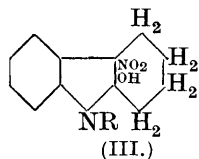
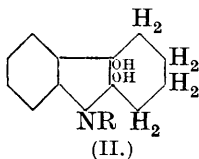
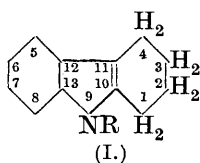


CCLVII.—*Derivatives of Tetrahydrocarbazole. Part VIII. Formation and Reactions of Nitric Acid Addition Products.*

By SYDNEY GLENN PRESTON PLANT and KENNETH HENRY RUTHERFORD.

SOME of the most interesting reactions of the derivatives of tetrahydrocarbazole (I; R = H) are those which take place between the 9-acyl compounds and nitric acid (Perkin and Plant, J., 1923, 123, 676; Manjunath and Plant, J., 1926, 2260; Plant and Rosser, J., 1928, 2454). In all these cases two products are formed: one is a simple nitro-derivative, but the formation of the other involves addition at the double linkage. When the substituent R is the acetyl, carbethoxyl, or phenylacetyl radical, this addition product



is of the type (II), but if R is the benzoyl group, the compound (III) results. This remarkable, and unexplained, difference between these substances has been found to extend, in general, to the acyl compounds of substituted tetrahydrocarbazoles (*e.g.*, the 3-methyl- and 6-chloro-derivatives). With the single exception of ethyl 6-chlorotetrahydrocarbazole-9-carboxylate, which gives a nitric acid addition product, the benzoylated compounds alone have given substances of the type (III).

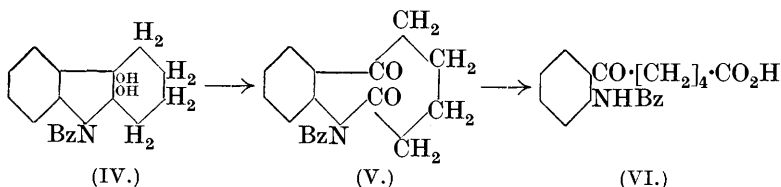
The present work was undertaken primarily in order (i) to discover how far the introduction of substituents into the benzoyl radical affects the reaction with nitric acid, and (ii) to investigate the relationship between the nitric acid addition products and those formed by the addition of two hydroxyl groups at the double bond. For this purpose the 9-*o*-, -*m*-, and -*p*-*toluoyltetrahydrocarbazoles* (I; R = CO·C<sub>6</sub>H<sub>4</sub>Me) and the 9-*o*-, -*m*-, and -*p*-*chlorobenzoyltetrahydrocarbazoles* (I; R = CO·C<sub>6</sub>H<sub>4</sub>Cl) have been prepared by the action of the appropriate acid chloride on the Grignard reagent (I; R = MgBr), and the constitutions have been confirmed in each case by hydrolysis to tetrahydrocarbazole and the corresponding acid. All of these substances, on treatment with nitric acid in glacial acetic acid solution, yielded the corresponding 5-nitro-substitution product, but from only two of them could a second

derivative be isolated. These two, the 9-*p*-toluoyl- and 9-*p*-chlorobenzoyl-compounds, gave the nitric acid addition products (III; R = CO·C<sub>6</sub>H<sub>4</sub>Me, or CO·C<sub>6</sub>H<sub>4</sub>Cl), and so conformed to the general rule. The constitution of the nitro-compounds was confirmed in each case by hydrolysis to 5-nitrotetrahydrocarbazole. Previous experience has shown that the formation of the addition products is favoured by the use of fuming nitric acid, but even under these conditions they could not be isolated from the *o*- and *m*-substituted benzoyl derivatives.

Although the reactions of nitric acid with many derivatives of tetrahydrocarbazole have now been investigated, no compound has so far been obtained in which both direct nitration and addition at the double linkage have occurred in the same molecule. It was considered of interest, therefore, to study the behaviour of 5-, 6-, 7-, and 8-nitro-9-benzoyltetrahydrocarbazole towards nitric acid under similar conditions. The first of these compounds has been obtained by the action of nitric acid on (I; R = Bz) (Perkin and Plant, *loc. cit.*), and the 6- and 7-nitro-derivatives have now been prepared by the action of benzoyl chloride on the corresponding nitrotetrahydrocarbazoles in acetone solution in the presence of potassium hydroxide (compare Stevens and Tucker, J., 1923, **123**, 2140), but nitric acid had no effect on these three substances in acetic acid solution. Attempts to benzoylate 8-nitrotetrahydrocarbazole have been unsuccessful. It has also been found that nitric acid does not react with (III; R = Bz) in acetic acid.

It has previously been noted (Plant and Rosser, *loc. cit.*) that ethyl 6-chloro-11-nitro-10-hydroxyhexahydrocarbazole-9-carboxylate is changed by boiling alcohol, apparently to give the corresponding 6-chloro-10:11-dihydroxy-ester by replacement of the nitro- by the hydroxyl group. This reaction has now been more closely investigated with the aid of (III; R = Bz), which, on being boiled in alcoholic solution for 45 minutes, yielded (IV), the constitution of which was established by treating it with boiling, aqueous-alcoholic potassium hydroxide, whereby it was converted into 11-hydroxytetrahydrocarbazolenine, identical with the substance obtained by similar treatment of (II; R = Ac) (Perkin and Plant, *loc. cit.*). The process of replacement of the nitro- by the hydroxyl-group is interesting, and results in the conversion of one of these two types of addition product into the other. It has previously been observed that (III; R = Bz) undergoes a remarkable change with boiling, aqueous-alcoholic potassium hydroxide during which  $\delta$ -*o*-benzamidobenzoylvaleric acid (VI) is produced, and it has been suggested (Perkin and Plant, *loc. cit.*) that this reaction primarily involves the formation of (IV), which is then

oxidised, possibly by potassium nitrite, to (V), which could yield (VI) on hydrolysis. The isolation of (IV) during the course of the present work has now made it possible to test these suggestions.



It has been found, however, that (IV) is unchanged by either potassium nitrite or potassium nitrate in boiling alcohol, and that, if potassium hydroxide is present in addition to one of these reagents, the product is 11-hydroxytetrahydrocarbazolenine. It is improbable, therefore, that (IV) is an intermediate stage in the conversion under discussion.

In view of the varied results so far obtained, it became of interest to study the effect of the cinnamoyl group upon the above addition reactions. Consequently, 9-cinnamoyltetrahydrocarbazole (I; R = CHPh·CH·CO) was prepared by the action of cinnamoyl chloride on (I; R = H) in acetone in the presence of potassium hydroxide, and, on treatment with nitric acid in acetic acid, it yielded a mixture of 5-nitro-9-cinnamoyltetrahydrocarbazole and 9-cinnamoyl-10:11-dihydroxyhexahydrocarbazole. It thus behaves like the majority of 9-acyltetrahydrocarbazole derivatives, and unlike the benzoyl compound.

#### E X P E R I M E N T A L.

**9-*o*-Toluoyltetrahydrocarbazole.**—Tetrahydrocarbazole (12 g.) was added gradually to a solution of magnesium (2 g.) in ethyl bromide (9 g.) and dry ether (200 c.c.); ethane was evolved, and the reaction was completed by warming the mixture for a few minutes on the steam-bath. *o*-Toluoyl chloride (14 g.) was then added, and, after a short time, the whole was boiled under reflux for 1 hour. After being shaken with ice and dilute hydrochloric acid, the ethereal solution was extracted with dilute aqueous ammonia to remove *o*-toluic acid, dried over calcium chloride, and the solvent removed. The residue was distilled under reduced pressure; a little tetrahydrocarbazole came over first, and then 9-*o*-toluoyltetrahydrocarbazole was collected as a pale brown oil, b. p. 260—270°/22 mm., which resisted all attempts at crystallisation (Found: N, 4.8. C<sub>20</sub>H<sub>19</sub>ON requires N, 4.8%). When a solution of this product in aqueous-alcoholic potassium hydroxide was boiled for ½ hour and then diluted with water, tetrahydrocarbazole was precipitated; after

concentrating the filtrate and acidifying it with hydrochloric acid, *o*-toluic acid was obtained.

Nitric acid (1.6 g., *d* 1.4), dissolved in a little acetic acid, was added to a solution of 9-*o*-toluoyltetrahydrocarbazole (4 g.) in glacial acetic acid (50 c.c.) at 60°. Since nothing separated from the solution on cooling, the whole was diluted with water, and the yellow product was crystallised from alcohol, from which 5-nitro-9-*o*-toluoyltetrahydrocarbazole was isolated in yellow prisms, m. p. 154° (Found : N, 8.2. C<sub>20</sub>H<sub>18</sub>O<sub>3</sub>N<sub>2</sub> requires N, 8.4%). When the nitration was carried out in a smaller quantity of solvent, or with fuming acid (*d* 1.5), this nitro-derivative was again the only product isolated in a crystalline condition. When a solution of this nitro-compound in aqueous-alcoholic potassium hydroxide was boiled and subsequently diluted with water, 5-nitrotetrahydrocarbazole was obtained, and after crystallisation from chloroform, proved to be identical with that previously described (Perkin and Plant, *loc. cit.*).

9-*m*-Toluoyltetrahydrocarbazole.—This substance, prepared as described for the ortho-derivative, was collected at 260—290°/12 mm. as a pale brown oil, which could not be made to crystallise (Found : N, 5.0%). When this was dissolved in acetic acid (2 g. in 10 c.c.) at 60° and treated with nitric acid (0.8 g., *d* 1.4), 5-nitro-9-*m*-toluoyltetrahydrocarbazole separated, after standing for several days, further quantities being obtained by diluting the mother-liquor with water; this compound crystallised from alcohol in yellow prisms, m. p. 148°.

9-*p*-Toluoyltetrahydrocarbazole.—This compound was collected at 250—280°/12 mm. as a viscous, brown oil, which solidified on treatment with alcohol, from which solvent it separated in colourless needles, m. p. 126° (Found : N, 5.3%). When a solution in glacial acetic acid (4 g. in 50 c.c.) at 60° was treated with nitric acid (1.6 g., *d* 1.4), dissolved in a little acetic acid, 11-nitro-9-*p*-toluoyl-10-hydroxyhexahydrocarbazole soon separated in colourless needles, m. p. 149° (decomp., with evolution of oxides of nitrogen) (Found : N, 7.8. C<sub>20</sub>H<sub>20</sub>O<sub>4</sub>N<sub>2</sub> requires N, 7.9%). After collecting this substance and diluting the filtrate with water, a yellow product was precipitated, and this, after crystallising two or three times from alcohol, yielded 5-nitro-9-*p*-toluoyltetrahydrocarbazole in yellow plates, m. p. 136° (Found : N, 8.3%).

9-*o*-Chlorobenzoyltetrahydrocarbazole.—Prepared by a process analogous to that used for the 9-*o*-toluoyl derivative, this compound was obtained as a yellow oil, b. p. 260—270°/20 mm., which crystallised from alcohol in colourless prisms, m. p. 117°. When its solution in acetic acid (5 g. in 75 c.c.) at 60° was treated with nitric acid

(2 g., *d* 1.4), 5-nitro-9-*o*-chlorobenzoyltetrahydrocarbazole rapidly separated, on cooling, in yellow prisms, which, after recrystallisation from alcohol, melted at 195°. A further quantity of the same substance was obtained by diluting the acetic acid solution with water and crystallising the product twice from alcohol. This same nitro-compound separated when an acetic acid solution of the 9-*o*-chlorobenzoyl derivative was treated with fuming nitric acid.

9-*m*-Chlorobenzoyltetrahydrocarbazole.—Prepared as above, the product distilled at 250—280°/15 mm., and separated from alcohol in colourless prisms, *m. p.* 93°. Nitration under conditions similar to those described for the ortho-compound gave 5-nitro-9-*m*-chlorobenzoyltetrahydrocarbazole, which separated from alcohol in yellow prisms, *m. p.* 155°.

9-*p*-Chlorobenzoyltetrahydrocarbazole.—This compound, prepared as above, was collected as a yellow oil, *b. p. ca.* 285°/18 mm., which, on crystallisation from alcohol, separated in colourless prisms, *m. p.* 106° (Found: N, 4.5.  $C_{19}H_{16}ONCl$  requires N, 4.5%). When its solution in acetic acid (1 g. in 15 c.c.) at 50° was treated with nitric acid (0.4 g., *d* 1.4), 11-nitro-9-*p*-chlorobenzoyl-10-hydroxyhexahydrocarbazole separated almost immediately, on stirring, in colourless needles, *m. p.* 153° (decomp.) (Found: N, 7.6.  $C_{19}H_{17}O_4N_2Cl$  requires N, 7.5%). When the acetic acid mother-liquor was diluted with water, a yellow product separated, and this, after crystallising twice from alcohol, yielded 5-nitro-9-*p*-chlorobenzoyltetrahydrocarbazole in yellow prisms, *m. p.* 148°.

6- and 7-Nitro-9-benzoyltetrahydrocarbazoles.—A solution of 6-nitrotetrahydrocarbazole (5 g., prepared by the direct nitration of tetrahydrocarbazole; Perkin and Plant, *J.*, 1921, **119**, 1825) in acetone (25 c.c.), to which potassium hydroxide (7 g. in 66% aqueous solution) had been added, was treated gradually with benzoyl chloride (7 g.), the mixture being well shaken. After addition of water, the solid product was crystallised from alcohol, from which 6-nitro-9-benzoyltetrahydrocarbazole separated in long yellow prisms, *m. p.* 180° (Found: N, 8.7.  $C_{19}H_{16}O_3N_2$  requires N, 8.7%).

7-Nitro-9-benzoyltetrahydrocarbazole, prepared in a similar way from 7-nitrotetrahydrocarbazole (obtained from cyclohexanone-*m*-nitrophenylhydrazone; Borsche, Witte, and Bothe, *Annalen*, 1908, **359**, 68), separated from alcohol in yellow needles, *m. p.* 138° (Found: N, 8.5%).

9-Benzoyl-10:11-dihydroxyhexahydrocarbazole.—A mixture of the addition product (III; R = Bz) (3 g.) and alcohol (25 c.c.) was boiled under reflux for 45 minutes, and the resulting solution was

concentrated; on cooling, the 10:11-*dihydroxy*-derivative separated in colourless prisms, m. p.  $142^{\circ}$  (Found: N, 4.4.  $C_{19}H_{19}O_3N$  requires N, 4.5%). When a mixture of the latter substance (1 g.), potassium hydroxide (3 g.), alcohol (15 c.c.), and water (10 c.c.) was boiled under reflux for  $\frac{1}{2}$  hour, cooled, and diluted with water, a yellow solid separated. After crystallising from petroleum, 11-hydroxytetrahydrocarbazolenine was obtained in long, yellow prisms, m. p.  $79^{\circ}$ , and shown to be identical with the product described by Perkin and Plant (*loc. cit.*) by a mixed m. p. determination, and by conversion into its colourless acetyl derivative (m. p.  $113^{\circ}$ ) with boiling acetic anhydride.

9-*Cinnamoyltetrahydrocarbazole*.—Cinnamoyl chloride (6 g., dissolved in a little acetone) was added gradually to a solution of tetrahydrocarbazole (4 g.) in acetone (20 c.c.), to which potassium hydroxide (7 g. in 66% aqueous solution) had been added. The solid which separated on dilution with water was crystallised from alcohol, and 9-*cinnamoyltetrahydrocarbazole* was obtained in yellow prisms, m. p.  $117^{\circ}$  (Found: N, 4.3.  $C_{21}H_{19}ON$  requires N, 4.7%). This compound (2 g.) in glacial acetic acid (35 c.c.) at  $70^{\circ}$  was treated with nitric acid (0.8 g., *d* 1.4), and, on cooling, a mixture (0.85 g.) of solid products separated. When this was dissolved in hot alcohol (80 c.c.) and the solution left undisturbed, 5-*nitro-9-cinnamoyltetrahydrocarbazole* (0.15 g.) separated in yellow needles, m. p.  $177^{\circ}$  (Found: N, 7.8.  $C_{21}H_{18}O_3N_2$  requires N, 8.1%), and, after being filtered, the mother-liquor deposited 9-*cinnamoyl-10:11-dihydroxyhexahydrocarbazole* (0.4 g.) in colourless prisms, m. p.  $204^{\circ}$  (Found: N, 4.2.  $C_{21}H_{21}O_3N$  requires N, 4.2%). The constitution of the former product was confirmed by hydrolysis to 5-*nitrotetrahydrocarbazole* and cinnamic acid.

THE DYSON PERRINS LABORATORY,  
OXFORD.

[Received, July 6th, 1929.]