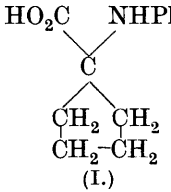
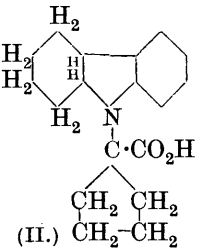
CCXLIX.—*The Condensation of Hexahydrocarbazole and of Tetrahydropentindole with* cyclo*Pentanone Cyanohydrin.*

By Sydney Glenn Preston Plant and Dorothy May Lyddon Rippon.

It has been observed by Plant and Facer (J., 1925, **127**, 2037) that the fusion of 1-anilino*cyclo*pentane-1-carboxylic acid (I) with potassium hydroxide yields carbazole, a reaction which involves the enlargement of the *cyclo*pentane ring, since 1-*p*-toluidino- and 1-*o*-toluidino-*cyclo*pentane-1-carboxylic acid yield 3-methyl- and 1-methyl-carbazole, respectively, under similar conditions (Oakeshott and Plant, J., 1926, 1210; 1927, 484). A similar process, starting with certain heterocyclic bases in the place of aniline, might be expected to give polynuclear carbazole derivatives, *e.g.*, from 1-(9′-hexahydrocarbazyl)*cyclo*pentane-1-carboxylic acid (II) a substance of the structure (III) might arise. Manjunath (*J. Indian*

Chem. Soc., 1927, **4**, 271) has prepared substances * which clearly contain the ring system present in (III). By reducing 9-nitrosohexahydrocarbazole with zinc dust and acetic acid in the presence of *cyclo*hexanone he obtained 8 : 9-(1′ : 2′-*cyclo*hexyl)tetrahydro-


(I.)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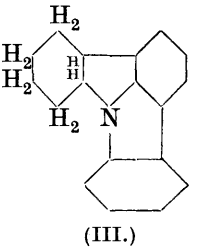
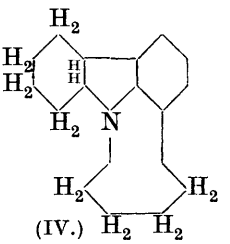

(III.)

carbazole, which, on electrolytic reduction, gave the corresponding 8 : 9-(1′ : 2′-*cyclo*hexyl)hexahydrocarbazole (IV).

Although, for reasons given below, it was not found possible during the course of the present work to synthesise a polynuclear carbazole of the type described, several interesting reactions have been brought to light. When hexahydrocarbazole (the ordinary *cis*-modification, m. p. 99°; see Gurney, Perkin, and Plant, J., 1927, 2676) was treated with *cyclo*pentanone and potassium cyanide in glacial acetic acid solution, 1-(9′-*hexahydrocarbazyl*)-1-*cyano*cyclo*pentane* (V) resulted. This nitrile, on boiling with concentrated hydrochloric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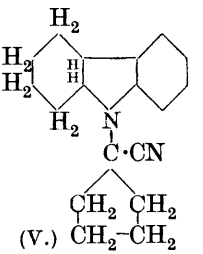
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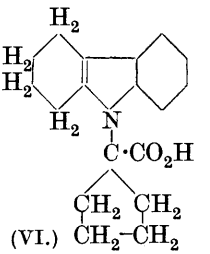

(VI.)

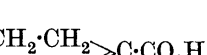
acid or with alcoholic hydrochloric acid, was hydrolysed with the formation of hexahydrocarbazole and *cyclo*pentanone, so this route to the corresponding acid could not be adopted. When a solution of the nitrile in concentrated sulphuric acid was left for two days, the corresponding *amide* was produced. Hydrolysis of this to the acid could not be carried out, the amide either remaining unchanged or breaking up with the production of hexahydrocarbazole under the conditions used. When the amide itself was heated with

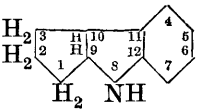
* The formulæ given for these substances in Manjunath's paper do not contain the ring system under discussion here and are obviously misprints, but there can be no doubt concerning the actual structure of the compounds described.

potassium hydroxide with a view to converting it directly into the polynuclear carbazole, it again broke up with the formation of hexahydrocarbazole.

As a possible alternative method for obtaining 1-(9′-hexahydrocarbazyl)*cyclo*pentane-1-carboxylic acid, the nitrosoamine of 1-anilino*cyclo*pentane-1-carboxylic acid (Plant and Facer, *loc. cit.*) was reduced with zinc dust and hot acetic acid in the presence of *cyclo*hexanone. This led to the formation of 1-(9′-*tetrahydrocarbazyl*)-cyclo*pentane*-1-*carboxylic acid* (VI), but reduction to the corresponding derivative of hexahydrocarbazole has not been brought about. However, the acid has some interesting reactions. When warmed with 60% aqueous sulphuric acid, when distilled, or when heated with solid potassium hydroxide, it dissociates into tetrahydrocarbazole and Δ^1-*cyclo*pentene-1-carboxylic acid (VII). It has previously been observed that 1-anilino*cyclo*pentane-1-carboxylic acid, on heating, yields the lactone of 1-1′-hydroxy*cyclo*pentane-1′-carboxylylanilino*cyclo*pentane-1-carboxylic acid (Plant and Facer, *loc. cit.*); but 1-anilino*cyclo*hexane-1-carboxylic acid behaves differently on heating alone, giving aniline and Δ^1-*cyclo*hexene-1-carboxylic acid, and ψ-indoxyl*spirocyclo*hexane results on fusion with potassium hydroxide (Betts, Muspratt, and Plant, J., 1927, 1310). 1-(9′-Tetrahydrocarbazyl)*cyclo*pentane-1-carboxylic acid, on heating, behaves like 1-anilino*cyclo*hexane-1-carboxylic acid, but lactone formation is here impossible in the absence of an unsubstituted >NH group.

The unexpected course of some of the above reactions suggested an investigation of similar reactions with *tetrahydropentindole* (VIII).

(VII.) 



(VIII.)

This base, which has been obtained by the electrolytic reduction of dihydropentindole, theoretically ought to exist in *cis*- and *trans*-modifications, analogous to the two forms of hexahydrocarbazole (see Gurney, Perkin, and Plant, *loc. cit.*); the *trans*-configuration, however, is very highly strained and its formation in appreciable quantities during the reduction of dihydropentindole is not to be expected. This point has been investigated, and the reduction product has been shown to consist essentially of a single substance, undoubtedly the *cis*-modification of tetrahydropentindole. It can be acetylated and benzoylated, and it is converted by the action of methyl iodide into 8-*methyltetrahydropentindole*, which yields a characteristic *methiodide*, m. p. 189°, that has been used for recognising tetrahydropentindole. When dissolved with *cyclo*pentanone

in glacial acetic acid and treated with potassium cyanide, tetrahydropentindole is converted into 1-(8′-*tetrahydropentindyl*)-1-*cyano*cyclo*pentane*. By a reaction analogous to that observed with the corresponding hexahydrocarbazole derivative, this nitrile is hydrolysed on boiling with concentrated hydrochloric acid with the formation of tetrahydropentindole and *cyclo*pentanone. In view of the ease with which these nitriles were hydrolysed it is interesting to point out that Kötz and Merkel (*J. pr. Chem.*, 1926, **113**, 75) observed that 1-piperidyl-1-cyano*cyclo*hexane was hydrolysed in a similar way, on boiling with aqueous-alcoholic potassium hydroxide. By allowing the solution of 1-(8′-tetrahydropentindyl)-1-cyano*cyclo*pentane in concentrated sulphuric acid to remain for two days, 1-(8′-*tetrahydropentindyl*)cyclo*pentane*-1-*carboxyamide* is produced. This amide decomposed with the formation of tetrahydropentindole when heated with solid potassium hydroxide. Many amides of this type seem to be hydrolysed to the corresponding acids only with difficulty, if at all (compare, *e.g.*, Kötz and Merkel, *loc. cit.*; Betts, Muspratt, and Plant, *loc. cit.*; Oakeshott and Plant, J., 1927, 492), and this fact, together with the alternative reactions outlined above, can account for the inability to prepare the acids from the amides described in the present work.

Experimental.

1-(9′-*Hexahydrocarbazyl*)-1-*cyano*cyclo*pentane* (V) soon began to separate when hexahydrocarbazole (21 g.), dissolved in a mixture of glacial acetic acid (210 c.c.) and *cyclo*pentanone (17·5 c.c.), was treated gradually with a solution of potassium cyanide (14 g.) in water (50 c.c.); after several hours, the mixture was diluted with water, and the product collected. It crystallised from dilute alcohol in colourless prisms, m. p. 76° (Found : N, 10·5. $C_{18}H_{22}N_2$ requires N, 10·5%).

A solution of this nitrile in an excess of concentrated hydrochloric acid was boiled under reflux for 3 hours and then distilled in steam for a short time. From the distillate, saturated with sodium chloride, ether extracted *cyclo*pentanone, b. p. 129—130°, which was identified by converting its phenylhydrazone into dihydropentindole (Perkin and Plant, J., 1923, **123**, 3242), m. p. and mixed m. p. 108°. The aqueous solution remaining after the steam distillation contained hexahydrocarbazole in good yield. The same reaction took place when the nitrile was boiled under reflux for 6 hours with alcohol saturated with hydrogen chloride.

1-(9′-*Hexahydrocarbazyl*)cyclo*pentane*-1-*carboxyamide*.—A solution of the nitrile (V) in concentrated sulphuric acid was kept for 2 days, poured on ice, and made alkaline with concentrated aqueous

ammonia. The solid product was ground with dilute aqueous ammonia to decompose any sulphate which might have been present, and then crystallised from alcohol, from which 1-(9′-*hexahydrocarbazyl*)cyclo*pentane*-1-*carboxyamide* was obtained in colourless plates, m. p. 160° (Found: N, 9·9. $C_{18}H_{24}ON_2$ requires N, 9·9%). This amide was not changed by boiling its solution in aqueous-alcoholic potassium hydroxide for 4 hours, or by heating it with 40% aqueous sulphuric acid. When its solution in concentrated hydrochloric acid was boiled under reflux for several hours, a considerable amount of hexahydrocarbazole was produced, which was removed from the solution, evaporated to small bulk and made alkaline with sodium hydroxide, by distillation in steam. When the amide was heated with powdered potassium hydroxide at 180—200°, in a copper tube fitted with a reflux air condenser, for 15 minutes, a considerable quantity of hexahydrocarbazole was produced. This was isolated by treating the cooled mixture with warm water and crystallising the precipitated solid from alcohol. The action of heat alone at 180—200° had no appreciable effect on the amide.

1-(9′-*Tetrahydrocarbazyl*)cyclo*pentane*-1-*carboxylic Acid* (VI).—The nitrosoamine of 1-anilino*cyclo*pentane-1-carboxylic acid (40 g., prepared as described by Plant and Facer, *loc. cit.*) was dissolved in a mixture of glacial acetic acid (560 c.c.) and water (240 c.c.), to which *cyclo*hexanone (56 c.c.) was added. With vigorous stirring, the mixture was warmed to 50°, and zinc dust (96 g.) was then gradually introduced, the temperature being raised slowly to 85°. The filtered solution was poured into *N*-sulphuric acid. When the solid product (yield, 25%) was crystallised from toluene, 1-(9′-*tetrahydrocarbazyl*)cyclo*pentane*-1-*carboxylic acid* separated in colourless prisms, m. p. 184° (Found: N, 5·0. $C_{18}H_{21}O_2N$ requires N, 4·9%).

When a solution of this acid (3 g.) in 60% aqueous sulphuric acid (180 c.c.) was left on the water-bath, crystals of Δ^1-*cyclo*pentene-1-carboxylic acid (m. p. and mixed m. p. 118°) gradually sublimed into the neck of the flask; dilution of the residual solution with water precipitated tetrahydrocarbazole. When a solution of 1-(9′-tetrahydrocarbazyl)*cyclo*pentane-1-carboxylic acid in cold concentrated sulphuric acid was left for several hours and then poured on ice, the acid was recovered unchanged. The acid resisted attempts to reduce it to the corresponding hexahydrocarbazole derivative by electrolytic reduction in alkaline solution, by sodium amalgam in alkaline solution, and by tin and alcoholic hydrochloric acid.

1-(9′-Tetrahydrocarbazyl)*cyclo*pentane-1-carboxylic acid was mixed with an excess of powdered potassium hydroxide and heated,

in a copper tube fitted with a reflux air condenser, at 320—340° for ½ hour. After cooling, the mixture was warmed with an excess of water. The insoluble portion, after crystallisation from aqueous alcohol, melted at 112° and was shown to be tetrahydrocarbazole by a mixed m. p. determination. The alkaline aqueous liquid, after filtering, was evaporated to a small volume, and acidified with concentrated hydrochloric acid, the mixture being kept cold. The solid which separated was crystallised from aqueous alcohol, Δ^1-*cyclo*pentene-1-carboxylic acid being obtained in colourless plates, m. p. 119° (Found : C, 64·1; H, 7·3. Calc.: C, 64·3; H, 7·1%). There is no doubt that this is identical with the Δ^1-*cyclo*pentene-1-carboxylic acid described by Haworth and Perkin (J., 1894, **65**, 101). A similar decomposition occurred on distilling 1-(9′ tetrahydrocarbazyl)*cyclo*pentane-1-carboxylic acid alone from a small distillation flask. The solid which collected in the side-tube yielded tetrahydrocarbazole (m. p. and mixed m. p. 114°) on treatment with dilute aqueous sodium hydroxide and filtration, and the alkaline filtrate, on evaporation to small bulk and acidification with concentrated hydrochloric acid, yielded Δ^1-*cyclo*pentene-1-carboxylic acid (m. p. and mixed m. p. 120°).

Tetrahydropentindole (VIII).—Dihydropentindole (5 g.) (Perkin and Plant, *loc. cit.*) was dissolved in sulphuric acid (140 c.c. of 60%) and submitted to electrolytic reduction at room temperature during 16 hours in the cathode compartment of an electrolytic cell, lead electrodes and a current of 5 amps. (0·03 amp. per sq. cm. of cathode) being used. From the solution, made alkaline with concentrated aqueous ammonia, ether extracted *tetrahydropentindole*, b. p. 152°/16 mm. (Found : C, 82·9; H, 8·3. $C_{11}H_{13}N$ requires C, 83·0; H, 8·2%). The tetrahydropentindole used in the present work was liquid, but a specimen was made to solidify and was found to melt at 21°.

A solution of tetrahydropentindole (3 g.) in hot acetic anhydride (30 c.c.) was boiled for 20 minutes, cooled, and shaken with water; the 8-*acetyltetrahydropentindole* obtained crystallised from alcohol in colourless prisms, m. p. 78° (Found : N, 6·9. $C_{13}H_{15}ON$ requires N, 7·0%). On shaking tetrahydropentindole (5 g.) with benzoyl chloride (5·5 g.) and an excess of dilute aqueous sodium hydroxide, 8-*benzoyltetrahydropentindole* separated as an oil, which gradually solidified; it crystallised from alcohol in colourless prisms, m. p. 86° (Found : N, 5·2. $C_{18}H_{17}ON$ requires N, 5·3%). When tetrahydropentindole (1·8 g.) and picric acid (2·5 g.) were mixed in hot toluene, the *picrate* separated; it crystallised from alcohol in yellow prisms, m. p. 159°.

8-*Methyltetrahydropentindole*.—An alcoholic solution of tetrahydropentindole (40 g.) and methyl iodide (45 g.) was boiled under reflux

for 24 hours, as much alcohol as possible was distilled off, and the residue was treated with an excess of dilute aqueous sodium carbonate and extracted with ether. After the extract had been dried over potassium carbonate and the solvent removed, the residual oil was boiled with an excess of acetic anhydride under reflux for an hour in order to acetylate any unchanged tetrahydropentindole. The cooled solution was shaken with an excess of water, concentrated hydrochloric acid (50 c.c.) added after 12 hours, the 8-acetyltetrahydropentindole removed by shaking twice with ether, and the aqueous solution made alkaline with sodium hydroxide and extracted with ether, which removed 8-*methyltetrahydropentindole*, b. p. 136—137°/15 mm. (Found : N, 7·8. $C_{12}H_{15}N$ requires N, 8·1%). From a solution of this (2 g.) and picric acid (2·6 g.) in hot alcohol, the *picrate* separated in yellowish-green plates, m. p. 116°, on cooling. When 8-methyltetrahydropentindole or tetrahydropentindole was warmed in alcohol with an excess of methyl iodide the *methiodide* of 8-methyltetrahydropentindole slowly separated in colourless prisms, m. p. 189° (Found : I, 40·2. $C_{13}H_{18}NI$ requires I, 40·3%).

1-(8′-*Tetrahydropentindyl*)-1-*cyano*cyclo*pentane*.—A solution of tetrahydropentindole (37 g.) and *cyclo*pentanone (25 c.c.) in glacial acetic acid was treated with a concentrated aqueous solution of potassium cyanide (27 g.). After several hours, the solution was poured into an excess of water and the oily product, which solidified when rubbed, was recrystallised from alcohol, 1-(8′-*tetrahydropentindyl*)-1-*cyano*cyclo*pentane* being obtained in colourless prisms, m. p. 51° (Found : N, 11·4. $C_{17}H_{20}N_2$ requires N, 11·1%). When this nitrile (1 g.) was mixed with picric acid (1·1 g.) in hot alcohol, and the solution was left, the *picrate* separated gradually in yellow prisms, m. p. 126°.

A solution of 1-(8′-tetrahydropentindyl)-1-cyano*cyclo*pentane in concentrated hydrochloric acid was boiled under reflux for 3 hours, and then submitted to steam distillation. From the distillate, ether extracted *cyclo*pentanone (identified by conversion into dihydropentindole as before). The acid solution, after being made alkaline with sodium hydroxide, was again submitted to steam distillation; the tetrahydropentindole isolated from the distillate by means of ether was identified by conversion into 8-methyltetrahydropentindole methiodide.

1-(8′-*Tetrahydropentindyl*)cyclo*pentane*-1-*carboxyamide*.—A solution of 1-(8′-tetrahydropentindyl)-1-cyano*cyclo*pentane in concentrated sulphuric acid was after 2 days poured on ice, and made alkaline with concentrated aqueous ammonia while being kept cool. The product, after being ground with dilute aqueous ammonia, was crystallised from alcohol, 1-(8′-*tetrahydropentindyl*)cyclo*pentane*-1-

carboxyamide separating in colourless prisms, m. p. 130° (Found : N, 10·3. $C_{17}H_{22}ON_2$ requires N, 10·4%).

A mixture of this amide with powdered potassium hydroxide was heated at 280—315° for ½ hour, and, after cooling, was treated with water and submitted to steam distillation. From the distillate, ether extracted tetrahydropentindole (identified by converting it into 8-methyltetrahydropentindole methiodide). No tetrahydropentindole could be detected when this amide was heated alone at 280—315° for ½ hour. Attempts to hydrolyse the amide to the corresponding acid by boiling its solution in concentrated hydrochloric acid or in aqueous sulphuric acid were not successful.

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