Metal Ions and Complexes in Organic Reactions. Part XVIII.[1] Structural Variations in the Production of Polycyclic Heterocyclic Systems by Iron-(II)-promoted Cyclisations of Nitro-substituted Precursors

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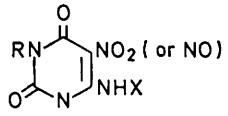
Syntheses are described involving intermediates with a nitro-substituent *ortho* to the internuclear linkage in structures X–Y or X–NH–Y, where X = phenyl and Y = thienyl, pyrazolyl, imidazolyl, or pyrimidinyl. Heating these compounds with iron(II) oxalate at *ca.* 280° gave chiefly the corresponding primary amines (up to *ca.* 65%), sometimes with the corresponding azo-compound. Competitive cyclisation, through the nitro-group, gave compounds (5—20%) in the following polycyclic series: thieno[2.3-*b*]quinoxaline (3), imidazo[1.2-*a*]quinoxaline (7), benzimidazo[1.2-*a*]quinoxaline (9), and benzo[*g*]pteridine (11): a 2-methyl substituent on an imidazole nucleus contributed to the central pyrazine ring in structures (7) and (9). *o*-Nitrodiphenylmethane gave *o*-aminobenzophenone and acridone. Nitro(pyridylamino)pyridines were synthesised as potential sources of dipyridopyrazines but they readily underwent fission to the corresponding aminonitropyridines.

In the preceding paper[1] we reported syntheses of pyridoquinoxalines by iron(II)-promoted deoxygenative thermal cyclisation, involving mixtures of iron(II) oxalate with nitro-substituted anilinopyridines, a transformation analogous to that of *o*-nitrodiarylamines into phenazines. Syntheses exemplifying other variations in component rings or in ring substituents have been described: *e.g.* in their original account of this synthesis of phenazines, Waterman and Vivian[2a] also demonstrated the production of carbazole, benzocinnoline, benzimidazole, and acridine ring systems from nitro-compounds of appropriate structure; later, pyrido- and benzofuro-phenazines were prepared.[2b] More recently, intramolecular reactions of uracil derivatives (1) (without a deoxygenating agent) have given alloxazines (X = Ar)[3] and pyrimidopteridines (X = another uracil system).[4]



(1)

We have applied a cyclisation procedure of the usual type [brief heating with iron(II) oxalate at *ca.* 280°] to a selection of compounds in which the common feature was a nitro-group adjacent to a linkage between two rings; the results are summarised in the Table. In compounds (2), (4), (5), (6), and (8), the linkage, direct or through –NH–, was between a phenyl group and a five-membered heterocycle; relative preparative convenience determined which ring should contain the nitro-group. In compounds (10) and (12) respectively, the linkage was with a pyrimidine nucleus *via* –NH–, and with a second benzene nucleus *via* $-CH_2-$.

As detailed below, the chief effect observed overall was not cyclisation through the nitro-group but reduction of it to give the corresponding primary amine (10—65%), and in some cases the corresponding azo-compound. Competitive cyclisation was effective, however, in five of the seven systems examined, giving the polycyclic compounds (3), (7), (9), (11), and (13) (5—20%). In syntheses of pyridoquinoxalines[1] reduction had been manifested only by the appearance of trace amounts of azo-compounds.

Thienoquinoxalines (*see Table*).—Alternative modes of fusion between thiophen and pyrazine rings are displayed in thieno[2,3-*b*]quinoxaline (3), which seems to be unrepresented in the literature, and by the [3,4-*b*]-isomer, which is represented by derivatives of a dihydroform.[5] Cyclisation of an intermediate with a nitro-group on the benzene ring could not be tested because of the failure of reaction between *o*-nitroaniline and 2-iodothiophen. However, 3-bromo-2-nitrothiophen was readily converted into the 3-anilino-compound (2) and this, when heated with iron(II) oxalate, cyclised to thieno[2,3-*b*]quinoxaline (3), in low yield; this was the only crystalline product. It resembled the pyridoquinoxalines[1] in its colour and u.v. spectrum, and in certain features of the mass and ^1H n.m.r. spectra. The latter showed the expected difference in the chemical shifts of the 5- and 8-protons relative to the 6- and 7-protons, and in shifts of the coupled 2- and 3-protons relative to the corresponding signals in thiophen.[6]

Uncertainty has been recorded[7] concerning the orientation of substituents in the bromonitrothiophen, which was prepared by nitration as the first step in the synthesis, but we found the n.m.r. spectrum to be in

[1] Part XVII, R. G. R. Bacon and S. D. Hamilton, preceding paper.

[2] (*a*) H. C. Waterman and D. L. Vivian, *J. Org. Chem.*, 1949, **14**, 289; (*b*) D. L. Vivian, J. L. Hartwell, and H. C. Waterman, *ibid.*, 1954, **19**, 1641; (*c*) D. L. Vivian and H. C. Waterman, *ibid.*, 1956, **21**, 914.

[3] H. Goldner, G. Dietz, and E. Carstens, *Annalen*, 1966, **694**, 142.

[4] Y. Maki, M. Sako, and E. C. Taylor, *Tetrahedron Letters*, 1971, 4271.

[5] C. G. Overberger, R. A. Gadea, J. A. Smith, and I. C. Kogon, *J. Amer. Chem. Soc.*, 1953, **75**, 2075.

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

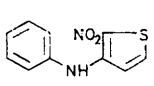
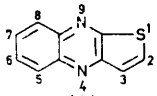
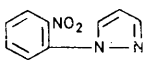
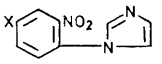
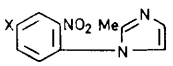
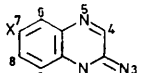
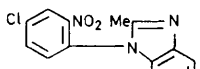
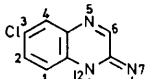
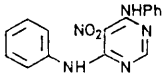
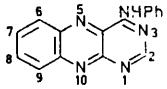
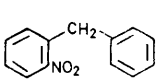
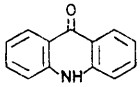
[7] W. Steinkopf, H. Jacob, and H. Penz, *Annalen*, 1934, **512**, 136; C. D. Hurd and K. L. Kreuz, *J. Amer. Chem. Soc.*, 1952, **74**, 2965; *cf.* H. D. Hartough, 'Thiophen and its Derivatives,' Interscience, New York, 1952, p. 223.

agreement with the 3-bromo-2-nitro-structure. Moreover, cyclisation necessitates the substituents being on adjacent carbon atoms, and, if the orientation was 3-bromo-4-nitro, the product would be thieno[3,4-*b*]-quinoxaline; this is disproved by the nature of the n.m.r. spectrum.

(5), but, in view of the capacity of the deoxygenated nitro-group to acquire hydrogen, cyclisation could conceivably give the imidazobenzimidazole structure (16), which is represented in the literature by the 2,3-diphenyl derivative.[9]

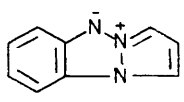
The desired polycyclic compounds were not isolated

Cyclisation of nitro-compounds with iron(II) oxalate

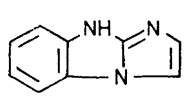
Nitro-compound	Cyclised compound	Yield (%)	Other products *	Yield (%)
 (2)	 (3)	5		
 (4)			Primary amine Azo-compound	29 Trace
 (5)			Primary amine	49 (X = H) 43 (X = Cl)
 (6)	 (7)	13 (X = H) 16 (X = Cl)	Primary amine	64 (X = H) 43 (X = Cl)
 (8)	 (9)	19	Primary amine Azo-compound	10 14
 (10)	 (11)	19		
 (12)	 (13)	9	*o*-Aminobenzophenone (14)	37

* Corresponding with the nitro-compound.

Cyclisations onto Azole Rings; Imidazo- and Benzimidazo-[1,2-a]*quinoxalines* (*see Table*).—Copper-catalysed substitution reactions between aryl halides and the NH< function of pyrazoles or imidazoles provide ready access to the 1-*o*-nitroaryl derivatives and thence, potentially, to polycyclic systems incorporating two fused azole rings. Thus, 1-*o*-nitrophenylpyrazole (4) gave pyrazo[1,2-*b*]benzotriazole (15) when heated with triethyl phosphite,[8] the cyclisation occurring, as expected (*cf.* ref. 1), onto the 2-nitrogen atom of the pyrazole ring. Corresponding cyclisation onto nitrogen is not possible in the case of 1-*o*-nitrophenylimidazole when either (4) or (5) was heated with iron(II) oxalate. The products, consisting of primary amines, with traces of the corresponding azo-compound, exemplify the



(15)



(16)

occurrence of NO_2 reduction without cyclisation, which has been noted in some previous cases. Thus, heating nitro-arenes with iron(II) oxalate gave azo- and azoxy-compounds,[10b] 2,4,6-trimethyl-2′-nitrobiphenyl gave the

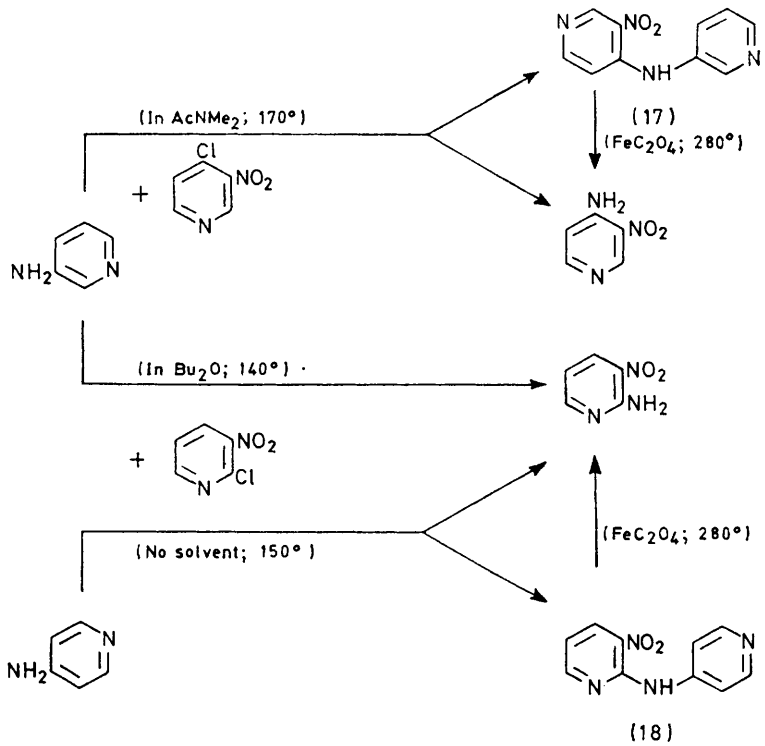
[8] B. M. Lynch and Y.-Y. Hung, *J. Heterocyclic Chem.*, 1965, **2**, 218.

[9] R. Gompper and F. Effenberger, *Chem. Ber.*, 1959, **92**, 1929.

[10] (*a*) R. A. Abramovitch, D. Newman, and G. Tertzakian, *Canad. J. Chem.*, 1963, **41**, 2390; (*b*) R. A. Abramovitch and B. A. Davis, *J. Chem. Soc.* (*C*), 1968, 119.

amine (in competition with cyclisation),[10a] and *o*-nitrodiphenyl sulphide gave the azo-compound, whilst the corresponding sulphone gave the amine.[2c] It has been pointed out [10a] that the hydrogen needed for amine production is presumably furnished by decomposition of some of the nitro-compound, the transfer perhaps being catalysed by iron species. A parallel case may be cited in the substitutive reduction of aryl halides (ArHal ⟶ ArH), with resinification of some of the halide, which may accompany Ullmann coupling (2ArHal ⟶ ArAr) in reactions involving copper at *ca.* 200°;[11] such metal-promoted reductions may be dominant in systems containing aryl halides, copper species, and various aromatic hydrogen donors, which include nitro-arenes.[12]

It is known that a suitably situated methyl group in one ring may interact with a nitro-group in the other, generating the central ring of the polycyclic product, *e.g.* producing a phenanthridine [with iron(II) oxalate] [10a] or a dibenzothiazepine (with triethyl phosphite).[13] Accordingly we prepared and tested the 2-methyl-1-*o*-nitroaryl-imidazoles (6) and -benzimidazole (8), in which a central pyrazine ring might thus be generated on heating with iron(II) oxalate. The desired cyclisation competed fairly successfully with the formation of reduced products in these cases. The 2-methyl-1-*o*-nitroarylimidazoles thus yielded the imidazo[1,2-*a*]quinoxalines (7; X = H or Cl); the parent heterocycle (X = H) was recently synthesised by a different route.[14] Likewise the benzimidazole derivative (8) yielded 3-chlorobenzimidazo[1,2-*a*]quinoxaline (9). In this latter reaction it was theoretically possible that cyclisation might alternatively occur at the 7-position in the benzimidazole system, giving an imidazophenazine, but no such product was detected. The ^{1}H n.m.r. spectra of the cyclisation products showed some similarities to those of the other quinoxalines synthesised.[1] The lowest-field signals were those of 4-H in (7) (τ 0·85) and 6-H in (9) (τ 0·83), *i.e.* similar to that of 6-H in phenanthridine (τ 0·87). The yield of accompanying amine was much higher than that of cyclised product from the imidazole derivatives (6), but in the case of the benzimidazole derivative (8) the effect was fairly evenly divided between reduction and cyclisation, and the reduced product consisted of comparable amounts of amine and azo-compound.



(18)

Having available 2-methyl-1-*o*-nitrophenylimidazole (6; X = H), we tested its reaction with methanolic alkali, which was found [15] to cyclise 2′-substituted 2-nitrobiphenyls to phenanthridines when the 2′-substituent was CH_2·CO_2Me, CH_2·CN, *etc.*, but not when it was Me. Cyclisation likewise failed with the methyl-substituted compound (6), which was reduced to the

[11] P. E. Fanta, *Chem. Rev.*, 1964, **64**, 613; R. G. R. Bacon and H. A. O. Hill, *Quart. Rev.*, 1965, **19**, 95.
[12] R. G. R. Bacon and O. J. Stewart, *J. Chem. Soc.* (*C*), 1969, 301.
[13] J. I. G. Cadogan and S. Kulik, *J. Chem. Soc.* (*C*), 1971, 2621.
[14] A. M. Simonov and I. G. Uryukina, *Khim. geterotsikl. Soedinenii*, 1971, **7**, 570 (*Chem. Abs.*, 1972, **76**, 25,242).
[15] C. W. Muth, J. C. Ellers, and O. F. Folmer, *J. Amer. Chem. Soc.*, 1957, **79**, 6500; C. W. Muth, N. Abraham, M. L. Linfield, R. B. Wotring, and E. A. Pacofsky, *J. Org. Chem.*, 1960, **25**, 736.

corresponding azo compound and amine, in major and minor yield respectively.

4-Anilinobenzo[g]*pteridine* (*see Table*).—Benzo[g]pteridine (pyrimido[4,5-*b*]quinoxaline) is of interest as being the parent ring system of the biologically important alloxazines. Accessible synthetic intermediates were 2,4- and 4,6-dichloro-5-nitropyrimidine. In the former compound the greater reactivity of the 4-chloro-substituent permitted preparation of either 4-anilino-2-chloro- or 2,4-dianilino-5-nitropyrimidine, but neither of these derivatives yielded identifiable products when heated with iron(II) oxalate. The equal reactivity of the two halogen atoms in 4,6-dichloro-5-nitropyrimidine resulted in production of 4,6-dianilino-5-nitropyrimidine (10) exclusively. Cyclisation of this compound was successful, giving 4-anilinobenzo[g]pteridine (11), and no amine or azo-compound was isolated. This compound gave a complex n.m.r. spectrum in which a low-field signal due to the 2-proton was distinguished.

Acridone (*see Table*).—It has been reported [16] that heating *o*-nitrodiphenylmethane (12) produced acridone (13) and a trace of *o*-aminobenzophenone (14), *i.e.* there are complex transformations involving deoxygenation of the nitro-group, oxidation at the benzylic centre, and cyclisation. It has been suggested [17] that oxygen transfer may involve an anthranil intermediate. There is also a report [2a] that heating *o*-nitrobenzophenone with iron(II) oxalate gave a trace of acridine, but the experimental evidence for this was inadequate. We heated *o*-nitrodiphenylmethane in the presence and in the absence of iron(II) oxalate and obtained acridone in both cases. *o*-Aminobenzophenone was produced in comparable amount when iron(II) oxalate was absent and was the major product in its presence.

Fission Reactions of Nitro(pyridylamino)pyridines.—We sought to extend the cyclisation procedure to the synthesis of dipyridopyrazines, of which the only representative to date appears to be the [3,4-*b*:3′,4′-*e*]-isomer.[18] For this purpose 3-nitro-4-(3-pyridylamino)-pyridine (17) and 3-nitro-2-(4-pyridylamino)pyridine (18) were prepared from an appropriate aminopyridine and chloronitropyridine: their cyclisation failed (see Scheme). This failure is apparently due to the instability of the nitro(pyridylamino)pyridines, which is manifested well below temperatures customary for cyclisation; fission occurs, with conversion of the pyridylamino- into an amino-substituent. This was observed not only when the nitro-amines were heated with iron(II) oxalate, but also during their preparation, which was carried out at 140—170°. An attempt to prepare 3-nitro-2-(3-pyridylamino)pyridine gave 2-amino-3-nitropyridine exclusively.

EXPERIMENTAL

As previously described,[1] cyclisations were attempted by heating the nitro-compound (5 mmol) with iron(II) oxalate at 260—280°, and the products were separated chromatographically on a column of deactivated alumina. M.p.s were determined on a Kofler block and n.m.r. spectra (unless otherwise stated) were taken at 60 MHz.

Thieno[2,3-b]*quinoxaline.*—3-Bromothiophen (5 g) in acetic anhydride was cooled to −5° and nitric acid (*d* 1·5; 5 g) in acetic anhydride (10 ml) was added dropwise over 1 h, keeping the temperature below 0°. The mixture was kept overnight in a refrigerator and the precipitate, augmented by material obtained by dilution with water, was purified by recrystallisation from ethanol and by chromatography, which afforded yellow 3-bromo-2-nitrothiophen (56%), m.p. 80° (lit.,[7] 80—81·5°, 81—83°), τ (100 MHz) 2·52 (d, 5-H), 2·91 (d, 4-H) ($J_{4,5}$ 6·0 Hz). A solution of aniline (20 mmol) and 3-bromo-2-nitrothiophen (10 mmol) in di-n-butyl ether (25 ml) was refluxed for 12 h. Aniline hydrobromide was filtered off, solvent evaporated, and the residue chromatographed. Light petroleum eluted a trace of 3-bromo-2-nitrothiophen and light petroleum–ether (5 : 1) gave orange *3-anilino-2-nitrothiophen* (2) (89%), m.p. 104° (Found: C, 54·5; H, 3·7; N, 12·9; S, 14·4. $C_{10}H_8N_2O_2S$ requires C, 54·6; H, 3·7; N, 12·8; S, 14·6%), *m/e* 220 (M^+), τ 3·18 (d, 4-H), 2·6—2·9 (m, all other H) ($J_{4,5}$ 6·0 Hz).

Heating this compound with iron(II) oxalate, followed by chromatography with light petroleum–ether (5 : 1) gave unchanged nitro-amine (12%), and then pale yellow *thieno*[2,3-b]*quinoxaline* (3) (0·047 g, 5%), m.p. 114° (Found: C, 64·5; H, 3·0; N, 15·1; S, 17·4. $C_{10}H_6N_2S$ requires C, 64·5; H, 3·25; N, 15·05; S, 17·25%), *m/e* 186 (M^+), 160 ($M - C_2H_2$), and 159 (M − HCN), $\nu_{max.}$ 1060, 750, and 685 cm^{-1}, $\lambda_{max.}$ (MeOH) 208 (log ε 4·15), 253 (4·76), and 341 nm (4·00), τ 1·55—1·83 (m, 5-H and 8-H), 1·88 (d, 3-H), 2·0—2·23 (m, 6-H and 7-H), and 2·35 (d, 2-H) ($J_{2,3}$ 6·0 Hz).

Pyrazole Derivatives.—1-*o*-Nitrophenylpyrazole (4) was prepared by an Ullmann-type condensation [19] and was obtained after chromatography as crystals (23%), m.p. 88° (lit.,[19] 85—87°). After heating with iron(II) oxalate the product was extracted with dichloromethane (other solvents yielded no further material) and the extract chromatographed with ether, yielding 1-*o*-*aminophenylpyrazole* (0·23 g, 29%), m.p. 45° (Found: C, 68·0; H, 5·4; N, 26·5. $C_9H_9N_3$ requires C, 67·9; H, 5·7; N, 26·4%), *m/e* 159 (M^+) and 132 (M − HCN), $\nu_{max.}$ 3440, 3350, and 750 cm^{-1}, τ 2·2—2·3 (6H, m), 3·57 (t, 4-H), 5·55br (s, NH_2) ($J_{3,4}$ and $J_{4,5}$ 2·0 Hz). This was followed by a trace of *oo*′-di-(pyrazol-1-yl)azobenzene (Found: M^+, 314·1278. Calc. for $C_{18}H_{14}N_6$: M, 314·1280), m.p. 167° (lit.,[8] 167°), *m/e* 314 (M^+, Ar_2N_2), 287 (M − HCN), 171 (M − Ar), 143 (Ar^+), and 116 (Ar − HCN).

Imidazole Derivatives.—An Ullmann-type condensation of imidazole with *o*-bromonitrobenzene [20] and chromatographic purification gave 1-*o*-nitrophenylimidazole (5; X = H) (54%), m.p. 96—98° (lit.,[20] 95—96°). After heating with iron(II) oxalate, chromatography with ether gave a trace of unchanged nitro-compound, whilst elution with chloroform afforded 1-*o*-aminophenylimidazole (0·39 g, 49%), m.p. 104° (lit.,[21] 106°), *m/e* 159 (M^+). Imidazole and 2,5-dichloronitrobenzene similarly gave 1-(4-chloro-2-nitrophenyl)imidazole (5; X = Cl) (53%), m.p. 77—79° (lit.,[20]

[16] A. Kliegl, *Ber.*, 1909, **42**, 591.
[17] J. D. Loudon and G. Tennant, *Quart. Rev.*, 1964, **18**, 389; P. N. Preston and G. Tennant, *Chem. Rev.*, 1972, **72**, 627.
[18] E. Koenigs and G. Jung, *J. prakt. Chem.*, 1933, **137**, 141.
[19] M. A. Khan and J. B. Polya, *J. Chem. Soc.* (*C*), 1970, 85.
[20] A. L. Johnson, J. C. Kauer, D. C. Sharma, and R. I. Dorfman, *J. Medicin. Chem.*, 1969, **12**, 1024.
[21] A. F. Pozharskii, A. M. Simonov, and L. M. Sitkina, *Khim. geterotsikl. Soedinenii*, 1969, **5**, 916 (*Chem. Abs.*, 1970, **72**, 111,427).

94—95°), *m/e* 225/223 (M^+), τ 1·97 (d, 3′-H), 2·23 (q, 5′-H), 2·35 (s, 2-H), 2·53 (d, 6′-H), 2·77 (s, 5-H), and 2·9 (s, 4-H) ($J_{3',5'}$ 2·0 and $J_{5',6'}$ 8·5 Hz). After heating with iron(II) oxalate a trace of unchanged nitro-compound was recovered, followed by 1-(2-*amino*-4-*chlorophenyl*)*imidazole* (0·42 g, 43%), m.p. 150° (Found: C, 55·5; H, 4·1; Cl, 18·4; N, 21·8. $C_9H_8ClN_3$ requires C, 55·8; H, 4·2; Cl, 18·3; N, 21·7%), *m/e* 195/193 (M^+), $\nu_{max.}$ 3400 and 3200 cm^{-1}, τ 2·41 (s, 2-H), 2·7—3·4 (m, all other nuclear H), and 6·2br (s, NH_2).

2-Methylimidazole Derivatives.—(*a*) 2-Methylimidazole and *o*-bromonitrobenzene were similarly converted into 2-methyl-1-*o*-nitrophenylimidazole (6; X = H) (38%), m.p. 88° (lit.,[21] 88—89°), *m/e* 203 (M^+). After heating with iron(II) oxalate, chromatography with ether gave crystals of imidazo[1,2-*a*]quinoxaline (7; X = H) (0·11 g, 13%), m.p. 115—118°, raised to 119° by sublimation (lit.,[14] 124°) (Found: C, 71·2; H, 4·2; N, 24·7. Calc. for $C_{10}H_7N_3$: C, 71·0; H, 4·2; N, 24·8%), *m/e* 169 (M^+) and 142 (M — HCN), $\nu_{max.}$ 1470, 1370, 1335, and 745 cm^{-1}, $\lambda_{max.}$ (MeOH) 210 (log ε 4·20), 229 (4·36), and 315 nm (3·98), τ 0·85 (s, 10-H) and 1·75—2·5 (m, all other protons). Further elution, with ether–chloroform (3 : 1) gave 1-*o*-aminophenyl-2-methylimidazole (0·55 g, 64%), m.p. 130—134°, raised to 136° by sublimation (lit.,[21] 135—136°), *m/e* 173 (M^+), $\nu_{max.}$ 3330 and 3250 cm^{-1}, τ 2·55—3·35 (m, all nuclear H), 6·25br (s, NH_2), and 7,75 (s, Me). Heating 2-methyl-1-*o*-nitrophenylimidazole alone for 30 min at 270—300° resulted in recovery of the nitro-compound (95%) and isolation of only a trace of imidazo[1,2-*a*]quinoxaline.

A solution of 2-methyl-1-*o*-nitrophenylimidazole (3 mmol) and potassium hydroxide (4 mmol) in methanol (30 ml) was refluxed for 1 h. Chromatography of the product with ether–chloroform (3 : 1) gave 1-*o*-aminophenyl-2-methylimidazole (14%), followed by red crystals of *oo′-bis*-(2-*methylimidazol*-1-*yl*)*azobenzene* (0·30 g, 58%), m.p. 227—229° (from acetone) (Found: C, 70·0; H, 5·4; N, 24·7. $C_{20}H_{18}N_6$ requires C, 70·2; H, 5·3; N, 24·5%), *m/e* 342 (M^+), τ 2·5 (s, all benzenoid H), 2·94 (d, all imidazole H), and 7·78 (s, 2 Me); decolourisation resulted on treatment with titanium(III) chloride in dilute hydrochloric acid.[1]

(*b*) 2-Methylimidazole and 2,5-dichloronitrobenzene similarly gave 1-(4-*chloro*-2-*nitrophenyl*)-2-*methylimidazole* (6; X = Cl) (33%), m.p. 105° (Found: C, 50·3; H, 3·3; Cl, 15·0; N, 17·7. $C_{10}H_8ClN_3O_2$ requires C, 50·5; H, 3·4; Cl, 14·9; N, 17·7%), *m/e* 239/237 (M^+), τ 1·92 (d, 3′-H), 2·22 (q, 5′-H), 2·57 (d, 6′-H), 2·93 (s, 5-H), 3·07 (s, 4-H), and 7·77 (s, Me) ($J_{3',5'}$ 2·0 and $J_{5',6'}$ 8·5 Hz). Heating with iron(II) oxalate and chromatography with ether gave 7-*chloroimidazo*[1,2-a]*quinoxaline* (7; X = Cl) (0·16 g, 16%), m.p. 226—230°, raised to 230° by sublimation (Found: C, 58·8; H, 2·8; Cl, 17·6; N, 20·5. $C_{10}H_6ClN_3$ requires C, 59·0; H, 2·9; Cl, 17·4; N, 20·6%), *m/e* 205/203 (M^+), $\nu_{max.}$ 1430, 1330, and 813 cm^{-1}, τ 0·91 (s, 4-H), 1·9br (s, 1- and 2-H), 2·1 (d, 9-H), 2·17 (d, 6-H), and 2·38 (q, 8-H) ($J_{6,8}$ 2·3 and $J_{8,9}$ 8·0 Hz). Elution with ether–chloroform (5 : 1) afforded 1-(2-*amino*-4-*chlorophenyl*)-2-*methylimidazole* (0·45 g, 43%), m.p. 174° (Found: C, 58·0; H, 4·8; Cl, 17·1; N, 20·5. $C_{10}H_{10}ClN_3$ requires C, 57·8; H, 4·9; Cl, 17·0; N, 20·2%), *m/e* 209/207 (M^+), $\nu_{max.}$ 3370 and 3210 cm^{-1}, τ 2·8—3·15 (m, all nuclear H), 6·2br (s, NH_2), and 7·78 (s, Me).

Benzimidazole Derivatives.—Reaction of 2-methylbenzimidazole and 2,5-dichloronitrobenzene similarly yielded a product which was purified chromatographically, giving yellow 1-(4-*chloro*-2-*nitrophenyl*)-2-*methylbenzimidazole* (8) (20%), m.p. 127° (Found: C, 58·3; H, 3·4; Cl, 12·3; N, 14·8. $C_{14}H_{10}ClN_3O_2$ requires C, 58·5; H, 3·5; Cl, 12·3; N, 14·6%), *m/e* 289/287 (M^+), τ 1·87 (d, 3′-H), 2·6 (d, 6′-H), 2·1—2·4 and 2·7—3·3 (m, 2 and 3 nuclear H), and 7·6 (s, Me) ($J_{3',5'}$ 2·2 and $J_{5',6'}$ 8·5 Hz). Heating with iron(II) oxalate and chromatography with ether gave 3-*chlorobenzimidazo*[1,2-a]*quinoxaline* (9) (0·24 g, 19%), m.p. 208—211°, raised to 212° by sublimation (Found: C, 66·4; H, 3·1; Cl, 14·0; N, 16·6. $C_{14}H_8ClN_3$ requires C, 66·3; H, 3·2; Cl, 14·0; N, 16·6%), *m/e* 255/253 (M^+), $\lambda_{max.}$ (MeOH) 208 (log ε 4·32), 242sh (4·42), 256 (4·54), and 340 nm (4·06), τ 0·83 (s, 6-H), 1·6—2·1 (m, 1-, 4-, 8-, and 11-H), and 2·25—2·55 (m, 2-, 9-, and 10-H). Elution with ether–chloroform (1 : 4) gave very sparingly soluble orange crystals (purified from hot acetone–methanol) of 5,5′-*dichloro*-2,2′-*bis*-(2-*methylbenzimidazol*-1-*yl*)*azobenzene* (0·18 g, 14%), m.p. >300° (Found: C, 65·9; H, 4·0; Cl, 13·7; N, 16·6. $C_{28}H_{20}Cl_2N_6$ requires C, 65·8; H, 3·9; Cl, 13·9; N, 16·4%), *m/e* 512/510 (M^+), $\nu_{max.}$ 1645, 1500, 1410, and 735 cm^{-1}; this decolourised a solution of titanium(III) chloride in dilute hydrochloric acid.[1] Further elution with the same solvent mixture gave 1-(2-*amino*-4-*chlorophenyl*)-2-*methylbenzimidazole* (0·14 g, 10%), m.p. 189° (Found: C, 65·1; H, 4·4; Cl, 13·9; N, 16·4. $C_{14}H_{12}ClN_3$ requires C, 65·3; H, 4·7; Cl, 13·8; N, 16·3%), *m/e* 259/257 (M^+), $\nu_{max.}$ 3400 and 3200 cm^{-1}, τ 2·2—3·15 (m, all nuclear H), 6·35br (s, NH_2), 7·4 (s, Me).

Pyrimidine Derivatives.—(*a*) Aniline (10 mmol) in di-n-butyl ether was added dropwise at ambient temperature to a stirred mixture of potassium carbonate (15 mmol) and 4,6-dichloro-5-nitropyrimidine (10 ml) in di-n-butyl ether. The precipitate was filtered off and washed with dichloromethane, and the filtrate and washings were evaporated and chromatographed, yielding no mono-anilino-derivative but 4,6-dianilino-5-nitropyrimidine (10) (3·6 mmol), m.p. 168° (lit.,[22] 168—169°), *m/e* 307 (M^+). By using an excess of aniline the yield was almost quantitative. After heating the nitro-amine with iron(II) oxalate, chromatography of the product with light petroleum–ether gave unchanged material (8%) and ether then eluted orange 4-*anilinobenzo*[g]*pteridine* (11) (0·26 g, 19%), m.p. 244° (Found: C, 70·4; H, 4·05; N, 25·5. $C_{16}H_{11}N_5$ requires C, 70·4; H, 4·05; N, 25·6%), *m/e* 273 (M^+), $\nu_{max.}$ 3360 cm^{-1}, $\lambda_{max.}$ (MeOH) 208 (log ε 4·56), 260 (4·54), and 446 nm (4·11), τ 1·0 (2-H) and 1·6—2·8 (m, all other H).

(*b*) 2,4-Dichloro-5-nitropyrimidine, prepared from uracil,[23] was a yellow oil, b.p. 96° at 10 mmHg, changing to a low-melting solid. Aniline (20 mmol) in dichloromethane was added dropwise to a stirred solution of the dichloro-compound (24 mmol) in dichloromethane at −5°. After filtration to remove aniline hydrochloride and partial evaporation of the filtrate, addition of ether precipitated 4-*anilino*-2-*chloro*-5-*nitropyrimidine* (7·6 mmol), m.p. 171—172° (from ether–dichloromethane) (Found: C, 47·8; H, 2·7; Cl, 14·3; N, 22·6. $C_{10}H_7ClN_4O_2$ requires C, 47·9; H, 2·8; Cl, 14·2; N, 22·4%), *m/e* 252/250 (M^+), $\nu_{max.}$ 3300 cm^{-1}, τ 0·0br (NH), 0·82 (s, 6-H), and 2·2—2·7 (m, aromatic H). Rapid reaction occurred between the dichloro-compound (10 mmol) and aniline (40 mmol) in dichloromethane at ambient temperature, yielding 2,4-dianilino-5-nitropyrimidine (94%), m.p. 209° (from dichloromethane–ether) (lit.,[22] 198—202°). The mono- and di-

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anilino-compounds were each heated with iron(II) oxalate; traces of the former and 8% of the latter were recovered, but no crystalline reaction products were detected.

Diphenylmethane Derivatives.—(*a*) *o*-Nitrodiphenylmethane, b.p. 104° at 0·1 mmHg, was prepared from *o*-nitrobenzyl chloride,[24] and a sample (5 mmol) was heated in a Pyrex tube for 15 min at 270—300°. Treatment of the product with dichloromethane left a yellow solid, identified as acridone (18%), m.p. 350—353° (lit.,[25] 354°), *m/e* 195 (M^+), 167 (M − CO), and 140 (M − CO − HCN), $\nu_{max.}$ 1650 cm^{-1}. Chromatography of the dichloromethane extract with petroleum afforded unchanged *o*-nitrodiphenylmethane (4%), and light petroleum–ether (5 : 1) eluted *o*-aminobenzophenone (0·14 g, 14%), m.p. 105° (lit.,[25] 105—106°), *m/e* 197 (M^+), $\nu_{max.}$ 3430, 3300, and 1640 cm^{-1}. Ether eluted black resin.

(*b*) An intimate mixture of iron(II) oxalate and *o*-nitrodiphenylmethane was heated at 270—300° for 15 min. A dichloromethane extract of the product yielded unchanged nitro-compound (8%) and *o*-aminobenzophenone (37%). An acetone extract of the residual crude product gave acridone (9%).

Pyridine Derivatives.—(*a*) A solution of 2-chloro-3-nitropyridine (10 mmol) and 3-aminopyridine (20 mmol) in di-n-butyl ether was refluxed for 3 h and the tarry product chromatographed. Light petroleum–ether (4 : 1) eluted unchanged nitro-compound (2 mmol), followed by unchanged aminopyridine (1 mmol). Elution with light petroleum–ether (2 : 1) then gave yellow 2-amino-3-nitropyridine (3 mmol), m.p. 163—164° (lit.,[26] 164°) (Found: M^+, 139·0382. Calc. for $C_5H_5N_3O_2$: M, 139·0382), $\nu_{max.}$ 3480 and 3380 cm^{-1}.

(*b*) A mixture of 2-chloro-3-nitropyridine (25 mmol) and 4-aminopyridine (50 mmol) was heated without solvent for 1 h at 150° and the resulting viscous oil was extracted with dichloromethane and the extract chromatographed with light petroleum–ether (3 : 1) to afford fractions consisting of a mixture of two yellow solids. Vacuum sublimation removed the more volatile 2-amino-3-nitropyridine (26%), spectroscopically identical with the product described in (*a*). Raising the temperature gave a sublimate of 3-*nitro*-2-(4-*pyridylamino*)*pyridine* (18) (26%), m.p. 165° (Found: C, 55·3; H, 3·8; N, 26·1. $C_{10}H_8N_4O_2$ requires C, 55·5; H, 3·7; N, 26·0%), *m/e* 216 (M^+), 215 (M − H), 169 (M − H − NO_2), and 142 (M − H − NO_2 − HCN), $\nu_{max.}$ 3320 cm^{-1}, τ (100 MHz) −0·25br (s, NH), 1·35—1·55 (m, 4-, 6-, 2′-, and 6′-H), 2·3 (q, 3′- and 5′-H), and 3·0 (q, 5-H) ($J_{4,5}$ 7·8, $J_{5,6}$ 5·2, $J_{2',3'}$ and $J_{5',6'}$ 5·0, and $J_{2',5'}$ and $J_{3',6'}$ 1·5 Hz). After being heated with iron(II) oxalate this compound yielded only 2-amino-3-nitropyridine (16%) and unchanged starting material.

(*c*) A solution of 4-chloro-3-nitropyridine (20 mmol) and 3-aminopyridine (40 mmol) in dimethylacetamide was refluxed for 3 h, the solvent removed, the viscous brown residue extracted with dichloromethane, and the extract chromatographed. Light petroleum–ether (4 : 1) successively eluted unchanged 3-aminopyridine (7 mmol), pale yellow 4-amino-3-nitropyridine (4 mmol), m.p. 198—200° (lit.,[26] 200°), *m/e* 139 (M^+), $\nu_{max.}$ 3380 and 3200 cm^{-1}, and yellow 3-*nitro*-4-(3-*pyridylamino*)*pyridine* (17) (1·25 g, 29%), m.p. 161° (from dichloromethane–ether–light petroleum) (Found: C, 55·6; H, 3·7; N, 26·2%), *m/e* 216 (M^+), $\nu_{max.}$ 3330 cm^{-1}, τ 0·35br (s, NH), 0·7 (s, 2-H), 1·36 (d, 2′-H), 1·40 (q, 6′-H), 1·68 (d, 6-H), 2·28 (sext, 4′-H), 2·52 (q, 5′-H), and 3·13 (d, 5-H) ($J_{2',4'}$ 2·0, $J_{4',6'}$ 1·9, $J_{5',6'}$ 4·0, $J_{4',5'}$ 7·9, and $J_{5,6}$ 6·1 Hz). A final chromatographic fraction was 1-acetyl-3-aminopyridine (1·7 g). After heating the compound (17) with iron(II) oxalate, chromatography afforded 4-amino-3-nitropyridine (17%), spectroscopically identical with the sample described above, followed by unchanged starting material (12%).

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