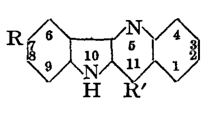
# **111.** *Carbazoles, Carbolines, and Related Compounds. Part I. Quindoline Derivatives.*

By S. J. Holt and V. Petrow.

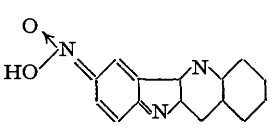
Improved methods for the preparation of quindoline [quinolo(2′ : 3′ : 3 : 2)indole] and its 11-carboxylic acid (I; R = H, R′ = $CO_2H$) have been developed. Bromination of these compounds has been found to give the 7-*bromo*-derivatives, identical with the compounds obtained by direct synthesis from 5-*bromo*-ON-*diacetylindoxyl* and isatin. Nitration of quindoline gives 7-*nitro*- (I; R = $NO_2$; R′ = H), 11-*nitro*- (I; R = H; R′ = $NO_2$), and 7 : x-*dinitro-quindoline*. The constitution of the first followed from its reduction to 7-*amino-quindoline* and conversion of the latter into 7-bromoquindoline. The structure of the second isomeride was determined by reduction to the amino-compound identical with 11-*amino-quindoline* obtained from quindoline-11-carboxylic acid.

The study of the chemistry of the heterocyclic ring systems of potential biological interest, now in progress in these laboratories, has been extended to the carbazole and azacarbazole (carboline) groups of compounds. Only 2-azacarbazole (β-carboline) has hitherto received any degree of attention, by virtue of its connection with the harmala alkaloids. We now report a study of some derivatives of quindoline (3 : 4-benz-δ-carboline). Their conversion into quaternary salts, and a brief reference to their biological properties, will be reported in Part II (forthcoming publication).

We were unable to obtain supplies of technical " indoxyl melt " required for the convenient preparation of quindoline-11-carboxylic acid described by Armit and Robinson (*J.*, 1922, **121**, 836), and so turned our attention to the alternative use of *ON*-diacetylindoxyl (" Friedländer," **5**, 940) and *N*-acetylindoxyl (*ibid*, p. 941). These two compounds have the added advantage of being very much less readily oxidised than the parent indoxyl. Condensation with isatinic acid in strongly alkaline solution led to formation of quindoline-11-carboxylic acid (I; R = H, R′ = $CO_2H$) in yields exceeding 90%. When lower concentrations of alkali were employed, variable amounts of indirubin were formed as a by-product. Both Fichter and Rohner (*Ber.*, 1910, **43**, 3489) and Armit and Robinson (*loc. cit.*) prepared quindoline (I; R = R′ = H) * from the 11-carboxylic acid by such methods as reduction with zinc dust in alkali, or with sodium amalgam, followed by oxidation with air. We now find that this procedure may be avoided, and the yield of quindoline raised above 90%, by direct decarboxylation of (I; R = H, R′ = $CO_2H$) at its melting point, or in liquid paraffin at 300°.



(I.)



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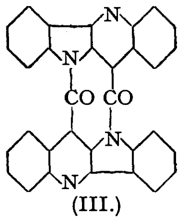

(III.)

The bromination of quindoline has been studied by Fichter and Rohner (*loc. cit.*), who obtained a product to which they assigned the 7-bromo-structure (I; R = Br, R′ = H). As 10-acetylquindoline would not brominate under the same conditions, but gave an unstable

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* The numbering of the quindoline ring system follows " The Ring Index " (Patterson and Capell).

" perbromide " which passed into the hydrobromide of 10-acetylquindoline on standing in air, they assumed the initial formation of 10-bromoquindoline, followed by rearrangement to the 7-bromo-isomeride. We have now confirmed structure (I; R = Br, R′ = H) by direct synthesis from 4-bromophenylglycine-*o*-carboxylic acid. It may be added that the formation of the latter compound by direct bromination of phenylglycine-*o*-carboxylic acid is claimed by the Badische Anilin- and Soda-Fabrik (G.P. 148,615), but evidence supporting this structure is not presented. We have now confirmed the constitution assigned to this compound by direct comparison with authentic 4-bromophenylglycine-*o*-carboxylic acid prepared by the method of Friedländer, Bruckner, and Deutsch (*Annalen*, 1912, **388**, 34). It gave 5-*bromo*-ON-*diacetylindoxyl* together with some 5-*bromo*-N-*acetylindoxyl* on ring closure, the diacetyl compound condensing with isatinic acid in alkaline solution to give 7-*bromoquindoline*-11-*carboxylic acid* (I; R = Br, R′ = $CO_2H$), also identical with the product we obtained by direct bromination of quindoline-11-carboxylic acid, to which must therefore be assigned the 7-bromo-structure. Decarboxylation of these bromo-acids gave the same 7-bromoquindoline, identical with the bromoquindoline prepared by the method of Fichter and Rohner (*loc. cit.*), and yielding identical *acetyl* derivatives.

Reaction of quindoline-11-carboxylic acid with thionyl chloride gave *quindoline*-11-*carboxyl chloride hydrochloride*, converted by heating in nitrobenzene into a bimolecular *product*, $C_{32}H_{16}O_2N_4$. We have termed this compound *bisquindolinoyl*, and have assigned it structure (III), a formulation which agrees well with its mode of formation, its molecular weight (Rast method), and its reconversion into quindoline-11-carboxylic acid on alkaline hydrolysis. *Quindoline*-11-*carboxyamide* (I; R = H, R′ = $CO{\cdot}NH_2$) failed to yield the corresponding amine on hypobromite oxidation, owing probably to the small solubility of the base. In common with the simpler γ-carboxyamidoquinolines (cf. Petrow, *J.*, 1945, 19) it gave 11-*cyanoquindoline* (I; R = H, R′ = CN) on sublimation.

11-*Aminoquindoline* (I; R = H, R′ = $NH_2$), prepared from the acid by the Curtius method, resembled 5-aminoacridine in that its dilute solutions were highly fluorescent, and reacted alkaline to litmus. Thus the pH of a 0·003M-solution in 50% alcohol was found to be 9·6. It formed only a *monohydrochloride*, and on acetylation gave a *triacetyl* derivative which was highly fluorescent in ultra-violet light (cf. Wilkinson and Finar, *J.*, 1946, 116).

The nitration of quindoline was studied by Fichter and Rohner (*loc. cit.*; see also Giraud, *Compt. rend.*, 1880, **90**, 1430), who described the formation of an orange dinitroquindoline. On repeating this work it soon became apparent that this was actually a mixture of two mononitroquindoline nitrates. These were separated by chromatographic adsorption on alumina, with benzene as solvent and elution agent, into a more strongly adsorbed yellow mononitroquindoline (80%) and a scarlet isomeride (10%). As indole derivatives usually nitrate *para*- to the indole nitrogen, we assigned the constitution of a 7-*nitroquindoline* (I; R = $NO_2$, R′ = H) to the yellow mononitration product. This assumption was supported by the behaviour of the compound with sodium hydroxide solution, whereupon, in common with such related compounds as 3-nitrocarbazole (cf. Stevens and Tucker, *J.*, 1923, 2141), a deep red coloration was obtained. This result is no doubt due to the formation of a salt of the *ψ*-nitro-acid (II). Attempts to confirm this structure by direct synthesis from 5-nitrodiacetylindoxyl were not successful. Although the necessary 4-nitrophenylglycine-*o*-carboxylic acid required for the preparation of the latter compound has been described by Hartmann (Diss., Halle, 1914, p. 41), in our hands the method gave poor yields (29%), and the same compound was finally obtained in 65% yield by direct condensation of 2-chloro-5-nitrobenzoic acid (Rupe, *Ber.*, 1897, **30**, 1099) with glycine by means of a copper-bronze catalyst. Ring closure gave 5-*nitro*-ON-*diacetylindoxyl*, but this compound failed to undergo the required condensation with isatinic acid. It was thought that removal of the *O*-acetyl group might facilitate the condensation, but attempts to carry this out using the " sulphite hydrolysis method " (Bayer & Co., G.P. 108,761) were unsuccessful. An alternative route would involve reduction of *o*-nitrobenylidene-5-nitroindoxyl, but attempts to prepare this compound from 5-nitrodiacetylindoxyl and *o*-nitrobenzaldehyde gave inconclusive results. The structure of the yellow mononitroquindoline was finally established by reduction to the amino-compound, followed by conversion into the bromoquindoline, which was found to be identical with the 7-bromo-isomeride (above). 7-*Aminoquindoline* (I; R = $NH_2$, R′ = H) was characterised by conversion into a *triacetyl* derivative and by formation of 7-*benzylideneaminoquindoline* (I; R = N:CHPh, R′ = H).

In contrast to 7-nitroquindoline, which readily gave an *acetyl* derivative, the scarlet nitroquindoline (above) resisted all attempts at acetylation, including the drastic conditions successfully employed by Preston, Tucker, and Cameron (*J.*, 1942, 500) for 1-nitrocarbazole.

It gave a weak purple coloration with alkali. Its formulation as an *11-nitroquindoline* (I; R = H, R′ = $NO_2$) followed from its reduction to 11-aminoquindoline. The nitration of quindoline in the 11-position finds a parallel in the reported formation of 4-nitro-3-acetamidoquinoline from 3-acetamidoquinoline (Renshaw and Friedman, *J. Amer. Chem. Soc.*, 1939, **61**, 3320), although the quinoline derivative differs in its resistance to reduction. It is noteworthy that nitration of quindoline may be effected with dilute nitric acid. For instance, prolonged heating with 0·5N-nitric acid gave the scarlet isomeride exclusively in 10% yield, with recovery of unchanged quindoline. The use of 2N-nitric acid gave the mixed isomers. A method is described for the exclusive preparation of each isomer in satisfactory yield. Nitration of quindoline-11-carboxylic acid gave the *nitrate* of 7-nitroquindoline-11-carboxylic acid (I; R = $NO_2$, R′ = $CO_2H$) The free *acid* gave 7-nitroquindoline on decarboxylation, and *7-aminoquindoline*-11-*carboxylic acid* (I; R = $NH_2$, R′ = $CO_2H$) on reduction. Nitration of quindoline with boiling concentrated nitric acid gave a low yield of 7 : x-*dinitroquindoline*, also formed by further nitration of 7-nitroquindoline, but not obtained from the 11-nitro-isomeride.

## EXPERIMENTAL.

(M. p.'s are corrected; semimicroanalyses are by Mr. S. Bance, B.Sc., A.R.I.C., Microanalytical Dept., May and Baker Ltd.).

*Quindoline*-11-*carboxylic Acid* (I; R = H, R′ = $CO_2H$).—A cooled solution of isatin (85 g.) in potassium hydroxide (515 g.) and water (2300 ml.) was run into a flask containing *N*-acetylindoxyl (100 g.) (or *ON*-diacetylindoxyl, 124 g.) in an atmosphere of coal-gas, and the mixture shaken until solution was complete. After 10 days water (1000 ml.) was added to the greenish-yellow crystalline mass, and air passed through the heated solution for 20 minutes, whereby any excess of indoxyl was oxidised to indigo. Concentrated hydrochloric acid was added to the hot filtrate with thorough stirring until a faint permanent precipitate was formed, followed by addition of charcoal (10 g.). The filtrate was added to an equal volume of alcohol, and the solution made acid to litmus with concentrated hydrochloric acid, giving quindoline-11-carboxylic acid, which was collected and washed twice with hot water and with alcohol. For further purification the crude acid in hot 2N-sodium hydroxide (300 ml.) and water (200 ml.) was treated with dilute hydrochloric acid until a slight permanent precipitate was obtained, charcoal (10 g.) added, and after addition of an equal volume of alcohol to the filtrate, concentrated hydrochloric acid added until the mixture was acid to litmus. Quindoline-11-carboxylic acid formed a bright yellow powder, m. p. 336—337° (decomp.) (Found: C, 73·4; H, 3·8; N, 10·9. Calc. for $C_{16}H_{10}O_2N_2$: C, 73·3; H, 3·8; N, 10·7%); yield 140 g. Its hydrochloride was obtained as a *monohydrate* (Found: N, 9·0; Cl, 11·2. $C_{16}H_{11}O_2N_2Cl,H_2O$ requires N, 8·9; Cl, 11·2%), an orange powder, when quindoline-11-carboxylic acid (2 g.) was heated under reflux for 1 hour with 5N-hydrochloric acid (5000 ml.), and the rapidly filtered solution allowed to cool. On heating, it lost hydrogen chloride to give the free acid. When quindoline-11-carboxylic acid (40 g.) in liquid paraffin (300 ml.) was kept at 290—300° until evolution of carbon dioxide had ceased with almost complete solution, and an equal volume of light petroleum (b. p. 40—60°) added to the cooled mixture, quindoline was obtained as yellow plates from toluene (1250 ml.), m. p. 251—252° (Found: C, 82·6; H, 4·3; N, 12·9. Calc. for $C_{15}H_{10}N_2$: C, 82·6; H, 4·6; N, 12·9%); yield 31·2 g.

*5-Bromo*-ON-*diacetylindoxyl*.—4-Bromophenylglycine-*o*-carboxylic acid (20 g.) was added in small portions to boiling acetic anhydride (100 ml.) containing fused sodium acetate (9·5 g.). After a further 5 mins. an equal volume of water was added, and the decomposed mixture decanted from a small quantity of tarry material. On cooling, crude *5-bromo*-ON-*diacetylindoxyl* (12 g.) was obtained, separating from acetic anhydride in white needles, m. p. 124—124·5° (Found: C, 48·7; H, 3·4; N, 4·8; Br, 27·2. $C_{12}H_{10}O_3NBr$ requires C, 48·7; H, 3·4; N, 4·7; Br, 27·0%); yield 7·2 g. (33%). Decomposition of the acetic anhydride mother-liquors with water gave *5-bromo*-N-*acetylindoxyl*, needles from methanol, m. p. 187—188° (Found: C, 47·3; H, 3·3; N, 5·7; Br, 31·7. $C_{10}H_8O_2NBr$ requires C, 47·2; H, 3·2; N, 5·5; Br, 31·5%); yield 900 mg.

*7-Bromoquindoline*-11-*carboxylic Acid* (I; R = Br, R′ = $CO_2H$).—(*a*) 5-Bromo-*ON*-diacetylindoxyl was condensed with potassium isatinate (as above), and *7-bromoquindoline*-11-*carboxylic acid* was obtained as an orange amorphous powder, m. p. 328—329° (decomp.) (Found: C, 56·3; H, 2·9; N, 8·1; Br, 23·2. $C_{16}H_9O_2N_2Br$ requires C, 56·4; H, 2·6; N, 8·2; Br, 23·4%); yield 88%. (*b*) Quindoline-11-carboxylic acid (3·5 g.) was triturated with glacial acetic acid (25 ml.), and a solution of bromine (1·6 ml.) in glacial acetic acid (10 ml.) added with stirring. The yellow suspension thickened and became purple. After 1 hour, water (100 ml.) was added, the precipitated solids were collected, washed with water, and dissolved in 2N-sodium hydroxide, and the solution boiled for 5 mins. and filtered. An equal volume of alcohol was added, followed by concentrated hydrochloric acid–alcohol (1 : 1) until a faint permanent precipitate was obtained. Charcoal was added, and 7-bromoquindoline-11-carboxylic acid obtained by addition of hydrochloric acid to the filtrate until acid to litmus (Found: N, 8·1; Br, 23·6%), m. p. 328—329° (decomp.), alone or in admixture with the bromo-acid prepared by method (*a*); yield 4 g. (87%).

*7-Bromoquindoline* (I; R = Br, R′ = H).—(*a*) Decarboxylation of 7-bromoquindoline-11-carboxylic acid in liquid paraffin at 285° gave 7-bromoquindoline in yellow needles or plates from alcohol, m. p. 314·5—315° (Found: C, 60·5; H, 3·0; N, 9·6; Br, 26·5. Calc. for $C_{15}H_9N_2Br$: C, 60·6; H, 3·0; N, 9·4; Br, 26·9%); yield 81%. (*b*) A solution of bromine (5 g.) in glacial acetic acid (100 ml.) was slowly added with stirring to quindoline (3·3 g.) in glacial acetic acid (66 ml.). The orange-yellow perbromide was collected, washed with water and, on warming with N-ammonium hydroxide, gave 7-bromoquindoline, identical in m. p. and mixed m. p. with the compound prepared by method (*a*). Fichter and Rohner (*loc. it.*) give m. p. 304°.

The *acetyl* derivative, pale yellow needles from alcohol, m. p. 174—174·5° (Found: N, 8·2. $C_{17}H_{11}ON_2Br$ requires N, 8·3%), was prepared by heating 7-bromoquindoline (1·5 g.) with acetic anhydride (15 ml.) for 35 minutes.

*Derivatives of Quindoline*-11-*carboxylic Acid.*—*Quindoline*-11-*carboxyl chloride hydrochloride* obtained (95% yield) when the pure acid was heated under reflux with thionyl chloride for 2 hours, formed a micro-crystalline scarlet powder which slowly lost hydrogen chloride on exposure to air (Found: Cl, 22·1. $C_{16}H_{10}ON_2Cl_2$ requires Cl, 22·4%).

*Bisquindolinoyl* (III), squat pale yellow needles from xylene, m. p. 365—367° [Found: C, 78·6; H, 3·2; N, 11·8; *M* (Rast), 466. $C_{32}H_{16}O_2N_4$ requires C, 78·7; H, 3·3; N, 11·5%; *M*, 488·5], was obtained when quindoline-11-carboxyl chloride hydrochloride (12 g.) was heated under reflux in nitrobenzene (25 ml.) until evolution of hydrogen chloride had ceased (*ca.* 45 mins.). On hydrolysis with 2N-sodium hydroxide for 10 hours, quindoline-11-carboxylic acid was obtained, m. p. 336—337°, alone or in admixture with an authentic specimen. Decarboxylation gave quindoline.

*Methyl quindoline*-11-*carboxylate*, yellow matted needles from 50% methanol, m. p. 154—155° (Found: N, 9·8. OMe, 10·8; Loss on drying, 3·2. $C_{17}H_{12}O_2N_2,\frac{1}{2}H_2O$ requires N, 9·8; OMe, 10·9; $H_2O$, 3·2%. The dried sample gave N, 10·4; OMe, 11·2. $C_{17}H_{12}O_2N_2$ requires N, 10·2; OMe, 11·2%), was obtained when the 11-carboxyl chloride hydrochloride (5 g.) in dry methanol (50 ml.) was heated under reflux for 30 mins.

*Quindoline*-11-*carboxyamide*, a very sparingly soluble yellow powder, m. p. 334—336° (Found: C, 73·6; H, 4·1; N, 16·0. $C_{16}H_{11}ON_3$ requires C, 73·5; H, 4·2; N, 16·1%), was prepared by sublimation at 300°/0·1 mm. of the product obtained when ammonium hydroxide (20 ml., *d* 0·880) was added to the acid chloride hydrochloride (5 g.); yield 3 g. (78%). Sublimation of the amide at 300° gave 11-*cyanoquindoline*, sparingly soluble yellow needles, m. p. 296° (Found: C, 79·0; H, 3·9; N, 17·6. $C_{16}H_9N_3$ requires C, 79·1; H, 3·7; N, 17·3%); yield 3·75 g. (81%). 11-Cyanoquindoline was also obtained (80%) when the amide (3 g.) was heated under reflux with acetic anhydride (20 ml.) for 1½ hrs., or (54%) when the amide (1 g.) was heated under reflux with phosphorus pentoxide (2 g.) in xylene (20 ml.).

11-*Aminoquindoline* (I; $R = H$, $R' = NH_2$).—The following experimental conditions must be strictly adhered to: Pure quindoline-11-carboxyl chloride hydrochloride (7·9 g.) was added to 95% hydrazine hydrate solution (7·5 ml.) in water (75 ml.) and stirred at 40—50° until a homogeneous suspension of the hydrazide was obtained. The filtered and water-washed product was stirred with N-hydrochloric acid (400 ml.) at 0° until a *homogeneous* suspension of the hydrazide hydrochloride was obtained. Sodium nitrite (2·0 g.) in a little water was then slowly added, and after 30 mins.' stirring at 0° the red azide was rapidly collected on a previously cooled 18-cm. Buchner filter. The cake of azide was washed with ice-water, and heated with 2N-hydrochloric acid (400 ml.) in a large beaker. Rapid evolution of nitrogen occurred with considerable frothing. After cooling, the crude amine hydrochloride was collected, recrystallised once (charcoal) from 50% alcohol (400 ml.), and the purified salt (6·35 g.) decomposed by warming with 2N-ammonium hydroxide. 11-*Aminoquindoline* formed yellow needles from 50% alcohol, m. p. *ca.* 297° (with previous blackening) (Found: C, 74·8; H, 4·7; N, 17·5; loss on drying, 3·7. $C_{15}H_{11}N_3,\frac{1}{2}H_2O$ requires C, 74·5; H, 4·9; N, 17·4; $H_2O$, 3·7%. The dried material gave N, 17·9. $C_{15}H_{11}N_3$ requires N, 18·0%); yield, 4·4 g. (83%). The *hydrochloride*, yellow needles from 50% alcohol, m. p. 350—380° (decomp.) (Found: N, 14·6; Cl, 12·2; loss on drying, 6·4. $C_{15}H_{12}N_3Cl,H_2O$ requires N, 14·6; Cl, 12·3; $H_2O$, 6·3%), was obtained when 11-aminoquindoline (400 mg.) in boiling alcohol (40 ml.) was treated with hot 2N-hydrochloric acid (4 ml.) in water (36 ml.). The *triacetyl* derivative formed colourless plates from alcohol, m. p. 190—191° (Found: C, 70·2; H, 4·9; N, 11·8. $C_{21}H_{17}O_3N_3$ requires C, 70·2; H, 4·7; N, 11·7%).

7-*Nitroquindoline* (I; $R = NO_2$, $R' = H$).—Quindoline (5 g.) was triturated with nitric acid (85 ml., *d* 1·42) at 0°, and after 12 hours at 15°, water (100 ml.) was added and the solids collected and basified by warming with N-ammonium hydroxide. The crude 7-nitro-derivative (5·8 g.) was freed from some 11-nitro-isomeride by heating it under reflux with chlorobenzene (100 ml.) for 30 mins. and allowing it to cool to 40°; it was then quickly collected and recrystallised from pyridine (40 ml.). Pyridine of crystallisation was removed in a vacuum over concentrated sulphuric acid, giving 7-*nitroquindoline*, flattened yellow needles on sublimation at 320°/11 mm., m. p. 322—323° (Found: C, 68·3; H, 3·5; N, 15·9. $C_{15}H_9O_2N_3$ requires C, 68·4; H, 3·4; N, 16·0%); yield, 66%. The acetic acid addition *compound* formed long yellow needles (Found: C, 63·1; H, 4·5; N, 12·8; loss on drying, 18·6. $C_{15}H_9O_2N_3,CH_3{\cdot}CO_2H$ requires C, 63·2; H, 4·0; N, 13·0; HOAc, 18·4%), losing acetic acid on warming. The *acetyl* derivative formed very pale yellow needles from glacial acetic acid, m. p. 259—260° (Found: N, 13·7. $C_{17}H_{11}O_3N_3$ requires N, 13·8%).

7-*Aminoquindoline* (I; $R = NH_2$, $R' = H$).—7-Nitroquindoline (7 g.), reduced iron (21·5 g.), anhydrous calcium chloride (1·35 g.), and 70% alcohol (105 ml.) were heated under reflux for 12 hrs. The mixture was immediately filtered into ice-cold, air-free water (110 ml.). Yellow needles were deposited on shaking (5·65 g.) which on recrystallisation from the minimum quantity of 50% alcohol gave, by rapid cooling and stirring, 7-*aminoquindoline*, orange-yellow glittering plates, m. p. 274·5° (preheated bath) (Found: C, 77·1; H, 5·0; N, 17·8. $C_{15}H_{11}N_3$ requires C, 77·2; H, 4·8; N, 18·0%); yield, 4·6 g. The compound undergoes rapid oxidation in hot solution. The *triacetyl* derivative formed very pale yellow needles from alcohol, m. p. 237—238° (Found: C, 70·1; H, 5·0; N, 11·7. $C_{21}H_{17}O_3N_3$ requires C, 70·2; H, 4·7; N, 11·7%). 7-*Benzylideneaminoquindoline*, bright yellow spangles from alcohol, m. p. 270—271° (Found: C, 81·8; H, 4·7; N, 13·2. $C_{22}H_{15}N_3$ requires C, 82·1; H, 4·7; N, 13·1%), was obtained when 7-aminoquindoline (580 mg.) in 2N-hydrochloric acid (2·5 ml.) and water (40 ml.) was treated with benzaldehyde (300 mg.), followed by crystalline sodium acetate (5·0 g.), and the mixture shaken for 20 minutes.

For conversion into 7-bromoquindoline, finely powdered anhydrous 7-aminoquindoline (1·17 g.) was added to 30% (w./v.) hydrobromic acid solution (30 ml.), and the suspension stirred at 0° for 15 minutes. Sodium nitrite (345 mg.) was then slowly added at 0°, and stirring continued for a further 30 mins. at this temperature. The suspension was then added to a solution of cuprous bromide (900 mg.) and sodium bromide (1·2 g.) in 30% (w./v.) hydrobromic acid solution at 0°. The mixture was warmed on the water-bath until evolution of nitrogen had ceased, an equal volume of water added, and the solids collected, basified by warming with N-ammonium hydroxide, and extracted with boiling alcohol (50 ml.), giving 7-bromoquindoline, m. p. 314·5—315° (Found : N, 9·4; Br, 26·6. Calc. for $C_{15}H_9N_2Br$ : N, 9·4; Br, 26·9%), not depressed in admixture with an authentic specimen; yield, 22%. The acetyl derivative, m. p. 174—174·5°, gave no depression in admixture with an authentic specimen.

5-*Nitro*-ON-*diacetylindoxyl*.—4-Nitrophenylglycine-*o*-carboxylic acid, long yellow needles from water, m. p. 226—227° in a sealed tube (lit. 226—227°) (Found : loss on drying, 13·2. Calc. for $C_9H_8O_6N_2,2H_2O$ : $H_2O$, 13·0%. Found for dried product : C, 45·0; H, 3·4; N, 11·6. Calc. for $C_9H_8O_6N_2$ : C, 45·0; H, 3·4; N, 11·7%), was prepared by heating 2-chloro-5-nitrobenzoic acid (10 g.), glycine (5·0 g.), anhydrous sodium carbonate (5·5 g.), copper powder (1·0 g.), and water (100 ml.) under reflux for 2 hours. The hot filtered solution was cooled, and the acid precipitated by addition of concentrated hydrochloric acid until the solution was acid to Congo-red. When the anhydrous acid was added to boiling acetic anhydride–sodium acetate as described above, it gave 5-*nitro*-ON-*diacetylindoxyl*, light yellow plates from glacial acetic acid, m. p. 219—220° (Found : C, 54·8; H, 4·0; N, 10·5. $C_{12}H_{10}O_5N_2$ requires C, 55·0; H, 3·8; N, 10·7%); yield 57%.

11-*Nitroquindoline* (I; R = H, R′ = $NO_2$).—Nitric acid (0·64 g., *d* 1·52) in glacial acetic acid (10 ml.) was added, during 60 mins., to a boiling, well-stirred solution of quindoline (2·18 g.) in glacial acetic acid (20 ml.). Heating under reflux was continued for 30 mins. after addition was complete. Water (100 ml.) was added to the cooled mixture, and the solids collected and extracted with boiling benzene (500 ml.). The cold filtered extract was passed through a column of alumina (2·5 × 15 cm.). The orange-red band was eluted with benzene, and the solution concentrated to 50 ml., giving 11-*nitroquindoline*, magnificent scarlet silky needles, m. p. 282° (Found : C, 68·3; H, 3·4; N, 16·1. $C_{15}H_9O_2N_3$ requires C, 68·4; H, 3·4; N, 16·0%); yield 400 mg. (15%). Reduction with reduced iron gave 11-aminoquindoline (Found : C, 74·4; H, 4·6; N, 17·5; loss on drying, 3·7. Calc. for $C_{15}H_{11}N_3,\frac{1}{2}H_2O$ : C, 74·5; H, 4·9; N, 17·4; $H_2O$, 3·7%. Found for dried material : N, 18·0. Calc. : N, 18·0%), identical with authentic 11-aminoquindoline, and converted into an identical triacetyl derivative.

7 : x-*Dinitroquindoline*.—Quindoline (5 g.) in nitric acid (80 ml., *d* 1·42) was heated under reflux for 15 mins. Water (10 ml.) was added, and when cold, the solids (5·1 g.) were collected and warmed for a few minutes with ammonium hydroxide. The product was crystallised from pyridine (90 ml.)–light petroleum (90 ml., b. p. 60—80°), then dissolved in hot pyridine (20 ml., charcoal), and light petroleum (10 ml.; b. p. 80—100°) added. 7 : x-*Dinitroquindoline* formed orange micro-needles, m. p. 303° (Found : C, 58·7; H, 3·0; N, 18·4. $C_{15}H_8O_4N_4$ requires C, 58·5; H, 2·6; N, 18·2%); yield, 1·5 g. (21%). The same compound (Found : N, 18·3%) was obtained when 7-nitroquindoline (3 g.) and nitric acid (40 ml., *d* 1·42) were heated under reflux for 15 mins., and water (5 ml.) added.

7-*Nitroquindoline*-11-*carboxylic acid*.—Quindoline-11-carboxylic acid (10 g.) was heated with nitric acid (80 ml., *d* 1·42) on the water-bath until solution was complete. After cooling, the solids were collected, washed with concentrated nitric acid, and dried over potassium hydroxide in a vacuum. 7-*Nitroquindoline*-11-*carboxylic acid nitrate* formed orange-yellow microcrystals, m. p. 332° (with previous darkening) (Found : C, 51·9; H, 3·0; N, 15·3. $C_{16}H_{10}O_7N_4$ requires C, 51·9; H, 2·7; N, 15·1%); yield, 11 g. (71%). The free *acid* formed a yellow, sparingly soluble, amorphous powder, m. p. 334—335° (sinters 327°) (Found: N, 13·6. $C_{16}H_9O_4N_3$ requires N, 13·7%). Decarboxylation of the acid (1 g.) gave 7-nitroquindoline, m. p. 332—333° (Found : N, 16·0%), not depressed in admixture with an authentic specimen; yield, 500 mg. (58%). 7-*Aminoquindoline*-11-*carboxylic acid*, a sparingly soluble, purplish-brown, amorphous powder, m. p. 311—312° (Found : C, 64·9; H, 4·4; N, 14·3; loss on drying, 6·0. $C_{16}H_{11}O_2N_3,H_2O$ requires C, 65·0; H, 4·4; N, 14·3; $H_2O$, 6·1. Found for dried product : N, 15·1. $C_{16}H_{11}O_2N_3$ requires N, 15·2%), was prepared by reduction of the nitro-acid with reduced iron, the filtrate made alkaline, warmed for 30 mins., filtered (charcoal), the new filtrate acidified with hydrochloric acid to Congo-red, and the amino-acid precipitated by addition of sodium acetate (30 g.); yield, 2·3 g. (78%).

*Fluorescence of Quindoline Derivatives in Ultra-violet Light*.—In general quindoline derivatives fluoresce both in the solid state and in solution. The colours vary from orange to dark blue.

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