Metal Ions and Complexes in Organic Reactions. Part XVII.[1] Iron(II)-promoted Conversions of Nuclear-substituted Anilinopyridines into Pyridoquinoxalines

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Brief heating of *o*-nitro-substituted anilinopyridines with iron(II) oxalate at ~280° resulted in 5—40% conversion into cyclised products; traces of azo-compounds and of unidentified dimers were also isolated. Two of the five isomeric nitro-amines thus tested gave pyrido[3,4-*b*]quinoxaline (1), one gave pyrido[2,3-*b*]quinoxaline (2), and one gave a mixture of the two. The procedure was applied to syntheses of pyridoquinoxalines containing a methyl or methoxy-group in the benzo-ring; in some of these cases cyclisation gave a mixture of isomers or occurred with displacement of a methoxy- or methyl group. N.m.r. and other spectral features of the pyridoquinoxalines are reported.

DURING an investigation[2] of copper-promoted substitutions between aryl halides and diarylamines, certain conditions incidentally led to the well-known conversion of *o*-nitrodiphenylamine into phenazine [reaction (1)].

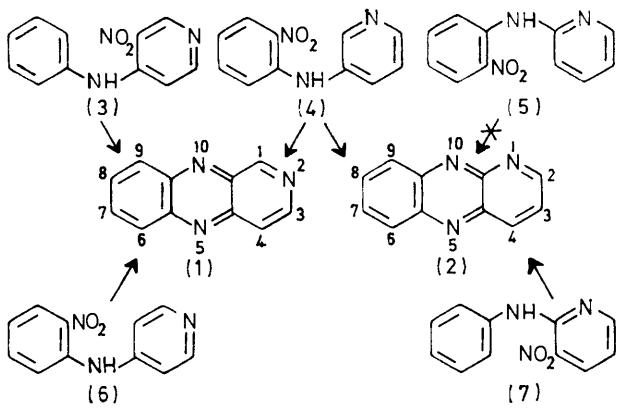
(1)

Cyclisations thus exemplified involve the aromatic nucleus and the $-NO_2$ and $-NH-$ groups with overall loss of two oxygen and two hydrogen atoms. This may occur under varied conditions.[3] A method often used[4-6] is heating the nitro-amine with iron(II) oxalate, which is considered to be an *in situ* source of iron(II) oxide, an oxygen acceptor. In this paper we describe application of this procedure to *o*-nitro-substituted anilinopyridines, whereby pyridoquinoxalines are obtained. Analogous syntheses of other polycyclic systems are reported in the following paper.[7]

Pyridoquinoxalines obtainable from the isomeric intermediates employed (Scheme 1) might incorporate pyridine and pyrazine rings fused in two ways, *i.e.*, as the [3,4-*b*]isomer (1), previously synthesised by a different route,[8] and as the [2,3-*b*]isomer (2), which has not hitherto been reported. A conventional procedure [brief heating at 260—280° with 2 mol. equiv. of iron(II) oxalate] resulted in production of the pyridoquinoxalines from four of the five isomeric nitro-substituted anilinopyridines tested.

The requisite nitro-amines were prepared by reaction of *o*-nitroaniline with halogenopyridines (generally with the aid of copper catalysis), or by reaction of aniline (or nuclear-substituted anilines in later cases) with 2- or 4-chloro-3-nitropyridine. After heating with iron(II) oxalate, the yields of cyclised products were in all cases low (usually 5—20%; highest observed, *ca.* 40%) and variable amounts of unchanged nitro-amines were recovered. Yields reported for phenazines are likewise generally poor, but may attain 50% or more in favourable cases. However, new heterocyclic compounds are thus potentially available from a relatively simple two-stage process.

Pyrido[3,4-*b*]quinoxaline (1) was produced (Scheme 1) from the nitro-amine (3) (21%) by cyclisation onto the



SCHEME 1

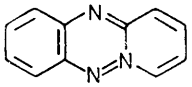
benzene ring, and, in much lower yield, from the isomer (6) by cyclisation onto the 3-position in the pyridine ring. Pyrido[2,3-*b*]quinoxaline (2) was produced from the nitro-amine (7) (20%) by cyclisation onto the benzene ring, but a better yield (27%) resulted in this case from the isomer (4), by cyclisation of the nitro-group onto the 2-position in the pyridine ring. The conversion (7) ⟶ (2) was also observed, in very low yield, when heating was carried out without iron(II) oxalate in diethylene glycol diethyl ether (*cf.* phenazine production, described in ref. 2).

In the reaction of the nitro-amine (4) a second possible

[1] Part XVI, R. G. R. Bacon and A. Karim, *J.C.S. Perkin I*, 1973, 278.
[2] R. G. R. Bacon and S. D. Hamilton, *J. Chem. Soc.* (*C*), 1972, 2391.
[3] B. Cross, P. J. Williams, and R. E. Woodall, *J. Chem. Soc.* (*C*), 1971, 2085, and references cited therein.
[4] (*a*) H. C. Waterman and D. L. Vivian, *J. Org. Chem.*, 1949, **14**, 289; (*b*) D. L. Vivian, G. Y. Greenberg, and J. L. Hartwell, *ibid.*, 1951, **16**, 1; (*c*) D. L. Vivian and J. L. Hartwell, *ibid.*, 1953, **18**, 1065; (*d*) D. L. Vivian, J. L. Hartwell, and H. C. Waterman, *ibid.*, 1954, **19**, 1136; (*e*) *idem.*, *ibid.*, p. 1641; and later papers.
[5] R. A. Abramovitch and B. A. Davis, *J. Chem. Soc.* (*C*), 1968, 119.
[6] H. Suschitzky and M. E. Sutton, *Tetrahedron Letters*, 1967, 3933; G. V. Garner and H. Suschitzky, *ibid.*, 1971, 169.
[7] R. G. R. Bacon and S. D. Hamilton, following paper.
[8] V. Petrow, J. Saper, and B. Sturgeon, *J. Chem. Soc.*, 1949, 2540.

site for ring closure is the 4-position in the pyridine ring. A minor amount of cyclisation did occur there, giving the isomeric pyrido[3,4-*b*]quinoxaline (1). The mixture of isomers was separable with an alumina column, on which the [2,3-*b*]-isomer was retained more strongly than the [3,4-*b*]-isomer. The observed ratio of isomers (~3 : 1 in favour of ring closure at the 2-position, as compared with the 4-position in pyridine) conforms with the behaviour of other types of 3-substituted pyridine derivatives on cyclisation: *e.g.*, heating 3-*o*-nitrosophenylpyridine with triethyl phosphite [9] gave a mixture of carbolines (pyridoindoles) in which the ratio of α- to γ-isomers was 4·4 : 1, and pyrolysis of 3-*o*-azidophenylpyridine [10] gave a similar mixture in 2 : 1 ratio.

Confirming an earlier report,[11] we found that heating 2-*o*-nitroanilinopyridine (5) with iron(II) oxalate gave only tars and unchanged nitro-amine. Conversion of this compound into pyrido[2,3-*b*]quinoxaline (2) would have involved cyclisation onto the 3-position in the pyridine ring. However, the preferred site for ring closure would be the nitrogen atom, giving a benzopyrido[1,2,4]triazine (24), which, if formed, may be thermally unstable. A parallel case is that of 2-*o*-nitrophenylpyridine, which gives pyrido[1,2-*b*]indazole (25), and not the isomeric pyrido[2,3-*b*]indole, when heated with iron(II) oxalate.[12]



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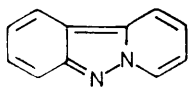
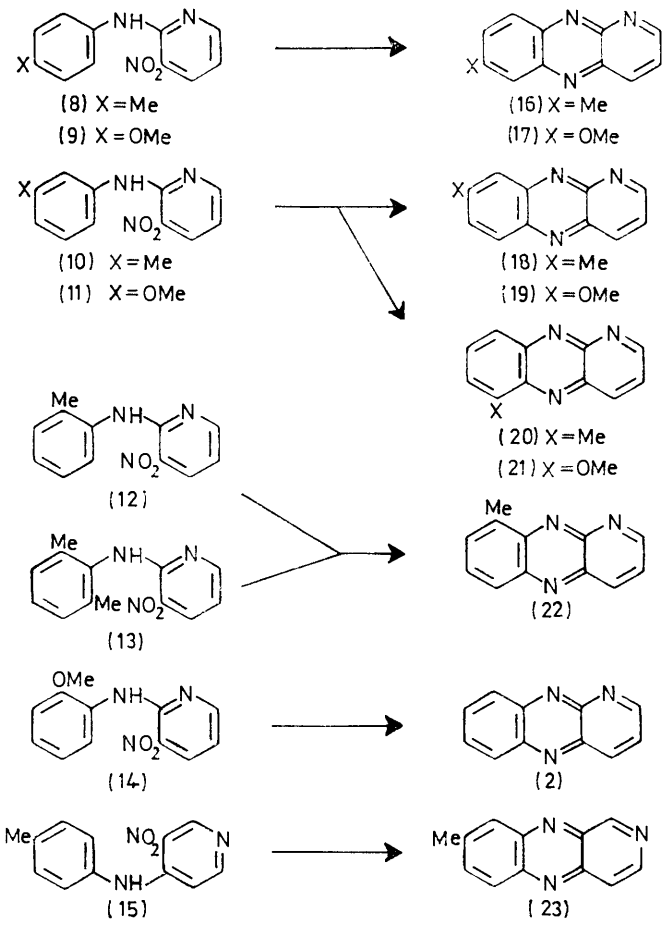


(25)

The iron(II) oxalate method was then applied (Scheme 2) to syntheses of pyrido[2,3-*b*]quinoxalines, containing a methyl or methoxy-substituent in the benzene ring, by routes analogous to the reaction (7) ⟶ (2). Also (Scheme 2), production of a methylpyrido[3,4-*b*]quinoxaline was exemplified, using a reaction analogous to (3) ⟶ (1).

In the case of the *o*-anisidinopyridine (14), the methoxy-group was eliminated in the cyclisation, which produced the parent heterocycle (2). This result is in harmony with observations [4b,d] that in analogous phenazine syntheses *ortho*-alkoxy-groups are eliminated in preference to *ortho*-hydrogen during ring closure. A different case of group displacement is shown by the 2,6-xylidino-derivative (13). The elimination of one of these methyl groups, giving the mono-methyl derivative (22) is unusual. When, in reactions with iron(II) oxalate, a six-membered central ring would thereby result, compounds containing blocking methyl groups generally contribute one of these groups to formation of the ring, as exemplified by production of an imidazoquinoxaline,[7] and by the conversion of 2,4,6-trimethyl-2′-nitrobiphenyl into 8,10-dimethylphenanthridine.[13] Among cyclisations effected by triethyl phosphite, the conversion of 2-nitrophenyl 2,6-xylyl sulphide into a dibenzothiazepine exemplifies formation of a seven-membered ring incorporating methyl-carbon.[14]



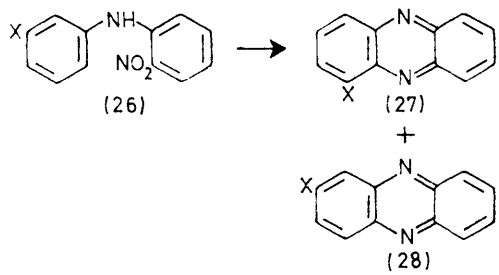
SCHEME 2

Cyclisations of the nitro-amines (10) and (11), containing respectively a 3-methyl or 3-methoxy-substituent in the benzene ring, could theoretically produce a mixture of 6- and 8-methyl(or methoxy)pyrido[2,3-*b*]quinoxalines (18)—(21), depending upon whether ring closure occurs at the 2- or 6-position in the benzene ring (*i.e.*, *ortho* or *para* to the substituent). Such mixtures did result and were not cleanly separable on chromatographic alumina, but integrals of n.m.r. spectra showed that the ratio of 6- to 8-isomer (*i.e.*, *o* : *p* substitution ratio) was 2·4 : 1 in the product from the methyl-substituted compound (10) and 1 : 2·5 in the product from the methoxy-substituted compound (11). It happens (and is possibly significant) that the *o* : *p* ratio given by the methoxy-compound (11) is in accord with that observed in most

[9] P. J. Bunyan and J. I. G. Cadogan, *J. Chem. Soc.*, 1963, 42.
[10] P. A. S. Smith and J. H. Boyer, *J. Amer. Chem. Soc.*, 1951, **73**, 2626.
[11] R. A. Abramovitch, *Chem. and Ind.*, 1957, 422.
[12] R. A. Abramovitch and K. A. H. Adams, *Canad. J. Chem.*, 1961, **39**, 2516.
[13] R. A. Abramovitch, D. Newman, and G. Tertzakian, *Canad. J. Chem.*, 1963, **41**, 2390.
[14] J. I. G. Cadogan and S. Kulik, *J. Chem. Soc.* (*C*), 1971, 2621.

electrophilic substitutions of anisole, in which polar and steric effects of OMe are considered to be operative.

It was of interest to discover whether the *ortho*-favoured cyclisation shown by 3-nitro-2-*m*-toluidinopyridine (10) would be paralleled if 3-methyl-2'-nitrodiphenylamine (26; X = Me) was heated with iron(II) oxalate. This proved to be the case; a mixture resulted in which the ratio, 1-methyl- : 2-methyl-phenazine, (27) : (28), was 2·2 : 1, *i.e.*, practically the same as (20) : (18). It is known [4b,c] that nitrodiphenylamines of the same type (26; X = Cl or OAlk) produce mixtures of isomeric phenazine derivatives when heated with iron(II) oxalate, but the relative proportions have not been determined. Further quantitative work is desirable.

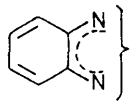


(26) (27) + (28)

The pyridoquinoxalines are yellow, crystalline solids which gradually darken on storage; on heating they sublime. The m.p. of each isomer is close to that of phenazine (171°), and the m.p. of the methylpyridoquinoxalines are *ca.* 20—40° lower. The mass spectra of the pyridoquinoxalines (see Experimental section) showed resemblances to those of phenazines; [15] prominent fragmentation modes are loss of HCN and C_2H_2.

The n.m.r. spectra of the parent heterocycles are considerably more complex than that of phenazine (see Experimental section). The protons in the pyrido-ring of the [2,3-*b*]-isomer gave signals *ca.* 0·5 p.p.m. to lower field than the corresponding protons of quinoline,[16] and in the same order (α- < γ- < β-proton), whilst 6-H and 9-H in the benzo-ring gave signals at lower field than 7-H and 8-H, corresponding with the pattern in phenazine. Similarly, the n.m.r. spectrum of pyrido-[3,4-*b*]quinoxaline showed correspondences with those of isoquinoline [16] and phenazine.

A noteworthy feature in the n.m.r. spectra of all the methylpyridoquinoxalines examined was the occurrence of the methyl signals as doublets, due to long-range benzylic spin–spin coupling (*J ca.* 1·0 Hz) with a nuclear proton.[16] The coupling assignments (see Experimental section), checked by spin–spin decoupling, were as follows: Me with 6-H in compound (16), with 7-H in (20), with 8-H in (22), and with 9-H in (18) and (23). These results are indicative of canonical forms in which there is a marked degree of bond-fixation (29) in the benzo-ring of the polycyclic structures.



(29)

Several of the pyridoquinoxalines shown in Schemes 1 and 2 were accompanied by trace amounts of by-products, isolated chromatographically. In five cases red solids were identified as azo-compounds corresponding with the nitropyridines used in the reactions. It is known [5] that azo- and azoxy-compounds may be major products when nitro-aromatic compounds are heated with iron(II) oxalate. Two other red solids were not identified but from mass spectral data they appeared to be pyridoquinoxaline dimers.

EXPERIMENTAL

M.p.s were determined on a Kofler block and, where necessary, were checked by observing samples in sealed capillary tubes. I.r. spectra were recorded with a Perkin-Elmer Infracord model 457, and mass spectra with an A.E.I. MS902 instrument. N.m.r. spectra were determined in deuteriochloroform, with tetramethylsilane as internal standard, either (where stated) at 100 MHz, with a Varian HA100 instrument, otherwise at 60 MHz with a Varian A60 instrument.

Separations of products were carried out on columns of alumina (Peter Spence, type H) which had been deactivated by adding 100 ml of 10% aqueous acetic acid to 2 kg of the powder and tumbling the mixture for 12 h on rollers. Successive chromatographic fractions were checked by m.p. and spectroscopy and were often analytically pure. For further purification vacuum sublimation was often effective. When recrystallisations were carried out, combinations of dichloromethane, ether, and light petroleum (b.p. 30—40°) were used.

All the by-products identified as azo-compounds responded by giving colourless solutions in a standard test [17] with 5% titanium(III) chloride in dilute hydrochloric acid. The by-products designated as (?) dimers did not have this effect.

Halogenopyridines.—2- and 3-Bromo-pyridine, 4-chloropyridine (as its hydrochloride), and 2-chloro-3-nitropyridine were from commercial suppliers. Conversion of 4-pyridone into 3-nitropyridin-4-ol (77%) and thence into 4-chloro-3-nitropyridine (60%) [18] gave the latter as a pale yellow liquid, b.p. 67° at 1 mmHg (lit.,[18] 95° at 5 mmHg); this was lachrymatory and unstable, and was stored in a refrigerator.

Anilino(nitro)pyridines and Nitroanilinopyridines.—A mixture of 2-bromopyridine (40 mmol), *o*-nitroaniline (33 mmol), potassium carbonate (33 mmol), and copper bronze (0·2 g) in nitrobenzene (50 ml) was stirred under reflux in an atmosphere of nitrogen for 17 h. Removal of solvent and chromatography of the residual oil yielded red crystals of 2-*o*-nitroanilinopyridine (5) (1·8 g, 25%), m.p.

[15] F. G. Holliman, R. A. W. Johnstone, and B. J. Millard, *J. Chem. Soc.* (*C*), 1967, 2351.

[16] L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' 2nd edn., Pergamon Press, London, 1969.

[17] H. T. Openshaw, 'A Laboratory Manual of Qualitative Organic Analysis,' Cambridge University Press, 3rd edn., 1965, p. 14.

[18] S. Kruger and F. G. Mann, *J. Chem. Soc.*, 1955, 2755.

68° (lit.,[11] 68—69°), eluted by light petroleum–ether (3 : 1), and unchanged *o*-nitroaniline (23 mmol), eluted by light petroleum–ether (1 : 1). Similar reaction (24 h) between 3-bromopyridine (45 mmol), *o*-nitroaniline (25 mmol), potassium carbonate (25 mmol), and copper bronze (0·2 g) in nitrobenzene yielded unchanged *o*-nitroaniline (5 mmol), eluted by light petroleum–ether (4 : 1), followed by red crystals of 3-*o*-nitroanilinopyridine (4) (4·0 g, 74%), m.p. 95° (lit.,[19] 95—96°), eluted by light petroleum–ether (1 : 1). A solution of 4-chloropyridine hydrochloride (40 mmol) and *o*-nitroaniline (33 mmol) in acetic acid (40 ml) was refluxed for 18 h. Solvent removal and chromatography yielded *o*-nitroacetanilide (19 mmol), m.p. 94°, eluted by light petroleum–ether (3 : 1), and then orange crystals of 4-*o*-nitroanilinopyridine (6) (1·6 g, 22%), m.p. 95° (lit.,[20] 80—81°), eluted by ether. When the preparation was carried out in refluxing dimethylacetamide the yield of the product, m.p. 93—95°, was only 6%.

A solution of 2-chloro-3-nitropyridine (20 mmol) and an excess of aniline (60 mmol) in di-n-butyl ether (25 ml) was heated under reflux (140°) for 2 h. Aniline hydrochloride was filtered off, solvent removed, and the residue chromatographed, yielding aniline, eluted by light petroleum, and red needles of 2-anilino-3-nitropyridine (7) (88%), m.p. 75° (lit.,[21] 75°), eluted by light petroleum–ether (2 : 1). Similar reactions were carried out (in di-n-butyl ether unless otherwise stated; period of refluxing shown in parentheses) on the following nuclear-substituted anilines. *o*-Toluidine (5 h) gave orange crystals of 3-nitro-2-*o*-toluidinopyridine (12) (70%), m.p. 125° (lit.,[22] 124—126°) after trituration of an oily product with methanol. *m*-Toluidine (5 g) gave orange crystals of 3-nitro-2-*m*-toluidinopyridine (10) (91%), m.p. 95° (from methanol) (lit.,[23] 95°). *p*-Toluidine (2 h, in refluxing dimethylacetamide) gave red crystals of 3-nitro-2-*p*-toluidinopyridine (8) (80%), m.p. 73° (from methanol) (lit.,[21] 73°); this was followed by the elution of *p*-toluidine (8 mmol) and then of *p*-methylacetanilide (10 mmol), identical with an authentic sample. 2,6-Xylidine (12 h, used in 4-fold excess) gave yellow crystals of 3-*nitro*-2-(2,6-*xylidino*)*pyridine* (13) (56%), m.p. 112° (Found: C, 64·1; H, 5·5; N, 17·1. $C_{13}H_{13}N_3O_2$ requires C, 64·3; H, 5·4; N, 17·3%), τ (100 MHz) 0·6 (s, NH), 1·51 (q, 4-H), 1·66 (q, 6-H), 2·83 (s, 3′-, 4′-, and 5′-H), 3·29 (q, 5-H), and 7·8 (s, 2′- and 6′-Me) ($J_{4.5}$ 8·3, $J_{4.6}$ 1·9, and $J_{5.6}$ 5·2 Hz); unchanged 2-chloro-3-nitropyridine (40%) was recovered. *o*-Anisidine (5 h) gave red crystals of 2-*o*-anisidino-3-nitropyridine (14) (79%), m.p. 151—152° (from methanol) (lit.,[24] 152—153°). *m*-Anisidine (3 h) gave red crystals of 2-*m*-anisidino-3-nitropyridine (11) (85%), m.p. 99—100° (from methanol) (lit.,[24] 100—101°). *p*-Anisidine (3 h) gave orange crystals of 2-*p*-anisidino-3-nitropyridine (9) (93%), m.p. 100° (from methanol) (lit.,[23] 83—84°).

4-Chloro-3-nitropyridine (40 mmol) was stirred with an excess of aniline (100 mmol) and the mixture kept for 1 h at 120°. Dichloromethane was added to the cold product, aniline hydrochloride filtered off, solvent removed and the residue chromatographed on silica gel. This gave the unchanged aniline, eluted by light petroleum–ether (7 : 3), followed by yellow crystals of 4-anilino-3-nitropyridine (3) (64%), m.p. 118° (lit.,[25] 118°), eluted by ether. Reaction between 4-chloro-3-nitropyridine (20 mmol) and *p*-toluidine (60 mmol) was carried out (2 h) in refluxing dimethylacetamide. Chromatography (light petroleum–ether) successively yielded yellow crystals of 3-nitro-4-*p*-toluidinopyridine (15) (80%), m.p. 123° (lit.,[21] 123°), *p*-toluidine (12 mmol), and *p*-methylacetanilide (6 mmol).

Cyclisation Procedure.—The nitro-amine (5 mmol) was intimately mixed in a mortar with iron(II) oxalate dihydrate (10 mmol). The mixture was transferred to a Pyrex tube fitted with an air condenser, lead shot (10 g) was mixed in as a heat conductor, and the tube heated in a Woods metal bath. At 200° water of hydration was evolved. The temperature was then raised to 260—280° and kept at this level for 10—15 min, when a vigorous reaction was generally visible, leaving a black powder. The tube was cooled, the contents extracted with dichloromethane, solvent removed, and the crude product chromatographed. The pyridoquinoxalines and, in some cases, trace amounts of by-products were thus isolated.

Pyrido[3,4-b]*quinoxaline* (1).—(*a*) Chromatography of the crude product from 4-anilino-3-nitropyridine (3) was carried out with light petroleum–ether (1 : 4) and yielded unchanged nitro-amine (1·3 mmol), followed by yellow crystals of pyrido[3,4-*b*]quinoxaline (0·19 g, 21%), m.p. 172°, unchanged by recrystallisation from light petroleum–ether or by sublimation (lit.,[8] m.p. 181—182°), *m/e* 181 (M^+), 154 (M − HCN), and 128 (M − HCN − C_2H_2), $\nu_{max.}$ 1590, 820, and 745 cm^{-1}, $\lambda_{max.}$ (MeOH) 209 (log ε 4·36), 248 (4·91), and 353 nm (3·94), τ (100 MHz) 0·28 (d, 1-H), 1·22 (d, 3-H), 1·65—1·85 (m, 6-H and 9-H), 2·01 (q, 4-H), and 2·05—2·2 (m, 7- and 8-H) ($J_{1.4}$ 0·8 and $J_{3.4}$ 6·0 Hz); the 4-H assignment was confirmed by spin–spin decoupling and by a 220 MHz spectrum. Continuation of chromatography with ether–chloroform (1 : 1) gave traces of a red (?) dimer, m.p. 263—265° (Found: M^+, 362·1280. Calc. for $C_{22}H_{14}N_6$: M, 362·1280), *m/e* 362, 361 (M − H), 209, and 182 ($M/2$ + H).

(*b*) The crude product from 4-*o*-nitroanilinopyridine (6) gave unchanged nitro-amine (0·4 mmol) and pyrido[3,4-*b*]-quinoxaline (0·055 g, 6%), identical in m.p. and spectroscopic properties with the product in (*a*).

(*c*) See under (*c*) for the [2,3-*b*]-isomer.

Pyrido[2,3-b]*quinoxaline* (2).—(*a*) Chromatography of the product from 2-anilino-3-nitropyridine (7) gave unchanged nitro-amine (2·5 mmol), eluted by light petroleum–ether (2 : 1). Ether then gave traces of a red solid, (?) 2,2′-*dianilino*-3,3′-*azopyridine*, m.p. 241—243° (Found: M^+, 366·1595. $C_{22}H_{18}N_6$ requires M, 366·1593), *m/e* 366, 183 ($M/2$), 182 ($M/2$ − H), and 169 ($M/2$ − N). Further elution, with chloroform, gave a black solid, which, on vacuum sublimation, afforded yellow crystals of *pyrido*-[2,3-b]*quinoxaline* (0·18 g, 20%), m.p. 176° (Found: C, 73·3; H, 4·2; N, 23·0. $C_{11}H_7N_3$ requires C, 73·0; H, 3·9; N, 23·1%), *m/e* 181 (M^+), 154 (M − HCN), and 128 (M − HCN − C_2H_2), $\nu_{max.}$ 1505, 1410, and 740 cm^-, $\lambda_{max.}$ (MeOH) 208 (log ε 4·34), 245 (4·67), and 358 nm (4·27), τ (100 MHz) 0·61 (q, 2-H), 1·39 (q, 4-H), 2·21 (q, 3-H), 1·5—1·8 (m, 6-H and 9-H), and 2·0—2·2 (m, 7-H and 8-H) ($J_{2.3}$ 3·9, $J_{2.4}$ 1·95, and $J_{3.4}$ 8·7 Hz).

(*b*) 2-Anilino-3-nitropyridine (5 mmol) was added to purified diethylene glycol diethyl ether (25 ml) alone, and the solution was refluxed (186°) under nitrogen for 24 h.

[19] R. A. Abramovitch, *Canad. J. Chem.*, 1960, **38**, 2273.
[20] A. T. Peters, *J. Soc. Dyers and Colourists*, 1970, **86**, 77.
[21] R. R. Bishop, E. A. S. Cavell, and N. B. Chapman, *J. Chem. Soc.*, 1952, 437.
[22] W. Gruber, *Canad. J. Chem.*, 1953, **31**, 1181.
[23] E. A. S. Cavell and N. B. Chapman, *J. Chem. Soc.*, 1953, 3392.
[24] M. G. W. Bell, M. Day, and A. T. Peters, *J. Chem. Soc.* (*C*), 1967, 132.
[25] O. Bremer, *Annalen*, 1934, **514**, 279.

Chromatography yielded unchanged nitro-amine (4 mmol), a trace of the presumed azo-compound, m.p. 242°, and pyrido[2,3-*b*]quinoxaline (30 mg, 3%), m.p. 176°.

(*c*) Chromatography of the product from 3-*o*-nitroanilinopyridine (4) gave pyrido[3,4-*b*]quinoxaline (0·09 g, 10%), eluted by light petroleum–ether (100 : 1), followed by pyrido[2,3-*b*]quinoxaline (0·24 g, 27%), eluted by light petroleum–ether (4 : 1). The two products were identical in m.p. and spectroscopic properties with those described above.

(*d*) The product from 2-*o*-anisidino-3-nitropyridine (14) gave unchanged nitro-amine (0·5 mmol), eluted by petroleum, followed by pyrido[2,3-*b*]quinoxaline (12%), m.p. 176°, eluted by ether–chloroform (50 : 1) and characterised spectroscopically.

(*e*) After treatment of 2-*o*-nitroanilinopyridine (5) the only crystalline material isolated was unchanged nitro-amine (2 mmol).

7-*Methylpyrido*[2,3-b]*quinoxaline* (16).—The product from 3-nitro-2-*p*-toluidinopyridine (8) yielded unchanged nitro-amine (2·8 mmol), eluted by light petroleum, followed by traces of a red solid, (?) 2,2′-*di*-p-*toluidino*-3,3′-*azopyridine*, m.p. 279° (Found: M^+, 394·1908. $C_{24}H_{22}N_6$ requires M, 394·1906), *m/e* 394, 197 ($M/2$), 196 ($M/2$ — H), 183 ($M/2$ — N), and 168 ($M/2$ — N — Me). Ether eluted yellow crystals of the *pyridoquinoxaline* (16) (0·11 g, 11%), m.p. 136—139°, raised to 140—141° by sublimation (Found: C, 73·7; H, 4·8; N, 21·4. $C_{12}H_9N_3$ requires C, 73·9; H, 4·6; N, 21·5%), *m/e* 195 (M^+), $\nu_{max.}$ 1510, 1420, and 790 cm^{-1}, τ 0·7 (q, 2-H), 1·45 (q, 4-H), 1·75 (d, 9-H), 2·02 (q, 6-H), 2·28 (q, 3-H), 2·3 (q, 8-H), 7·35 (d, Me) [$J_{2.3}$ 4·0, $J_{2.4}$ 2·0, $J_{3.4}$ 8·5, $J_{8.9}$ 8·9, and $J_{6.Me}$ 1·1 Hz (assignment checked by spin–spin decoupling)].

6- *and* 8-*Methylpyrido*[2,3-b]*quinoxaline*.—The product from 3-nitro-2-*m*-toluidinopyridine (10) similarly gave unchanged nitro-amine (1·5 mmol) and traces of (?) 2,2′-*di*-m-*toluidino*-3,3′-*azopyridine*, m.p. 265° (Found: M^+, 394·1905). Elution with light petroleum–ether (4 : 1) gave yellow crystalline fractions (0·09 g, 9%), m.p. 120—150°, consisting of 6- and 8-methylpyrido[2,3-*b*]quinoxaline (18) and (20) (Found: C, 73·6; H, 4·7; N, 21·6%), *m/e* 195 (M^+), τ 0·68 (q, 2-H), 1·42 (q, 4-H), 1·6—2·5 (m, all other nuclear H), 7·1 (d, 6-Me), and 7·35 (d, 8-Me) ($J_{7.6\text{-Me}}$ 1·1 and $J_{9.8\text{-Me}}$ 1·0 Hz); the ratio 6-Me : 8-Me, from the integral curve, was 2·4 : 1.

9-*Methylpyrido*[2,3-b]*quinoxaline* (22).—(*a*) The product from 3-nitro-2-*o*-toluidinopyridine (12) similarly gave unchanged nitro-amine (0·8 mmol) and traces of (?) 2,2′-*di*-o-*toluidino*-3,3′-*azopyridine*, m.p. 263° (Found: M^+, 394·1906). Elution with light petroleum–ether (4 : 1) then gave yellow crystals of the *methylquinoxaline* (22) (0·12 g, 12%), m.p. 132—134°, raised to 135° by sublimation (Found: C, 74·0; H, 4·6; N, 21·7%), τ 0·62 (q, 2-H), 1·37 (q, 4-H), 1·7—2·35 (m, 3-, 6-, 7-, and 8-H), and 7·0 (d, Me) ($J_{2.3}$ 4·0, $J_{2.4}$ 1·9, $J_{3.4}$ 8·7, and $J_{8.Me}$ 1·0 Hz).

(*b*) The product from 3-nitro-2-(2,6-xylidino)pyridine (13) gave unchanged nitro-amine (0·6 mmol) and yellow crystals of 9-methylpyrido[2,3-*b*]quinoxaline (0·04 g, 4%), identical in m.p. and spectroscopic properties with the product obtained in (*a*).

8-*Methylpyrido*[3,4-b]*quinoxaline* (23).—The product from 3-nitro-4-*p*-toluidinopyridine (15) gave unchanged nitro-amine (1 mmol). Elution by light petroleum–ether (4 : 1) then gave yellow crystals of the pyridoquinoxaline (23) (0·1 g, 10%), m.p. 152—153° (lit.,[8] 148°), *m/e* 195 (M^+), $\nu_{max.}$ 2920, 1440, and 815 cm^{-1}, τ 0·32 (d, 1-H), 1·23 (d, 3-H), 1·92 (d, 6-H), 2·03 (q, 4-H), 2·05 (q, 9-H), 2·31 (q, 7-H), and 7·38 (d, Me) [$J_{1.4}$ 0·9, $J_{3.4}$ 6·0, $J_{6.7}$ 8·7, $J_{7.9}$ 2·0, and $J_{9.Me}$ 1·0 Hz (assignment checked by spin–spin decoupling)]. Elution by ether afforded a trace of a red (?) dimer, m.p. 252° (Found: M^+, 390·1593. Calc. for $C_{24}H_{18}N_6$: M, 390·1593).

7-*Methoxypyrido*[2,3-b]*quinoxaline* (17).—Elution of the product from 2-*p*-anisidino-3-nitropyridine (9) with light petroleum gave unchanged nitro-amine (0·5 mmol). Ether–chloroform (1 : 1) gave yellow crystals of the *pyridoquinoxaline* (17) (0·06 g, 6%), m.p. 196—199°, raised to 200° by sublimation (Found: C, 68·2; H, 4·5; N, 19·8. $C_{12}H_9N_3O$ requires C, 68·35; H, 4·3; N, 19·9%), *m/e* 211 (M^+), 196 (M — Me), 181 (M — CH_2O), and 168 (M — COMe), τ 0·72 (q, 2-H), 1·48 (q, 4-H), 1·75 (d, 9-H), 2·26 (q, 3-H), 2·44 (q, 8-H), 2·61 (d, 6-H), and 5·95 (s, Me) ($J_{2.3}$ 3·7, $J_{2.4}$ 1·9, $J_{3.4}$ 8·8, $J_{6.8}$ 2·5, and $J_{8.9}$ 9·4 Hz).

6- *and* 8-*Methoxypyrido*[2,3-b]*quinoxaline*.—Elution with light petroleum of the product from 2-*m*-anisidino-3-nitropyridine (11) gave unchanged nitro-amine (2 mmol), followed by trace amounts of red crystals of (?) 2,2′-*di*-m-*anisidino*-3,3′-*azopyridine*, m.p. 149° (Found: M^+, 426·1804. $C_{24}H_{22}N_6O_2$ requires M, 426·1804), *m/e* 426, 213 ($M/2$), 212 ($M/2$ — H), and 199 ($M/2$ — N). Chloroform eluted yellow crystals, m.p. 150—190°, consisting of a mixture of 6- and 8-methoxypyrido[2,3-*b*]quinoxaline (19) and (21) (0·17 g, 16%) (Found: C, 68·4; H, 4·1; N, 20·1%); superimposed n.m.r. spectra, τ 0·65 (q, 2-H), 1·25 (q, 4-H), and 5·83 (s, 6-OMe) for the 6-isomer, 0·72 (q, 2-H), 2·46 (q, 4-H), and 5·97 (s, 8-OMe) for the 8-isomer, 1·8—2·6 (m, all other nuclear protons); ratio, 6-methoxy- : 8-methoxy-isomer, 1 : 2·5 from the integral curve.

1- *and* 2-*Methylphenazine*.—A mixture of *m*-toluidine (80 mmol), *o*-chloronitrobenzene (40 mmol), and anhydrous sodium acetate (40 mmol) was kept at 180° for 50 h and the product chromatographed. Light petroleum eluted unchanged *o*-chloronitrobenzene (15 mmol), followed by a red oil, which, when triturated with methanol, gave red crystals of 3-methyl-2′-nitrodiphenylamine (26; X = Me) (4·4 g, 48%), m.p. 74° (lit.,[26] 70—71°). After heating the nitro-amine (5 mmol) with iron(II) oxalate, chromatography with light petroleum gave unchanged nitro-amine (1·3 mmol), followed by fractions, m.p. 105—115° consisting of 1- and 2-methylphenazine (27) and (28) (X = Me) (0·51 g, 53%) (lit.,[4e] m.p. 107—108° for the 1-methyl- and 117° for the 2-methyl-isomer), τ 1·6—2·5 (all nuclear H), 7·08 (d, 1-Me), and 7·4 (d, 2-Me) ($J_{2.1\text{-Me}}$ 0·9 and $J_{1.2\text{-Me}}$ 0·9 Hz); ratio, 1-methyl- : 2-methyl-isomer, 2·2 : 1 from the integral curve.

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[26] J. G. Belton and M. McInerney, *Proc. Roy. Irish Acad., Section B*, 1970, **69**, 21.