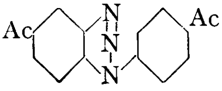
166. *The Friedel and Crafts Reaction in the Carbazole Series.*

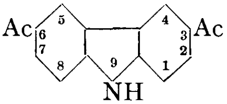
By S. G. P. Plant, (Miss) K. M. Rogers, and S. B. C. Williams.

An examination of the few recorded instances of the use of simple acid halides in Friedel and Crafts reactions in the carbazole series suggests that there may be a profound difference in the course adopted when the reaction is applied to 9-acylcarbazoles on the one hand and carbazoles with a free >NH group on the other. In the latter class carbazole itself appears to undergo substitution in both the 3- and the 6-position, even in the presence of a limited amount of the acid halide, and in 3-substituted carbazoles the process is completed by the introduction of a single acyl group in the 6-position (Plant and Tomlinson, J., 1932, 2188). The reaction with 9-acylcarbazoles appears to involve substitution of a single acyl radical into the 2-position (Borsche and Feise, *Ber.*, 1907, **40**, 378; I. G. Farbenind. Akt.-Ges., D.R.-P. 555,312; Plant and Williams, J., 1934, 1142). The main object of the present work has been to investigate the validity of this generalisation.

When carbazole was treated with acetyl bromide (two molecular proportions) and aluminium chloride in carbon disulphide, a diacetylcarbazole (m. p. 232°) was obtained. The use of restricted amounts of acetyl bromide in efforts to prepare a monoacetyl derivative resulted in the recovery of considerable quantities of carbazole. Attempts to identify this product have involved the synthesis along the usual lines of 5 : *4′-diacetyl-1-phenylbenzotriazole* (I) and *5-acetyl-1-phenyl-4′-ethylbenzotriazole*, but efforts to convert these substances into carbazole derivatives with loss of nitrogen were unsuccessful. The latter would have given 3-acetyl-6-ethylcarbazole, but it was hoped to identify the 3 : 6-diethyl-

(I.)





(II.)

carbazole obtained on reduction with the product obtained by reducing the diacetyl compound of m. p. 232°.

Ultimately 3 : 6-*diethylcarbazole* was synthesised by condensing 4-ethyl*cyclo*hexanone with *p*-ethylphenylhydrazine, converting the hydrazone by Fischer's reaction into 3 : 6-*diethyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, and oxidising the latter with sulphur in boiling quinoline. It proved to be identical with the product obtained by applying Clemmensen's method of reduction to the diacetyl compound mentioned above, and it therefore follows that the Friedel and Crafts reaction with carbazole and acetyl bromide leads to 3 : 6-*diacetylcarbazole* (II).

The generalisation has been further tested by treating, first, 3-benzoylcarbazole with acetyl bromide and aluminium chloride, and, secondly, 3-acetylcarbazole with benzoyl chloride and aluminium chloride. The products were identical, from which it follows that they must be 3-*benzoyl*-6-*acetylcarbazole*.

In order to study the reaction with the 9-alkylcarbazoles, 9-methylcarbazole was treated with acetyl bromide and aluminium chloride in carbon disulphide; the product was 3 : 6-*diacetyl*-9-*methylcarbazole*, identical with the substance obtained by methylating the 3 : 6-diacetylcarbazole described above. The use of only one molecular proportion of acetyl bromide also resulted in the formation of a considerable quantity of the diacetyl compound, there being no indication of the presence of any appreciable amount of a monoacetyl derivative.

In the conversion of 9-benzoylcarbazole by benzoyl chloride and aluminium chloride into 3 : 6-dibenzoylcarbazole (Plant and Tomlinson, *loc. cit.*) migration of the benzoyl group to the 3-position, which is known to be induced by aluminium chloride, must precede substitution. In several attempts to repeat the preparation of 3 : 6-dibenzoylcarbazole in this way, however, the main product has been the isomeric 2 : 9-*dibenzoylcarbazole*, formed in accordance with the generalisation mentioned above. It was found to be easily hydrolysed to 2-*benzoylcarbazole*, the constitution of which was proved by the fact that it gave carbazole-2-carboxylic acid on fusion with potassium hydroxide. These discordant observations in this particular reaction have not been traced to any obvious variations in conditions, and are probably due to very minor changes in the quality of the materials used.

9-Acetylcarbazole has been converted by a similar process into 2-*benzoyl*-9-*acetylcarbazole*, which has also yielded 2-benzoylcarbazole on hydrolysis. This preparation and characterisation of 2-benzoylcarbazole is of interest in view of a statement (D.R.-P. 555,312) to the effect that 2-benzoylcarbazole results as a compound melting above 360° from the benzoylation of 9-acetylcarbazole in carbon tetrachloride with aluminium chloride and a little iodine, and subsequent hydrolysis. In the absence of further details it is impossible to say what this product can be, but it is apparently not 2-benzoylcarbazole.

EXPERIMENTAL.

3 : 6-*Diacetylcarbazole*.—A mixture of carbazole (6 g.), carbon disulphide (50 c.c.), and pulverised aluminium chloride (10 g.) was treated with acetyl bromide (9 g.), the whole refluxed for an hour, and the solvent allowed to evaporate. The 3 : 6-*diacetylcarbazole* obtained by treating the residue with ice–dilute hydrochloric acid was isolated in colourless prisms, m. p. 232°, after two crystallisations from alcohol (Found : C, 76·4; H, 5·5. $C_{16}H_{13}O_2N$ requires C, 76·5; H, 5·2%).

When a solution of this substance (1 g.) in acetone (20 c.c.) was shaken with aqueous potassium hydroxide (3 g. of 35%) and acetyl chloride (3 c.c.) for 10 minutes and then diluted with water, 3 : 6 : 9-*triacetylcarbazole*, colourless needles, m. p. 220°, from acetic acid, was obtained (Found : C, 73·7; H, 5·2. $C_{18}H_{15}O_3N$ requires C, 73·7; H, 5·1%). By a similar process, using methyl sulphate instead of acetyl chloride, 3 : 6-*diacetyl*-9-*methylcarbazole*, colourless prisms, m. p. 192°, from acetic acid, was prepared (Found : C, 76·8; H, 5·6. $C_{17}H_{15}O_2N$ requires C, 77·0; H, 5·7%).

5 : 4′-*Diacetyl*-1-*phenylbenzotriazole*.—A mixture of *p*-aminoacetophenone (5·3 g.), 4-bromo-3-nitroacetophenone (9 g.), and potassium carbonate (4·5 g.) with a little copper powder was heated in an oil-bath at 150° and stirred until frothing ceased and a pasty mass resulted. The product was extracted several times with alcohol, and the united extracts boiled for 10 minutes

with charcoal. 2-*Nitro*-4 : 4′-*diacetyldiphenylamine*, red prisms, m. p. 177°, from methyl alcohol, was precipitated in poor yield when the filtered solution was poured into dilute hydrochloric acid (Found : C, 63·7; H, 4·9; N, 9·8. $C_{16}H_{14}O_4N_2$ requires C, 64·4; H, 4·7; N, 9·4%). A solution of this compound (1·1 g.) in glacial acetic acid (15 c.c.) was boiled with stannous chloride (5 g.) and concentrated hydrochloric acid (12 c.c.) for 10 minutes, cooled, and made alkaline with concentrated aqueous sodium hydroxide. The resulting amine, which was extracted with ether and recovered by evaporation of the dried solution, was dissolved in warm acetic acid (10 c.c.) and treated with sodium nitrite (0·3 g. in a little water). The addition of more water completed the precipitation of 5 : 4′-*diacetyl*-1-*phenylbenzotriazole*, colourless plates, m. p. 224°, from alcohol (Found : N, 15·1. $C_{16}H_{13}O_2N_3$ requires N, 15·1%).

5-*Acetyl*-1-*phenyl*-4′-*ethylbenzotriazole*.—Prepared from *p*-aminoethylbenzene by a process similar to that described above for 2-nitro-4 : 4′-diacetyldiphenylamine, but with the omission of the copper powder, 2-*nitro*-4-*acetyl*-4′-*ethyldiphenylamine* separated from methyl alcohol in red prisms, m. p. 85° (Found : N, 10·0. $C_{16}H_{16}O_3N_2$ requires N, 9·9%). The nitro-compound was converted as before into the corresponding amine, yellow prisms, m. p. 106°, from alcohol, and then into 5-*acetyl*-1-*phenyl*-4′-*ethylbenzotriazole*, colourless needles, m. p. 143°, from alcohol (Found : N, 16·2. $C_{16}H_{15}ON_3$ requires N, 15·9%).

3 : 6-*Diethylcarbazole and its Synthesis*.—Granulated zinc (200 g.) was left in aqueous mercuric chloride (400 c.c. of 5%) for an hour, the solution was poured away, and 3 : 6-diacetylcarbazole (3 g.) added. The mixture was shaken with concentrated hydrochloric acid (50 c.c.) for a few minutes and left over-night. After the addition of anisole (5 c.c.) and more concentrated hydrochloric acid (20 c.c.), the whole was refluxed for 12 hours, and the product extracted with ether. The extract was washed with dilute hydrochloric acid, water, and aqueous sodium carbonate, then dried and evaporated, the anisole being removed from the residue by steam distillation. The product was taken up in ether and purified by distillation under reduced pressure; the distillate solidified, and, on crystallisation from acetic acid, 3 : 6-*diethylcarbazole* was obtained in colourless plates, m. p. 119° (Found : C, 85·5; H, 7·4; N, 6·3. $C_{16}H_{17}N$ requires C, 86·1; H, 7·6; N, 6·3%).

p-Ethylphenol, b. p. 212—215° (compare Beilstein and Kuhlberg, *Annalen*, 1870, **156**, 206), prepared from sodium *p*-ethylbenzenesulphonate (Sempotowski, *Ber.*, 1889, **22**, 2662) by fusion with sodium hydroxide, was reduced to 4-ethyl*cyclo*hexanol, b. p. 194—196° (compare von Braun, Mannes, and Reuter, *Ber.*, 1933, **66**, 1499), by passing its vapour together with hydrogen slowly over nickel on pumice at 220°, a certain amount of the unchanged phenol being recovered from the product by extraction with alkali. 4-Ethyl*cyclo*hexanone (5·5 g., b. p. 192—194°; compare von Braun, Mannes, and Reuter, *loc. cit.*), obtained from the ethyl*cyclo*hexanol as described by Baeyer (*Annalen*, 1894, **278**, 100) for *cyclo*hexanone, was warmed on the steam-bath for a few minutes with *p*-ethylphenylhydrazine (7 g.; see Plant and Williams, *loc. cit.*), and the product boiled for 10 minutes with water (135 c.c.) and concentrated sulphuric acid (15 c.c.). The 3 : 6-*diethyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, colourless prisms (5 g.), m. p. 87—88°, from methyl alcohol, which separated as an oil and solidified on cooling (Found : N, 6·4. $C_{16}H_{21}N$ requires N, 6·2%), was boiled (4·35 g.) with sulphur (1·25 g.) in pure quinoline (30 c.c.) for ½ hour. The product obtained when the resulting solution was poured (cold) on ice–dilute hydrochloric acid was extracted with ether, and the extract dried and evaporated. After the solid residue had been distilled under reduced pressure with a small quantity of iron filings, 3 : 6-diethylcarbazole, identified by mixed m. p. with the substance described above, was obtained; it was isolated in colourless plates, m. p. 117—119°, after crystallisation from acetic acid and then methyl alcohol.

3-*Benzoyl*-6-*acetylcarbazole*.—Further experience of the method described by Plant and Williams (*loc. cit.*) for converting 9-acetylcarbazole into 3-acetylcarbazole by heating with aluminium chloride has shown that the procedure is not always entirely satisfactory and on several occasions the reaction has proved to be more complex than the simple isomeric change. It has now been found that the process is very much more reliable when carried out in nitrobenzene. A solution of 9-acetylcarbazole (14 g.) in nitrobenzene (120 c.c.) was treated with aluminium chloride (10 g.), warmed to 120°, and kept at that temperature with occasional shaking for 15 minutes. The whole was poured, when cold, into dilute hydrochloric acid, and the nitrobenzene removed in steam. The residue was boiled in alcohol with charcoal, and the product precipitated from the filtered solution by pouring into dilute hydrochloric acid. When this was crystallised from toluene, reasonably pure 3-acetylcarbazole (5·6 g.), m. p. 162° after softening from 157°, was obtained.

A solution of 3-acetylcarbazole (1·5 g.), aluminium chloride (2 g.), and benzoyl chloride (2 g.)

in nitrobenzene (50 c.c.) was kept at room temperature for a day. The product, isolated as above, was boiled in acetone with charcoal, and 3-*benzoyl*-6-*acetylcarbazole*, grey prisms, m. p. 210°, after being recrystallised from toluene and then twice from acetic acid, was isolated after filtration by precipitation with dilute hydrochloric acid (Found : C, 80·6; H, 4·5. $C_{21}H_{15}O_2N$ requires C, 80·5; H, 4·8%). The same substance (mixed m. p.) was also obtained when the reactants were refluxed in carbon disulphide for an hour.

Aluminium chloride (1·3 g.) and then acetyl bromide (1·5 c.c.) were added to 3-benzoylcarbazole (1·3 g.; Plant and Tomlinson, *loc. cit.*) in carbon disulphide (30 c.c.), the mixture was refluxed for 6 hours, the solvent allowed to evaporate, and the residue treated with ice–dilute hydrochloric acid. After the whole had been warmed on the steam-bath for a few minutes, the aqueous liquid was removed by decantation, and the sticky residue purified by boiling in alcohol (170 c.c.) with charcoal for 10 minutes. The 3-benzoyl-6-acetylcarbazole which was recovered from the solution separated in pale green prisms, m. p. 209—210°, after crystallisation from acetic acid and then alcohol, and was identified (mixed m. p.) with the compound described above.

3 : 6-*Diacetyl*-9-*methylcarbazole*.—Prepared from 9-methylcarbazole by a process similar to that described for 3 : 6-diacetylcarbazole, 3 : 6-diacetyl-9-methylcarbazole was purified by crystallisation from alcohol and then acetic acid, and identified by mixed m. p. with the product mentioned above.

2-*Benzoylcarbazole and its Derivatives*.—9-Benzoylcarbazole (5 g., prepared as described by Mazzara, *Ber.*, 1891, **24**, 278) was refluxed for 4 hours in carbon disulphide (30 c.c.) with benzoyl chloride (3 c.c.) and aluminium chloride (15 g.), the solvent was allowed to evaporate, and the residue treated with ice–dilute hydrochloric acid. When the product was crystallised from alcohol (about 300 c.c.), 2 : 9-*dibenzoylcarbazole*, colourless prisms, m. p. 140—142°, from toluene, was obtained (Found : N, 3·7. $C_{26}H_{17}O_2N$ requires N, 3·7%). By a similar procedure 2-*benzoyl*-9-*acetylcarbazole*, pale brown needles, m. p. 136—137°, from alcohol, was prepared from 9-acetylcarbazole (Found : N, 4·3. $C_{21}H_{15}O_2N$ requires N, 4·5%).

Both of these substances were hydrolysed by refluxing with aqueous–alcoholic potassium hydroxide for an hour, 2-*benzoylcarbazole*, greenish-yellow plates, m. p. 163°, from glacial acetic acid, being precipitated from the resulting solution by the addition of water (Found : C, 83·9; H, 4·9; N, 5·3. $C_{19}H_{13}ON$ requires C, 84·1; H, 4·8; N, 5·2%). This compound was rebenzoylated by heating with benzoyl chloride at 160—170° for 2 hours, and re-acetylated by refluxing for 2 hours with acetic anhydride containing a trace of sulphuric acid, the products being identified with the substances described above by mixed m. p.

2-Benzoylcarbazole (1·5 g.) was added gradually with stirring to a molten mixture of potassium hydroxide (15 g.) and water (0·75 g.). After the cold residue had been dissolved in water, the addition of sulphuric acid to the filtered solution precipitated carbazole-2-carboxylic acid, colourless prisms, m. p. 320—322°, after crystallisation from aqueous alcohol. This compound was identified by mixed m. p. with an authentic specimen (Plant and Williams, *loc. cit.*) and by conversion into its ethyl ester, m. p. 184°.

THE DYSON PERRINS LABORATORY, OXFORD.

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