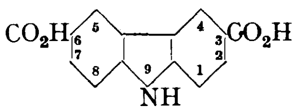
279. *The Friedel–Crafts Reaction in the Carbazole Series. Part II.*

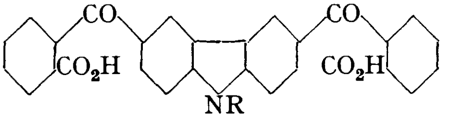
By D. R. Mitchell and S. G. P. Plant.

Hitherto none of the carbazoledicarboxylic acids has been definitely characterised. A dibasic acid, m. p. above 340° (decomp.), obtained by the action of carbon dioxide at a high temperature on potassium carbazole has been mentioned (D.R.PP. 263,150, 442,609; *Chem. Zentr.*, 1913, ii, 730; 1927, ii, 639), but without any statement regarding the positions of the substituents. The preparation of authentic samples of various 3 : 6-diacylcarbazoles (Plant and Tomlinson, J., 1932, 2188; Plant, Rogers, and Williams, J., 1935, 741) has now made it possible to obtain carbazole-3 : 6-dicarboxylic acid (I). The acid itself, which resulted from the fusion of 3 : 6-dibenzoylcarbazole with potassium hydroxide, melts above 370° (decomp.), but gives a well-characterised *ethyl* ester suitable for its identification. In a similar manner 3 : *6-dibenzoyl-9-methylcarbazole* has been converted into 9-methylcarbazole-3 : 6-dicarboxylic acid, which also melts at a high temperature with decomposition, but gives a satisfactory *ethyl* ester.

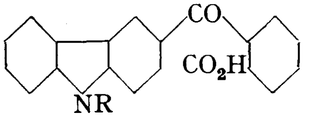
The observation that various acid halides react with carbazole and its 9-alkyl (but not 9-acyl) derivatives in the presence of aluminium chloride to give 3 : 6-diacylcarbazoles (Plant, Rogers, and Williams, *loc. cit.*) makes it probable that a similar process with acid anhydrides would lead to substitution in one or both of the 3- and the 6-positions. This has to some extent been confirmed by the fact that the use of acetic and benzoic anhydride has given with carbazole the corresponding 3 : 6-diacyl derivatives. The point is of considerable interest in connexion with the structure of substances obtained from carbazole and its 9-methyl and 9-ethyl derivatives with the aid of phthalic anhydride and aluminium chloride (Scholl and Neovius, *Ber.*, 1911, **44**, 1249; Ehrenreich, *Monatsh.*, 1911, **32**, 1103; D.R.P. 261,495; *Chem. Zentr.*, 1913, ii, 396; Copisarow and Weizmann, J., 1915, **107**, 878; Ignatjuk-Maistrenko and Tichonow, *Chem. Zentr.*, 1935, i, 2894). Diphthaloylic acids of the formula (II) are supposed to result, accompanied in the case of the 9-alkyl compounds by the monobasic acids (III). The former have been converted by the elimination of two molecules of water in each case into anthraquinone-like substances which have found some application as dyes, but there appears to be no proof that the acids have their substituents in the positions indicated. In view of the fact that anomalous results are

(I.)

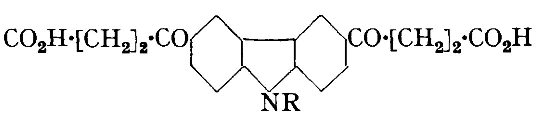




(II.)



(III.)

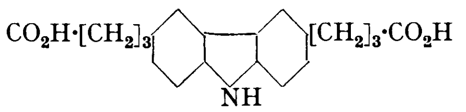


(IV.)

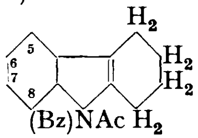
common in Friedel–Crafts reactions in this series (Plant, Rogers, and Williams, *loc. cit.*), it was decided to examine these substances and remove any possible ambiguity regarding their structure.

The dibasic acid from carbazole, which melts with decomposition, has been decarboxylated to 3 : 6-dibenzoylcarbazole, identical with the product of Plant and Tomlinson (*loc. cit.*), and its well-defined *ethyl* ester has been converted by fusion with potassium hydroxide into carbazole-3 : 6-dicarboxylic acid (I). The ethyl ester was also converted on methylation and ethylation into *ethyl* 9-*methylcarbazole*-3 : 6-*diphthaloylate* (as II; R = Me) and the corresponding 9-*ethyl* compound (as II; R = Et), which proved to be identical with the substances obtained by the esterification of the acids derived from 9-methyl- and 9-ethyl-carbazole respectively with phthalic anhydride. It is thus established that these dibasic acids have been correctly designated. The fact that the monobasic acid derived from 9-methylcarbazole is accurately represented by the formula (III; R = Me) has been proved by its decarboxylation to 3-*benzoyl*-9-*methylcarbazole*, identical with a compound obtained by the methylation of 3-benzoylcarbazole.

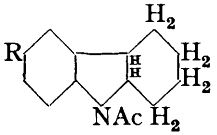
The reaction between carbazole and succinic anhydride in the presence of aluminium chloride gave a satisfactory product only if carried out below room temperature, but under these conditions a good yield of a dibasic acid resulted. It has not been possible to degrade the substance into a compound which would furnish a rigid proof of its structure, but in view of the uniformity of the results obtained with other acid anhydrides there can be no doubt that it is *carbazole*-3 : 6-*bis*-γ-*ketobutyric acid* (IV; R = H). The acid had m. p. 285° (decomp.), but gave characteristic methyl and *ethyl* esters, and when reduced by the Clemmensen method it was converted into *carbazole*-3 : 6-*dibutyric acid* (V). Similarly, 9-methylcarbazole has been converted into the corresponding acid (IV; R = Me), the *ethyl* ester of which was found to be identical with the compound obtained by the methylation of the ethyl ester of the acid (IV; R = H).



(V.)



(VI.)



(VII.)

In view of the fact that the application of the Friedel–Crafts reaction to 9-acylcarbazoles results in the introduction of a single substituent in the 2-position, and 9-acyltetrahydrocarbazoles (VI) give the analogous 7-substituted products (Plant, Rogers, and Williams, *loc. cit.*; Plant and Rogers, this vol., p. 40), it became of interest to study the reaction with 9-acetylhexahydrocarbazole (VII; R = H). It was found that the action of acetyl chloride and aluminium chloride gave a good yield of 6 : 9-*diacetylhexahydrocarbazole* (VII; R = Ac), which has been hydrolysed to 6-*acetylhexahydrocarbazole*. The constitution of this product has been established by reducing it to 6-*ethylhexahydrocarbazole*, which gave a well-defined 9-p-*nitrobenzoyl* derivative and proved to be identical with the base obtained by the reduction of the 6-ethyltetrahydrocarbazole previously synthesised by Plant and Williams (J., 1934, 1142). It thus follows that 9-acetylhexahydrocarbazole differs fundamentally from the other carbazole compounds mentioned and behaves more like a simple benzene derivative, as would be expected from the fact that one of the carbon rings is fully reduced.

EXPERIMENTAL.

Ethyl Carbazole-3 : 6-*dicarboxylate and its* 9-*Methyl Derivative*.—3 : 6-Dibenzoylcarbazole (2 g.) was added to potassium hydroxide (20 g.) which had been melted with a little water (2 c.c.), and the temperature was slowly raised until reaction occurred. When cold, the mixture was dissolved in water, and the addition of hydrochloric acid to the filtered solution then precipitated carbazole-3 : 6-dicarboxylic acid (1 g.). The acid melts above 370° (decomp.) and is very sparingly soluble in the common solvents, but dissolves freely in dilute alkalis to give a bright yellow solution. Its suspension in alcoholic hydrogen chloride was refluxed for 6 hours, the solvent distilled off, and the residue shaken with dilute aqueous sodium carbonate to remove any unchanged acid. After crystallisation from alcohol, *ethyl carbazole*-3 : 6-*dicarboxylate* was obtained in almost colourless plates, m. p. 203° (Found : C, 69·2; H, 5·6. $C_{18}H_{17}O_4N$ requires C, 69·4; H, 5·5%).

After a solution of 3 : 6-dibenzoylcarbazole (3 g.) in acetone (60 c.c.) had been vigorously shaken with methyl sulphate (3 c.c.) and potassium hydroxide (3 g. in 1·5 c.c. of water), the addition of water precipitated 3 : 6-*dibenzoyl*-9-*methylcarbazole*, colourless prisms, m. p. 220°, from glacial acetic acid, in practically quantitative yield (Found : C, 83·4; H, 5·0. $C_{27}H_{19}O_2N$ requires C, 83·3; H, 4·9%). On fusion with potassium hydroxide, as above, this product gave the corresponding dicarboxylic acid, m. p. above 350° (decomp.), in poor yield, and subsequent esterification as before led to *ethyl* 9-*methylcarbazole*-3 : 6-*dicarboxylate*, colourless plates, m. p. 161—163°, from alcohol (charcoal) (Found : C, 70·2; H, 5·9. $C_{19}H_{19}O_4N$ requires C, 70·2; H, 5·8%).

3 : 6-*Diacetyl- and* 3 : 6-*Dibenzoyl-carbazole*.—After a mixture of carbazole (5 g.), nitrobenzene (70 c.c.), acetic anhydride (7 g.), and aluminium chloride (17 g.) had been kept at 0° for 8 hours, it was poured on ice–dilute hydrochloric acid, and the nitrobenzene removed in steam. When the residual solid had been washed with a little ether and then crystallised successively from acetone and alcohol, 3 : 6-diacetylcarbazole, identical (mixed m. p.) with the product of Plant, Rogers, and Williams (*loc. cit.*), was obtained in almost colourless prisms, m. p. 233°.

After carbazole had been similarly reacted upon with the corresponding quantity of benzoic anhydride, and the crude product treated with aqueous sodium carbonate to remove benzoic acid, and then crystallised successively from alcohol and acetic acid, 3 : 6-dibenzoylcarbazole was isolated. Its identity was confirmed by conversion into the 9-methyl derivative as described above, a mixed m. p. showing no depression.

Ethyl Carbazole-3 : 6-*diphthaloylate and its* 9-*Methyl and* 9-*Ethyl Derivatives*.—Prepared as described by Scholl and Neovius (*loc. cit.*), carbazole-3 : 6-diphthaloylic acid melted with decomposition at 315° if rapidly heated, but at a lower temperature (298—302°) when heated more slowly. When a mixture of the acid (2 g.) and quinoline (5 c.c.) containing a little copper oxide was gradually heated, effervescence began at 160°. After the whole had been kept at 170—220° for an hour, it was cooled, poured into dilute hydrochloric acid, and the resulting solid treated with aqueous sodium carbonate. The residue was crystallised from glacial acetic acid, and an almost quantitative yield of 3 : 6-dibenzoylcarbazole was obtained. Its identity was confirmed by conversion into the 9-methyl derivative, as already described, a mixed m. p. showing no depression.

Ethyl carbazole-3 : 6-*diphthaloylate*, colourless needles, m. p. 195°, from alcohol, was obtained when the acid was refluxed for 6 hours with alcoholic hydrogen chloride and the residue, after evaporation, shaken with aqueous sodium carbonate (Found : C, 73·9; H, 4·8. $C_{32}H_{25}O_6N$ requires C, 74·0; H, 4·8%). When this ester was treated with molten potassium hydroxide as described in the case of 3 : 6-dibenzoylcarbazole, carbazole-3 : 6-dicarboxylic acid was obtained; it was identified by conversion into the corresponding ethyl ester (m. p. 203°), the m. p. of which showed no depression on admixture with the authentic specimen.

After ethyl carbazole-3 : 6-diphthaloylate (1 g.) in acetone (20 c.c.) had been shaken with methyl sulphate (2 c.c.) and sodium hydroxide (2 g. in 2 c.c. of water) for several minutes, water precipitated the product as a sticky solid. On crystallisation from alcohol (charcoal), a small amount of resinous material separated first, but, after filtration, the mother-liquor then yielded *ethyl* 9-*methylcarbazole*-3 : 6-*diphthaloylate* in minute, colourless needles, m. p. 135° (Found : C, 74·4; H, 5·2. $C_{33}H_{27}O_6N$ requires C, 74·3; H, 5·1%).

9-Methylcarbazole-3-phthaloylic and 3 : 6-diphthaloylic acids were obtained from 9-methylcarbazole as described by Ehrenreich (*loc. cit.*). The latter was converted, as in the case of the corresponding carbazole derivative, into its ethyl ester, which separated from alcohol in colourless needles, m. p. 134—135°, and was identified by a mixed m. p. with the ester described immediately above. The former acid was decarboxylated by heating (0·5 g.) with quinoline (3 c.c.) and copper-bronze at 170—220° for 2 hours; 3-*benzoyl*-9-*methylcarbazole*, almost colourless prisms, m. p. 84—85°, from alcohol (charcoal), was obtained when the resulting mixture was treated successively with dilute hydrochloric acid and aqueous sodium hydroxide (Found : C, 84·3; H, 5·3. $C_{20}H_{15}ON$ requires C, 84·2; H, 5·3%). 3-Benzoyl-9-methylcarbazole was also prepared by shaking 3-benzoylcarbazole (described by Plant and Tomlinson, *loc. cit.*) in acetone with methyl sulphate and potassium hydroxide for 10 minutes, the identity of the substances being established by mixed m. p.

9-Ethylcarbazole-3 : 6-diphthaloylic acid, m. p. 268°, was prepared as described in D.R.P. 261,495 and also by the method of Ignatjuk-Maistrenko and Tichonow (*loc. cit.*), and was converted by the usual process into *ethyl* 9-*ethylcarbazole*-3 : 6-*diphthaloylate*, colourless prisms,

m. p. 178°, after being twice recrystallised from alcohol (charcoal) (Found: C, 74·4; H, 5·4. $C_{34}H_{29}O_6N$ requires C, 74·6; H, 5·3%). The same ester (mixed m. p.) was obtained when ethyl carbazole-3 : 6-diphthaloylate was ethylated with ethyl sulphate and alkali in acetone as described for the analogous 9-methyl derivative.

Carbazole-3 : 6-*bis*-γ-*ketobutyric Acid and its Derivatives*.—Carbazole (10 g.) and succinic anhydride (12 g.) in nitrobenzene (140 c.c., purified by distillation in steam) were treated with aluminium chloride (34 g.) below 0°, and the solution was kept at 0° for 8 hours. The yellow solid obtained when the mixture was then poured on ice–dilute hydrochloric acid was collected and dissolved in aqueous sodium carbonate. The solution was filtered from a trace of carbazole, and shaken with ether to remove any nitrobenzene. On addition of hydrochloric acid, *carbazole*-3 : 6-*bis*-γ-*ketobutyric acid* (12 g.), minute, colourless needles, m. p. 285° (decomp.), from glacial acetic acid, was precipitated (Found: C, 64·6; H, 4·8. $C_{20}H_{17}O_6N$ requires C, 65·4; H, 4·6%). The acid was very sparingly soluble in the common solvents. Its methyl ester, colourless plates, m. p. 195°, from methyl alcohol, and its *ethyl* ester, colourless prisms, m. p. 173°, from alcohol (Found: C, 67·9; H, 6·0. $C_{24}H_{25}O_6N$ requires C, 68·1; H, 5·9%), were prepared by the usual procedure.

9-*Methylcarbazole*-3 : 6-*bis*-γ-*ketobutyric acid*, colourless prisms, m. p. 268° (decomp.), from glacial acetic acid (Found: C, 65·3; H, 5·0. $C_{21}H_{19}O_6N$ requires C, 66·1; H, 5·0%), and its *ethyl* ester, colourless needles, m. p. 142°, from alcohol (charcoal) (Found: C, 69·0; H, 6·2. $C_{25}H_{27}O_6N$ requires C, 68·6; H, 6·2%), were similarly prepared from 9-methylcarbazole. The latter ester (mixed m. p.) was also obtained when ethyl carbazole-3 : 6-bis-γ-ketobutyrate (above) was shaken in acetone with methyl sulphate and potassium hydroxide; the product was precipitated with water and crystallised from alcohol.

The keto-acid (4 g.) was refluxed with glacial acetic acid (40 c.c.) and amalgamated zinc (40 g.) while concentrated hydrochloric acid (40 c.c.) was added in portions during 4 hours. After filtration, *carbazole*-3 : 6-*dibutyric acid*, m. p. 197—198° (after recrystallisation from aqueous acetic acid), separated in colourless plates (2 g.), on cooling (Found: C, 70·6; H, 6·2. $C_{20}H_{21}O_4N$ requires C, 70·8; H, 6·2%). No satisfactory product was obtained during several attempts to effect cyclisation in this substance with the formation of a diketo-octahydrodinaphthacarbazole.

6-*Acetyl- and* 6-*Ethyl-hexahydrocarbazole*.—A mixture of 9-acetylhexahydrocarbazole (5 g.), carbon disulphide (30 c.c.), and acetyl chloride (3 c.c.) was treated gradually with aluminium chloride (15 g.), and, after being kept for 3 hours, was refluxed for a further hour. After the solvent had been distilled off, the residue was scraped on to ice–dilute hydrochloric acid, and the product crystallised from alcohol; 6 : 9-*diacetylhexahydrocarbazole* was obtained in colourless prisms (4 g.), m. p. 123—125° (Found: N, 5·4. $C_{16}H_{19}O_2N$ requires N, 5·5%). It was hydrolysed by refluxing for ½ hour with concentrated hydrochloric acid. The product was isolated by making the solution alkaline with ammonia, extracting the base with ether, drying with potassium carbonate, and evaporating the extract. After purification by distillation under reduced pressure, 6-*acetylhexahydrocarbazole*, b. p. 251°/25 mm., was obtained as a very viscous, yellow oil which slowly solidified on keeping (Found: C, 78·1; H, 8·0. $C_{14}H_{17}ON$ requires C, 78·1; H, 7·9%); it melted again at 73°.

A solution of 6-ethyltetrahydrocarbazole (3 g., Plant and Williams, *loc. cit.*) in sulphuric acid (150 c.c. of 60%) was reduced in the cathode compartment of an electrolytic cell during 15 hours at room temperature, lead electrodes and a current of 4 amps. (approx. 0·02 amp./sq. cm. of cathode) being used. The oily base, liberated when the solution was diluted with water and made alkaline with ice–ammonia, was extracted with ether. After the extract had been dried and evaporated, the residual 6-*ethylhexahydrocarbazole*, b. p. 182°/20 mm., was distilled under reduced pressure (Found: C, 83·4; H, 9·5. $C_{14}H_{19}N$ requires C, 83·6; H, 9·4%). The colourless oil solidified in a freezing mixture and melted again at 30—32°. When the base was shaken in acetone with potassium hydroxide and the theoretical amount of *p*-nitrobenzoyl chloride, and the mixture diluted with water, 9-p-*nitrobenzoyl*-6-*ethylhexahydrocarbazole*, pale yellow prisms, m. p. 153°, from alcohol, was precipitated (Found: C, 72·0; H, 6·4. $C_{21}H_{22}O_3N_2$ requires C, 72·0; H, 6·3%).

6-Acetylhexahydrocarbazole (4 g.), or its 9-acetyl derivative, was refluxed with amalgamated zinc (30 g.), concentrated hydrochloric acid (90 c.c.), and water (25 c.c.) for 10 hours. After the solution had been filtered (hot) and made alkaline with sodium hydroxide, 6-ethylhexahydrocarbazole (0·6 g.) was obtained by distillation in steam. It was isolated by extraction with ether and purification as before, and its identity confirmed by conversion into the 9-*p*-nitrobenzoyl derivative, m. p. and mixed m. p. 153°.

THE DYSON PERRINS LABORATORY, OXFORD. [*Received, July* 18*th*, 1936.]