# CCLVII.—*Stereoisomerism in Polycyclic Systems. Part VIII.*

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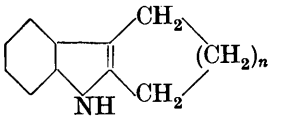
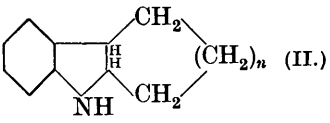
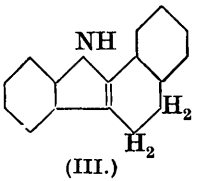
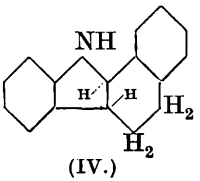
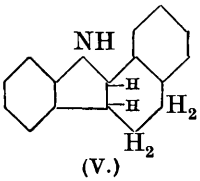
IN Part V (J., 1928, 2583) it was shown that the reduction of 2 : 3 : 4 : 5-tetrahydroheptindole (I; $n = 3$) with tin and alcoholic hydrochloric acid gives essentially one form (m. p. 77°) of 2 : 3 : 4 : 5 : 11 : 12-hexahydroheptindole (II; $n = 3$) (two forms are theoretically possible from the *cis*- and *trans*-unions respectively of the two reduced ring systems). Owing to the fact that the *trans*-configuration is the more highly strained, the form which was isolated was presumed to be the *cis*-compound. By reducing a much larger quantity (62 g.) of the indole it has now been possible to isolate a small amount (1 g.) of a second form (m. p. 92°) of the *hexahydro-base*, which undoubtedly has the *trans*-configuration.

(I.)   (II.)

It then became of interest to extend these investigations to a study of the reduction of 5 : 6-dihydro-αβ-naphthacarbazole (III). Theoretical considerations indicate that the *trans*-modification (IV)

 (III.)  (IV.)  (V.)

of 5 : 6 : 12 : 13-tetrahydro-αβ-naphthacarbazole is again much more highly strained than the corresponding *cis*-form (V). It has been

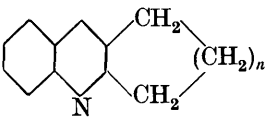
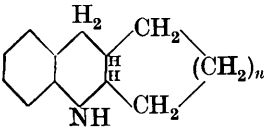
found that the action of tin and alcoholic hydrochloric acid on the indole (III) leads to a mixture of the two forms of the *tetrahydro-base*, and that these can be separated by the fractional crystallisation of the corresponding *acetyl* derivatives. One modification, undoubtedly the *cis*-, constitutes almost the entire product, and only a relatively small quantity of the *trans*-base was obtained.

During this series of investigations the reduction of three members of the polycyclic indole type, *viz.*, tetrahydrocarbazole (I; $n = 2$) and the two cases now under consideration, has been studied. Since the *trans*-form of the reduced base in every instance is by far the more highly strained, there can be no doubt that the modification which greatly preponderates in the reduction product has the *cis*-configuration. It is well known that in cases of simple geometrical isomerism associated with a double linkage or a single reduced ring system, the *trans*-modification melts, as a general rule, at a higher temperature than the corresponding *cis*-form, and it is interesting to consider whether this generalisation can be extended to the more complex fused ring systems now under investigation. Table I indicates quite definitely that it does, in fact, apply, so far without exception, not only to the reduced indoles, but to their simple derivatives.

TABLE I.

| | M. p. of *trans*-. | M. p. of *cis*-. |
|---|---|---|
| Hexahydrocarbazole (II; $n = 2$) | 127° | 99° |
| 9-Acetylhexahydrocarbazole | 113 | 98 |
| 9-Benzoylhexahydrocarbazole | 133 | 106 |
| Picrate of hexahydrocarbazole | 179 | 166 |
| Hexahydroheptindole (II; $n = 3$) | 92 | 77 |
| Picrate of hexahydroheptindole | 191 | 176 |
| *Tetrahydro-aβ-naphthacarbazole* (IV and V) | 102 | 48 |
| 11-*Acetyltetrahydro-aβ-naphthacarbazole* | 140 | 118 |
| 11-*Benzoyltetrahydro-aβ-naphthacarbazole* | 151 | 135 |
| 11-*Nitrosotetrahydro-aβ-naphthacarbazole* | 87 | 83 |

During the reduction of polycyclic quinoline derivatives of the type (VI), in which the strain in the *trans*-configuration of the corresponding tetrahydro-base (VII) is not greatly different from that in the *cis*-, relatively considerable quantities of both forms of

(VI.)   (VII.)

the product have been isolated. It is impossible in such cases to say from strain considerations which of the two products has the *cis*- and which the *trans*-configuration, and in this series of communic-

ations the higher-melting form has been called (A), and the lower-melting (B). A study of Table II shows that, with very few exceptions, the derivatives of the (A) form of a given compound also melt at a higher temperature than the corresponding derivatives of the (B) form. It thus appears probable that the above generalisation applies to the reduced polycyclic quinolines, and that the forms previously designated by (A) have the *trans*-configuration.

TABLE II.

| | M. p. of (A). | M. p. of (B). |
|---|---|---|
| Hexahydro-β-quinindene (VII; $n = 1$) | 67° | Liquid |
| 5-Acetylhexahydro-β-quinindene | 102 | 87° |
| 5-Benzoylhexahydro-β-quinindene | 174 | 161 |
| Picrate of hexahydro-β-quinindene | 193 | 158 |
| Octahydroacridine (VII; $n = 2$) | 82 | 72 |
| 10-Acetyloctahydroacridine | 86 | 136 |
| 10-*Benzoyloctahydroacridine* | 185 | 86 |
| 10-*Nitroso-octahydroacridine* | 125 | 95 |
| Picrate of octahydroacridine | 195 | 175 |
| Octahydroheptaquinoline (VII; $n = 3$) | 61 | Liquid |
| Hydrochloride of octahydroheptaquinoline | 245 | 145 |
| 5-Phenylcarbamyloctahydroheptaquinoline | 144 | 112 |
| 5-Benzoyloctahydroheptaquinoline | 140 | 146 |
| Picrate of octahydroheptaquinoline | 168 | 196 |

This view is confirmed when it is considered how far this generalisation applies to other cases of stereoisomerism dependent upon the *cis*- and *trans*-unions of two fused ring systems, and in Table III the m. p.'s of the best known examples, in which the configurations of the various forms have been established by their method of preparation or by their degradative reactions, have been collected.

TABLE III.

| | M. p. of *trans*-. | M. p. of *cis*-. |
|---|---|---|
| α-Decalone | 33° | 2° |
| β-Decalone | 6 | −14 |
| Hexahydro-β-hydrindone | −12 | 10 |
| Hexahydrohomophthalic anhydride | 83 | 59 |
| Anhydride of *cyclo*hexane-1 : 2-dicarboxylic acid | 144 | 32 |

It will be seen that, in general, a given *trans*-modification melts at a higher temperature than its *cis*-isomeride, although there is apparently one notable exception. Hückel and Friedrich (*Annalen*, 1927, **451**, 132) state that *cis*-hexahydro-β-hydrindone melts at + 10°, whilst the m. p. of the *trans*-form is − 12°. It is important to note, however, that the semicarbazone of the former melts at 215—216° and the oxime at 80°, whilst the m. p.'s of the analogous derivatives of the *trans*-modification are respectively 243° and 161°.

It is apparent, therefore, that this generalisation can be used with reasonable safety for the allocation of the configurations of reduced polycyclic types, especially when the m. p.'s of some simple derivatives are also taken into consideration.

## EXPERIMENTAL.

trans-2 : 3 : 4 : 5 : 11 : 12-*Hexahydroheptindole.*—A mixture of 2 : 3 : 4 : 5-tetrahydroheptindole (62 g., prepared as described by Perkin and Plant, J., 1928, 2586), alcohol (200 c.c.), concentrated hydrochloric acid (200 c.c.), and granulated tin (200 g.) was boiled for 5 hours and then filtered. The tin residues were washed with hot alcohol, and as much alcohol as possible was removed from the united filtrates by heating on the steam-bath. The solution was then made alkaline with sodium hydroxide (200 g. in concentrated aqueous solution), and, after being cooled, the product was collected by filtration through asbestos. Both the filtrate and the solid were twice extracted with ether, and the united ethereal solutions were dried with potassium carbonate. After the solvent had been removed, the base (55 g.) solidified, and, on being crystallised from alcohol, it yielded *cis*-2 : 3 : 4 : 5 : 11 : 12-hexahydroheptindole (30 g., m. p. 77°) in a pure condition. When the mother-liquor had been concentrated, a further quantity (5·5 g., m. p. 69—70°) of the *cis*-base was obtained almost pure. The alcoholic filtrate was then completely evaporated, the residue was dissolved in ether and extracted with dilute sulphuric acid. The ethereal solution, after being dried and evaporated, gave no appreciable residue, so the reduction of the tetrahydroheptindole had been completed. After the aqueous sulphuric acid solution had been made alkaline with ammonia, the base was extracted with ether, the solvent removed, and the base recrystallised from a small amount of alcohol. A further quantity (2 g.) of rather impure *cis*-base (m. p. 59—66°) was obtained. When the mother-liquor had been completely evaporated, the residue was dissolved in benzene and shaken with dilute aqueous sodium hydroxide and benzoyl chloride (20 g.). After an hour, the benzene layer was dried with calcium chloride, and then evaporated. The residual oil was crystallised from alcohol, and practically pure 10-benzoyl-*cis*-2 : 3 : 4 : 5 : 11 : 12-hexahydroheptindole (2 g., m. p. 112—114°) separated. The mother-liquor was then boiled with charcoal, filtered, and evaporated, and, when the residue was again crystallised from a little alcohol, a further quantity (2·5 g., m. p. 106—109°) of the almost pure *cis*-benzoyl derivative was obtained. The alcoholic filtrate was treated with potassium hydroxide (10 g. in concentrated aqueous solution); the mixture was boiled under reflux for $5\frac{1}{2}$ hours, and then shaken with ether and water. The

ethereal layer was extracted with dilute sulphuric acid, and then, after being dried and evaporated, it yielded only a small quantity (1 g.) of a thick brown oil. The aqueous sulphuric acid solution was made alkaline with ammonia and the base was collected in ether. When the extract had been dried and evaporated, the residual oil was distilled under reduced pressure, and, after being twice recrystallised from light petroleum, trans-2 : 3 : 4 : 5 : 11 : 12-*hexahydroheptindole* (1 g.) was then obtained in colourless silky needles, m. p. 92° (Found : C, 83·4; H, 8·9. $C_{13}H_{17}N$ requires C, 83·4; H, 9·1%). A mixture with the *cis*-modification was completely liquid at 64°.

The picrate of the *trans*-base separated from alcohol in small yellow plates, m. p. 190—191° (decomp.).

*Reduction of* 5 : 6-*Dihydro*-αβ-*naphthacarbazole.*—A mixture of 5 : 6-dihydro-αβ-naphthacarbazole (50 g., prepared from the phenylhydrazone of 1-keto-1 : 2 : 3 : 4-tetrahydronaphthalene as described by Bryant and Plant, this vol., p. 103), alcohol (500 c.c.), and granulated tin (350 g.) was boiled under reflux for 20 hours, whilst concentrated hydrochloric acid (800 c.c.) was added in portions from time to time. The whole was filtered, the tin residues washed with boiling alcohol, and the alcohol removed from the united filtrates by distillation in steam. After the mixture had been made alkaline by the addition of sodium hydroxide (800 g. in concentrated aqueous solution), the product was extracted with ether, and the ethereal solution dried with potassium carbonate. The solvent was then removed, and the residual oil was distilled under reduced pressure. Almost the entire product distilled at 215—220°/14 mm. as a nearly colourless oil (38 g.). Since a test portion, on treatment with dilute sulphuric acid, was found to contain a very small quantity of non-basic, insoluble material, the whole was dissolved in ether and extracted with dilute sulphuric acid. The basic product was recovered from the aqueous solution by making it alkaline and extracting it with ether. It was then boiled in acetic anhydride solution for ½ hour, and the whole was well shaken with much water and left for 12 hours. The solid product was extracted with ether, and the ethereal solution shaken with aqueous sodium carbonate, dried, and evaporated. When the residue was crystallised from methyl alcohol, 11-*acetyl*-cis-5 : 6 : 12 : 13-*tetrahydro*-αβ-*naphthacarbazole* (27 g.) separated in colourless needles, m. p. 118° (Found : C, 82·1; H, 6·6. $C_{18}H_{17}ON$ requires C, 82·1; H, 6·5%). The mother-liquor, on being concentrated, yielded a solid (9 g.) which melted at 110—115°, but its m. p. was depressed by admixture with the acetyl compound described above. When this product was recrystallised from alcohol, a substance (2 g.), m. p. 134—139°, was obtained, and, on further recrystallisation from glacial acetic acid,

11 - *acetyl* - trans- 5 : 6 : 12 : 13 - *tetrahydro*-αβ-*naphthacarbazole* was isolated pure in colourless prisms, m. p. 140° (Found : C, 82·0; H, 6·2%). The alcoholic and methyl-alcoholic mother-liquors from the separation of the above products were united and evaporated. The residual syrup was treated with boiling aqueous-alcoholic potassium hydroxide for 6 hours, the alcohol distilled off, and the remainder shaken with ether and water. The ethereal layer was extracted with dilute sulphuric acid, and, on subsequent evaporation, it yielded a small quantity of a thick, dark brown oil. The aqueous sulphuric acid solution was made alkaline with ammonia, and, after the basic material had been extracted with ether and the extract evaporated, the residue was acetylated, as before, by boiling its solution in acetic anhydride for ½ hour. An investigation of the product by the method used for the original mixture yielded a further quantity (8·5 g.) of the pure *cis*-acetyl compound, but no additional amount of the *trans*-isomeride was obtained.

cis-5 : 6 : 12 : 13-*Tetrahydro*-αβ-*naphthacarbazole*.—The *cis*-acetyl compound, the m. p. of which was unchanged by further recrystallisation, was hydrolysed by boiling its solution in aqueous-alcoholic potassium hydroxide for 6 hours. The alcohol was distilled off, and, after the addition of water, the base was extracted with ether. After the ethereal solution had been dried with potassium carbonate and evaporated, the residual oil was crystallised from light petroleum, and cis-5 : 6 : 12 : 13-*tetrahydro*-αβ-*naphthacarbazole* was isolated in colourless prisms, m. p. 47—48° (Found : C, 86·9; H, 6·9. $C_{16}H_{15}N$ requires C, 86·9; H, 6·8%). Its picrate separated from toluene in red prisms, m. p. 158° (decomp.).

A solution of the *cis*-base (2·2 g.) in benzene was shaken for 5 minutes with dilute aqueous sodium hydroxide and benzoyl chloride (1·5 c.c.). The benzene solution was washed with water, dried with calcium chloride, and evaporated. When the residue was crystallised from methyl alcohol, 11-*benzoyl*-cis-5 : 6 : 12 : 13-*tetrahydro*-αβ-*naphthacarbazole* was obtained in colourless prisms, melting at 135° to a cloudy liquid which became clear at 142° (Found : C, 85·0; H, 6·0. $C_{23}H_{19}ON$ requires C, 84·9; H, 5·8%).

When a solution of the *cis*-base (1·5 g.) in iced dilute sulphuric acid was treated with an aqueous solution of sodium nitrite (0·5 g.), 11-*nitroso*-cis-5 : 6 : 12 : 13-*tetrahydro*-αβ-*naphthacarbazole* separated. It crystallised from alcohol in yellow needles, m. p. 83° (Found : N, 11·2. $C_{16}H_{14}ON_2$ requires N, 11·2%).

trans-5 : 6 : 12 : 13-*Tetrahydro*-αβ-*naphthacarbazole*.—The *trans*-acetyl compound described above was hydrolysed by a process similar to that used for the *cis*-isomeride, and, after the product had been crystallised from methyl alcohol, trans-5 : 6 : 12 : 13-*tetra*-

*hydro-αβ-naphthacarbazole* was obtained in colourless needles, m. p. 102° (Found : C, 87·1 ; H, 7·0%).

11-*Benzoyl*-trans-5 : 6 : 12 : 13-*tetrahydro-αβ-naphthacarbazole*, prepared from the *trans*-base by a process analogous to that used for the *cis*-isomeride, separated from alcohol in colourless needles, m. p. 150—151° (Found : N, 4·5. $C_{23}H_{19}ON$ requires N, 4·3%). When admixed with the *cis*-benzoyl compound, it melted at 112—117°.

11-*Nitroso*-trans-5 : 6 : 12 : 13-*tetrahydro-αβ-naphthacarbazole*, prepared like the corresponding *cis*-compound, was obtained from alcohol in yellow prisms, m. p. 87° (Found : N, 11·4%). A mixture with the *cis*-isomeride melted at 53—58°.

*Derivatives of the Octahydroacridines.*—The two stereoisomeric octahydroacridines (A) and (B), were prepared and separated by the method described in Part V (J., 1928, 2589). A solution of the base (A) in a mixture of equal volumes of alcohol and dilute hydrochloric acid was treated, whilst cold, with aqueous sodium nitrite. After the product had been crystallised from alcohol, 10-*nitroso-octahydroacridine* (A) was obtained in yellow needles, m. p. 125° (Found : N, 13·0. $C_{13}H_{16}ON_2$ requires N, 13·0%). 10-*Nitroso-octahydroacridine* (B), obtained by a similar process from a solution of the base (B) in dilute hydrochloric acid, separated from alcohol in pale yellow plates, m. p. 95° (Found : N, 13·1%).

A solution of the base (A) in benzene was shaken with benzoyl chloride and dilute aqueous sodium hydroxide, washed with water and dried. After the solvent had been distilled off, the residual solid was crystallised from alcohol, and 10-*benzoyloctahydroacridine* (A) was obtained in colourless plates, m. p. 185° (Found : N, 4·9. $C_{20}H_{21}ON$ requires N, 4·8%). 10-*Benzoyloctahydroacridine* (B), obtained by an analogous procedure, separated from light petroleum in colourless prisms, m. p. 86° (Found : N, 5·0%).

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