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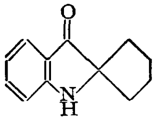
437. *The Structure of Certain Compounds derived from Tetrahydrocarbazole.*

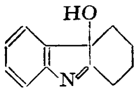
By S. G. P. Plant and Muriel L. Tomlinson.

The substance obtained from the product of bromination of certain acyltetrahydrocarbazoles (*J.*, 1931, 3324), and previously thought to be 11-hydroxy-2 : 3 : 4 : 11-tetrahydrocarbazole, has been shown to be 1-hydroxy-1 : 2 : 3 : 4-tetrahydrocarbazole, while an isomeric compound obtained from the bromination of 1 : 2 : 3 : 4-tetrahydrocarbazole itself (*J.*, 1933, 298), and regarded as 10-hydroxy-1 : 2 : 3 : 10-tetrahydrocarbazole, is 11-hydroxytetrahydrocarbazolenine. Both isomers gave, on dehydration, a substance originally thought to be 2 : 3-dihydrocarbazole, but which is, in fact, 1 : 2 : 3 : 4 : 1′ : 2′ : 3′ : 4′-octahydro-1 : 9-9′ : 1′-dicarbazolylene, as shown by dehydrogenation and determination of molecular weight.

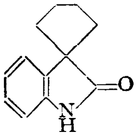
It has recently been shown (Plant and Robinson, *Nature*, 1950, **165**, 36) that it is necessary to revise the structures previously assigned to two isomeric compounds, $C_{12}H_{13}ON$, derived from tetrahydrocarbazole and regarded as *cyclo*pentane*spiro*-2-ψ-indoxyl (I) and 11-hydroxytetrahydrocarbazolenine (II) respectively. The same conclusions were reached independently by Witkop (*J. Amer. Chem. Soc.*, 1950, **72**, 614), and conclusive evidence has been adduced that the former is *cyclo*pentane*spiro*oxindole (III) and the latter authentic *cyclo*pentane*spiro*-2-ψ-indoxyl (I). It has been realised for some time that revision must be made of the structures assigned to two other isomeric compounds of the composition $C_{12}H_{13}ON$, and their derivatives, also obtained from tetrahydrocarbazole (see Plant, Robinson, and Tomlinson, *Nature*, 1950, **165**, 928), and investigations into some of the problems involved are in progress. A recent communication by Patrick and Witkop (*J. Amer. Chem. Soc.*, 1950, **72**, 633) in which reference is made to certain of these compounds makes it desirable to record some of our experimental results at this stage.



(I.)

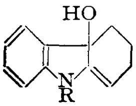


(II.)

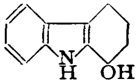


(III.)

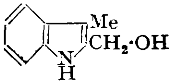
When 9-benzoyl(and 9-cinnamoyl)-tetrahydrocarbazole were treated with bromine in acetic acid, and the solutions immediately poured into water, compounds described as 11-hydroxy-9-benzoyl(or -cinnamoyl)-2 : 3 : 4 : 11-tetrahydrocarbazole (IV; R = Bz or CHPh:CH·CO) were obtained (*J.*, 1931, 3324). They were hydrolysed and subsequently benzoylated to the so-called 11-hydroxy- (IV; R = H) and 11-benzoyloxy-2 : 3 : 4 : 11-tetrahydrocarbazole. The possibility has existed that these substances are 1-hydroxy-1 : 2 : 3 : 4-tetrahydrocarbazole (V) and the corresponding acyl derivatives, and, in fact, an analogous compound obtained from 1-acetyl-2 : 3-dimethylindole was regarded as 3-methyl-2-hydroxymethylindole (VI) rather than the isomeric (VII) (*J.*, 1933, 955) (in this connection see Taylor, *Helv. Chim. Acta*, 1950, **33**, 164). The correctness of the alternative formulation has now been established by the preparation of (V), together with 1-hydroxyhexahydrocarbazole, by the reduction of 1-ketotetrahydrocarbazole with sodium and boiling alcohol. Ultra-violet light absorption spectra of the substances 1-hydroxy-9-benzoyl-, 9-benzoyl-, 1-hydroxy-, and 1-benzoyloxy-tetrahydrocarbazole (Fig. 1) in methanol confirm that they are all of the type represented by (V) and are evidence against the possibility that the first is (IV; R = Bz) and undergoes the requisite structural change on hydrolysis.



(IV.)



(V.)



(VI.)

A different compound, $C_{12}H_{13}ON$, has been obtained by the bromination of tetrahydrocarbazole under similar conditions, and this was first formulated as (VIII) (*J.*, 1933, 298). It has now been found that the dye obtained from it by diazotisation and coupling with β-naphthol has the composition $C_{22}H_{20}O_3N_2$ (Found: C, 72·9; H, 5·7; N, 7·9. Required: C, 73·3; H, 5·55;

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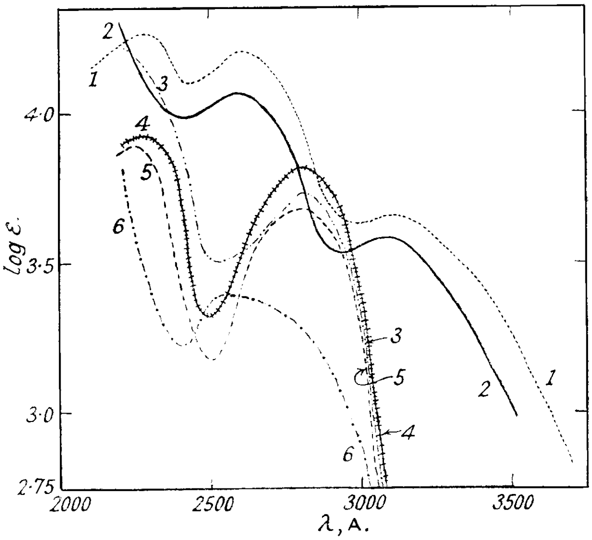
FIG. 1.

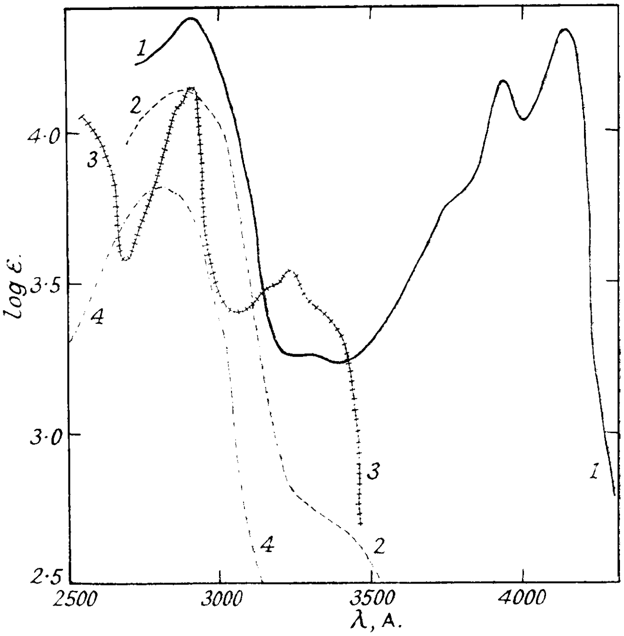
Ultra-violet absorption spectra.



1, 9-*Benzoyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*. 2, 1-*Hydroxy*-9-*benzoyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*. 3, 1-*Benzoyloxy*-1 : 2 : 3 : 4-*tetrahydrocarbazole*. 4, 1 : 2 : 3 : 4-*Tetrahydrocarbazole*. 5, 1-*Hydroxy*-1 : 2 : 3 : 4-*tetrahydrocarbazole*. 6, 11-*Hydroxytetrahydrocarbazolenine*. (*All determined in methanol solution.*)

FIG. 2.

Ultra-violet absorption spectra.



1, 1 : 9-9′ : 1′-*Dicarbazolylene*. 2, 1 : 2 : 3 : 4 : 1′ : 2′ : 3′ : 4′-*Octahydro*-1 : 9-9′ : 1′-*dicarbazolylene*. (1 *and* 2 *in dioxan solution.*) 3, *Carbazole*. 4, 1 : 2 : 3 : 4-*Tetrahydrocarbazole*. (3 *and* 4 *in methanol solution.*)

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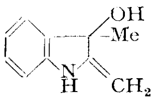
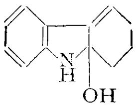
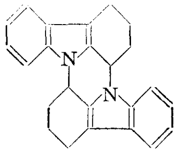
N, 7·8%), and not $C_{22}H_{18}O_2N_2$, and the substance is the authentic 11-hydroxytetrahydrocarbazolenine (II) as also stated by Patrick and Witkop (*loc. cit.*).



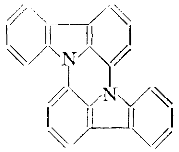
(VII.)



(VIII.)



(IX.)



(X.)

The compound obtained from both 1-hydroxytetrahydrocarbazole and 11-hydroxytetrahydrocarbazolenine by dehydration with boiling acetic anhydride and in other ways (*J.*, 1931, 3324; 1933, 298), and previously called "2 : 3-dihydrocarbazole," is evidently 1 : 2 : 3 : 4 : 1′ : 2′ : 3′ : 4′-octahydro-1 : 9-9′ : 1′-dicarbazolylene (IX). This follows not only from its molecular weight but from the fact that the product of dehydrogenation with sulphur in boiling quinoline (Tomlinson, D.Phil. Thesis, Oxford, 1933) was not carbazole, but a substance of the composition $C_{24}H_{14}N_2$, which must be 1 : 9-9′ : 1′-dicarbazolylene (X). The formulations (IX) and (X) are supported by ultra-violet absorption spectra (Fig. 2).

EXPERIMENTAL.

1-*Hydroxy*-1 : 2 : 3 : 4-*tetrahydrocarbazole* [with B. P. MOORE].—Sodium (6 g.) was added in portions to a boiling solution of 1-keto-1 : 2 : 3 : 4-tetrahydrocarbazole (2 g.) in absolute (Mg-dried) ethanol (80 c.c.) under reflux. After the mixture had been poured into water and the product extracted with ether, the extract was washed with water, dried (Na_2SO_4), and concentrated to small bulk (9 c.c.). When this was cooled below 0°, 1-*hydroxy*-1 : 2 : 3 : 4 : 10 : 11-*hexahydrocarbazole* (0·5 g., soluble in dilute mineral acids), colourless plates, m. p. 140° (from ethanol), separated (Found : C, 76·6; H, 7·9. $C_{12}H_{15}ON$ requires C, 76·2; H, 7·9%). Benzoylation with benzoyl chloride and sodium hydroxide gave a monobenzoyl compound, colourless needles, m. p. 136—137° [from light petroleum (b. p. 60—80°)], evidently 1-*hydroxy*-9-*benzoyl*-1 : 2 : 3 : 4 : 10 : 11-*hexahydrocarbazole* since it is insoluble in dilute hydrochloric acid (Found : C, 77·8; H, 6·2. $C_{19}H_{19}O_2N$ requires C, 77·8; H, 6·5%). After the above basic product had been removed, the solution was gradually diluted with light petroleum (b. p. 60—80°) in order to effect the separation of a small quantity (about 0·2 g.) of unchanged ketotetrahydrocarbazole. This was removed by filtration, the solution evaporated, the yellow gummy residue dissolved in a little warm benzene, and the mixture treated drop-wise with light petroleum (b. p. 60—80°) until crystallisation started, and cooled below 0°. 1-Hydroxy-1 : 2 : 3 : 4-tetrahydrocarbazole (0·2 g.) then separated in colourless prisms, m. p. 112—115°, identical (mixed m. p.) with a specimen of the substance obtained by Plant and Tomlinson (*J.*, 1931, 3324) from 9-benzoyltetrahydrocarbazole and previously regarded as 11-hydroxy-2 : 3 : 4 : 11-tetrahydrocarbazole. Both specimens gave, with concentrated sulphuric acid, a carmine colour which faded slowly when the solution was kept and rapidly when it was treated with nitric acid, and both gave a yellow solution in concentrated nitric acid. The use of 1-hydroxy-1 : 2 : 3 : 4-tetrahydrocarbazole in pharmacological tests is mentioned by Eddy (*J. Pharm. Exp. Ther.*, 1939, **65**, 308), and its m. p. is stated to be 118·5°, but no analysis or details of its preparation seem to have been published. In the absence of such information it is thought possible that the substance used by Eddy may have been tetrahydrocarbazole, m. p. 118°, which can be obtained by reduction of the keto-compound under certain conditions (see Mears, Oakeshott, and Plant, *J.*, 1934, 272).

1 : 2 : 3 : 4 : 1′ : 2′ : 3′ : 4′-*Octahydro*-1 : 9-9′ : 1′-*dicarbazolylene*.—(*a*) When 1-hydroxytetrahydrocarbazole (from 1-ketotetrahydrocarbazole) was boiled for 15 minutes with acetic anhydride, this compound separated in colourless prisms, m. p. 290—293°, identical (mixed m. p.) with the substance (previously regarded as 2 : 3-dihydrocarbazole) obtained by Plant and Tomlinson (*J.*, 1933, 298) from the product of bromination of tetrahydrocarbazole. This substance is not dissolved by dilute hydrochloric acid.

(*b*) A boiling solution of 1-ketotetrahydrocarbazole (3 g.) in commercial absolute alcohol (150 c.c.) was treated with sodium (9 g.), as much alcohol as possible was removed on a steam-bath under reduced pressure, and the residue was diluted with water and just acidified with acetic acid. The sticky precipitate was taken up in ether and, when the extract was dried ($CaCl_2$) and concentrated, a crystalline product (0·6 g.) separated. After this had been recrystallised from benzene, the octahydro-compound, m. p. 290—293°, was obtained. The true m. p. of the substance was determined by heating it rapidly in a capillary tube. When heated slowly it melted at 257—260° and partly resolidified as observed by Patrick and Witkop (*loc. cit.*). This phenomenon is evidently due to some dehydrogenation to the more aromatic compound described below, since the material which had been kept at 265° for some minutes dissolved in hot toluene to give the characteristic fluorescence and deposited solid, m. p. 320—325°, raised to 325—330° by admixture with the dehydrogenation product.

The molecular weight of the octahydro-compound was difficult to determine with accuracy by Rast's method owing to the small solubility of the substance in camphor, and values ranging between 274 and 344 were obtained, but these serve to establish the fact that the compound is derived from two tetrahydrocarbazole components ($C_{24}H_{22}N_2$ requires *M*, 338).

With concentrated sulphuric acid the octahydro-compound gave a faint brown colour which was changed to a deep orange-brown by a drop of nitric acid (tetrahydrocarbazole gives a colourless, changed

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to faintly yellow, solution). When the compound was melted with oxalic acid a brown colour appeared (tetrahydrocarbazole gives a red colour).

1 : 9-9′ : 1′-*Dicarbazolylene.*—A solution of the above octahydro-compound (0·6 g.) in quinoline (20 c.c.) to which sulphur (0·116 g.) had been added, was boiled for ½ hour, and poured into ice–dilute hydrochloric acid. The precipitate was dried and heated with iron filings under reduced pressure, and, when the crystalline sublimate had been extracted with hot toluene, the solution gave 1 : 9-9′ : 1′-*dicarbazolylene*, on cooling, in greenish yellow needles, m. p. 337° (Found: C, 87·6; H, 4·5. $C_{24}H_{14}N_2$ requires C, 87·3; H, 4·2%). It showed a brilliant violet fluorescence in benzene or toluene. The same substance was obtained when the octahydro-compound was dehydrogenated with chloranil in boiling xylene (compare Barclay and Campbell, *J.*, 1945, 530), or heated with palladised charcoal in hydrogen. The compound gave a green colour, becoming violet, with concentrated sulphuric acid, changed to emerald green by nitric acid (carbazole: yellow, changed to intense green). The melt with oxalic acid was yellowish-green (carbazole gives a blue melt).

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