

## The Kinetics and Mechanism of the Electrophilic Substitution of Hetero-aromatic Compounds. Part XLVIII.<sup>1</sup> Nitration of Pyrazoles in the 3- and 5-Positions

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The kinetics of nitration of 1,4-dimethyl- and 4-methyl-1-*p*-nitrophenylpyrazole at the 3-position, and of 1,4-dimethyl-3-nitropyrazole at the 5-position show that these reactions all proceed on free base species. Standard rate constants ( $k_0$ ) are calculated and compared with those for the nitration of related compounds.

WHEREAS the direct nitration of the pyrazole nucleus at the 4-position has been long known, such nitration reactions at the 3- and 5-positions have been reported only recently. Habraken and her co-workers converted several 4-alkylpyrazoles into 3-nitro-derivatives<sup>2</sup> with acetyl nitrate whereas 1-methyl-4-phenylpyrazole thus

also yielded considerable amounts of 3,2'-dinitro-product.<sup>3</sup> The same group have also rearranged 1-nitro- to 3(5)-nitro-pyrazoles,<sup>4,5</sup> and nitrated indazoles at the 3-position.<sup>6</sup> Coburn has reported that 4-(2,4-dinitrophenyl)- (1) and 4-(2,4,6-trinitrophenyl)-1-methylpyrazole are nitrated in the 3- and 5-positions<sup>7</sup> as is 4-bromo-1-methylpyrazole.<sup>8</sup> He studied<sup>9</sup> the kinetics

<sup>1</sup> Part XLVII, A. R. Katritzky, M. Konya, H. O. Tarhan, and A. G. Burton, preceding paper.

<sup>2</sup> C. L. Habraken, P. Cohen-Fernandes, S. Balian, and K. C. van Erk, *Tetrahedron Letters*, 1970, 479.

<sup>3</sup> P. Cohen-Fernandes and C. L. Habraken, *Rec. Trav. chim.*, 1972, **91**, 1185.

<sup>4</sup> J. W. A. M. Janssen and C. L. Habraken, *J. Org. Chem.*, 1971, **36**, 3081.

<sup>5</sup> J. W. A. M. Janssen, H. J. Koeners, C. G. Kruse, and C. L. Habraken, *J. Org. Chem.*, 1973, **38**, 1777.

<sup>6</sup> P. Cohen-Fernandes and C. L. Habraken, *J. Org. Chem.*, 1971, **36**, 3084.

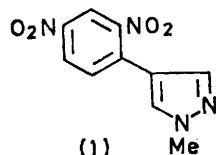
<sup>7</sup> M. D. Coburn, *J. Heterocyclic Chem.*, 1970, **7**, 707.

<sup>8</sup> M. D. Coburn, *J. Heterocyclic Chem.*, 1971, **8**, 153.

<sup>9</sup> M. D. Coburn, *J. Heterocyclic Chem.*, 1971, **8**, 293.

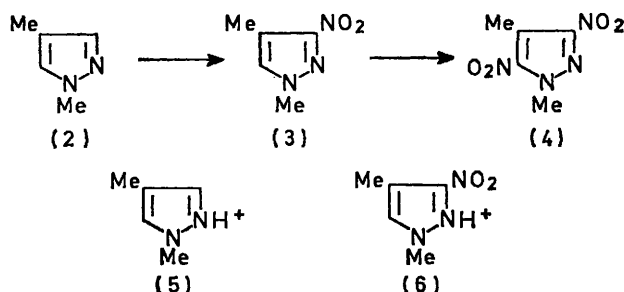
of nitration of (1) in nitric acid and found that both the 3- and 5-nitro-derivatives were formed but that the latter then decomposed in further reactions. Nitration of 5-methyl-1-phenylpyrazole in acetic anhydride is reported<sup>10</sup> to give a mixture of 3- (42%) and 4-nitro-isomers (14%), but 3-methyl-1-phenylpyrazole yielded solely the 4-nitro-product.

In none of the above work was the species undergoing nitration elucidated, although it was surmised<sup>6</sup> that for



the indazoles the free base reacted at the 2- and 3-positions but the conjugate acid in the benzo-ring. We showed earlier<sup>11</sup> that 4-nitration of pyrazoles occurred

4-Methyl-1-(*p*-nitrophenyl)pyrazole (7) also underwent nitration in both acetic anhydride and sulphuric acid to



yield the previously unreported 3-nitro-derivative (8). This nitration appeared to occur only at the 3-position: a single 4-methyl peak was observed and any 5-nitro-product formed was probably present to the extent of less than 5%.

TABLE I  
Proton chemical shifts ( $\delta$  values) and coupling constants (Hz) at 60 MHz of substituted pyrazoles  
Pyrazole ring position

Compound	1				3	4	5
	Subst.	$J^a$					
(2) <sup>b</sup>	Me	4.33			H 8.08	Me 2.38	H 8.12
(3) <sup>b</sup>	Me	4.68			NO <sub>2</sub>	Me 2.68	H 8.46
(4) <sup>c</sup>	Me	4.30			NO <sub>2</sub>	Me 2.60	NO <sub>2</sub>
(7) <sup>b</sup>	<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	8.69, 7.96	8.8		H 8.40	Me 2.40	H 8.40
(8) <sup>b</sup>	<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	8.69, 7.96	9.0		NO <sub>2</sub>	Me 2.80	H 8.64
(9) <sup>c</sup>	2,4-(NO <sub>2</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	9.12, 8.70, 7.85	1.8, 8.4		NO <sub>2</sub>	Me 2.80	NO <sub>2</sub>

<sup>a</sup> Coupling constants (Hz) for *p*-nitrophenyl and 2,4-dinitrophenyl substituents. <sup>b</sup> Relative to internal standard, tetramethylammonium sulphate in 90% H<sub>2</sub>SO<sub>4</sub> solvent. Chemical shifts given are for the compounds in their protonated species. <sup>c</sup> Relative to internal standard Me<sub>4</sub>Si, in CDCl<sub>3</sub> as solvent.

on the conjugate acid species, and we have now examined the mechanism of 3- and 5-nitration and elucidated the reactivity of these ring positions towards electrophiles.

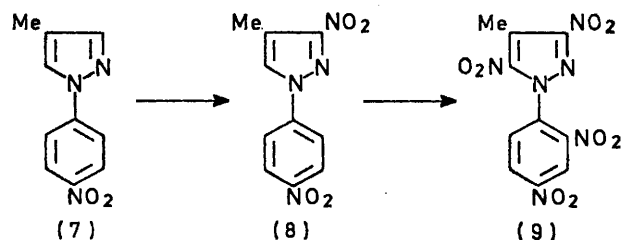
**Preparation of Compounds.**—1,4-Dimethylpyrazole (2) underwent nitration to give the 3-nitro-analogue (3), in acetic anhydride as previously reported,<sup>12</sup> and also in sulphuric acid. In sulphuric acid, the crude nitro-compound was isolated in 62% yield; it was shown by n.m.r. spectroscopy to contain less than 5% of other isomers, and recrystallisation gave pure 1,4-dimethyl-3-nitropyrazole in 40% yield. The nitration in sulphuric acid was also followed by n.m.r.: the pattern changed from that of (5) to that of (6) (Table I); however the appearance of small peaks at  $\delta$  4.30–4.70 for *N*-methyl and  $\delta$  2.65–2.95 for *C*-methyl provided evidence for the formation of some 1,4-dimethyl-5-nitropyrazole; the proportion was *ca.* 10–15% of the amount of the 3-nitro-analogue found by integration.

Further nitration of (3), and also vigorous nitration of (2), gave the 3,5-dinitropyrazole (4), the n.m.r. spectra of which showed solely two methyl groups,  $\delta$  4.30 and 2.70 (in CDCl<sub>3</sub>).

<sup>10</sup> M. R. Grimmett, S. R. Hartshorn, K. Schofield, and J. B. Weston, *J.C.S. Perkin II*, 1972, 1654.

<sup>11</sup> A. G. Burton, P. P. Forsythe, C. D. Johnson, and A. R. Katritzky, *J. Chem. Soc. (B)*, 1971, 2365.

Compound (8) was resistant to further nitration under all but forcing conditions, which produced the tetranitro-compound (9). The structure of (9) was confirmed by



the n.m.r. spectrum which showed an ABC pattern for the trisubstituted phenyl ring and a methyl proton peak. It was not possible to nitrate (8) to give a trinitro-compound.

**Kinetics.**—The nitrations (2)  $\rightarrow$  (3), (3)  $\rightarrow$  (4), and (7)  $\rightarrow$  (8) proceeded smoothly at 80 °C. However the further nitration of (8) was not easy to follow kinetically.

#### EXPERIMENTAL

The following were prepared by the literature methods quoted: 1,1-diethoxypropane, b.p. 122–124° at 760 mmHg

<sup>12</sup> C. L. Habraken, P. Cohen-Fernandes, S. Balian, and K. C. van Erk, *Tetrahedron Letters*, 1970, 479.

(lit.<sup>13</sup> 122—124° at 760 mmHg); 1-ethoxypropene, b.p. 65—75° at 760 mmHg (lit.<sup>14</sup> 69° at 760 mmHg); 1,1,3,3-tetraethoxy-2-methylpropane, b.p. 89—92° at 5 mmHg (lit.<sup>15</sup> 65—67° at 1 mmHg); 1,4-dimethylpyrazole, b.p. 146—148° at 760 mmHg (lit.<sup>16</sup> 146—147° at 760 mmHg).

in acetic anhydride for 12 h, just for the preparation of 1,4-dimethyl-3-nitropyrazole. The pyrazole crystallized from benzene as pale yellow needles (0.43 g, 35%), m.p. 192° (Found: C, 48.2; H, 3.4; N, 22.5. C<sub>10</sub>H<sub>8</sub>N<sub>4</sub>O<sub>4</sub> requires C, 48.4; H, 3.3; N, 22.9%);  $\delta$  [(CD<sub>3</sub>)<sub>2</sub>SO] 8.43—8.27

TABLE 2  
U.v. and pK<sub>a</sub> data for substituted pyrazoles

Substituents				$\lambda_{\text{max.}}/\text{nm}$ (log $\epsilon$ )		Proton addition				
1	3	4	5	Neutral species	Cationic species <sup>b</sup>	$\lambda^a$	$\lambda/\text{nm}$	$H_0(\frac{1}{2})$	$m$	pK <sub>a</sub>
Me	H	Me	H	230 (3.75) <sup>c,d</sup>	232 (3.68) <sup>d</sup>	265	240	2.93		2.93
Me	NO <sub>2</sub>	Me	H	276—279 (3.83) <sup>c</sup>	234 (3.79), 270 (3.81)	250	240	—4.33	0.78	—3.38
Me	NO <sub>2</sub>	Me	NO <sub>2</sub>	255—257 (3.99) <sup>e</sup>	224 (3.95), 277 (3.65)		220, 258	—9.01	0.89	—8.02
<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	H	Me	H	225—230 (3.90), 327—330 (4.16) <sup>e,f</sup>	292—294 (4.12) <sup>f</sup>	335			1.00 <sup>g</sup>	—0.16 <sup>h</sup>
<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	NO <sub>2</sub>	Me	H	278—280 (4.16) <sup>e</sup>	269 (4.16)		250	—4.33	0.78	—3.48
2,4-(NO <sub>2</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	NO <sub>2</sub>	Me	NO <sub>2</sub>	243 (4.41)	240—243 (4.43)					

<sup>a</sup>  $\lambda$  For study of nitration kinetics (nm). <sup>b</sup> Measured in 98% H<sub>2</sub>SO<sub>4</sub> ( $H_0$  ca. —9). <sup>c</sup> Measured in acetate buffer at pH 5. <sup>d</sup> Similar values have been reported (J. Elguero, R. Jacquier, and H. C. N. Tien Duc, *Bull. Soc. chim. France*, 1966, 3744). <sup>e</sup> Measured in 35% H<sub>2</sub>SO<sub>4</sub> ( $H_0$  ca. —2). <sup>f</sup> Similar values have been reported (ref. 18). <sup>g</sup> E. Gonzalez and R. Jacquier, *Bull. Soc. chim. France*, 1968, 5006. <sup>h</sup> J. Elguero, E. Gonzalez, and R. Jacquier, *Bull. Soc. chim. France*, 1968, 5009.

The following were prepared by the reactions of 1,1,3,3-tetraethoxy-2-methylpropane with methylhydrazinium sulphate, phenylhydrazine hydrochloride, and *p*-nitrophenylhydrazinium sulphate, respectively, according to the method reported for 1,4-dimethylpyrazole:<sup>16</sup> 4-methyl-1-phenylpyrazole (73%), m.p. 42—43° (lit.,<sup>17</sup> 41.5—42.5°); 4-methyl-1-(*p*-nitrophenyl)pyrazole (67%), m.p. 125—126° (lit.,<sup>18</sup> 125—125.5°).

**1,4-Dimethyl-3-nitropyrazole.**—Nitric acid (70%; 6.0 g) in acetic anhydride (50 ml) was added dropwise at 0 °C to 1,4-dimethylpyrazole (2 g) in acetic anhydride (10 ml). After 5 h at 0 °C the mixture was poured onto water (200 ml) and extracted with ether (2 × 50 ml). The extracts were washed with aqueous sodium hydrogen carbonate and water, dried (MgSO<sub>4</sub>), and evaporated. The resulting 4-methyl-3-nitropyrazole (0.65 g, 22%) crystallized from water as yellow needles, m.p. 97° (lit.<sup>12</sup> 97°). The compound was homogeneous by g.l.c. (SE30 on Chromosorb W AW-DMCS);  $\delta$  (CDCl<sub>3</sub>) 7.40 (1 H, s), 4.01 (3 H, s), and 2.35 (3 H, s). In H<sub>2</sub>SO<sub>4</sub>, the yield increased to 40%.

**1,4-Dimethyl-3,5-dinitropyrazole.**—(a) Nitric acid (70%; 3.5 g) in sulphuric acid (92%; 25 ml) was added dropwise to 1,4-dimethyl-3-nitropyrazole (0.2 g) in sulphuric acid (92%; 10 ml). The solution was stirred for 12 h at 100 °C, cooled, and poured onto crushed ice (100 g). The precipitated dinitropyrazole crystallized from water as plates (19%; 0.05 g), m.p. 101—102° (Found: C, 31.3; H, 3.6; N, 28.6. C<sub>5</sub>H<sub>6</sub>N<sub>4</sub>O<sub>4</sub> requires C, 32.3; H, 3.3; N, 30.1%);  $\delta$  (CDCl<sub>3</sub>) 4.30 (3 H, s) and 2.70 (3 H, s).

(b) 1,4-Dimethylpyrazole (0.5 g), fuming nitric acid (5.0 ml), and sulphuric acid (75 ml) were heated under reflux gently for 24 h, and the product was worked up as before to give the dinitropyrazole (0.23 g, 24%), m.p. and mixed m.p. 101—102°.

**4-Methyl-3-nitro-1-(*p*-nitrophenyl)pyrazole.**—(a) 4-Methyl-1-(*p*-nitrophenyl)pyrazole (1 g) was treated with nitric acid

(2 H, d, *J* 9 Hz), 7.92—7.76 (2 H, d, *J* 9 Hz), 7.88 (1 H, s), and 2.40 (3 H, s).

TABLE 3  
Rate constants for the nitration of 4-methylpyrazoles at 80 °C

(i) 1,4-Dimethylpyrazole				
H <sub>2</sub> SO <sub>4</sub>	—H <sub>0</sub>	—(H <sub>R</sub> + log $a_{\text{H}_2\text{O}}$ )	—log $k_2(\text{obs})$	log $k_2(\text{fb})$
97.80	9.24		2.32	9.85
95.79	8.79		1.96	9.76
94.51	8.57		1.03	10.47
93.08	8.32		0.89	10.36
89.00	7.72		0.67	9.98
88.00	7.59		0.84	9.68
85.80	7.32		1.24	9.01
84.00	7.04	14.59	1.42	8.55
81.58	6.67	13.54	1.74	7.86
79.58	6.39	12.82	2.06	7.26
77.92	6.15	12.26	2.67	6.41
76.71	5.97	11.93	2.79	6.11
(ii) 1,4-Dimethyl-3-nitropyrazole				
% H <sub>2</sub> SO <sub>4</sub>	—H <sub>0</sub>	—log $k_2(\text{obs})$	log $k_2(\text{fb})$	
95.79	8.76	2.54	0.91	
93.26	8.34	2.14	0.99	
91.94	8.16	1.91	1.07	
87.92	7.57	1.74	0.78	
86.20	7.37	1.96	0.41	
83.99	7.04	2.15	—0.04	
(iii) 4-Methyl-1-( <i>p</i> -nitrophenyl)pyrazole				
% H <sub>2</sub> SO <sub>4</sub>	—H <sub>0</sub>	—(H <sub>R</sub> + log $a_{\text{H}_2\text{O}}$ )	—log $k_2(\text{obs})$	log $k_2(\text{fb})$
97.80	9.24		2.97	6.11
95.79	8.79		2.43	6.20
93.58	8.40		1.87	6.37
91.20	8.05		1.56	6.33
87.81	7.56		1.98	5.42
85.80	7.32		2.17	4.99
81.58	6.67	13.54	2.68	4.13
79.58	6.39	12.82	2.86	3.66
77.97	6.16	12.27	3.17	2.83

(b) To 4-methyl-1-(*p*-nitrophenyl)pyrazole (0.5 g) in sulphuric acid (92%; 20 ml) was added 70% nitric acid (0.5 g)

<sup>13</sup> H. Adkins and B. H. Nissen, *J. Amer. Chem. Soc.*, 1922, **44**, 2749.

<sup>14</sup> 'Beilsteins Handbuch der Organischen Chemie,' eds. B. Prager, P. Jacobson, P. Schmidt, and D. Stern, Springer-Verlag, Berlin, 1918, vol. 1, p. 435.

<sup>15</sup> L. A. Yanovskaya, S. S. Yufit, and V. F. Kucherov, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1960, 1246 (*Chem. Abs.*, 1960, **54**, 24,452i).

<sup>16</sup> V. F. Bystrov, I. I. Grandberg, and G. I. Sharova, *Zhur. obshchei Khim.*, 1965, **35**, 293.

<sup>17</sup> R. Huisgen, R. Grashey, and H. Gotthardt, *Chem. Ber.*, 1968, **101**, 829.

<sup>18</sup> J. Elguero and R. Jacquier, *Bull. Soc. chim. France*, 1962, 233.

in sulphuric acid (92%; 50 ml). The solution was stirred at 50 °C for 4 h, cooled, and poured onto crushed ice (300 g). The precipitated dinitropyrazole was crystallized from benzene; yield 0.26 g (43%), m.p. and mixed m.p. 192°.

1-(2,4-Dinitrophenyl)-4-methyl-3,5-dinitropyrazole.—Fuming nitric acid (90%; 2.0 ml) in sulphuric acid (102%; 40 ml) was added dropwise to 4-methyl-3-nitro-1-(*p*-nitrophenyl)pyrazole (0.5 g) in sulphuric acid (92%; 20 ml). The mixture was stirred at 120 °C for 24 h, cooled, and poured over crushed ice (200 g). The precipitated pyrazole crystallized from ethanol as pale yellow plates (0.20 g, 29%), m.p. 153° (Found: C, 35.4; H, 2.0; N, 24.7. C<sub>10</sub>H<sub>7</sub>N<sub>5</sub>O<sub>8</sub>

numerator. For 1,4-dimethyl-3-nitropyrazole it was not possible to follow the kinetics at acidities below 84% as decomposition leading to loss of u.v. absorption then occurred rapidly. However for all these compounds the  $d[\log k_2(\text{obs})]/d(-H_0)$  values lie in the range 0.7–1.2, which is within the range expected<sup>19</sup> for minority species reactions, *i.e.* less than 1.7.

*Standard Rates.*—Table 5 gives  $\log k_0$  values which refer to  $H_0 = -6.6$  and 25 °C and were calculated by the standard procedure.<sup>19</sup> The  $\log k_0$  value for 1,4-dimethylpyrazole, 3.55, is significantly greater than that for

TABLE 4  
Slopes of the rate profiles for nitration of 4-methylpyrazoles

Substrate	T/°C	Low acidity range				High acidity range	
		$m_1^a$	$m_2^b$	$m_3^c$	Reactive species <sup>d</sup>	$m_4^e$	Reactive species <sup>d</sup>
1,4-Dimethylpyrazole	80	0.54	0.93	1.18	F.B.	1.69	F.B.
1,4-Dimethyl-3-nitropyrazole	80			0.75		1.03	F.B.
4-Methyl-1-( <i>p</i> -nitrophenyl)pyrazole	80	0.38	1.00	0.81	F.B.	1.21	F.B.

<sup>a</sup>  $m_1 = d[\log k_2(\text{obs})]/d[-(H_R + \log a_{H_2O})]$ . <sup>b</sup>  $m_2 = d[\log k_2(\text{fb})]/d[-(H_R + \log a_{H_2O})]$ . <sup>c</sup>  $m_3 = d[\log k_2(\text{obs})]/d(-H_0)$ ; the ranges are recorded in Table 5. <sup>d</sup> F.B. = free base. <sup>e</sup>  $m_4 = d[\log k_2(\text{obs})]/d(-H_0)$ .

TABLE 5  
Standard rate constants for the nitration of 4-methylpyrazoles at 80 °C

Compounds	Range (% H <sub>2</sub> SO <sub>4</sub> )	Range (-H <sub>0</sub> )	$d[\log k_2(\text{obs})]/d(-H_0)$	$-\log k$	$-\log k_{25}$	$\log k(\text{fb})$	$\log k^0$
1,4-Dimethylpyrazole	89–76	7.7–6.0	1.18	1.98	5.98	3.55	3.55
1,4-Dimethyl-3-nitropyrazole	88–84	7.6–7.0	0.75	2.50	6.50	-4.73	-4.73
4-Methyl-1-( <i>p</i> -nitrophenyl)pyrazole	88–78	7.6–6.1	0.81	2.75	6.75	-0.31	-0.31

requires C, 35.5; H, 1.8; N, 24.8%);  $\delta$  (CDCl<sub>3</sub>) 9.14–9.11 (1 H, d, *J* 1.8 Hz), 8.78–8.61 (1 H, q, *J* 1.8 and 8.4 Hz), 7.92–7.78 (1 H, d, *J* 8.4 Hz), and 2.80 (3 H, s).

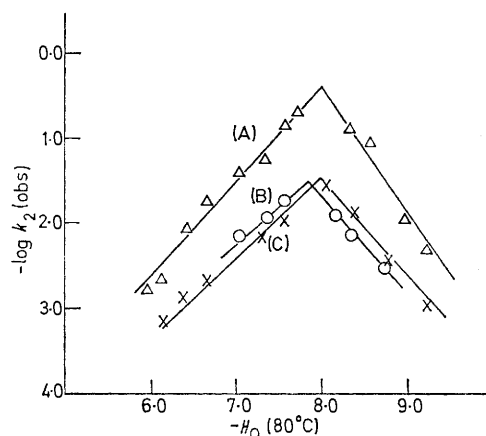
*Spectroscopy and Kinetics.*—N.m.r. spectra were recorded at 60 MHz with a Perkin-Elmer R12 spectrometer and tetramethylammonium sulphate or Me<sub>4</sub>Si as internal standard. The  $pK_a$  determinations and kinetics were followed by Unicam SP 800 self-recording and SP 500 manual spectrometers.  $pK_a$  values, obtained by the u.v. method, are recorded in Table 2.

Kinetics were measured under pseudo-first-order conditions by the procedure previously reported;<sup>19</sup> results are given in Table 3, and the analytical wavelengths for the kinetics are given in Table 2.

## RESULTS AND DISCUSSION

*Nature of Species undergoing Nitration.*—The rate profiles (Figure) show clearly that all the reactions studied proceed on minority species, *i.e.* on the free pyrazole bases. Thus the high acidity slopes (Table 4) are all greater than 1.0: we have shown<sup>20</sup> that for majority species slopes are expected to be in the range 0.2–0.6. In the low acidity range also, the  $d[\log k_2(\text{obs})]/d[-(H_R + \log a_{H_2O})]$  slopes<sup>21</sup> are low and approach unity only when  $\log k_2(\text{fb})$  is used in the

toluene at the *ortho*-position ( $\log k_0 + 1.9$ )<sup>19</sup> but detailed consideration is hindered by the fact that it is comparable



Rate profiles for nitration of (A) 1,4-dimethylpyrazole; (B) 1,4-dimethyl-3-nitropyrazole; (C) 4-methyl-1-(*p*-nitrophenyl)pyrazole, all at 80 °C in aqueous sulphuric acid

with the encounter rate. (Precise calculation of the encounter rate at elevated temperature is difficult.<sup>22</sup>) Clearly, the activation by the pyrrole-like nitrogen atom

<sup>19</sup> A. R. Katritzky, B. Terem, E. V. Scriven, S. Clementi, and H. O. Tarhan, *J.C.S. Perkin II*, 1975, 1600.

<sup>20</sup> A. G. Burton, Ph.D. Thesis, University of East Anglia, 1971.

<sup>21</sup> J. G. Hoggett, R. B. Moodie, J. R. Penton, and K. Schofield, 'Nitration and Aromatic Reactivity,' Cambridge University Press, 1971, p. 147.

<sup>22</sup> See B. Terem, Ph.D. Thesis, University of East Anglia, 1975, for full discussion.

is greater than the deactivation by the pyridine-like nitrogen, but comparison of the effect with that for hydrogen exchange cannot be made. The  $k_0$  value for hydrogen exchange at the 3-position of 1,4-dimethylpyrazole<sup>23</sup> is  $-4.2$ , much less negative than that for toluene at the *ortho*-position<sup>24</sup> ( $-8.3$ ).

The 1-*p*-nitrophenyl group deactivates the ring considerably towards nitration at the 3-position:  $\log k_0$  is  $-0.31$  indicating a reactivity less than that of benzene. We have previously reported that 4-nitration of 1-*p*-nitrophenylpyrazole proceeds on the free base<sup>25</sup> with  $\log k_0 -1.57$  (recalculated in ref. 19). Comparison of these figures, and taking into account the activating influence of the 4-methyl group in the former, it is seen that the difference in the susceptibility of the 3- and

4-positions in the *free-base form* of pyrazole towards nitration is a relatively small factor in favour of the 4-position (*ca.* 1 log unit). Doubtless, for the more usual substitution *via* the conjugate acid, the difference is considerably greater.

Comparison of the  $\log k_0$  values for the first and second nitrations of 1,4-dimethylpyrazole indicates that the *meta*-nitro-group deactivates by 8.2 log units: this is nearly as much as the deactivation in benzene of 8.7 log units.<sup>19</sup>

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