Synthesis of Polynuclear Heterocycles. Part II.[1] Cyclisations of 2- and 4-Substituted 3-Amino- and 3-Nitro-pyridines

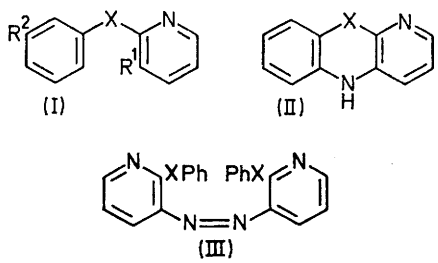
By **J. J. Eatough, L. S. Fuller, R. H. Good, and R. K. Smalley,*** Department of Pure and Applied Chemistry, University of Salford, Salford M5 4WT, Lancs.

Treatment of 2- and 4-phenoxy-3-nitropyridine with triethyl phosphite failed to yield the expected pyridobenzoxazines; 2- and 4-phenylthio-3-nitropyridine, however, cyclised to give 5*H*-pyrido[2,3-*b*][1,4]benzothiazine and 5*H*-pyrido[3,4-*b*][1,4]benzothiazine respectively, albeit in poor yield. Similar results were obtained by thermolytic decomposition of the corresponding 2- and 4-substituted 3-azido-pyridines. 9-Hydroxypyrido-[2,3-*b*]1,4,5-benzoxadiazepine has been synthesised.

An improved synthesis of pyrido[2,3-*c*]furoxan is reported, and its n.m.r. spectrum has been measured at various temperatures.† Attempts to prepare the unknown isomeric pyrido[3,4-*c*]furoxan have failed.

PHENOXAZINES and phenothiazines have found wide application as chemotherapeutic agents and more recently their aza-analogues, in particular the pyridobenzothiazines, have been found to be of pharmacological importance.[2] It was of interest, therefore, to investigate potential synthetic routes to these aza-analogues.

Phenothiazine has been prepared[3] by reductive cyclisation of phenyl *o*-nitrophenyl sulphide with triethyl phosphite. We found that similar treatment of the nitropyridyl sulphide (I; $R^1 = NO_2$, $R^2 = H$, X = S) yielded 5*H*-pyrido[2,3-*b*][1,4]benzothiazine (II; X = S) (30%), together with the azo-compound (III; X = S). The isomeric nitropyridyl sulphide (IV; $R = NO_2$, X = S) under the same conditions gave only a poor yield (20%) of 5*H*-pyrido[3,4-*b*][1,4]benzothiazine (V; X = S) together with an intractable tar. The nitropyridyl ethers (I; $R^1 = NO_2$, $R^2 = H$, X = O) and (IV; $R = NO_2$, X = O); like their benzene analogues,[3] cyclised neither in hot triethyl phosphite nor when treated with triethyl-phosphite in a high boiling inert solvent, *e.g.* dodecane. The azo-compound (III; X = O) was the only identifiable product obtained in these reactions. Cadogan has commented on the difficulty of six-membered ring formation with triethyl phosphite, and, in fact, phenothiazine formation may well proceed *via* a five-membered ring intermediate.[4]



Both phenoxazine and phenothiazine have been isolated in poor yield from the thermolytic decomposition of *o*-azidophenyl phenyl ether and *o*-azidophenyl phenyl

† During the course of this work (J. J. Eatough, M.Sc. Thesis, University of Salford, September 1969) a report appeared (see ref. 6) which indicated that isomer (VIIIa) formed *ca.* 7% of the equilibrium mixture at −50°.

[1] Part I is considered to be R. K. Smalley, *J. Chem. Soc.*, 1966, 80.

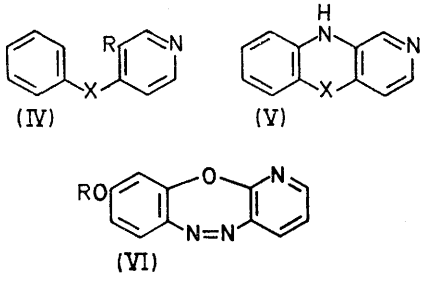
[2] E. Schenker and H. Herbst, *Progr. Drug Res.*, 1963, **5**, 269.

[3] J. I. G. Cadogan, R. K. Mackie, and M. J. Todd, *Chem. Comm.*, 1966, 491.

[4] J. I. G. Cadogan, *Quart. Rev.*, 1968, **22**, 222.

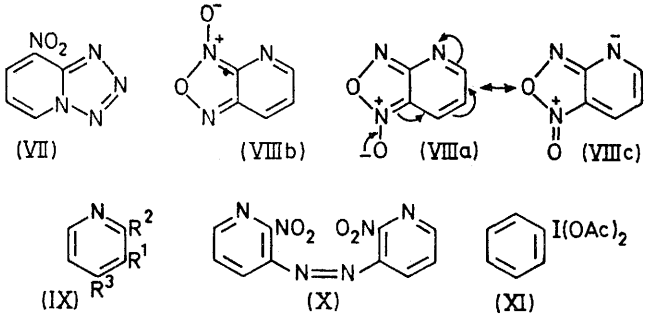
sulphide, respectively.[5] Accordingly, the 3-azidopyridyl ethers (I; $R^1 = N_3$, $R^2 = H$, X = O) and (IV; R = N_3, X = O) and the 3-azidopyridyl sulphides (I; $R^1 = N_3$, $R^2 = H$, X = S) and (IV; R = N_3, X = S) were prepared from the corresponding amines. Decomposition of (I; $R^1 = N_3$, $R^2 = H$, X = S) in boiling bromobenzene yielded 5*H*-pyrido[2,3-*b*][1,4]-benzothiazine (II; X = S) in moderate yield (40%). Similarly the isomeric azide (IV; $R^1 = N_3$, X = S) gave a poor yield (17%) of 5*H*-pyrido[3,4-*b*]benzothiazine (V; X = S). In each case azo-compound and polymeric material were also isolated. The azide (IV; R = N_3; X = S) proved somewhat difficult to obtain pure since the amino-sulphide (IV; R = NH_2, X = S) cleaved easily during diazotisation in cold hydrochloric acid to yield benzenethiol. This undoubtably accounts for the isolation of diphenyl disulphide from the decomposition of this azide in hot bromobenzene. Decomposition of the azidopyridyl ethers under identical conditions to those described failed to yield any cyclised products. In each case only azo-compound and polymeric material were isolated.

The hydroxyphenyl nitropyridyl ether (I; $R^1 = NO_2$, $R^2 = OH$, X = O) was prepared by condensing 2-chloro-3-nitropyridine with resorcinol in ethanol solution. Catalytic reduction of the nitro-compound and subsequent diazotisation of the resulting amine gave a solution of the diazonium chloride (I; $R^1 = N_2^+Cl^-$, $R^2 = OH$, X = O), which when treated with sodium acetate gave 9-hydroxypyrido[2,3-*b*][1,4,5]benzoxadiazepine (VI; R = H), a hitherto unreported ring system. Treatment of (VI; R = H) with acetic anhydride gave the acetyl derivative (VI; R = Ac). That cyclisation had not taken place *ortho* to the hydroxy-group of the phenyl ring was shown by the ^1H n.m.r. spectra of both the hydroxy-compound and its acetyl derivative. In each case a *meta*-coupled single hydrogen (attributable to 10-H) was observed at δ 6·6 and 7·1 p.p.m. respectively.



Benzofuroxans have been prepared by the thermolysis of *o*-nitrophenyl azides.[6] All attempts to prepare 2-azido-3-nitropyridine, however, have failed since immediate isomerisation of the azide to the nitropyridotetrazole (VII) occurred.[7] Pyrolysis of solid (VII) however, was found [7] to yield pyrido[2,3-*c*]furoxan (VIII). We found that thermolysis of solid (VII) gave substantial amounts of charred material and that a better yield of cleaner product was obtained by decomposing (VII) in boiling diphenyl ether. Pyrido[2,3-*c*]furoxan should also be the thermolytic decomposition product of 3-azido-2-nitropyridine (IX; $R^1 = N_3$, $R^2 = NO_2$, $R^3 = H$). Recent attempts [8] to prepare this azide have failed. We have obtained the nitro-azide in good yield (78%) by diazotisation of 3-amino-2-nitropyridine (IX; $R^1 = NH_2$, $R^2 = NO_2$, $R^3 = H$) in cold 5N-hydrochloric acid, and subsequent treatment of the resulting diazonium chloride solution with sodium azide. However, on decomposition of the azide in various solvents, no pyrido[2,3-*c*]furoxan was detected. For example, in boiling *o*-dichlorobenzene, azo-compound (X) was the only identifiable product, whereas thermolysis of the nitro-azide in boiling acetic anhydride yielded the same azo-compound. The nitro-azide was recovered virtually unchanged (85%) after being heated in boiling toluene for 16 h.

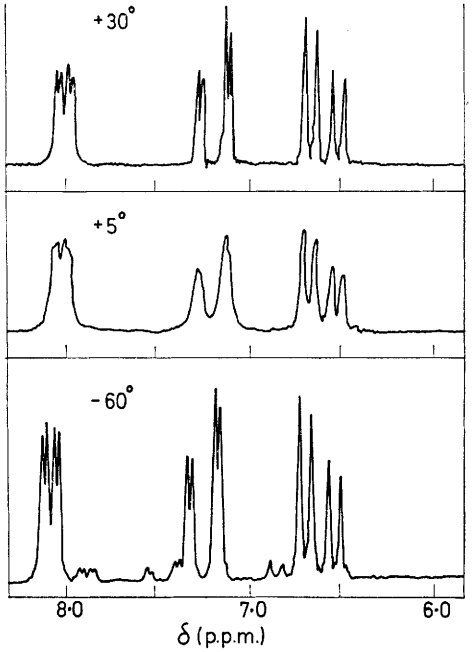
Oxidation of 3-amino-2-nitropyridine (IX; $R^1 = NH_2$, $R^2 = NO_2$, $R^3 = H$) with sodium hypochlorite in solution in ethanol (a successful method for the preparation of benzofuroxan [9]) also failed to yield pyrido[2,3-*c*]furoxan. The azo-compound (X) was again the only product isolated. Pausacker [10] has prepared benzofuroxans by the oxidation of *o*-nitro-anilines by use of (diacetoxyiodo)benzene (XI). We have found this to be the best method of preparation of pyrido[2,3-*c*]furoxan, since oxidation of 3-amino-2-nitropyridine with (XI) in acetone solution gave the required pyrido-furoxan in 80% yield.



Recent ^1H n.m.r. studies have shown that many benzo-, naphtho-, and quinolino-furoxans exist as tautomeric mixtures at room temperature.[6] We have now studied the ^1H n.m.r. spectrum of pyrido[2,3-*c*]-furoxan at various temperatures and in various solvents. At room temperature in deuteriochloroform (with

[5] P. A. S. Smith, B. B. Brown, R. K. Putney, and R. F. Reinisch, *J. Amer. Chem. Soc.*, 1953, **75**, 6335.
[6] A. J. Boulton and P. B. Ghosh, *Adv. Heterocyclic Chem.*, 1969, **10**, 1.
[7] J. H. Boyer, D. I. McCane, W. J. McCarville, and A. T. Tweedie, *J. Amer. Chem. Soc.*, 1953, **75**, 5298.
[8] P. B. Ghosh and M. W. Whitehouse, *J. Medicin. Chem.*, 1969, **12**, 505.
[9] F. B. Mallory, *Org. Synth.*, 1963, Coll. Vol. IV, 74.
[10] L. K. Dyall and K. H. Pausacker, *Austral. J. Chem.*, 1958, **11**, 491.

tetramethylsilane as internal reference) the n.m.r. spectrum of (VIII) showed only three quartets centred at δ 7·30 (β-proton), 7·92 (γ-proton), and 8·48 (α-proton) p.p.m. with $J_{\alpha\beta}$ 3·5 Hz, $J_{\alpha\gamma}$ 1·5 Hz, and $J_{\beta\gamma}$ 8·0 Hz. A similar spectrum at room temperature was observed for solutions in both acetone and trimethyl phosphate. At −60° for solution in acetone, however, the n.m.r. spectrum of (VIII) (Figure) indicated the presence of a



^{1}H N.m.r. spectrum of pyrido[2,3-*c*]furoxan in solution in acetone

mixture of two forms [(VIIIa) ⇌ (VIIIb)] in the ratio 12·3 : 1. This gave a value of 1·1 kcal/mol for the difference in free energy between the two tautomers (VIIIa and b). A coalescence temperature of 278 ± 3 K was observed for the α-proton together with a chemical shift of 11 Hz. Application of the Eyring equation [11] yielded a value of 14·5 ± 0·5 kcal for ΔG^* (the activation energy for the tautomerism). Obviously at room temperature rapid interchange occurs between the two forms (VIIIa and b), whereas at low temperatures the two forms are capable of separate existence. Form (VIIIa) (*i.e.* the 3-oxide form) appears to be the most stable isomer since (i) favourable resonance structures of type (VIIIc), in which the negative charge is borne on the pyridine ring nitrogen, are possible, and (ii) form (VIIIb) would be rendered somewhat unstable by unfavourable electrostatic interactions between the *N*-oxide group and the lone-pair electrons of the pyridine nitrogen.

Attempts to prepare the hitherto unknown isomeric pyrido[3,4-*c*]furoxan have failed. We have confirmed that decomposition of solid 4-azido-3-nitropyridine (IX; $R^1 = NO_2$, $R^2 = H$, $R^3 = N_3$) gave only an intractable tar.[12] Decomposition of the nitro-azide in boiling diphenyl ether gave only polymeric material, while thermolysis of the azide in either toluene or acetic anhydride gave only polymer and starting material.

Oxidation of 4-amino-3-nitropyridine (IX; $R^1 = NO_2$, $R^2 = H$, $R^3 = NH_2$) with either sodium hypochlorite or (diacetoxyiodo)benzene also failed to yield the required pyrido[3,4-*c*]furoxan. These results are perhaps somewhat surprising since in both the naphtho- and quinolino-furoxan series it has been found [13] that the angular rather than the linear furoxan is more readily prepared.

EXPERIMENTAL

^{1}H N.m.r. spectra were measured for solution in deuteriochloroform unless otherwise stated, with a Varian A60A instrument, with tetramethylsilane as internal reference. Variable-temperature n.m.r. spectra were measured on a V-6040 N.M.R. Variable Temperature Controller with a liquid nitrogen-cooled probe. The reported coalescence temperature was calibrated against the hydroxy-line of methanol as indicated in the Varian Associate Publication No. 87–202–00, p. 27.

Preparation of Nitro-compounds.—Unless otherwise indicated the required nitro-compounds were prepared by literature methods and are listed in the Table.

2-(m-*Hydroxyphenoxy*)-3-*nitropyridine.*—To a boiling ethanolic solution (45 ml) of 2-chloro-3-nitropyridine (9·5 g) and resorcinol (13·2 g) was added slowly during 1 h a solution of potassium hydroxide (3·4 g) in ethanol (55 ml). The solution was then heated under reflux for a further 6 h. The ethanol was removed under reduced pressure and a solution of the residual oil in ether (100 ml) was extracted with warm water (3 × 50 ml), dried ($MgSO_4$), and then evaporated to yield a yellow solid (9 g, 65%). 2-(m-*Hydroxyphenoxy*)-3-*nitropyridine* formed yellow prisms, m.p. 168° (from aqueous ethanol) (Found: C, 56·5; H, 3·3; N, 12·4. $C_{11}H_8N_2O_4$ requires C, 56·9; H, 3·4; N, 12·05%).

Preparation of Amines.—In each case the required amines (see Table) were obtained in high yield by catalytic reduction (Raney nickel–hydrogen at atmospheric pressure) of the nitro-compound in either benzene or ethanol solution.

Preparation of Azides.—The azides listed in the Table were prepared by treating the diazotised amine with sodium azide in the presence of a sodium acetate buffer. The resulting azides were chromatographed on alumina with diethyl ether as eluant and all showed characteristic absorption at *ca.* 2120 cm^{-1} [ν(N_3)] in their i.r. spectra.

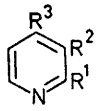
Cyclisations with Triethyl Phosphite.—General method. The nitro-compound (1 g) was heated under reflux either in triethyl phosphite or triethyl phosphite–dodecane (7 ml) under nitrogen for 0·5 h. Excess of triethyl phosphite was removed under reduced pressure and the residue was examined by t.l.c. In all cases the formation of a multitude of products was indicated. The mixture was chromatographed on alumina with various solvents.

[11] A. J. Boulton, A. R. Katritzky, M. J. Sewell, and B. Wallis, J.. *Chem Soc.* (*B*), 1967, 914.

[12] J. H. Boyer and S. Kruger, *J. Amer. Chem. Soc.*, 1957, **79**, 3552.

[13] A-ur Rahmann, A. J. Boulton, D. P. Clifford, and G. J. T. Tiddy, *J. Chem. Soc.* (*B*), 1968, 1516.

Results. Elution of the reaction mixture from 3-nitro-2-phenylthiopyridine with benzene gave 5*H*-pyrido[2,3-*b*]-[1,4]benzothiazine as a pale yellow solid (0·25 g), m.p. 238° [from light petroleum (b.p. 100—120°)] (lit.,[14] m.p. 242°) (Found: C, 66·15; H, 4·05; N, 13·85; S, 16·0. Calc. for $C_{11}H_8N_2S$: C, 66·0; H, 4·1; N, 14·0; S, 16·0%). Further elution with diethyl ether gave traces of unidentified products. Elution with chloroform gave a deep red azo-compound identical to that obtained from decomposition of 3-azido-2-phenylthiopyridine. Similar treatment of the reaction mixture from 3-nitro-4-phenylthiopyridine gave 5*H*-pyrido[3,4-*b*][1,4]benzothiazine as a yellow solid (0·18 g), m.p. 163° [from light petroleum (b.p. 100—120°)] (lit.,[15] m.p. 165°) (Found: C, 66·2; H, 4·2; N, 13·75%). In all the corresponding nitro-compound. Further elution with chloroform gave 2,2′-*bis*(*phenylthio*)-3-*azopyridine* as a deep red solid (0·3 g), m.p. 151° (Found: C, 66·4; H, 3·9; N, 13·8; S, 15·9. $C_{22}H_{16}N_4S_2$ requires C, 66·0; H, 4·1; N, 14·0; S, 16·0%). The product from 3-*azido*-4-*phenylthiopyridine* gave, after chromatography with benzene as eluant, diphenyl disulphide, m.p. 58°, identical with an authentic sample prepared by oxidation of benzenethiol with hydrogen peroxide. Elution with chloroform gave 5*H*-pyrido[3,4-*b*][1,4]benzothiazine as a yellow solid (0·15 g) (17%), m.p. 162°. Further elution with chloroform gave a trace of a deep red solid which rapidly decolourised titanium(III) chloride solution and which was probably an azo-compound. The product from 3-*azido*-4-*phenoxypyridine*



			M.p. (decomp. temp.)	Lit. m.p.	Found (%)			Mol. formula	Required (%)		
R^1	R^2	R^3			C	H	N		C	H	N
OPh	NO_2	H	94°	94° [a]							
,,	NH_2	,,	106 [b]		70·8	5·3	14·9	$C_{11}H_{10}N_2O$	71·0	5·4	15·05
,,	N_3	,,	40 (130)		62·1	3·9	26·0	$C_{11}H_8N_4O$	62·3	3·9	26·4
SPh	NO_2	,,	103	103 [c]							
,,	NH_2	,,	68	68 [c]							
,,	N_3	,,	65 (130)		58·3	3·3	24·1	$C_{11}H_8N_4S$	57·9	3·5	24·6
H	NO_2	OPh	72	73 [d]							
,,	NH_2	,,	*								
,,	N_3	,,	†								
,,	NO_2	SPh	84	86 [d]							
,,	NH_2	,,	107	108 [d]							
,,	N_3	,,	25 (120)		58·2	3·6	24·0	$C_{11}H_8N_4S$	57·9	3·5	24·6
m-HO·C_6H_4	NH_2	H	170 [e]		65·7	5·1	14·0	$C_{11}H_{10}N_2O_2$	65·3	4·95	13·9

* Picrate from ethanol, m.p. 229° (lit.,[c] m.p. 230°). † Isolated as brown oil, picrate from ethanol, m.p. 145° (decomp.).

[a] T. Takahashi and J. Shibasaki, *J. Pharm. Soc., Japan*, 1949, **69**, 408. [b] From light petroleum (b.p. 100—120°) needles, which rapidly darkened in air. [c] T. Takahashi and J. Shibasaki, *J. Pharm. Soc., Japan*, 1952, **72**, 1141. [d] S. Kruger and F. G. Mann, *J. Chem. Soc.*, 1955, 2755. [e] From light petroleum (b.p. 100—120°), grey-green needles.

the other reductions with triethyl phosphite, only tarry materials were obtained, from which no identifiable materials could be isolated.

Decomposition of Azides.—General method. A solution of the azide (1 g) in bromobenzene (50 ml) was added dropwise over 10 min to boiling bromobenzene (50 ml). Nitrogen was evolved spontaneously and t.l.c. examination of the deep red reaction mixture showed that azide decomposition was complete after *ca.* 5 min. The excess of solvent was removed under reduced pressure and the resulting dark red oil was decantated with light petroleum (b.p. 40—60°) to remove residual bromobenzene; the resulting dark brown solid (*ca.* 0·8 g) was chromatographed on alumina. In all cases an unidentified high melting (>300°) amorphous solid was isolated.

Results. The product from 3-*azido*-2-*phenoxypyridine* gave, after chromatography with chloroform as eluant, 2,2′-*diphenoxy*-3-*azopyridine* (0·45 g) as a deep red solid which sintered at 170—175° (Found: C, 72·2; H, 4·6; N, 14·8. $C_{22}H_{16}N_4O_2$ requires C, 71·8; H, 4·35; N, 15·2%). No other identifiable products were isolated. The product from 3-*azido*-2-*phenylthiopyridine* gave, after chromatography with chloroform as eluant, 5*H*-pyrido[2,3-*b*]-[1,4]benzothiazine (0·35 g) which was identical with the product obtained from the triethyl phosphite reduction of gave, after chromatography, only trace amounts of unidentifiable products together with polymeric material (0·5 g).

9-*Hydroxypyrido*[2,3-b][1,4,5]*benzoxadiazepine.*—3-*Amino*-2-(m-*hydroxyphenoxy*)*pyridine* (0·6 g) was diazotised at 0—5° with sodium nitrite (0·3 g). The resulting diazonium chloride solution was filtered into a rapidly stirred cold solution of sodium acetate (20 g) in water (50 ml). The orange precipitate which rapidly formed was filtered off, dried by suction, and then chromatographed on silica with ethanol as eluant. 9-*Hydroxypyrido*[2,3-b][1,4,5]*benzoxadiazepine* was obtained as an orange solid, (0·4 g) which had m.p. 245° (decomp.) (from ethanol) (Found: C, 61·6; H, 3·6; N, 20·2. $C_{11}H_7N_3O_2$ requires C, 62·0; H, 3·3; N, 19·7%) *M* (mass spectrum) 213, δ [$(CD_3)_2SO$] 6·58 (d, *J* 2·5 Hz, 10-H), 6·8—6·98 (q, *J ca.* 8·0 and 2·5 Hz, 8-H), 7·5—7·8 (m, 3- and 7-H), 8·15—8·25 (q, 4-H), and 8·3—8·45 (q, 2-H) p.p.m. 9-*Acetoxypyrido*[2,3-b][1,4,5]*benzoxadiazepine* (prepared by use of acetic anhydride), formed yellow crystals, and had m.p. 140° (from ethanol) (Found: C, 61·0; H, 3·3; N, 16·1. $C_{13}H_9N_3O_3$ requires C, 61·2; H, 3·5; N, 16·5%) δ 7·1 (d, *J* 2 Hz, 10-H), 7·2—8·0 (m, 3-, 7-, and 8-H), and 8·2—8·5 (m, 2- and 4-H) p.p.m.

[14] B.P. 791,190.
[15] A. J. Saggiomo, P. N. Craig, and M. Gordon, *J. Org. Chem.*, 1958, **23**, 1906.

Preparation of 3-*Azido*-2-*nitropyridine*.—A solution of 3-amino-2-nitropyridine [16] (8·4 g) in concentrated hydrochloric acid (30 ml) and water (30 ml) was diazotised at 0—5° *with* sodium nitrite. The resulting pale yellow diazonium chloride solution was added dropwise during 0·5 h to a cold stirred solution of sodium azide (8 g) and sodium acetate (100 g) in water (250 ml). Nitrogen was evolved spontaneously and 3-azido-2-nitropyridine separated as a buff solid. The azide was filtered off, air dried, and chromatographed on alumina with diethyl ether as eluant. 3-*Azido*-2-*nitropyridine* was obtained as pale yellow crystals (7 g), m.p. 45° (decomp. temp. 140—145°) (Found: N, 41·9. $C_5H_3N_5O_2$ requires N, 42·4%) $\nu_{max.}$ (Nujol) 2110 and 2140 (N_3) and 1560 and 1310 (NO_2) cm^{-1}, δ 8·26—8·1 (q, $J_{\alpha\beta}$ 4·5 Hz and $J_{\alpha\gamma}$ 2 Hz, H_α), 7·65—7·42 (q, $J_{\beta\gamma}$ 8·5 Hz, H_γ), and 7·42—7·15 (q, H_β) p.p.m.

Preparation of Pyrido[2,3-c]*furoxan*.—*Method* (a). *Decomposition of* 4-*nitro*-1,2,3,4-*tetrazolo*[4,5-a]*pyridine*. 4-Nitro-1,2,3,4-tetrazolo[4,5-a]pyridine was prepared by the method of Boyer [7] and also by diazotisation of 2-hydrazino-3-nitropyridine.[17] The nitro-tetrazole (1 g) was added slowly during 20 min to diphenyl ether (25 ml) at 170—175°. The resulting deep red solution was heated at 175° for a further 20 min then concentrated to low bulk (*ca.* 5 ml) under reduced pressure. On addition of light petroleum (b.p. 40—60°) to the residual oil, pyrido[2,3-*c*]furoxan slowly crystallised as a brown solid (0·6 g) which was recrystallised from ethyl acetate–light petroleum (b.p. 60—80°) as pale yellow needles, m.p. 53—54° (lit.,[7] m.p. 54°).

Method (b). *Decomposition of* 3-*azido*-2-*nitropyridine*. (i) *In* o-*dichlorobenzene*. A suspension of 3-azido-2-nitropyridine (2·4 g) in *o*-dichlorobenzene (30 ml.) was added dropwise during 20 min to boiling *o*-dichlorobenzene (70 ml). T.l.c. examination indicated that the azide had disappeared completely after 20 min. No pyrido[2,3-*c*]furoxan could be detected. After removal of the solvent, the residual oil was washed with light petroleum (b.p. 40—60°) to yield a high melting (>300°) brown polymeric material. The light petroleum washings, on evaporation, gave a brown semi-solid (0·8 g) which was chromatographed on alumina. Elution with benzene gave 2,2′-*dinitro*-3-*azopyridine* (0·2 g), m.p. 229—234° (Found: C, 43·5; H, 2·8. $C_{10}H_6N_6O_4$ requires C, 43·8; H, 2·2%). Further elution with chloroform gave a brown shellac (0·4 g), m.p. >300°, which was not identified. Finally elution with ethanol gave further amounts of brown polymeric material.

(ii) *In toluene*. A solution of 3-azido-2-nitropyridine (2·4 g) in toluene (100 ml) was heated under reflux for 16 h. After removal of the solvent under reduced pressure, the residual oil was chromatographed on alumina to yield starting material (2·2 g) and a brown shellac (0·11 g), m.p. >300°.

(iii) *In acetic anhydride*. A solution of 3-azido-2-nitropyridine (2·5 g) in acetic anhydride (100 ml) was heated under reflux for 3 h. Treatment as before and chromatography on alumina with benzene as eluant gave 2,2′-dinitro-3-azopyridine (0·5 g), m.p. 230°, identical with the azo-compound previously prepared.

Method (c). *Oxidation of* 3-*amino*-2-*nitropyridine*. (i) *With sodium hypochlorite*. Oxidation of 3-amino-2-nitropyridine (1 g) in ethanol solution with sodium hypochlorite gave 2,2′-dinitro-3-azopyridine as the only identifiable product.

(ii) *With* (*diacetoxyiodo*)*benzene*. Finely ground 3-amino-2-nitropyridine (2·5 g) was added slowly to a well stirred solution of (diacetoxyiodo)benzene (6·4 g) in AnalaR acetone (200 ml). The mixture was stirred for 18 h at room temperature after which time t.l.c. indicated that the nitro-amine had almost completely disappeared, and that a single compound had been formed. The solvent was removed under reduced pressure and the semi-solid residue was extracted with hot benzene. The benzene extracts were concentrated and then chromatographed on alumina with benzene as eluant. A yellow band rapidly separated which on evaporation gave pyrido[2,3-*c*]furoxan (2 g, 83%) as a pale yellow solid, m.p. 53°.

Attempted Preparation of Pyrido[3,4-c]*furoxan*.—4-Hydrazino-3-nitropyridine [18] was diazotised to give 4-azido-3-nitropyridine as a brown solid which crystallised from ethanol as yellow needles, m.p. 85—87° (decomp.) (lit.,[13] m.p. 89°). The nitro-azide (1 g) was decomposed in boiling toluene during 4·5 h and gave only an amorphous brown solid (0·9 g), m.p. >250°. A similar product was obtained when the azide was decomposed in boiling acetic anhydride during 3 h. 4-Amino-3-nitropyridine [18] (1 g) was oxidised with sodium hypochlorite as in the previous example. Treatment of the reaction mixture as previously described gave an unidentified red oil and starting material (0·4 g). Oxidation of the nitro-amine with (diacetoxyiodo)benzene in acetone solution even during 5 days yielded only trace amounts of products, none of which were identified as pyrido[3,4-*c*]furoxan.

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