91. *The Preparation of 1-Substituted Carbazoles.*

By Neil Campbell and J. A. R. MacLean.

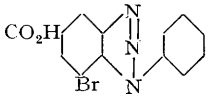
One successful and several unsuccessful attempts to prepare 1-substituted carbazoles are recorded. 3 : 6-Dibromo-1-aminocarbazole, when heated with concentrated hydriodic acid and red phosphorus, gives 1-aminocarbazole. *7-Bromo-1-phenylbenztriazole-5-carboxylic acid* loses bromine during the Graebe–Ullmann reaction to give carbazole. 9-Acetylcarbazole, when nitrated with Menke's reagent, gave little or no 1-nitrocarbazole and oxidation of 1-methylcarbazole yielded alkali-insoluble products which are probably dicarbazyls.

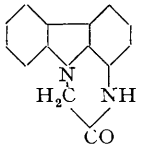
Mecke's reagent (selenious acid in sulphuric acid) is not specific for phenols, as it gives colorations also with diphenylamine, carbazole, and their derivatives.

The bromocarbazoles show characteristic orange fluorescence.

The preparation of 1-substituted carbazoles is difficult. Ullmann (*Annalen*, 1904, **332**, 84) obtained 1-methylcarbazole by the Graebe–Ullmann synthesis and Lindemann and Wessel (*Ber.*, 1925, **58**, 1221) prepared 1-aminocarbazole by a tedious process. This compound is obtained in good yield from 1-nitrocarbazole (Lindemann and Werther, *Ber.*, 1924, **57**, 1316), but the latter is obtained in poor yield by the nitration of carbazole (Lindemann, *ibid.*, p. 555; Morgan, J., 1931, 3283). Carbazole-1-carboxylic acid has been prepared (Ciamician and Silber, *Gazzetta*, 1882, **12**, 272; cf. Briscoe and Plant, J., 1928, 1990) with much loss in yield during purification. Gilman (*J. Org. Chem.*, 1937, **1**, 146) prepared the same acid by metalation. Other attempts to prepare 1-substituted carbazoles have been unsuccessful, Plant and Tomlinson (J., 1928, 2188), for example, failing to obtain 1-benzoylcarbazole by the Graebe–Ullmann synthesis. The present paper gives an account of attempts to find methods for preparing 1-substituted carbazoles.

3 : 4-Dibromo-5-nitrotoluene did not condense with aniline to give the required diphenylamine, the methyl group in the *p*-position apparently decreasing the reactivity of the 4-bromo-group. A similar effect has been noted with other bromonitrotoluenes (Lindemann and Pabst, *Annalen*, 1928, **462**, 24; Campbell, Anderson, and Gilmore, J., 1940, 446). The methyl group was therefore oxidised to carboxyl : the resulting acid condensed readily with aniline to give *2-bromo-6-nitrodiphenylamine-4-carboxylic acid* (cf. Schöpf, *Ber.*, 1889, **22**, 3281), from which *7-bromo-1-phenylbenztriazole-5-carboxylic acid* (I) was prepared. This compound, when heated at 360° with quicklime, yielded carbazole and not the expected 1-bromocarbazole.

(I.) 

 (II.)

The Graebe–Ullmann method has therefore certain limitations. Bremer (*Annalen*, 1934, **514**, 279) also noted this, though he indicated that monosubstituted carbazoles are readily prepared by the method.

It is well known that nitration with Menke's reagent (*Rec. Trav. chim.*, 1925, **44**, 141, 269) frequently gives *o*-substituted derivatives where other reagents give *p*-compounds. The nitration of 9-acetylcarbazole with this reagent was therefore investigated in the hope that the main product would be 1-nitro-9-acetylcarbazole. The results were unsatisfactory, but it was established that the yield of 1-nitrocarbazole was small.

1-Methylcarbazole (Ullmann, *loc. cit.*) was oxidised with various agents, but no carboxylic acid was obtained, the products being insoluble in alkali. They are probably dicarbazyls (cf. Tucker and Perkin, J., 1921, **119**, 217).

Finally we prepared 1-aminocarbazole by the following series of reactions : Carbazole ⟶ 3 : 6-dibromocarbazole ⟶ 3 : 6-dibromo-1-nitrocarbazole ⟶ 3 : 6-dibromo-1-aminocarbazole ⟶ 1-aminocarbazole. The first three reactions are known to work smoothly (Lindemann and Mühlhaus, *Ber.*, 1925, **58**, 2371). The removal of the bromine atoms by boiling with concentrated hydriodic acid gave a 35% yield of 1-aminocarbazole and thus afforded the best-known method of obtaining this compound. The compound was characterised by the preparation of *2′-ketopiperazino*(6′ : 4′ : 1 : 9)*carbazole* (II).

Mecke's reagent is a sensitive test for many alkaloids, but Levine's statement (*Centr.*, 1926, II, 925) that it is specific for phenolic compounds is incorrect, for it gives colorations with many derivatives of diphenylamine, carbazole, etc. The colorations are also obtained if selenic acid is substituted for selenious acid.

The fluorescence of the bromocarbazoles may be used for their detection and identification, brilliant orange fluorescence being observed in ultra-violet light.

Experimental.

Unless otherwise stated, the preparation, properties, and purification of compounds used are those given in the literature. M. p.'s were determined in Kofler's apparatus (*Mikrochem.*, 1934, **15**, 242) and analyses were done by Drs. Weiler and Strauss, Oxford. Fluorescence observations were made with ultra-violet light from a Hanovia mercury lamp provided with a filter to eliminate visible waves.

Attempted Preparation of 2-Bromo-6-nitro-4-methyldiphenylamine.—3 : 4-Dibromo-5-nitrotoluene (Cohen and Dutt, J., 1914, **105**, 510) was treated under different conditions with aniline, but even in the presence of copper bronze or anhydrous sodium acetate no condensation products were obtained. That the 4-bromo-group is not completely inactive was shown by heating the compound with piperidine at 50° for 2 hours; on cooling, yellow plates of piperidine hydrobromide, m. p. 210—225°, separated.

2-Bromo-6-nitrodiphenylamine-4-carboxylic Acid.—3 : 4-Dibromo-5-nitrotoluene (60 g.) and nitric acid (*d* 1·2; 1450 c.c.) were refluxed for 24 hours. The solution, when cooled, deposited a solid, which was shaken with sodium hydroxide solution; after filtration, the liquid was acidified with concentrated hydrochloric acid. Crystallisation from boiling water yielded 20 g. (30%) of 3 : 4-dibromo-5-nitrobenzoic acid in needles, m. p. 180—182° (lit., 183°). Other methods of oxidation gave less satisfactory results. The acid was heated over a naked flame with excess of aniline for 40 minutes. Concentrated hydrochloric acid was then added, and the mixture poured into water. *2-Bromo-6-nitrodiphenylamine-4-carboxylic acid* was obtained in golden-yellow crystals from benzene, m. p. 207—208°. It sublimed in lustrous plates (Found: C, 46·3; H, 2·8; Br, 23·7. $C_{13}H_9O_4N_2Br$ requires C, 46·3; H, 2·7; Br, 23·7%). The *methyl* ester, obtained in similar manner from methyl 3 : 4-dibromo-5-nitrobenzoate, formed light brown prisms, m. p. 151—152°, from benzene (Found: N, 8·4. $C_{14}H_{11}O_4N_2Br$ requires N, 8·0%).

7-Bromo-1-phenylbenztriazole-5-carboxylic Acid.—The preceding acid (6 g.) was heated for 24 hours on a water-bath with crystalline sodium sulphide (18 g.) and water (25 c.c.). Glacial acetic acid gave a precipitate, which was shaken with warm sodium carbonate solution; after filtration to remove sulphur, acidification with glacial acetic acid yielded *2-bromo-6-aminodiphenylamine-4-carboxylic acid*, which was crystallised from alcohol; m. p. 244—245°. It sublimed in colourless plates (Found: N, 9·2. $C_{13}H_{11}O_2N_2Br$ requires N, 9·1%). Yield, 4·5 g. (80%). The *acetyl* derivative, prepared by shaking the compound (0·2 g.) with water (1 c.c.) and acetic anhydride (12 drops) for 15 minutes, crystallised from methyl alcohol in white needles, m. p. 163—164° (Found: N, 8·2. $C_{15}H_{13}O_3N_2Br$ requires N, 8·0%). The amino-compound (4·5 g.) was dissolved in water (50 c.c.) containing sodium carbonate (1·8 g.) and, after slow addition of sodium nitrite (2·3 g.) in the minimum amount of water, was added drop by drop to well-stirred sulphuric acid (10%). Stirring was continued for 15 minutes, and the solution then kept at room temperature for 2 hours. *7-Bromo-1-phenylbenztriazole-5-carboxylic acid* separated and was obtained in almost quantitative yield from aqueous methyl alcohol, m. p. 215—217°. It sublimed in colourless needles or cubes (Found: N, 13·3. $C_{13}H_8O_2N_3Br$ requires N, 13·2%).

Graebe–Ullmann Reaction with 7-Bromo-1-phenylbenztriazole-5-carboxylic Acid.—The triazole (1·5 g.) was ground with freshly prepared quicklime (3 g.) and heated in a distilling flask to 360°. Micro-extraction of the sublimate and oily distillate yielded a light brown compound (0·1 g.), m. p. 220—230°, which did not contain bromine and proved to be carbazole (violet fluorescence; deep green colour with sulphuric acid and a trace of nitric acid; mixed m. p.).

2-Chloro-2'-nitrodiphenylamine.—*o*-Bromonitrobenzene (3 g.) was heated with excess of *o*-chloroaniline, potassium carbonate (1 g.), and a trace of copper bronze at 160—170° for 15 hours. The mixture was extracted with concentrated hydrochloric acid, and the residue with light petroleum (b. p. 100—120°). *2-Chloro-2'-nitrodiphenylamine* separated and was obtained in red prisms, m. p. 114°, from alcohol; yield, 1·1 g. (20%) (Found: C, 58·1; H, 3·5. $C_{12}H_9O_2N_2Cl$ requires C, 57·9; H, 3·6%).

1-Aminocarbazole.—3 : 6-Dibromo-1-aminocarbazole was obtained in 54% yield from 3 : 6-dibromo-1-nitrocarbazole (Lindemann and Mühlhaus, *loc. cit.*, give no yield). The acetyl compound sublimed in white lustrous plates, m. p. 262—264° (Found: N, 7·3. Calc. for $C_{14}H_{10}ON_2Br_2$: N, 7·3%). Lindemann and Mühlhaus (*loc. cit.*) did not give a m. p.

3 : 6-Dibromo-1-aminocarbazole (10 g.) was refluxed for 4 hours with hydriodic acid (*d* 1·94; 40 g.) and red phosphorus (3·5 g.), boiling water (25 c.c.) added, and the liquid filtered hot. The filtrate was treated until neutral with a saturated solution of sodium acetate, and the resulting 1-aminocarbazole crystallised from benzene, giving colourless needles, m. p. 193—195° (lit., 195°). Yield, 1·7 g. (30%) (Found: N, 15·3. Calc. for $C_{12}H_{10}N_2$: N, 15·4%).

2'-Ketopiperazino(6' : 4' : 1 : 9)carbazole.—1-Aminocarbazole (1·0 g.) in benzene (25 c.c.) was refluxed with bromoacetyl bromide (0·5 c.c.) in benzene (5 c.c.) for 30—35 minutes, and the solution kept overnight; it was then filtered and evaporated to half volume in a vacuum at room temperature. *1-ω-Bromoacetamidocarbazole* was obtained in colourless or pale green prisms, m. p. 188° (Found: Br, 26·1. $C_{14}H_{11}ON_2Br$ requires Br, 26·4%). 1-ω-Bromoacetamidocarbazole (0·5 g.), ethyl alcohol (100 c.c.), and 50% aqueous potassium hydroxide (1 c.c.) were refluxed for 30 minutes, and the solution kept overnight and then poured into 50 c.c. of concentrated hydrochloric acid. The precipitate was triturated with water and then with methyl alcohol and crystallised from xylene; it had m. p. 255°, subliming in colourless prisms. Yield, poor (Found: N, 12·0. $C_{14}H_{10}ON_2$ requires N, 12·5%).

Bromocarbazoles and Hydriodic Acid.—3 : 6-Dibromocarbazole (4 g.), hydriodic acid (*d* 1·94; 20 c.c.), and red phosphorus (1 g.) were refluxed for 4 hours, and the mixture poured into potassium iodide solution. The precipitate was extracted with alcohol and yielded carbazole (1·2 g.), m. p. and mixed m. p. 239°. The same result was obtained with 1 : 3 : 6-tribromo- and 3 : 6-di-iodo-carbazole.

Bromocarbazoles and Stannous Chloride–Hydrochloric Acid.—3 : 6-Dibromocarbazole (4 g.), glacial acetic acid (50 c.c.), concentrated hydrochloric acid (20 c.c.), and stannous chloride (4·7 g.) were refluxed for 3 hours. A quantitative yield of carbazole, m. p. 240°, was obtained. 1 : 3 : 6-Tribromocarbazole (4 g.) was not attacked under these conditions, but after 48 hours' refluxing, carbazole (0·1 g.) was isolated, most of the original compound being recovered.

Selenious Acid Colorations.—The following colorations were obtained with Mecke's reagent: Pyrrole, brown; indole, magenta → green (heat); diphenylamine, blue (heat); 2-aminodiphenylamine, magenta; 2-nitrodiphenylamine, violet; triphenylamine, cobalt-blue; carbazole, 1-methylcarbazole, 1-aminocarbazole, and 3 : 6-dibromocarbazole, dark green; 3 : 6-di-iodocarbazole, bluish-green; tribromocarbazole and tetrabromocarbazole, none. Magenta colorations were also obtained with several substituted *o*-amino- and *o*-nitro-diphenylamines. No colours were obtained with pyridine, 2-phenylindole, and indazole.

Fluorescence of Substituted Carbazoles.—In the crystalline state the bromocarbazoles have characteristic fluorescence which offers a ready means of detection and identification. 3 : 6-Dibromo- (yellowish-orange), 1 : 3 : 6-tribromo- (reddish-orange), 1 : 3 : 6 : 8-tetrabromo-carbazole (deep orange-red).

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University of Edinburgh. [*Received, December 18th*, 1941.]