Ring Opening or Rearrangement *versus* *N*-Oxidation in the Action of Peracids upon Pyrrolo[2,3-*b*]pyridines, Pyrrolo[2,3-*b*]pyrazines, and Triazolo[1,5-*a*]- and Triazolo[4,3-*a*]-pyrazine. Some Chemical and Spectroscopic Properties of the Triazolopyrazines and Their *N*-Oxides

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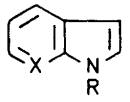
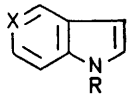
Peracid oxidation of the title heterocycles has shown a variety of reaction pathways. 1-Methyl-2,3-diphenyl-1*H*-pyrrolo[2,3-*b*]pyridine (8) gave a ring-opened product (13), while 3-methyl-2-phenyl-1*H*-pyrrolo[2,3-*b*]-pyrazine gave *N*-benzoylurea. In contrast, triazolo[1,5-*a*]pyrazine (36) undergoes smooth *N*-oxidation to the 7-oxide (37), triazolo[4,3-*a*]pyrazine (41) gives the *N*-oxide (42) less efficiently, and the pyrrolopyrazine (26) undergoes rearrangement and *N*-oxidation to give the spiro-compound (28). Triazolo[4,3-*a*]pyrazine 7-oxide (42) is readily obtained from 2-hydrazinopyrazine 4-oxide (45). The *N*-alkylation of the 2,3-diphenyl-1*H*-pyrrolo[2,3-*b*]pyridines (5) and (6), certain useful features of the n.m.r. spectra of the triazolopyrazines, (36) and (41), and their *N*-oxides, and some reactions of these *N*-oxides are reported.

MUCH work has been done on the *N*-oxidation of monocyclic azines and on bicyclic systems containing two fused rings, *e.g.* quinoline and the naphthyridines.[1] However, there has been less attention paid to the action of *N*-oxidising agents on nitrogen-containing heterocycles having both fused five- and six-membered rings. The two notable exceptions to this are the biologically important systems, indole and purine, and these two heterocycles behave in very different ways. The oxidation of indoles, where formation of an *N*-oxide is not expected, has been studied under a wide variety of conditions, and in the presence of peracids they undergo either ring opening or rearrangement by attack at the 2- and 3-positions.[2] The action of peracids on purines causes *N*-oxidation of the nitrogen atoms of the pyrimidine moiety but opening of the five-membered ring, though potentially possible, does not occur to a significant extent.[3] We report here an extension of our investigation of the reactions of peracids with compounds which may be thought of as lying between indole (monoazaindene) and purine (tetra-azaindene).



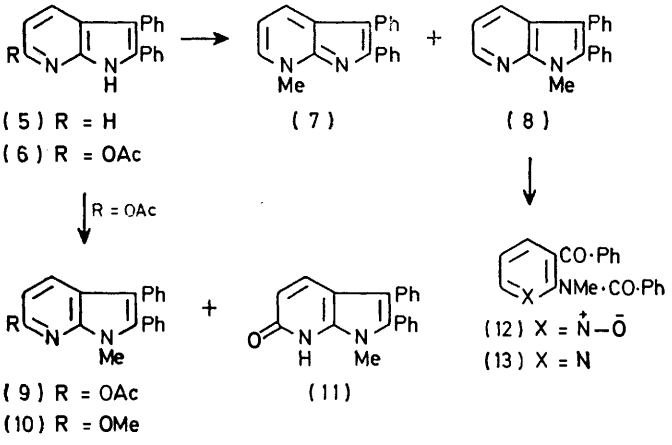
(1) X = N, R = Ac
(2) X = N̂–Ō, R = H



(3) X = N, R = Ac
(4) X = N̂–Ō, R = H

We have shown [4,5] that the 1-acetyl derivatives of 1*H*-pyrrolo[2,3-*b*]- (1) and 1*H*-pyrrolo[3,2-*c*]-pyridine (3) give the corresponding *N*-oxides (2) and (4), though both give ring-opened products with hydrogen peroxide in acetic anhydride.[6] It seemed likely that 1-methyl-2,3-diphenyl-1*H*-pyrrolo[2,3-*b*]pyridine (8) would give a higher and more reliable yield of the corresponding *N*-oxide with *m*-chloroperbenzoic acid than had been obtained [4] with the unsubstituted compound (1), and we therefore attempted to prepare the required (8) (Scheme 1) by methylation [7] of 2,3-diphenyl-1*H*-pyrrolo[2,3-*b*]-pyridine. The product contained (8) with its isomer (7). A similar procedure with the 6-acetoxy-derivative (6) gave the expected 1-alkylated derivatives (9) and (11) together with the 6-methoxy-compound (10), the last presumably formed by nucleophilic displacement of the acetoxy-group. No product corresponding to (7) was isolated. Both the 6-acetoxy- (9) and 6-methoxy- (10) derivatives could be converted into (11) and, in turn, (11) readily yielded (9) or (10).

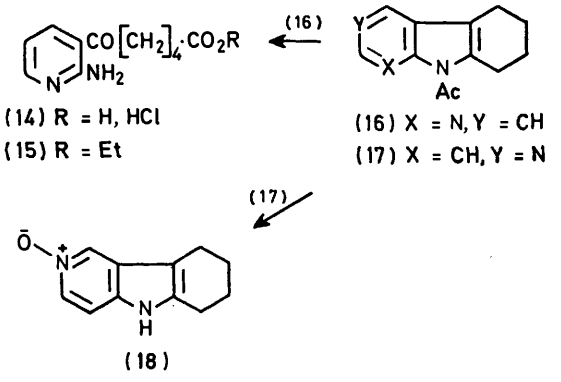
Treatment of 1-methyl-2,3-diphenyl-1*H*-pyrrolo[2,3-*b*]-pyridine (8) with *m*-chloroperbenzoic acid gave two



SCHEME 1

products each of which contained two different carbonyl groups. The minor component was the *N*-oxide of the major product, and spectroscopic and analytical data indicated them to be (13) and (12), respectively. The action of *m*-chloroperbenzoic acid on the 2,3-disubstituted pyrrolo[2,3-*b*]pyridine, 5,6,7,8-tetrahydro-9*H*-pyrido[2,3-*b*]indole (16), also gave a ring-opened product (Scheme 2) isolated as the amino-acid ester (15) [presumably formed when the hydrochloride (14) was treated with hot ethanol in the purification process]. This is the type of reaction undergone by the corresponding pyrrolo[3,2-*c*]pyridine system (17) with hydrogen peroxide and acetic anhydride,[6] but with *m*-chloroperbenzoic acid (17) gives the *N*-oxide (18) in high yield.[5] Thus,

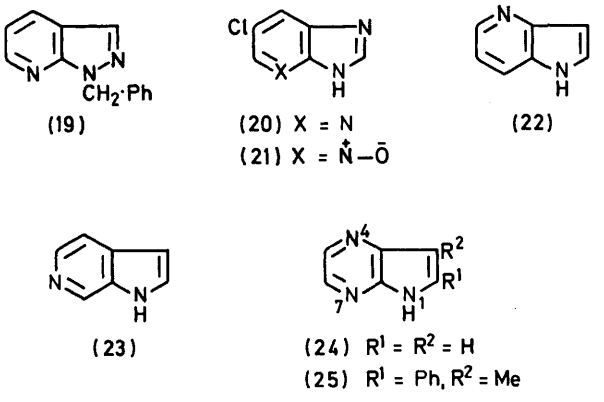
from the limited evidence available it appears that the pyrrolo[2,3-*b*]pyridine nucleus is more readily opened at the 2,3-positions by attack of *m*-chloroperbenzoic acid than is the pyrrolo[3,2-*c*]pyridine ring, and the aryl or alkyl substituents at the 2- and 3-positions increase this tendency to undergo ring opening. The ring fission



SCHEME 2

must be much more rapid than *N*-oxidation so that the peracid is exhausted before *N*-oxidation can occur to any significant extent.

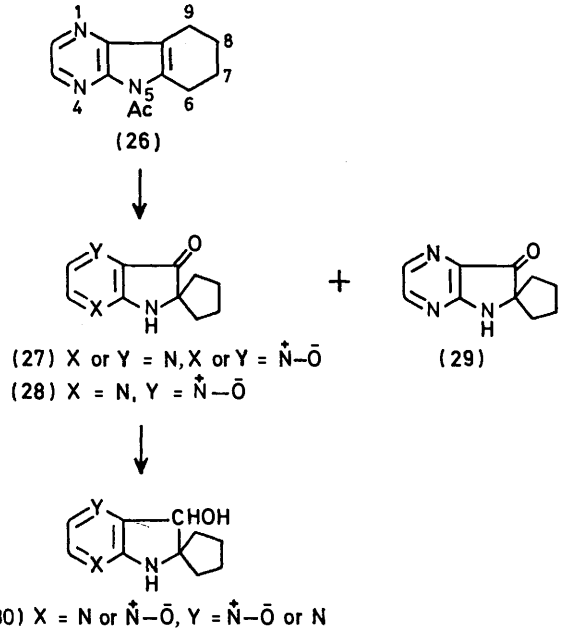
Nitrogen atoms might be considered to be introduced into the indole nucleus in either the five- or six-membered rings. *m*-Chlorobenzoic acid causes oxidation of 1-benzyl-1*H*-pyrazolo[3,4-*b*]pyridine (19) on the pyridyl



nitrogen atom only.[8] This is in direct contrast to the case of the pyrrolo[2,3-*b*]pyridines and indicates that the presence of a second nitrogen atom in the five-membered ring causes the system as a whole to be more resistant to oxidative cleavage. This is supported by the observation[9] that 6-chloro-1*H*-imidazo[4,5-*b*]pyridine (20) undergoes *N*-oxidation even in peracetic acid. Nitration of 1-benzyl-1*H*-pyrazolo[3,4-*b*]pyridine *N*-oxide gave the 4-nitrobenzyl derivative,[8] while attempted nitration of (21) produced only deoxygenation.

The influence of additional nitrogen atoms in the six-membered ring on the course of the oxidation process is not so readily predictable. We have already noted the difference in behaviour between the pyrrolo[2,3-*b*]- (16) and pyrrolo[3,2-*c*]-pyridine (17). Nothing is known about the behaviour of 1*H*-pyrrolo[3,2-*b*]- (22) and 1*H*-pyrrolo[2,3-*c*]-pyridine (23) under these oxidation conditions. 1*H*-Pyrrolo[2,3-*b*]pyrazine (24) is a little-studied[10] heterocycle related to the pyrrolo[2,3-*b*]-pyridine (16) and the behaviour of this ring system was investigated. The 3-methyl-2-phenyl derivative (25) gave a complex mixture with *m*-chloroperbenzoic acid but with peracetic acid extensive oxidative degradation occurred to give benzoic acid and benzoylurea, the latter being formed from the phenyl substituent, C_2, N_1, and N_7, and a bridgehead carbon atom. In the light of previous evidence, cleavage at the 2,3-bond is not surprising, but oxidative degradation of the pyrazine is not expected, since benzopyrazine 1-oxide and benzopyrazine 1,4-dioxide have been prepared under similar conditions.[11] *m*-Chloroperbenzoic acid gave complex mixtures which we were unable to separate.

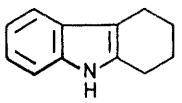
Attention was now turned to the oxidation of 5-acetyl-6,7,8,9-tetrahydro-5*H*-pyrazino[2,3-*b*]indole (26) with *m*-chloroperbenzoic acid (Scheme 3). This might be



SCHEME 3

expected to give a ring-opened product if it behaved like the deaza-compound (16), or a complex mixture with extensive degradation, if it behaved like the other 2,3-disubstituted pyrrolo[2,3-*b*]pyrazine (25). The product of the reaction was yellow and consisted of a major and minor component. The latter was an *N*-oxide, as indicated by an $M - 16$ peak in the mass spectrum. The remainder of the spectrum of the minor component was identical to that of the other product; neither showed the retro-Diels–Alder fragmentation characteristic of (26) and similar compounds. That the major component was the *N*-oxide of the minor product was confirmed by catalytic reduction of the former to afford the latter. Each component of the oxidation reaction

mixture showed a single carbonyl peak in the i.r. spectrum and an absorption due to NH. It seemed likely that the major reaction had been oxidative rearrangement to a spirocyclopentane, either (27) or (28), together with *N*-oxidation. Similar oxidative rearrangements of the tetrahydrocarbazole (31) under basic conditions are well known,[2] but had not been found with ' azatetrahydrocarbazoles ' (16) and (17). Sodium borohydride reduction of the *N*-oxide ($C_{10}H_{11}N_3O_2$) gave the deoxygenated compound as a minor product together with a compound having a molecular formula, $C_{10}H_{13}N_3O_2$, and containing both an NH and $\overset{+}{N}\text{–}\overset{-}{O}$ function, but no CO group. That a secondary alcohol was present was shown by the n.m.r. spectrum which exhibited spin–spin coupling between the OH and methine protons. The spiro-compound therefore has the structure (27) rather than its isomer (32). The assignment of the position of the *N*-oxide function is more tentative. If it is assumed that the 5-H in a pyrrolo[2,3-*b*]pyrazine nucleus (24) will be at higher field than the 6-H, as is the case for indole, then the 2-H



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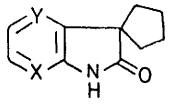
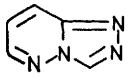
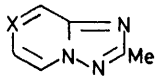


(32) X or Y = N, X or Y = $\overset{+}{N}\text{–}\overset{-}{O}$



(33)

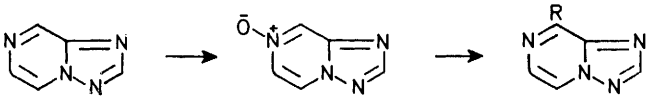


(34) X = N
(35) X = $\overset{+}{N}\text{–}\overset{-}{O}$

in the pyrazino[2,3-*b*]indole (26) will be expected to be at higher field than the 3-H, *i.e.* at δ 8.07 and 8.23, respectively.[10] The spiro-compound has chemical shifts for the pyrazine protons of δ 8.27 and 8.90, and the latter value may reflect the large effect of the *N*-oxide function on the adjacent α-proton, while the β-proton is little affected. The structure (28) is tentatively suggested for the spiro-compound.

We also studied the action of peracids on related heterocycles containing a bridgehead nitrogen atom. The literature indicates that there might be a wide variety of behaviour from related structures. For instance, the triazolopyridazine (33) undergoes oxidation only under severe conditions,[12] while the 2-methyltriazolopyrazine (34) readily gives the *N*-oxide (35) with peracetic acid.[13]

Oxidation of 1,2,4-triazolo[1,5-*a*]pyrazine (36) with either peracetic or *m*-chloroperbenzoic acid gave the stable 7-oxide (37) in good yield (Scheme 4). In contrast, the oxidation of 1,2,4-triazolo[4,3-*a*]pyrazine (41) with peracetic acid (Scheme 5) gave a pure solid only after repeated recrystallisation. On the basis of mass (*M* — 16 peak) and n.m.r. spectral evidence (discussed later), the compound was thought to be the 7-oxide (42). Reduction of the *N*-oxide gave the parent triazolopyrazine, showing that no rearrangement had occurred. The same compound (42) was obtained (27%) from 2-hydrazinopyrazine 4-oxide (45) [obtained from the corresponding chloro-compound (44)] by treatment with refluxing formic acid. Under milder conditions only

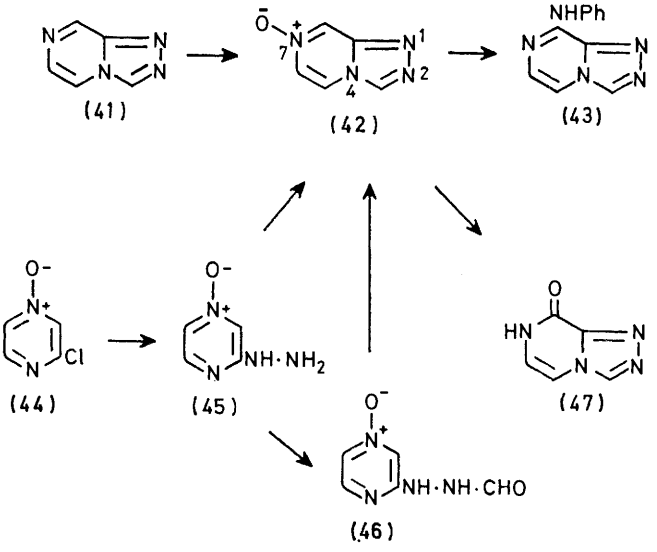


(36) (37) (38) R = NHPh (39) R = Cl (40) R = NH·NH$_2$

SCHEME 4

2-(2-formylhydrazino)pyrazine 4-oxide (46) was obtained. It seemed likely that the low yield in the cyclisation reaction was due to the acidic conditions, and a reaction of (45) with triethyl orthoformate gave (42) in 63% yield. This not only provided an efficient route to the 7-oxide (35% overall yield from 2-chloropyrazine) but also confirmed the structure of the oxide.

We have studied some reactions and properties of the triazolopyrazine oxides. Both (37) and (42) gave anilino-derivatives on treatment with phenyl isocyanate.[14] The ^{1}H n.m.r. spectrum of each product showed a pair of doublets with *J* 5 Hz which corresponds with $J_{5,6}$, and the products were thought to be (38) and (43), respectively. Treatment of triazolo[1,5-*a*]pyrazine 7-oxide (37) with phosphorus oxychloride gave only the 8-chlorotriazolopyrazine (39). The chlorine atom was readily replaced by hydrazine to give (40), but not by



(41) (42) (43) (44) (45) (46) (47)

SCHEME 5

aniline. Treatment of the triazolo[4,3-*a*]pyrazine 7-oxide with acetic anhydride gave a low yield of triazolo[4,3-*a*]pyrazin-8(7*H*)-one (47).

The chemical shifts for C-2 in the ^{13}C n.m.r. spectrum of the triazolo[1,5-*a*]pyrazine (36) was consistently greater than for C-3 of the corresponding triazolo[4,3-*a*]-pyrazine system (41) and affords a useful method of

distinguishing between the isomeric systems. Deshielding of carbon atoms in the pyrazine moiety would be expected to be significant only in the case of C-8 due to bond localisation, and the signal at 143 p.p.m. was assigned to C-8. The presence of the 7-oxide function resulted in shielding of C-8 in both heterocyclic systems and this, together with an increase in coupling (C-8–8-H), indicating an increased electron density at C-8. The respective absorptions due to C-5 and C-6 remain unassigned.

The relative positions of the signals due to 2-H and 3-H in the ^{1}H n.m.r. spectra of (36) and (41) were found to be the reverse of those observed for the corresponding C atoms in the ^{13}C spectra. Probably this is because there is a significant amount of shielding by the lone pair of electrons on basic nitrogen, and this is greatest in (36). The presence of an *N*-oxide function in a heteroaromatic system causes shielding of *o*- and *p*-protons relative to the parent heterocycle. Although 8-H in both *N*-oxides, (37) and (42), was apparently slightly shielded compared to the corresponding proton in the parent heterocycle, the signal due to 6-H in both *N*-oxides showed a large downfield shift indicating deshielding of the 6-proton relative to the parent heterocycle. In view of the donation of negative charge to the 8-position by the *N*-oxide function (as shown by the ^{13}C spectra), it seems that the anisotropy of the *N*-oxide acts to cause deshielding of both 6-H and 8-H and that the result is the observed downfield shift for 6-H and the reduced upfield shift for 8-H. Signals for 5-H were also shifted upfield compared with the corresponding signals in the parent heterocycle but an explanation for this is not so apparent.

EXPERIMENTAL

I.r., ^{1}H n.m.r., and mass spectra were recorded as previously described.[5] ^{13}C N.m.r. spectra were recorded on a Varian CFT 20 spectrometer with dimethyl sulphoxide as internal standard.

Methylation of 6-*Acetoxy*-2,3-*diphenyl*-1H-*pyrrolo*[2,3-b]-*pyridine* (6).—A mixture of 6-acetoxy-2,3-diphenyl-1*H*-pyrrolo[2,3-*b*]pyridine (6) [15] (8.0 g), potassium hydroxide (5.6 g), and dry dimethyl sulphoxide (100 cm^3) was stirred for 1 h. Methyl iodide (8.6 g) was then added and the mixture stirred for a further 1 h. Addition of water (50 cm^3) produced a precipitate which was removed and dried. Chromatography on silica gel with benzene gave 6-*methoxy*-1-*methyl*-2,3-*diphenyl*-1H-*pyrrolo*[2,3-b]*pyridine* (10) (1.7 g, 22%), m.p. 136—138° (Found: C, 80.0; H, 5.6; N, 9.1. $C_{21}H_{18}N_2O$ requires C, 80.2; H, 5.6; N, 9.1%), δ(CDCl$_3$) 7.9 (1 H, d, $J_{4,5}$ 8.5 Hz, 4-H), 7.3 (5 H, m, Ph), 7.2 (5 H, m, Ph), 4.9 (1 H, d, $J_{4,5}$ 8.5 Hz, 5-H), 4.0 (3 H, s, OMe), and 3.7 (3 H, s, NMe). Elution with chloroform then gave a solid which crystallised from benzene–light petroleum (b.p. 60—80°) as 6-*acetoxy*-1-*methyl*-2,3-*diphenyl*-1H-*pyrrolo*[2,3-b]*pyridine* (9) (2.1 g, 25%), m.p. 196—197° (Found: C, 77.4; H, 5.5; N, 7.9. $C_{22}H_{18}N_2O_2$ requires C, 77.2; H, 5.3; N, 8.2%), $\nu_{max.}$ 1 762 cm^{-1} (CO), δ(CDCl$_3$) 8.13 (1 H, d, *J* 8.5 Hz, 4-H), 7.40 (5 H, s, Ph), 7.28 (5 H, s, Ph), 6.88 (1 H, d, *J* 8.5 Hz, 5-H), 3.75 (3 H, s, NMe), and 2.41 (3 H, s, COMe). A third component was obtained upon elution with ether; crystallisation from benzene gave 1-*methyl*-2,3-*diphenyl*-1H-*pyrrolo*[2,3-b]*pyridin*-6(7H)-*one* (11) (2.7 g, 37%), m.p. 283—285° (Found: C, 80.1; H, 5.6; N, 9.1. $C_{20}H_{16}N_2O$ requires C, 80.0; H, 5.4; N, 9.3%), $\nu_{max.}$ 1 644 cm^{-1} (CO), δ[(CD$_3$)$_2$SO] 8.03 (1 H, d, *J* 8.5 Hz, 4-H), 7.46 (5 H, s, Ph), 7.28 (5 H, s, Ph), 6.82 (1 H, s, exchanged with D$_2$O, NH), 6.56 (1 H, d, *J* 8.5 Hz, 5-H), and 3.63 (3 H, s, Me).

Hydrolysis of either compounds (10), in boiling ethanolic hydriodic acid, or (9), in boiling ethanolic hydrochloric acid, gave the lactam (11) (82 and 63%, respectively).

Treatment of the ketone (11) with methyl iodide by Heaney's method [7] gave the 6-methoxy-derivative (80%), while treatment with acetic anhydride gave the 6-acetoxy-derivative (88%).

1-*Methyl*-2,3-*diphenyl*-1H-*pyrrolo*[2,3-b]*pyridine* (8) *and* 7-*Methyl*-2,3-*diphenyl*-7H-*pyrrolo*[2,3-b]*pyridine* (7).—A mixture of 2,3-diphenyl-1*H*-pyrrolo[2,3-*b*]pyridine (5) (0.54 g), potassium hydroxide (0.23 g), and dimethyl sulphoxide (30 cm^3) was heated to 70 °C for 2 h. Methyl iodide (0.58 g) was then added to the cooled solution and the mixture stirred at room temperature for 2 h. Addition of water (50 cm^3) gave a yellow solid which was chromatographed on silica gel. Elution with dichloromethane gave the 1-*methyl derivative* (8) (0.26 g, 46%), m.p. 135—136° (from benzene) (Found: C, 84.7; H, 5.8; N, 10.0. $C_{20}H_{16}N_2$ requires C, 84.5; H, 5.7; N, 9.85%), δ[(CD$_3$)$_2$CO] 8.38 (1 H, dd, *J* 2 and 4.5 Hz, 6-H), 8.05 (1 H, dd, *J* 2 and 8 Hz, 4-H), 7.47 (5 H, s, Ph), 7.28 (5 H, s, Ph), 7.15 (1 H, dd, *J* 4.5 and 8 Hz, 5-H), and 3.73 (3 H, s, Me).

Further elution with ethyl acetate gave the yellow 7-*methyl derivative* (7) (0.13 g, 23%), m.p. 158—160° [from benzene–light petroleum (b.p. 60—80°)] (Found: C, 84.2; H, 5.7; N, 10.1. $C_{20}H_{16}N_2$ requires C, 84.5; H, 5.7; N, 9.85%), δ[(CD$_3$)$_2$CO] 8.13—7.83 (4 H, m, 4- and 6-H and *o*-H of 2-Ph), 7.44 (5 H, s, 3-Ph), 7.53—7.30 (3 H, m, *m*- and *p*-H of 2-Ph), 6.95 (1 H, t, *J* 7 Hz, 5-H), and 4.42 (3 H, s, Me).

3-*Benzoyl*-2-(N-*methylbenzoylamino*)*pyridine* (12) *and* 3-*Benzoyl*-2-(N-*methylbenzoylamino*)*pyridine* 1-*Oxide* (13).—A mixture of *m*-chloroperbenzoic acid (0.43 g, 85%), 1-methyl-2,3-diphenyl-1*H*-pyrrolo[2,3-*b*]pyridine (8) (0.28 g), and dichloromethane (30 cm^3) was allowed to stand at room temperature for 24 h. The mixture was washed with aqueous sodium hydrogencarbonate and then water, and evaporated to dryness. The residue was chromatographed on silica gel with chloroform to give the *amide* (12) (0.13 g, 41%), m.p. 90—92° (from benzene) (Found: C, 76.05; H, 5.3; N, 9.1. $C_{20}H_{16}N_2O_2$ requires C, 75.9; H, 5.1; N, 8.85%), $\nu_{max.}$ 1 665 (CO) and 1 648 cm^{-1} (CO), δ(CDCl$_3$) 8.68 (1 H, dd, *J* 2 and 4.5 Hz, 6-H), 7.70 (1 H, dd, *J* 2 and 8 Hz, 4-H), 7.19 (1 H, dd, *J* 4.5 and 8 Hz, 5-H), 7.40 (5 H, s, Ph), 7.10 (5 H, s, Ph), and 3.31 (3 H, s, Me).

Elution with ether gave the N-*oxide* (13) (0.09 g, 27%), m.p. 180—182° (from acetone–ether) (Found: C, 72.5; H, 5.1; N, 8.1. $C_{20}H_{16}N_2O_3$ requires C, 72.3; H, 4.85; N, 8.4%), $\nu_{max.}$ 1 671 (CO) and 1 656 cm^{-1} (CO), δ[(CD$_3$)$_2$CO] 8.62 (1 H, dd, *J* 2 and 4.5 Hz, 6-H), 7.66 (1 H, dd, *J* 2 and 8 Hz, 4-H), 7.40—7.13 (11 H, m, 2 × Ph and 5-H), and 3.13 (3 H, s, Me).

9-*Acetyl*-5,6,7,8-*tetrahydro*-9H-*pyrido*[2,3-b]*indole* (16).—Treatment of 5,6,7,8-tetrahydro-9*H*-pyrido[2,3-*b*]indole [16] (5.0 g) with acetic anhydride (12 cm^3) on a steam-bath for 2 h afforded the *acetyl derivative* (16) (4.9 g, 79%), m.p. 48—50° [from light petroleum (b.p 40—60°)] (Found: C,

72.9; H, 6.6; N, 13.1. $C_{13}H_{14}N_2O$ requires C, 72.9; H, 6.6; N, 13.1%), $\nu_{max.}$ 1 702 cm^{-1} (CO), δ($CDCl_3$) 8.29 (1 H, dd, *J* 2 and 5 Hz, 4-H), 7.68 (1 H, dd, *J* 2 and 8 Hz, 2-H), 7.14 (1 H, dd, *J* 5 and 8 Hz, 3-H), 3.10 (2 H, m, 8-H), 3.07 (3 H, s, Me), 2.65 (2 H, m, 5-H), and 1.87 (4 H, m, 6- and 7-H).

Ethyl 6-(2-*amino*-3-*pyridyl*)-6-*oxohexanoate* (15).—A mixture of *m*-chloroperbenzoic acid (2.3 g, 85%), 9-acetyl-5,6,7,8-tetrahydro-9*H*-pyrido[2,3-*b*]indole (16) (2.0 g), and dichloromethane (45 cm^3) was allowed to stand for 3 days at room temperature. The mixture was filtered and the filtrate extracted with hydrochloric acid (3M). Evaporation of the aqueous phase gave a residue which was refluxed in ethanol (charcoal). The solution was evaporated and the residue separated by preparative t.l.c. on alumina with chloroform–ethyl acetate (19 : 1). One component (R_F 0.38) was 5,6,7,8-tetrahydro-9*H*-pyrido[2,3-*b*]indole (0.32 g, 20%). The second component (R_F 0.65) was the *ethyl ester* (15) (0.53 g, 23%), m.p. 59—61° (from benzene) (Found: C, 62.6; H, 7.2; N, 11.35. $C_{13}H_{18}N_2O_3$ requires C, 62.4; H, 7.25; N, 11.2%), $\nu_{max.}$ 3 280 (NH), 1 722 (CO), and 1 658 cm^{-1} (CO), δ[$(CD_3)_2SO$] 8.28 (2 H, d, *J* 7 Hz, 4′- and 6′-H), 7.70 (2 H, s, exchanged with D_2O, NH_2), 6.70 (1 H, t, *J* 7 Hz, 5′-H), 4.13 (2 H, q, *J* 7 Hz, CH_2), 3.0 (2 H m, 6-H), 2.37 (2 H, m, 1-H), 1.63 (4 H, m, 3- and 4-H), and 1.20 (3 H, t, *J* 7 Hz, Me).

Action of Peracetic Acid on 3-*Methyl*-2-*phenyl*-1H-*pyrrolo*-[2,3-b]*pyrazine* (25).—Hydrogen peroxide (4 cm^3, 30%), 3-methyl-2-phenyl-1*H*-pyrrolo[2,3-*b*]pyrazine (25) [10] (0.8 g), and glacial acetic acid were heated together at 70—80 °C for 2 h. Evaporation of the solvent gave a residue which was dissolved in chloroform, and the solution was washed with aqueous sodium hydrogencarbonate and water, and then evaporated to dryness. Crystallisation from benzene gave *N*-benzoylurea (0.23 g, 37%), m.p. 213—214° (lit.,[17] 215°). Acidification of the basic extract yielded benzoic acid (0.15 g, 32%).

5-*Acetyl*-6,7,8,9-*tetrahydro*-5H-*pyrazino*[2,3-b]*indole* (26).—A mixture of 6,7,8,9-tetrahydro-5*H*-pyrazino[2,3-*b*]-indole [10] (2.0 g) and acetic anhydride (10 cm^3) heated on a steam-bath for 2 h yielded the 5-*acetyl compound* (26) (1.7 g, 68%), m.p. 101—103°, $\nu_{max.}$ 1 720 cm^{-1} (CO), δ($CDCl_3$) 8.48 (1 H, d, *J* 2 Hz, 2-H), 8.25 (1 H, d, *J* 2 Hz, 3-H), 3.23 (2 H, m, CH_2), 3.02 (3 H, s, Me), 2.83 (2 H, m, CH_2), and 1.90 (4 H, m, 2 × CH_2).

7-*Oxo*-6,7-*dihydro*-5H-*pyrrolo*[2,3-b]*pyrazine*-6-*spirocyclopentane* (29) *and its* 1-*Oxide* (28).—A mixture of *m*-chloroperbenzoic acid (8.0 g, 85%), 5-acetyl-6,7,8,9-tetrahydro-5*H*-pyrazino[2,3-*b*]indole (26) (2.6 g), and dichloromethane (120 cm^3) was allowed to stand at room temperature in the dark for 5 days. The solid was removed and the filtrate evaporated. The residue was dissolved in aqueous sodium carbonate and continuously extracted with dichloromethane. The extract yielded a yellow solid which was separated by preparative t.l.c. on silica gel with acetone–ethyl acetate (1 : 1). The component (R_F 0.11) was the N-*oxide* (28) (0.6 g, 24%), m.p. 215° (decomp.) (from benzene) (Found: C, 58.2; H, 5.2; N, 20.2%; M^+, 205.0849. $C_{10}H_{11}N_3O_2$ requires C, 58.5; H, 5.4; N, 20.4%; *M*, 205.0851), $\nu_{max.}$ 3 220 (NH) and 1 710 cm^{-1} (CO), δ[$(CD_3)_2SO$] 10.10 (1 H, s, exchanged in D_2O, NH), 8.90 (1 H, d, *J* 4 Hz, 2-H), 8.27 (1 H, d, *J* 4 Hz, 3-H), and 1.98 (8 H, s, 4 × CH_2). A second component (R_F 0.41) gave the *spiro-compound* (29) (40 mg, 2%), m.p. 118—120° (from benzene) (Found: C, 63.3; H, 5.3; N, 22.1%, M^+, 189.0907. $C_{10}H_{11}N_3O$ requires C, 63.5; H, 5.9; N, 22.2%; *M*, 189.0902), $\nu_{max.}$ 3 190 (NH) and 1 709 cm^{-1} (CO).

Reduction of 7-oxo-6,7-dihydro-5*H*-pyrrolo[2,3-*b*]pyrazine-6-spirocyclopentane 1-oxide (28) (50 mg) in methanol (20 cm^3) with hydrogen (2 atm.) over palladium–charcoal (15 mg, 10%) for 3 h gave the deoxygenated spiro-compound (29) (24 mg, 52%).

7-*Hydroxy*-6,7-*dihydro*-5H-*pyrrolo*[2,3-b]*pyrazine*-6-*spirocyclopentane* 1-*Oxide* (30).—A solution of sodium borohydride (0.10 g) in methanol (50 cm^3) was added dropwise during 0.5 h to 7-oxo-6,7-dihydro-5*H*-pyrrolo[2,3-*b*]pyrazine-6-spirocyclopentane 1-oxide (28) (0.25 g) in methanol (30 cm^3) at room temperature. After evaporation of the reaction mixture, the residue was dissolved in water (50 cm^3) and the solution continuously extracted with chloroform. The extract yielded a solid which was separated by preparative t.l.c. [silica gel; acetone–ethyl acetate (1 : 4)] to give the spiro-compound (29) (R_F 0.44) (15 mg, 6%) and the N-*oxide* (30) (R_F 0.15) (0.16 g, 62%), m.p. 167—169° (decomp.) (Found: M^+, 207.1006. $C_{10}H_{13}N_3O_2$ requires *M*, 207.1008), $\nu_{max.}$ 3 188 cm^{-1} (NH), δ[$(CD_3)_2SO$] 7.77 (1 H, d, *J* 4 Hz, 3-H), 7.67 (1 H, s, exchanged in D_2O, NH), 7.38 (1 H, d, *J* 4 Hz, 2-H), 5.86 (1 H, d, *J* 7 Hz, exchanged in D_2O, 7-OH), 4.73 (1 H, d, *J* 7 Hz, becomes s in D_2O, 7H), and 1.67 (8 H, br m, 4 × CH_2).

1,2,4-*Triazolo*[1,5-a]*pyrazine* 7-*Oxide* (37).—A mixture of *m*-chloroperbenzoic acid (3.4 g, 85%), 1,2,4-triazolo[1,5-*a*]-pyrazine (36),[18] and dichloromethane (400 cm^3) was allowed to stand for 2 days. The solvent was removed, the residue dissolved in aqueous sodium carbonate, and the solution continuously extracted with dichloromethane. The extract yielded the 7-*oxide* (37) (0.85 g, 75%), m.p. 215—217° (from ethanol) (Found: C, 44.3; H, 3.1; N, 41.2. $C_5H_4N_4O$ requires C, 44.1; H, 3.0; N, 41.1%), $\nu_{max.}$ 1 224 cm^{-1} ($\overset{+}{N}\overset{-}{O}$), δ[$(CD_3)_2SO$] 9.08 (1 H, d, *J* 6 Hz, 6-H), 9.06 (1 H, d, *J* 1.5 Hz, 8-H), 8.62 (1 H, s, 2-H), and 8.03 (1 H, dd, *J* 1.5 and 6 Hz, 5-H).

The same compound was obtained (71%) when a mixture of hydrogen peroxide (3 cm^3; 30%), the triazolopyrazine (1.0 g), and glacial acetic acid (15 cm^3) was heated to 90 °C for 4 h.

2-*Hydrazinopyrazine* 4-*Oxide* (45).—A mixture of hydrazine hydrate (10 cm^3, 98%), 2-chloropyrazine 4-oxide (4.0 g), and ethanol (200 cm^3) was heated under reflux for 1.5 h. After cooling, the mixture yielded the *hydrazine* (45) (3.3 g, 77%), m.p. 196° (decomp.) (from methanol) (Found: C, 38.1; N, 4.7; N, 44.35%; M^+, 126.0549. $C_4H_6N_4O$ requires C, 38.1; H, 4.8; N, 44.4%; *M*, 126.0542), $\nu_{max.}$ 3 250 (NH) and 1 222 cm^{-1} ($\overset{+}{N}\overset{-}{O}$), δ[$(CD_3)_2SO$] 7.88 (1 H, s, exchanged in D_2O, NH), 7.70 (1 H, d, *J* 4 Hz, 5-H), 7.50 (1 H, s, 3-H), 7.27 (1 H, d, *J* 4 Hz, 6-H), and 4.20 (2 H, s, exchanged in D_2O, NH_2).

2-(2-*Formylhydrazino*)*pyrazine* 4-*Oxide* (46).—The aforementioned *N*-oxide (45) (1.6 g) and formic acid (10 cm^3, 98%) were heated together at 60—65 °C for 0.5 h to yield the *hydrazide* (46) (1.1 g, 56%), m.p. 186—188° (from methanol–benzene) (Found: C, 38.9; H, 4.0; N, 36.2. $C_5H_6N_4O_2$ requires C, 39.0; H, 3.9; N, 36.35%), $\nu_{max.}$ 3 300 (NH) and 1 678 cm^{-1} (CO), δ[$(CD_3)_2SO$] 9.50 (2 H, s, exchanged in D_2O, NH·NH), 8.03 (1 H, s, 2-H), 7.95 (1 H, d, *J* 4 Hz, 5-H), 7.58 (1 H, d, *J* 4 Hz, 6-H), and 7.55 (1 H, s, CHO).

1,2,4-*Triazolo*[4,3-a]*pyrazine* 7-*Oxide* (42).—*Method* A. 2-(2-Formylhydrazino)pyrazine (0.5 g) was refluxed in

formic acid (10 cm³, 98%) for 4 h to yield the N-*oxide* (42) (0.12 g, 27%), m.p. 120° (decomp.) [from ethanol (charcoal)] (Found: C, 43.9; H, 3.1; N, 41.15. $C_5H_4N_4O$ requires C, 44.1; H, 3.0; N, 41.1%), $\nu_{max.}$ 1 220 cm^{-1} ($\overset{+}{N}\overset{-}{O}$), δ[$(CD_3)_2SO$] 9.50 (1 H, s, 3-H), 9.28 (1 H, d, *J* 1.5 Hz, 8-H), 8.85 (1 H, d, *J* 6 Hz, 6-H), and 7.88 (1 H, dd, *J* 1.5 and 6 Hz, 5-H).

Method B. Triethyl orthoformate (5 cm³), 2-hydrazinopyrazine 4-oxide (6.0 g), and xylene (100 cm³) were heated together at 100—110 °C until evolution of ethanol ceased. The mixture gave the triazolopyrazine 7-oxide (42) (4.1 g, 63%).

Method C. 1,2,4-Triazolo[4,3-*a*]pyrazine (41) [19] (1.0 g), glacial acetic acid (20 cm³), and hydrogen peroxide (3 cm³, 30%) were heated at 70—80 °C for 2 h. The cold solution yielded a buff solid which quickly became a tar after isolation. Extraction of the tar with ethanol gave a solution which yielded a solid. Recrystallisation from ethanol gave the *N*-oxide (42) (0.17 g, 15%).

The *N*-oxide (42) was reduced to 1,2,4-triazolo[4,3-*a*]pyrazine (66%) in ethanol with hydrogen (1 atm) over palladium–charcoal for 2 h.

1,2,4-*Triazolo*[4,3-a]*pyrazin*-8(7H)-*one* (47).—A mixture of 1,2,4-triazolo[4,3-*a*]pyrazine 7-oxide (42) (1.0 g), anhydrous sodium acetate (0.3 g), and acetic anhydride (30 cm³) was heated under reflux for 0.5 h, and then evaporated to dryness. A dichloromethane extract of the aqueous sodium carbonate solution of the residue yielded the *amide* (47) (0.17 g, 17%), m.p. 224—227° (decomp.) [from benzene–light petroleum (b.p. 60—80°)] (Found: C, 43.8; H, 3.1; N, 41.5. $C_5H_4N_4O$ requires C, 44.1; H, 3.0; N, 41.1%), $\nu_{max.}$ 3 280 (NH) and 1 657 cm^{-1} (CO), δ[$(CD_3)_2SO$] 9.15 (1 H, s, 3-H), 7.72 (1 H, d, *J* 4 Hz, 5-H), 7.38 (1 H, s, exchanged in D_2O, NH), and 7.17 (1 H, d, *J* 4 Hz, 6-H).

8-*Anilino*-1,2,4-*triazolo*[4,3-a]*pyrazine* (43).—1,2,4-Triazolo[4,3-*a*]pyrazine 7-oxide (42) was added to a solution of phenyl isocyanate (1.75 g) in dimethylformamide (25 cm³) and the mixture heated for 1 h at 110—120 °C. After the reaction mixture had been poured into water, continuous extraction with chloroform yielded 8-*anilino*-1,2,4-*triazolo*[4,3-a]*pyrazine* (0.6 g, 39%), m.p. 192—193° (from methanol) (Found: C, 62.95; H, 4.3; N, 32.9. $C_{11}H_9N_5$ requires C, 62.6; H, 4.3; N, 33.2%), $\nu_{max.}$ 3 276 cm^{-1} (NH), δ[$(CD_3)_2SO$] 10.02 (1 H, s, exchanged in D_2O, NH), 9.23 (1 H, s, 3-H), 8.06 (1 H, d, *J* 1 Hz, 2′-H), 7.92 (1 H, d, *J* 1 Hz, 6′-H), 7.90 (1 H, d, *J* 5 Hz, 5-H), 7.36 (1 H, d, *J* 5 Hz, 6-H), 7.40—6.97 (3 H, m, 3′-, 4′-, and 5′-H).

8-*Anilino*-1,2,4-*triazolo*[1,5-a]*pyrazine* (38).—A reaction analogous to that used for the aforementioned isomer (43) gave the *anilinotriazolopyrazine* (38) (0.45 g, 58%), m.p. 129—131° (from benzene) (Found: C, 62.7; H, 4.6; N, 33.1. $C_{11}H_9N_5$ requires C, 62.6; H, 4.3; N, 33.2%), $\nu_{max.}$ 3 370 cm^{-1} (NH), δ[$(CD_3)_2SO$] 9.80 (1 H, s, exchanged in D_2O, NH), 8.53 (1 H, d, *J* 1 Hz, 2′-H), 8.28 (1 H, d, *J* 5 Hz, 5-H), 8.02 (1 H, d, *J* 1 Hz, 6′-H), 7.90 (1 H, s, 2-H), 7.62 (1 H, d, *J* 5 Hz, 6-H), and 7.40—6.95 (3 H, m, 3′-, 4′-, and 5′-H).

8-*Chloro*-1,2,4-*triazolo*[1,5-a]*pyrazine* (39).—A mixture of 1,2,4-triazolo[1,5-*a*]pyrazine 7-oxide (37) (1.0 g) and phosphorus oxychloride (25 cm³) was heated under reflux for 1 h, the excess of acid chloride was then distilled off, and the residue poured into ice–water. Continuous extraction with chloroform of the basified ($NaHCO_3$) solution yielded a product which was separated on silica gel plates with chloroform to give a solid (R_F 0.34). Sublimation at 100° and 0.01 mmHg afforded the *chloro-compound* (39) (0.32 g, 37% based on recovered starting material), m.p. 132—134° (Found: C, 38.3; H, 2.1; N, 36.9. $C_5H_3N_4Cl$ requires C, 38.9; H, 2.1; N, 36.9%), δ[$(CD_3)_2SO$] 8.83 (1 H, d, *J* 5 Hz, 5-H), 8.51 (1 H, s, 2-H), and 7.88 (1 H, d, *J* 5 Hz, 6-H).

Reaction of this chloro-compound with hydrazine hydrate (98%) gave 8-hydrazino-1,2,4-triazolo[1,5-*a*]pyrazine (40) (72%), m.p. 247—249° (lit.,[20] 248—250°) (Found: M^+, 150. Calc. for $C_5H_6N_6$: *M*, 150).

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