutral molecule at a rate less than or equal to 0.01% the rate of encounter.

*Arrhenius Parameters.*—These (Table 8) were calculated from the rate profiles (Figure 3) using media of equal  $H_0$  (and not of equal % sulphuric acid). There is a well-defined change in the region of  $H_0$  –8.5. At acidities weaker than this  $\Delta S$  is ca. +30 e.u. and  $\Delta H$  is ca. 35 kcal mol<sup>-1</sup> whereas at stronger acidities  $\Delta S$  is ca. –45 e.u. and  $\Delta H$  ca. 10 kcal mol<sup>-1</sup>.

The activation energies for the nitration of 3-methyl- and 5-methyl-2-pyridone suggest that at elevated temperatures, the 3-nitration of 5-methyl-2-pyridone would become faster than 5-nitration of 3-methyl-2-pyridone. This is comparable to the predominance of 3-nitration of unsubstituted 2-pyridone at elevated temperatures.

Previously,<sup>19</sup> we have considered that the apparent entropies of activation for reaction between two positively charged species are more negative than those for reaction

between an ion and a neutral molecule. The large variations of the activation parameters with acidity found in the present work emphasise that this criterion must be applied with great caution.

*Previous Work on Change of Nitration Orientation with Acidity.*—Cases of change in orientation with acidity as a result of reaction of species of differing charge are well authenticated; e.g., quinoline 1-oxide undergoes nitration as the free base at the 4-position and as conjugate acid at the 5- and 8-positions and the proportion of products found changes as expected with the acidity.<sup>20,21</sup> However, it is also quite clear that considerable variation in isomer proportion can also arise from other causes: thus Hartshorn and Ridd<sup>22</sup> ascribe the considerable variation in product composition in the nitration of aniline to ‘differential salt effects on substitution at the *o*-, *m*-, and *p*-positions in the anilinium ion.’ There are considerable variations in the isomer proportion in the nitration of electron withdrawing-substituted thiophenes with medium and temperature,<sup>23</sup> which cannot be attributed to competitive reaction of differently charged species, and although such hypotheses have been made, e.g. for the nitration of benzaldehyde,<sup>24</sup> this is at best doubtful. A review by Taylor<sup>25</sup> has rationalised changing *o-p* ratios in terms of selectivity, pointing out that log  $f_o$  : log  $f_p$  ratios should be sought rather than those involving  $\frac{1}{2}o$  : *p* ratios. Recently, Allan<sup>26</sup> has suggested that in strongly acid media proton loss may become partially rate-determining for nitration and that this may affect isomer ratios.

*General Conclusions.*—The work described in this paper highlights a major deficiency of present theoretical treatments of reactivity which neglect medium considerations (e.g. ‘the position 3 ought to be slightly more reactive than the position 5’ for 1-methyl-2-pyridone from MO calculations<sup>27</sup>).

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