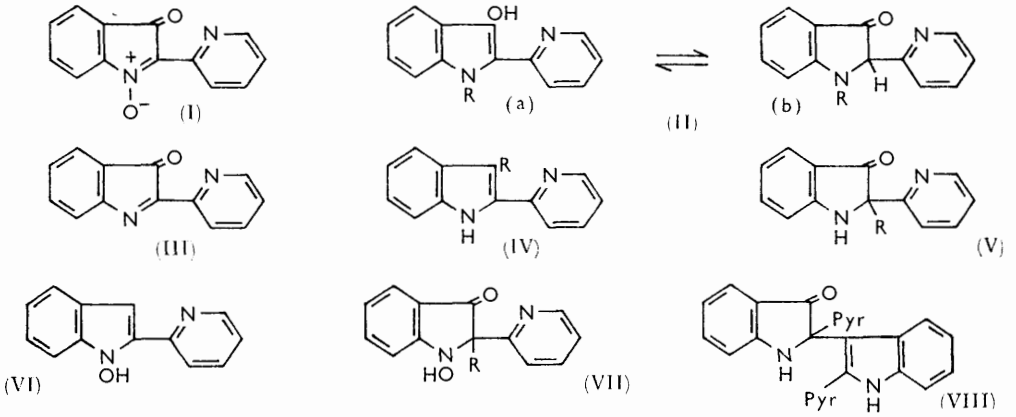
319. *Isatogens. Part II.*[1] 2-2′-*Pyridylisatogen*

By D. A. Patterson and D. G. Wibberley

The reduction of 2-2′-pyridylisatogen with phenylhydrazine has been shown to yield 2-2′-pyridylindoxyl and not, as hitherto suggested,[2] 2-2′-pyridylindolone.—The " indolone hydrate " which is also isolated from the same reaction is 2-hydroxy- and not 1-hydroxy-1,2-dihydro-2-2′-pyridylindolone. The nature of the products obtained from 2-2′-pyridylisatogen and piperidine, both alone, and in the presence of active methylene compounds is postulated, and a novel synthesis of 1-hydroxy-2-2′-pyridylindole is described.

It has been shown in these laboratories that 2-2′-pyridylisatogen (I) has *in vitro* antibacterial activity. We were therefore interested in the preparation of the related compounds, 2-2′-pyridyl-indolone (III), -indoxyl (IV; R = OH), and -indole (IV; R = H), and 1-hydroxy-2-2′-pyridylindole (VI). Ruggli and Cuenin [2] claimed that reduction of the isatogen (I) with phenylhydrazine yielded the indolone (III) as orange-brown plates, and its hydrate, 1,3-dihydroxy-2-2′-pyridylindole (IIa; R = OH) as green-yellow needles. Treatment of either of these products, or of the isatogen itself, with piperidine gave the same yellow piperidine adduct which was formulated as 3-hydroxy-1-piperidino-2-2′-pyridylindole (IIa; R = NC_5H_{10}).



We obtained the same three compounds from 2-2′-pyridylisatogen by the methods of Ruggli and Cuenin,[2] but suggest on the basis of the following evidence that the orange-brown compound is the indoxyl (IV; R = OH), the green-yellow hydrate is 1,2-dihydro-2-hydroxy-2-2′-pyridylindolone (V; R = OH), and the piperidine adduct the closely related 1,2-dihydro-2-piperidino-2-2′-pyridylindolone (V; R = NC_5H_{10}). (i) The analysis of the orange-brown compound corresponds more closely to $C_{13}H_{10}N_2O$ than to $C_{13}H_8N_2O$.

[1] Part I, Coutts, Hooper, and Wibberley, *J.*, 1961, 5205.
[2] Ruggli and Cuenin, *Helv. Chim. Acta*, 1944, **27**, 649.

(ii) All three compounds show NH absorption in their infrared spectra and form nitrosamines with nitrous acid. (iii) The infrared spectrum of the orange-brown compound showed no carbonyl absorption in the solid state or in chloroform, although a weak absorption was present in dioxan solution. The compound thus cannot be the indolone (III). Indoxyls are stated [3] to exist in both the carbonyl, *e.g.*, (IIb; R = H), and the " enolic " form, *e.g.*, (IIa; R = H), but in 2-2′-pyridylindoxyl (IIa; R = H or IV; R = OH) strong intramolecular hydrogen bonding would be expected between the 3-hydroxyl and the pyridine ring-nitrogen except in polar solvents. A closely similar example has been found in 2-2′-quinolylcyclohexanone which also shows no carbonyl absorption.[4] (iv) Ruggli and Cuenin [2] claimed that reduction of the orange-brown compound with zinc and acetic acid in the presence of acetic anhydride yielded 3-acetoxy-2-2′-pyridylindole (IV; R = OAc). This was shown to be true but the same compound was isolated with acetic anhydride alone. A longer reaction time yielded 3-acetoxy-1-acetyl-2-2′-pyridylindole (*i.e.*, *N*,*O*-diacetylindoxyl) again without the use of any reducing agent.

The indolone structure (III) would seem to be suggested by the formation of the piperidine adduct (V; R = NC_5H_{10}) from the orange-brown compound, but when this reaction is carried out in the absence of air only unchanged indoxyl is isolated. Strong evidence for the formation of the indolone (III) as an intermediate, in the preparation of 1,2-dihydro-2-piperidino-2-2′-pyridylindolone from the indoxyl, is provided by the reaction of 2-phenylindolone with piperidine to yield 1,2-dihydro-2-phenyl-2-piperidinoindolone. Not only have the two products almost identical infrared spectra but the latter is additionally obtained from 2-phenylindoxyl and piperidine. The reactivity of the –C=N– grouping in indolenines [5] and other *N*-heteroaromatic systems is well known, and the oxidative dimerization of indoles is presumed to proceed through the nucleophilic addition of indoles to indolones.[6] Nucleophilic addition of piperidine to the indolone could only yield the 2-substituted adduct (V; R = NC_5H_{10}). A similar intermediate formation of the indolone (III) from the indoxyl (IV; R = OH) by aerial oxidation must be postulated to account for the formation of 3-nitroso-2-2′-pyridylindole (IV; R = NO) by the prolonged action of hydroxylamine on the indoxyl. The known 2-phenylindoxyl, in exactly the same manner, yielded 3-nitroso-2-phenylindole which was identical to a sample prepared by nitrosation of 2-phenylindole.[7] 3-Nitroso-2-2′-pyridylindole was prepared more rapidly from the " indolone hydrate " (V; R = OH) and hydroxylamine, or, together with the 3-nitropyridylindole, by treatment of 2-2′-pyridylindole with amyl nitrite. Both the nitroso- and nitro-compounds, on reduction with sodium dithionite, yielded 3-amino-2-2′-pyridylindole (IV; R = NH_2); the latter yielded 3-diazo-2-2′-pyridylindolenine with nitrous acid and 3-acetamido-2-2′-pyridylindole (IV; R = NHAc) on acetylation.

The isolation of 2-2′-pyridylindolone has continued to elude us. Reduction of the isatogen with tin and hydrochloric acid yielded the indoxyl again, catalytic reduction gave the " indolone hydrate " and attempted oxidation of 2-2′-pyridylindole with peracetic acid yielded 2-2′-pyridyl-2-(2-2′-pyridylindol-3-yl)indoxyl (VIII). Further evidence for the difficulty of the preparation of indolones is afforded by the recent demonstration [8] that the supposed 2-methylindolone [9] was in fact 2,2′-dimethyl-2,2′-di-indoxylyl.

The formation of the piperidine adduct (V; R = NC_5H_{10}) from 2-2′-pyridylisatogen has been mentioned earlier. Under milder conditions, however, a direct adduct (VII; R = NC_5H_{10}) is produced which appears to be an intermediate in the formation of compounds (VII; R = $CH(CN)CO_2Et$) from the isatogen with ethyl cyanoacetate and (VII; R = $CH(COPh)CO_2Et$) with ethyl benzoylacetate.

[3] Katritzky and Lagowski, " Heterocyclic Chemistry," Methuen, London, 1960, 191.
[4] Hamana and Noda, *Chem. and Pharm. Bull.* (*Japan*), 1963, **11**, 1331.
[5] Elderfield, " Heterocyclic Compounds," Wiley, New York, 1952, Vol. III, p. 108.
[6] Witkop and Patrick, *J. Amer. Chem. Soc.*, 1951, **73**, 713.
[7] Kalb and Bayer, *Ber.*, 1912, **45**, 2150.
[8] Giovannini, Farkas, and Rosales, *Helv. Chim. Acta*, 1963, **46**, 1326.
[9] Neunhoffer and Lehrmann, *Chem. Ber.*, 1961, **94**, 2960.

Two alternative syntheses of 2-2′-pyridylisatogen were investigated. In the first, which was a modification of Kröhnke's method [10] for 2-phenylisatogen, a solution of 1-[2-hydroxy-2-(2-nitrophenyl)-1-(2-pyridyl)ethyl]pyridinium bromide was exposed to sunlight for 18 days, to give a low yield of the pyridylisatogen. The quaternary salt, is very easily degraded to α′-amino-2′-nitrostyrylpyridine which, with nitrous acid, yields 2-nitrobenzyl 2-pyridyl ketone. Both compounds, on treatment with sodium borohydride and palladium–charcoal,[11] are converted into 1-hydroxy-2-2′-pyridylindole (VI). Nitrosation of this *N*-hydroxy-indole yielded the oxime of 2-2′-pyridylisatogen which, however, resisted hydrolysis to the isatogen (I).

2-4′-Pyridylisatogen was prepared by Ruggli's method for the 2-isomer; it yielded 1,2-dihydro-2-piperidino-2,4′-pyridylindolone on treatment with piperidine.

Experimental

Infrared spectra were, unless otherwise stated, taken in chloroform solution with a Unicam S.P. 200 spectrophotometer. Equivalent weights were determined by non-aqueous titration with perchloric acid.

1-[2-*Hydroxy*-2-(2-*nitrophenyl*)-1-(2-*pyridyl*)*ethyl*]*pyridinium Bromide*.—A solution of 2-bromomethylpyridine (2·0 g.) in ether (20 ml.) was added dropwise to pyridine (10 ml.) in ether (20 ml.) and the mixture refluxed for 15 min. The 2′-pyridylpyridinium bromide, which separated as an oil, was washed with dry ether, dissolved in ethanol (19·5 ml.) and treated with *o*-nitrobenzaldehyde (1·5 g.) followed by 50% potassium hydroxide solution (0·2 ml.). The solution was stirred at room temperature for 4 hr. to yield the *quaternary salt* (3·7 g.) as colourless prisms, m. p. 198—200° (from acetic acid) (Found: C, 53·6; H, 4·1; N, 10·4. $C_{18}H_{16}BrN_3O_3$ requires C, 53·7; H, 4·0; N, 10·4%).

2-2′-*Pyridylisatogen* (I).—(*a*) The method of Ruggli and Cuenin [2] from 2-2′-nitrostyrylpyridine gave the isatogen (28%) as orange plates, m. p. 183—184°, $\nu_{max.}$ 1705s and 1720(sh)s (C=O), 1400s cm.$^{-1}$ (*N*-oxide).

(*b*) A solution of the above pyridinium bromide (0·25 g.) in 50% acetic acid solution (10 ml.) was exposed to spring sunlight for 18 days. Evaporation to dryness followed by trituration with 5% sodium hydrogen carbonate solution gave the isatogen (0·04 g.).

The identity of samples prepared by methods (*a*) and (*b*) in this, and in subsequent examples, was shown by their undepressed mixed m. p. and identical infrared spectra.

1,2-*Dihydro*-2-*hydroxy*-2-2′-*pyridylindolone* (V; R = OH).—(*a*) Treatment of 2-2′-pyridylisatogen with phenylhydrazine [2] yielded the " *indolone hydrate* " (V; R = OH) as green-yellow needles, m. p. 171—173° (from ethanol) (Found: C, 69·2; H, 4·6; N, 12·6%; Equiv., 229. $C_{13}H_{10}N_2O_2$ requires C, 69·0; H, 4·4; N, 12·4%; Equiv., 226), $\nu_{max.}$ 3370m (N–H), 1700s cm.$^{-1}$ (C=O).

(*b*) A suspension of 2-2′-pyridylisatogen (0·45 g.) in ethanol (20 ml.) was shaken with hydrogen at 1 atm. and at room temperature in the presence of 10% palladium–charcoal (0·04 g.). The catalyst was removed and the green-yellow fluorescent solution concentrated to yield the " indolone hydrate " (V; R = OH), m. p. 167—168° (from ethanol). The product, on treatment with nitrous acid, gave an oily nitrosamine which gave a positive Liebermann reaction. The hydrochloride had m. p. >300° and basification of an aqueous solution liberated unchanged " indolone hydrate."

2-2′-*Pyridylindoxyl* (IV; R = OH).—(*a*) Concentration of the liquors [2] after removal of the above 1,2-dihydro-2-hydroxy-2-2′-pyridylindolone yielded the *indoxyl* (IV; R = OH) as orange-brown plates, m. p. 194—195° (from ethanol) (Found: C, 74·5; H, 4·9; N, 13·3%; Equiv., 216. $C_{13}H_{10}N_2O$ requires C, 74·3; H, 4·8; N, 13·3%; Equiv., 210. Calc. for the indolone $C_{13}H_8N_2O$: C, 75·0; H, 3·9; N, 13·5%), $\nu_{max.}$ (Nujol) 3350m cm.$^{-1}$ (N–H), no absorption in 1600—1800 cm.$^{-1}$ region; $\nu_{max.}$ (dioxan) 1705, 1720m cm.$^{-1}$ (split C=O). The indoxyl gave a positive test for a secondary amine and formed a sparingly soluble hydrochloride, m. p. *ca.* 260° (decomp.), from which it was recovered unchanged on basification of an aqueous solution.

(*b*) 2-2′-Pyridylisatogen was warmed with tin and dilute hydrochloric acid for 10 min. A clear orange solution formed initially, to be followed by the separation of the yellow indoxyl

[10] Kröhnke and Vogt, *Chem. Ber.*, 1952, **85**, 376.
[11] Coutts and Wibberley, *J.*, 1963, 4610.

hydrochloride, m. p. *ca.* 260° (decomp.). Basification of an aqueous solution of the hydrochloride liberated the free indoxyl, m. p. 194—195°.

1,2-*Dihydro*-2-*piperidino*-2-2′-*pyridylindolone* (V; R = NC_5H_{10}).—(*a*) 2-2′-Pyridylisatogen and piperidine gave [2] after 3 hr. reflux the *piperidine adduct* as green-yellow needles, m. p. 180—181° (from ethanol) (Found: C, 73·5; H, 6·5; N, 14·3%; Equiv., 152. $C_{18}H_{19}N_3O$ requires C, 73·7; H, 6·5; N, 14·3%; Equiv., 146·5), $\nu_{max.}$ 3400m (N–H), 1710s cm.$^{-1}$ (C=O).

(*b*) 2-2′-Pyridylindoxyl (0·09 g.), piperidine (0·1 ml.), and ethanol (2·0 ml.) were refluxed for 3 hr. Dilution of the solution gave the adduct (0·06 g.), m. p. 180—181°. A similar yield of the adduct was obtained after only 30 min. reflux when oxygen was bubbled through the solution. When nitrogen was bubbled through the solution, under otherwise comparable conditions, only unchanged indoxyl (74%) could be isolated. The piperidine adduct gave a positive test for a secondary amine. It was converted into a hydrochloride of m. p. >300° with dilute hydrochloric acid. Basification of an aqueous solution of this hydrochloride yielded 1,2-dihydro-2-hydroxy-2-2′-pyridylindolone.

1,2-*Dihydro*-2-*piperidino*-2-*phenylindolone*.—(*a*) 2-Phenylindolone [7] (0·2 g.), piperidine (0·2 ml.), and ethanol (2·0 ml.) were refluxed for 3 hr. to yield the *piperidine adduct* (0·14 g.) as green-yellow needles, m. p. 150—151° (from ethanol) (Found: C, 78·0; H, 6·5; N, 9·4%; Equiv., 300. $C_{19}H_{20}N_2O$ requires C, 78·0; H, 6·8; N, 9·6%; Equiv., 292), $\nu_{max.}$ 3500w (N–H), 1720s cm.$^{-1}$ (C=O). Apart from these two absorptions the infrared spectrum of this compound and 1,2-dihydro-2-piperidino-2-2′-pyridylindolone (V; R = NH_5H_{10}) were identical.

(*b*) 2-Phenylindoxyl [7] (0·05 g.) under identical conditions yielded the same adduct (0·04 g.), m. p. 150—151°.

3-*Acetoxy*-2-2′-*pyridylindole* (IV; R = OAc).—2-2′-Pyridylindoxyl (0·15 g.) and acetic anhydride (1·0 ml.) were refluxed for 5 min. The solution was diluted with ethanol, evaporated to dryness and the residue crystallised from ethanol to yield the monoacetyl derivative (0·12 g.) as colourless needles, m. p. 128—129° alone and mixed with a sample prepared by the reduction [2] of 2-2′-pyridylisatogen with zinc and acetic acid (Found: C, 71·4; H, 4·8; N, 11·2. Calc. for $C_{15}H_{12}N_2O_2$: C, 71·4; H, 4·8; N, 11·1%), $\nu_{max.}$ 3490m (N–H), 1770s cm.$^{-1}$ (acetoxyl C=O). A similar reaction with the prior addition of zinc dust (0·3 g.) and acetic acid (0·45 ml.) gave [2] the same monoacetyl derivative.

3-*Acetoxy*-1-*acetyl*-2-2′-*pyridylindole*.—The above reaction was repeated but with a reflux time of 1 hr. The *diacetylindoxyl* (0·14 g.) was obtained as colourless prisms, m. p. 139—140° (from ethanol) (Found: C, 69·3; H, 4·85; N, 9·4. $C_{17}H_{14}N_2O_3$ requires C, 69·3; H, 4·8; N, 9·5%), $\nu_{max.}$ 1780s (acetoxyl C=O), 1720s cm.$^{-1}$ (amide C=O).

3-*Nitroso*-2-2′-*pyridylindole*.—(*a*) 2-2′-Pyridylindole (1·0 g.), amyl nitrite (0·7 ml.), and benzene (25 ml.) were stirred at room temperature for 12 hr. The nitrosoindole (0·84 g.), which separated from the solution in two crops, crystallized from benzene as orange-yellow prisms, m. p. 186—187°, alone and mixed with a sample prepared [2] by the action of hydroxylamine hydrochloride on 2-2′-pyridylindoxyl (Found: C, 70·1; H, 4·2%; Equiv., 221. Calc. for $C_{13}H_9N_3O$: C, 69·9; H, 4·1%; Equiv., 223).

(*b*) The use of 1,2-dihydro-2-hydroxy-2-2′-pyridylindolone in place of the pyridylindoxyl in (*a*) and a reflux time of 3 hr. yielded the nitrosoindole (0·08 g.), m. p. 186—187°.

3-*Nitroso*-2-*phenylindole*.—2-Phenylindoxyl [7] (0·135 g.), hydroxylamine hydrochloride (0·4 g.), and ethanol (10 ml.) were refluxed for 15 hr. The solution was diluted with water (12 ml.) to yield the nitrosoindole (0·14 g.) as prisms, m. p. 264—265° (from ethanol). The product was identical with one obtained by nitrosation of 2-phenylindole (cf. Kalb and Bayer [7]).

3-*Nitro*-2-2′-*pyridylindole*.—2-2′-Pyridylindole (0·2 g.), amyl nitrite (0·6 g.), and benzene (25 ml.) were refluxed for 6 hr. The solution was concentrated to yield the *nitroindole* (0·15 g.) as yellow needles, m. p. 204—205° (from ethanol) (Found: C, 64·8; H, 4·0%; Equiv., 231. $C_{13}H_9N_3O_2$ requires C, 65·2; H, 3·8%; Equiv., 239).

3-*Amino*-2-2′-*pyridylindole* (IV; R = NH_2).—Sodium dithionite (0·75 g.) was added to a solution of 3-nitroso-2-2′-pyridylindole (0·35 g.) in ethanol (2·0 ml.) and 2N-sodium hydroxide (4·0 ml.), and the mixture heated on a water-bath for 4 min. to yield the *amine* (0·3 g.) as yellow plates, m. p. 171—172° (from ethyl acetate) (Found: C, 74·6; H, 5·3; N, 20·4. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3; N, 20·1%). Reduction of the 3-nitroindole gave a similar yield of the same amine.

3-*Diazo*-2-2′-*pyridylindolenine*.—Sodium nitrite (0·2 g.) in water (1·0 ml.) was added dropwise to a solution of 3-amino-2-2′-pyridylindole (0·4 g.) in water (20 ml.) and concentrated sulphuric

acid (1·4 ml.) at 0° and the mixture stirred for 20 min. The diazoniumsulphate which separated was collected and triturated with 20% sodium carbonate solution to yield the 3-*diazoindolenine* (0·27 g.) as yellow needles, m. p. 97—98° (from benzene–light petroleum) (Found: C, 70·7; H, 3·7; N, 25·4. $C_{13}H_8N_4$ requires C, 70·9; H, 3·6; N, 25·5%), $\nu_{max.}$ 2100s cm.$^{-1}$ (C=$\overset{+}{N}$=$\overset{-}{N}$).

3-*Acetamido*-2-2′-*pyridylindole* (IV; R = NHAc).—3-Amino-2-2′-pyridylindole (0·1 g.) and acetic anhydride (1·0 ml.) were refluxed together for 1 min. to yield the 3-acetamidoindole (IV; R = NHAc) as colourless needles, m. p. 193—194° (from ethanol), alone and with a sample prepared by treatment of 3-nitroso-2-2′-pyridylindole with zinc, acetic acid, and acetic anhydride [2] (Found: C, 71·1; H, 5·45; N, 16·7. Calc. for $C_{15}H_{13}N_3O$: C, 71·6; H, 5·2; N, 16·7%), $\nu_{max.}$ 3400w (N–H), 1670s (amide C=O).

2-2′-*Pyridyl*-2-(2-2′-*pyridylindol*-3-*yl*)*indoxyl* (VIII).—2-2′-Pyridylindole (0·5 g.), peracetic acid (0·6 ml.), and chloroform (10 ml.) were refluxed for 1 hr. The solution was cooled, washed with water and evaporated to dryness to yield the *indolylindoxyl* (0·1 g.) as yellow prisms, m. p. 236—237° (from ethanol) (Found: C, 77·4; H, 4·8; N, 13·6. $C_{26}H_{18}N_4O$ requires C, 77·7; H, 4·5; N, 13·9%), $\nu_{max.}$ 3500w and 3400w (N–H), 1715s cm.$^{-1}$ (C=O).

1,2-*Dihydro*-1-*hydroxy*-2-*piperidino*-2-2′-*pyridylindolone* (VII; R = NC_5H_{10}).—2-2′-Pyridylisatogen (0·5 g.), piperidine (0·37 ml.), and ethanol (8·0 ml.) were stirred at room temperature for 1 hr. to yield the *piperidine adduct* (VII; R = NC_5H_{10}) (0·53 g.) as green-yellow prisms, m. p. 127—128° (from ethyl acetate) (Found: C, 69·6; H, 6·2; N, 13·5. $C_{18}H_{19}N_3O_2$ requires C, 69·9; H, 6·15; N, 13·6%), $\nu_{max.}$ 3200—3400m (O–H), 1710s cm.$^{-1}$ (C=O).

Ethyl α-*Cyano*-α-(2,3-*dihydro*-1-*hydroxy*-3-*oxo*-2-2′-*pyridylindol*-2-*yl*)*acetate* (VII; R = $CH(CN)CO_2Et$).—2-2′-Pyridylisatogen (0·23 g.), ethyl cyanoacetate (0·11 g.), piperidine (0·1 ml.), and ethanol (4·0 ml.) were stirred together at room temperature for 16 hr. to yield the *cyanoacetate* (VII; R = $CH(CN)CO_2Et$) (0·1 g.) as colourless prisms, m. p. 165—166° (from ethanol) (Found: C, 63·75; H, 4·4; N, 12·55. $C_{15}H_{15}N_3O_4$ requires C, 64·1; H, 4·45; N, 12·4%). The same product was isolated by the reaction of the piperidine adduct (VII; R = NC_5H_{10}) with ethyl cyanoacetate.

Ethyl α-*Benzoyl*-α-(2,3-*dihydro*-1-*hydroxy*-3-*oxo*-2-2′-*pyridylindol*-2-*yl*)*acetate* (VII; R = $CH(COPh)CO_2Et$).—2-2′-Pyridylisatogen (0·23 g.), ethyl benzoylacetate (0·19 g.), piperidine (0·1 ml.), and ethanol (4·0 ml.) were stirred together at room temperature for 16 hr. to yield the *benzoylacetate* (VII; R = $CH(COPh)CO_2Et$) (0·23 g.) as cream prisms, m. p. 163—164° (from ethanol) (Found: C, 69·2; H, 5·1; N, 6·6. $C_{24}H_{20}N_2O_4$ requires C, 69·2; H, 4·8; N, 6·7%).

1-(2-*Nitro*-α-*pyridylstyryl*)*pyridinium Bromide*.—1-[2-Hydroxy-2-(2-nitrophenyl)-1-(2-pyridyl)ethyl]pyridinium bromide (2·0 g.), pyridine (2·0 ml.), and acetic anhydride (6·0 ml.) were refluxed for 2 hr. The solution was cooled, to yield the *quaternary salt* (1·3 g.) as colourless prisms, m. p. 258—260° (from acetic acid) (Found: C, 56·75; H, 3·6; N, 11·2. $C_{18}H_{19}BrN_3O_2$ requires C, 56·3; H, 3·65; N, 10·9%).

α-*Amino*-2-*nitrostyrylpyridine*.—1-(2-Nitro-α-pyridylstyryl)pyridinium bromide (3·0 g.) and piperidine (30 ml.) were heated together on a water-bath for 5 min. The deep red solution was poured into water (300 ml.) to precipitate the aminostyrylpyridine (0·95 g.) as orange needles, m. p. 93—94° (from ethanol). The amine darkened on storage and was not obtained analytically pure (Found: C, 63·6; H, 4·5; N, 15·9. Calc. for $C_{13}H_{11}N_3O_2$: C, 64·7; H, 4·6; N, 17·4%).

2-*Nitrobenzyl* 2-*pyridyl Ketone*.—A solution of α-amino-2-nitrostyrylpyridine (0·3 g.) in dilute hydrochloric acid (10 ml.) was stirred at 0° during the addition of sodium nitrite (0·3 g.) in water (5·0 ml.). The clear solution was stirred at room temperature for 30 min. and made alkaline with 2N-sodium hydroxide to give the *ketone* (0·29 g.) as colourless prisms, m. p. 84—85° (from aqueous acetic acid) (Found: C, 64·15; H, 4·3; N, 11·5. $C_{13}H_{10}N_2O_3$ requires C, 64·4; H, 4·6; N, 11·6%), $\nu_{max.}$ 1700s (C=O), 1350s, 1530s cm.$^{-1}$ (NO_2).

1-*Hydroxy*-2-2′-*pyridylindole* (VI).—A solution of 2-nitrobenzyl 2-pyridyl ketone (0·35 g.) in dioxan (6·0 ml.) was added to a stirred suspension of palladium–charcoal (0·18 g.) and sodium borohydride (0·35 g.) in 2% sodium hydroxide. A stream of nitrogen was passed through the mixture for 30 min., the catalyst was removed and the filtrate acidified strongly with concentrated hydrochloric acid. The clear solution was boiled and cooled to yield the N-hydroxyindole (0·29 g.) as yellow needles, m. p. 199—201° (from ethanol) (Found: C, 74·1; H, 5·3; N, 13·3. $C_{13}H_{10}N_2O$ requires C, 74·2; H, 4·8; N, 13·3%), $\nu_{max.}$ (KCl) 3400w (free OH), 2500—2900s cm.$^{-1}$ (bonded OH).

2-2′-*Pyridylisatogen Oxime*.—A solution of 1-hydroxy-2-2′-pyridylindole (0·06 g.) in N-hydrochloric acid (0·3 ml.) and water (5·0 ml.) was treated with sodium nitrite (0·02 g.) in water (0·5 ml.). Within a few minutes the solution had turned red and the oxime (0·04 g.) precipitated. Crystallization from ethanol gave yellow prisms, m. p. 214—216°, alone and with a sample prepared from 2-2′-pyridylisatogen and hydroxylamine.[2]

2-4′-*Pyridylisatogen*.—The method of Ruggli and Cuenin [2] for the 2′-isomer was carried out from 4-2′-nitrostyrylpyridine without isolation of the intermediate 4-(α,β-dichloro-2-nitrophenethyl)pyridine or 4-2′-nitrophenylethynylpyridine to yield the isatogen (10%) as orange plates, m. p. 200—201° (from ethanol) (Found: C, 69·4; H, 3·8; N, 12·7. $C_{13}H_8N_2O_2$ requires C, 69·6; H, 3·6; N, 12·5%), $\nu_{max.}$ 1705s and 1725(sh)s (C=O), 1405s cm.$^{-1}$ (*N*-oxide).

1,2-*Dihydro*-2-*piperidino*-2-4′-*pyridylindolone*.—A solution of 2-4′-pyridylisatogen (0·2 g.) and piperidine (0·2 ml.) in ethanol (4·0 ml.) was refluxed for 3 hr. to yield the piperidine adduct (0·1 g.) as green-yellow plates, m. p. 200—201° (from ethanol) (Found: C, 73·8; H, 6·8; N, 14·1. $C_{18}H_{19}N_3O$ requires C, 73·7; H, 6·5; N, 14·3%), $\nu_{max.}$ 3400m (N–H), 1710s cm.$^{-1}$ (C=O)

SCHOOL OF PHARMACY, SUNDERLAND TECHNICAL COLLEGE,
SUNDERLAND, CO. DURHAM.

[*Received, June 30th*, 1964.]