881. *Tryptamines, Carbolines, and Related Compounds. Part III.*[1] 1-*Methyl- and* 1 : N-*Dimethyl-tryptamines.*

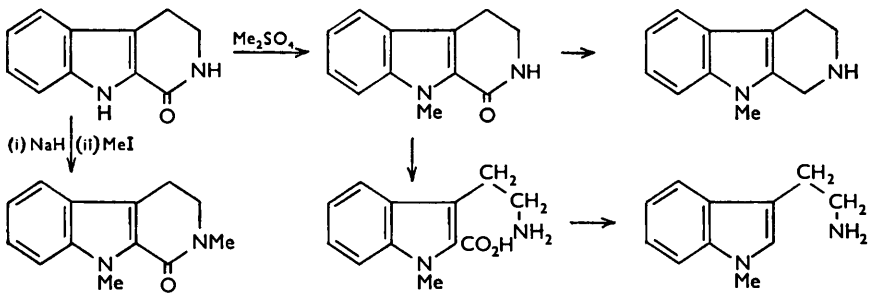
By R. A. Abramovitch.

The scope of the synthesis of tryptamines from 1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carbolines has been examined. Substituents in the benzene ring affect the ease of decarboxylation of the tryptamine-2-carboxylic acids, in the order OMe > Me > H > Cl > NO_2: an explanation is suggested. Tetrahydro-oxocarbolines with dimethyl sulphate give the 9-methyl compounds from which the 1-methyltryptamines can be obtained; the amide group is unreactive but can be methylated by prolonged treatment with sodium hydride followed by methyl iodide, to give the 2 : 9-dimethyl compound in which the amide group now behaves normally, though it is resistant to alkaline hydrolysis. Acid hydrolysis leads to *NN'*-dimethyltryptamine. Cyclisation of 2 : 3-dioxopiperidine 3-*m*-methoxyphenylhydrazone by formic acid gives a mixture of isomers, whereas ethanolic hydrogen chloride gives only the 7-methoxy-compound which, contrary to report, is hydrolysed normally to the amino-acid.

The infrared spectra of some of the intermediates have been examined and are discussed.

The scope of the tryptamine synthesis reported in the preceding paper [1] has been examined in view of divergent experience in the hydrolysis [1,2] and decarboxylation [1] involved, and in methylations [2,3] in this series. In particular, *N*-methyl derivatives have been investigated.

1 : 2 : 3 : 4-Tetrahydro-1-oxo-β-carboline with dimethyl sulphate in aqueous alkali gave, in a few minutes, a high yield of the 9-methyl compound. The position of the methyl group was determined by alkaline hydrolysis to oily 1-methyltryptamine which was identified as its crystalline picrate, which gave no depression of the m. p. when mixed with a specimen [4,5] kindly supplied by Professor Gaddum. The methylcarboline was reduced with sodium and butanol to 1 : 2 : 3 : 4-tetrahydro-9-methyl-β-carboline, an oil (picrate, m. p. 240°; Groves and Swan [6] give m. p. 242°), whereas 1 : 2 : 3 :4-tetrahydro-2-methyl-



β-carboline [7] is a solid, m. p. 208—210° (picrate, m. p. 216—217°). For this reduction lithium aluminium hydride failed as in the case of the unmethylated compound, starting material being recovered, also indicating that the unreactive secondary amide group was still present. Finally, whereas both 1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carboline and its 6-methoxy-derivative showed an NH band at 1575 $cm.^{-1}$ (cyclic imides do not show NH

[1] Part II, Abramovitch and Shapiro, preceding paper.
[2] Nishikawa, Perkin, and Robinson, *J.*, 1924, **125**, 658.
[3] King and Stiller, *J.*, 1937, 466.
[4] Manske, *Canad. J. Res.*, 1931, **5**, 592.
[5] Snyder and Eliel, *J. Amer. Chem. Soc.*, 1948, **70**, 1703.
[6] Groves and Swan, *J.*, 1952, 650.
[7] Boekelheide and Ainsworth, *J. Amer. Chem. Soc.*, 1950, **72**, 2132; Witkop and Goodwin, *ibid.*, 1953, **75**, 3376.

bands in this region [8]) the methylated product does not show this band. The *ind-N*-methylation was somewhat unexpected, since an indole-nitrogen atom is not usually methylated under such mild conditions, whereas some amide nitrogen atoms are.[9] Thus, indole is methylated by methyl toluene-*p*-sulphonate by boiling in xylene in 90 hr.[10a] Alternatively, the indole-nitrogen atom can be methylated by forming the sodium salt in liquid ammonia and treating it with methyl iodide.[10b] King and Stiller [3] showed that methylation of methyl 1 : 2-dihydro-1-oxo-β-carboline 3-orthoformate in acetone with methyl sulphate and potassium carbonate for 3 hr. gave methyl 1 : 2-dihydro-2 : 9-dimethyl-1-oxo-β-carboline-3-carboxylate, but that, if the potassium salt of the orthoformic ester was treated with methyl iodide or the orthoformic ester itself was treated with diazomethane, methylation took place at the amide-nitrogen atom. In our hands, treatment of 1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carboline in acetone with dimethyl sulphate and potassium carbonate (anhydrous conditions) still gave the 9-methyl compound, even in the presence of an excess of dimethyl sulphate. Diazomethane did not methylate the compound at all. Dimethylation (no NH band in the 3 μ region, amide-CO band at 1650 cm.$^{-1}$) was achieved by forming the disodio-derivative with sodium hydride in toluene and treating this with methyl iodide. On use of shorter reaction times only partial formation of the disodium salt occurred, for on methylation 1 : 2 : 3 : 4-tetrahydro-9-methyl-1-oxo-β-carboline was also obtained. 1 : 2 : 3 : 4-Tetrahydro-2 : 9-dimethyl-1-oxo-β-carboline could now be reduced with lithium aluminium hydride, to give 1 : 2 : 3 : 4-tetrahydro-2 : 9-dimethyl-β-carboline (no bands in the 3 and the 6 μ region). It could not, however, be hydrolysed under alkaline conditions. Acid hydrolysis gave 1-methyl-3-2′-methylaminoethylindole. These methylations thus lay the basis for convenient syntheses of 1-methyl- and 1 : *N*-dimethyltryptamine.

Preliminary experiments showed that the cyclic amide group was unreactive even towards phosphorus pentachloride, both in 1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carboline and its 9-methyl derivative, starting material being recovered under the conditions under which 1 : 2-dihydro-1-oxo-β-carboline-3-carboxylic acid [3] and 1 : 2-dihydro-9-methyl-1-oxo-β-carboline [11] and its 6-methoxy-derivative [12] were converted into the 1-chloro-compound. [In connection with the unreactivity of this amide group, it is interesting that 1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carboline condenses readily with methyl anthranilate in the presence of phosphorus trichloride [13] to give rutaecarpine.[14]]

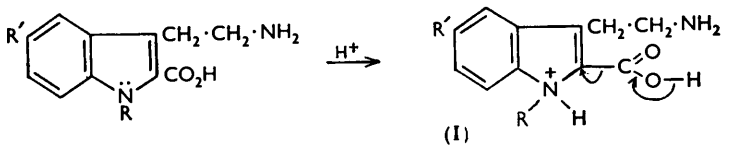
Extension of the synthesis to 6-methoxytryptamine is of two-fold interest: first, there is the question of the direction of ring-closure in the Fischer cyclisation *ortho* or *para* to the methoxyl group; and then there is the report [2] that 1 : 2 : 3 : 4-tetrahydro-7-methoxy-1-oxo-β-carboline [15] is not hydrolysed to the amino-acid by ethanolic alkali. The conditions for the reaction of diazotised *m*-anisidine with 2-oxopiperidine-3-carboxylic acid are critical, the optimum pH being 3·6—4, above or below which only tar is obtained. Kermack, Perkin, and Robinson [16] showed that with ethanolic hydrogen chloride indole-ring formation of a *m*-methoxyphenylhydrazone takes place only *para* to the methoxyl group, though exceptions are now known.[17] 2 : 3-Dioxopiperidine 3-*m*-methoxyphenylhydrazone was cyclised in boiling 70% formic acid to a mixture of the 1 : 2 : 3 : 4-tetrahydro-5- and -7-methoxy-1-oxo-β-carboline, but ethanolic hydrogen chloride gave only the 7-methoxy-compound (poor yield). The latter was readily hydrolysed to the amino-acid with aqueous-ethanolic potassium hydroxide and then decarboxylated smoothly with 5% hydrochloric acid to 6-methoxytryptamine.[18] Again, in contrast to the results of Nishikawa *et al.*,[2]

[8] Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen & Co. Ltd., London, 1954, p. 176.
[9] Abramovitch, Hey, and Long, unpublished results.
[10] (*a*) Shirley and Roussel, *J. Amer. Chem. Soc.*, 1953, **75**, 377; (*b*) Potts and Saxton, *J.*, 1954, 2641; Anet, Chakravarti, Robinson, and Schlittler, *J.*, 1954, 1254.
[11] Kermack, Perkin, and Robinson, *J.*, 1922, **121**, 1884.
[12] Kermack and Tebrich, *J.*, 1940, 314.
[13] Asahina, Manske, and Robinson, *J.*, 1927, 1708.
[14] Cf. Asahina and Ohta, *J. Pharm. Soc. Japan*, 1928, **48**, 313.
[15] Manske and Robinson, *J.*, 1927, 240.
[16] Kermack, Perkin, and Robinson, *J.*, 1921, **119**, 1602; see also Mentzer, *Compt. rend.*, 1946, **222**, 1176; Borsche, *Annalen*, 1908, **359**, 49.
[17] Koelsch, *J. Org. Chem.*, 1943, **8**, 295; Schofield and Theobald, *J.*, 1949, 796.
[18] Akabori and Saito, *Ber.*, 1930, **63**, 2245.

1 : 2 : 3 : 4-tetrahydro-7-methoxy-1-oxo-β-carboline was methylated with dimethyl sulphate and aqueous alkali to a product which is assumed to be the 9-methyl derivative by analogy with the results reported above.

2:3-Dioxopiperidine 3-*p*-nitrophenylhydrazone was readily formed (also a *p*-chlorophenylhydrazone), in agreement with the effect of electron-attractive substituents in the ring on the reactivity of the diazonium cation.[19] This phenylhydrazone was not cyclised by boiling formic or acetic acid, but polyphosphoric acid gave a good yield of 1 : 2 : 3 : 4-tetrahydro-6-nitro-1-oxo-β-carboline. Attempts to decarboxylate 5-nitrotryptamine-2-carboxylic acid failed. In view of the high melting point of both the carboline and the amino-acid, experiments on thermal decarboxylations were carried out with tryptamine-2-carboxylic acid. No product could be obtained with copper or its salts and quinoline;[20] when heated in resorcinol at 235°[21] or in glycerol at 210°,[22] the compound cyclised, to give 1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carboline (similar results were obtained with 5-chlorotryptamine-2-carboxylic acid) without decarboxylation. *ind-N*-Methylation of the imide followed by alkaline hydrolysis gave 1-methyl-5-nitrotryptamine-2-carboxylic acid, and though this was not affected by the usual mild acid treatment much more vigorous and prolonged (10 days) treatment gave a small amount of 1-methyl-5-nitrotryptamine. Similar results were obtained with 5-chlorotryptamine-2-carboxylic acid. This was decarboxylated under vigorous acid conditions in 18 hr., whereas 5-chloro-1-methyltryptamine-2-carboxylic acid only required 2 hr. under the same conditions to give 5-chloro-1-methyltryptamine. Reduction of 6-chloro-1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carboline with sodium and *n*-butyl alcohol resulted in elimination of the halogen and formation of 1 : 2 : 3 : 4-tetrahydro-β-carboline. The synthesis of 7-methyltryptamine was unexceptional and the decarboxylation stage was somewhat easier than for the unsubstituted compound.

The ease of decarboxylation of the tryptamine-2-carboxylic acids in acid media decreases in the order OMe > Me > H > Cl > NO_2 of substituents in the benzene ring, whereas *ind-N*-methylation facilitates decarboxylation under these conditions. This order is the reverse of that expected for normal decarboxylations, the electron-attractive nitro-group generally greatly favouring the heterolysis of the C–C bond linking the carboxyl group or carboxylic anion.[23] Again, it is difficult to see a *direct* influence of the 5-substituent on $C_{(2)}$ of the indole ring. The order of substituents is, however, that of decreasing electron density at the ring-nitrogen atom and it would, therefore, seem that the first stage in the decarboxylation mechanism is co-ordination of a proton at this nitrogen, thus forming a positive centre which will attract electrons from $C_{(2)}$ and favour the heterolysis :



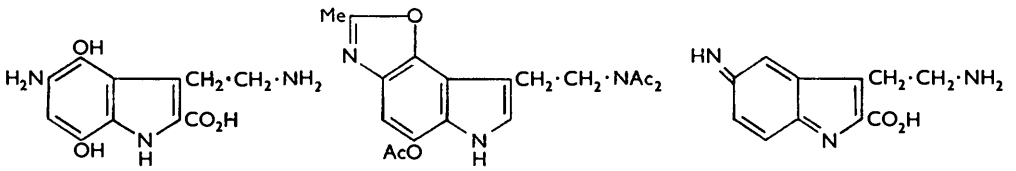
(I)

Only a small amount of the intermediate (I) need be formed. The effect of the indole-*N*-methyl group (R = Me) is in agreement with such a mechanism since it increases the availability of electrons at the nitrogen atom. A 5-benzyloxy-substituent should then favour the ease of decarboxylation and it is hoped to re-examine the decarboxylation of 5-benzyloxytryptamine-2-carboxylic acid later.

Catalytic reduction of 1 : 2 : 3 : 4-tetrahydro-6-nitro-1-oxo-β-carboline gave the 6-amino-compound. Though stannous chloride reduction gave a better yield the product could not be freed from some inorganic material (low analysis for carbon) and the m. p. remained constant on repeated recrystallisations. Its infrared absorption was identical

[19] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell & Sons, London, 1953, p. 298.
[20] Ruggli and Brandt, *Helv. Chim. Acta*, 1944, **27**, 274.
[21] Plieninger, *Chem. Ber.*, 1950, **83**, 268.
[22] Burton and Stoves, *J.*, 1937, 1726.
[23] Brown, *Quart. Rev.*, 1951, **5**, 131.

with that of the product obtained from the catalytic reduction except that the former had, in addition, a very weak band at 952 cm.$^{-1}$. Both compounds gave positive diazo-coupling tests for primary amines, and on hydrolysis by aqueous-ethanolic potassium hydroxide both gave good yields of the same amino-acid (II) which, however, was not the expected



(II) (III) (IV)

5-aminotryptamine-2-carboxylic acid. This product had an infrared spectrum characteristic [24] of this series of amino-acids (see p. 4599), but in addition, a shoulder at 3571 cm.$^{-1}$ seems to indicate the presence of a hydroxyl group. It is insoluble in organic solvents but soluble in aqueous acids and alkalis, giving reddish-purple solutions (the compound itself is brownish-purple). It contains a high proportion of oxygen, compatible with its being 5-amino-(?4 : 7)-dihydroxytryptamine-2-carboxylic acid (II). Acetylation gives a product whose infrared spectrum (p. 4599) and analysis ($C_{18}H_{13}O_5N_3$) indicate that it may have structure (III). The acetyl determination indicates the presence of 3—4 acetyl groups (oxazoline rings can open on alkaline hydrolysis: [25a] presumably this hydrolysis was incomplete). The presence of phenolic hydroxyl groups in (II) is to this extent confirmed [chelated-ester band at 1715 cm.$^{-1}$ in (III)]. Also, benzoxazoles are known [25b] to give strong bands at 1724—1692 cm.$^{-1}$, where our acetate absorbs. The acetate is insoluble in alkali, so that a band at 1701 cm.$^{-1}$ is not due to a carboxyl group but is attributed to one of the carbonyl groups in the *N*-diacetyl derivative. The possibility that one of the carbonyl groups of an *N*-diacetyl compound behaves more like a normal keto-group was indicated by the fact that 2-*o*-aminobenzoyl-1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carboline gives the Schiff's base rutaecarpine.[14] This possibility is also supported by the observation that 2-acetyl-1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carboline (obtained by acetylation of 1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carboline) shows two strong bands at 1701 and 1672 cm.$^{-1}$, the latter being the normal amide I band in a monosubstituted amide. The indole-NH band for our acetate is very weak, probably because of chelation with the adjacent acetate grouping. Aerial oxidation during the alkaline hydrolysis is not entirely unexpected, since a 5-amino-indole derivative can be considered as a substituted *p*-phenylenediamine. It is possible that oxidation first leads to a quinone di-imine type of structure (IV) which is then hydrated to give the dihydroxyamine.

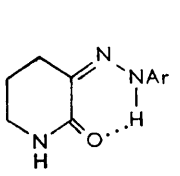
The infrared spectra of the 2 : 3-dioxopiperidine 3-phenylhydrazones were examined during this study. A feature of their spectra is the absence of two distinct bands for the amide-carbonyl and C=N groups, both bands overlapping at 1664—1667 cm.$^{-1}$. It would have been expected that hydrogen bonding between the amide-carbonyl and the hydrazone-NH groups would have lowered the carbonyl absorption in the same way as in vomicine and in *N*-acetyl-4-hydroxyproline.[26] Thus, diacetyl monophenylhydrazone (V) in which hydrogen bonding similarly lowers the ketonic absorption frequency to 1658 cm.$^{-1}$ again shows no distinct band for the C=N grouping, whereas pyruvamide phenylhydrazone (VI) (which is an open-chain analogue of 2 : 3-dioxopiperidine 3-phenylhydrazone) exhibits the C=N stretching band at 1667 cm.$^{-1}$ and the hydrogen-bonded amide I band at 1650 cm.$^{-1}$ as a slightly more intense peak. The absence of evidence for hydrogen bonding in the dioxopiperidine phenylhydrazones might be explained on the basis of a preferred *anti*-structure (VII) for these compounds. Pyruvamide phenylhydrazone (yellow needles,

[24] Bellamy, *op. cit.*, p. 202.

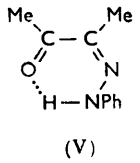
[25] (*a*) Gilman, "Organic Chemistry," Wiley & Sons Ltd., New York, 1953, Vol. IV, p. 808; Meyer and Jacobson, "Lehrbuch der Organischen Chemie," De Gruyter & Co., Berlin, 1920, Band 2, 3 Teil, p. 527; (*b*) Randall, Fuson, Fowler, and Dangl, "Infra-Red Determination of Organic Substances," Van Nostrand Co., New York, 1949, pp. 214—215.

[26] Witkop and Hull, *J. Amer. Chem. Soc.*, 1955, **77**, 6592; Ek and Witkop, *ibid.*, 1954, **76**, 5579.

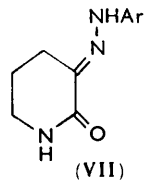
m. p. 118—119°) is interesting from two other points of view. Gastaldi [27] claims to have obtained this compound as white plates, m. p. 144° (only N analysis given), by the sodium amalgam reduction of the phenylhydrazone of *N*-hydroxypyruvamide, whereas it was prepared in this work from pyruvamide and phenylhydrazine (all the phenylhydrazones with an α-carbonyl group examined so far here are yellow). Again, its infrared spectrum in



(V)



(VI)



(VII)

Nujol mull is interesting because it shows six bands in the 3 μ region : at 3534, 3484, 3425, 3322, 3247, and 3185 cm.$^{-1}$ (shoulder). These might be explained by the slight solubility of the compound in Nujol leading to some unbonded –NH– stretching bands (the three bands at the higher wave numbers are of lower intensity than the others) owing to the Nujol *solution* of the amide, whereas the other bands are due to the mull proper.

Note added September 27th, 1956.—Since this paper was submitted Hodson and Smith [27a] have shown that the main degradation product ($C_{12}H_{16}N_2$) of folicanthine [27b] is identical with 1-methyl-3-2′-methylaminoethylindole which they prepared from 1-methyltryptamine by formylation followed by reduction with lithium aluminium hydride. They record m.p. 161—173° for the picrate (ours has m.p. 161—169°). The infrared spectrum of our free base is also identical with the one reported by Eiter and Svierak [34] for the folicanthine degradation product, thus confirming the structure deduced by Hodson and Smith for that compound.

Experimental

Infrared spectra were measured on a Grubb-Parsons S4 double-beam spectrometer.

1 : 2 : 3 : 4-*Tetrahydro-9-methyl-1-oxo-β-carboline.*—1 : 2 : 3 : 4-Tetrahydro-1-oxo-β-carboline (2 g.) in acetone (8 c.c.) and 20% aqueous sodium hydroxide (6 c.c.) was boiled under reflux and treated with dimethyl sulphate (3·2 c.c.). After vigorous stirring and boiling under reflux for 5 min., 20% aqueous sodium hydroxide (4 c.c.) was added, and the solution boiled for a further minute and poured into cold water. The oil which separated solidified (2·1 g.) and after being washed with water the solid was recrystallised from dilute methanol, giving colourless 1 : 2 : 3 : 4-*tetrahydro-9-methyl-1-oxo-β-carboline*, m. p. 157—158° (Found : C, 71·6; H, 5·9; N, 13·8; *N*-Me, 8·65. $C_{12}H_{12}ON_2$ requires C, 72·0; H, 6·0; N, 14·0; *N*-Me, 7·5%), main infrared bands (in Nujol mull) at 3268, 3175, 1647, 1605, 1534, 1453, 1311, 1292, 741 cm.$^{-1}$.

1-*Methyltryptamine-2-carboxylic Acid.*—The crude methylated product (0·75 g.) was boiled under reflux for 6 hr. with a 60% aqueous-ethanolic solution (20 c.c.) of potassium hydroxide (2·2 g.), the ethanol partially evaporated and replaced by water, and the solution filtered and brought to pH 6 with acetic acid. The *amino-acid* (0·32 g.), m. p. 243—244°, was filtered off; the mother-liquor deposited a further crop (0·22 g.) overnight. The product recrystallised from very dilute alcohol as colourless plates, m. p. 253—254° (decomp.) (Found : C, 65·8; H, 6·7; N, 12·8. $C_{12}H_{14}O_2N_2$ requires C, 66·1; H, 6·4; N, 12·8%).

1-*Methyltryptamine.*—1-Methyltryptamine-2-carboxylic acid (0·32 g.) was boiled under reflux with 10% hydrochloric acid (5 c.c.) for 1 hr. The solution was made alkaline, the base extracted with ether, and the extract dried ($MgSO_4$) and evaporated, giving an oil (0·27 g.). It was purified as the picrate, m. p. 179—180° (from alcohol containing benzene), undepressed on admixture with the picrate prepared from 1-methyltryptamine kindly supplied by Professor Gaddum (Found : C, 50·4; H, 4·3; N, 16·7. Calc. for $C_{11}H_{14}N_2,C_6H_3O_7N_3$: C, 50·6; H, 4·2; N, 17·4%). Manske [4] gives m. p. 180—181° for 1-methyltryptamine picrate.

1 : 2 : 3 : 4-*Tetrahydro-9-methyl-β-carboline.*—The *ind-N*-methylamide (1 g.) in dry *n*-butyl alcohol (30 c.c.) was stirred and boiled under reflux (oil-bath at 140°) and treated as quickly as

[27] Gastaldi, *Gazzetta*, 1924, **54**, 212.
[27a] Hodson and Smith, *Chem. and Ind.*, 1956, 740.
[27b] Eiter and Svierak, *Monatsh.*, 1952, **83**, 1453.

possible with pieces of sodium (2·5 g.). Heating and stirring were continued to complete dissolution of the sodium, the cooled solution was treated with 90% ethanol (20 c.c.) and then water (25 c.c.), and the mixture steam-distilled. The residual oil was extracted with ether, and the extract dried ($MgSO_4$). Evaporation of the solvent gave 1 : 2 : 3 : 4-tetrahydro-9-methyl-β-carboline (0·78 g.) as a brown oil, b. p. 95—120°/0·01 mm., which gave the picrate (from ethanol–acetone) as orange-red needles, m. p. 240° (decomp.) (Found: C, 52·2; H, 4·5. Calc. for $C_{12}H_{14}N_2,C_6H_3O_7N_3$: C, 52·1; H, 4·1%). Groves and Swan[6] give m. p. 242°. The base gave a purple colour in the sulphuric acid-oxidising test,[6] whereas the unmethylated base gives a blue colour.[28].

2 : 3-*Dioxopiperidine* 3-p-*Nitrophenylhydrazone*.—*p*-Nitroaniline (1·52 g.) was dissolved in hot water (30 c.c.) containing concentrated hydrochloric acid (2·5 g.), and the stirred cold suspension diazotised with sodium nitrite (0·9 g.) in water (5 c.c.). The solution was filtered and added at 5—10° to a solution of ethyl 2-oxopiperidine-3-carboxylate (1·7 g.) in water (20 c.c.) containing potassium hydroxide (0·6 g.), which had been kept at 30° overnight, and the suspension stirred at that temperature for 3½ hr. until carbon dioxide was no longer evolved. The product (2·8 g.), m. p. 213—215° (decomp.), was collected, washed with water, and recrystallised from dilute acetic acid, giving the 3-p-*nitrophenylhydrazone* as golden-yellow needles, m. p. 220—221° (decomp.) (Found: C, 53·0; H, 4·9. $C_{11}H_{12}O_3N_4$ requires C, 53·2; H, 4·9%).

1 : 2 : 3 : 4-*Tetrahydro*-6-*nitro*-1-*oxo*-β-*carboline*.—The hydrazone (1 g.) was heated to 110° with polyphosphoric acid (5 c.c.) until complete dissolution had occurred and no more heat was evolved. The solution was poured into ice-water, and the solid (0·9 g.) filtered off, dried, and recrystallised from 90% acetic acid (charcoal), giving the *carboline* as pale yellow needles, m. p. >300°, which became deeper yellow in air (Found: C, 56·8; H, 3·8; N, 18·2. $C_{11}H_9O_3N_3$ requires C, 57·15; H, 3·9; N, 18·2%).

5-*Nitrotryptamine*-2-*carboxylic Acid*.—The oxocarboline (1 g.; crude) was boiled under reflux for 24 hr. with potassium hydroxide (2·2 g.) in 60% aqueous ethanol (20 c.c.). The deep reddish-brown solution was diluted with water (40 c.c.), filtered, and made acid with glacial acetic acid. The canary-yellow precipitate of the *amino-acid* (0·8 g.) did not melt below 300°, could not be recrystallised (sodium salt separates from hot water as orange plates), and was purified by repeated precipitations from the hot alkaline solution (Found: C, 52·6; H, 4·8; N, 16·7. $C_{11}H_{11}O_4N_3$ requires C, 53·0; H, 4·4; N, 16·9%). The usual methods attempted for decarboxylation failed to give the required base.

1 : 2 : 3 : 4-*Tetrahydro*-9-*methyl*-6-*nitro*-1-*oxo*-β-*carboline*.—1 : 2 : 3 : 4-Tetrahydro-6-nitro-1-oxo-β-carboline (1 g.) in acetone (20 c.c.) and aqueous 20% potassium hydroxide (3 c.c.) was stirred and heated under reflux and treated with dimethyl sulphate (1·6 c.c.); the solid went into solution (red colour) and after a few seconds yellow needles separated. The mixture was diluted with water and filtered, and the *product* (0·82 g.), m. p. 291° (decomp.), washed with cold alcohol and recrystallised from 96% acetic acid, giving pale yellow needles, m. p. 297—298° (decomp.) (Found: C, 58·8; H, 4·9; N, 17·6; *N*-Me, 5·35. $C_{12}H_{11}O_3N_3$ requires C, 59·05; H, 4·5; N, 17·1; *N*-Me, 6·1%).

1-*Methyl*-5-*nitrotryptamine*-2-*carboxylic Acid*.—The nitro-oxocarboline (0·75 g.) was hydrolysed as described for the unmethylated product, giving the *amino-acid* (0·75 g.), which was purified by precipitation from hot alkaline solution as pale-yellow needles, m. p. 307° (decomp.; shrinking at 258°), which became orange-brown in a vacuum over phosphoric oxide at 100° (Found: C, 54·4; H, 5·1. $C_{12}H_{13}O_4N_3$ requires C, 54·75; H, 4·9%).

Decarboxylation. The amino-acid (0·5 g.) in 25% hydrochloric acid (10 c.c.) and glacial acetic acid (4 c.c.) was boiled under reflux for 10 days; most of the solid dissolved, to give a deep brown solution which was filtered, cooled, and made alkaline. The oil was extracted repeatedly with ether, dried ($MgSO_4$), and recovered. The residual oil gave a very impure picrate (from 90% ethanol on standing) which, after a number of recrystallisations from 90% ethanol, gave deep red needles of 1-*methyl*-5-*nitrotryptamine picrate*, m. p. 232—233° (Found: C, 15·8; H, 3·8. $C_{11}H_{13}O_2N_3,C_6H_3O_7N_3$ requires C, 45·5; H, 3·6%).

Formation of 6-*Amino*-1 : 2 : 3 : 4-*tetrahydro*-1-*oxo*-β-*carboline*.—(i) *Catalytically*. 1 : 2 : 3 : 4-Tetrahydro-6-nitro-1-oxo-β-carboline (1 g.) was dissolved in hot glacial acetic acid (75 c.c.) and reduced hot with hydrogen in the presence of 5% palladium–charcoal (1 g.). The filtrate was evaporated to dryness *in vacuo*, and the residue was treated with water, filtered off, and recrystallised from dilute ethanol, giving the *amine* (0·5 g.) as tiny plates, m. p. 281—282° (decomp.) after sintering at 270° (Found: C, 65·55; H, 5·4; N, 20·7. $C_{11}H_{11}ON_3$ requires C, 65·7; H, 5·5; N,

[28] Harvey, Miller, and Robson, *J.*, 1941, 153.

20·9%), main infrared bands (in Nujol) at 3425, 3236, 1675, 1650 sh., 1587, 1558, 1502 sh., 1335, 1302, 1285, 1229, 1125, 775, 722 cm.$^{-1}$.

(ii) *With stannous chloride.* The nitroamide (1 g.) in glacial acetic acid (25 c.c.) containing concentrated hydrochloric acid (2·2 c.c.; *d* 1·19) and stannous chloride (3 g.; dihydrate) was boiled under reflux for 1 hr. The cooled suspension was filtered and the solid complex decomposed with an excess of 20% aqueous sodium hydroxide. The solid (0·7 g.), m. p. 230° (decomp.), recrystallised from dilute ethanol (charcoal) as plates, m. p. 231—233° (decomp.). The carbon analysis (six determinations) was unsatisfactory, and though the m. p. was unchanged after repeated crystallisations it seems probable that it contains some inorganic impurity (Found: C, 62·6; H, 5·25; N, 21·0%).

Hydrolysis of 6-*Amino*-1 : 2 : 3 : 4-*tetrahydro*-1-*oxo*-β-*carboline.*—The amine (1 g.) was hydrolysed as usual with potassium hydroxide (2·2 g.) in 60% aqueous ethanol (20 c.c.) for 5 hr., the purple solution filtered from some insoluble material and evaporated partially, and glacial acetic acid added dropwise. The product (0·62 g.) was filtered, washed with water and alcohol, and dried. It could not be recrystallised from the usual solvents and when dissolved in dilute alkali was not precipitated on careful acidification. It was purified as much as possible by extraction with boiling water, alcohol, and benzene, and dried *in vacuo* at 100°. The 5-*amino*-(?4 : 7)-*dihydroxytryptamine*-2-*carboxylic acid*, m. p. 257—258° (decomp.), was brownish with a violet tinge (Found: C, 52·6; H, 5·5; N, 17·2; O, 20·7. $C_{11}H_{13}O_4N_3$ requires C, 52·6; H, 5·2; N, 16·7; O, 25·5%) and had infrared bands (in Nujol mull) at 3571 sh., 3484 m, 3401 w, 3195 broad, 2667 broad, 1642 (NH_3^+), 1560 s(CO), 1534, 1519 m, 1511 sh., 1493 sh., 1445, 1406, 1383, 1359, 1344, 1302, 1272, 1239, 1223, 1145, 942, 858, 810 cm.$^{-1}$ (abbreviations have the usual meanings). The amino-acid, when boiled with acetic anhydride and 3 drops of glacial acetic acid for 2 hr., gave a low yield of an acetylated *product*, m. p. 204—205°, white plates (from alcohol) (Found: C, 60·2; H, 5·2; Ac, 40·3. $C_{18}H_{19}O_5N_3$ requires C, 60·5; H, 5·3; 3 × Ac, 36·2; 4 × Ac, 48·0%), insoluble in alkalis, having infrared bands (in Nujol mull) at 3425 vw, 1724 s, 1715 s, 1701 s, 1675 m, sh., 1656 m, sh., 1592 w, broad, 1563 w, broad, 1422, 1379, 1348, 1302, 1279, 1248, 1196, 1140, 1095, 1080, 1052, 1038, 1028, 1016, 986, 976, 950, 826 m, 762 (m) cm.$^{-1}$.

2-*Acetyl*-1 : 2 : 3 : 4-*tetrahydro*-1-*oxo*-β-*carboline.*—1 : 2 : 3 : 4-Tetrahydro-1-oxo-β-carboline (0·5 g.) was boiled under reflux for 2 hr. with acetic anhydride (5 c.c.) containing glacial acetic acid (5 drops). The mixture was poured into cold water, and the solid recrystallised from alcohol, giving a nearly quantitative yield of 2-*acetyl*-1 : 2 : 3 : 4-*tetrahydro*-1-*oxo*-β-*carboline* as colourless needles, m. p. 230—231° (Found: C, 68·1; H, 5·2; Ac, 20·4. $C_{13}H_{12}O_2N_2$ requires C, 68·4; H, 5·3; Ac, 18·9%), infrared bands (in Nujol mull) at 3289, 1701, 1672, 1653 sh., 1631, 1582, 1560, 1538 sh., 1486, 1468, 1439, 1397, 1372, 1325, 1299, 1263, 1242, sh., 1235, 1209, 1203 sh., 1183 sh., 1136, 1075, 1045, 1008, 1000, 948, 930, 913, 768, 748, 728, 702, 680 cm.$^{-1}$.

Action of Heat on Tryptamine-2-carboxylic Acid.—(i) Tryptamine-2-carboxylic acid (0·5 g.) in glycerol (5 c.c.) was heated under nitrogen at 230° until gas evolution (water vapour) ceased (10 min.). Water was added to the cooled solution, and the precipitated solid was washed with water and dried, giving 1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carboline (0·25 g.), m. p. and mixed m. p. 182—183°

(ii) A similar result was obtained by fusing the acid with resorcinol at 225° and isolating the product by extracting the phenol with aqueous alkali.

2 : 3-*Dioxopiperidine* 3-p-*Chlorophenylhydrazone.*—This was prepared as in the previous cases from *p*-chloroaniline (1·3 g.) and 2-oxopiperidine-3-carboxylic acid (from 1·7 g. of the ester) at pH 4. The *phenylhydrazone* (1·98 g.) was obtained as yellow prisms, m. p. 216—217° (from ethyl alcohol), insoluble in hot water and only slightly soluble in hot alcohol, but readily soluble in hot dilute alcohol (Found: C, 55·5; H, 5·13. $C_{11}H_{12}ON_3Cl$ requires C, 55·6; H, 5·05%).

6-*Chloro*-1 : 2 : 3 : 4-*tetrahydro*-1-*oxo*-β-*carboline.*—The chlorophenylhydrazone (1 g.) on refluxing with 90% formic acid as described for the other compounds, gave the *carboline* (0·75 g.), m. p. 219—221°, which on recrystallisation from dilute acetic acid (charcoal) gave colourless needles, m. p. 224·5—225·5° (Found: C, 59·4; H, 4·2. $C_{11}H_9ON_2Cl$ requires C, 59·9; H, 4·1%). Its *picrate* (from ethanol) had m. p. 239—240° (Found: C, 45·7; H, 2·6. $C_{11}H_9ON_2Cl,C_6H_3O_7N_3$ requires C, 45·4; H, 2·7%).

5-*Chlorotryptamine*-2-*carboxylic Acid.*—The carboline (1 g.) gave the *amino-acid* (1 g.), m. p. 257—258° (decomp.), which could not be recrystallised but was purified by precipitation from alkaline solution (Found: C, 53·1; H, 5·1. $C_{11}H_{11}O_2N_2Cl,\frac{1}{2}H_2O$ requires C, 53·3; H, 5·25%).

5-Chlorotryptamine.—(i) The amino-acid was unaffected by refluxing 10% hydrochloric acid. (ii) Fusion of the amino-acid with resorcinol at 230° gave 6-chloro-1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carboline, m. p. and mixed m. p. 223—224°, which gave a picrate, m. p. and mixed m. p. 239—240°.

(iii) The amino-acid (3·25 g.) was boiled under reflux with 20% hydrochloric acid (70 c.c.) and glacial acetic acid (20 c.c.) until complete dissolution occurred (18 hr.). The cooled solution, from which the base hydrochloride separated, was made alkaline and extracted with ether, and the ether dried ($MgSO_4$) and evaporated, giving the base as a brown oil (2·12 g.), which was taken up in ether. Dry hydrogen chloride was passed through the solution and the *hydrochloride*, which separated quantitatively, recrystallised from ethanol–ether as plates, m. p. 296—297° (Found: C, 52·2; H, 5·3; N, 11·8. $C_{10}H_{11}N_2Cl,HCl$ requires C, 51·95; H, 5·2; N, 12·1%). The free base gave *5-chlorotryptamine picrate* as orange-red needles, m. p. 253° (decomp.) (from ethanol) (Found: C, 45·6; H, 3·3; N, 17·0. $C_{10}H_{11}N_2Cl,C_6H_3O_7N_3$ requires C, 45·3; H, 3·3; N, 16·5%), depressed to 215—220° on admixture with the picrate of the oxocarboline obtained under (ii).

Attempted Preparation of 6-Chloro-1 : 2 : 3 : 4-tetrahydro-β-carboline.—6-Chloro-1 : 2 : 3 : 4-tetrahydro-1-oxo-β-carboline (1 g.) in boiling *n*-butyl alcohol (25 c.c.) was stirred in an oil-bath at 140° and treated with sodium (2·5 g.). After all the sodium had dissolved, 90% ethanol (25 c.c.) and then water (25 c.c.) were added, the mixture was steam-distilled, and the residue (0·38 g.) was recrystallised from very dilute alcohol, giving 1 : 2 : 3 : 4-tetrahydro-β-carboline, m. p. 206—207° (Found: C, 76·2; H, 6·9. Calc. for $C_{11}H_{12}N_2$: C, 76·8; H, 7·0%); the picrate had m. p. 253—254° (decomp.) (Found: C, 50·9; H, 3·8. Calc. for $C_{11}H_{12}N_2,C_6H_3O_7N_3$: C, 50·9; H, 3·7%); both m. p.s were undepressed on admixture with authentic specimens.

5-Chloro-1-methyltryptamine-2-carboxylic Acid.—The chloro-oxocarboline (3·5 g.) was methylated as in the case of the nitro-compound, giving the *9-methyl* derivative (3·0 g.), m. p. 204—205·5°, which on recrystallisation from dilute ethanol had m. p. 207—207·5° (Found: C, 61·4; H, 8·2. $C_{12}H_{11}ON_2Cl$ requires C, 61·4; H, 8·3%). This (2 g.), on alkaline hydrolysis for 5 hr. as usual, gave *5-chloro-1-methyltryptamine-2-carboxylic acid* (2·1 g.) as plates (from large volume of dilute ethanol), m. p. 249—250° (decomp.) (Found: C, 56·5; H, 5·2. $C_{12}H_{13}O_2N_2Cl$ requires C, 57·0; H, 5·15%).

5-Chloro-1-methyltryptamine.—The amino-acid (0·5 g.) was boiled under reflux with 20% hydrochloric acid (10 c.c.) and acetic acid (5 c.c.) until complete dissolution had taken place (2 hr.). The solution was made alkaline and extracted with ether, and the extract dried ($MgSO_4$) and evaporated, giving the base (0·31 g.) which solidified overnight when a few drops of ether were added. The solid, m. p. 87—89°, was purified and analysed as the *picrate*, m. p. 203—204° (from 90% ethanol) (Found: C, 47·0; H, 3·5. $C_{11}H_{13}N_2Cl,C_6H_3O_7N_3$ requires C, 46·6; H, 3·7%).

7-Methyltryptamine.—Diazotised *o*-toluidine (from 2·14 g. of base) and 2-oxopiperidine-3-carboxylic acid (from 3·4 g. of ester) gave *2 : 3-dioxopiperidine 3-o-methylphenylhydrazone* (3·3 g.) as pale yellow needles, m. p. 138—139°, from dilute alcohol (Found: C, 66·2; H, 7·0. $C_{12}H_{15}ON_3$ requires C, 66·4; H, 6·9%). The phenylhydrazone (1 g.) with 90% acetic acid (5 c.c.) gave *1 : 2 : 3 : 4-tetrahydro-8-methyl-1-oxo-β-carboline* (0·72 g.) which, recrystallised from dilute acetic acid, had m. p. 195—196° (Found: C, 71·8; H, 6·0. $C_{12}H_{12}ON_2$ requires C, 72·0; H, 6·0%), and gave a brown ⟶ olive-green colour in the sulphuric acid–oxidising agent test. Hydrolysis of the amide (2·8 g.) with aqueous-alcoholic potassium hydroxide for 5 hr. gave *7-methyltryptamine-2-carboxylic acid* (2·3 g.), m. p. 248° (decomp.) (from water) (Found: C, 65·6; H, 6·5. $C_{12}H_{14}O_2N_2$ requires C, 66·1; H, 6·4%). This (0·5 g.), with boiling 10% hydrochloric acid, gave 7-methyltryptamine (0·27 g.), whose picrate (from ethanol) had m. p. 231° (decomp.) (Found: C, 50·2; H, 4·1; N, 17·2. Calc. for $C_{11}H_{14}N_2,C_6H_3O_7N_3$: C, 50·6; H, 4·2; N, 17·4%). Gaddum *et al.*[29] give m. p. 236° (decomp.) for 7-methyltryptamine picrate.

2 : 3-Dioxopiperidine 3-m-Methoxyphenylhydrazone.—*m*-Anisidine (2·5 g.) in water (30 c.c.) and concentrated hydrochloric acid (5 c.c.) was diazotised with sodium nitrite (1·4 g.) in water (10 c.c.). The solution was brought to pH 4 with saturated aqueous sodium acetate. A solution of ethyl 2-oxopiperidine-3-carboxylate (3·6 g.) in water (40 c.c.) containing potassium hydroxide (1·2 g.), which had been left at room temperature overnight, was added to the cold diazonium solution and stirring continued, the pH being kept at 3·6—4·0 all the time (in more acid medium decomposition takes place, whereas at a higher pH the phenylazo-compound separates out and decomposes very quickly). At first a small amount of tar separated and then the yellow solid product. The suspension was allowed to reach room temperature after 2 hr.,

[29] Gaddum, Hameed, Hathway, and Stephens, *Quart. J. Expt. Physiol.*, 1955, **40**, 49.

the liquid was decanted off, and the tarry solid residue boiled for a short while with a little alcohol. The orange-yellow solid was filtered from the cold mixture, washed with a little alcohol, and dried, giving the 3-m-*methoxyphenylhydrazone* (1·92 g.), m. p. 209—210° (decomp.). Recrystallisation from dilute alcohol gave orange-red crystals, m. p. 212—213° (decomp.) (Found: C, 61·5; H, 6·4. $C_{12}H_{15}O_2N_3$ requires C, 61·8; H, 6·5%).

Cyclisation of 2 : 3-*Dioxopiperidine* 3-m-*Methoxyphenylhydrazone.*—(i) *By use of* 70% *formic acid.* The hydrazone (0·5 g.) was boiled under reflux for ½ hr. with 70% formic acid (2·5 c.c.), the solution diluted with water, and the dark oil which separated partially solidified. The mother-liquor was decanted off and the residue taken up in boiling alcohol and cooled. 1 : 2 : 3 : 4-*Tetrahydro-5-methoxy-1-oxo-β-carboline* (0·06 g.), m. p. 208—210°, separated and was recrystallised from ethanol as cream-coloured needles, m. p. 212—213° (Found: C, 66·8; H, 5·2. $C_{12}H_{12}O_2N_2$ requires C, 66·65; H, 5·6%). The alcohol mother-liquor, on being partially evaporated and cooled, gave 1 : 2 : 3 : 4-tetrahydro-7-methoxy-1-oxo-β-carboline (0·10 g.), m. p. 192—193° which, on recrystallisation from dilute ethanol, gave colourless prisms, m. p. 199—200° (Found: C, 66·9; H, 5·8%). Barrett, Perkin, and Robinson [30] give m. p. 198° for this compound. A mixture of the above two carbolines melted at 180—185°.

(ii) *By use of alcoholic hydrogen chloride.* The phenylhydrazone (4·6 g.) in alcohol (100 c.c.) was saturated with dry hydrogen chloride, the solution being allowed to get hot. It was then kept at room temperature overnight (stoppered flask) and the solid (0·96 g.) collected and washed with a little cold alcohol. The alcoholic mother-liquor was evaporated to a small bulk and cooled, and the solid obtained (0·6 g.) added to the first lot and recrystallised from dilute ethanol, giving 1 : 2 : 3 : 4-tetrahydro-7-methoxy-1-oxo-β-carboline, m. p. 198—200°.

1 : 2 : 3 : 4-*Tetrahydro-7-methoxy-9-methyl-1-oxo-β-carboline.*—The methoxy-amide (0·9 g.) was methylated with dimethyl sulphate and sodium hydroxide as described above, giving the ind-N-*methyl* derivative (0·91 g.), m. p. 195—196°, which recrystallised from ethanol as clusters of rods, m. p. 202—203° (Found: C, 67·9; H, 6·2. $C_{13}H_{14}O_2N_2$ requires C, 67·8; H, 6·1%), depressed to 163—165° on admixture with the starting material.

6-*Methoxytryptamine-2-carboxylic Acid* (cf. ref. 2).—1 : 2 : 3 : 4-Tetrahydro-7-methoxy-1-oxo-β-carboline (0·35 g.) was boiled under reflux with a 60% aqueous-ethanolic solution (10 c.c.) of potassium hydroxide (1·1 g.) for 5 hr. and worked up as usual, to give the amino-acid (0·35 g.), m. p. 253—254°, which on recrystallisation from very dilute alcohol gave colourless platelets, m. p. 257—258° (decomp.) (Found: C, 61·6; H, 5·9. Calc. for $C_{12}H_{14}O_3N_2$: C, 61·5; H, 6·0%). Nishikawa, Perkin, and Robinson [2] report that this compound darkens at 220° and progressively decomposes from 220—250° without melting. Its main infrared bands (in Nujol mull) were at 3484, 3401, 3175 broad, 2500 broad, 1639, 1577, 1553, 1522, 1433, 1379, 1299, 1285, 808 cm.$^{-1}$.

6-*Methoxytryptamine.*—The amino-acid (0·2 g.) was boiled with 5% hydrochloric acid (2 c.c.) for 10 min., the solution made strongly alkaline and extracted with ether, and the dried ($MgSO_4$) ether evaporated, giving the tryptamine (0·15 g.), m. p. 144—145°. Akabori and Saito [18] give m. p. 142·5—143·5° for 6-methoxytryptamine. The *picrate* separated from ethanol containing a little dioxan as ruby-red prisms, m. p. 221° (decomp.) (Found: C, 48·8; H, 4·15. $C_{11}H_{14}ON_2,C_6H_3O_7N_3$ requires C, 48·7; H, 4·1%). From water containing a few drops of ethanol the picrate separated as violet needles, m. p. 220—221° (decomp.).

Action of Diazomethane on 1 : 2 : 3 : 4-*Tetrahydro-1-oxo-β-carboline.*—The amide (1 g.) in methyl alcohol (100 c.c.) was treated with diazomethane (5 mols.) in ether and kept at room temperature for 24 hr. Starting material (0·95 g.), m. p. 185—186°, was recovered.

1 : 2 : 3 : 4-*Tetrahydro-2 : 9-dimethyl-1-oxo-β-carboline.*—1 : 2 : 3 : 4-Tetrahydro-1-oxo-β-carboline (1·86 g.) was dissolved in boiling dry toluene (150 c.c.), the cooled solution treated with sodium hydride (0·60 g., excess), and the mixture boiled under reflux for 18 hr. Methyl iodide (6 c.c.) was added to the mixture, which was boiled for another 4 hr., filtered hot, and evaporated *in vacuo*. The residual oil was distilled, giving 1 : 2 : 3 : 4-*tetrahydro-2 : 9-dimethyl-1-oxo-β-carboline* (1·95 g.) as a pale yellow oil, b. p. 150—152°/0·04 mm., m. p. 65—66° (Found: C, 72·4; H, 6·5; *N*-Me, 16·3. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·5; *N*-Me, 14·0%), infrared bands (in Nujol mull) at 1653, 1626, 1546, 1504, 1479, 1431, 1406, 1387, 1362, 1323, 1259, 1244, 1082, 747, and 739 cm.$^{-1}$. The *picrate* (from very dilute ethanol) was orange needles, m. p. 113—113·5° (Found: C, 51·45; H, 4·0. $C_{13}H_{14}ON_2,C_6H_3O_7N_3$ requires C, 51·5; H, 3·8%). If the toluene solution of the amide was refluxed with sodium hydride (0·40 g.) for only 6 hr. before treatment with methyl iodide, evaporation of the solvent to a small volume gave first 1 : 2 : 3 : 4-tetrahydro-9-methyl-1-oxo-β-carboline (0·50 g.), m. p. and mixed m. p. 157°. The mother-liquors gave the *NN'*-dimethylamide (0·8 g.) b. p. 136—138°/0·02 mm., m. p. 65—66°.

[30] Barrett, Perkin, and Robinson, *J.*, 1929, 2942.

Hydrolysis of 1 : 2 : 3 : 4-*Tetrahydro*-2 : 9-*dimethyl*-1-*oxo*-β-*carboline*.—(i) Attempts to effect hydrolysis under alkaline conditions as usual or by boiling overnight failed to give any product and starting material was recovered. (ii) The *NN'*-dimethylamide (0·25 g.) was boiled under reflux with 15% hydrochloric acid (15 c.c.) for 24 hr., by which time all the oil had dissolved. The solution was diluted with water (10 c.c.), filtered, and made alkaline, and the oil which separated extracted with ether. The dried ($MgSO_4$) ether extract was evaporated, yielding an oil (0·19 g.), b. p. 190°/18 mm., from which a deep-red picrate was prepared. Recrystallisation from ethanol gave 1-*methyl*-3-2'-*methylaminoethylindole picrate* as deep-red needles, m. p. 168—169° (Found: C, 51·4; H, 4·7. $C_{12}H_{16}N_2,C_6H_3O_7N_3$ requires C, 51·8; H, 4·6%). The free base gives a positive Ehrlich reaction. Its infrared absorption spectrum (liquid film) shows the absence of carbonyl groups, a very weak band at 1667 cm.$^{-1}$ probably being due to an indole ring vibration.

1 : 2 : 3 : 4-*Tetrahydro*-2 : 9-*dimethyl*-β-*carboline*.—The *NN'*-dimethylamide (0·5 g.) in a Soxhlet extractor was boiled with lithium aluminium hydride (0·5 g.) in dry ether (150 c.c.) for 6 hr. The excess of hydride was decomposed with ethyl acetate, and the complex decomposed with water. The water layer was extracted with ether, and the ether layers were combined, dried ($MgSO_4$), and evaporated, giving 1 : 2 : 3 : 4-*tetrahydro*-2 : 9-*dimethyl*-β-*carboline* (0·31 g.) as an oil which solidified and recrystallised from light petroleum (b. p. 60—80°) as colourless rods, m. p. 95·5—96·5° (Found: C, 77·6; H, 7·8. $C_{13}H_{16}N_2$ requires C, 78·0; H, 8·0%). The *picrate* (from ethanol) gives yellow needles, m. p. 210° (from acetone) (Found: C, 53·4; H, 4·2. $C_{13}H_{16}N_2,C_6H_3O_7N_3$ requires C, 53·1; H, 4·4%). The infrared spectrum of the base (liquid film) has no >NH (or —OH) band, and no amide band in the 6 μ region.

Pyruvamide Phenylhydrazone.—Pyruvamide [31] and phenylhydrazine in very dilute alcohol gave the *phenylhydrazone* as yellow needles, m. p. 118—119°, from dilute ethanol (Found: C, 61·5; H, 6·4. $C_9H_{11}ON_3$ requires C, 61·0; H, 6·2%) [Gastaldi [27] gives m. p. 144° for a colourless product claimed to be pyruvamide phenylhydrazone (only N analysis given) prepared by an ambiguous route]. The infrared spectrum (in Nujol mull) had bands at 3534, 3484, 3425, 3322, 3247, 3185 sh., 1667, 1650, 1608, 1572 broad, 1546, 1504, 1471, 1404, 1385, 1311, 1299 sh., 1264, 1235, 1217, 1174, 1163, 1151, 1075, 891, 774, 746, and 694 cm.$^{-1}$.

Diacetyl monophenylhydrazone was prepared by Benary's method [32] from ethyl methyl ketone and ethyl formate, followed by reaction of the product with benzenediazonium chloride and had infrared bands (in Nujol mull) at 3279, 3145, 1658, 1608, 1570, 1550 sh., 1511, 1484, 1466, 1453, 1429, 1377 sh., 1368, 1342, 1304, 1295, 1252, 1242 sh., 1208, 1185, 1176 sh., 1166, 1159, 1152, 1116, 1000, 995, 939, 758, and 697 cm.$^{-1}$.

The author thanks Professor J. H. Gaddum for a specimen of 1-methyltryptamine. This work was carried out during the tenure of an I.C.I. Research Fellowship.

KING'S COLLEGE (UNIVERSITY OF LONDON),
STRAND, LONDON, W.C.2.

[*Received, July 11th*, 1956.]

[31] Ankers, *J. Biol. Chem.*, 1949, **176**, 1334.
[32] Benary, *Ber.*, 1926, **59**, 2198.