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Preparation and antibacterial activity of isatogens and related compounds

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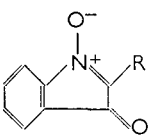
A number of 2-substituted isatogens are shown to possess moderate *in vitro* antibacterial properties. The syntheses of closely related compounds in the pyrrolo-[2,3-*c*]pyridine and pyrrolo[3,2-*b*]pyridine series are described. Antibacterial activities of these compounds, of the structurally similar indolones, *N*-hydroxyindoles, indoxyls and indoles are recorded, together with those of certain styryl compounds required as intermediates.

IN routine *in vitro* antibacterial screening tests we found that 2-pyrid-2′-ylisatogen (I; R = pyrid-2-yl) showed interesting activity. This led us to prepare a short series of closely related isatogens and some aza-analogues (II and III). 2-Phenylisatogen (I; R = Ph) (Pfeiffer, 1916),



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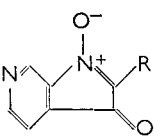

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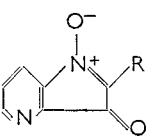
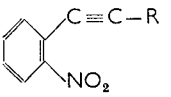


(III)

methyl isatogenate (I; R=CO·O·Me) (Alessandrai, 1928) and 2-pyrid-4′-ylisatogen (I; R=pyrid-4-yl) (Patterson & Wibberley, 1965) were obtained from the isomeric acetylenes (IV) under conditions previously described in the literature. Closely related to these acetylenes is 3-nitro-4- phenylethynylpyridine (V; R=Ph), which was derived from 3-nitro-4-styrylpyridine by chlorination followed by dehydrochlorination, and which yielded 3-oxo-2-phenyl-3*H*-pyrrolo[2,3-*c*]pyridine 1-oxide (II; R=Ph) on treatment with nitrosobenzene. The dehydrohalogenation of 4-(1,2-dichloro-2-pyrid-2′-ylethyl)-3-nitropyridine failed to yield any 3-nitro-4-pyrid-2′-ylethynylpyridine (V; R=pyrid-2-yl) and thus frustrated our attempts to prepare the 2-pyrid-2′-ylpyrrolopyridine 1-oxide (II; R=pyrid-2-yl). Several other attempted dehydrohalogenations also failed and in the case of 4-($\alpha\beta$-dibromophenethyl)-3-nitropyridine the main product of reaction was 3-nitro-4-styrylpyridine.

Splitter & Calvin (1955) showed that isatogens may be synthesised from the corresponding styryl compounds, in certain instances, on exposure to sunlight of their solutions in benzene. We have now demonstrated that the method is also successful for the synthesis of 2-*p*-dimethylaminophenyl-3-oxo-3*H*-pyrrolo[2,3-*c*]pyridine 1-oxide (II; R=*p*-$Me_2N{\cdot}C_6H_4$) from 4-*p*-dimethylaminostyryl-3-nitropyridine (VI; R=Me_2N) and for the synthesis of 2-*p*-dimethylaminophenyl-3-oxo-3*H*-pyrrolo[3,2-*b*]pyridine 1-oxide (III; R=*p*-$Me_2N{\cdot}C_6H_4$) from 2-*p*-dimethylaminostyryl-3-nitro pyridine (VII; R=Me_2N).

From the School of Pharmacy, The Technical College, Sunderland.



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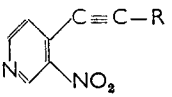

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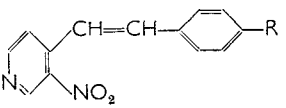

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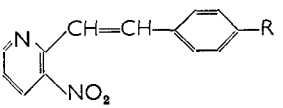
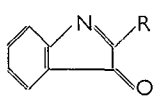


(VII)

Traces of a product, suggested by the evidence of its infrared spectrum to be 2-*p*-hydroxyphenyl-3-oxo-3*H*-pyrrolo-[2,3-*c*]pyridine 1-oxide (II; R=*p*-HO·C_6H_4), were obtained by irradiation of the sparingly soluble hydroxy-compound (VI; R=OH), but attempts to prepare 3-oxo-3*H*-pyrrolo[3,2-*c*]pyridine 1,5-dioxides by irradiation of solutions of 4-nitro-3-styrylpyridine *N*-oxides were unsuccessful.

Indole derivatives such as the 3*H*-indolones (VIII), the *N*-hydroxyindoles (X) and the indoxyls (XI; R_1=OH) may all be considered to be derived theoretically from the corresponding isatogens by reduction. However, we have recently shown that the compound previously thought to be 2-pyrid-2′-yl-3*H*-indolone (VIII; R = pyrid-2-yl) is in fact 2-pyrid-2′-yl-indoxyl (Patterson & Wibberley, 1965). We also find that the compound hitherto thought to be 2-methoxycarbonyl-3*H*-indolone (VIII; R = CO·O·Me) shows NH absorption in its infrared spectrum, has an ultraviolet spectrum closely similar to that of other 2,2′-disubstituted di-indoxyls (Hassner & Haddadin, 1963), and is therefore presumably 2,2′-dimethoxycarbonyl-2,2′-di-indoxyl (IX; R=CO·O·Me). 2-Phenyl-3*H*-indolone (VIII; R=Ph) was the only authentic indolone we were able



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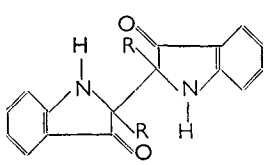

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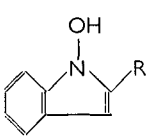

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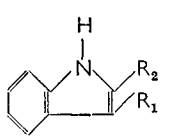

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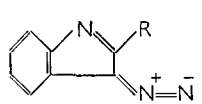

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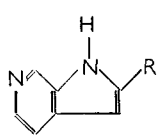

(XIII)

to test. The four *N*-hydroxyindoles recorded in Table 1 were prepared by methods described in the literature. The four known indoxyls were prepared by reduction of the corresponding isatogens with phenylhydrazine.

The literature contains several references to the antibacterial activity of indole itself (e.g. Sandholzer & Tittsler, 1934); it was of interest therefore to prepare 2-phenyl-, 2-pyrid-2′-yl-, and 2-pyrid-4′-yl-indoles for

comparison of their activity with the corresponding isatogens. The three compounds were obtained by a Fischer-type synthesis using polyphosphoric acid (Sugasawa & others, 1957). Such methods are not readily applicable in the pyridine series and the aza-analogues 2-phenyl-, 2-pyrid-2′-yl and 2-pyrid-4′-yl-pyrrolo[2,3-*c*]pyridine (XIII) were prepared by the Madelung-type cyclisation of the corresponding amides (cf. Clayton & Kenyon, 1950). Treatment of 3-amino-2-pyrid-2′-ylindole with nitrous acid had yielded 3-diazo-2-pyrid-2′-yl-3*H*-indole (Patterson & Wibberley, 1965) and the corresponding derivatives of 2-phenyl- and 2-pyrid-4′-yl-indole have now been prepared.

ANTIBACTERIAL ACTIVITIES

The results of antibacterial screening tests are in Table 1. The isatogens and 3-oxo-3*H*-pyrrolopyridine 1-oxides were all effective against Gram-positive organisms, but only 2-phenylisatogen and 2-pyrid-2′-ylisatogen

TABLE 1. MINIMAL INHIBITORY CONCENTRATION (MG/100 ML) OF ISATOGENS AND RELATED COMPOUNDS

Compound	Formula	Test organisms				
		Staph. aureus	*B. subtilis*	*E. coli*	*S. typhi*	*P. vulgaris*
Methyl isatogenate	I; R = CO·O·Me	2·5	10	>40	20	>40
2-Phenylisatogen	I; R = Ph	10	10	20*	20*	20*
2-Pyrid-2′-ylisatogen	I; R = pyrid-2-yl	2·5	2·5	10	10	20
2-Pyrid-4′-ylisatogen	I; R = pyrid-4-yl	5	5	>40	>40	>40
3-Oxo-2-phenyl-3*H*-pyrrolo[2,3-*c*]pyridine 1-oxide	II; R = Ph	1·25	5	2·5	>40	>40
2-*p*-Dimethylaminophenyl-3-oxo-3*H*-pyrrolo[2,3-*c*]pyridine 1-oxide	II; R = $Me_2N·C_6H_4$	2·5*	0·6*	20*	>40*	>40*
2-*p*-Dimethylaminophenyl-3-oxo-3*H*-pyrrolo[2,3-*b*]pyridine 1-oxide	III; R = $Me_2N·C_6H_4$	>40	>40	20	>40	10
1-Hydroxy-2-phenylindole	X; R = Ph	0·31	0·31	1·25*	10*	40*
Methyl indoxylate	XI; R_1 = OH, R_2 = CO·OMe	2·5	10	5	10	40
2-Pyrid-2′-ylindole	XI; R_1 = H, R_2 = pyrid-2-yl	<0·31	0·31	>40	5	>40
2-Pyrid-4′-ylindole	XI R_1 = H, R_2 = pyrid-4-yl	1·25	2·5	>5*	>5*	>5*
3-Nitroso-2-pyrid-4′-ylindole	XI; R_1 = NO, R_2 = pyrid-4-yl	10	10	10	>40	>40
3-Amino-2-pyrid-2′-ylindole	XI; R_1 = NH_2, R_2 = pyrid-2-yl	10	>40	5	>40	2·5
3-Amino-2-pyrid-4′-ylindole	XI; R_1 = NH_2, R_2 = pyrid-4-yl	<1·25	10	10	10	>40
3-Diazo-2-phenyl-3*H*-indole	XII; R = Ph	<0·31	<0·31	1·25	1·25	5
3-Diazo-2-pyrid-2′-yl-3*H*-indole	XII; R = pyrid-2-yl	0·31	0·31	1·25	0·62	5
3-Diazo-2-pyrid-4′-yl-3*H*-indole	XII; R = pyrid-4-yl	1·25	1·25	1·25	1·25	1·25
2-Pyrid-2′-ylpyrrolo[2,3-*c*]pyridine	XIII; R = pyrid-2-yl	1·25	1·25	10	10	20
2-Pyrid-4′-ylpyrrolo[2,3-*c*]pyridine	XIII; R = pyrid-4-yl	2·5	10	5	10	10
4-Nitro-3-styryl-pyridine 1-oxide		5	5	5	5	5

*Tested as a suspension in ethanol.

The following compounds had MIC 40 or >40 against all the Gram-negative organisms; any activity against Gram-positive organisms is indicated. 6-Nitro-2-phenylisatogen (*Staph. aureus* 10*, *B. subtilis* 10*), 2-phenyl-3*H*-indolone, 2,3-dihydro-2-hydroxy-2-pyrid-2′-ylindolone, 1-hydroxyindole-2-carboxylic acid, 1,2-dihydroxyindole, 1-hydroxy-2-pyrid-2′-ylindole (*Staph. aureus* 2·5), 2-phenylindoxyl (*Staph. aureus* 1·25), 6-nitro-2-phenylindoxyl, 2-pyrid-2′-ylindoxyl (*Staph. aureus* 0·62, *B. subtilis* 5), 2,2′-diphenyl-2,2′-di-indoxyl (*Staph. aureus* 2·5, *B. subtilis* 1·25), 2,2′-dimethoxycarbonyl-2,2′-di-indoxyl, 2-phenylindole, 3-nitroso-2-phenylindole (*Staph. aureus* 10), 3-nitroso-2-pyrid-2′-ylindole, 3-amino-2-phenylindole, 2-phenylpyrrolo-[2,3-*c*]pyridine, 5-methyl-2-phenylpyrrolo[3,2-*b*]pyridine, 3-*p*-dimethyl-aminostyryl-4-nitropyridine 1-oxide (*Staph. aureus* 10), 3-*p*-hydroxystyryl-4-nitropyridine 1-oxide, 3-nitro-2-styrylpyridine, 2-*p*-dimethylamino-styryl-3-nitropyridine, 3-nitro-4-styrylpyridine (*Staph. aureus* 2·5, *B. subtilis* 20), 4-*p*-dimethylaminostyryl-3-nitropyridine, 4-*p*-hydroxystyryl-3-nitropyridine.

showed a broad spectrum of activity. The inactivity of 2-phenyl-2*H*-indolone and the "hydrate" of 2-pyrid-2′-yl-3*H*-indolone suggests that the 1-oxide group is essential for growth inhibition. With the exception of 1-hydroxy-2-phenylindole the 1-hydroxyindoles and indoxyls were of little interest.

The pyrrolo[2,3-*c*]pyridines were generally more effective than the analogous indoles although the 3-diazo-group conferred a broad spectrum of activity in the 2-substituted indoles. The literature contains several references to the growth-inhibitory properties of styryl compounds (Rubtsov, Pershin, Novitskaya, Milovanova & Vichkanova, 1960) and nitrostyryl *N*-oxides (Buchmann & Kirstein, 1962). The activity of one of our intermediates, 4-nitro-3-styrylpyridine 1-oxide, is therefore not surprising.

Experimental

General method for the preparation of the styrylpyridines. A solution of the picoline (0·025 mole), the aldehyde (0·03 mole) and piperidine (0·005 mole) in methanol (10 ml) was refluxed for 24 hr. The solution was cooled, the styryl compound collected and crystallised from the stated solvent.

4-p-*Hydroxystyryl*-3-*nitropyridine* (VI; R=OH) (40%) separated from ethanol in orange needles, m.p. 257–259°. Found: C, 64·3; H, 4·1; N, 11·4. $C_{13}H_{10}N_2O_3$ requires C, 64·4; H, 4·2; N, 11·55%. A solution of the styryl compound (0·34 g) in benzene (250 ml) was exposed to sunlight for one week. The solution was concentrated to dryness and the residue triturated with ethanol to yield a maroon solid (0·006 g), m.p. > 360°. ν_{max} ($CHCl_3$) 1390s (*N*-oxide), 1710s cm^{-1} (C=O).

4-p-*Dimethylaminostyryl*-3-*nitropyridine* (VI; R=Me_2N) (82%) separated from ethanol as dark green needles, m.p. 162–163°. Found: C, 66·3; H, 5·6; N, 15·7. $C_{15}H_{15}N_3O_2$ requires C, 66·9; H, 5·6; N, 15·6%.

3-*Nitro*-4-(2-*pyrid*-2′-*ylvinyl*)*pyridine* (81%) separated from ethanol as yellow prisms, m.p. 110–111°. Found: C, 63·6; H, 4·0; N, 18·3. $C_{12}H_9N_3O_2$ requires C, 63·5; H, 4·0; N, 18·5%.

3-*Nitro*-2-*styrylpyridine* (VII; R=H) (12·2%) separated from aqueous methanol as yellow needles, m.p. 107–108°. A better yield (33%) was obtained by using acetic anhydride (0·038 mole) in place of the piperidine and methanol. Found: C, 68·8; H, 4·45; N, 12·35. $C_{13}H_{10}N_2O_2$ requires C, 69·0; H, 4·45; N, 12·4%.

2-p-*Dimethylaminostyryl*-3-*nitropyridine* (VII; R=Me_2N) (53%) was obtained after 4-days' reflux. It separated from methanol as dark-red needles, m.p. 148–149°. Found: C, 66·4; H, 5·4; N, 15·3. $C_{15}H_{15}N_3O_2$ requires C, 66·9; H, 5·6; N, 15·6%.

3-p-*Dimethylaminostyryl*-4-*nitropyridine* 1-*oxide* (28%) separated from 2-ethoxyethanol as dark-red needles, m.p. 207–208°. Found: C, 63·1; H, 5·5; N, 14·5. $C_{15}H_{15}N_3O_3$ requires C, 63·15; H, 5·3; N, 14·7%. Irradiation of a solution in benzene for 10 days yielded no pyrrolopyridine 1,5-dioxide.

3-p-*Hydroxystyryl*-4-*nitropyridine* 1-*oxide* (15·5%). Separated from acetic acid as orange needles, m.p. > 360°. Found: C, 60·2; H, 4·1; N, 10·7. $C_{13}H_{10}N_2O_4$ requires C, 60·5; H, 3·9; N, 10·8%.

4-(αβ-*Dichlorophenethyl*)-3-*nitropyridine*. A solution of 3-nitro-4-styrylpyridine (1·9 g) in glacial acetic acid was saturated with chlorine. The precipitate was collected and triturated with dilute aqueous ammonia to yield the *dichloro*-compound (1·3 g) as colourless prisms, m.p. 133–134° (from methanol). Found: C, 52·6; H, 3·3; Cl, 23·7; N, 9·4. $C_{13}H_{10}Cl_2N_2O_2$ requires C, 52·7; H, 3·4; Cl, 23·8; N, 9·4%.

4-(αβ-*Dibromophenethyl*)-3-*nitropyridine*. A solution of 3-nitro-4-styrylpyridine (3·8 g) in acetic acid (25 ml) and bromine (4·0 g) was maintained at 60–70° for 40 min. The product was collected and triturated with dilute aqueous ammonia to yield the *dibromo*-compound (3·1 g) as colourless prisms, m.p. 222–224° (from methanol). Found: C, 40·8; H, 2·6; Br, 40·9; N, 7·0. $C_{13}H_{10}Br_2N_2O_2$ requires C, 40·4; H, 2·6; Br, 41·4; N, 7·2%.

4-(1,2-*Dichloro*-2-*pyrid*-2′-*ylethyl*)-3-*nitropyridine*. Chlorination of 3-nitro-4-(2-pyrid-2′-ylvinyl)pyridine (2·0 g) under similar conditions yielded the *dichloro*-compound (0·6 g) as colourless prisms, m.p. 135–136° (from ethanol). Found: C, 48·0; H, 3·2; Cl, 23·5; N, 14·2. $C_{12}H_9Cl_2N_3O_2$ requires C, 48·3; H, 3·0; Cl, 23·8; N, 14·1%.

3-(αβ-*Dichlorophenethyl*)-4-*nitropyridine* 1-*oxide*. Chlorination of 4-nitro-3-styrylpyridine 1-oxide (2·0 g) under the above conditions yielded the *dichloro*-compound (1·2 g) as yellow prisms, m.p. 177–178° (from ethyl acetate). Found: C, 50·6; H, 3·4; N, 9·0. $C_{13}H_8Cl_2N_2O_3$ requires C, 50·3; H, 2·6; N, 9·0%.

3-*Oxo*-2-*phenyl*-3-*Hpyrrolo*[2,3-*c*]*pyridine* 1-*oxide* (II; R=Ph). A solution of 4-(αβ-dichlorophenethyl)-3-nitropyridine (1·3 g) and potassium hydroxide (0·52 g) in ethanol (5·0 ml) was refluxed for 2 hr and then concentrated to dryness. The residue was extracted with benzene (20 ml) and the extract passed down a column of silica gel (10 g) and Celite (5 g). The column was eluted with benzene and the eluate collected (500 ml) until its infrared spectrum no longer showed a peak at 2200 cm^{-1} (C≡C absorption of 3-nitro-4-phenylethynylpyridine). The solution was evaporated to yield the nitropyridine (V; R=Ph) (0·4 g) which, without further purification, was dissolved in chloroform (5·0 ml) and refluxed for 1 hr with nitrosobenzene (0·25 g). The solution was concentrated to low bulk when the *pyrrolopyridine* 1-*oxide* (0·32 g) crystallised out. It separated from ethanol as orange plates, m.p. 171–172°. Found: C, 69·5; H, 3·4; N, 12·4. $C_{13}H_8N_2O_2$ requires C, 69·6; H, 3·6; N, 12·5%. ν_{max} ($CHCl_3$) 1400s (*N*-oxide) 1710s cm^{-1} (C=O).

2-p-*Dimethylaminophenyl*-3-*oxo*-3H-*pyrrolo*[3,2-*b*]*pyridine* 1-*oxide* (III; R=$Me_2N{\cdot}C_6H_4$). A solution of 2-*p*-dimethylaminostyryl-3-nitropyridine (0·25 g) in benzene (250 ml) was exposed to sunlight for two weeks. The dark-blue solution was filtered and the filtrate evaporated to dryness. The residue was stirred with ethanol (5·0 ml) to yield the *pyrrolopyridine* 1-*oxide* (0·073 g) as dark-blue needles, m.p. 212° (decomp.) (from 2-ethoxyethanol). Found: C, 67·3; H, 5·0; N, 15·7. $C_{15}H_{13}N_3O_2$ requires

C, 67·5; H, 4·9; N, 15·7%. ν_{max} ($CHCl_3$) 1380s (*N*-oxide), 1715s cm^{-1} split (C=O).

2-p-*Dimethylaminophenyl*-3-*oxo*-3H-*pyrrolo*[2,3-c]*pyridine* 1-*oxide* (II; R=$Me_2N{\cdot}C_6H_4$). In a similar irradiation 4-*p*-dimethylaminostyryl-3-nitropyridine (VI; R=Me_2N) (0·5 g) after four days yielded the *pyrrolo*-[2,3-*c*]*pyridine* 1-*oxide* (0·145 g) as dark-blue needles, m.p. 206° (decomp.) (from ethanol). Found: C, 66·9; H, 5·0; N, 15·6. $C_{15}H_{13}N_3O_2$ requires C, 67·5; H, 4·9; N, 15·7%. ν_{max} ($CHCl_3$) 1380s (*N*-oxide), 1705s cm^{-1} (C=O).

2,2′-*Dimethoxycarbonyl*-2,2′-*di-indoxyl* (IX; R=CO·O·Me) (a) A solution of methyl indoxylate (0·3 g) and benzoyl peroxide (1·2 g) in acetone (50 ml) was allowed to evaporate to dryness at room temperature. The residue was boiled with benzene (10 ml), and the hot suspension filtered to yield the *di-indoxyl* (0·3 g). It separated from nitrobenzene as yellow needles, m.p. 255° (decomp.). Found: C, 63·4; H, 4·4; N, 7·7. $C_{20}H_{16}N_2O_6$ requires C, 63·2; H, 4·2; N, 7·4%. ν_{max} (Nujol) 1730s (ester C=O), 1700s (ring C=O), 3400m cm^{-1} (N–H). λ_{max} (ethanol) 235 mμ (log ϵ 4·27), 265 (3·75), 390 (3·40) (Hassner & Haddadin state λ_{max} 235, 255, 395 mμ for 2,2′-di-indoxyls). (b) Treatment of methyl isatogenate with phenylhydrazine under the conditions described by Ruggli & Bollinger (1921) for the preparation of 2-methoxycarbonyl-3*H*-indolone yielded the same di-indoxyl of identical infrared spectrum and undepressed mixed m.p.

3-*Picolinamido*-4-*picoline*. Picolinic acid (7·5 g) and thionyl chloride (20 ml) were refluxed together for 20 min and the excess thionyl chloride removed under vacuum. An extract in benzene (20 ml) of the residue was added to a solution of 3-amino-4-picoline (3·25 g) in benzene (20 ml) over 10 min. After 1 hr the precipitated amide hydrochloride was collected, treated with dilute ammonia solution until alkaline, and the mixture evaporated to dryness. The residue was extracted with boiling light petroleum (120°–160°) from which the *amide* (4·1 g) separated as pink needles, m.p. 141–142°. Found: C, 67·8; H, 5·3; N, 19·5. $C_{12}H_{11}N_3O$ requires C, 67·5; H, 5·2; N, 19·7%.

3-*Isonicotinamido*-4-*picoline*. A similar treatment of 3-amino-4-picoline (7·5 g) with freshly prepared isonicotinoyl chloride (from 24·7 g of isonicotinic acid) yielded the amide hydrochloride, which was converted into the *amide* (12·9 g) by basification of its aqueous solution. The amide crystallised as a *dihydrate*, m.p. 82–84° (from aqueous ethanol). Found: C, 57·5; H, 6·1; N, 18·5. $C_{12}H_{11}N_3O{\cdot}2H_2O$ requires C, 57·8; H, 6·0; N, 17·9%.

3-*Benzamido*-4-*picoline monohydrate*. A solution of 3-amino-4-picoline (5·6 g) and benzoyl chloride (8·0 ml) in pyridine (20 ml) was stirred at room temperature for 1 hr and then poured into water (125 ml). The oil which separated was extracted with chloroform and the extracts washed with water, dried, and evaporated to yield the amide monohydrate (6·9 g) as colourless needles, m.p. 80–82° (from aqueous ethanol). Found: C, 68·0; H, 6·0; N, 12·4. $C_{13}H_{12}N_2O.H_2O$ requires C, 67·8; H, 6·1; N, 12·2%. (Koenigs & Fulde, 1927, state m.p. 81° for the anhydrous compound).

2-Pyrid-2'-ylpyrrolo[2,3-c]*pyridine* (XIII; R=pyrid-2-yl). A solution of 3-picolinamido-4-picoline (1 g) and sodium ethoxide (0·7 g) in absolute ethanol (50 ml) was distilled during the passage of a stream of nitrogen. The bath temperature was raised to 325° where it was maintained for 10 min. Water (10 ml) was added to the cooled residue and the solution extracted with chloroform. Evaporation of the extracts followed by sublimation of the residue yielded the *pyrrolopyridine* (0·29 g) as prisms, m.p. 205–206° (from ethanol). Found: C, 73·7; H, 4·7; N, 21·6. $C_{12}H_9N_3$ requires C, 73·9; H, 4·6; N, 21·5%.

2-Pyrid-4'ylpyrrolo[2,3-c]*pyridine* (XIII; R=pyrid-4-yl). Similar treatment of 3-isonicotinamido-4-picoline at 300° for 10 min yielded the *pyrrolopyridine* (12%) as colourless prisms, m.p. 251–252° (from dioxan). Found: C, 73·5; H, 4·7; N, 21·7. $C_{12}H_9N_3$ requires C, 73·9; H, 4·6; N, 21·5%.

2-Phenylpyrrolo[2,3-c]*pyridine* (XIII; R=Ph). 3-Benzamido-4-picoline at 320° for 20 min yielded the *2-phenylpyrrolopyridine* (24%) as colourless needles, m.p. 229–231° (from aqueous ethanol). Found: C, 79·6; H, 5·2; N, 13·9. $C_{13}H_{10}N_2$ requires C, 80·3; H, 5·2; N, 14·4%.

3-Nitroso-2-pyrid-4'-ylindole (XI; R_1=NO,R_2=pyrid-4-yl). 2-Pyrid-4'-ylindole (0·4 g), sodium nitrite (0·2 g) and acetic acid (10 ml) were stirred at room temperature for 10 min. Filtration yielded the nitrosoindole (0·43 g) as yellow needles, m.p. 249–250° (from 2-ethoxyethanol). Found: C, 70·1; H, 4·2; N, 18·75. $C_{13}H_9N_3O$ requires C, 69·9; H, 4·1; N, 18·8%.

3-Amino-2-pyrid-4'-ylindole (XI; R_1=NH_2,R_2=pyrid-4-yl). Sodium dithionite (0·75 g) was added to a solution of 3-nitroso-2-pyrid-4'-ylindole (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 (0·25 g) as yellow-green prisms, m.p. 219–220° (from ethanol). Found: C, 74·8; H, 5·3; N, 19·9. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3; N, 20·1%.

3-Diazo-2-pyrid-4'-yl-3H-*indole* (XII; R=pyrid-4-yl). A solution of sodium nitrite (0·2 g) in water (1·0 ml) was added dropwise to a suspension of 3-amino-2-pyrid-4'-ylindole (0·2 g) in water (10 ml) and concentrated sulphuric acid (0·75 ml) at 0° and the mixture stirred for 20 min. Neutralisation with sodium carbonate solution yielded the *diazoindole* (0·16 g) as yellow needles, m.p. 101–102° (from light petroleum). Found: C, 70·4; H, 4·0; N, 25·0. $C_{13}H_8N_4$ requires C, 70·9; H, 3·7; N, 25.5%. The solid discoloured on the surface after exposure to the air and light for several hours.

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