CCXXXVIII.—*Stereoisomerism in Polycyclic Systems. Part VII. The Reduction of 7 : 8 : 9 : 10-Tetrahydroheptaquinoline.*

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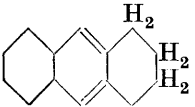
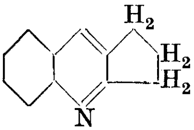
In Part V of this series (Perkin and Plant, J., 1928, 2583) it was pointed out that, since tetrahydroacridine (I) and 2 : 3-dihydro-β-quinindene (II) readily take up four atoms of hydrogen on treatment with tin and aqueous-alcoholic hydrochloric acid to give in each case a mixture of two stereoisomerides, 7 : 8 : 9 : 10-tetrahydroheptaquinoline (III) ought under similar conditions to give the two analogous forms of 5 : 7 : 8 : 9 : 10 : 11 : 14 : 15-octahydroheptaquinoline (IV). The existence of these stereoisomerides depends upon the *cis*- and *trans*-unions respectively of the two reduced ring systems. It was found, however, that the reduction of (III) in this way led to an oily base which appeared to be essentially a single substance, since its benzoylation product melted at 133—137° in the crude state and at 145° after recrystallisation.



(I.)



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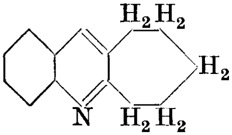
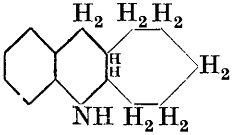
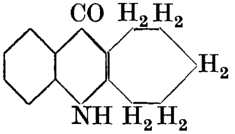


(III.)

(IV.)





(V.)

As a result of more recent work on the reduction of quinoline derivatives under various conditions, part of which will form the subject of a future communication (see also Plant and Rosser, J., 1929, 1861), it has become apparent that the isolation of both stereoisomeric modifications of (IV) is much more likely to be accomplished if the reduction of (III) is carried out in boiling absolute alcohol by the addition of sodium. It has now been found that this procedure does, in fact, lead to a mixture of the two octahydro-bases, (A), m. p. 61·5°, and (B), an oil, which can be separated by crystallisation of the mixed hydrochlorides, as described in the experimental section. The latter of these two modifications, which are present in approximately equal amounts, is identical with the form previously described (Perkin and Plant, *loc. cit.*). The modification with the higher melting point is designated (A) in accordance with the custom adopted throughout this series. The *octahydro-base* (*A*) gives a *hydrochloride* (m. p. 244—245°), a picrate (m. p. 167—168°), a *phenylcarbamyl* derivative (m. p. 144°), and a *benzoyl* derivative (m. p. 139—140°), whilst the stereoisomeride (B) gives a hydrochloride (m. p. 143—145°), a picrate (m. p. 196°), a *phenylcarbamyl* derivative (m. p. 112·5°), and a benzoyl derivative (m. p. 146·5°).

It will be noticed that the melting points of the two stereoisomeric benzoyl derivatives lie very close together, and it was observed that the depression in melting point produced by mixing the substances is surprisingly small. For this reason, it became apparent that the method employed for examining the reduction product in the previous investigation, *viz.*, the crystallisation of the benzoyl derivative, which has been successful in analogous cases, was unsatisfactory in this particular instance. It was decided, therefore, to re-investigate the product obtained by reducing (III) with tin and aqueous-alcoholic hydrochloric acid, using the method of separation now devised, and it was found that a small quantity of the octahydro-base (A) was, in reality, present, although the main product was the stereoisomeride (B) previously isolated. The tetrahydro-compound (III) has also now been reduced electrolytically and with zinc and alcoholic hydrochloric acid, and, in both cases, considerable quantities of the two stereoisomeric octahydro-bases were isolated.

Furthermore, it was previously reported (Perkin and Plant, *loc. cit.*), from an examination of the benzoyl derivative of the product, that the reduction of 11-keto-5 : 7 : 8 : 9 : 10 : 11-hexahydroheptaquinoline (V) with sodium amalgam also yielded a single form (B) of (IV), but, on re-examination by the more satisfactory process now described, it has been found that here again a small, but definite, quantity of the stereoisomeride (A) is formed at the same time.

EXPERIMENTAL.

Reduction of 7 : 8 : 9 : 10-*Tetrahydroheptaquinoline.*—(a) *With sodium and alcohol.* A solution of the base (4·8 g., prepared from suberone and isatin as described by Borsche, *Annalen*, 1910, **377**, 122) in absolute alcohol (165 c.c.) was kept boiling and treated gradually with sodium (25 g.). A further quantity of alcohol was added to effect complete solution of the sodium, and the mixture was then submitted to steam distillation during several hours. The first portion of the distillate, which consisted largely of alcohol, was treated with hydrochloric acid, the alcohol distilled off, the residue made alkaline to liberate the bases present, and then added to the main part of the steam distillate. These united distillates were then shaken with ether, the ethereal solution was dried with potassium carbonate, and the solvent removed. After the residue had been dissolved in a small quantity of dry ether and treated with dry hydrogen chloride, a colourless solid was obtained, and, on crystallisation from absolute alcohol, this yielded the *hydrochloride* of 5 : 7 : 8 : 9 : 10 : 11 : 14 : 15-octahydroheptaquinoline (A) in colourless prisms, which melted, on rapid heating, at 244—245° (Found : C, 70·5; H, 8·4. $C_{14}H_{20}NCl$ requires C, 70·7; H, 8·4%). After further quantities of this hydrochloride had been obtained by the gradual addition of dry ether to the alcoholic mother-liquor, the remaining solution was evaporated, and the residue shaken with ether and aqueous alkali. The ethereal solution was dried, the solvent removed, and the residue shaken with benzoyl chloride and dilute aqueous sodium hydroxide. After being kept for some time, the solid was collected and crystallised from alcohol, 5-benzoyl-5 : 7 : 8 : 9 : 10 : 11 : 14 : 15-octahydroheptaquinoline (B) being obtained in colourless prisms, m. p. 146·5°. The total amounts of these two substances obtained indicated that the corresponding octahydro-bases were present in approximately equal quantities in the reduction product.

(b) *Electrolytic reduction.* A solution of the base (3 g.) in sulphuric acid (100 c.c. of 20%) was reduced at 95° in an electrolytic cell, lead electrodes and a current of 6 amps. (0·07 amp. per sq. cm. of cathode) being used during 10 hours. After being made alkaline with concentrated aqueous sodium hydroxide, the mixture was steam-distilled, and the basic product so obtained was examined as described above. The results showed that the octahydro-bases (A) and (B) were present in the ratio of approximately 3 : 4.

(c) *With zinc and alcoholic hydrochloric acid.* A mixture of the base (2 g.), alcohol (50 c.c.), and zinc dust (32·5 g.) was kept boiling whilst concentrated hydrochloric acid (70 c.c.) was added in portions at intervals during 48 hours. The hot mixture was then filtered, the residue washed with alcohol, and as much alcohol as possible removed from the united filtrates by distillation. The residue was made alkaline with sodium hydroxide (70 g. in concentrated aqueous solution), and extracted with ether. After drying the extract with potassium carbonate and removing the ether, the basic product was dissolved in dry ether and examined by the method described above. The results indicated that the two octahydro-bases, (A) and (B), were present in the ratio of approximately 3 : 5.

(d) *With tin and alcoholic hydrochloric acid.* A mixture of the base (3 g.), alcohol (30 c.c.), concentrated hydrochloric acid (30 c.c.), and granulated tin (30 g.) was boiled for 20 hours, a further quantity

(10 c.c.) of hydrochloric acid being added after 5 hours, and the subsequent procedure was then similar to that adopted when zinc was used. The octahydro-bases, (A) and (B), were found to be present in the ratio of approximately 1 : 6.

5 : 7 : 8 : 9 : 10 : 11 : 14 : 15-*Octahydroheptaquinoline* (*A*).—The hydrochloride (A) was shaken with aqueous sodium hydroxide, and the product extracted with ether. After the extract had been dried with potassium carbonate and the ether removed, the residue was crystallised from petroleum (b. p. 60—80°), 5 : 7 : 8 : 9 : 10 : 11 : 14 : 15-*octahydroheptaquinoline* (*A*) being obtained in colourless prisms, m. p. 61·5° (Found : C, 83·5; H, 9·5. $C_{14}H_{19}N$ requires C, 83·6; H, 9·4%). The picrate of this base separated from alcohol in yellow prisms, m. p. 167—168°; a mixture with the picrate (m. p. 196°) of the stereoisomeric base (B) melted at 145—147°.

A solution of the base in benzene was treated with a small excess of phenyl *iso*cyanate and boiled for ten minutes. After the addition of a little water, the whole was boiled and shaken until most of the benzene had evaporated, the residue was extracted with ether, and the ethereal solution dried with sodium sulphate. After the solution had been evaporated, carbanilide was isolated from the residue by crystallisation from benzene. The benzene mother-liquor was then evaporated, and the product was crystallised from alcohol, whereby 5-*phenylcarbamyl*-5 : 7 : 8 : 9 : 10 : 11 : 14 : 15-*octahydroheptaquinoline* (*A*) was obtained in colourless prisms, m. p. 144° (Found : N, 9·2. $C_{21}H_{24}ON_2$ requires N, 8·8%).

When the base was shaken with benzoyl chloride and aqueous sodium hydroxide, and the resulting product crystallised from alcohol, 5-*benzoyl*-5 : 7 : 8 : 9 : 10 : 11 : 14 : 15-*octahydroheptaquinoline* (*A*) was isolated in colourless plates, m. p. 139—140° (Found : C, 82·6; H, 7·7. $C_{21}H_{23}ON$ requires C, 82·6; H, 7·5%). The m. p. of a mixture with the 5-benzoyl derivative of the stereoisomeric base (B) was also 139—140°.

5 : 7 : 8 : 9 : 10 : 11 : 14 : 15-*Octahydroheptaquinoline* (*B*).—This base was isolated as a liquid from its benzoyl derivative by the method of Perkin and Plant (*loc. cit.*). Its hydrochloride separated when dry hydrogen chloride was passed into a solution of the base in dry ether, and, after recrystallisation from ether, it was obtained in colourless prisms, m. p. 143—145°. The 5-*phenylcarbamyl* derivative, prepared by the process described for its stereoisomeride, separated from alcohol in colourless prisms, m. p. 112·5° (Found : N, 9·2. $C_{21}H_{24}ON_2$ requires N, 8·8%).

Reduction of 11-*Keto*-5 : 7 : 8 : 9 : 10 : 11-*hexahydroheptaquinoline*.—A solution of this keto-compound (4 g., prepared as described by Perkin and Plant, *loc. cit.*) in boiling alcohol (200 c.c.), to which a little sodium bicarbonate had been added, was treated gradually at 80° with sodium amalgam (300 g. of 4%), the whole being vigorously stirred and carbon dioxide being passed continuously. After 8 hours, the mixture was filtered, the solid was washed with hot alcohol, and the united filtrates were submitted to steam distillation and subsequent examination as described for the reduction of the 7 : 8 : 9 : 10-tetrahydro-compound with sodium and alcohol. A small quantity (0·2 g.) of the hydrochloride (A) (m. p. 244—245°) was first isolated and then the benzoyl compound (B) (m. p. 144°) was obtained. The identity of the latter was confirmed by hydrolysis and subsequent conversion of the base into its 5-phenylcarbamyl derivative (m. p. 112·5°).

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