CCLIX.—*Syntheses in the Indole Series. Part IV. Derivatives of 2 : 3-Benz-γ-carboline.*

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The aim of this work was to prepare derivatives of 2 : 3-benz-γ-carboline (I) * in order to ascertain whether they possess chemotherapeutic activity. γ-Carboline was prepared from 4-chloro-

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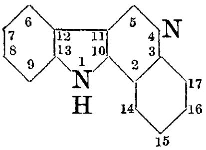
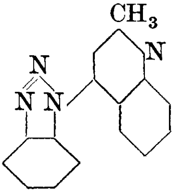
* The numbering of the benzcarboline nucleus is based on the suggestion of Gulland, Robinson, Scott, and Thornley (J., 1929, 2926).

pyridine and *o*-phenylenediamine by Robinson and Thornley (J., 1924, **125**, 2169), *via* 4-*o*-aminophenylaminopyridine, and the triazole derivative. In an analogous way, 4-o-*aminophenylamino-2-methylquinoline* was obtained when 4-chloro-2-methylquinoline and *o*-phenylenediamine were heated together at 140° under a pressure of 20—30 mm., and this base was readily converted into 4-(*benztriazolyl*-3′)-2-*methylquinoline* (II).

(I.)



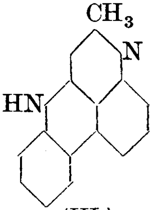


(II.)

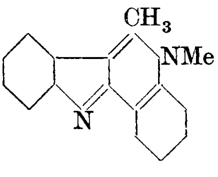
The latter compound was heated in syrupy phosphoric acid until the evolution of nitrogen had ceased, and from the resulting solution a crystalline base, m. p. 298°, was isolated, the properties (*e.g.*, fluorescence) of which indicated that it was the desired 5-*methyl*-2 : 3-*benz*-γ-*carboline*.

By an analogous series of reactions from 4-chloro-6-methoxy-2-methylquinoline, there were prepared 4-o-*aminophenylamino*-6-*methoxy*-2-*methylquinoline*, 4-(*benztriazolyl*-3′)-6-*methoxy*-2-*methylquinoline*, and a base, m. p. 236°, which was presumably 15-*methoxy*-5-*methyl*-2 : 3-*benz*-γ-*carboline*.

The method of synthesis of these two bases does not, however, decide their constitution unambiguously, for it is possible that a base possessing structure (III) might have arisen from the triazole compound at the final stage.



(III.)



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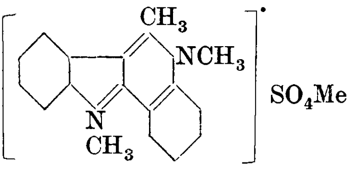


(V.)

Besides the general similarity of these new bases to the isomeric 4 : 5-benz-β-carboline (5 : 6-benz-4-carboline) previously prepared (Kermack and Slater, J., 1928, 32), and the agreement of their properties with those to be expected of derivatives of 2 : 3-benz-γ-carboline, the further evidence given below appears to leave little doubt that these bases have the assigned constitutions.

When equimolecular quantities of *p*-anisidine and ethyl methylacetoacetate were kept at 37° for several days, and the water formed was removed, a solid separated, but the mixture did not form a hard mass as happened, for example, when *p*-anisidine and ethyl acetoacetate were similarly treated. When the soft mixture was rapidly heated to 250° it was converted in 55% yield into 4-*hydroxy*-6-*methoxy*-2 : 3-*dimethylquinoline*.

By treatment with phosphorus oxychloride at 130°, this compound yielded 4-*chloro*-6-*methoxy*-2 : 3-*dimethylquinoline*, which reacted with *o*-phenylenediamine at 140° under diminished pressure to form 4-o-*aminophenylamino*-6-*methoxy*-2 : 3-*dimethylquinoline*. When this was treated with nitrous acid in the cold, 4-(*benztriazolyl*-3′)-6-*methoxy*-2 : 3-*dimethylquinoline* was formed, but all attempts to obtain from this compound, by heating with phosphoric acid, a crystalline base, or a substance exhibiting a violet fluorescence were unsuccessful.

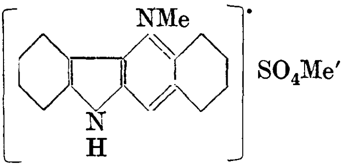
This affords negative evidence in favour of the benzcarboline constitution of the fluorescing bases described above, since in this case position 3 in the quinoline nucleus is blocked, but position 5 is open. If the fluorescing bases had the constitution of the type (III), it is probable that an analogous compound would have been obtained from 4-(benztriazolyl-3′)-6-methoxy-2:3-dimethylquinoline, whereas, of course, the formation of a benzcarboline derivative would have been impossible.

More direct evidence was sought by attempting new methods of synthesis, which, independently, or along with the synthesis previously mentioned, might remove ambiguity.

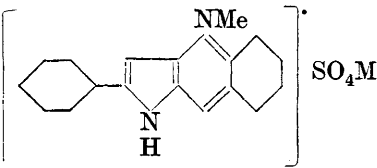
4-(β-*Phenyl*-β-*methylhydrazino*)-2-*methylquinoline* was prepared from 4-chloro-2-methylquinoline and phenylmethylhydrazine by heating them together at 160—180°. Attempts to convert this compound, by an extension of Fischer's indole synthesis analogous to that employed by Schoff (*Ber.*, 1896, **29**, 267), Japp and Findlay (J., 1897, **71**, 1117), and Japp and Maitland (J., 1903, **83**, 269), into 1 : 5-dimethyl-2 : 3-benz-γ-carboline were unsuccessful. Phosphoryl chloride in boiling toluene solution appeared to be without effect, and anhydrous zinc chloride at 140—180° caused considerable decomposition, but neither a crystalline base nor any substance exhibiting fluorescence could be isolated.

The following method of synthesising 1 : 5-dimethyl-2 : 3-benz-γ-carboline proved successful: *o*-Acetamidoacetophenone, obtained by the reduction of *o*-nitroacetophenone (Kermack and Smith, J., 1929, 814) and acetylation of the *o*-aminoacetophenone, was converted into its *phenylmethylhydrazone*, and when this compound was treated in boiling toluene solution with phosphoryl chloride a base, m. p. 173—174°, was obtained, which yielded fluorescent solutions and was apparently 1 : 5-*dimethyl*-2 : 3-*benz*-γ-*carboline*.

To settle the question, an attempt was made to prepare a common derivative of the two bases of m. p.'s 298° and 173—174°. The former was converted into its *methosulphate*, m. p. 277° (decomp.), by treatment with methyl sulphate in dry toluene, and from this the *anhydronium base*, m. p. 262°, was obtained by treatment with alkali. This base, presumably 4 : 5-*dimethyl*-2 : 3-*benz*-γ-ψ-*carboline* (IV), yielded a *methosulphate* (V), m. p. 292°, when treated with methyl sulphate in dry benzene solution. This salt should be identical with the methosulphate of the supposed 1 : 5-dimethyl-2 : 3-benz-γ-carboline, m. p. 173—174°. This latter compound, of which only a limited quantity was available, was therefore treated with methyl sulphate in dry toluene solution; the methosulphate obtained was somewhat impure and its m. p. could not be raised above 281°, but the m. p. of an intimate mixture of the two compounds was 286°, and microscopic examination of the crystals showed them to be similar, except that those obtained by the second method were slightly contaminated by amorphous material. In other respects the compounds exhibited the same behaviour, so there seems little doubt that they are identical, and the proposed structures are confirmed.



(VI.)



(VII.)

It also follows that the anhydronium base derived from the methosulphate by treatment with alkali has the constitution (IV), similar to that postulated by Kermack, Perkin, and Robinson (J., 1922, **121**, 1877) in the case of derivatives of β-carboline and other analogous compounds, and confirmed by Kermack and Slater (J., 1928, 32) in the case of 4 : 5-benz-β-carboline.

Although Armit and Robinson (J., 1922, **121**, 827) failed to obtain an anhydronium base from the methosulphate of 3 : 4-benz-δ-carboline (VI), Mrs. Robinson (J., 1929, 2948) found that 2 : 3-(2′-phenylpyrrolo)(4′ : 5′)-quinoline methosulphate (VII), in which the relationship between the nitrogen atoms is very closely similar, does yield an anhydronium base. She suggests that in the second case the valency changes involved can occur over a more direct path and do not have to proceed round the greater part of the benzene nucleus as in 3 : 4-benz-δ-carboline. No short peripheral path presents itself in the case of 2 : 3-benz-γ-carboline now investigated, but if *p*-linkages are permissible, only a very simple series of valency changes need be postulated in the formation of this anhydronium base.

EXPERIMENTAL.

4 - o -*Aminophenylamino* - 2 - *methylquinoline*.—4-Chloro-2-methylquinoline (10 g.) and *o*-phenylenediamine (6 g.) were heated together at 140° in an oil-bath under a pressure of 20—30 mm. for 2 hours. The yellow solid which separated was extracted with boiling dilute hydrochloric acid (10%), and the solution filtered. The filtrate on cooling deposited a greyish-green mass of prismatic crystals of the *dihydrochloride*, yield 13 g., m. p. 301° (Found: Cl, 22·3. $C_{16}H_{15}N_3,2HCl$ requires Cl, 22·1%).

The *base* precipitated by alkali from an aqueous solution of this salt was recrystallised from benzene, separating in clumps of white prismatic needles, m. p. 220° (Found: C, 77·6; H, 6·3. $C_{16}H_{15}N_3$ requires C, 77·2; H, 6·0%). It is soluble in dilute mineral acids and dissolves readily in benzene, alcohol, and chloroform, but is almost insoluble in either light petroleum or water. Its solution in concentrated sulphuric acid exhibits a faint greenish fluorescence in the arc light.

4-(*Benztriazolyl*-3′)-2-*methylquinoline*.—A solution of sodium nitrite (1·6 g.) in water (20 c.c.) was slowly added with constant stirring to a well-cooled solution of 4-*o*-aminophenylamino-2-methylquinoline (6·4 g.) in 3% hydrochloric acid (about 400 c.c.) until a slight excess of sodium nitrite was present. The voluminous white precipitate of the *hydrochloride* which separated was filtered, washed with water, and recrystallised from boiling water, forming fine colourless needles, m. p. 210° (Found: Cl, 10·7; loss at 110°, 11·1. $C_{16}H_{12}N_4,HCl,2H_2O$ requires Cl, 10·7; $2H_2O$, 10·8%).

The *base* precipitated from the hot solution of the hydrochloride by alkali was filtered, dried, and recrystallised from hot aqueous alcohol, separating as slender, colourless needles, m. p. 149° (yield 4 g.) (Found: C, 73·7; H, 4·6. $C_{16}H_{12}N_4$ requires C, 73·8; H, 4·6%). It is soluble in dilute nitric, sulphuric, acetic, phosphoric, and lactic acids, moderately soluble in benzene, very soluble in alcohol, but insoluble in either light petroleum or water. Its clear solution in cold concentrated sulphuric acid exhibits a light blue fluorescence in the arc light; when the solution is heated, brisk effervescence takes place and the resulting brown solution exhibits a strong bluish-violet fluorescence, presumably due to the formation of 5-methyl-2 : 3-benz-γ-carboline.

5-*Methyl*-2 : 3-*benz*-γ-*carboline*.—Anhydrous 4-(benztriazolyl-3′)-2-methylquinoline (5 g.) was heated in syrupy phosphoric acid (50 c.c.) until the evolution of nitrogen ceased. The yellow precipitate separating from the cool solution on basification was filtered, dried, and recrystallised from methyl alcohol; it formed light brown needles, m. p. 298° (Found: C, 82·6; H, 5·3. $C_{16}H_{12}N_2$ requires C, 82·8; H, 5·2%). This *compound* is insoluble in water and in light petroleum, sparingly soluble in benzene and in ether, moderately soluble in ethyl and still more soluble in methyl alcohol. The hydrochloride is sparingly soluble in water, but the base is readily soluble in dilute phosphoric, lactic, and acetic acids. In all solutions, neutral and acid, 5-methyl-2 : 3-benz-γ-carboline exhibits a strong bluish-violet fluorescence. Its clear solution in concentrated sulphuric acid assumes a bluish colour on heating. It is sparingly soluble in concentrated nitric acid, but easily dissolves on warming to yield a pale yellow solution, which when cool deposits a yellow solid.

4-o-*Aminophenylamino-6-methoxy-2-methylquinoline.*—4-Chloro-6-methoxy-2-methylquinoline (6·9 g.) and *o*-phenylenediamine (4 g.) were condensed together at 140° under reduced pressure (12 mm.) until the contents had become solid (1—2 hours). The yellow product was extracted with boiling water, and the hot solution filtered; the *monohydrochloride* separated from the filtrate, on cooling, in the form of pale yellow needles, m. p. 294° (yield 90%) (Found: Cl, 10·0. $C_{17}H_{17}ON_3,HCl,2H_2O$ requires Cl, 10·1%).

The *base*, obtained as a white precipitate by addition of caustic soda to an aqueous solution of the hydrochloride, separated from hot aqueous alcohol as pink, slender, rectangular prisms, m. p. 188° (Found: N, 15·1. $C_{17}H_{17}ON_3$ requires N, 15·1%). It is fairly soluble in dilute mineral acids, much more so in dilute acetic and lactic acids, moderately soluble in alcohol, sparingly soluble in hot benzene, and insoluble in both light petroleum and water. It dissolves very readily in concentrated nitric acid to yield a yellow solution which becomes crimson on heating.

4-(*Benztriazolyl*-3')-*6-methoxy-2-methylquinoline.*—To a well-cooled solution of the preceding base (8 g.) in 3% hydrochloric acid (400 c.c.), a solution of sodium nitrite (2 g. in 10 c.c. of water) was added until a slight excess was present. The white gelatinous precipitate of the *hydrochloride* of the base obtained was filtered off and recrystallised from boiling water, separating in the form of white needles, m. p. 221° (Found: Cl, 8·8. $C_{17}H_{14}ON_4,HCl,4H_2O$ requires Cl, 8·9%).

The *base* was obtained, on basifying a hot aqueous solution of the hydrochloride, as a light-coloured voluminous precipitate, and was subsequently recrystallised from hot aqueous alcohol, separating as large, pink, rhombohedra, m. p. 144° (yield 4·7 g.) (Found: C, 70·6; H, 4·9. $C_{17}H_{14}ON_4$ requires C, 70·3; H, 4·8%). This base forms very sparingly soluble salts with dilute mineral acids, and even its salts with acetic and lactic acids are only moderately soluble in the hot and sparingly so in the cold; these last two solutions exhibit a light blue fluorescence in the arc light. It dissolves in cold concentrated sulphuric acid with difficulty, and the clear solution, which gives a faint greenish fluorescence, darkens and effervesces slightly on warming, and then exhibits a very strong violet fluorescence [compare the behaviour of 4-(benztriazolyl-3′)-2-methylquinoline].

15-*Methoxy*-5-*methyl*-2 : 3-*benz*-γ-*carboline*.—4-(Benztriazolyl-3′)-6-methoxy-2-methylquinoline (1 g.) was heated in syrupy phosphoric acid (10 c.c.) until effervescence had ceased. The resulting dark liquid was poured into a large excess of water (400 c.c.) and neutralised with caustic soda, and the yellow solid which separated was filtered off at the pump, dried on the water-bath, extracted with ammoniacal methyl alcohol, and the extract filtered hot; the *base* separated on cooling as dark brown rhombic crystals (containing 1 mol. of methyl alcohol) apparently of the hemimorphic class, m. p. 236° (Found: C, 73·7; H, 6·6; N, 9·3. $C_{17}H_{14}ON_2,CH_3OH$ requires C, 73·8; H, 6·2; N, 9·5%). The solubilities of this base in methyl alcohol, ethyl alcohol, benzene, etc., are very similar to those of the 5-methyl analogue (p. 2004). It is sparingly soluble in dilute mineral acids, moderately soluble in acetic and lactic acids, all these solutions (particularly the acid ones) exhibiting a bluish-violet fluorescence. The solution in cold concentrated sulphuric acid, in which the base is sparingly soluble in the cold, exhibits a violet fluorescence, darkening to reddish-brown on warming. The base dissolves in cold concentrated nitric acid to form a dark yellow solution which exhibits scarcely any fluorescence; after being heated and then cooled, however, it deposits yellow crystals.

4-*Hydroxy*-6-*methoxy*-2 : 3-*dimethylquinoline*.—Equimolecular quantities of *p*-anisidine (31 g.) and ethyl methylacetoacetate (36 g.) were warmed together on the water-bath until the former had dissolved completely. The layer of water which separated on standing for 3—4 days at 37° was subsequently removed in the vacuum desiccator, leaving a semi-solid, dark brown, crystalline mass of the condensation product. This was rapidly heated to 250°, whereupon a vigorous reaction took place. The residue in the flask was extracted with boiling water, from which, on filtering and cooling, light yellow crystals of the *monohydrate* of 4-*hydroxy*-6-*methoxy*-2 : 3-*dimethylquinoline*, m. p. 294°, separated. This monohydrate was obtained from aqueous alcohol as nearly colourless needles (Found: loss at 110°, 8·0. $C_{12}H_{13}O_2N,H_2O$ requires loss, 8·1%. Found, on anhydrous base: N, 6·8. $C_{12}H_{13}O_2N$ requires N, 6·9%).

The base may also be obtained from the cooled reaction mixture more conveniently (yield 55%) but in a less pure form by extracting it with dilute hydrochloric acid (3%) and basifying the extract. It is moderately soluble in hot dilute mineral acids, cold dilute acetic and lactic acids, and alcohol, but insoluble in either benzene or light petroleum. Its solution in concentrated sulphuric acid, which exhibits a faint blue fluorescence in the arc light, darkens very considerably on warming. It readily dissolves in concentrated nitric acid to yield a reddish solution unaltered by heating.

4-*Chloro*-6-*methoxy*-2 : 3-*dimethylquinoline*.—The foregoing hydroxy-compound (16 g.) was heated with phosphoryl chloride (32 g.) at 130—140° for 1—2 hours, the product cautiously decomposed by addition of water, and the mixture made alkaline with sodium hydroxide and steam-distilled. 4-*Chloro*-6-*methoxy*-2 : 3-*dimethylquinoline* was obtained by filtering the distillate as a white solid, which was less volatile in steam than the 2-monomethyl compound; it separated from alcohol as long colourless needles, m. p. 111° (Found : N, 6·2. $C_{12}H_{12}ONCl$ requires N, 6·3%).

This base is soluble in dilute mineral acids, the solutions exhibiting a strong blue fluorescence in the arc light. It is moderately soluble in alcohol, benzene, and light petroleum, but sparingly soluble in dilute lactic acid. With concentrated sulphuric and nitric acids it yields solutions which exhibit a very strong blue fluorescence in the arc light but do not undergo any colour changes on warming.

4-o-*Aminophenylamino*-6-*methoxy*-2 : 3-*dimethylquinoline*.—The preceding compound (7·4 g.) was heated with *o*-phenylenediamine (4 g.) under the same conditions as for the monomethyl analogue, and bronze-coloured needles of the *monohydrochloride*, m. p. 125° (decomp.), were obtained (Found : Cl, 9·9. $C_{18}H_{19}ON_3,HCl,2H_2O$ requires Cl, 9·7%). When dilute hydrochloric acid (5%) was used to extract the condensation product, green crystals of the *dihydrochloride*, m. p. 284° (decomp.), separated (Found : Cl, 17·9. $C_{18}H_{19}ON_3,2HCl,2H_2O$ requires Cl, 17·7%).

The *base* was obtained from an aqueous solution of either of the hydrochlorides as a light yellow precipitate on neutralisation with caustic soda. When recrystallised from hot aqueous alcohol, it separated in the form of yellow-brown cubes and short rectangular prisms, m. p. 193° (Found : N, 14·5. $C_{18}H_{19}ON_3$ requires N, 14·3%). Its solubilities are similar to those of the monomethyl compound. It is sparingly soluble in concentrated sulphuric acid, yielding a reddish-brown solution which loses its reddish tinge on heating, and darkens slightly. It is soluble in concentrated nitric acid, yielding a dark red solution which darkens still more on heating.

4-(*Benztriazolyl*-3′)-6-*methoxy*-2 : 3-*dimethylquinoline*.—A solution of the preceding base (8·8 g.) in 3% hydrochloric acid (300 c.c.)

was treated with sodium nitrite as for the monomethyl analogue. No precipitate of the hydrochloride was formed, but the *base* was obtained on basification as a white voluminous precipitate, which separated from alcohol as white, hexagonal prisms, m. p. 201° (Found : N, 18·7. $C_{18}H_{16}ON_4$ requires N, 18·4%).

The solubilities of the salts of this compound are similar to those of the monomethyl compound, the solutions, especially those in dilute acetic and lactic acids, exhibiting a faint violet fluorescence in the arc light. The base dissolves with difficulty in cold concentrated sulphuric and nitric acids to yield yellow solutions which exhibit a faint bluish-green fluorescence in the arc light. No change takes place on heating the latter solution, but the former develops a dark green colour on warming for some time, without, however, effervescing in the slightest [compare 4-(benztriazolyl-3′)-2-methyl- and -6-methoxy-2-methyl-quinoline].

4-(β-*Phenyl*-β-*methylhydrazino*)-2-*methylquinoline*.—4-Chloro-2-methylquinoline (3 g.) and phenylmethylhydrazine (2·5 g.) were heated together at 160—180° for 2 hours under an air condenser. The sticky yellow solid which had formed was extracted with hot dilute hydrochloric acid (3%), and the extract filtered; the hydrochloride separated from the filtrate on cooling as yellow rectangular prisms, m. p. 172°. The *base*, obtained as a light yellow precipitate by the addition of ammonium hydroxide to a hot aqueous solution of the hydrochloride, separated from benzene in the form of short yellow needles, m. p. 237° (Found : N, 16·1. $C_{17}H_{17}N_3$ requires N, 16·0%). This compound is sparingly soluble in alcohol and in benzene, and is insoluble in either light petroleum or water. It is very sparingly soluble in dilute hydrochloric acid in the cold but easily dissolves on warming to yield a yellow solution from which yellow crystals separate on cooling. The base dissolves readily in cold dilute sulphuric acid; it is moderately soluble in concentrated sulphuric acid, yielding a dark brown solution which on heating darkens to crimson and exhibits a bluish-violet fluorescence. It dissolves immediately with frothing when treated with concentrated nitric acid, yielding a crimson solution, and is sparingly soluble in dilute acetic and lactic acids.

o-*Acetamidoacetophenone Phenylmethylhydrazone*.—Solutions of *o*-acetamidoacetophenone (2 g.) and of phenylmethylhydrazine, each in 10 c.c. of acetic acid (50%), were mixed and heated on the water-bath for 30 minutes. The yellow crystals which separated on standing for a few hours were filtered off and dried (yield 0·7 g.). When recrystallised from light petroleum, this *compound* separated in the form of tetragonal bipyramids, m. p. 131—132° (Found : C, 72·7; H, 6·5. $C_{17}H_{19}ON_3$ requires C, 72·6; H, 6·8%); it is moderately soluble in alcohol, benzene, and hot light petroleum, but insoluble in water. It is sparingly soluble in dilute mineral acids but dissolves readily when warmed. In dilute, but not concentrated, nitric acid it dissolves to form a reddish-purple solution, the colour gradually fading on warming or standing for some time. A similar colour is also observed when a drop of dilute sodium nitrite solution is added to a solution of the compound in dilute hydrochloric acid. When a solution of the compound in dilute acetic acid, but not lactic acid, is kept over-night, the reddish-purple colour which develops does not fade on heating or standing. The compound dissolves with difficulty in cold concentrated sulphuric acid to form a yellow solution which darkens on heating, and then exhibits a greenish fluorescence in the arc light.

1 : 5-*Dimethyl*-2 : 3-*benz*-γ-*carboline*.—A solution of the foregoing phenylmethylhydrazone (2 g.) and phosphorus oxychloride (4 c.c.) in dry toluene (10 c.c.) was refluxed for 2 hours; a dark viscous oil adhering to the sides of the flask gradually separated. The toluene was decanted off, and the sticky residue washed several times with light petroleum. The residue was then boiled with alcoholic potassium hydroxide (20%), and the insoluble potassium phosphate filtered off. The dark filtrate was poured into a large excess of water; the yellow solid which separated was so finely divided that it passed through filter paper, but after being coagulated by the addition of a little sodium chloride solution, it could be separated without difficulty, and was then dried on the water-bath. This *base* may be recrystallised from benzene or ligroin, separating from the latter solvent in characteristic yellow, sharp-pointed, petal-like crystals arranged radially, m. p. 173—174° (Found: C, 81·8; H, 5·7; N, 11·4. $C_{17}H_{14}N_2$ requires C, 82·9; H, 5·7; N, 11·4%).

This compound, which is readily soluble in alcohol, moderately soluble in benzene and in ligroin, and sparingly soluble in dilute mineral acids with a bluish-violet fluorescence, dissolves readily in dilute acetic and lactic acids with an intense green fluorescence. When treated with concentrated sulphuric acid, it yields a reddish-brown solution, exhibiting a light blue fluorescence; on warming, the solution loses its reddish tinge, and the fluorescence changes to violet.

5-*Methyl*-2 : 3-*benz*-γ-*carboline Methosulphate*.—A suspension of 5-methyl-2 : 3-benz-γ-carboline (1·5 g.) in 50 c.c. of benzene (freshly distilled over phosphoric oxide) was boiled with a slight excess of methyl sulphate (1·5 g.) for 2 hours under reflux. The hot solution was filtered at the pump, and the light-coloured residue treated with water; all the methosulphate easily dissolved and was thus separated from any unchanged benzcarboline. The aqueous solution was evaporated to dryness, and the residue extracted with boiling alcohol and filtered. On cooling, fine white needles of the *methosulphate* separated from the strongly fluorescing solution. These were again crystallised from alcohol and then melted at 277° (decomp.) (Found : N, 8·2. $C_{16}H_{12}N_2,Me_2SO_4$ requires N, 7·8%).

This compound exhibits a very strong blue fluorescence in all its solutions. It is extremely soluble in water, but sparingly so in alcohol and in hot benzene. Its aqueous solution is precipitated by ammonium hydroxide. It dissolves readily in cold concentrated sulphuric acid to give a colourless solution (exhibiting the usual strong blue fluorescence), which on warming rapidly becomes blue, thus resembling the behaviour of the parent base when similarly treated. It is very sparingly soluble in cold concentrated nitric acid, but easily dissolves on warming and is reprecipitated on cooling or on dilution with water.

4 : 5-*Dimethyl*-2 : 3-*benz*-γ-ψ-*carboline*.—An aqueous solution of the above methosulphate was made alkaline with ammonium hydroxide, and the pale yellow solid which separated was filtered, air-dried, and recrystallised from aqueous alcohol, separating as pale yellow needles, m. p. 262°, of the *monohydrate* of the base (Found : loss at 110°, 6·5. $C_{17}H_{14}N_2,H_2O$ requires loss, 6·8%. Found, in anhydrous *base* : C, 82·1 ; H, 5·9 ; N, 11·4. $C_{17}H_{14}N_2$ requires C, 82·9 ; H, 5·7 ; N, 11·4%).

This base was soluble in dilute hydrochloric or sulphuric acid, but sparingly soluble in dilute nitric acid. It is more soluble, however, in dilute acetic and lactic acids, giving a much stronger fluorescence than with the mineral acids. It is sparingly soluble in water, the solution exhibiting a faint blue fluorescence. It easily dissolves in cold concentrated sulphuric acid to form a clear solution showing a strong light blue fluorescence, which on warming yields first a violet and finally a Prussian-blue colour. It is soluble in concentrated nitric acid to form a light yellow solution, which changes to reddish-brown on warming, but reverts to its original colour on continued heating ; on dilution a white solid is precipitated.

Methosulphate. A solution of the base (2 g.) and methyl sulphate (2 g.) in dry toluene (10 c.c.) was refluxed for 1—2 hours. The light-coloured solid which separated was filtered off, dissolved in water, and the solution filtered and evaporated to dryness ; the residue was dissolved in alcohol, from which the *methosulphate* was obtained after two recrystallisations as fine white needles, m. p. 292° (Found : N, 7·7. $C_{17}H_{14}N_2,Me_2SO_4$ requires N, 7·5%).

A solution of this compound in water, in which it is extremely soluble, exhibits a very strong blue fluorescence, but, unlike the methosulphate of the 5-monomethyl compound, it is unaffected by treatment with ammonium hydroxide solution, although with dilute sodium hydroxide solution a canary-yellow precipitate is obtained which easily dissolves on addition of a slight excess of dilute hydrochloric acid. It dissolves freely in cold concentrated sulphuric acid to yield a yellow solution which, on warming, changes to royal blue and finally to Prussian blue. With concentrated nitric acid this compound behaves in a similar manner to the original base. It is sparingly soluble in alcohol and in hot benzene, in which solvents it exhibits a bluish-violet fluorescence in the arc light.

1 : 5-*Dimethyl*-2 : 3-*benz*-γ-*carboline Methosulphate.*—A solution of the base (0·3 g.) and methyl sulphate (0·3 g.) in toluene was worked up as in the preceding case, and the product obtained melted not very sharply about 260°. When it was recrystallised twice from ethyl alcohol, slightly greyish, thin needles were obtained, m. p. 281°, which when examined microscopically appeared to be contaminated with a small quantity of amorphous material. An intimate mixture of this compound with an approximately equal amount of the 4 : 5-dimethyl methosulphate melted without previous softening at 286°. The solubilities of this compound are indistinguishable from those of the 4 : 5-dimethyl methosulphate; its colourless aqueous solution exhibits a beautiful blue fluorescence readily visible in diffused daylight, and is unaffected by ammonium hydroxide, but sodium hydroxide produces a canary-yellow precipitate soluble in excess of hydrochloric acid.

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