83. *The Action of Halogens on Polycyclic Indole Derivatives. Part III.*

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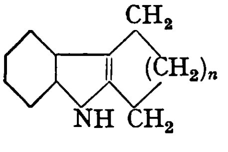
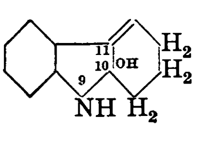
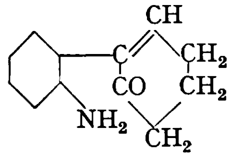
Earlier investigations of the bromination of tetrahydrocarbazole (I; $n = 2$) have not yielded any simple, well-defined products (cf., *e.g.*, Borsche, Witte, and Bothe, *Annalen*, 1908, **359**, 49), but it has now been found that under the appropriate conditions (see Experimental) a compound, $C_{12}H_{13}ON$, can be isolated in good yield. This is isomeric with the 11-hydroxy-2 : 3 : 4 : 11-tetrahydrocarbazole (V; R = H) described in Part I (J., 1931, 3324) and it is evidently 10-*hydroxy*-1 : 2 : 3 : 10-*tetrahydrocarbazole* (II). Its formation clearly involves the primary addition of bromine at the double linkage in (I; $n = 2$), the removal of hydrogen bromide, and the ultimate replacement of the remaining bromine by hydroxyl. The preferential elimination of the bromine in the 11-position during the second stage is easily understood from the basic character of the primary dibromide. That no appreciable quantity of a bromo-substitution product is formed was indicated by the fact that the crude bromination product contained only 0·3% of bromine. The compound (II) was readily transformed by loss of water to a dihydrocarbazole, while the fact that it was diazotised in acid solution and then coupled with β-naphthol to give a red dye indicates that it can readily react in the isomeric form (III). The chlorination of tetrahydrocarbazole under similar conditions has also given the compound (II) in good yield.



(I.)

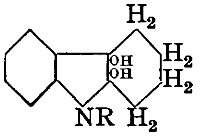


(II.)

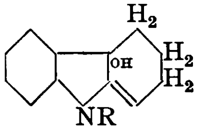


(III.)

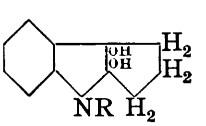
The bromination of certain 9-acyl derivatives of tetrahydrocarbazole has been described in Part I, and the chlorination of these compounds has now been investigated. Under the various conditions recorded in the experimental section the products (IV; R = Ac, CO_2Et, and CHPh:CH·CO) have been isolated. 9-Benzoyltetrahydrocarbazole has given not only (IV; R = Bz) but also (V; R = Bz). Thus the results obtained differ in many respects from those observed during bromination, although, as in the latter process, they involve the primary addition of halogen at the double linkage followed by the facile replacement of the halogen by hydroxyl. The ready isolation of compounds which have resulted from the loss of hydrogen chloride from the primary dichloride is not, however, a feature of the chlorination process. Such compounds may, nevertheless, be formed, since in some cases it has been found impossible to obtain more than a small proportion of the reaction product in a crystalline form. In this respect the chlorination process is less satisfactory than bromination.



(IV.)



(V.)



(VI.)

Earlier efforts (see Part I) to obtain crystalline products from the bromination of dihydropentindole (I; $n = 1$) and some of its acyl derivatives were unsuccessful, but we have now developed conditions for halogenation which have led to interesting substances. The bromination of dihydropentindole itself has given 9 : 10-*dihydroxytetrahydropentindole* (VI; R = H), while the chlorination of 8-acetyl- and 8-benzoyl-dihydropentindole has yielded the *compounds* (VI; R = Ac) and (VI; R = Bz). These products have undoubtedly resulted from the primary addition of bromine at the double linkage, followed by hydrolysis, and special interest attaches to their isolation. Analogous compounds (IV) can readily be obtained by the nitration of several acyl derivatives of tetrahydrocarbazole (Perkin and Plant, J., 1923, **123**, 676), but the nitration of the corresponding acyldihydropentindoles proceeds along other lines, and simple products of the constitution (VI) have not hitherto been prepared (Plant, J., 1929, 2493; Massey and Plant, J., 1931, 1990, 2218).

The compounds (IV) undergo some interesting reactions such as the formation of 11-hydroxytetrahydrocarbazolenine on boiling for a short time with aqueous alcoholic alkali, and of derivatives of ψ-indoxyl*spirocyclo*pentane on heating alone or with acetic anhydride (Perkin and Plant, *loc. cit.*). The substance (VI; R = Ac) has not been made to undergo analogous transformations; it was not appreciably changed by boiling aqueous alcoholic potassium hydroxide after an hour, but it was converted by boiling aqueous alkali into (VI; R = H). No definite product has been obtained from it by heating alone or by boiling with acetic anhydride.

EXPERIMENTAL.

Bromination of Tetrahydrocarbazole.—A solution of tetrahydrocarbazole in AcOH at room temp. was treated with an equimol. quantity of Br (in AcOH), immediately diluted with an excess of H_2O, and made alk. with NH_3 aq. The product, which was extracted with Et_2O and dried with Na_2SO_4, gave 10-*hydroxy*-1 : 2 : 3 : 10-*tetrahydrocarbazole* in colourless prisms, m. p. 153°, on crystn. from C_6H_6 (Found: C, 77·0; H, 6·8. $C_{12}H_{13}ON$ requires C, 77·0; H, 7·0%).

When a solution of the latter in Ac_2O had been boiled for an hr. and then cooled, 2 : 3-dihydrocarbazole (identified by mixed m. p. with the specimen described in Part I), colourless prisms, m. p. 293—295°, from C_6H_6, separated. The same compound separated when 10-hydroxy-1 : 2 : 3 : 10-tetrahydrocarbazole was refluxed with abs. EtOH for 5 hr.; from the alc. filtrate a very small quantity of a substance which has not been identified, m. p. 196—198°, after repeated crystn. from petroleum (b. p. 100—120°), was obtained on concn.

The 10-hydroxy-compound was converted into the 11-hydroxytetrahydrocarbazolenine of Perkin and Plant (*loc. cit.*) by refluxing for ½ hr. with EtOH aq., or better with aq.-alc. KOH; the product was isolated by dilution with H_2O and identified by mixed m. p.

When a solution of the 10-hydroxy-compound (1 g.) in dil. HCl was diazotised and added to β-naphthol (0·66 g.) in H_2O containing NaOH (0·33 g.) and AcONa (1 g.), the corresponding *azo-dye*, red prisms, m. p. 143°, from EtOH, was pptd. (Found: N, 7·9. $C_{22}H_{18}O_2N_2$ requires N, 8·2%).

Chlorination of 9-*Acetyl-*, 9-*Carbethoxy-*, *and* 9-*Cinnamoyl-tetrahydrocarbazole.*—9-Acetyltetrahydrocarbazole in AcOH was treated with an equimol. quantity of Cl (dissolved in either AcOH or CCl_4), the whole being well shaken, then immediately stirred vigorously with an excess of H_2O and made alk. with NH_3 aq. When the ppt. was crystallised from EtOH, 10 : 11-dihydroxy-9-acetylhexahydrocarbazole (yield 50—60%) was obtained in colourless plates, m. p. 203° (identified with the product of Perkin and Plant, *loc. cit.*, by a mixed m. p.).

By similar methods the 9-carbethoxy-compound gave ethyl 10 : 11-dihydroxyhexahydrocarbazole-9-carboxylate (approx. 50% yield), colourless needles, m. p. 133°, from EtOH (identified with the product of Perkin and Plant, *loc. cit.*, by mixed m. p.), while the 9-cinnamoyl derivative gave 10 : 11-dihydroxy-9-cinnamoylhexahydrocarbazole, colourless prisms, m. p. 204° (after repeated crystn. from EtOH, C_6H_6, and acetone), identical (mixed m. p.) with the substance of Plant and Rutherford (J., 1929, 1970). The latter compound, on being refluxed with aq.-alc. KOH, gave 11-hydroxytetrahydrocarbazolenine, while 6-*cinnamoyl*-ψ-*indoxyl*spirocyclo*pentane*, pale yellow needles, m. p. 165°, from EtOH, separated from its solution in Ac_2O after being refluxed for 4 hr. and then cooled (Found: C, 79·5; H, 5·9. $C_{21}H_{19}O_2N$ requires C, 79·5; H, 6·0%). The same product was obtained when ψ-indoxyl*spirocyclo*pentane (Perkin and Plant, *loc. cit.*) was shaken in acetone with conc. KOH aq. and cinnamoyl chloride; it was isolated by pptn. with H_2O.

Chlorination of 9-*Benzoyltetrahydrocarbazole.*—(a) This compound in AcOH was treated with an equimol. quantity of Cl (dissolved in AcOH); the product, which was pptd. by the immediate addition of H_2O, gave 11-hydroxy-9-benzoyl-2 : 3 : 4 : 11-tetrahydrocarbazole (small yield), colourless prisms, m. p. 144—146° (identified by mixed m. p. with the substance described in Part I), when crystallised several times from petroleum (b. p. 60—80°).

(b) The compound in AcOH was treated with an equimol. quantity of Cl, dissolved in CCl_4, the whole being quickly shaken and then immediately diluted with H_2O. After the sticky ppt. had been removed with Et_2O, the aq. layer, on being made alk. with NH_3 aq., deposited a small quantity of 10 : 11-dihydroxy-9-benzoylhexahydrocarbazole (identified by mixed m. p. with the product of Plant and Rutherford, *loc. cit.*), colourless prisms, m. p. 147°.

Bromination of Dihydropentindole.—Dihydropentindole in AcOH was treated quickly with an equimol. quantity of Br (dissolved in AcOH) and the solution was then immediately diluted with an excess of ice–H_2O and made alk. with NH_3 aq. The aq. liquid was filtered from a ppt. from which nothing cryst. was obtained and was then extracted with Et_2O. After the ethereal solution had been dried (Na_2SO_4) and evaporated, the residue gave 9 : 10-*dihydroxytetrahydropentindole* (yield, 10%), colourless plates, m. p. 140°, on crystn. from C_6H_6 (Found : C, 69·3; H, 7·2. $C_{11}H_{13}O_2N$ requires C, 69·1; H, 6·8%). This compound readily dissolved in dil. HCl and, after diazotisation, it coupled with β-naphthol in alk. solution to give a red dye. Its solution in acetone was shaken with conc. KOH aq. and AcCl, diluted with H_2O, and filtered from an uncrystallisable ppt.; Et_2O then extracted a small quantity of 9 : 10-dihydroxy-8-acetyltetrahydropentindole, identical (mixed m. p.) with the product described below.

Chlorination of 8-Acetyl- and 8-Benzoyl-dihydropentindole.—8-Acetyldihydropentindole was treated rapidly in small quantities in AcOH with an equimol. amount of Cl (dissolved in AcOH); H_2O was immediately added and the whole well shaken. After the solution had been filtered from a small amount of unchanged 8-acetyl compound and made alk. (NH_3 aq.), Et_2O extracted 9 : 10-*dihydroxy-8-acetyltetrahydropentindole* (yield 50%), colourless prisms, m. p. 152°, from C_6H_6 (Found : C, 67·3; H, 6·7. $C_{13}H_{15}O_3N$ requires C, 66·9; H, 6·4%). When the latter had been boiled for an hr. with KOH aq. (15%), 9 : 10-dihydroxytetrahydropentindole (identified by mixed m. p.) separated slowly from the filtered solution when this was made just acid with AcOH.

8-Benzoyldihydropentindole was chlorinated as above and the solution immediately diluted with much H_2O. The sticky ppt. yielded nothing cryst., but, after the filtered solution had been made alk. (NH_3 aq.), Et_2O extracted 9 : 10-*dihydroxy-8-benzoyltetrahydropentindole* (yield, *ca.* 5%), colourless prisms, m. p. 149°, from C_6H_6 (Found : C, 73·0; H, 5·5. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8%). It was hydrolysed, as for the corresponding acetyl compound, to 9 : 10-dihydroxytetrahydropentindole.

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