786. *Heterocyclic Fluorine Compounds. Part I. Monofluoro-1 : 2 : 3 : 4-tetrahydrocarbazoles and Monofluorocarbazoles.*

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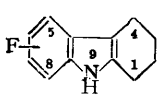
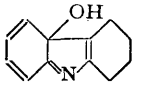
The four monofluorocarbazoles and monofluoro-1 : 2 : 3 : 4-tetrahydrocarbazoles substituted in the benzene ring have been prepared by a Borsche synthesis and suitably characterised. Since the Borsche method led to an ambiguous result with 2- and 4-fluorocarbazole, these compounds were also made by an unambiguous route. The preparation of 1- and 3-fluorocarbazole by Balz–Schiemann reaction of the corresponding aminocarbazoles is also described.

5-, 6-, 7-, and 8-Fluoro-1 : 2 : 3 : 4-tetrahydrocarbazoles (as I) have been made by a Borsche synthesis from the *o*-, *m*-, and *p*-fluorophenylhydrazones of *cyclo*hexanone (cf. *J.*, 1953, 3326). Cyclisation of *cyclo*hexanone *m*-fluorophenylhydrazone led to a mixture of 5-fluoro- and 7-fluoro-1 : 2 : 3 : 4-tetrahydrocarbazole. An attempt to separate the mixture by chromatography in ultra-violet light led to decomposition of the substances, and a liquid chromatogram had to be used. The constituents were indirectly identified by dehydrogenating them to the corresponding fluorocarbazoles which were then compared with unambiguously synthesised reference compounds. The preparation of 7-fluoro-1 : 2 : 3 : 4-tetrahydrocarbazole as a reference compound from the corresponding amino-

compound by a Balz–Schiemann reaction was unsuccessful. A fluorine-free substance of high melting point was obtained which is reminiscent of the Bismarck brown formation. The two chromatographically separated fluorotetrahydrocarbazoles, m. p.s 18° and 142°, yielded 4- and 2-fluorocarbazole on dehydrogenation, and were therefore 5- and 7-fluorotetrahydrocarbazoles, respectively. Cyclisation of *cyclo*hexanone *o*-fluorophenylhydrazone in glacial acetic acid yielded only 8-fluoro-1 : 2 : 3 : 4-tetrahydrocarbazole. When, however, dilute sulphuric acid was used, a small quantity of a by-product, m. p. 167°, was isolated, possessing phenolic properties and containing no fluorine. This is possibly identical with the so-called " 1 : 2 : 3 : 4-tetrahydro-12-hydroxy*iso*carbazole " (II), m. p. 172° (Barnes, Pausacker, and Schubert, *J.*, 1949, 1381), which has recently been regarded as 1 : 2 : 3 : 4-tetrahydro-6-hydroxycarbazole by Milne and Tomlinson (*J.*, 1952, 2789).



(I)



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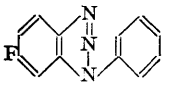

(III)

The fluorotetrahydrocarbazoles were converted into the corresponding fluorocarbazoles by refluxing them with chloranil in sulphur-free xylene (Barclay and Campbell, *J.*, 1945, 530). This dehydrogenation required longer reflux times and gave smaller yields than that of the corresponding chloro- and bromo-compounds (cf. *idem, loc. cit.*). Since 2- and 4-fluorocarbazole were needed as reference compounds in the ambiguous ring-closure of *cyclo*hexanone *m*-fluorophenylhydrazone, they were prepared by an additional synthesis. 2-Fluorocarbazole was obtained by a Graebe–Ullmann synthesis : 5-fluoro-2-nitrodiphenylamine (in the press) was reduced to the 2-amino-compound which on diazotisation afforded the fluorobenzotriazole (III). Prolonged strong heating of (III) in a sealed tube yielded a small quantity of 2-fluorocarbazole. Low yields attending a Graebe–Ullmann reaction with negatively substituted triazoles appear to be general (cf. Preston, Tucker, and Cameron, *J.*, 1942, 500; Clifton and Plant, *J.*, 1951, 461).

4-Fluorocarbazole was made by a Borsche reaction from *cyclo*hexanone 3-fluoro-6-methylphenylhydrazone (Suschitzky, in the press). Treatment with acetic acid gave the 5-fluoro-1 : 2 : 3 : 4-tetrahydro-8-methylcarbazole which on dehydrogenation with chloranil gave 4-fluoro-1-methylcarbazole and a small quantity of the 1-carboxylic acid; the latter presumably arising by oxidation of the methyl group.

The methyl group, which had prevented the cyclisation of the hydrazone taking place in two directions, was eliminated by oxidation of the methylcarbazole to the carboxylic acid with selenium dioxide and hydrogen peroxide, followed by decarboxylation with copper chromite (Plant and Wilson, *J.*, 1939, 237). It is of interest that this 1-methyl group responds to oxidative attack by selenium dioxide in a manner generally observed with activated methyl groups in heterocyclic compounds.

2- and 4-Fluorocarbazole were also made by dehydrogenation of the mixture of the 5- and 7-fluorotetrahydrocarbazoles, followed by chromatographic separation of the reaction product in ultra-violet light. It was observed that the adsorptive behaviour of the 2- and 4-fluorocarbazole is similar to that of their parent tetrahydrocarbazoles. This relationship seems to indicate that the extent of hydrogen-bond association is of the same order in both series of compounds (Hoyer, *Kolloid Z.*, 1951, **121**, 121).

The identities of 1- and 3-fluorocarbazole were confirmed by a Balz–Schiemann reaction on the corresponding aminocarbazoles.

Experimental

Diazonium borofluorides were decomposed in dry nitrogen. Diazonium nitrogen in diazonium borofluorides was estimated by Schiemann and Pillarsky's method (*Ber.*, 1929, **62**, 3035). In chromatograms activated alumina, type H (P. Spence), was used.

Fluorine-substituted Tetrahydrocarbazoles.—The *cyclo*hexanone fluorophenylhydrazones (Suschitzky, in the press) were cyclised by refluxing them with five times their weight of glacial acetic acid for 0·5—1 hr., except that the *o*-fluorophenylhydrazone had to be heated

for 3 hr. The crude product obtained by dilution of the reaction mixture with aqueous ethanol or water was washed free from acid (dilute ammonia solution) and then recrystallised. The *m*-fluorophenylhydrazone (6 g.) yielded a mixture (5·4 g.; 6 : 5) of 5-fluoro- and 7-fluoro-1 : 2 : 3 : 4-tetrahydrocarbazole; these were separated in benzene solution (350 c.c.) on alumina (40 cm. × 1·5 cm.). The chromatogram was developed with light petroleum (b. p. 60—80°)–benzene (1 : 9) to which in the later stages 1% of carbon tetrachloride was added. The least strongly adsorbed fraction yielded the 7-fluoro-isomer; the 5-fluoro-isomer was obtained from subsequent percolates.

5-*Fluoro*-1 : 2 : 3 : 4-*tetrahydrocarbazole* (39·4%), m. p. 18°, was unstable to light (Found: C, 76·1; H, 6·1; N, 7·7. $C_{12}H_{12}NF$ requires C, 76·2; H, 6·3; N, 7·4%). The *picrate* formed small red needles, m. p. 156°, from ethanol (Found: N, 13·2. $C_{18}H_{15}O_7N_4F$ requires N, 13·4%), and the s-*trinitrobenzene* derivative blood-red needles, m. p. 175°, from ethanol (Found: N, 13·6. $C_{18}H_{15}O_6N_4F$ requires N, 13·9%).

6-*Fluoro*-1 : 2 : 3 : 4-*tetrahydrocarbazole* was obtained as plates (71·8%), m. p. 103—104°, from benzene–light petroleum (1 : 1) (Found: C, 76·0; H, 6·5; N, 7·1%). The *picrate* formed copper-coloured, feathery crystals, m. p. 140°, from ethanol (Found: N, 13·4%), and the s-*trinitrobenzene* derivative dark-red needles, m. p. 150° (Found: N, 14·1%).

7-*Fluoro*-1 : 2 : 3 : 4-*tetrahydrocarbazole* (29·6%), plates (from ethanol), m. p. 142°, was unstable to light (Found: C, 76·2; H, 6·1; N, 7·3%). The *picrate* was obtained as long, red needles, m. p. 129°, from ethanol (Found: N, 13·2%), and the s-*trinitrobenzene* derivative as red, feathery needles, m. p. 156°, also from ethanol (Found: N, 14·0%).

In another experiment, 7-amino-1 : 2 : 3 : 4-tetrahydrocarbazole hydrochloride (1·5 g.), made by Perkin and Plant's method (*J.*, 1921, 1825; 1923, 676), was diazotised in 40% aqueous acetic acid with solid sodium nitrite at low temperature in the presence of sodium borofluoride. Strong effervescence was observed, and the product, a dark-brown solid, m. p. 240—300°, containing a trace of fluorine, was not further investigated.

8-*Fluoro*-1 : 2 : 3 : 4-*tetrahydrocarbazole* was obtained as plates (56%), m. p. 71°, from benzene–light petroleum (3 : 2) (Found: C, 76·3; H, 6·6; N, 7·6%). The *picrate* formed blood-red needles, m. p. 128—129°, from ethanol (Found: N, 13·6%), and the s-*trinitrobenzene* derivative dark-red needles, m. p. 126° (Found: N, 14·2%).

In a second experiment *cyclo*hexanone *o*-fluorophenylhydrazone (4 g.) was heated with aqueous sulphuric acid (1 : 8 by vol.; 40 g.) for 1 hr. Extraction of the syrupy product with light petroleum (b. p. 60—80°) yielded 8-fluoro-1 : 2 : 3 : 4-tetrahydrocarbazole (29%). Treatment of the oily residue with saturated ethanolic picric acid and basification (ammonia) of the resulting dark-red solution afforded a solid, m. p. 165—167° (0·05 g.) which might have been the 6-hydroxy-compound or (II). It gave a negative test for fluorine and was soluble in sodium hydroxide solution.

5-*Fluoro*-1 : 2 : 3 : 4-*tetrahydro*-8-*methylcarbazole* formed small needles (74·5%), m. p. 43°, from light petroleum (b. p. 40°) which were unstable to light (Found: C, 77·0; H, 7·0; N, 6·6. $C_{13}H_{14}NF$ requires C, 76·8; H, 6·9; N, 6·9%). The *picrate* formed dark-red rosettes, m. p. 137°, from ethanol or benzene (Found: N, 13·3. $C_{19}H_{17}O_7N_4F$ requires N, 12·9%).

Fluorocarbazoles.—The fluorotetrahydrocarbazoles were dehydrogenated with chloranil in boiling xylene (Barclay and Campbell, *J.*, 1945, 530). After evaporation of the solvent on a steam-bath, the residue was refluxed with 3N-alcoholic potassium hydroxide (5% ethanol) for 0·5 hr., collected, washed with 3N-sodium hydroxide until the wash liquid was colourless, and finally recrystallised and sublimed. Details are given in the Table.

Tetrahydrocarbazole	Carbazole	Time of reflux, hr.	Yield, %
8-Fluoro-	1-*Fluoro*-	30	37
7-Fluoro-	2-*Fluoro*-	26	54
6-Fluoro-	3-*Fluoro*-	28	42
5-Fluoro-	4-*Fluoro*-	24	36
5-Fluoro-8-methyl-	4-*Fluoro*-1-*methyl*-	26	38

The product (2·0 g.) obtained by dehydrogenation of the mixture of 5- and 7-fluoro-tetrahydrocarbazole (see above) was resolved in benzene solution (2%) on alumina (28 cm. × 1·5 cm.). Benzene–light petroleum (5%; b. p. 40°) was used as developer until two distinct bands of bluish fluorescence (ultra-violet light) were obtained. Extraction of the lower and the upper band with ethanol yielded crude 2- and 4-fluorocarbazole, respectively. Results of dehydrogenation experiments are quoted under (*a*).

1-*Fluorocarbazole.* (*a*) This *carbazole* formed plates, m. p. 145°, from benzene (Found: C, 77·7; H, 4·2; N, 7·8. $C_{12}H_8NF$ requires C, 77·8; H, 4·3; N, 7·6%). The *picrate* was obtained

as red needles, m. p. 152—153°, from ethanol (Found: N, 13·3. $C_{18}H_{11}O_7N_4F$ requires N, 13·5%), and the s-*trinitrobenzene* derivative as orange needles, m. p. 156—160° (Found: N, 14·4. $C_{18}H_{11}O_6N_4F$ requires N, 14·1%). The N-*nitroso*-derivatve was prepared in glacial acetic acid with aqueous sodium nitrite (20%; 1 equiv.) and formed lemon-coloured plates, m. p. 106°, from ethanol (Found: N, 13·4. $C_{12}H_7ON_2F$ requires N, 13·1%).

(*b*) In another preparation, *o*-nitrophenylhydrazine (10 g.), prepared by Bischler's method (*Ber.*, 1889, **22**, 2801), was condensed with *cyclo*hexanone (6·4 g.), and the resulting hydrazone boiled with aqueous sulphuric acid (1 acid : 9 water, v/v) for 3 hr. The resulting tetrahydro-8-nitrocarbazole (69·2%) yielded 1-nitrocarbazole, m. p. 186° (51%), on treatment with chloranil. The nitro-compound (3 g.) was dissolved in a hot mixture of ethanol (40 c.c.) and 40% aqueous potassium hydro xide solution (12 c.c.), and 20% aqueous sodium dithionite solution (60 c.c.) added dropwise until the mixture became colourless. Addition of a large excess of water yielded 1-aminocarbazole, greyish needles (from benzene), m. p. 190° (decomp.) [Lindemann and Werther (*Ber.*, 1924, **57**, 1316) give m. p. 193°]. This (1·5 g.) was triturated with concentrated hydrochloric acid (20 c.c.) and water (10 c.c.) and then diazotised at −20° with solid sodium nitrite (0·7 g.). Addition of sodium borofluoride solution (40%; 5 c.c.) yielded *carbazole-1-diazonium borofluoride* as a pale-green solid (56%), decomp. 107—110° (Found: diazonium N, 10·5. $C_{12}H_8N_3F_4B$ requires diazonium N, 10·0%). Its pyrolysis afforded 1-fluorocarbazole (16%), m. p. 140° raised by admixture with sample (*a*) to 142—144°.

2-*Fluorocarbazole*. (*a*) The 2-*fluoro*-compound formed plates (sublimation), m. p. 221° (Found: C, 77·6; H, 4·5; N, 7·8%). It gave a *picrate*, light-red needles, m. p. 169° (Found: N, 13·6%), s-*trinitrobenzene* derivative, orange needles, m. p. 178° (Found: N, 14·0%), and N-*nitroso*-compound, pale green needles and plates, m. p. 88° (Found: N, 13·1%).

(*b*) An ethanolic solution of 3-fluoro-6-nitrodiphenylamine (5 g.) (Suschitsky, in the press) was added gradually to hot ethanolic stannous chloride (15 g. of the dihydrate) containing concentrated hydrochloric acid (50 c.c.). 6-*Amino*-3-*fluorodiphenylamine* (70·6%), m. p. 87°, was obtained in greyish needles (from benzene) (Found: C, 71·1; H, 5·4; N, 14·1. $C_{12}H_{11}N_2F$ requires C, 71·3; H, 5·4; N, 13·8%). Alternatively the reduction was carried out in higher yield (77%) by addition of sodium dithionite (excess) to the nitro-compound (5 g.) dissolved in ethanol (200 c.c.) and 40% potassium hydroxide (100 c.c.). The amine (2 g.) was diazotised in 10% sulphuric acid (15 c.c.) containing some ethanol (2 c.c.) with solid sodium nitrite (0·7 g.) at 0°. After 2 hr. at room temperature the mixture deposited a solid which was purified by sublimation yielding 6-*fluoro*-1-*phenylbenzotriazole* as needles (62%), m. p. 113—115° (Found: C, 67·7; H, 3·4; N, 19·6. $C_{12}H_8N_3F$ requires C, 67·6; H, 3·7; N, 19·7%). The triazole (2 g.) was heated in a sealed tube at 350—380° for 2 hr. and the product extracted with light petroleum (b. p. 60—80°). 2-Fluorocarbazole was obtained on sublimation as iridescent plates (21%), m. p. and mixed m. p. with a sample from (*a*) 218—220°.

3-*Fluorocarbazole*. (*a*) The 3-*isomer* crystallised from ethanol in plates, m. p. 202—203° (Found: N, 7·4%). The *picrate*, rosettes of red needles, had m. p. 157—159° (Found: N, 13·9%), the s-*trinitrobenzene* derivative, red needles, m. p. 175° (Found: N, 14·2%), and the N-*nitroso*-derivative, lemon-coloured plates, m. p. 116° (Found: N, 13·0%).

(*b*) Carbazole residues (containing 40% of carbazole) were purified by several recrystallisations from toluene. To remove anthracene, the product (16 g.), m. p. 242°, and maleic anhydride (2 g.) were refluxed in toluene (270 c.c.) for 5 hr., slightly cooled, and filtered. The filtrate deposited pure carbazole in plates, m. p. 246° (corr.); a solution in concentrated sulphuric acid was colourless. 3-Nitrocarbazole (10 g.), prepared by Lindemann's method (*Ber.*, 1924, **57**, 555), was dissolved in a mixture of ethanol (125 c.c.) and aqueous potassium hydroxide (50 c.c.; 40%) and reduced with 20% sodium dithionite solution (200 c.c.). Addition of water (500 c.c.) afforded 3-aminocarbazole (77%), silver-grey plates (from toluene), m. p. 250° (Found: C, 79·2; H, 5·3; N, 15·0. Calc. for $C_{12}H_{10}N_2$: C, 79·1; H, 5·5; N, 15·3%). Ruff and Stein (*Ber.*, 1901, **34**, 1668) give m. p. 254°. The amine (3 g.) was triturated with hydrochloric acid (50 c.c.; containing 15 c.c. of concentrated hydrochloric acid) and then diazotised with 20% sodium nitrite solution at 8—10°. The filtrate deposited brown needles which were collected and dissolved in lukewarm water. Addition of hydroborofluoric acid (5 c.c.; 34% w/w) yielded pale-green, light-sensitive *carbazole-3-diazonium borofluoride* (89%), m. p. 145° (decomp.) (from aqueous acetone) (Found: diazonium N, 10·2. $C_{12}H_8N_3F_4B$ requires diazonium N, 10·0%). Decomposition of the borofluoride was accompanied by sublimation of dark-green particles with bluish fluorescence. The brown residue was extracted with warm light petroleum (b. p. 60—80°), and the extract washed with sodium hydroxide solution (20%), dried, and evaporated. Sublimation of the residue afforded plates of 3-fluorocarbazole (38%),

m. p. 204—205°, mixed m. p. with a sample from (*a*) 204° (Found: C, 77·8; H, 4·4; N, 7·3. $C_{12}H_8NF$ requires C, 77·8; H, 4·3; N, 7·6%).

4-*Fluorocarbazole*. (*a*) The 4-*fluoro*-compound formed plates, m. p. and mixed m. p. with a sample from (*b*) 105° (Found: C, 77·7; H, 4·0; N, 7·8%). The *picrate* formed blood-red needles, m. p. 150° (Found: N, 13·7%), the s-*trinitrobenzene* derivative, orange needles, m. p. 157° (Found: N, 14·0%), and the N-*nitroso*-derivative, greenish plates, m. p. 119° (Found: N, 13·3%).

(*b*) The crude product from the chloranil treatment of 5-fluoro-1 : 2 : 3 : 4-tetrahydro-8-methylcarbazole was dissolved in a saturated ethanolic solution of picric acid. Cooling precipitated a dark-red solid which was decomposed with ice-cold ammonia solution and the product extracted with cold dioxan. A small residue was recognised as 4-*fluorocarbazole*-1-*carboxylic acid* (see below). Evaporation of the extract afforded 4-fluoro-1-methylcarbazole in small plates (from ethanol), m. p. 106—108° (Found: C, 78·2; H, 4·8; N, 7·3. $C_{13}H_{10}NF$ requires C, 78·3; H, 5·0; N, 7·0%). The *picrate* formed bright-red plates, m. p. 114° (Found: N, 12·8. $C_{19}H_{13}O_7N_4F$ requires N, 13·0%). To a well-stirred solution of 4-fluoro-1-methylcarbazole (1·2 g.) in decalin (40 c.c.) kept at about 170° selenium dioxide (0·7 g.) was gradually added, and after 2 hr. the mixture was cooled and filtered. The dark-brown oil obtained on evaporation of the filtrate under reduced pressure was treated with acetone (10 c.c.) and hydrogen peroxide (2 c.c.; 30%) and set aside for 16 hr. After addition of water (50 c.c.) the mixture was refluxed for several hours and the light-brown solid filtered off and recrystallised from aqueous acetone. 4-Fluorocarbazole-1-carboxylic acid was obtained as a white powder (32%), m. p. 287—289° (Found: C, 67·9; H, 3·6; N, 6·4. $C_{13}H_8O_2NF$ requires C, 68·1; H, 3·5; N, 6·1%). The acid (1 g.) and copper chromite (0·13 g.) were heated at about 195° in quinoline (25 c.c.) (Plant and Wilson, *J.*, 1939, 237) until evolution of gas had ceased (approx. 3 hr.); the mixture was then cooled, the solvent removed with hydrochloric acid, and the residue extracted with ether. Washing of the ethereal extract with sodium hydroxide solution and sublimation of the residue obtained from evaporation of the solvent afforded 4-fluorocarbazole (22%), m. p. 104°.

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