N-Oxides and Related Compounds. Part XLVI.[1] Chemical and Physical Properties of Pyridine 1-Nitroimides and Comparison with Quantum Chemical Predictions

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Molecular orbital treatment of pyridine 1-nitroimide predicts well the site of protonation, u.v. spectrum, and reactivity. The ring resists electrophilic attack but α-protons are readily replaced by deuterium in the presence of base. The mass spectral fragmentation is elucidated.

FOLLOWING the preparation of diverse *N*-nitroimides,[2-4] we reported briefly on their crystal structure and a comparison of their reactivity with theoretical predictions.[1] We now give further details of this and related work. The CNDO/2 and CNDO/S study (original parameterisation[5]) used bond lengths and angles from the *X*-ray structure of 3-bromopyridine 1-nitroimide,[6] and gave $\theta = 43°$ for the pyridine ring to $N-N-NO_2$ plane angle (experimental *ca.* 70°).[1] The oxygen atoms are strongly and the central nitrogen less strongly negatively charged; the terminal nitrogens are negatively charged. Ring carbon atoms are charged positively at 2, 4, and 6 and negatively at 3 and 5, the opposite to pyridine 1-oxide.[1] The adjacent hydrogen atom on the same side of the ring as the NO_2 group carries a considerable positive charge and is expected to show marked acid character. The weak polarisation of the ring carbon atoms relative to the $N-N-NO_2$ group is expected to favour ionic reactions at the $N-NO_2$ group.

U.v. Spectrum.—Pyridine 1-nitroimide absorbs in three regions (Table 1) in agreement with the CNDO2/S calculated spectrum of two rather weak transitions at 300—340 nm essentially due to NO_2 and two stronger transitions at 260—280 nm. Change of solvent from H_2O to MeCN significantly affects the experimental spectrum (Table 1). Solvation energy terms (Table 1), calculated from the electrostatic energy of transfer from vapour to a homogeneous medium of dielectric constant equal to the solvent,[7] are larger for the ground state than for the excited states, indicating that a hypsochromic shift should be found, in agreement with experiment.

Protonation of N-*Nitroimides.*—pK_a Values for proton addition to various *N*-nitroimides (Table 2) show the compounds to be weak bases. We gave previously[1] reasons for the expected predominance of *O*-protonated [*cf.* (2)] rather than *N*-protonated [*cf.* (1)] cations. The cation shows a weak band at 359 nm (ε 1) in agreement with the spectrum calculated from the *O*-protonated form (Table 1).

TABLE 1

Calculated and experimental u.v. spectral maxima (nm) and ε values for pyridine 1-nitroimides

	Neutral form						Cation					
	Calculated		Found CH_3CN		Found H_2O		Calculated *N*-protonation		Calculated *O*-protonation		Found (in 80% H_2SO_4)	
λ	*A*[a]	*b*	λ	ε	λ	ε	λ	*A*	λ	*A*	λ	ε
339	0.012	0.056 56	320	3 200	300	1 800	306	0.036	388	0.003	359	1
296	0.010	0.057 95										
277	0.045	0.054 79	265	*c*	260	4 400	276	0.053	289	0.006		
261	0.025	0.026 771					250	0.048	256	0.146	256	5 950
230	0.203	0.065 41	232	12 900	224	7 000	230	0.017	221	0.082	213	3 850
216	0.062	0.036 001					214	0.010	206	0.008		

[a] Oscillator strength. [b] Energy of ground state less energy of excited state with energy of solvation (atomic units). [c] Shoulder.

Other Reactions with Electrophiles.—Pyridine 1-nitroimide and phosphorus trichloride gave pyridine in good yield, a behaviour analogous to that of pyridine *N*-oxide[8] and a heteroaromatic *N*-imide.[9] Whereas pyridine *N*-oxides and *N*-imides yield pyridones[10] and *N*-acylated products[11] with acetic anhydride, the *N*-nitroimide again gives pyridine (50%). Pyridine 1-nitroimide could not be alkylated (MeI or CF_3SO_3Me),

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nitrated ($AcONO_2$, $PhCO_2NO_2$,[12] NO_2BF_4,[4] NaOEt–$C_5H_{11}ONO_2$ [4]), brominated,[13] or mercuriated.[14]

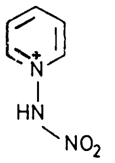
Base-catalysed Hydrogen Exchange.—Base-catalysed hydrogen–deuterium exchange, which we believe occurs by deprotonation to an ylide type intermediate, is followed by n.m.r.[15] (Table 3). The 2- and 6-positions of pyridine 1-nitroimide are rapidly exchanged at 25 °C, but not the 4-proton under conditions which do not cause ring opening. This orientation reflects the positive charge found on the α-protons by the MO calculations.[1] By comparison, exchange at the 2- and 6-positions in pyridine requires 200 °C;[16] in pyridine *N*-oxide base-catalysed 2,6-exchange occurs at 100 °C,[17] whilst the 3-, 4-, and 5-protons are exchanged at 180 °C.

TABLE 2

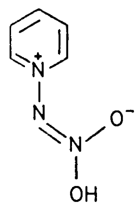
N-Nitroimide pK_a values at 25 °C

Compound	pK_a	m [a]	Analytical λ/nm
Pyridine 1-nitroimide	−4.6 [b]		
2-Methylpyridine 1-nitroimide	−3.57	1.11	245
1,2,4-Triazole 4-nitroimide	−3.29	1.10	245
Trimethylammonium *N*-nitroimide	−4.2 [c]		
1-Methyl-1,2,4-triazole 4-nitroimide	−3.20	1.06	245

[a] d(log I)/dH_0. [b] From ref. 2. [c] Determined by n.m.r. method (J. Epsztajn and A. R. Katritzky, *Tetrahedron Letters*, 1969, 4739).

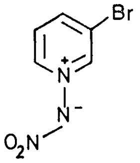


(1)



(2)

Rapid exchange occurs of the methyl protons in 2- and 4-methylpyridine 1-nitroimide and in the 2,4- and 2,6-dimethyl analogues (Table 3). Surprisingly, no ring-proton exchange was detected in these cases, although the 3-methyl derivative *did* exchange at the 2- and 6-positions. 3-Bromopyridine 1-nitroimide underwent exchange at the 6-position only, whereas 3-bromopyridine 1-oxide exchanges more readily at the 2-position.[18] By contrast, 3-methoxypyridine 1-nitroimide exchanges readily only the 2-proton, although the easy ring-opening of this compound hinders detailed study. These results, together with the MO calculations of charge on the individual ring hydrogen atoms,[1] suggest that the 3-bromo- and 3-methoxy-compounds exist in conformations (3) and (4) respectively in solution:



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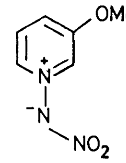

(4)

however, X-ray analysis [6] demonstrates a conformation of type (4) for the bromo-compound at least for the solid state.

Ring-opening.—Pyridine 1-nitroimide in 0.2N-NaOD–D_2O rapidly gave the ABB′ spectrum of the 2,6-dideuterio-nitroimide (6); the 4-proton shows as a quartet at δ 8.6 and the 3,5-protons as a multiplet at δ 8.18. With 2N-NaOD at 60 °C superimposed on the above low field resonances were the higher field spectra of the two partially deuteriated ring-opened products (8) and (9). The shifts and coupling constants for (8) and (9) are similar to those previously found [19] for other glutaconic aldehyde derivatives (Table 4). Ring opening of pyridine 1-nitroimide also occurs with ethoxide in ethanol at 80 °C.

TABLE 3

Base-catalysed hydrogen–deuterium exchange of pyridine *N*-nitroimides and related compounds

Substituents in pyridinium ring						[NaOD]/		Temp.	Time for exchange (h) [a]		
1	2	3	4	5	6	N	Solvent	(°C)	Methyl	H-2	H-6
N–NO_2	H	H	H	H	H	0.5	D_2O	25		0.2	0.2
N–NO_2	Me	H	H	H	H	0.2	D_2O	35	<0.2		>20
N–NO_2	H	Me	H	H	H	0.2	D_2O	25	Fast	>6	>6
N–NO_2	Me	H	Me	H	H	0.2 [b]	D_2O	25	2.5		>20
N–NO_2	Me	H	H	H	Me	0.2	D_2O	25	0.3		
N–NO_2	H	Br	H	H	H	0.2	$(CD_3)_2SO$	25		>20	Fast
N–NO_2	H	OMe	H	H	H	0.5	D_2O	25		1.5	>20
N–SO_2Ph	H	OMe	H	H	H	0.5	$(CD_3)_2SO$	25		1.5	>20
N–SO_2Ph	H	H	H	H	H [c]	0.5	D_2O	35		0.2	0.2

[a] No exchange was found in the 3-, 4-, or 5-positions (20—60 h). [b] Imide concentrations only 0.1 of usual value due to solubility problem. [c] From ref. 2.

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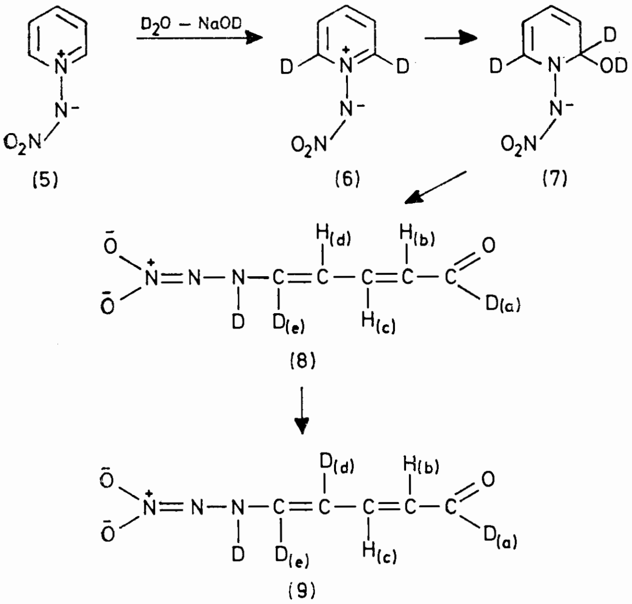
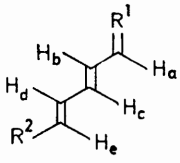
Other Reactions.—Pyridine 1-nitroimide and potassium cyanide give pyridine (40%) whereas many *N*-oxides form Reissert compounds. No reaction occurred with aniline and benzylamine. Grignard[20] and organolithium reagents afford complex mixtures, probably by attack at the nitro-group.[21] Irradiation of pyridine 1-nitroimide in methanol or dichloromethane gave pyridine (30%), but starting material (96%) was recovered after irradiation in benzene. Heteroaromatic *N*-imides can act as 1,3-dipoles;[22] pyridine 1-nitroimide and dimethyl acetylenedicarboxylate gave dimethyl pyrazolo[1,5-*a*]pyridine-2,3-dicarboxylate, a product previously obtained[22c] from pyridine *N*-imide itself. 2-Methylpyridine 1-nitroimide reacted with 2,5-dimethyl-1-phenylpyrrole-3-carboxaldehyde to yield (11).



SCHEME 1



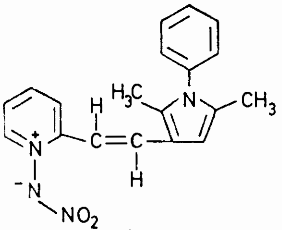
(10)

TABLE 4

N.m.r. shifts (δ) for glutaconic aldehyde derivatives (10)

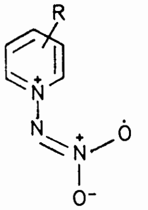
Ref.	Formula (10) R¹	Formula (10) R²	H$_b$	H$_c$	H$_d$	J_{bc}/Hz	J_{cd}/Hz	Solvent
†	O [a]	N·NDNO$_2^-$	6.2	7.5	5.8	15	12	D$_2$O–NaOD
†	O [a]	N·NDNO$_2^-$	6.2	7.5		15		D$_2$O–NaOD
19 [a]	O	OSO$_2$Ph	6.14	7.03	6.18	15.1	10.9	CDCl$_3$
19 [a]	O	NMe$_2$	5.80	7.20	5.28	14.4	11.8	CDCl$_3$
19 [a]	O	NCS	6.21	7.44	6.15	15.4	11.1	CDCl$_3$

[a] D$_a$ for H$_a$ in formula (10). † This work.

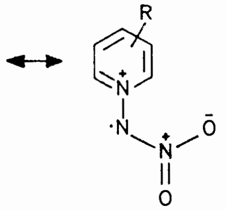


(11)

Mass Spectra of N-*Nitroimides*.—*N*-Ethoxycarbonyl-, *N*-acyl-, *N*-benzoyl-, and *N*-phenylsulphonyl-imides all show molecular ions and frequently also a strong $M - 1^+$ ion due to ring H expulsion.[23,24] By contrast *N*-nitroimides do not show any strong molecular ion [(12a) ⟶ (12b)]. The major fragmentation patterns (Table 5) are believed to involve the loss of neutral fragments (*a*) N_2O_2, to give (13) which fragments further by well established routes,[23] (*b*) NO_2, to give (14) fragmenting in the expected manner (*cf*. ref. 24), or (in some



(12a)



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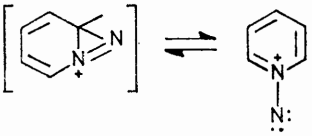

(14a) (14b)

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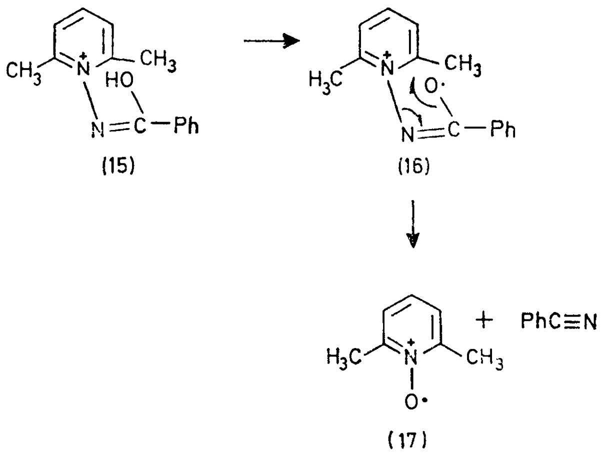
cases) (*c*) N_2O, *via* the *N*-oxide ion (17), with subsequent breakdown corresponding to that found for pyridine *N*-oxides.[23] The formation of such an ion was previously observed by Ikeda[23] from 2,6-dimethylpyridine *N*-benzoylimide and ascribed as arising *via* a concerted four-atom process [(16) ⟶ (17)] favoured by the steric effects of the 2,6-methyl groups. Quinoline and isoquinoline *N*-nitroimide fragmentation are in agreement with analogous routes implied[23] for isoquinoline *N*-benzoylimides.

TABLE 5

Relative intensities of primary fragment ions for *N*-nitroimides (as % of base peak)

N-Nitroimide					
Ring	Substituent(s)	M^+	$M^+ -$ N_2O_2	$M^+ -$ NO_2	$M^+ -$ N_2O
Pyridine		29	72	100	
Pyridine	2-Me		100	63	
Pyridine	3-Me	12	100	12	
Pyridine	3-Br	1.3	100	9	
Pyridine	3-OMe	3.2	100	24	
Pyridine	2,4-Me_2	5	73	100	
Pyridine	2,6-Me_2		100		12
Quinoline			100		60
Isoquinoline			100		85



SCHEME 2

Routes corresponding to (*a*) and (*b*) above have recently been invoked by Abramovitch[25] in the mass spectral fragmentation of pyridine *N*-phenylsulphonylimides.

EXPERIMENTAL

Spectroscopy.—The mass spectra were recorded using a Hitachi–Perkin-Elmer RMU 6-E single focusing mass spectrometer. I.r. spectra were measured using KBr discs on a Perkin-Elmer model 127 i.r. spectrophotometer. pK_a Measurements were carried out in sulphuric acid by the u.v. spectrophotometric method. U.v. spectra were recorded on Unicam SP 500 and SP 800 spectrophotometers.

Dimethyl Pyrazolo[1,5-a]*pyridine*-2,3-*dicarboxylate*.—Pyridine *N*-nitroimide (0.5 g, 0.0036 mol) was heated under reflux with dimethyl acetylenedicarboxylate (2 g) in MeCN (30 ml) for 6 days. After removal of solvent under vacuum, the residue was thick layer chromatographed (silica; $CHCl_3$ eluant). The ester was crystallised from ether–light petroleum (40—60 °C), m.p. 66—66.5 °C (lit.,[26] 69—70 °C) (42%) (Found: C, 56.1; H, 4.3; N, 12.3. Calc. for $C_{11}H_{10}N_2O_4$: C, 56.4; H, 4.3; N, 12.0%); $\nu_{max.}$ (Nujol) 1 690 and 1 730 (C=O) cm^{-1}; τ (CCl_4) 6.2 (3 H, s), 6.1 (3 H, s), 3.2—2.5 (2 H, m), 2.6 (1 H, d, *J* 7.5 Hz), and 1.5 (1 H, d, *J* 6 Hz).

2-[2-(2,5-*Dimethyl*-1-*phenylpyrrol*-3-*yl*)*vinyl*]*pyridine* 1-*Nitroimide* (11).—2-Methylpyridine 1-nitroimide (0.156 g, 0.001 mol), 2,5-dimethyl-1-phenylpyrrole-3-carbaldehyde (0.199 g, 0.001 mol), ethanol (30 ml), and piperidine (0.1 g), were kept at 20 °C for 12 h and then at 40 °C for 6 h. The precipitate crystallised from *N*-methyl-2-pyrrolidone as yellow plates of the condensation *product* (90%), m.p. 187 °C (Found: C, 67.4; H, 5.6; N, 16.7. $C_{19}H_{18}N_4O_2$ requires C, 68.0; H, 5.7; N, 16.7%).

Reaction of Pyridine 1-*Nitroimide with Acetic Anhydride*.—Pyridine 1-nitroimide (0.5 g, 0.0036 mol) and Ac_2O (30 ml) were heated under reflux for 30 min, neutralised, and extracted with ether to give pyridine, characterised as the picrate (0.55 g, 50%), m.p. 165 °C (lit.,[27] 167—168 °C).

Reaction between Pyridine 1-*Nitroimide with Phosphorus Trichloride*.—Pyridine 1-nitroimide (1.0 g, 0.0072 mol) and phosphorus trichloride (2.5 ml) were heated at 100 °C for 30 min, diluted with water, and the mixture made alkaline. Extraction with $CHCl_3$ followed by evaporation of the dried extract gave an oil (0.4 g, 80%). I.r., n.m.r., and examination of the picrate derivative indicated it to be pyridine.

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[5/304 *Received*, 13*th February*, 1975]

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