Studies in Azole Chemistry. Part 2.[1] Nitration of 1,4,5-Trimethylimidazole 3-Oxide and 1-Methylpyrazole 2-Oxide, and Some Reactions of the Products

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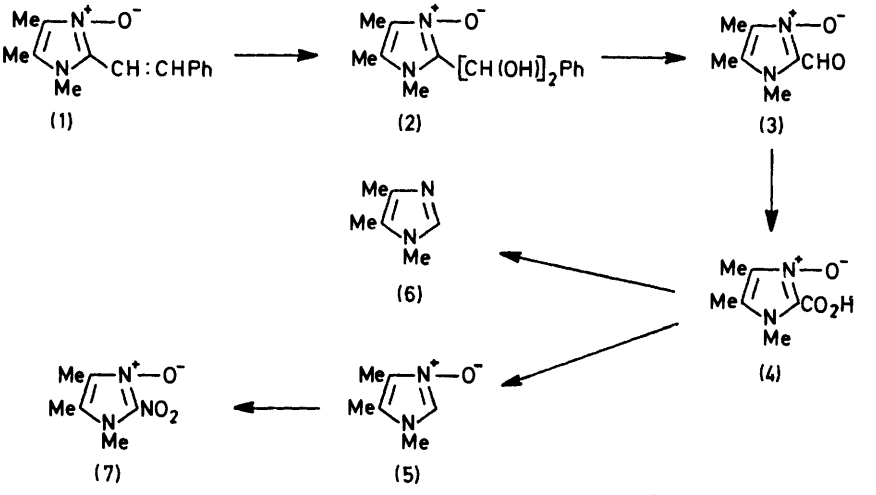
In sulphuric acid, 1,4,5-trimethylimidazole 3-oxide and 1-methylpyrazole 2-oxide are nitrated as the free bases at C-2 and C-5, respectively. At high acidities the pyrazole gives 1-methyl-3,5-dinitropyrazole 1-oxide. With phosphorus trichloride the pyrazole oxides were deoxygenated, and with phosphoryl chloride, 1-methylpyrazole 2-oxide gave 5-chloro-1-methylpyrazole. 1-Methyl-5-nitropyrazole 2-oxide with acetyl chloride gave 5-chloro-1-methyl-4-nitropyrazole.

We describe here a study of the nitration of some azole *N*-oxides, and also some of their general reactions. We previously reported [1] the synthesis of imidazole 3-oxides unsubstituted at C-2 and C-4, and some of the nucleophilic reactions which they underwent. However, for the purpose of studying electrophilic substitution, in particular nitration, these *N*-oxides were not particularly suitable as they contained more than one aromatic nucleus. Consequently we designed a route (Scheme) to 1,4,5-trimethylimidazole 3-oxide, in which electrophilic substitution, if it occurred, would be unambiguous. Nitration of an imidazole 3-oxide unsubstituted at C-2 was of particular interest, for the oxide function might be expected to activate C-2 towards electrophilic substitution (*cf.* activation of C-4 in pyridine 1-oxide [2]). This would lead directly to the pharmaceutically interesting 2-nitroimidazoles,[3] which previously have had to be prepared indirectly, usually *via* the corresponding 2-aminoimidazoles.[4] Nitration at C-2 would be in contrast to the orientation observed with simple imidazoles, which afford 4(5)-nitroimidazoles *via* the conjugate acid.[5]

The precursor, 1,4,5-trimethyl-2-styrylimidazole 3-oxide (1), was obtained from *N*-cinnamylidenemethylamine and biacetyl mono-oxime in acetic acid. Of the possible reactions which presented themselves for the next step, the most successful was the oxidation of the styrylimidazole to 2-(1,2-dihydroxy-2-phenylethyl)-1,4,5-trimethylimidazole 3-oxide (2), with osmium tetraoxide in pyridine. The diol was easily cleaved with lead tetra-acetate in acetic acid to give 1,4,5-trimethylimidazole-2-carbaldehyde 3-oxide (3). Oxidation of the aldehyde (3) with silver oxide gave 1,4,5-trimethylimidazole-2-carboxylic acid 3-oxide (4), which was difficult to isolate owing to its marked solubility in water.



SCHEME

The carboxylic acid (4) was readily decarboxylated by heating, to give 1,4,5-trimethylimidazole 3-oxide (5). If heating *in vacuo* was prolonged, decarboxylation was accompanied by deoxygenation to give 1,4,5-trimethylimidazole (6).

Pyrazole *N*-oxides other than 1-hydroxypyrazole 2-

[1] Part 1, I. J. Ferguson and K. Schofield, *J.C.S. Perkin I*, 1975, 275.
[2] E. Ochiai, *Proc. Japan Acad.*, 1942, **18**, 561; H. J. den Hertog and J. Overhoff, *Rec. Trav. chim.*, 1950, **69**, 468.
[3] *E.g.* G. Lancini and E. Lazzari, *Chem. Abs.*, 1971, **75**, 140,848.
[4] A. G. Beaman, R. Duschinsky, and W. P. Tautz, U.S.P., 1966, 3,355,201 (*Chem. Abs.*, 1966, **65**, 13724).
[5] M. W. Austin, J. R. Blackborow, J. H. Ridd, and B. V. Smith, *J. Chem. Soc.*, 1965, 1051.

oxides are rare compounds.[6] 1-Methylpyrazole 2-oxide can be prepared by oxidising 1-methylpyrazole,[7] and 1-methyl-5-nitropyrazole 2-oxide by oxidising 5-amino-1-methylpyrazole.[8]

The mononitrations of 1-methylpyrazole 2-oxide and 1,4,5-trimethylimidazole 3-oxide in sulphuric acid were studied kinetically (see Table). Over the acidity ranges studied the values of $d(\log k_2)/d(-H_R + \log a_{H_2O})$ at 25.0 °C for the two compounds were 0.53 and 0.59, respectively, clearly showing that each reacts as the free base.[9,10] Ionisation constants for the two compounds are unknown, but likely values indicate the bases to be more reactive than benzene, and to be nitrated at the encounter rate.[9]

With 1-methylpyrazole 2-oxide, nitration at acidities higher than those tabulated gave unsatisfactory kinetics, perhaps because of dinitration. Nitration of the oxide in 88% sulphuric acid for a short time gave 1-methyl-3,5-dinitropyrazole 2-oxide as well as 1-methyl-5-nitropyrazole 2-oxide. The dinitro-compound could also be obtained by nitrating 1-methyl-5-nitropyrazole 2-oxide. Under some nitrating conditions deoxygenation led to the production of 1-methyl-3,5-dinitropyrazole rather than its *N*-oxide.

The orientation of the dinitro-compounds was proved by mass spectrometry, and from the known properties of the non-oxygenated base.[11]

For mass spectrometric comparisons we prepared 1-methyl-3- and 1-methyl-5-nitropyrazole, by methylating 3(5)-nitropyrazole.[12] The nitro-compounds were readily reduced to the amines, which this route makes readily available.

Having available three pyrazole *N*-oxides, we examined their behaviour in typical oxide reactions. 1-Methyl-3-nitro- and 1-methyl-3,5-dinitro-pyrazole 2-oxide were deoxygenated by phosphorus trichloride. With phosphoryl chloride, 1-methylpyrazole 2-oxide gave 5-chloro-1-methylpyrazole. The mononitro-oxide did not react with acetic anhydride or dimethyl acetylenedicarboxylate. Surprisingly, the chief product obtained by treating 1-methyl-5-nitropyrazole 2-oxide with acetyl chloride was 5-chloro-1-methyl-4-nitropyrazole; two other products may have been 5-chloro-1-methylpyrazol-3-one and 5-chloro-1-methyl-4-nitropyrazole 2-oxide.

The mass spectra of several of the *N*-oxides were examined.[13] In every case the characteristic fragments $M - 16$ (−O) and $M - 17$ (−OH) were observed. The aldehyde oxide (3) lost CO, as does 1-methylimidazole-2-carbaldehyde.[14] The nitro-oxide (7) gave the expected fragments by loss of O, OH, NO, and NO_2 but also lost HCO. The mass spectra of a number of pyrazoles were also recorded.[13] A useful observation was that 1-methyl-5-nitropyrazoles lose HCO, perhaps by intramolecular reaction between the 1-methyl and the 5-nitro-group.

EXPERIMENTAL

Elemental analyses were performed by Ilse Beetz. I.r. spectra were obtained with a Hilger H90 Infrascan spectrophotometer, low resolution mass spectra with a Perkin-Elmer Hitachi RMU 60 spectrometer, high resolution mass spectra from the P.C.M.U., Harwell, and ^1H n.m.r. spectra (60 and 100 MHz) with a Perkin-Elmer R60 and a JEOL JMH/100 spectrometer, respectively. Analytical g.l.c. was performed with a Pye Unicam 104 Chromatograph (15% SE30 on Chromosorb W). Preparative g.l.c. was performed with an Aerograph Autoprep 700 instrument (30% SE30 on Chromosorb W). T.l.c. was carried out with Kieselgel GF_{254} (Merck).

Kinetics.—Rates of nitration were determined by following the increase in absorption of the reaction solution at 336 nm (Pye Unicam SP 1800 spectrophotometer). The general conventional procedure has been described.[15] Results are given in the Table.

Nitration of 1-methylpyrazole 2-oxide (A) and 1,4,5-trimethylimidazole 3-oxide (B) in sulphuric acid (25.0 ± 0.1 °C) *

(A)		(B)	
H_2SO_4(%)	10^3k_2/ dm^3 mol^{-1} s^{-1}	H_2SO_4(%)	$10^3k_2'$ dm^3 mol^{-1} s^{-1}
65.80	3.92	73.26	4.51
68.44	11.9	74.13	6.05
70.10	28.0	76.94	22.3
73.26	158	79.17	67.2
75.48	461	81.73	222

* [Oxide] *ca.* 10^{-4} mol dm^{-3}; [HNO_3] *ca.* 10^{-1}—10^{-2} mol dm^{-3}. Rate constants relate to the equation, rate = k_2[ArH] [HNO_3].

1,4,5-*Trimethyl-2-styrylimidazole* 3-*Oxide.*—*N*-Cinnamylidenemethylamine (72.5 g) was added carefully to a stirred solution of biacetyl mono-oxime (50.0 g) in glacial acetic acid (50 cm^3) cooled in ice. After 6 h at room temperature the solution had set to a solid mass. The solid was washed with ether and then with a little cold acetone. Crystallisation from acetone gave pale yellow prisms of 1,4,5-trimethyl-2-styrylimidazole 3-oxide (58.0 g), m.p. 192 °C, τ ($CDCl_3$; 60 MHz) 7.84 (3 H, s, CH_3), 7.81 (3 H, s, CH_3), 6.44 (3 H, s, NCH_3), 3.16 (1 H, d, =CH), 2.52 (5 H, m, Ph), and 1.30 (1 H, d, =CH), *m/e* 228 (M^+). The *hydrochloride*, m.p. 252 °C (Found: C, 63.8; H, 6.6; N, 10.7. $C_{14}H_{17}ClN_2O$ requires C, 63.5; H, 6.5; N, 10.6%), was obtained as a white powder from methanol.

2-(1,2-*Dihydroxy-2-phenylethyl*)-1,4,5-*trimethylimidazole* 3-*Oxide.*—1,4,5-Trimethyl-2-styrylimidazole 3-oxide (0.9 g), osmium tetraoxide (1 g), and pyridine (15 cm^3) were stirred

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[7] E. W. Parnell, *Tetrahedron Letters*, 1970, 3941.
[8] M. D. Coburn, *J. Heterocyclic Chem.*, 1970, **7**, 455.
[9] J. G. Hoggett, R. B. Moodie, J. R. Penton, and K. Schofield, 'Nitration and Aromatic Reactivity,' Cambridge University Press, 1971.
[10] See I. J. Ferguson, M. R. Grimmett, and K. Schofield, *Tetrahedron Letters*, 1972, 2771, for a preliminary report.
[11] M. D. Coburn, *J. Heterocyclic Chemistry*, 1971, **8**, 153.
[12] J. W. A. M. Janssen and C. L. Habraken, *J. Org. Chem.*, 1971, **36**, 3081.
[13] For full details see I. J. Ferguson, Ph.D. Thesis, University of Exeter, 1973.
[14] J. H. Bowie, R. G. Cooks, S. O. Lawesson, and G. Schroll, *Austral. J. Chem.*, 1967, **20**, 1613.
[15] R. G. Coombes, R. B. Moodie, and K. Schofield, *J. Chem. Soc.* (*B*), 1968, 800.

together for 2 h. A solution of sodium hydrogen sulphite (1.8 g) in water (30 cm³) and pyridine (20 cm³) was added and the resulting solution extracted with dichloromethane. Removal of dichloromethane and pyridine and crystallisation of the residue from methanol gave prisms of the *diol* (0.51 g), m.p. 236 °C (Found: C, 64.1; H, 6.6; N, 10.5. $C_{14}H_{18}N_2O_3$ requires C, 64.1; H, 6.9; N, 10.7%), τ (CD_3OD; 100 MHz) 8.12 (3 H, s, CH_3), 7.92 (3 H, s, CH_3), 6.76 (3 H, s, NCH_3), 4.86 (2 H, 2d, HC:CH), and 2.64 (5 H, m, Ph), *m/e* 262 (M^+).

1,4,5-*Trimethylimidazole*-2-*carbaldehyde* 3-*Oxide*.—Lead tetra-acetate (2.25 g) was added in small portions to a solution of the foregoing diol (1.3 g), in glacial acetic acid (10 cm³). The mixture was stirred for 2 h and then filtered, and the acetic acid was removed. The residue was extracted with dichloromethane and the extract washed with aqueous sodium carbonate. The aqueous phase was further extracted with dichloromethane. The dichloromethane extracts were combined and the solvent removed. After being washed with a little ether, the solid residue was collected and crystallised from benzene or chloroform–di-isopropyl ether to give needles of the *aldehyde* (0.32 g), m.p. 186 °C (Found: C, 54.8; H, 6.6. $C_7H_{10}N_2O$ requires C, 54.5; H, 6.5%), τ ($CDCl_3$; 100 MHz) 7.80 (3 H, s, CH_3), 7.77 (3 H, s, CH_3), 6.14 (3 H, s, NCH_3), and −0.10 (1 H, s, O:CH).

1,4,5-*Trimethylimidazole*-2-*carboxylic Acid* 3-*Oxide*.—The foregoing aldehyde (0.616 g) was added to a stirred suspension of silver oxide [from silver nitrate (1.36 g), sodium hydroxide (0.8 g), and water (5 cm³)]. The mixture was stirred for a further 5 min and the precipitate of silver then filtered off and washed with hot water. The filtrate and washings were combined and acidified to pH 3 with concentrated hydrochloric acid. Extraction with dichloromethane, removal of solvent, and washing with a little ether afforded the *acid* (0.508 g), m.p. 158 °C (Found: C, 50.7; H, 5.9; N, 16.3. $C_7H_{10}N_2O_3$ requires C, 49.4; H, 5.9; N, 16.5%); $\nu_{max.}$ 1 660 cm⁻¹ (C=O), τ ($CDCl_3$; 100 MHz) 7.72 (6 H, s, $2CH_3$) and 6.02 (3 H, s, NCH_3). Attempts to crystallise the acid from various solvents afforded an oil (by decarboxylation?).

1,4,5-*Trimethylimidazole* 3-*Oxide*.—The foregoing acid (0.11 g) was heated and stirred at 140—150 °C for 3 min. Crystallised from ether, 1,4,5-*trimethylimidazole* 3-*oxide* (0.08 g), m.p. 68 °C (Found: C, 57.3; H, 9.2; N, 21.9. $C_6H_{10}N_2O$ requires C, 57.1; H, 8.0; N, 22.2%), was obtained as a hygroscopic solid, τ ($CDCl_3$; 60 MHz) 7.86 (6 H, s, $2CH_3$), 6.15 (3 H, s, NCH_3), and 2.03 (1 H, s, CH).

1,4,5-*Trimethylimidazole*.—Sublimation of 1,4,5-trimethylimidazole-2-carboxylic acid 3-oxide at 140 °C and 0.1 mmHg afforded a liquid, τ ($CDCl_3$; 60 MHz) 7.92 (6 H, s, $2CH_3$), 6.56 (3 H, s, NCH_3), and 2.76 (1 H, s, CH). The picrate was obtained from methanol as a yellow powder, m.p. 214—216 °C (lit.,[16] 218 °C).

1,4,5-*Trimethyl*-2-*nitroimidazole* 3-*Oxide*.—A solution of 1,4,5-trimethylimidazole 3-oxide (0.126 g) in 74% sulphuric acid (10 cm³) was cooled in ice and treated with a solution of nitric acid (0.9 cm³; *d* 1.5) in 74% sulphuric acid (5 cm³). After 12 h the solution was poured onto ice and the resulting aqueous solution continuously extracted with dichloromethane for 24 h. After removal of the solvent preparative t.l.c. (1 : 9 methanol–chloroform) gave the product (0.058 g). Crystallisation from dichloromethane–ether gave as a yellow powder the *nitroimidazole*, m.p. 132 °C (Found: C, 42.2; H, 5.6; N, 24.5%; M^+, 171.0643. $C_6H_9N_3O_3$ requires C, 42.1; H, 5.3; N, 24.6%; *M*, 171.0644), τ ($CDCl_3$; 60 MHz) 7.79 (3 H, s, CH_3), 7.69 (3 H, s, CH_3), and 6.09 (3 H, s, NCH_3).

1-*Methyl*-5-*nitropyrazole* 2-*Oxide*.—A solution of 1-methylpyrazole 2-oxide (0.59 g) in 65.8% sulphuric acid was cooled in an ice-bath and treated dropwise with a solution of nitric acid (1 cm³; *d* 1.5) in 65.8% sulphuric acid (5 cm³). After 12 h at room temperature the solution was poured onto ice. Continuous extraction with dichloromethane for 16 h gave, on removal of solvent, the nitropyrazole (0.78 g). Crystallisation from heptane gave a yellow powder, m.p. 109 °C (lit.,[8] 109 °C) (Found: C, 33.5; H, 3.5; N, 29.4. Calc. for $C_4H_5N_3O_3$: C, 33.6; H, 3.5; N, 29.4%), τ ($CDCl_3$; 100 MHz) 5.87 (3 H, s, NCH_3) and 2.77 (2 H, 2 d, *J* 3.04 Hz, H-3 and -4), *m/e* 143 (M^+), homogeneous on t.l.c. (1 : 4 toluene–chloroform).

1-*Methyl*-3,5-*dinitropyrazole* 2-*Oxide*.—(*a*) A solution of 1-methylpyrazole 2-oxide (0.25 g) in 87% sulphuric acid (1.5 cm³) was cooled to 0 °C, and treated dropwise with a solution of nitric acid (0.5 cm³; *d* 1.5) in 87% sulphuric acid (2.5 cm³). After 75 min at room temperature the solution was poured onto ice, and a yellow solid separated (0.295 g). Crystallised from methanol, the *dinitropyrazole* was obtained as a yellow powder, m.p. 186—188 °C (Found: C, 25.6; H, 2.2. $C_4H_4N_4O_5$ requires C, 25.5; H, 2.1%), τ [$(CD_3)_2SO$; 100 MHz] 5.97 (3 H, s, NCH_3) and 1.66 (1 H, s, CH), *m/e* 188 (M^+).

(*b*) 1-Methyl-5-nitropyrazole 2-oxide (0.4 g) was added in portions to a solution of nitric acid (1 cm³; *d* 1.5) in 88% sulphuric acid (6 cm³) cooled in ice. After 12 min the solution was poured onto ice and extracted with dichloromethane. Preparative t.l.c. (1 : 4 toluene–chloroform) afforded the dinitropyrazole (0.125 g). ^1H N.m.r. spectra and m.p. were identical with data given above. 1-Methyl-5-nitropyrazole (0.014 g) was also obtained (identified by ^1H n.m.r. spectra and t.l.c.).

Varying Conditions for the Nitration of 1-*Methyl- and* 1-*Methyl*-5-*nitro-pyrazole* 2-*Oxide*.—(*a*) 1-Methylpyrazole 2-oxide (0.6 g) in 88% sulphuric acid (2 cm³) was treated at 0 °C with a solution of nitric acid (1 cm³; *d* 1.5) in 88% sulphuric acid (1 cm³). After 15 s the solution was poured onto ice and extracted with dichloromethane. Removal of the solvent gave a yellow solid. T.l.c. (1 : 4 toluene–chloroform) and ^1H n.m.r. spectroscopy showed the solid to be principally a mixture of 1-methyl-3,5-dinitropyrazole 2-oxide and 1-methyl-5-nitropyrazole 2-oxide. Chromatography on neutral alumina (1 : 3 toluene–chloroform) afforded 1-methyl-3,5-dinitropyrazole 2-oxide (0.049 g), m.p. 185 °C (from methanol), and 1-methyl-5-nitropyrazole 2-oxide (0.125 g), m.p. 108.5 °C (from heptane).

(*b*) 1-Methyl-5-nitropyrazole 2-oxide (0.5 g) was added to an ice-cooled, stirred solution of urea (0.5 g) and nitric acid (1 cm³; *d* 1.5) in 88% sulphuric acid (11 cm³). After 1 h the solution was poured onto ice and extracted with dichloromethane. Preparative t.l.c. (1 : 4 toluene–chloroform) afforded 1-methyl-3,5-dinitropyrazole 2-oxide (0.06 g), m.p. 185 °C, and 1-methyl-3,5-dinitropyrazole (0.062 g), m.p. 62 °C.

1-*Methyl*-3,5-*dinitropyrazole*.— 1-Methyl-3,5-dinitropyrazole 2-oxide (0.5 g) and freshly distilled phosphorus trichloride (10 cm³) were boiled together for 62 h. The solution was then poured onto ice, basified with aqueous sodium carbonate, and continuously extracted with di-

[16] F. L. Pyman, *J. Chem. Soc.*, 1927, 3128.

chloromethane for 12 h. Removal of solvent afforded a pale yellow solid which, when crystallised from heptane, gave yellow needles of 1-methyl-3,5-dinitropyrazole (0.175 g), m.p. 66 °C (lit.,[15] 62 °C) (Found: C 27.7; H, 2.3; N, 32.4 $C_4H_4N_4O_4$ requires C, 27.9; H, 2.3; N, 32.6%), τ [$(CD_3)_2SO$; 100 MHz] 5.72 (3 H, s, NCH_3) and 1.91 (1 H, s, CH), *m/e* 172 (M^+).

1-Methyl-5-nitropyrazole.—1-Methyl-5-nitropyrazole 2-oxide (2.0 g) and freshly distilled phosphorus trichloride (25 cm³) were boiled together for 72 h. The solution was poured onto ice, basified with aqueous sodium carbonate, and extracted with chloroform. Removal of solvent afforded a liquid which was distilled to give 1-methyl-5-nitropyrazole (0.8 g), b.p. 186 °C, τ ($CDCl_3$; 100 MHz) 5.71 (3 H, s, NCH_3), 2.90 (1 H, d, *J* 2.34 Hz, CH), and 2.44 (1 H, d, *J* 2.34 Hz, CH), *m/e* 127 (M^+). T.l.c. (1 : 9 light petroleum–chloroform) showed the distillate to be homogeneous. G.l.c. t_R 110 s at 172 °C.

Reaction of 1-Methylpyrazole 2-Oxide with Phosphoryl Chloride.—1-Methylpyrazole 2-oxide (0.78 g) was added carefully to freshly distilled phosphoryl chloride (4 cm³) at 0 °C. The solution was warmed on a steam-bath for 30 min then poured with stirring onto crushed ice and made basic with concentrated ammonia. Extraction with chloroform afforded a liquid which by preparative g.l.c. gave 5-chloro-1-methylpyrazole (0.582 g), b.p. 134 °C (Found: C, 40.1; H, 3.6. $C_4H_5ClN_2$ requires C, 41.2; H, 4.3%) (better figures could not be obtained), τ ($CDCl_3$; 100 MHz) 6.18 (3 H, s, NCH_3), 3.86 (1 H, d, CH), and 2.66 (1 H, d, CH), *m/e* 116/118 (M^+). Qualitative g.l.c. (84 °C) of the product gave 5-chloro-1-methylpyrazole, t_R 346 s, and also showed a small peak (< 1%), t_R 215 s, tentatively regarded as being due to 3-chloro-1-methylpyrazole.

5-Chloro-1-methyl-4-nitropyrazole.—A solution of 5-chloro-1-methylpyrazole (0.66 g) in 98% sulphuric acid (3 cm³) was slowly added to one of nitric acid (1 cm³; *d* 1.5) in 98% sulphuric acid (3 cm³). After being heated on a steam-bath for 3 h the solution was poured onto ice, basified with aqueous sodium carbonate, and extracted with dichloromethane. The residue left after removal of solvent was extracted with hot heptane to give cubes of 5-chloro-1-methyl-4-nitropyrazole (0.543 g). Sublimation at 75 °C and 0.1 mmHg gave white crystals, m.p. 59 °C (Found: C, 30.0; H, 2.8. $C_4H_4ClN_3O_2$ requires C, 29.8; H, 2.5%), τ ($CDCl_3$; 100 MHz) 7.08 (3 H, s, NCH_3) and 1.92 (1 H, s, CH), *m/e* 161/163 (M^+).

Reaction of 1-Methyl-5-nitropyrazole 2-Oxide with Acetyl Chloride.—1-Methyl-5-nitropyrazole 2-oxide (1.0 g) was added cautiously to freshly distilled acetyl chloride (5 cm³) and the mixture was heated on a steam-bath for 30 min. Nitrogen dioxide was given off. The solution was cooled, poured into water, and made basic with aqueous sodium carbonate. Extraction with dichloromethane afforded, on evaporation, an amber oil (0.803 g). Column chromatography on neutral alumina (1 : 1 light petroleum–chloroform; 1 : 4 light petroleum–chloroform; 1 : 19 methanol–chloroform; 1 : 1 methanol–chloroform) gave three principal compounds: (*a*) 5-chloro-1-methyl-4-nitropyrazole, a white solid (0.125 g), m.p. 59—60 °C (from heptane) (Found: M^+, 160.9993. Calc. for $C_4H_3ClN_3O_2$: *M*, 160.9991), τ ($CDCl_3$; 100 MHz) 6.08 (3 H, s, NCH_3) and 1.92 (1 H, s, CH); (*b*) an off-white solid (0.088 g) which after crystallisation from heptane had m.p. 106—107 °C (Found: C, 36.2; H, 4.0. Calc. for $C_4H_5ClNO_2$: C, 36.4; H, 3.8%), τ ($CDCl_3$; 100 MHz) 6.34 (3 H, s, NCH_3) and 2.90 (1 H, s, CH), *m/e* 132/134 (M^+), $\nu_{max.}$ 1 620 cm⁻¹ (C=O); and (*c*) a dark red oil (0.315 g) which afforded a red solid (0.055 g), m.p. 250—254 °C (from methanol), *m/e* 172/174 (M^+), considered to be impure 5-chloro-1-methyl-4-nitropyrazole 2-oxide.

1-Methyl-3- and 1-Methyl-5-nitropyrazole.—3(5)-Nitropyrazole[12] (3.39 g) was dissolved in absolute ethanol (5 cm³) and water (1 cm³) containing potassium hydroxide (1.68 g, 0.003 mol). Methyl iodide (4.26 g) in ether (10 cm³) was then added dropwise to the stirred solution cooled in ice. After the solution had been boiled for 1 h the precipitate of potassium iodide was filtered off, water (10 cm³) was added, and the solution was extracted with dichloromethane. Removal of solvent afforded a pale yellow solid; t.l.c. (1 : 4 light petroleum–chloroform) showed one major and one minor product. Washing the product with a small amount of ether–petroleum left the major component undissolved; crystallised from water it gave white needles of *1-methyl-3-nitropyrazole* (1.94 g), m.p. 81 °C (Found: C, 37.5; H, 3.9; N, 32.8. $C_4H_5N_3O_2$ requires C, 37.8; H, 4.0; N, 33.1%), τ ($CDCl_3$; 100 MHz) 5.92 (3 H, s, NCH_3), 3.08 (1 H, d, *J* 2.50 Hz, CH), and 2.42 (1 H, d, *J* 2.50 Hz, CH), *m/e* 127 (M^+). *1-Methyl-5-nitropyrazole*, b.p. 186 °C, was obtained from the ether–petroleum washings after evaporation and distillation. G.l.c. showed the original product mixture to contain 25.9% of 1-methyl-5-nitropyrazole and 74.1% of 1-methyl-3-nitropyrazole.

5-Amino-1-methylpyrazole.— 1-Methyl-5-nitropyrazole (0.087 g), methanol (30 cm³), and 10% palladised charcoal (0.05 g) were stirred together under hydrogen until uptake ceased. Filtration through a small amount of Kieselguhr, removal of the solvent, and sublimation of the residue (75 °C and 0.1 mmHg) gave 5-amino-1-methylpyrazole (0.27 g), m.p. 72 °C (lit.,[17] 71—72 °C), identical (^1H n.m.r. and i.r. spectra) with an authentic sample.

3-Amino-1-methylpyrazole.—Similar reduction of 1-methyl-3-nitropyrazole (0.521 g) gave 3-amino-1-methylpyrazole (0.35 g), b.p. 64 °C at 0.1 mmHg, as a clear liquid, τ ($CDCl_3$; 100 MHz) 6.44br (2 H, s, NH_2), 6.32 (3 H, s, CH_3), 4.52 (1 H, d, *J* 2.32 Hz, CH), and 3.00 (1 H, d, *J* 2.32 Hz, CH), *m/e* 95 (M^+).

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