143. *The Influence of Structure on the Ultra-violet Absorption Spectra of Heterocyclic Systems.*

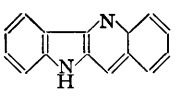
By G. R. Clemo and D. G. I. Felton.

The synthesis of a number of indoloquinolines is described. Their ultra-violet absorption spectra are recorded and compared with those of certain other related heterocylic systems.

Ultra-violet absorption spectra have frequently been used as confirmatory evidence in the identification of heterocyclic compounds, but there are, as far as we are aware, comparatively few data available on heterocyclic systems possessing two or more hetero-atoms. A valuable survey of the simpler heterocyclic systems has been given by Braude (*Ann. Reports*, 1945, **42**, 128), in which these systems are compared with their carbocyclic analogues, but, apart from this, data are scattered in individual papers. Before the undoubtedly valuable potentialities of ultra-violet absorption spectra can be fully used as a diagnostic tool, a greater accumulation and empirical correlation of such data are necessary. It is for this reason that we present these results.

In the simplest heterocyclic systems, the spectral characteristics of those in which the nitrogen atom is bound to carbon by single bonds, *e.g.*, pyrrole, indole, carbazole, are not appreciably different from those of their carbocyclic analogues containing instead a methylene group. Similarly the series in which the nitrogen atom replaces a methine group, *e.g.*, pyridine, quinoline, acridine, show absorptions which are very similar to the aromatic analogues (Braude, *loc. cit.*). The similarity does not extend to cover the intensities which tend to be higher in the heterocyclic series owing to the increased mobility of the π electrons.

Fusion of two such systems might be expected to lead to modifications of the spectra, through the interaction of the two chromophoric systems. Such fused systems include the carbolines, pyrroloquinolines, indoloquinolines, and indolo*iso*quinolines, many of which have been found or postulated in alkaloids or alkaloid degradation products. A certain amount of information concerning the absorption of carbolines and pyrroloquinolines is to be found in the literature, but



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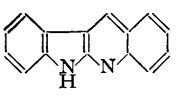

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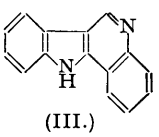

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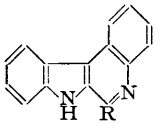
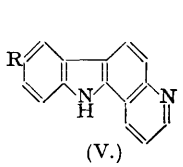


(IV.)

no information concerning that of indolo-quinolines or -*iso*quinolines is available. To date four of the possible fundamental indoloquinolines are known: indolo(3′ : 2′-2 : 3)quinoline (I) " quindoline ") (Fichter and Rohner, *Ber.*, 1910, **43**, 3490; Noelting and Steuer, *ibid.*, p. 3512),

indolo(2′ : 3′-2 : 3)quinoline (II) (" quinindoline ") (Borsche, Wagner-Roemmich, and Barthenheier, *Annalen*, 1942, **550**, 160), indolo(3′ : 2′-3 : 4)quinoline (III) (3 : 4-quinindoline) (Clemo and Perkin, *J.*, 1924, **125**, 1608), and indolo(2′ : 3′-3 : 4)quinoline (IV; R = H) (Kermack and Slater, *J.*, 1928, 32). Recently Manske and Kulka (*Canad. J. Res.*, 1949, **27**, *B*, 291) have reported the synthesis of some indolo*iso*quinolines in which the indole moiety is fused to the benzenoid side of the *iso*quinoline molecule. Indoloquinolines in which the indole moiety is attached to the benzenoid ring of quinoline have been prepared in the form of their tetrahydro-compounds (Nandi, *J. Indian Chem. Soc.*, 1940, **17**, 449; Dewar, *J.*, 1944, 615).

In this study we have prepared indolo(2′ : 3′-5 : 6)quinoline (V; R = H), indolo(3′ : 2′-5 : 6)quinoline (VI; R = H), indolo(3′ : 2′-7 : 8)quinoline (VII; R = H), and their respective 5′-methyl homologues (V, VI, and VII; R = Me), from the 5-, 6-, and 8-quinolylhydrazones of *cyclo*hexanone (or 4-methyl*cyclo*hexanone) by ring closure with sulphuric acid in acetic acid, followed by dehydrogenation of the resultant tetrahydroindoloquinolines by means of palladised charcoal. The assumption is made in the case of (VI), where ring closure may occur in two ways, that it does so to yield the angular compound.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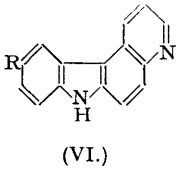
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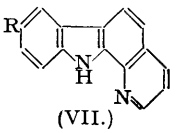

(VII.)

We have also prepared indolo(2′ : 3′-3 : 4)quinoline (IV; R = H) by a modification of Kermack and Slater's method (*loc. cit.*) which is simpler and offers higher yields. This procedure starts with the phenylhydrazone of ethyl *o*-nitrophenylpyruvate which undergoes the Fischer indole ring closure on boiling an ethanolic solution saturated with hydrogen chloride, to yield the crystalline ethyl 3-*o*-nitrophenylindole-2-carboxylate (previously reported as an oil). This on reduction over Adams's platinic oxide catalyst readily yields, by elimination of ethanol during the reduction, 2-hydroxyindolo(2′ : 3′-3 : 4)quinoline [1 : 2-dihydro-2-ketoindolo(2′ : 3′-3 : 4)quinoline]; replacement of oxygen by chlorine is effected by phosphorus pentachloride in phosphoryl chloride (Kermack and Tebrich, *J.*, 1940, 314) and this is then removed by catalytic hydrogenolysis. This procedure obviates the need for decarboxylation of the indole, followed by a Bischler–Napieralski type of ring closure of the reduced intermediate. The yields on each stage are of the order of 90% or more, and consequently indolo(2′ : 3′-3 : 4)quinoline is readily accessible. In contrast to the ease of reduction and simultaneous ring closure of ethyl 3-*o*-nitrophenylindole-2-carboxylate, the catalytic reduction of 3-*o*-nitrophenylindole-2-carboxylic acid proved very sluggish and yielded 3-*o*-aminophenylindole-2-carboxylic acid, which however, when heated, lost water by ring closure and in fact melted at the same temperature as the lactam.

The 2-methyl homologue (IV; R = Me) was prepared by the dehydrogenation of 4′ : 5′ : 6′ : 7′-tetrahydro-2-methylindolo(2′ : 3′-3 : 4)quinoline (Robinson and Robinson, *J.*, 1924, **125**, 837) by means of palladised charcoal. This preparation, involving the Fischer indole ring closure of the 3-quinaldylhydrazone of *cyclo*hexanone, was also adapted for the independent synthesis of (IV; R = H). 3-Quinolylhydrazine, from 3-aminoquinoline (Clemo and Swan, *J.*, 1945, 867), was condensed with *cyclo*hexanone, and the product cyclised with sulphuric acid in acetic acid to yield the tetrahydro-compound, which on dehydrogenation yielded (IV; R = H).

The ultra-violet absorption spectra of (IV, V, VI, and VII; R = H and Me in each case) were determined in ethanol, and the values of $\lambda_{max.}$ and log $\varepsilon_{max.}$ are recorded in Table I (cf. Fig. 1).

TABLE I.

	$\lambda_{max.}$, A.	log $\varepsilon_{max.}$	$\lambda_{max.}$, A.	log $\varepsilon_{max.}$		$\lambda_{max.}$, A.	log $\varepsilon_{max.}$	$\lambda_{max.}$, A.	log $\varepsilon_{max.}$
(IV; R = H)	2590	4·61	3275	4·20	(VI; R = Me)	2480	4·40	2830	4·41
(IV; R = Me)	2580	4·58	3250	4·11				3450	3·97
(V; R = H)	2450	4·48	2920	4·58	(VII; R = H)	2430	4·58	2920	4·67
(V; R = Me)	2460	4·53	2970	4·57	(VII; R = Me)	2450	4·53	2940	4·60
(VI; R = H)	2455	4·48	2800	4·50					
			3410	3·98					

With the methyl homologues, there is in general a very slight bathochromic shift of *ca.* 20 A., with a very slight lowering of the intensity. Fig. 1 shows that the absorptions of the indolo-

quinolines in which the indole portion is attached to the benzenoid ring of the quinoline are fairly similar [(VI) has a third maximum where (V) and (VII) have inflexions], while there is a more profound difference when the indole system is fused to the heterocyclic ring of the quinoline. Thus there is a minimum in the case of (IV) where the others exhibit a maximum, though the inflexion shown by (V) and (VII) is reproduced by (IV), at a longer wave-length however. The close similarity between (V) and (VII) shows that the position in the quinoline ring of the heterocyclic nitrogen is of little consequence. A similar phenomenon is found in the benzoquinoline series (Johnson and Mathews, *J. Amer. Chem. Soc.*, 1944, **66**, 210).

The pyrroloquinolines, (VIII), (IX), and (X), corresponding to (V), (VI), and (VII) respectively, have been prepared and their absorption charted by Horner (*Annalen*, 1939, **540**, 73), while (XI), corresponding to (IV), has recently been reported by Eiter and Nagy (*Sitzungsber. Akad. Wien*, 1949, **158**, *IIb*, 607). These data are collected in Fig. 2. The striking difference

FIG. 1.

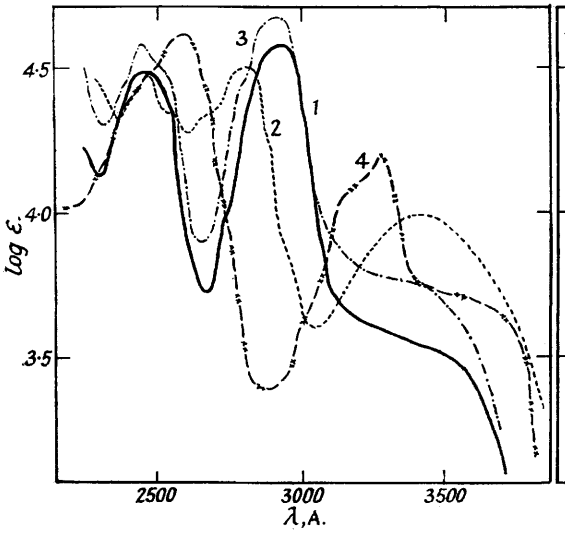


FIG. 2.

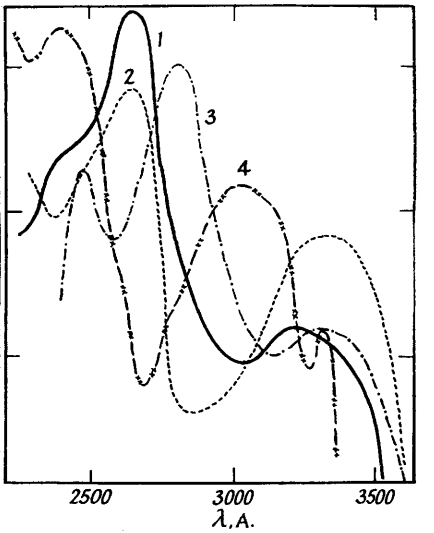
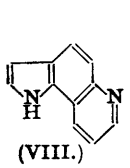
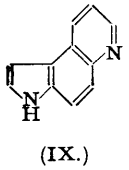


FIG. 1. ——————— *Indolo*(2′ : 3′-5 : 6)*quinoline* (V; R = H).
— — — — — — — — *Indolo*(3′ : 2′-5 : 6)*quinoline* (VI; R = H).
— · — · — · — · — *Indolo*(3′ : 2′-7 : 8)*quinoline* (VII; R = H).
× × — — × × — — *Indolo*(2′ : 3′-3 : 4)*quinoline* (IV; R = H).

FIG. 2. ——————— *Pyrrolo*(2′ : 3′-5 : 6)*quinoline* (VIII).
— — — — — — — — *Pyrrolo*(3′ : 2′-5 : 6)*quinoline* (IX).
— · — · — · — · — *Pyrrolo*(3′ : 2′-7 : 8)*quinoline* (X).
× × — — × × — — *Pyrrolo*(2′ : 3′-3 : 4)*quinoline* (XI).

between the curve for the pyrroloquinoline (XI), in which the pyrrole ring is fused to the heterocyclic ring of the quinoline, and those of the other three, in which it is attached to the benzenoid ring, is again noteworthy though it is somewhat obscured by the differences between the latter three compounds. These differences are larger than those between their benzo-analogues (V, VI, and VII), but close scrutiny of Fig. 2 reveals the same general interrelation between the curves. Thus while pyrrolo(3′ : 2′-5 : 6)quinoline (IX) shows a pronounced maximum in the region of


(VIII.)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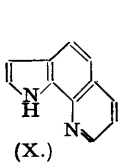
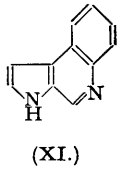

(X.)


(XI.)

3300 A., pyrrolo(2′ : 3′-5 : 6)- (VIII) and pyrrolo(3′ : 2′-7 : 8)-quinoline (X) show slight humps in this region, corresponding respectively to the pronounced maximum at 3400 A. for (VI) and the inflexions exhibited by (V) and (VII). That in fact it is the overall " shape " of the molecule

which determines the absorption is confirmed by the similarity in curves obtained with (IX) and (XI), though that of (IX) is shifted to longer wave-lengths; the same is partly true for (IV) and (VI), although there are complicating features in the spectra of (IV) and (XI), caused perhaps by the proximity of the heterocyclic rings.

Since the replacement of a methine group by a nitrogen atom produces only a slight change in absorption in the monoheteroatomic series, *e.g.*, pyridine, quinoline, compared with their aromatic analogues, we may look on the indolo- and pyrrolo-quinolines as isosterically related to indolo- and pyrrolo-naphthalenes and, simplifying still further, to naphthylamines. The conclusion reached concerning the " shape " of the above compounds then finds a logical basis since (V) and (VII), (VIII) and (X), the spectra of which appear to be closely related, are structural analogues of α-naphthylamine, while the other pairs, (IV) and (VI), (IX) and (XI), are modelled on β-naphthylamine. We may expect a closer resemblance to the corresponding aminoquinolines.

TABLE II.

	$\lambda_{max.}$, A.	log $\varepsilon_{max.}$	$\lambda_{max.}$, A.	log $\varepsilon_{max.}$	$\lambda_{max.}$, A.	log $\varepsilon_{max.}$
Indole [1]	2150	4·25	2650 f	3·80	—	—
Carbazole [2]	2420	4·38	2910	4·28	3300	3·50
Quinoline [1]	—	—	2750 f	3·65	3110 f	3·80
β-Carboline [5]	2400	4·60	2850	4·40	3400	3·85
α-Naphthylamine [3]	2400	4·08	—	—	3200	3·52
β-Naphthylamine [3]	2370	4·52	2800	3·61	3400	3·11
3-Aminoquinoline [3]	2420	4·21	2720 †	3·55	3500	3·45
5-Aminoquinoline [3]	2520	4·18	—	—	3430	3·20
6-Aminoquinoline [3]	2450	4·40	2800 *	3·45	3520	3·45
8-Aminoquinoline [3]	2590	4·18	—	—	3390	3·20
Pyrrolo(2′ : 3′-3 : 4)quinoline [4]	2400	4·65	3000	4·10	3300	3·60
Indolo(2′ : 3′-3 : 4)quinoline	2590	4·60	3275	4·20	3600 *	3·70
Pyrrolo(2′ : 3′-5 : 6)quinoline [5]	2650	4·70	—	—	3200	3·60
Indolo(2′ : 3′-5 : 6)quinoline	2450	4·48	2920	4·58	3350 *	3·60
Pyrrolo(3′ : 2′-5 : 6)quinoline [5]	2640	4·43	—	—	3310	3·98
Indolo(3′ : 2′-5 : 6)quinoline	2455	4·48	2800	4·50	3410	3·98
Pyrrolo(3′ : 2′-7 : 8)quinoline [5]	2480	4·10	2810	4·52	3300	3·60
Indolo(3′ : 2′-7 : 8)-quinoline	2430	4·58	2920	4·67	3300 *	3·76

f, Subsidiary maxima. * Inflexion. † Incipient point of inflexion.

[1] Braude (*loc. cit.*). [2] Pruckner and Witkop (*Annalen*, 1943, **554**, 130). [3] Steck and Ewing (*loc. cit.*). [4] Eiter and Nagy (*loc. cit.*). [5] Horner (*loc. cit.*).

The spectra of naphthylamines and the aminoquinolines have been studied very thoroughly by Steck and Ewing (*J. Amer. Chem. Soc.*, 1948, **70**, 3397). Data from their paper are included in Table II in which are summarised the principal bands of some of the heterocyclic systems containing two nitrogen atoms for comparison with the parent monoheteroatomic systems. The values of $\lambda_{max.}$ are grouped into sets of what appear to us to be comparable bands, although we do not attempt to correlate them to particular chromophoric systems.

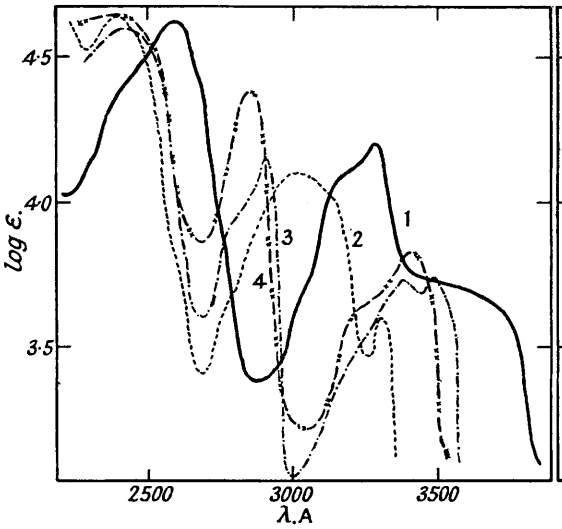
For the pyrroloquinolines (VIII and IX) compared with the parent aminoquinolines, cyclisation to a pyrrole involves a bathochromic shift of about 100 A., though for (X) there is a corresponding hypsochromic shift of about the same amount with splitting of the first maximum. This is undoubtedly caused by interaction of the acidic pyrrole hydrogen with the basic quinoline nitrogen atom, as is to be expected from the basicity studies of the aminoquinolines carried out by Albert and Goldacre (*Nature*, 1944, **153**, 468). Addition of a further benzene ring, to give the indoloquinolines (V and VI), intensifies the bathochromic tendency and leads to the splitting of the first maximum into two maxima, one higher and the other lower in wave-length than the corresponding band in the pyrroloquinoline. The interaction of the acidic hydrogen of the indole with the basic nitrogen atom of the quinoline in (VII) is even more strongly marked than with the corresponding pyrroloquinoline, and there is a further hypsochromic shift of the first maximum.

Indolo(2′ : 3′-3 : 4)quinoline (IV; R = H) contains a β-carboline system. Fig. 3 shows its spectrum, along with that of β-carboline itself (Horner, *loc. cit.*; Pruckner and Witkop, *loc. cit.*), that of a typical carboline obtained from an indole alkaloid, *viz.*, yobyrine (Clemo and Swan, *J.*, 1946, 618), and also that of the pyrroloquinoline (XI) containing the analogous arrangement of heterocyclic rings. While the two true carbolines have very closely similar spectra, that of (IV) shows a bathochromic shift of about 250 A. and the shape of the minimum is considerably broadened; the shape of the second maximum, at 3275 A., closely resembles that of yobyrine at 2900 A., having a small peak on top and to the longer-wave side of a broad band.

A similar outline is reproduced in the third maximum of β-carboline at 3410 A., but this peak is probably not comparable with the other two. The pyrroloquinoline absorption is intermediate between that of (IV) and of β-carboline, the first maximum at 2400 A. being identical with β-carboline, while the second is not shifted so far towards longer wave-lengths as for (IV).

We have also studied the effect of a tetramethylene bridge on the absorption of the pyrroloquinoline (XI), by charting the spectra of 4′ : 5′ : 6′ : 7′-tetrahydroindolo(2′ : 3′-3 : 4)quinoline and its 2-methyl derivative (Fig. 4). The first maximum shows a slight hypsochromic tendency (maxima at 2315 A. and inflexions at *ca.* 2420 A.), while the second maximum undergoes a bathochromic shift of 200—250 A. (to 3200 and 3250 A. respectively). This is larger than the

FIG. 3.



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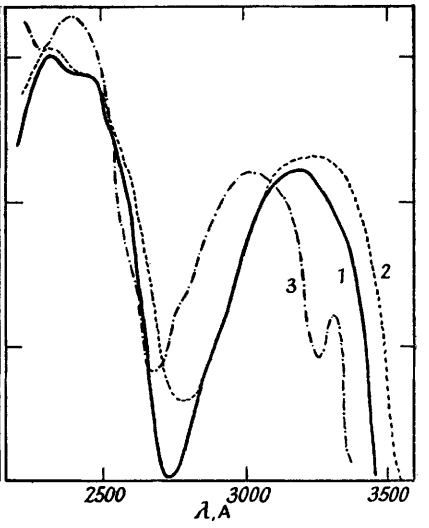

FIG. 3. ——————— *Indolo*(2′ : 3′-3 : 4)*quinoline* (IV; R = H).
— — — — — — — — *Pyrrolo*(2′ : 3′-3 : 4)*quinoline* (XI).
— · — · — · — · — *Yobyrine.*
× × — — × × — — β-*Carboline.*

FIG. 4. ——————— 4′ : 5′ : 6′ : 7′-*Tetrahydro-2-methylindolo*(2′ : 3′-3 : 4)*quinoline.*
— — — — — — — — 4′ : 5′ : 6′ : 7′-*Tetrahydroindolo*(2′ : 3′-3 : 4)*quinoline.*
— · — · — · — · — *Pyrrolo*(2′ : 3′-3 : 4)*quinoline.*

effect of alkyl groups in dienes (50 A. per alkyl substituent), but corresponds to the effect in the more mobile systems (100 A. per alkyl group) (Braude, *loc. cit.*, p. 120).

EXPERIMENTAL.

4′ : 5′ : 6′ : 7′-*Tetrahydroindolo*(2′ : 3′-5 : 6)*quinoline.*—5-Quinolylhydrazine dihydrochloride (5 g.) was condensed with *cyclo*hexanone (2·13 g.) in the presence of sodium acetate (5·91 g.), water (37 ml.), and ethanol (20 ml.) by refluxing the mixture on the steam-bath for 1 hour. The oily hydrazone obtained on cooling was extracted with chloroform, and the residue obtained on evaporation was cyclised by heating the solution in acetic acid (30 ml.) with sulphuric acid (2 ml.) at 100° for 10 minutes. The crystalline orange sulphate was collected and suspended in water, and the base liberated with aqueous ammonia, collected, and crystallised from aqueous pyridine, from which it was obtained in rectangular plates, m. p. 293—294° (Dewar, *loc. cit.*, gives m. p. 288—289°). The *picrate*, prepared in ethanol, crystallised from *cyclo*hexanone in minute yellow solvated prisms, m. p. 255° (decomp.) (Found, on a sample dried at 100° : C, 58·5; H, 4·8. $C_{15}H_{14}N_2,C_6H_3O_7N_3,0{\cdot}75C_6H_{10}O$ requires C, 58·3; H, 4·7. Found, on a sample dried at 180° in a vacuum : C, 56·8; H, 3·8; loss, 8·0. $C_{15}H_{14}N_2,C_6H_3O_7N_3,0{\cdot}25C_6H_{10}O$ requires C, 56·8; H, 4·1; loss, 9·3%).

Indolo(2′ : 3′-5 : 6)*quinoline* (V; R = H).—The above tetrahydro-compound (100 mg.) was intimately mixed with palladised charcoal (*ca.* 50 mg.) in a test-tube (3 × ¼″), and the tube, attached to the pump, was placed in a heated metal block. At 290—300°/10 mm., a white sublimate was obtained; this was remixed with the catalyst, and the mixture resublimed. The *product* (80 mg.) was removed and resublimed at 300°/10 mm., whereafter it formed long, very pale yellow prisms, m. p. 334—335° (decomp.) (Found : C, 82·4; H, 4·8; N, 12·6. $C_{15}H_{10}N_2$ requires C, 82·6; H, 4·6; N, 12·85%). The *picrate*, prepared in ethanol, crystallised from aqueous ethanol in microscopic yellow needles, m. p. 277° (decomp.) (Found : C, 55·7; H, 3·8. $C_{15}H_{10}N_2,C_6H_3O_7N_3,C_2H_5{\cdot}OH$ requires C,

56·0; H, 3·9. Found, in a sample dried at 120° in a vacuum: C, 56·6; H, 2·6. $C_{15}H_{10}N_2,C_6H_3O_7N_3$ requires C, 56·4; H, 2·9%).

4′ : 5′ : 6′ : 7′-Tetrahydro-5′-methylindolo(2′ : 3′-5 : 6)quinoline.—5-Quinolylhydrazine dihydrochloride (4·2 g.), sodium acetate (5·0 g.), and 4-methyl*cyclo*hexanone, condensed in aqueous ethanol, yielded an oily hydrazone, which after extraction was cyclised with sulphuric acid (2 ml.) in acetic acid (25 ml.). The *base*, liberated from the solid sulphate which was formed, crystallised from aqueous pyridine, forming flat needles, m. p. 298·5° (decomp.), after softening at 287° (Found: C, 81·6; H, 6·6. $C_{16}H_{16}N_2$ requires C, 81·4; H, 6·8%). The *picrate* formed minute rosettes of yellow microscopic needles (from *cyclo*hexanone), m. p. 259—260° (decomp.) (Found, on a sample dried at 100° in a vacuum: C, 58·5; H, 5·15. $C_{16}H_{16}N_2,C_6H_3O_7N_3,0{\cdot}5C_6H_{10}O$ requires C, 58·4; H, 4·7. Found, on a sample dried at 180° in a vacuum: C, 57·3; H, 4·05; loss, 9·9. $C_{16}H_{16}N_2,C_6H_3O_7N_3$ requires C, 56·8; H, 4·1; loss, 9·5%).

5′-Methylindolo(2′ : 3′-5 : 6)quinoline (V; R = Me).—Dehydrogenation over palladised charcoal at 300°/10 mm. yielded the *indoloquinoline*, which, after resublimation at 300°/10 mm., formed very pale yellow prisms, m. p. 335° (Found: C, 82·8; H, 5·0. $C_{16}H_{12}N_2$ requires C, 82·7; H, 5·2%). The mixed m. p. with indolo(2′ : 3′-5 : 6)quinoline (m. p. 334—335°) was 306°. The *picrate* crystallised from *cyclo*hexanone in yellow needles, decomposing over the range 280—287° (Found: C, 59·4; H, 4·2. $C_{16}H_{12}N_2,C_6H_3O_7N_3,0{\cdot}75C_6H_{10}O$ requires C, 59·5; H, 4·2. Found, on a sample dried at 180° in a vacuum: C, 57·5; H, 3·1; loss, 13·2. $C_{16}H_{12}N_2,C_6H_3O_7N_3$ requires C, 57·3; H, 3·25; loss, 13·8%).

4′ : 5′ : 6′ : 7′-Tetrahydroindolo(3′ : 2′-5 : 6)quinoline.—Prepared according to Dewar (*loc. cit.*), this formed colourless prisms, m. p. 205° (Dewar, m. p. 201—202°). The *picrate* formed orange-yellow needles (from *cyclo*hexanone), m. p. 241—242° (decomp.) (Found, on a sample dried at 180° in a vacuum: C, 56·6; 56·4, 56·5; H, 4·1, 4·1, 4·3. $C_{15}H_{14}N_2,C_6H_3O_7N_3,0{\cdot}25C_6H_{10}O$ requires C, 56·8; H, 4·1%). Strenuous efforts to remove the solvent proved unavailing. Drying at a temperature in excess of 180° led to darkening.

Indolo(3′ : 2′-5 : 6)quinoline (VI; R = H).—Dehydrogenation over palladised charcoal of the above tetrahydro-compound by sublimation at 270°/10 mm. yielded the *indoloquinoline* as very pale yellow massive prisms, m. p. 211° (mixed m. p. with the parent tetrahydro-compound, 178—179°) (Found: C, 82·7; H, 4·7. $C_{15}H_{10}N_2$ requires C, 82·6; H, 4·6%). The *picrate* crystallised from aqueous ethanol in bright yellow prisms, m. p. 275° (decomp.) (Found: C, 54·2; H, 3·6. $C_{15}H_{10}N_2,C_6H_3O_7N_3,H_2O$ requires C, 54·2; H, 3·2%).

4′ : 5′ : 6′ : 7′-Tetrahydro-5′-methylindolo(3′ : 2′-5 : 6)quinoline.—This was obtained in the usual way from 6-quinolylhydrazine dihydrochloride (6·0 g.), sodium acetate (7·1 g.), and 4-methyl*cyclo*hexanone (2·9 ml.). The *base* formed short pale yellow prisms, m. p. 258°, from acetone (Found: C, 81·6; H, 7·2. $C_{16}H_{16}N_2$ requires C, 81·4; H, 6·8%). The *picrate* crystallised from *cyclo*hexanone in clumps of small, fine needles, m. p. 254° (decomp.) (Found, on a sample dried at 180° in a vacuum: C, 56·5; H, 4·1. $C_{16}H_{16}N_2,C_6H_3O_7N_3$ requires C, 56·8; H, 4·1%).

5′-Methylindolo(3′ : 2′-5 : 6)quinoline (VI; R = Me).—Dehydrogenation at 280°/10 mm. over palladised charcoal and resublimation at 270°/10 mm. afforded this *compound* as pale yellow massive needles, m. p. 307° (slight decomp.) (Found: C, 82·5; H, 5·2. $C_{16}H_{12}N_2$ requires C, 82·7; H, 5·2%). The *picrate* formed very small bright yellow needles, m. p. 270° (decomp.), from *cyclo*hexanone (Found: C, 58·2; H, 3·6. $C_{16}H_{12}N_2,C_6H_3O_7N_3,0{\cdot}25C_6H_{10}O$ requires C, 58·1; H, 3·6. Found, on a sample dried at 180° in a vacuum: C, 57·1; H, 3·1. $C_{16}H_{12}N_2,C_6H_3O_7N_3$ requires C, 57·3; H, 3·25%).

4′ : 5′ : 6′ : 7′-Tetrahydroindolo(3′ : 2′-7 : 8)quinoline.—Prepared in the usual manner, this base formed large, lustrous prisms, m. p. 151—152°, from ethyl acetate (Dewar, *loc. cit.*, gives m. p. 151°). The *picrate* crystallised from *cyclo*hexanone as fine, deep-yellow needles, m. p. 250° (decomp.) (Found: C, 57·6; H, 4·4. $C_{15}H_{14}N_2,C_6H_3O_7N_3,0{\cdot}5C_6H_{10}O$ requires C, 57·6; H, 4·4. Found, on a sample dried at 180° in a vacuum: C, 56·1; H, 3·6. $C_{15}H_{14}N_2,C_6H_3O_7N_3$ requires C, 55·9; H, 3·8%).

Indolo(3′ : 2′-7 : 8)quinoline (VII; R = H).—After dehydrogenation of the tetrahydro-compound in the usual manner at 270°/10 mm., the resublimed product formed white needles, m. p. 165° depressed to 141—144° on admixture with the parent tetrahydroindoloquinoline (m. p. 151—152°). Recrystallisation from ethanol afforded *indolo(3′ : 2′-7 : 8)quinoline* as very long, silky, white needles, m. p. 169° (Found: C, 82·3; H, 4·9; N, 12·8. $C_{15}H_{10}N_2$ requires C, 82·6; H, 4·6; N, 12·85%). The *picrate* formed spherular clusters of small needles, m. p. 265° (decomp.), from *cyclo*hexanone (Found, on a specimen dried at 100° in a vacuum: C, 58·9, 58·9; H, 4·0, 3·8. $C_{15}H_{10}N_2,C_6H_3O_7N_3,0{\cdot}75C_6H_{10}O$ requires C, 58·8; H, 3·9. Found, on a sample dried at 180° in a vacuum: C, 56·6; H, 3·1. $C_{15}H_{10}N_2,C_6H_3O_7N_3$ requires C, 56·4; H, 2·9%).

4′ : 5′ : 6′ : 7′-Tetrahydro-5′-methylindolo(3′ : 2′-7 : 8)quinoline.—Prepared in the usual way from 8-quinolylhydrazine dihydrochloride and 4-methyl*cyclo*hexanone, this *base* crystallised from ethyl acetate, in which it was considerably soluble, in pale yellow needles, m. p. 152° (Found: C, 81·7; H, 6·65. $C_{16}H_{16}N_2$ requires C, 81·4; H, 6·8%). The *picrate* crystallised from *cyclo*hexanone as very fine, deep yellow needles, m. p. *ca.* 250° with preliminary darkening and decomposition at 230—240° (Found, on a sample dried at 180° in a vacuum: C, 57·1; H, 4·3. $C_{16}H_{16}N_2,C_6H_3O_7N_3$ requires C, 56·8; H, 4·1%).

5′-Methylindolo(3′ : 2′-7 : 8)quinoline (VII; R = Me).—Dehydrogenation was accomplished by sublimation from palladised charcoal at 250°/10 mm. After resublimation, the *indoloquinoline* formed colourless needles, m. p. 193—194° (Found: C, 82·4; H, 5·0; N, 12·3. $C_{16}H_{12}N_2$ requires C, 82·7; H, 5·2; N 12·1%). The *picrate* separated from *cyclo*hexanone as bright yellow needles, decomposing above 220° with no definite m. p. (Found: C, 59·1; H, 3·9. $C_{16}H_{12}N_2,C_6H_3O_7N_3,0{\cdot}5C_6H_{10}O$ requires C, 58·8; H, 3·9. Found, in a sample dried at 180° in a vacuum: C, 58·1; H, 3·7. $C_{16}H_{12}N_2,C_6H_3O_7N_3,0{\cdot}25C_6H_{10}O$ requires C, 58·1; H, 3·6%).

3-*Quinolylhydrazine*.—3-Aminoquinoline (Clemo and Swan, *J.*, 1945, 867) (1·0 g.) in concentrated hydrochloric acid (10 ml.) and water (4 ml.) was diazotised with sodium nitrite (0·5 g.) in water (17 ml.) and reduced by addition to stannous chloride (4·8 g.) in concentrated hydrochloric acid (5 ml.) and water (8·5 ml.). The tin was removed by precipitation with hydrogen sulphide, and the filtrate and washings were concentrated under reduced pressure and basified with sodium hydroxide solution (40%) with cooling. The solution was extracted with ethyl acetate and after being dried ($MgSO_4$), the extract was evaporated and 3-*quinolylhydrazine* crystallised from ethyl acetate as frond-like fawn needles, m. p. 176—177° (Found : C, 67·9; H, 5·3. $C_9H_9N_3$ requires C, 67·9; H, 5·7%).

cyclo*Hexanone* 3-*Quinolylhydrazone*.—This was obtained by condensing 3-quinolylhydrazine (0·8 g.) with *cyclo*hexanone (0·5 g.) in ethanol at 100° for 3 minutes in the presence of a trace of acetic acid. Dilution with water yielded the *hydrazone*, which formed pale yellow lozenge-shaped plates, m. p. 150—151°, from aqueous ethanol (Found : C, 75·1; H, 7·0. $C_{15}H_{17}N_3$ requires C, 75·3; H, 7·1%).

4′ : 5′ : 6′ : 7′-*Tetrahydroindolo*(2′ : 3′-3 : 4)*quinoline*.—The above hydrazone (0·4 g.) was cyclised by sulphuric acid (5 drops) in acetic acid (2 ml.). The *product* was precipitated by the addition of ammonia and after drying was dissolved in benzene and run on to a column of alumina, and impurities were removed by exhaustive elution with benzene. The alumina was then dried and extracted continuously with methanol. Evaporation of the solvent afforded a crystalline residue, which was sublimed at 260°/10 mm. to yield very pale cream-coloured needles, m. p. 265—266° (Found : C, 80·6; H, 6·15. $C_{15}H_{14}N_2$ requires C, 81·1; H, 6·3%).

Indolo(2′ : 3′-3 : 4)*quinoline* (IV; R = H).—Dehydrogenation of the tetrahydro-compound yielded nearly colourless needles, m. p. 249°, undepressed on admixture with an authentic specimen (see below).

2-*Methylindolo*(2′ : 3′-3 : 4)*quinoline* (IV; R = Me).—The corresponding tetrahydro-compound (Robinson and Robinson, *loc. cit.*) on dehydrogenation in the usual way and resublimation at 240°/10 mm. yielded colourless prisms, m. p. 200—201° (Found : C, 82·6; H, 5·2. Calc. for $C_{16}H_{12}N_2$: C, 82·7; H, 5·2%). Kermack and Slater (*loc. cit.*) describe this product as pale yellow needles (from benzene–light petroleum), m. p. 204—205°.

Ethyl 3-o-*Nitrophenylindole-2-carboxylate*.—Ethyl *o*-nitrophenylpyruvate phenylhydrazone (5·0 g.) (Wislicenus and Thoma, *Annalen*, 1924, **436**, 45) in ethanol (20 ml.) was rapidly saturated with dry hydrogen chloride, and the solution refluxed on the water-bath for 30 minutes, becoming dark brown and ammonium chloride being precipitated. The solution was cooled and diluted and, after scratching, the precipitated brown oil formed an orange-yellow solid (4·3 g., 91%). On crystallisation from ethanol, the *indole* ester formed orange-yellow needles, m. p. 131° (Found : C, 65·5; H, 4·7. $C_{17}H_{14}O_4N_2$ requires C, 65·8; H, 4·5%). Hydrolysis of the ester (2·0 g.) with alcoholic potash (20 ml. of 3%) for 2 hours, followed by acidification with dilute hydrochloric acid, yielded the corresponding acid, crystallising from ethanol as yellow needles, m. p. 274° (Kermack and Slater give m. p. 276°) (Found : C, 63·5; H, 3·55. Calc. for $C_{15}H_{10}O_4N_2$: C, 63·8; H, 3·55%).

2-*Hydroxyindolo*(2′ : 3′-3 : 4)*quinoline* (IV; R = OH).—The foregoing ester (6 g.) in ethyl acetate (70 ml.) was hydrogenated over Adams's platinic oxide at room temperature and 6 atms. Evaporation of the filtered solution, followed by crystallisation of the residue from methanol, afforded the lactam (yield, quantitative) as colourless needles, m. p. 313° (Kermack and Slater, *loc. cit.*, record m. p. >316°) (Found : C, 77·0; H, 4·4. Calc. for $C_{15}H_{10}ON_2$: C, 76·9; H, 4·3%).

3-o *Aminophenylindole-2-carboxylic Acid*.—Reduction of 3-*o*-nitrophenylindole-2-carboxylic acid (2 g.) in ethyl acetate (40 ml.) by hydrogen and platinic oxide (room temperature, 6 atms.) was extremely slow. A white precipitate formed during the reduction was taken up in more ethyl acetate, and the hot solution freed from catalyst by filtration. Evaporation left a white solid, which on crystallisation from acetic acid yielded the *indole amino-acid* as colourless thin rods, m. p. 312—313° (efferv.) (Found : C, 71·8; H, 4·7. $C_{15}H_{12}O_2N_2$ requires C, 71·4; H, 4·8%).

Indolo(2′ : 3′-3 : 4)*quinoline* (IV; R = H).—The lactam obtained above (1 g.) was converted into the corresponding chloro-compound, needles (from benzene), m. p. 185° (Kermack and Tebrich, *loc. cit.*, give m. p. 182°), by means of a mixture of phosphorus pentachloride (2·5 g.) in phosphoryl chloride (10 ml.) at 130° under reflux. The chloro-compound, dissolved in acetic acid, was hydrogenated over palladised charcoal at room temperature and 6 atms. The solution, after removal of the catalyst, was very pale yellow with a very intense, brilliant blue-green fluorescence. After removal of the solvent, the base was liberated from its hydrochloride and purified by sublimation at 250°/10 mm., forming colourless silky needles, m. p. 249° (Found : C, 82·7; H, 4·5. Calc. for $C_{15}H_{10}N_2$: C, 82·6; H, 4·6%). Kermack and Slater (*loc. cit.*) describe the compound as pale yellow needles (from benzene), m. p. 245°.

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