RECENT ADVANCES IN THE CHEMISTRY OF CARBAZOLE

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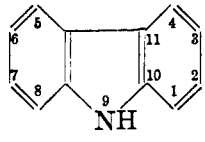
I. INTRODUCTION

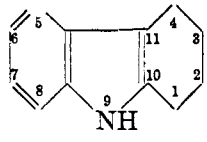
In spite of the publication of much interesting work on carbazole during the past twenty-five years, Cohn's monograph, *Die Carbazolgruppe* (1919), is the last comprehensive survey of this heterocyclic, coal-tar product. It seems appropriate, therefore, to give a brief, critical résumé of recent advances in this field. Emphasis is accordingly laid on the work of the late W. H. Perkin, Jr., and S. G. P. Plant at Oxford, S. H. Tucker at Glasgow, and Hans Lindemann at Brunswick, etc., although reference to the pioneer work of Graebe, Ullmann, Borsche, and others is naturally not neglected. No finality or completeness is claimed, our aim being to give a broad rather than a detailed picture.

II. PROPERTIES OF CARBAZOLE

In the present review, carbazole and tetrahydrocarbazole are represented by the following formulae:



Carbazole



Tetrahydrocarbazole

Various systems of numbering the carbon and nitrogen atoms are to be found in the literature. The one adopted here is that used in most American and British journals.

Carbazole is a white substance which crystallizes in beautiful flakes from hot alcohol, glacial acetic acid, benzene, or toluene. The preparation of pure carbazole is not easy, and it is not surprising that the melting points quoted in the literature vary considerably. Probably the most reliable are those of Tucker (87), 245°C.; Aristov (2), 246°C.; Senseman and Nelson (85), 244.8°C.; Zelinsky, Titz, and Gaverdowskaja (102), 245.6°C.; and Kirby (44), 247°C. It is clear from these figures that a decisive value for the melting point of carbazole is still lacking. Most samples of carbazole melt considerably below the above figures, a value of 235°C. being frequently encountered. Pure carbazole fluoresces only slightly (17, 18, 87), and it is therefore noteworthy that Aristov's sample fluoresced brilliantly.

Many color tests are used for the detection of carbazole (see Cohn's monograph, page 42). The best known is the bluish-green color observed when a trace of carbazole is dissolved in concentrated sulfuric acid and a drop of nitric acid added. Campbell and Maclean (21) found that many carbazoles—e.g., carbazole, 1-methylcarbazole, 1-aminocarbazole, 3,6-dibromocarbazole, etc.—give a dark green color with Mecke's reagent (selenious acid in concentrated sulfuric acid). The test is not specific for carbazoles, since Dewey and Gelman (26) showed that many other nitrogen compounds also give characteristic colors. Levine's statement (45) that the reagent is specific for phenolic compounds is manifestly incorrect.

Commercial carbazole gives a yellow solution in concentrated sulfuric acid, but when the carbazole is pure the solution is colorless (102).

As an indole derivative carbazole gives a red color when the vapor of its alcoholic solution comes in contact with a pine splint soaked in hydrochloric acid.

Carbazole is identified by its picrate (bright red needles, m.p. 185°C.) and trinitrobenzene derivative (red needles, m.p. 166°C.). Substituted carbazoles are similarly identified.

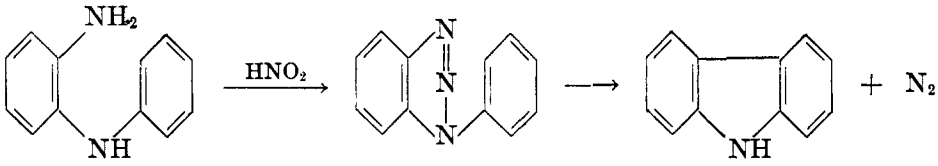
III. PREPARATION OF CARBAZOLE AND SUBSTITUTED CARBAZOLES

The main source of carbazole is coal tar, from which carbazole is obtained in large quantities. To eliminate all the impurities present, such as anthracene, is no easy task, and pure carbazole is best prepared synthetically. A few of the synthetic methods are sufficiently important to warrant some discussion here.

A. Graebe–Ullmann method

The method of Graebe and Ullmann (36) is of wide application and is exemplified by the treatment of *o*-aminodiphenylamine with nitrous acid to give 1-phenyl-1,2,3-benzotriazole, which when heated loses nitrogen to give a quantitative yield of carbazole (see page 361).

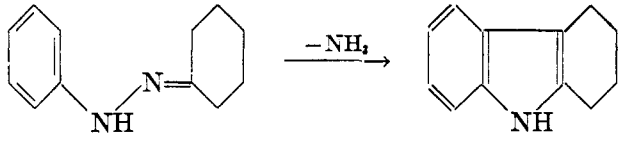
Ullmann (97) synthesized a number of carbazoles by this method, but other workers found that the presence of unsaturated groups gave negative results.



Preston, Tucker, and Cameron (93) were the first to show that nitrocarbazoles (trace), acetylcarbazoles (22 per cent), and cyanocarbazoles (34 per cent) can be obtained, although, as is clear from the yields given in parentheses, the results are not very satisfactory.

B. Borsche's method

Cyclohexanone phenylhydrazone is converted to tetrahydrocarbazole when heated with dilute sulfuric acid (5, 6, 13, 27), the process being completely analogous to the formation of indoles by the Fischer process. Borsche (13) was the first to realize the full scope of the reaction, and by it prepared many substituted tetrahydrocarbazoles. Reagents other than sulfuric acid may be used; glacial acetic acid, for example, has been found to give cleaner products (63).

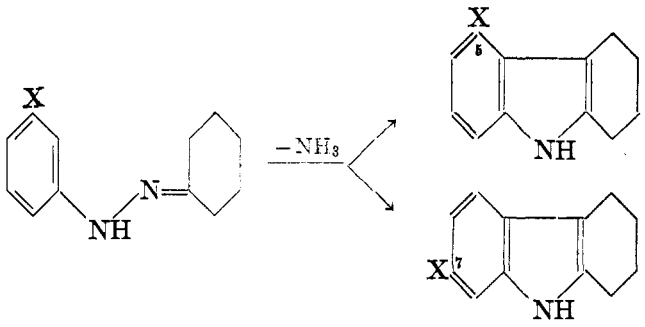


The value of the method is obviously dependent on a suitable means of effecting dehydrogenation. Many reagents have been tried, the yields obtained in most cases being small. Borsche (13) used lead oxide; Perkin and Plant (63, 64) mercurous acetate or sulfur; and Cooke and Gulland (25) palladous chloride. None of these was completely satisfactory. Barclay and Campbell (19) found chloranil to be an excellent reagent for the purpose, many substituted carbazoles being obtained in good yields. Arnold (3, 4) had previously used chloranil successfully to prepare polynuclear aromatic hydrocarbons.

An interesting dehydrogenation was accomplished by Hoshino and Takiura (39) with cinnamic acid and palladium black. The cinnamic acid was reduced to hydrocinnamic acid and carbazole was obtained in excellent yield.

Borsche's method, like that of Graebe and Ullmann, serves both for the preparation of substituted carbazoles and for the determination of their structure. Ambiguity arises, however, when the *m*-substituted phenylhydrazones of cyclohexanone are used. Two products, 5- and 7-substituted tetrahydrocarbazoles, are theoretically possible and are frequently obtained in practice (see page 362).

Plant and his collaborators have examined several reactions of this type. For example, both the 5- and the 7-carboxylic acids were obtained from *m*-hydrazinobenzoic acid (71), and their structures were later proved by Moggridge and Plant (73). Plant (69) showed also that the product from cyclohexanone *m*-nitrophenylhydrazone is a mixture of 5- and 7-nitrotetrahydrocarbazoles and not a single substance, as claimed by Borsche (13). Plant succeeded in isolating the



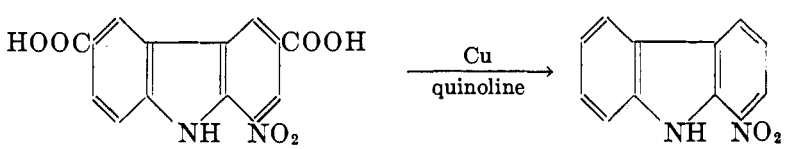
7-isomer, and Barclay and Campbell (19), using chromatographic adsorption, isolated both isomers.

C. Substitution

A limited number of substituted carbazoles can be obtained by nitration, halogenation, sulfonation, etc. but care must be exercised, since mixtures which are difficult to separate are often obtained. Mixtures containing mono-, di-, and tri-substituted isomers sometimes result. The 3- and 6-positions and to a lesser extent the 1- and 8-positions are the most reactive in carbazole. This is clearly demonstrated by nitration, which gives 75 per cent of 3-nitro- and 4 per cent of 1-nitro-carbazole (46), and by exhaustive nitration which yields 1,3,6,8-tetranitrocarbazole.

The reactivity of the carbon atoms ortho and para to the imino group in carbazole results in the formation not only of mono- but also of di-, tri-, and tetra-substituted carbazoles. By bromination, for example, 3-bromo-, 3,6-dibromo-, 1,3,6-tribromo-, and 1,3,6,8-tetrabromo-carbazoles may be prepared, depending on the quantity of bromine used. It is at once obvious that the preparation of 2- and 4-isomers by direct substitution is not possible.

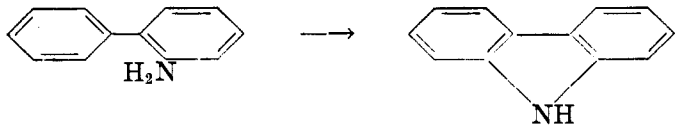
Substitution is most often used to prepare the 3-substituted carbazoles. The 1-isomers are generally separated with difficulty. Morgan and Mitchell (54), for example, separated 1- and 3-nitrocarbazoles by making use of their different basicities, but Preston, Tucker, and Cameron (93) obtained more satisfactory results by chromatographic analysis. 1-Substituted carbazoles may, however, be conveniently prepared from 1,3,6-trisubstituted carbazoles by removal of the groups in the 3- and 6-positions. Tucker and coworkers (93), for example, nitrated 3,6-carbazoledicarboxylic acid to give 1-nitro-3,6-carbazoledicarboxylic acid, and then decarboxylated the acid to 1-nitrocarbazole.



D. Miscellaneous methods

Other methods have also been used to prepare carbazole and its derivatives, many of them, however, being of little practical importance (see Cohn's mono-

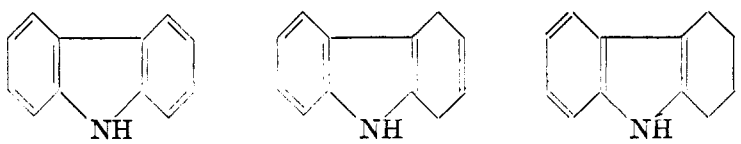
graph, page 6 *et seq.*). Mention may be made of the preparation of carbazoles from derivatives of 2,2′-diaminodiphenyl by treatment of the tetrazotized compound with copper or from *o*-xenylamine by catalytic pyrolysis. By the latter method Morgan and Walls obtained particularly pure carbazole (56).



A promising method is that given in a German patent (30), according to which aromatic amines and 2-chlorocyclohexanone interact to give good yields of tetrahydrocarbazoles. The possibilities of the method are being investigated in our laboratories.

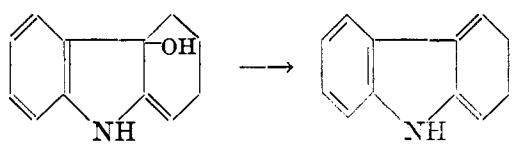
IV. REDUCTION OF CARBAZOLE

By analogy with naphthalene it might be expected that hydrogenation of carbazole would yield first 1,4-dihydro- and then 1,2,3,4-tetrahydrocarbazole.



Carbazole 1,4-Dihydrocarbazole Tetrahydrocarbazole

Schmidt and Schall (83) did claim to have prepared the dihydro compound by reduction of carbazole with sodium and boiling amyl alcohol, but a critical examination of the resulting so-called 1,4-dihydrocarbazole by Barclay, Campbell, and Gow (20) proved it to be a mixture containing at least 50 per cent of carbazole. This means that the only known dihydrocarbazole is 2,3-dihydrocarbazole, prepared by Plant and Tomlinson (77) by the dehydration of 11-hydroxy-2,3,4,11-tetrahydrocarbazole (see page 367).

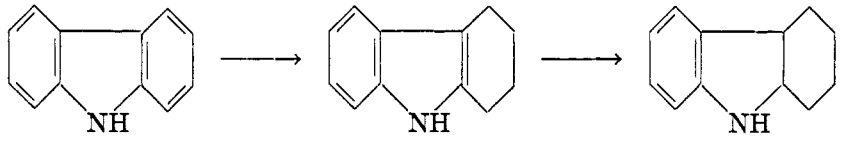


2,3-Dihydrocarbazole

There is no ambiguity about 1,2,3,4-tetrahydrocarbazole prepared either by reduction of carbazole with sodium and alcohol (101) or more conveniently from cyclohexanone phenylhydrazone by the Borsche method (page 361). It has been stated that tetrahydrocarbazole decomposes on standing in air, but this holds only for the impure substance. When crystallized from light petroleum (100–120°C.) it separates as a colorless, stable substance, m.p. 116°C.

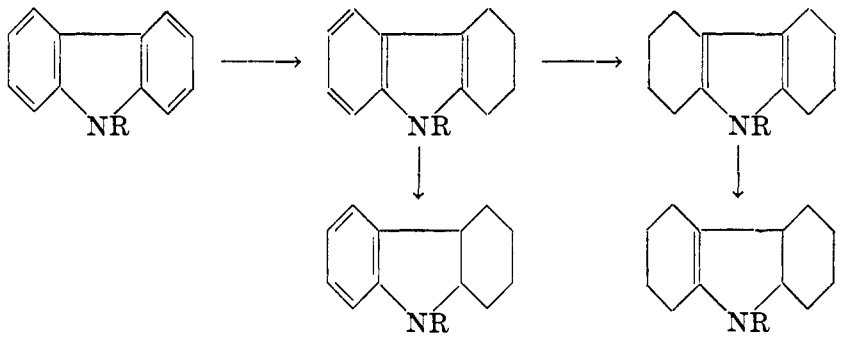
1,2,3,4,10,11-Hexahydrocarbazole may be obtained by reducing carbazole with hydriodic acid and phosphorus at 130°C. (84), but at higher temperatures a hydrocarbon, probably 3,3′-dimethyldicyclopentyl, is obtained. The hexahy-

dro derivative is best prepared either by the reduction of tetrahydrocarbazole with tin and hydrochloric acid (13) or in quantitative yield by electrolytic reduction (Perkin and Plant (65)).



Tetrahydrocarbazole Hexahydrocarbazole

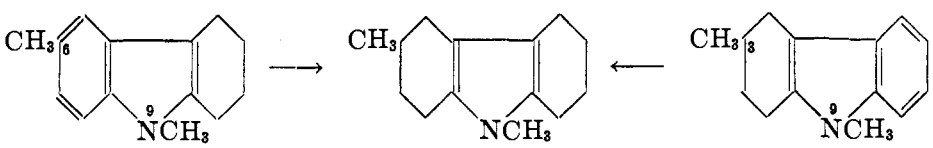
Reduction under more vigorous conditions has been investigated. von Braun and Ritter (14) found that *N*-methyl- or *N*-ethyl-carbazole with hydrogen at 210°C. and 25 atm. pressure in the presence of a nickel catalyst gives a mixture of tetra- and octa-hydrocarbazoles along with unchanged material.



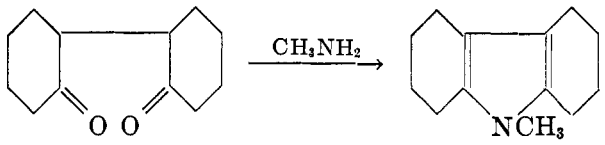
Curiously enough, the double bonds of the "pyrrole ring" in both products remain intact, but may be attacked by tin and hydrochloric acid to give hexahydro- and a decahydro-carbazole, respectively (in the form of their *N*-methyl or *N*-ethyl derivative).

The latter is extremely resistant to further reduction. Carbazole, even when purified, is not attacked under the above conditions, but this is probably due to traces of impurity.

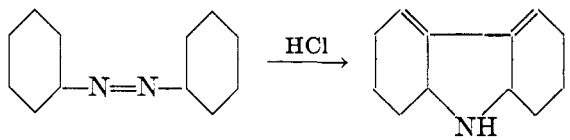
The position of the double bonds in the octahydro compound was demonstrated in two ways. von Braun and Schörnig (16) reduced 6,9-dimethyl- and 3,9-dimethyl-1,2,3,4-tetrahydrocarbazoles and obtained the same octahydro product in both cases. This result is consistent only with a pyrrole structure of the octahydrocarbazole as formulated below.



The correctness of von Braun's conclusion was confirmed by Plant's synthesis (68) from 2,2′-dicyclohexanone and methylamine—an extension of the well-known synthesis of pyrroles from 1,4-diketones.

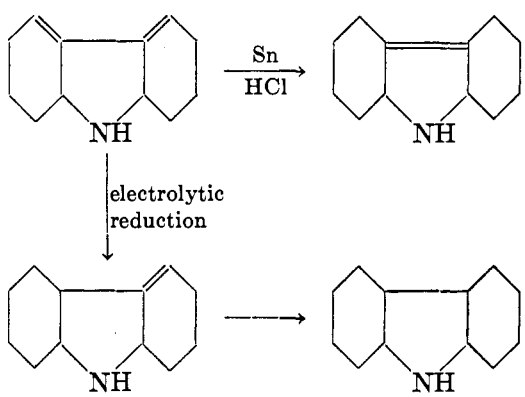


Perkin and Plant (65) prepared a second octahydrocarbazole by treating cyclohexylidine azine with hydrochloric acid.



It is highly probable that the substance has the above structure, first suggested by von Braun and Schörnig (16), but this has still to be proved. The same compound was also obtained by Benary (7) by treatment of the azine with chloroacetyl chloride at room temperature, followed by hydrolysis.

More highly reduced carbazoles have also been prepared. Perkin and Plant (65) obtained a decahydrocarbazole by reduction of their octahydrocarbazole with tin and hydrochloric acid and dodecahydrocarbazole (perhydrocarbazole) by electrolytic reduction. The decahydrocarbazole was stable to electrolytic reduction and could not therefore be an intermediate in the reduction to perhydrocarbazole. The latter substance is possibly formed as shown below:



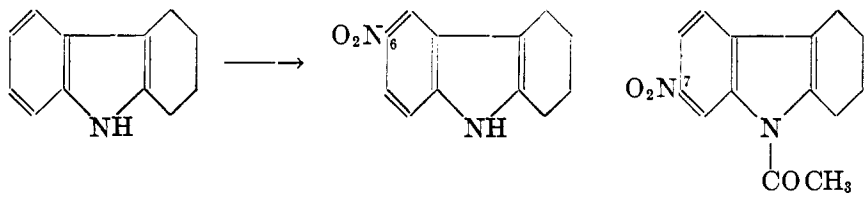
Of considerable interest are the results of Adkins and Coonvadt (1), who studied the hydrogenation of carbazole with copper chromite and Raney nickel catalysts. 1,2,3,4-Tetrahydrocarbazole, *cis*-1,2,3,4,10,11-hexahydrocarbazole, or dodecahydrocarbazole was obtained, according to the catalyst and conditions employed.

A. Properties of tetrahydrocarbazole

Tetrahydrocarbazole with its remarkably reactive 10,11-double bond is the most interesting of the hydrogenated carbazoles.

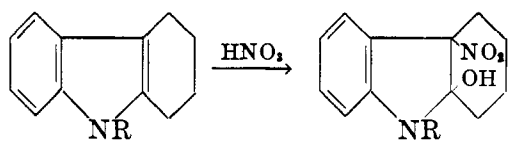
Nitration of tetrahydrocarbazole or its *N*-methyl derivative with concentrated

nitric and sulfuric acids at −5°C. gives 6-nitrotetrahydrocarbazole or its *N*-methyl derivative, while the *N*-acetyl compound nitrates in the 7-position.

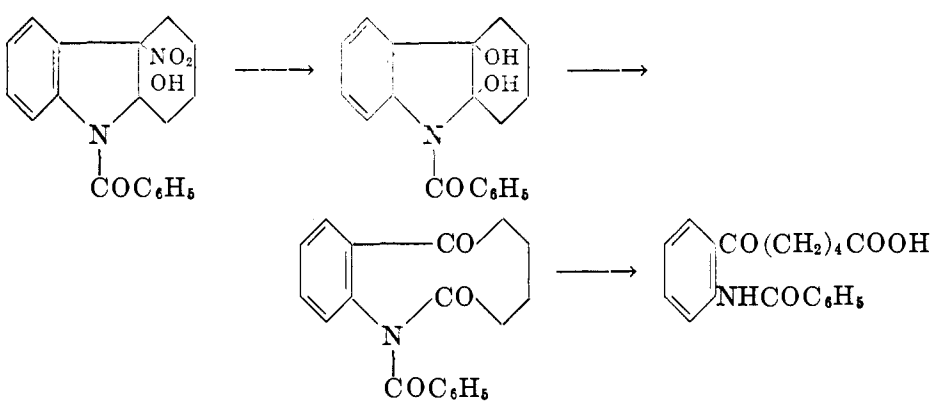


The *N*-benzoyl derivative reacts like the *N*-acetyl. Perkin and Plant (63) concluded that the *N*-benzoyltetrahydrocarbazole nitrates in the 5-position, but Plant (69) later proved this to be erroneous.

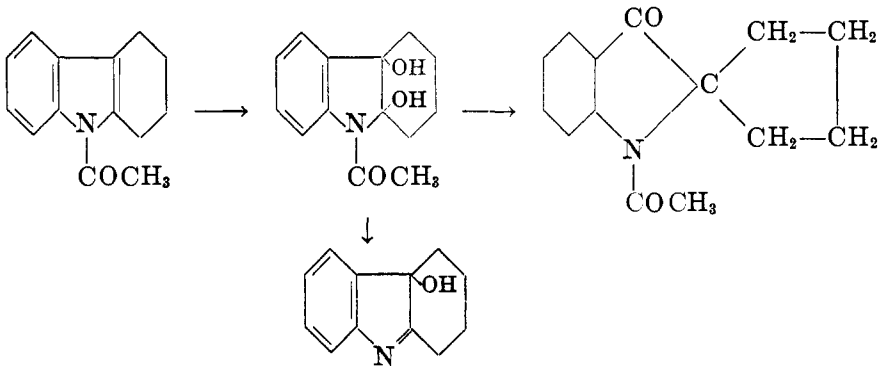
Under suitable conditions, however, *N*-substituted tetrahydrocarbazoles react with nitric acid in quite a different manner, addition of the nitric acid occurring at the double bond of the reduced ring (64). *N*-Benzoyltetrahydrocarbazole, for example, gives mainly 10-hydroxy-9-benzoyl-11-nitrohexahydrocarbazole (or, less likely, the 11-hydroxy-10-nitro derivative).



Ring fission occurs with alkali, and δ-(*o*-benzoylaminobenzoyl)valeric acid is formed. Perkin and Plant (64) pictured this reaction as taking place in the following stages.

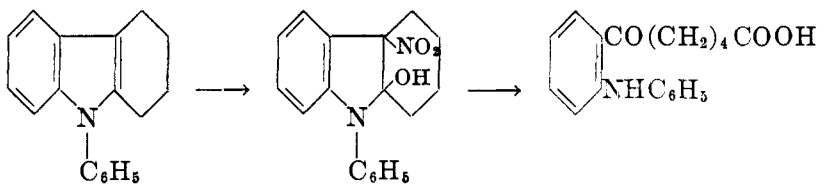


N-Acetyltetrahydrocarbazole reacts differently, 10,11-dihydroxyhexahydrocarbazole being formed. This difference is curious and difficult to explain satisfactorily. The dihydroxy derivative yields with alkali a red product, possibly 11-hydroxytetrahydrocarbazolenine, and with acetic acid a spirane, probably by a pinacol change.

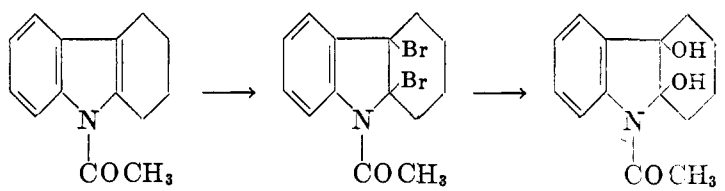


11-Hydroxytetrahydrocarbazolenine

Linnell and Perkin (62) found that *N*-phenyltetrahydrocarbazole behaves like the *N*-benzoyl compound, and 11-nitro-10-hydroxy-9-phenylhexahydrocarbazole is formed. It decomposes into *o*-anilinobenzoylvaleric acid when heated with potassium hydroxide.



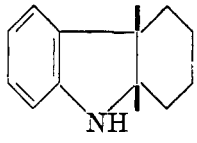
Bromination of *N*-substituted tetrahydrocarbazoles leads to the formation of unstable 10,11-dibromo derivatives, which react instantly with water to give the corresponding dihydroxy compounds or their anhydro derivatives (77). Thus, *N*-acetyltetrahydrocarbazole yields the *N*-acetyl derivatives of 10,11-dihydroxyhexahydrocarbazole.



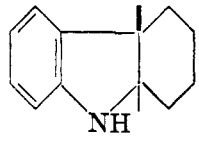
Again the benzoyl compounds behave differently from the acetyl. An intermediate dibromo product is obtained as before, but only one of the bromine atoms reacts with water, the other uniting with a neighboring hydrogen atom to form hydrobromic acid. The product is probably the benzoyl derivative of 11-hydroxy-2,3,4,11-tetrahydrocarbazole, into which it is converted on hydrolysis with alcoholic potassium hydroxide. Its conversion into 2,3-dihydrocarbazole has already been noted on page 363.

B. Properties of hexahydrocarbazole

The most interesting property of hexahydrocarbazole is its existence in two forms—*cis* and *trans*.



cis



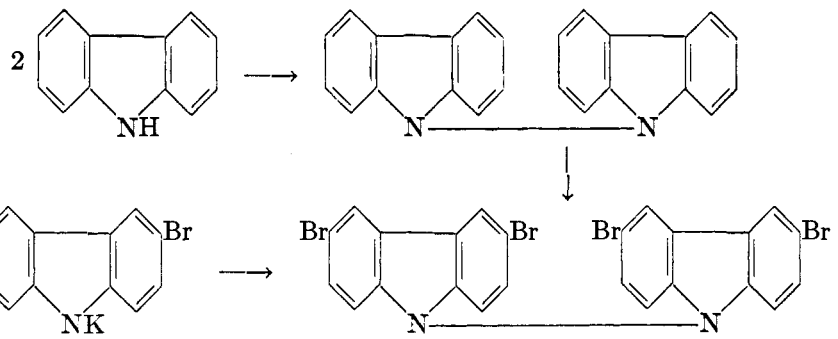
trans

Models show that the *cis* form is much less strained than the *trans*, and consequently is more stable. It is therefore to be anticipated that hydrogenation of tetrahydrocarbazole will give a great preponderance of the *cis* isomer. Gurney, Perkin, and Plant found this to be so (61), the *trans* form amounting only to 1–2 per cent of the product.

V. OXIDATION OF CARBAZOLE

Carbazoles may be oxidized by sodium dichromate in a mixture of sulfuric and acetic acids (Wieland's method (100)) or potassium permanganate in acetone. With the latter reagent Perkin and Tucker (67) isolated three products: A, m.p. 220°C.; B, m.p. 265°C.; and C (amorphous), m.p. about 175°C. A and B were shown to be dicarbazyls.

In view of the reactivity of the hydrogen atom in the 9-position it was not surprising that Tucker and McLintock (90) proved A to be 9,9′-dicarbazyl, since it gave on bromination 3,6,3′,6′-tetrabromodicarbazyl, the constitution of which followed from its preparation by the action of powdered potassium hydroxide followed by iodine on 3,6-dibromocarbazole.



It was expected that the product B would be 3,3′-dicarbazyl, but Tucker (88) synthesized this compound and showed it to be different from B. 3,3′-Dicarbazyl was, however, obtained by the oxidation of carbazole with Wieland's reagent.

The possibility that B might be 1,1′- or 3,9′-dicarbazyl was ruled out by Tucker's synthesis of these substances (91, 92). Their properties differed from those of B, which is presumably 1,3′- or 1,9′-dicarbazyl.

VI. SIMPLE DERIVATIVES OF CARBAZOLE

It is only in recent times that many of the simple carbazole derivatives have been prepared, and a short account of them is therefore in order.

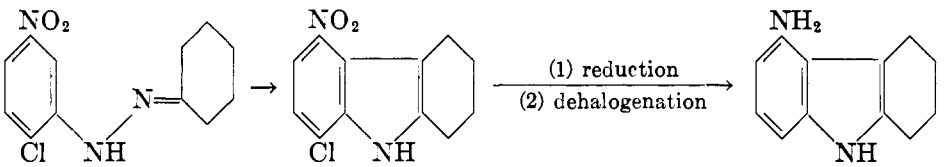
A. Nitrocarbazoles

3-Nitrocarbazole (m.p. 214°C.) is the most accessible of the nitrocarbazoles and is best prepared by modifications of the method of Ruff and Stein (43, 46, 82, 94), by the action of nitric acid on *N*-nitrosocarbazole. The nitroso group is then readily removed by heating with alkali or glacial acetic acid.

Two other mononitrocarbazoles have been reported in the literature. One, m.p. 187°C., was first isolated by Votocek (98) in 1896. Lindemann (46) showed that it is obtained during the preparation of 3-nitrocarbazole in about 4 per cent yield, and proved it to be 1-nitrocarbazole by reducing it to 1-aminocarbazole, identical with a sample synthesized by the Graebe–Ullmann method (48, 49). The other nitro compound, m.p. 164°C., was obtained by Ziersch (103) and was for long mistaken for 1-nitrocarbazole, but Morgan and Mitchell (54) showed it to be a molecular compound of 1- and 3-nitrocarbazoles. Failure to realize that it was a mixture has led to some confusion (see, for example, Whitner (99)).

1-Nitrocarbazole may be prepared from 1-nitro-3,6-carbazoledicarboxylic acid (see page 362) or by removal of the sulfonyl groups from 1-nitro-3,6,8-carbazoletrisulfonic acid (58).

Borsche, Witte, and Bothe (13) obtained a supposedly single product from the ring-closure of cyclohexanone *m*-nitrophenylhydrazone, but Plant (69) showed that in reality it was a mixture of 5- and 7-nitrotetrahydrocarbazoles, although a pure sample of the 5-isomer was not obtained. The structures of these compounds were settled by reduction to the corresponding amines and comparison of their properties with a sample of 5-aminotetrahydrocarbazole, the constitution of which follows from its synthesis from cyclohexanone 2′-chloro-5′-nitrophenylhydrazone.



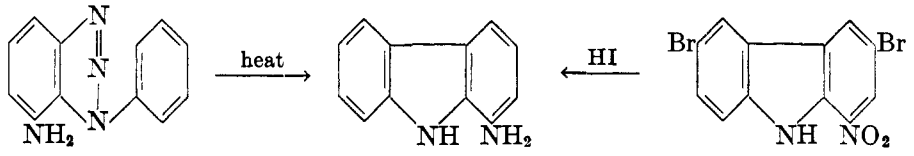
Barclay and Campbell (19) succeeded in obtaining pure samples of both the 5- and the 7-nitrotetrahydrocarbazoles by chromatographic separation, and prepared 2- and 4-nitrocarbazoles from them by dehydrogenation with chloranil.

B. Aminocarbazoles

Our knowledge of the amines is, of course, dependent on the isolation of the corresponding nitrocarbazoles. It follows that 3-aminocarbazole, readily prepared in quantity by the reduction of 3-nitrocarbazole (43, 99), has been thoroughly studied. Of the other isomers, 1-aminocarbazole has been prepared, 2-aminocarbazole *may* have been obtained, and 4-aminocarbazole has not been described in the literature.

Lindemann and Werther (48) were the first to prepare pure 1-aminocarbazole. This was done both by the reduction of 1-nitrocarbazole and by synthesis from

1-phenyl-7-aminobenzotriazole, but neither method gave large yields. Better results were obtained from 1-phenyl-5-carboxy-7-aminobenzotriazole (Lindemann and Wessel (49)), but this method is also unsuitable for large-scale preparations. A more promising method is that of Campbell and Maclean (21), in which 3,6-dibromo-1-nitrocarbazole is treated with hydriodic acid. Reduction of the nitro group is accompanied by removal of the bromine atoms. The method suffers from the disadvantage that the resulting 1-aminocarbazole is sometimes difficult to purify. Better results might be obtained by the use of a milder reagent, such as Raney nickel.



1-Aminocarbazole

A product claimed by Whitner (99) to be 1-aminocarbazole was probably impure 3-aminocarbazole.

2-Aminocarbazole is stated in the literature to be a substance, m.p. 238°C., isolated by Blank (10) from the pyrolysis of "diphenylin" (presumably 2,4'-diaminodiphenyl). Blank's claims are of doubtful validity, as his paper contains several unsatisfactory features, such as lack of details regarding his starting material and no analytical figures for the resulting aminocarbazole.

C. Halogenocarbazoles

Halogenation of carbazole proceeds as would be expected, 3-halogenocarbazoles being first formed. These, however, readily react with more halogen to give 3,6-dihalogenocarbazoles, and these are the most accessible halogen derivatives of carbazole. The isolation of 3-carbazolediazonium chloride in a crystalline condition by Morgan and Read (55) opened up another route for the preparation of halogenocarbazoles, and Tucker (89) used it for this purpose.

All the monochlorocarbazoles have been prepared. Moggridge and Plant (73) obtained 5- and 7-chlorotetrahydrocarbazoles (the former impure) from cyclohexanone *m*-chlorophenylhydrazone, and prepared 2- and 4-chlorocarbazoles from them by dehydrogenation with sulfur in quinoline. Barclay and Campbell (19) obtained all the chlorocarbazoles by chloranil dehydrogenation of the corresponding chlorotetrahydrocarbazoles. The four bromocarbazoles have been prepared by this method.

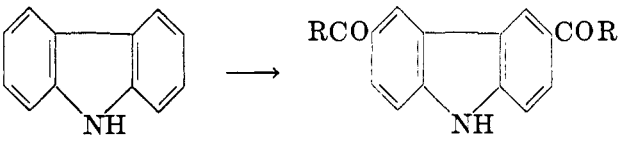
Tucker (87) was the first to prepare pure iodocarbazoles by the action of potassium iodide and potassium iodate on carbazole in glacial acetic acid. The main product was 3-iodocarbazole, identical with a specimen prepared by the diazotization of 3-aminocarbazole. Tucker also prepared 3,6-diiodocarbazole and showed that Classen's diiodocarbazole (24) was an impure product. The positions of the iodo groups are not proved, but are almost certainly 3 and 6 by analogy with other disubstitution products of carbazole. Moreover, Gilman

and Kirby (33) showed that *N*-ethylcarbazole on iodination gave the 3,6-diiodo-*N*-ethylcarbazole.

D. Carbazyl ketones

The acylcarbazoles are prepared by the Friedel–Crafts reaction and have been thoroughly studied by Plant and his coworkers. The course of the acylation depends on several factors (see below).

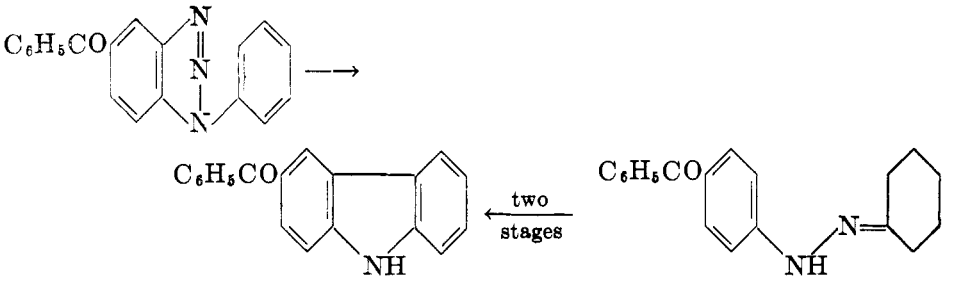
Carbazole with aluminum chloride and acid chlorides (even in limited quantities) in carbon disulfide yields 3,6-disubstituted products, monosubstituted derivatives being obtained only in limited quantities. In this way Plant (76, 78) obtained 3,6-dibenzoyl- and 3,6-diacetyl-carbazoles.



R = CH_3 or C_6H_5.

The structures of these compounds were determined by comparison with samples synthesized by unambiguous methods.

3-Benzoylcarbazole was prepared from 5-benzoyl-1-phenylbenzotriazole by Hunter and Darling (42) and from *p*-hydrazinobenzophenone and cyclohexanone by Plant and Tomlinson (78). Both syntheses proved the structure of the product.



Attempts to prepare 1-benzoylcarbazole from 7-benzoyl-1-phenyltriazole failed.

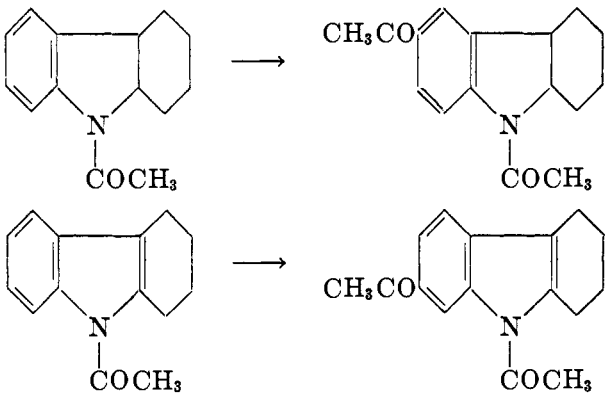
3-Benzoylcarbazole was also obtained by "baking" (Scholl process) *N*-benzoylcarbazole with aluminum chloride at 120°C. (78), and the 3-acetyl compound was obtained in an analogous manner (79). The constitution of the latter substance was proved by reduction to 3-ethylcarbazole, whose structure was determined by synthesis. Plant (76) and Meitzner (52) obtained the best results with nitrobenzene as solvent, and Meitzner succeeded in isolating some 1-acetylcarbazole in addition to the main product, 3-acetylcarbazole (50–60 per cent).

9-Alkylcarbazoles react with acyl chlorides and aluminum chloride in the same way as carbazole, 9-methylcarbazole, for example, giving with acetyl bromide and aluminum chloride 3,6-diacetyl-9-methylcarbazole (76). 9-Acylcarbazoles, on the other hand, give 2,9-derivatives. Plant and Williams

(79) found that 9-acetylcarbazole gave 2,9-diacetylcarbazole (*cf.* Borsche and Feise (12)). Results with 9-benzoylcarbazole have not been consistent. Plant and Tomlinson (78) found that it yielded with benzoyl chloride and aluminum chloride 3,6-dibenzoylcarbazole, but later Plant, Williams, and Rogers (76) were unable to repeat this result and obtained instead 2,9-dibenzoylcarbazole. These discordant observations have not been completely explained. The reactivity of the 2-position in the above experiments was also shown by Ruberg and Small (81), who obtained 2-chloroacetyl-9-acetylcarbazole from 9-acetylcarbazole and chloroacetyl chloride.

Hydrolysis of the 2,9-derivatives gives 2-acetyl- and 2-benzoylcarbazoles. Plant, Rogers, and Williams (76) obtained 2-benzoylcarbazole (m.p. 163°C.), different from the substance (m.p. 350°C.) previously regarded as having this structure (31).

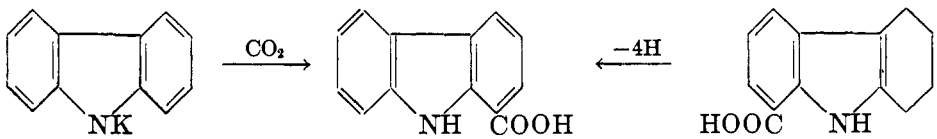
Another factor affecting the course of the Friedel–Crafts reaction is the degree of reduction of the carbazole. Mitchell and Plant (72) obtained 6,9-diacetylhexahydrocarbazole from 9-acetylhexahydrocarbazole, but Plant and Rogers (75) found the product from 9-acetyltetrahydrocarbazole to be 7,9-diacetyltetrahydrocarbazole.



E. Carbazolecarboxylic acids

The carbazolecarboxylic acids are not readily prepared in large quantities, but 1-, 2-, and 3-carbazolecarboxylic acids have been prepared and characterized.

Ciamician and Silber (23) obtained a monocarboxylic acid, m.p. 271–272°C., by passing carbon dioxide into potassium carbazole, followed by treatment with dilute sulfuric acid. The assumption that it was the 1-carboxylic acid was proved many years later, when Briscoe and Plant (70) showed it to be identical with the dehydrogenation product of 1,2,3,4-tetrahydro-8-carbazolecarboxylic acid.

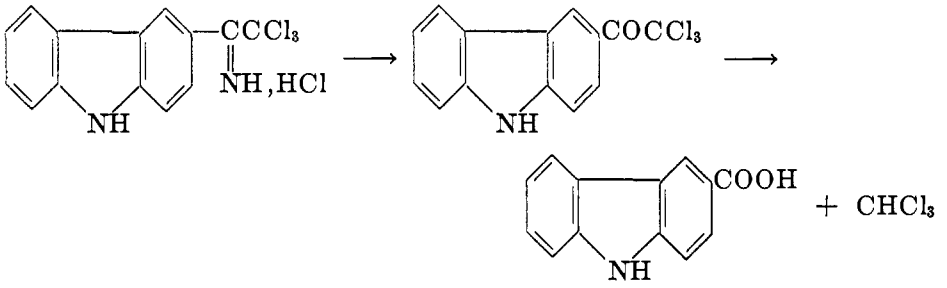


Gilman and Kirby (33) found that interaction of carbazole and *n*-butyllithium followed by carbonation gave 1-carbazolecarboxylic acid in very poor yield. Better results were obtained with *N*-ethylcarbazole, the resulting 9-ethyl-1-carbazolecarboxylic acid being identical with that obtained by treating 1-carbazolecarboxylic acid with diethyl sulfate and potassium hydroxide.

2-Carbazolecarboxylic acid was prepared by Borsche and Feise (12) by fusing 2-acetylcarbazole with potassium hydroxide (*cf.* Plant and Williams (79)); by Moggridge and Plant (73) by dehydrogenation of 1,2,3,4-tetrahydro-7-carbazolecarboxylic acid with palladized charcoal; and from 2-benzoylcarbazole by fusion with potassium hydroxide (76).

3-Carbazolecarboxylic acid has been prepared by similar methods: fusion of 3-acetylcarbazole with potassium hydroxide (79); dehydrogenation of the methyl ester of the corresponding tetrahydrocarbazolecarboxylic acid (73); and mercuration of *N*-ethylcarbazole and suitable treatment of the product (33), 9-ethyl-3-carbazolecarboxylic acid being obtained. It is of interest that whereas metallation of *N*-ethylcarbazole with lithium gives a 1-lithium compound, mercuration occurs in the 3-position.

More recently Dunlop and Tucker (89) have prepared the acid by the Houben–Fischer method (40, 41). Trichloroacetonitrile acted on carbazole in chlorobenzene solution with aluminum chloride and dry hydrogen chloride, followed by hydrolysis, to give 3-trichloroacetylcarbazole. Alkaline hydrolysis split off chloroform and yielded 3-carbazolecarboxylic acid.



4-Carbazolecarboxylic acid has not yet been prepared, since efforts to dehydrogenate 1,2,3,4-tetrahydro-5-carbazolecarboxylic acid were not successful (73).

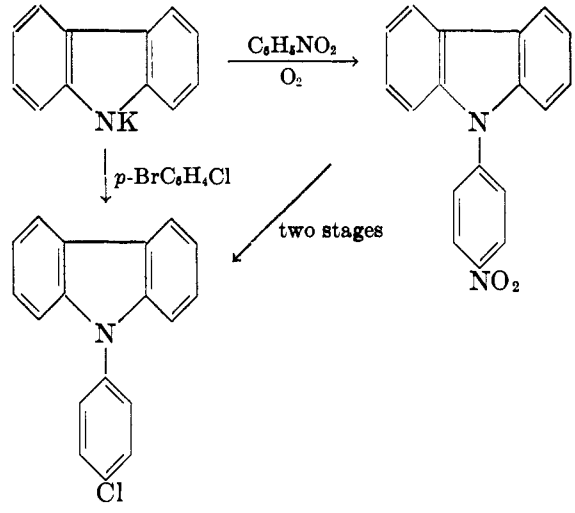
A carbazoledicarboxylic acid is stated in the patent literature to have been prepared by the action of carbon dioxide on potassium carbazole (29), but no proof of structure is given. Mitchell and Plant (72) were the first to prepare 3,6-carbazoledicarboxylic acid and prove its structure by showing it to be identical with the product of fusion of 3,6-dibenzoylcarbazole with potassium hydroxide. It has also been prepared by the Houben–Fischer method (89).

F. N-Substituted carbazoles

N-Alkyl, -aryl, or -acyl derivatives have been obtained by the action of the appropriate reagents on (*1*) carbazole, (*2*) potassium carbazole, (*3*) or carbazole-

magnesium iodide. For example, Boeseken (11) prepared *N*-acetylcarbazole in good yield by the action of acetic anhydride containing a trace of sulfuric acid on carbazole. None of these methods is completely satisfactory, and it was therefore a considerable advance when Tucker and Stevens (94) showed that nearly quantitative yields of *N*-derivatives are obtained by the action at room temperature of the appropriate alkylating or acylating reagent upon carbazole in acetone or alcohol solution in the presence of sodium or potassium hydroxide. These authors also found that the greater the acidity of the imino hydrogen, the more successful is the method. The process has occasionally proved to be capricious or ineffective. Tucker (87) found that vigorous shaking must be avoided in the preparation of *N*-benzoylcarbazole, and Ruberg and Small (81) were able to methylate 2-chloroacetylcarbazole only to a slight extent. Nevertheless the method is of wide application. It may be noted that the *N*-benzoyl compound is obtained in 60 per cent yield by heating carbazole with anhydrous potassium carbonate and benzoyl chloride in the presence of copper bronze (89).

An interesting reaction is the oxidative condensation of *N*-potassium carbazole with nitrobenzene (53). It was shown by de Montmollin and de Montmollin (53) that condensation occurred in the para position of the nitrobenzene. The 9-*p*-nitrophenylcarbazole on reduction, followed by diazotization, etc., gave a product identical with that prepared from *N*-potassium carbazole and *p*-chlorobromobenzene.



This was confirmed by the synthesis of the nitro compound by Nelmes and Tucker (92) from carbazole and *p*-chloronitrobenzene in the presence of potassium carbonate.

Patterson and Adams (59) studied other *N*-phenylcarbazole derivatives and showed that while *N*-*o*-carboxyphenylcarbazole could not be resolved, *N*-*o*-carboxyphenyl-3-nitrocarbazole (see page 376) could be resolved. The lack of symmetry in this case is clearly due to restricted rotation.

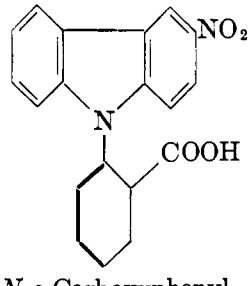
TABLE 1

Simple derivatives of carbazole

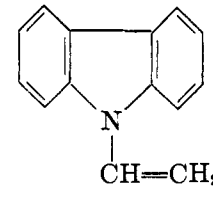
(For numbering of ring, see page 359)

COMPOUND	MELTING POINT	REFERENCES
	°C.	
1-Nitrocarbazole	187	(46, 93)
	185–187	(19)
2-Nitrocarbazole	165–166	(19)
3-Nitrocarbazole	214	(46)
	209–210	(82)
	203–206	(19)
	No. m.p.	(94)
4-Nitrocarbazole	182–183	(19)
3,6-Dinitrocarbazole	320	(103)
1-Aminocarbazole	193	(21, 48)
2-Aminocarbazole	238	(10)
3-Aminocarbazole	254	(99)
	259	(82)
1-Chlorocarbazole	125	(58)
	109–110	(19)
2-Chlorocarbazole	244	(97)
	242	(19, 73)
	201.5	(97)
3-Chlorocarbazole	195	(86)
	199–200	(19)
4-Chlorocarbazole	96	(19, 73)
1,4-Dichlorocarbazole	84–85	(19)
3,6-Dichlorocarbazole	202–203	(51)
1-Bromocarbazole	111–112	(19)
2-Bromocarbazole	250–251	(19)
3-Bromocarbazole	197	(64)
	194–195	(86)
	201–202	(19)
4-Bromocarbazole	104–105	(19)
3,6-Dibromocarbazole	213	(47)
3,6-Dibromo-1-nitrocarbazole	260	(47)
3,6-Dibromo-1-aminocarbazole	192	(47)
3-Iodocarbazole	192–194	(86, 87)
3,6-Diiodocarbazole	202–204	(87)
1-Acetylcarbazole	136	(52)
2-Acetylcarbazole	227	(12, 79)
3-Acetylcarbazole	167	(79)
	162	(76)
	165	(93)
3,6-Diacetylcarbazole	232	(76)
2-Benzoylcarbazole	163	(76)
3-Benzoylcarbazole	203–205	(42)
	206	(78)
3,6-Dibenzoylcarbazole	258	(78)
3-Ethoxycarbazole	106–107	(39)
	105–106	(19)

COMPOUND	MELTING POINT	REFERENCES
	°C.	
2-Ethylcarbazole	225	(79)
3-Ethylcarbazole	144	(79)
3,6-Diethylcarbazole	119	(76)
1-Methylcarbazole	120.5	(97)
	110–114	(19)
2-Methylcarbazole	259	(13, 19)
3-Methylcarbazole	207	(96, 74)
	203	(13, 97)
	199–202	(19)
1-Carbazolecarboxylic acid	270–271	(70, 73)
	271–273	(19)
2-Carbazolecarboxylic acid	320–322	(76, 79)
3-Carbazolecarboxylic acid	276–278	(73, 79)
	272–274	(19)
9-Acetylcarbazole	69	(35)
	75	(64)
	76	(11)
	No m.p.	(8)
9-Benzoylcarbazole	95.5	(9)
	98.5	(50)
	98	(87, 94)
	No m.p.	(89)
9-Ethylcarbazole	70	(95)
	No m.p.	(94)
9-Methylcarbazole	85–86	(63, 64)
	87	(34)
	88	(95)
	No m.p.	(94)
9-Phenylcarbazole	82–84	(22)
	88–89	(19, 38)
	91–93	(89)
	94–95	(28)
3,9-Diacetylcarbazole	153	(79)
3,9-Dibenzoylcarbazole	170	(78)
9-Acetyl-3-benzoylcarbazole	154	(78)
9-Benzoyl-2-acetylcarbazole	153	(79)
9-Methyl-2-acetylcarbazole	122	(79)
9-Methyl-3-acetylcarbazole	102	(79)



N-*o*-Carboxyphenyl-3-nitrocarbazole



N-Vinylcarbazole

TABLE 2

Simple derivatives of tetrahydro- and hexahydro-carbazoles

(For numbering of ring, see page 359)

COMPOUND	MELTING POINT	REFERENCES
	°C.	
Tetrahydrocarbazole	116	(13)
	119	(63)
Hexahydrocarbazole	96	(13)
	99	(65)
5-Nitrotetrahydrocarbazole	155–156	(19)
6-Nitrotetrahydrocarbazole	174	(13, 63)
7-Nitrotetrahydrocarbazole	172	(19, 69)
8-Nitrotetrahydrocarbazole	148–149	(13)
	149–150	(66)
7-Nitrohexahydrocarbazole	69	(69)
5-Aminotetrahydrocarbazole	163	(69)
6-Aminotetrahydrocarbazole	152	(63)
7-Aminotetrahydrocarbazole	101	(69)
8-Aminotetrahydrocarbazole	163–164	(66)
5-Chlorotetrahydrocarbazole	Syrup	(19, 73)
6-Chlorotetrahydrocarbazole	138	(13, 19)
7-Chlorotetrahydrocarbazole	181	(19, 73)
8-Chlorotetrahydrocarbazole	55–56	(13, 19)
5,8-Dichlorotetrahydrocarbazole	91–93	(19)
5-Bromotetrahydrocarbazole	Syrup	(80)
	131–132	(19)
6-Bromotetrahydrocarbazole	153	(13, 19)
7-Bromotetrahydrocarbazole	183	(80)
	171–172	(19)
8-Bromotetrahydrocarbazole	Syrup	(19)
1-Methyltetrahydrocarbazole	72	(37)
2-Methyltetrahydrocarbazole	98–100	(13)
	94	(19)
6-Methyltetrahydrocarbazole	141–142	(13, 19)
8-Methyltetrahydrocarbazole	97–98	(19)
6-Ethoxytetrahydrocarbazole	87–88	(13)
	105–106	(39)
	102–104	(19)
3-Carboxytetrahydrocarbazole	195	(60)
5-Carboxytetrahydrocarbazole	210	(57, 71, 73)
6-Carboxytetrahydrocarbazole	282	(57, 71)
7-Carboxytetrahydrocarbazole	287	(57, 71, 73)
8-Carboxytetrahydrocarbazole	203	(57, 71)
9-Acetyltetrahydrocarbazole	77	(63)
9-Benzoyltetrahydrocarbazole	85	(64)
9-Methyltetrahydrocarbazole	50	(63, 94)
9-Phenyltetrahydrocarbazole	86	(62)

Finally, *N*-vinylcarbazole (see page 376) may be mentioned. It is prepared in a number of ways, including the interaction of carbazole and acetylene with an alkali catalyst under pressure and at moderate temperatures (32). It readily

yields a transparent thermoplastic polymer with the very high softening temperature of 250°C. It comes on the market as Luvican.

VII. TABLES OF DERIVATIVES

Table 1 lists the names and melting points of simple derivatives of carbazole, while table 2 gives the names and melting points of simple derivatives of reduced carbazoles.

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