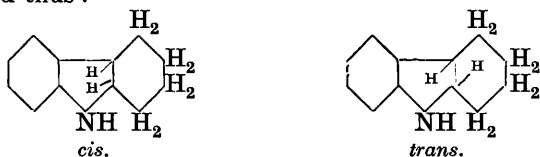


CCCLV.—A New Stereoisomeride (trans-) of Hexahydrocarbazole.

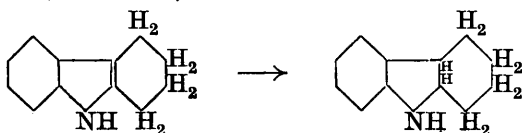
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DURING the course of experiments on octahydroacridine, Perkin and Sedgwick (*J.*, 1924, **125**, 2437) showed that this substance exists in two stereoisomeric, externally compensated modifications, namely (A), m. p. 82°, and (B), m. p. 72°, and these they subsequently resolved (*J.*, 1926, 438) each into its optically active components. In the earlier paper, it was pointed out that hexahydrocarbazole also should exist in two analogous stereoisomeric forms, which may be represented thus :



and it was proposed to investigate this point.

Hitherto only one form of hexahydrocarbazole (m. p. 99°) has been described. Although this substance has been obtained by the reduction of carbazole under various conditions (Graebe and Glaser, *Ber.*, 1872, **5**, 14; *Annalen*, 1872, **163**, 352; Schmidt and Sigwart, *Ber.*, 1912, **45**, 1784), the only practicable method for preparing relatively large quantities is by the hydrogenation of the double bond in tetrahydrocarbazole (Borsche, Witte, and Bothe, *Annalen*, 1908, **359**, 70; Carrasco, *Gazzetta*, 1908, **38**, ii, 303; Perkin and Plant, *J.*, 1924, **125**, 1512).



By reducing a large quantity (900 g.) of tetrahydrocarbazole with tin and hydrochloric acid we have now succeeded in isolating a small amount (about 12 g.) of the second isomeride of hexahydrocarbazole, and we find that this melts at 127°. Its identity has been confirmed by making the *picrate* and *acetyl* and *benzoyl* derivatives, and comparing these with the corresponding derivatives of the ordinary form. Both modifications of hexahydrocarbazole have been shown to be unimolecular, they distil unchanged at the ordinary pressure at approximately the same temperature, and are both exceptionally volatile in steam.

The existence of two stereoisomerides of hexahydrocarbazole can be predicted from the Sachse-Mohr theory of multiplanar rings and forms an interesting addition to the cases of this kind which have been already described. This type of stereoisomerism has been recently well established by several investigators in the decahydro-naphthalene series, and in a few other dicyclic systems composed of two six-membered rings (see, *e.g.*, Windaus, Hückel, and Revere, *Ber.*, 1923, 56, 91; Perkin and Sedgwick, *loc. cit.*; Helfer, *Helv. Chim. Acta*, 1926, 9, 814; Hückel and Stepf, *Annalen*, 1927, 453, 163). In all these cases, both the *cis*- and the *trans*-modifications can be regarded as strainless. The points of particular interest involved in the case of hexahydrocarbazole are (1) that the stereoisomerism is a feature of a dicyclic system composed of one six-membered carbon ring and one five-membered ring containing nitrogen, and (2) that both isomerides are produced together from the same substance in the same reaction. It is quite apparent that in this system there is far more strain in the *trans*-structure than in the *cis*-, a fact which is easily demonstrated with the aid of models. It is to be expected, therefore, that in the formation of such a dicyclic system by the hydrogenation of the double bond common to both rings the *cis*-modification will be produced to a much greater extent than the *trans*-modification, and this is exactly what is observed in the case of the hexahydrocarbazoles. There can be little doubt that the modification, m. p. 99°, which constitutes almost the entire product, is the *cis*-, and that the new substance, present to the extent of 1—2%, is the corresponding *trans*-form.

Hückel and Friedrich (*Annalen*, 1926, 451, 132) have isolated the *cis*- and *trans*-modifications of the hexahydro- β -hydrindones and the three hexahydro- β -hydrindols, which contain dicyclic carbon systems composed of one six-membered and one five-membered ring, but each of these isomerides was obtained synthetically by independent reactions starting with the *cis*- and *trans*-forms of ethyl cyclohexane-1 : 2-diacetate, respectively. These authors also point

out that the *trans*-configuration in these systems is marked by considerable strain. The anhydrides of *cis*- and *trans*-cyclohexane-1:2-dicarboxylic acid (Windaus and Hüchel, *Nachr. Ges. Wiss. Göttingen, Math.-physik. Klasse*, 1920, **11**, ii, 181) also may be considered as examples of the type of dicyclic system which is being discussed in this communication. We are engaged in the attempt to resolve the *cis*- and *trans*-modifications of hexahydrocarbazole into their active components.

EXPERIMENTAL.

A mixture of tetrahydrocarbazole (900 g.), alcohol (1800 c.c.), concentrated hydrochloric acid (1800 c.c.), and granulated tin (1800 g.) (compare Borsche, Witte, and Bothe, *loc. cit.*) was heated on the steam-bath for 5 hours, as much alcohol as possible was then distilled off and the residue was poured into beakers and allowed to cool. The product partly solidified to a crystalline mass, which was pulverised, and the whole was then made strongly alkaline by the addition of concentrated aqueous sodium hydroxide. The solid was collected on asbestos, pressed as dry as possible, and then extracted in portions twice with ether. The solid remaining was ground to a paste with more aqueous sodium hydroxide, collected, and again extracted twice with ether. After removal of the ether by distillation, the crude reduction product was crystallised from alcohol and a large quantity of *cis*-hexahydrocarbazole (m. p. 99°) was obtained. By concentrating the mother-liquor three times, further quantities of *cis*-hexahydrocarbazole were obtained. The alcohol was then removed as completely as possible on the steam-bath from the remaining mother-liquor, the residual product dissolved in 60% sulphuric acid, and the solution poured into much water. The small quantity (38 g.) of unchanged tetrahydrocarbazole thus precipitated was removed, and the aqueous solution made alkaline by the addition of concentrated ammonia, which precipitated the crude mixture of the hexahydrocarbazoles as a colourless solid. The product was made into a paste with water, added to an excess of dilute aqueous sodium hydroxide, and shaken with an equal weight (130 g.) of benzoyl chloride. After a few hours, the solid product was collected and crystallised from alcohol; a considerable amount of practically pure 9-benzoyl-*cis*-hexahydrocarbazole then separated. After filtration, the alcoholic mother-liquor was added to an excess of aqueous-alcoholic potassium hydroxide, the mixture boiled under reflux for 3 hours, as much alcohol as possible distilled off, and the residual mixture diluted with water. The sticky product was washed by decantation and crystallised from alcohol; almost pure *trans*-hexahydrocarbazole then separated.

On recrystallisation from alcohol, it was obtained in colourless needles (about 12 g.), m. p. 127° (Found : C, 83.2; H, 8.7; N, 8.1. $C_{12}H_{15}N$ requires C, 83.2; H, 8.7; N, 8.1%). Molecular-weight determinations by Rast's method (*Ber.*, 1922, 55, 1051) gave for *trans*-hexahydrocarbazole a value of 170 and for the *cis*-form 163, theory requiring 173. *trans*-Hexahydrocarbazole, like the *cis*-modification, is readily soluble in dilute hydrochloric acid and is precipitated on addition of ammonia. Both modifications distilled unchanged : *trans*-, b. p. 286°/769 mm.; *cis*-, b. p. 280°/769 mm.

trans-Hexahydrocarbazole (0.5 g.) and picric acid (0.65 g.) were mixed in hot alcohol; the *picrate* separated, on cooling, in yellow needles, m. p. 179° (Found : N, 13.9. $C_{18}H_{18}O_7N_4$ requires N, 13.9%). The *picrate* of the ordinary *cis*-modification, prepared in the same way, was obtained in yellow needles, m. p. 166° (Found : N, 13.7%).

After *trans*-hexahydrocarbazole had been boiled with an excess of acetic anhydride for an hour, the mixture shaken with much water, and the product crystallised from dilute alcohol, 9-*acetyl-trans-hexahydrocarbazole* separated in long, colourless needles, m. p. 113° (Found : N, 6.4. $C_{14}H_{17}ON$ requires N, 6.5%). 9-Acetyl-*cis*-hexahydrocarbazole melts at 98° (Graebe and Adlerskron, *Annalen*, 1880, 202, 25).

When *trans*-hexahydrocarbazole was made into a paste with water, an excess of dilute aqueous sodium hydroxide added, and the mixture shaken with benzoyl chloride, 9-*benzoyl-trans-hexahydrocarbazole* separated; it crystallised from alcohol in colourless needles, m. p. 133° (Found : N, 5.2. $C_{19}H_{19}ON$ requires N, 5.1%). The m. p. of 9-*benzoyl-cis-hexahydrocarbazole* is 106° (Gurney and Plant, this vol., p. 1320).

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