STUDIES ON CARBAZOLE

and

ITS DERIVATIVES

By

JAMES ALISTAIR ROSS MACLEAN, B.Sc.

Thesis submitted for the degree of

Doctor of Philosophy.

May, 1941.

University of Edinburgh.

INDEX.

---oOo---

LIST OF PREPARATIONS

LIST OF PREPARATIONS (Contd.)

LIST OF PREPARATIONS (Contd.)

INTRODUCTION.

In the year 1872 yet another compound was added to the rapidly mounting list obtained from coal tar, when Graebe and Glaser [B, (1872), 5, 12] and [A (1872), 163, 343] discovered a substance which they called carbazole. These workers were investigating a process for purifying anthracene, communicated to them by Perkin in England. The residue from the distillation of crude anthracene with hot 50% KOH produced a potassium compound which in turn gave an insoluble residue on treatment with water. From this residue carbazole sublimed. Graebe obtained the same compound by passing aniline through a red-hot tube [A, (1873), 167, 125]. He posuulated the correct constitution of the compound and, with Ullmann, discovered a valuable method of synthesis [A, (1896), 291, 16]. All the carbazole used in industry or dyestuff manufacture is extracted from coal tar. It is found in the anthracene oil fraction i.e. the oil which distills between 270 and 400° C. (approx.) and consists essentially of anthracene and phenanthrene but contains other hydrocarbons e.g. naphthalene, fluoranthene. On cooling this distillate a semi-fluid is obtained which, by suction, filtration, and centrifuging gives the "crude-anthracene"/

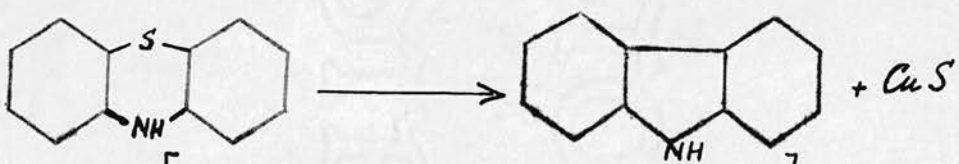
"crude-anthracene" which contains approx. 20% carbazole. In addition to the KOH fusion and subsequent decomposition with water many industrial methods have been devised for the production of pure carbazole, two being worthy of mention. The first entails the use of the so-called 'polishing-oil' - an oil which boils between 170-200° C. or the use of naphthalene oil solutions which dissolve carbazole more readily than anthracene. The best results are obtained by dissolving "crude anthracene" uncentrifuged in the naphthalene oil, cooling to 40°C, filtering and centrifuging when carbazole is precipitated in addition to the bulk of the anthracene. The carbazole can then be separated by KOH fusion and water decomposition. This method is much more economical than using 'polishing-oil' as much less of the former is required as a solution medium and it can also be recovered for further use. In the other method of note pyridine bases are employed as solution media in place of 'polishing' or naphthalene oils and have the advantage over the latter that carbazole is very soluble in them whilst anthracene is almost insoluble. On distilling off the pyridine a residue rich in carbazole remains which can then be treated with polishing oil in order to separate it from phenanthrene and/

and other impurities and thus obtain the pure product. [Akt. Ges. fürTeer und Erdöl industrie DRP 111, 359 Kl 12 (1899)]. A great improvement in this method resulted from Frankhänel's work in Darmstadt. [DRP. 226 112 Kl 120, (1909)]. He injected pyridine vapour at 230°C into the "crude anthracene" (3:1), the product being collected in a cooled receiver. 96% pure anthracene was obtained by filtration, the filtrate containing mainly carbazole which was collected by distillation. If a quantitative estimation of the carbazole content is desired a simple method of Kraemer and Spilker can be utilised. By this method all existing bases are removed by extracting with warm dilute H_2SO_4, the nitrogen in the residue calculated by Kjeldahl's method, and hence the carbazole content. Before leaving the subject of the origin of carbazole at should be noted that it can be obtained from the naturally-occurring alkaloids, strychnine and brucine, by zinc dust distillation. In addition to many by-products such as H_2 NH_3 etc. a sublimate of carbazole forms. cf. [Loebisch and Schoop, M (1886), 7, 611.] This method of production has not been investigated fully but it is not very probable that the carbazole ring pre-exists in these alkaloids.

Carbazole/

Carbazole occurs in the literature under such names as Imino-diphenyl and dibenzo-pyrrole as, in spite of its nitrogen content, it has the characteristics of a hydrocarbon. Its structure was fixed by evidence supplied by many investigators. The presence of a diphenyl nucleus was shown by conversion into perchlor-diphenyl and the existence of an imino-group by the preparation of a potassium compound, in addition to alkyl and acyl derivatives.

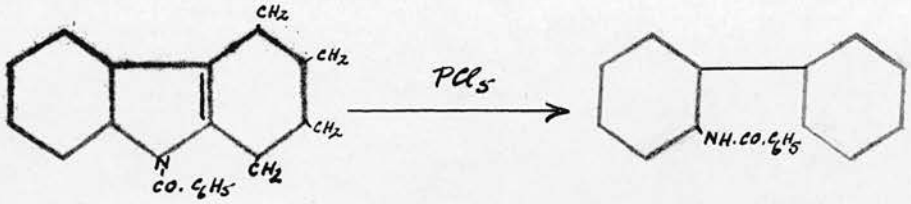
The positions at which the rings were linked was illustrated by synthesising carbazole from thio-diphenylamine, whose structure was proved by heating it with copper powder Bernthsen [B, (1886(, 19, 3255]



Ackermann, [DRP, 222, 879, Kl 12 p. (1909)].

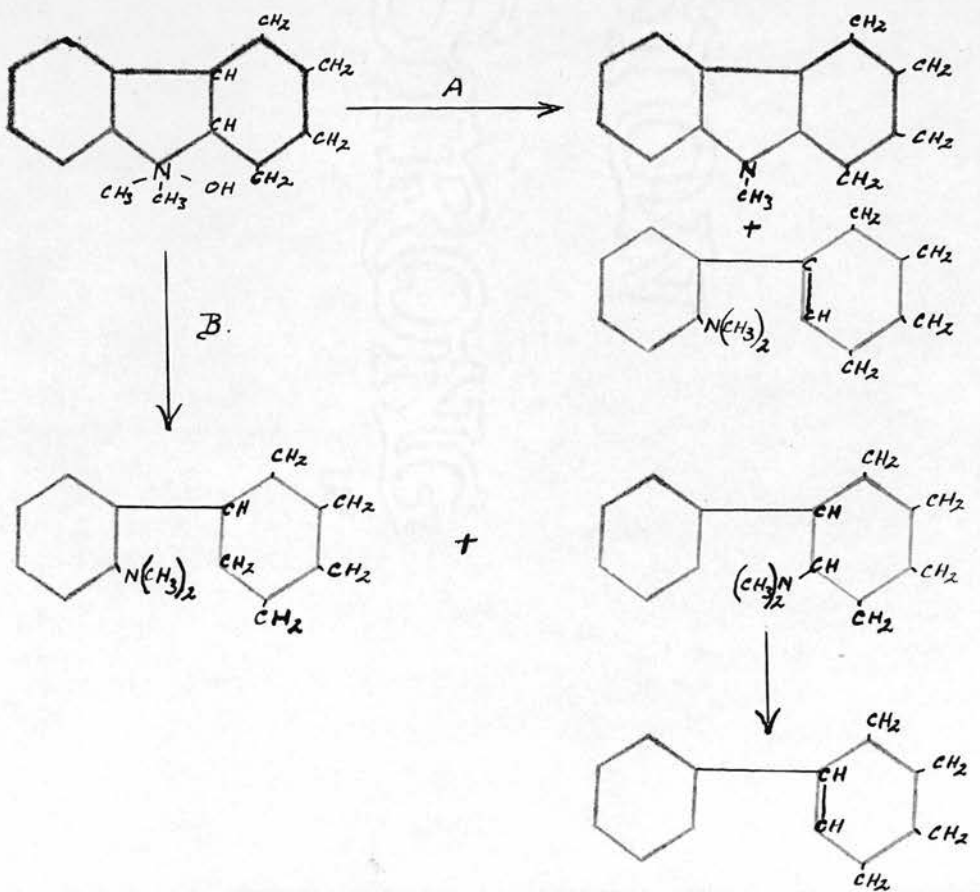
Final proof of its structure is given by syntheses from diphenylamine and diphenylamine derivatives, as will be shown later, and is confirmed by the results of standard methods such as those of Von Braun and Hofmann. By benzoylation of tetrahydro-carbazole and subsequent treatment with phosphorus pentachloride benzoyl/

benzoyl-o-aminodiphenyl is obtained.

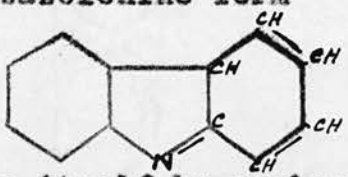


Degradation methods yield various compounds according to the experimental conditions employed. e.g. Decomposition of hexahydrocarbazole-dimethyl-ammonium hydroxide produced o-dimethylamino-phenyl-1-cyclohexene as well as N-methyl-hexahydrocarbazole.

Under different conditions the same quaternary ammonium base can be decomposed into o-dimethylamino-phenyl -cyclohexane and to o-phenyl dimethylamino-cyclohexane. Von Braun, Heider and Neumann, [B, (1916), 49, 2618.] These reactions can be graphically represented thus:-

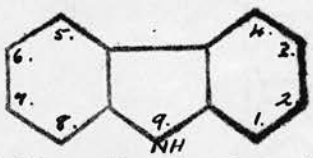


From these reactions the presence of a diphenyl nucleus and an imino group is corroborated. The positions at which the rings are linked may also be determined. A final structural point of interest lies in the fact that carbazole was found to exist in a methylene form as the existence of some of the tetrahydro-carbazoles could only be explained by the presence of a carbazolenine form



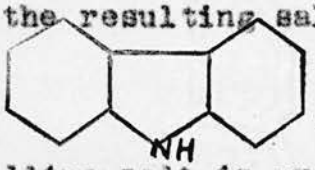
This form suggests itself by analogy with the pyrrolenine and indolenine forms, as the structural resemblance, as well as the similarity in reactions and modes of formation between pyrrole, indole and carbazole is obvious.

The most usual nomenclature of carbazole and derivatives corresponds to the following scheme:-



[Ullmann, B, (1898), 31,1697]

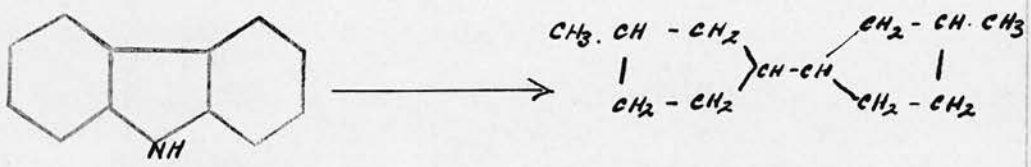
Many of the physical and chemical properties of carbazole can be predicted form its structure. It crystallises in colourless flakes from alcohol or glacial acetic acid but is very sparingly soluble in the other organic solvents. Tucker and Stevens, [J.C.S. (1923), 2146]. It sublimes very easily, the sublimate melting at 246°C. and fluoresces in ultra-violet light. As is to be expected with the presence of a diphenyl/

diphenyl nucleus carbazole is chemically exceedingly stable, being unaffected by conc. HCl in a sealed tube at 300°C. [Graebe,and Glaser, A, (1872), 163, 347] or by phosgene at 200°C. The imino group is responsible for the characteristic reaction of carbazole. As final proof of its stability it distills without decomposition. As carbazole gives a potassium compound on fusion with KOH and reacts much less readily with NaOH it may be said to possess slight acidic properties. Its slight basicity is proved by the formation of a perchlorate with 70% perchloric acid, the resulting salt having the formula 

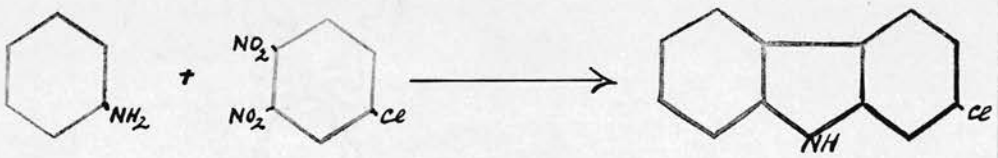
, $HClO_4$. A colourless crystalline salt is produced which, like the potassium compound, is immediately decomposed by water. Carbazole is therefore amphoteric.

Although the carbazole nucleus is very stable, it gives substituted carbazoles and carbazole addition products. Thus reduction of carbazole by boiling with sodium and amyl alcohol gives di- and tetrahydrocarbazole whilst the hexahydro-compound is obtained by the action of tin and hydrochloric acid on tetrahydrocarbazole [Graebe and Glaser, A, (1872), 163, 352]. Catalytic hydrogenation with nickel and catalyst yields α : β -diethylindole [Padoa and Chiaves, R.A.L. 5 , (1908) 16, II, 762] whilst/

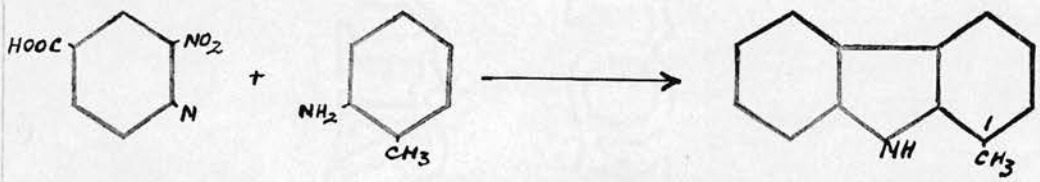
whilst energetic reduction with hydriodic acid leads to 33' dimethyl-dicyclopentyl



Halogenated carbazoles can be obtained directly the 3- and then the 3:6-substituted derivatives being formed or the Graebe-Ullmann method may be used e.g.[Ullmann, B. (1898), 31, 1697)]



Iodine also can be introduced into the molecule, the iodine atoms in all probability occupying the 3- and 6-positions [Tucker, J.C.S. (1926), 546].
In 1904 Ullmann prepared an ethyl carbazole by the following synthesis:-



In this case 1-methyl-carbazole results [A, (1904), 332, 84] but the 2- and 3-methyl compounds in addition to di-, tri- and tetra-methyl carbazoles are/

are prepared by syntheses similar to the above using the appropriately substituted starting materials. For the formation of 9-aryl compounds the method of Graebe and Adlerskron [A. (1880). 202. 23] may be used.

A better method however has been given by Stevens and Tucker [J. (1923). 123. 2140], who acted on carbazole or a derivative, dissolved in alcohol or acetone, with aqueous solutions of potassium or sodium hydroxide in the presence of the appropriate alkylating or acylating reagent at, or slightly above, room temperature. Oxidation of carbazole [Perkin and Tucker, J.C.S. (1921), 216] yields unusual results, a mixture of dicarbazyls being formed. Their structure is still the subject of investigation. The reaction, carried out with acetone and potassium permanganate, demonstrates the extreme stability of the carbazole nucleus.

Of very much greater interest and importance are the carbazole carboxylic acids which are formed by the action of carbon dioxide on potassium carbazole, at high temperatures under pressure. According to the temperature and length of heating mono- or di-carboxylic acids result. Carbazole also/

also forms the extremely reactive organo-magnesium compounds by its action with methyl magnesium iodide. The action of carbon dioxide on this Mg compound at low temperature yields the 9-carboxylic acid whilst the 1-acid is formed at high temperatures 270°C. approx. With acid chlorides the corresponding 9-acyl compound is produced in almost quantitative yield. [Oddo, G, (1911), 41, I, 255].

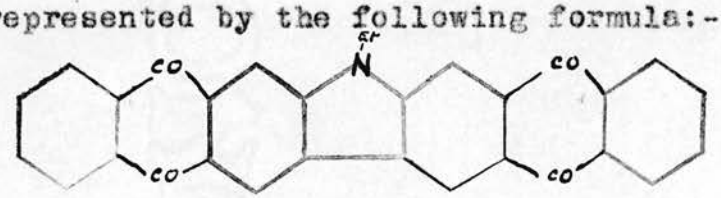
Mainly due to the work of [Lindemann and Ber, (1924), 57, 1316; 555 and Gilbert Morgan J.C.S. (1931), 3283] the nitration of carbazole has been effected and the position of the groups, especially in the mono-nitro compounds, fixed. [P. Ziersch, B, (1909), 42 3798] showed that, using the correct molecular proportions of conc. HNO_3, under carefully regulated temperature conditions, di- and tetranitro-carbazoles could be prepared and Zeidler [A, (1878), 191, 304] obtained a 9-nitroso-carbazole by adding nitrous acid to a glacial acetic acid solution of carbazole. Here carbazole resembles diphenylamine and the nitroso-compound is suitable for rearrangement into a nuclear derivative. [Schott, DRP. (1901), 134, 983, Kl. 12 pp.]

Aminocarbazoles, which are of greater technical importance than the nitro-compounds, are prepared/

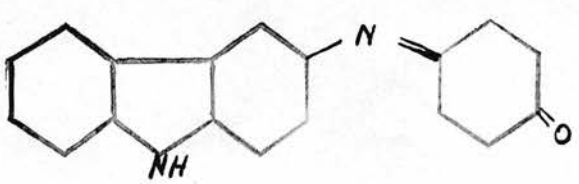
prepared by reduction of the corresponding nitro-compounds [Lindemann, Ber, (1924), 57, 1316; 555].

Like many other hydrocarbons and bases carbazole unites with a number of nitro-compounds to form addition products which serve for purposes of purification, characterisation and identification. Foremost among such products is carbazole picrate [Graebe and Glaser, B, (1872), 5, 14], which forms orange-red needles with a sharp melting point at 186°C. In addition to this picrate, carbazole-picryl chloride, carbazole-trinitrobenzene and trinitrotoluene can be prepared.

For several years investigators entertained strong hopes of utilising the amino-compounds by coupling their diazotisation products with phenols and/or amines and thus forming dyestuffs of technical importance. The real technical significance of carbazole was discovered by the chemists Haas and Herz who established the fact that from it Hydron dyestuffs can be formed. This group of dyes have carbazole derivatives as nuclei e.g. Hydron yellow G which is represented by the following formula:-



and Hydron blue:-

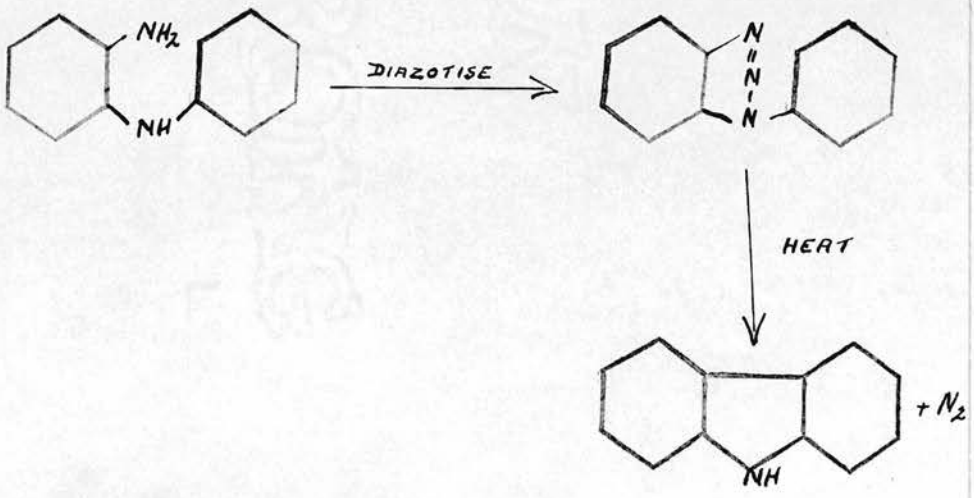


With certain reagents carbazole forms characteristic colours which are utilised for its detection in mixtures and in confirmatory tests for its identification. [Graebe and Glaser A, (1872), 163, 347] describe a reaction in which carbazole, like diphenylamine, gives an intense blue colour when dissolved in H_2SO_4 and a trace of nitrous acid or some other oxidation medium e.g. chromic acid, is added.

Like pyrrole and indole, carbazole gives an intense red colour on exposing a pine splint soaked in HCl vapour to an alcoholic solution of the compound. Isatin and conc. H_2SO_4 reacting on an alcoholic carbazole solution give a deep blue but if glacial acetic acid is used as solvent a fuschin red colour results, water precipitating a brownish-red dyestuff in flakes. Chroranil colours an ethereal solution of carbazole red, N-methyl indole colours it blue and a whole series of carbohydrates give intensive colours with cold saturated solutions of carbazole and indole, in the presence of HCl or H_2SO_4. Finally hot solutions of carbazole give a number of vivid colours with various aldehydes in the presence of H_2SO_4. All the foregoing colour reactions/

reactions have yet to be thoroughly investigated, the dyes obtained being probably nearly related to the technically important triphenyl-methane group. It is significant to note that the fusion of carbazole with water-free oxalic acid gives carbazole blue, a triphenyl-methane dye which is a related dye of diphenylamine blue Suida, [B, (1879), 12, 1403]. It may be mentioned at this point that the similarity between many of the diphenylamine, pyrrole and indole colour reactions and those of carbazole give additional evidence of the chemical similitude of these compounds.

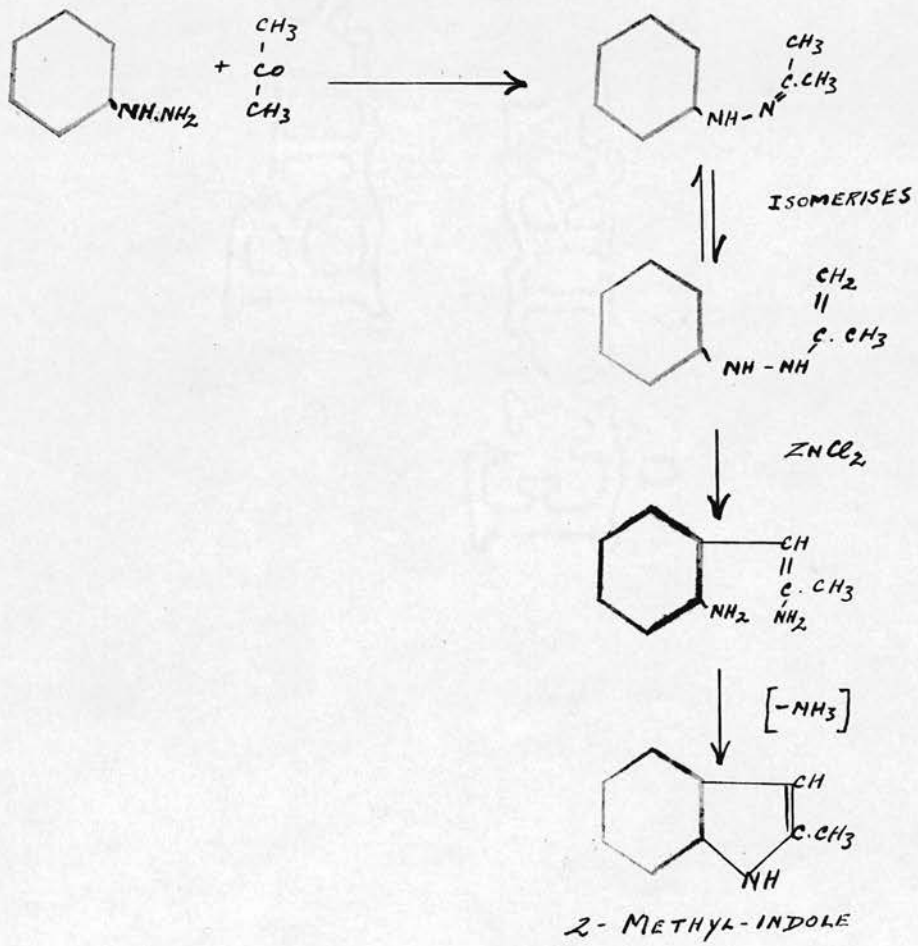
A great deal has been said of the occurrence of carbazole in "crude anthracene" and the technical methods employed for obtaining it chemically pure. Several laboratory methods are also used, many of which are however only of academic interest. The method of Graebe and Ullmann (see p. 8) is undoubtedly the most useful. Their starting product was o-aminodiphenylamine:-



By the use of appropriately substituted diphenylamines this method can be adopted for the preparation of a large number of substituted carbazoles.

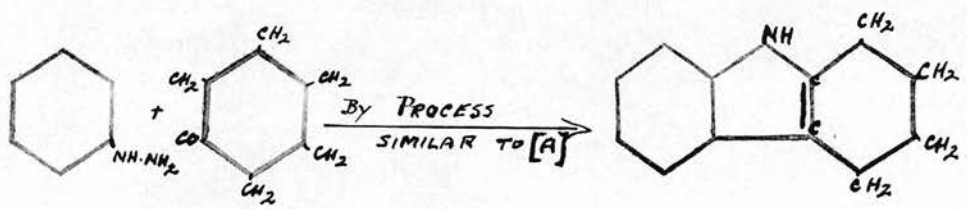
One other laboratory method is suitable for the preparation of carbazole derivatives and is analogous with the Fischer synthesis of indole [A]. Thus tetrahydrocarbazole can be prepared from phenylhydrazine and cyclohexanone [B].

A.



2-METHYL-INDOLE

B.



If the tetrahydro-compound is distilled over lead oxide carbazole is formed [Borsche, Witte and Bothe, A, (1908), 359, 74]. From the foregoing laboratory syntheses alone, the basic structure of carbazole can be elucidated.

In recent years valuable results have been obtained by the study of Friedel and Craft's reaction on carbazole, a field of study in which S.C.P. Plant and co-workers have been singularly successful. Carbazole can, of course, be acetylated [Boëseken, R, (1912), 31, 350] and benzoylated [Mazzara, B (1891), 24, 278] by using the appropriate reagents, the acetyl- and benzoyl-groups entering the 9-position or nucleus. By treatment with nitrobenzene and aluminium chloride Plant found that the acetyl- and benzoyl-groups migrate into the nucleus to give the 3-substituted carbazole [J.C.S., (1936), 40, ibid, (1932), 2188]. The behaviour of these carbazole ketones is rather unusual as N-acetyl carbazole gives the 2-acetyl compound on treatment with acetyl chloride and aluminium chloride [J.C.S. (1934), 1142]. The N-benzoyl compound behaves similarly on treatment with benzoyl chloride and $AlCl_3$ [J.C.S. (1932), 2188]. In 1935 Plant and co-workers clarified the position with regard

to/

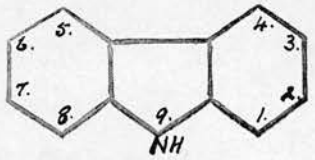
to substitution in the carbazole nucleus and found that the position occupied by a substituent depends on whether the 9-position is already occupied (i) or not (ii).

(i) 9-acyl carbazoles

(ii) carbazoles with a free NH group

Carbazole undergoes substitution in the 3- and 6-positions even with a small amount of acid halide, and in 3-substituted carbazoles a second acyl group goes into the 6-position. Plant and Tomlinson, [J.C.S. (1932), 2188]. From the orientation of substituted carbazoles it is clear that the most reactive positions are the 3-, 6- and 9. This is not surprising. An amino- or imino-group is generally reactive and facilitates further substitutions in the ortho- and para-positions. The 3- and 6-positions in carbazole are para to the imino group and accordingly reactive. It is to be expected that the 1- and 8-positions i.e. ortho to the imino-group will also be somewhat reactive. This is indeed the case; 3:6 dibromo-carbazole, for instance, yields 3:6-dibromo-1-nitrocarbazole Lindemann and Mühlhaus, [Ber. (1925), 58, 2371]. It follows, in view of the greater reactivity of the 3- and 6-positions that direct preparation of 1-substituted carbazoles is a matter of/

of difficulty. For example, nitration of carbazole yields 70-75% of the 3-nitro and only 3-4% of the 1-nitrocarbazole. [Gilbert Morgan, J.C.S. (1931), 3283 and Lindemann, Ber. (1924), 57, 555].



In other words one of the numerous problems in the carbazole series still awaiting solution is the preparation of 1-substituted derivatives in good yield. Some 1-substituted derivatives have been obtained but only by tedious methods and in poor yields. [Lindemann and Wessel, Ber. (1925), 58 1221, ibid, Lindemann, (1924), 57 555]. Gilbert Morgan's method for the preparation of 1-nitrocarbazole (loc. cit.) did not produce a very substantial yield, (see above). As a final example 1-acetylcarbazole has not yet been prepared and attempts by Plant and co-workers to synthesise 1-benzoylcarbazole have so far been unsuccessful. [J.C.S. (1932), 2188].

OBJECT OF RESEARCH.

It was therefore decided to attempt the preparation of 1-derivatives of carbazole. Success in this project would have a dual significance. Not only would a preparatory method be developed but the resulting product could, in many cases, forge the essential link in proving the structure of poly-substituted compounds which have not yet been oriented, e.g. In tetra-bromo-carbazole the position of 2 bromine atoms is still obscure [Votoček Ch. I. Rep. (1896), 20, 190]; two of the bromine atoms are known to occupy the 3- and 6-positions and it has been suggested that further substitution occurs in the 1- and 8-positions. A synthesis of 1-bromo-carbazole would therefore fix the position of a third bromine atom and by analogy the fourth atom would occupy position 8. Such a synthesis was therefore attempted. Several other carbazole derivatives may also have their structures defined by such means.

Improved methods of preparation for some of the simpler substituted carbazoles were also desirable as the yield and purity in many cases were unsatisfactory. It was therefore decided to investigated preparatory methods for the mono-halogenated derivatives [Gazz. (1896), 238 and Zeit. angew. Chem. (1901), 748] and the use/

use of reagents such as phenyl-iodo-dichloride and iodine bromide for obtaining increased yields and higher degrees of purity. There are a great number of preparative and structural problems involved in the study of this subject and this thesis is mainly devoted to them.

EXPERIMENTAL WORK.

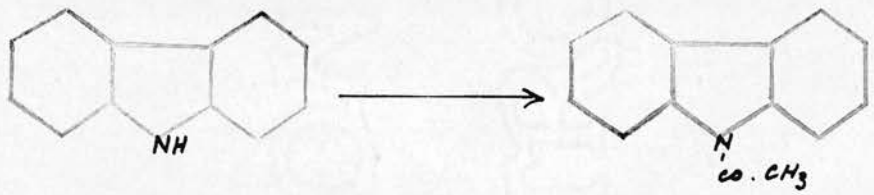
The experimental work carried out is described in the following pages. Yields are quoted as percentages of the theoretical amount obtainable. Since, in many cases, the yields were small, the majority of the melting point determinations were performed on a special micro-melting point apparatus consisting of an electrically heated plate, with thermometer incorporated, mounted on the stage of a low power microscope. Kofler, [Mikrochem., (1934), 15, 242].

All new compounds obtained in the pure state were analysed by micro methods by Dr Weiler of Oxford or by Mr W. Brown of the Department of Medical Chemistry of the University of Edinburgh.

EXPERIMENTAL.

I. Preparation of 9-acetyl-1-nitrocarbazole.

A. 9-acetylcarbazole. [Boëseken, R (1912) 31,350].



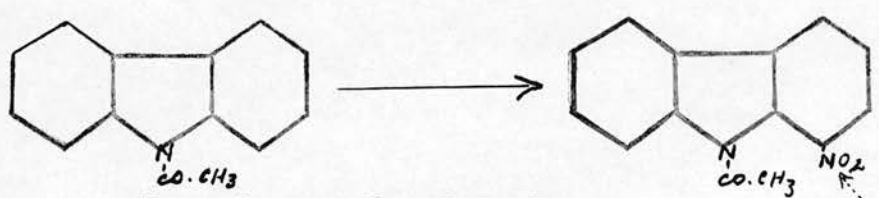
15 g. Carbazole.

22.5 c.c. Acetic anhydride containing 0.4 c.c. conc. H_2SO_4 per 20 c.c. acetic anhydride .

The following was a modification of Boëseken's procedure. The mixture was heated in an open vessel for 5 mins., the fluid obtained being then poured into 100 c.c. water. The dark brown solid which resulted was crystallised from alcohol.

Yield = 10.2 g. m.p. = 76°C. (lit.)

B. Nitration of 9-acetylcarbazole. [Cf. Menke, Rec. Trav. chim. (1925), 44, 141 and 269].



5 g. 9-acetylcarbazole.

30 c.c. acetic anhydride.

12 g. copper nitrate.

The acetylcarbazole was dissolved in the acetic anhydride and the copper nitrate was added in small portions with continuous stirring, the temperature being kept below 30°C. The mixture was allowed to stand at room temperature for 1 hour and then poured into 150 c.c. water. The yellow solid obtained was filtered and dried.

Yield = 5 g. m.p. = 130°-180°C.

The solid was suspected to contain a mixture of substances and a separation was effected by boiling with aqueous alcohol for 15-20 mins.

Soluble fraction. Yield = 3.2 g. m.p. 163-168°C. This fraction sublimed in yellow needles but was discarded as it consisted chiefly of the 3-compound.

Insoluble fraction. m.p. = 193-198°C.

This fraction was recrystallised three times from glacial acetic acid, the light brown solid obtained giving no m.p. up to 300°C., but showed signs of decomposition.

Yield = 0.2 g. This solid had a microscopic appearance of clusters of light brown needles.

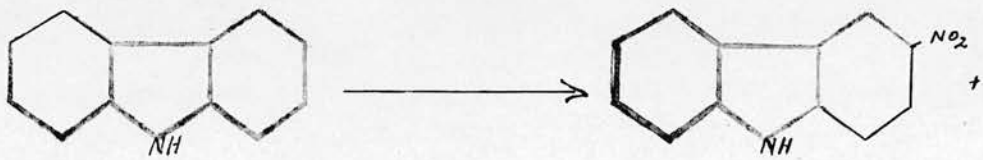
Analysis of insoluble fraction. N fd. = 12.86%

$C_{14}H_{10}O_3N_2$ requires N = 11.1%.

II. Preparation of 1-nitro-9-acetylcarbazole.

[Gilbert Morgan, J.C.S. (1931), 3283].

A. 1-nitro-carbazole.



+ Molecular Compd.

50 g. carbazole.

100 c.c. water.

45 c.c. 60% nitric acid.

Experimental procedure followed the above reference. A yellow product of m.p. = 156-159°C. was obtained.

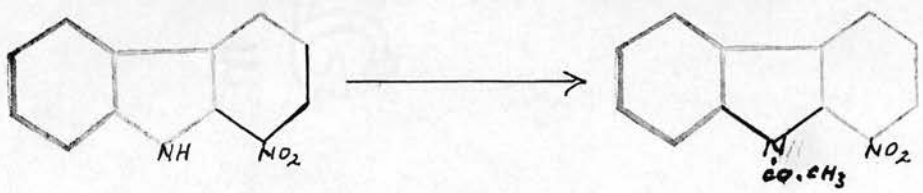
Yield of 3-nitrocarbazole = 57 g.

Yield of molecular compound = 14 g.

This molecular compound of 1- and 3-nitrocarbazole was then dissolved in warm pyridine 14.8 c.c. and, on addition of 3 vols. of alcohol followed by cooling, 1-nitrocarbazole separated. It was recrystallised from glacial acetic acid, the dark yellow plates obtained having a m.p. = 180-182°C.

Yield = 3 g.

B. Acetylation of 1-nitrocarbazole.



0.2 g. 1-nitrocarbazole.

5 c.c. acetic anhydride [H_2SO_4 (conc.)

0.4 c.c. per 20 c.c. acetic anhydride].

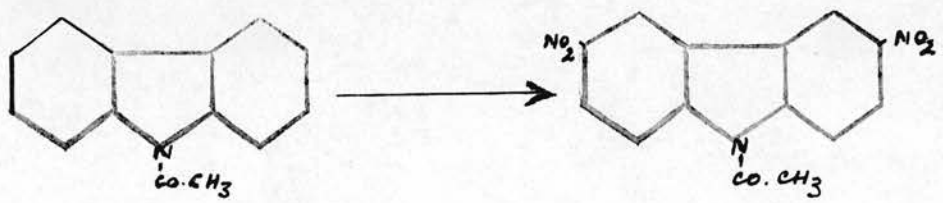
The 1-nitrocarbazole and acetic anhydride were placed in a narrow-necked bottle and the mixture shaken for 14 hrs. The resulting suspension was filtered and the yellow solid found to melt over a very wide range. A molecular compound was suspected and, on warming it with 2 c.c. pyridine a soluble and insoluble fraction was obtained.

Insoluble fraction : m.p. = 238-245°C.

Soluble fraction : This fraction, on cooling and addition of methyl alcohol yielded a light brown solid. m.p. = Nil up to 300°C. but signs of decomposition were evident. Yield = 0.002 g.

The microscopic appearance of both the nitration of 9-acetylcarbazole and the acetylation of 1-nitrocarbazole were similar viz. clusters of light brown needles. The yield was however extremely poor. Attempts to acetylate this compound by warming it with the acetylation mixture of acetic anhydride and H_2SO_4 (conc.) were unsuccessful. A charred mass being obtained even with 5 mins. heating.

Dinitro-9-acetylcarbazole.



2 g. 9-Acetylcarbazole.

15 c.c. Glacial acetic acid.

3.6 c.c. Nitric acid (conc.).

The acetylcarbazole was dissolved in the glacial acetic acid by warming to 80°C. and the nitric acid was then added dropwise with stirring. The mixture was finally heated at 100°C. for half an hour. The yellow compound which separated was recrystallised three times from glacial acetic acid.

Yield = 1.2 g. = [43%] m.p. = 217-218°C. with sublimation in rosettes of needles.

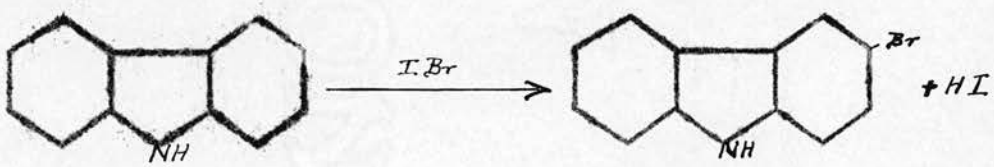
m.p. of sublimate = 232-233°C.

Analysis : N fd = 13.5%

$C_{14}H_9O_5N_3$ requires N = 14.00%

Bromination of Carbazole with Iodine Bromide.

Cf. [Militzer J.A.C.S., (1938), 60, 256].



$$IBr + HI \longrightarrow I_2 + HBr$$

10 g. Carbazole

100 c.c. Carbon tetrachloride.

The carbazole and carbon tetrachloride were stirred until a uniform suspension resulted. Two molecular proportions of iodine bromide, prepared by adding the calculated quantity of bromine to iodine in carbon tetrachloride, were added in three portions at intervals of 10 mins. at 50°C. The mixture was maintained between 50°C. and 60°C. until evolution of hydrobromic acid had ceased, was then cooled and filtered. The solid obtained was a mixture of iodine and the brominated carbazole. The iodine was dissolved out by shaking with excess sulphurous acid and subsequent boiling with carbon tetrachloride.

Yield of impure compound = 7 g. [50%] m.p. = 170-80°C.

Purification of the dark brown solid obtained was effected by extraction with light petroleum (100-120°).

Yield = 1.5 g. [11%]. m.p. = 197-198°C.
lit. = 199°C .

The 3-bromocarbazole so formed was converted to the picrate. This was done by adding a boiling concentrated solution of the compound in benzene to a similar solution of picric acid in benzene. A perceptible darkening in the colour of the solution was immediately noticeable and, on cooling, a dark-red solid separated out.

It was extremely unstable, decomposed readily and recrystallisation from benzene did not purify it.

m.p. = 155-180°C. Long red needles.

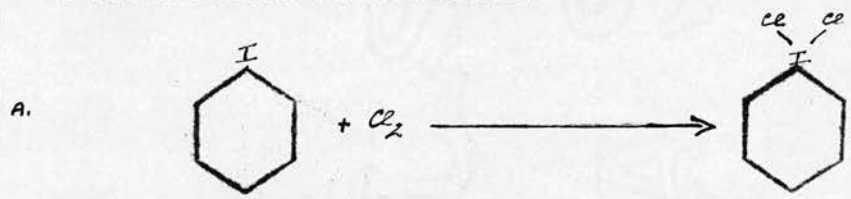
The compound was obviously very impure and was not analysed. Carbazole picrate was prepared in a similar fashion using glacial acetic acid instead of benzene. Decomposition of this picrate was also observed and recrystallisation from glacial acetic acid did not purify it.

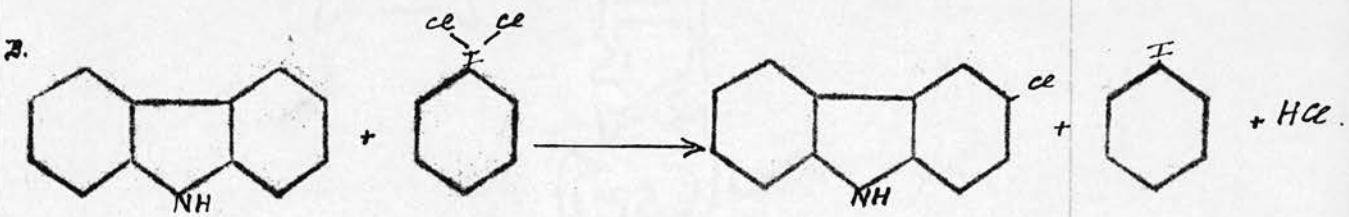
m.p. = 168-182°C.

Chlorination of Carbazole with Phenyl-iodo-dichloride.

Cf. [J.A.C.S. (1937), 59, 1827].

Chlorination of Carbazole.





9.5 g. Carbazole.

23 g. Phenyl-iodo-dichloride [1.5 mols.]

150 c.c. Chloroform.

The mixture of carbazole and phenyl-iodo-dichloride in chloroform was heated slowly until complete solution resulted, a procedure which took 15 mins. Refluxing of the solution was continued for 3 hours,

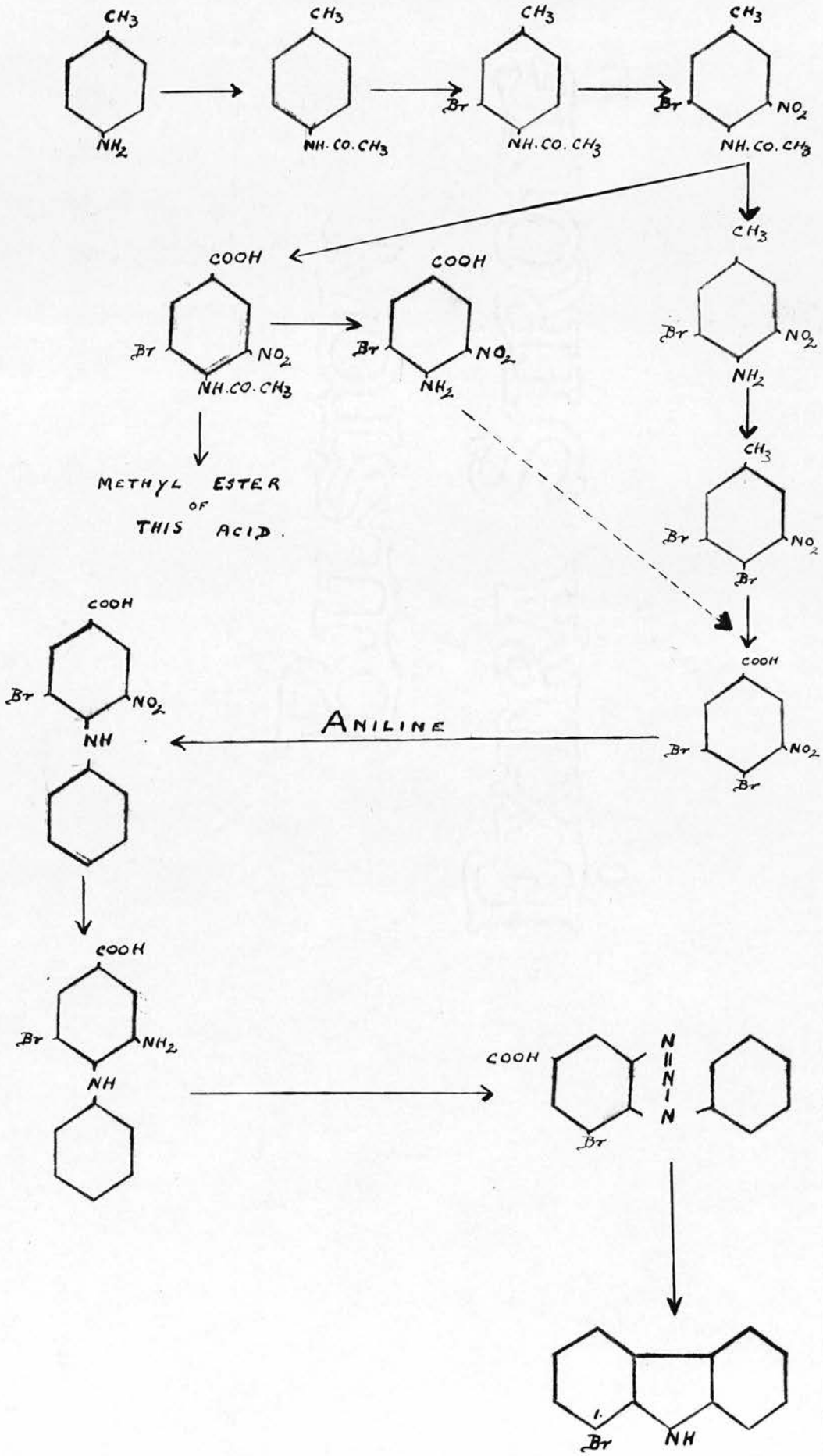
When/

when all the hydrochloric acid gas fumes ceased to be evolved, the chloroform and iodobenzene were removed by steam distillation, the yellow-greenish coloured residue being recrystallised from glacial acetic acid.

Yield = 7 g. [70%]. m.p. = 198°C. lit. = 201.5°C.

Modifications of B using less than 1.5 molecular proportions of phenyl iodo-dichloride gave smaller yields and less pure products.

Attempted Synthesis of 1-Bromocarbazole.



I. Preparation of p-Acetotoluidide.

[Ber. (1909), 42, 3481].

[Org. Synthesis, 6, 8-9].

100 g. p-toluidine

100 g. acetic anhydride

250 c.c. benzene.

Yield = 130 g. [95%] m.p. = 153-5°C. -white prisms from ligroin

lit. m.p. = 155°C.

II. 3-Bromo-4-acetamidotoluene.

[Ann. (1872), 168, 153 and Ann. (1878), 192, 202].

130 g. p-acetotoluidide

130 g. bromine

500 c.c. glacial acetic acid.

Yield = 165 g. [85%] m.p. = 115-117°C.

lit. m.p. = 117-118°C.

The solid sublimes in rosettes of white needles.

III. 3-Bromo-5-nitro-4-acetamidotoluene.

[J.C.S. (1914), 105, 510].

165 g. 3-bromo-4-acetamidotoluene

165 c.c. fuming HNO_3

550 c.c. glacial acetic acid.

The fuming nitric acid was added dropwise with continual stirring to the solution of 3-bromo-4-acetamidotoluene in glacial acetic acid, the temperature being kept between 5-10°C. When all the nitric acid had been added the mixture was heated until it boiled and was poured into a litre of cold water. The pale yellow compound obtained was recrystallised from alcohol.

Yield = 160 g. [80%]. m.p. 207-9°C.
lit.m.p. 210°C.

This solid also sublimed in rosettes of white needles.

IV. 3-Bromo-5-nitro-4-aminotoluene.

100 g. 3-Bromo-5-nitro-4-acetamidotoluene.
550 c.c. alcohol
550 c.c. conc. HCl.

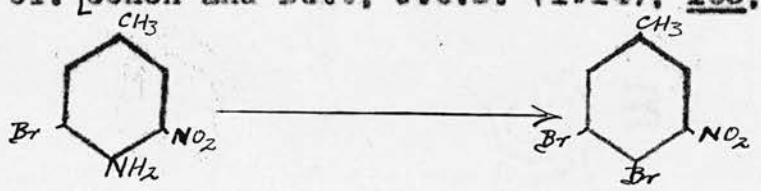
The above compounds were mixed and heated on a water-bath for 3½ hours. The solution was poured into cold water and the orange-red solid which separated was recrystallised from methyl alcohol.

Yield = 87 g. Quantitative. m.p. = 63-5°C. - Prisms.
lit. m.p. = 64-5°C.

V./

V. 3:4-Dibromo-5-nitrotoluene.

Cf. [Cohen and Dutt, J.C.S. (1914), 105, 510).]



The base [87 g.] was dissolved in warm glacial acetic acid, the calculated quantity of concentrated HCl [109 c.c.] added, and the diazotisation effected with sodium nitrite [35 g.] The whole of the solid passed into solution and this was added dropwise with continuous stirring to an ice-cooled solution of cuprous bromide in hydrobromic acid.

The cuprous bromide was prepared by mixing solutions of copper sulphate [175 g.] and potassium bromide [74 g.] in water and passing in sulphur dioxide. The white precipitate of cuprous bromide is filtered off and is dissolved, when dried, in hydrobromic acid.

The diazotised mixture thus formed was warmed on a water-bath until evolution of nitrogen ceased and steam was then passed in for a few minutes. The brown oil which separated, solidified on cooling to a crystalline mass. It was filtered off and recrystallised from alcohol.

Yield = 70 g. [66%]. m.p.=63-65°C. - Prisms.

lit. m.p. = 63-65°C.

Mixed m.p. with previous compound = 30-50°C.

Several unsuccessful attempts were made to condense the 3:4-dibromo-5-nitrotoluene with aniline.

Heating of the compound with aniline both in open vessels and sealed tubes from 2-24 hours with

(a) Copper bronze

(b) Sodium acetate and alcohol

(c) Aluminium chloride

(d) Sodium hydroxide and alcohol

yielded in each case charred masses or tars. Under milder conditions such as heating on a water bath charred masses were again obtained. In order to determine whether the Br atom in the para position is reactive or not the following experiment was carried out.

0.3 g. 3-4-dibromo-5-nitrotoluene

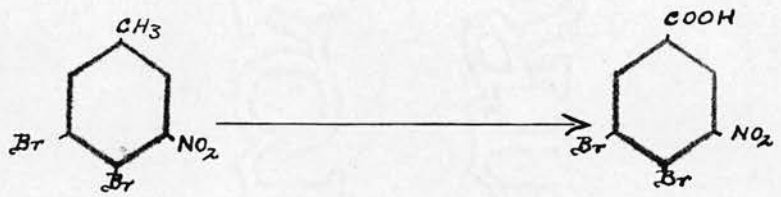
2 c.c. piperidine.

The above compounds were heated for 2 hours at 50°C. and, on cooling, pale yellow plates formed. m.p. = 235°C. They were very soluble in water and were probably piperidine hydrobromide which has a m.p. = 235°C. Hydrobromic acid was probably given off during the reaction and has united with the piperidine. This indicates that the main reaction has proceeded to some extent and it may therefore be concluded/

concluded that the Br in the para position of the nucleus is reactive but not sufficiently reactive to condense with aniline.

VI. In view of the foregoing experiments it was decided to oxidise the 3:4-dibromo-5-nitrotoluene.

3:4-Dibromo-5-nitrobenzoic acid.



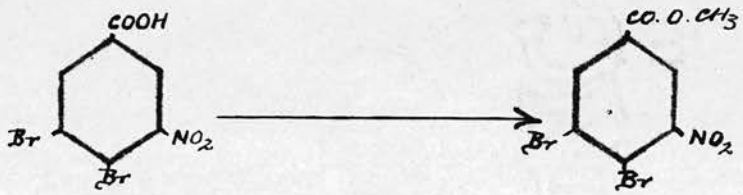
60 g. 4:5-dibromo-3-nitrotoluene.
1450 c.c. nitric acid [density 1.2].

The above quantities of the compounds were boiled for 24 hours. On cooling a solid separated. Sodium hydroxide was added and any remaining solid was filtered off. The acid was recrystallised from the filtrate by adding HCl (conc.) until the filtrate is acid. Recrystallisation is effected from boiling water.

Yield = 20 g. [33%]. m.p. = 180-2°C. - Needles.
lit. m.p. = 183°C.

This method was considered much superior to that of Blanksma [C, (1912), II, 1965.] who obtained this acid/

acid by $KMnO_4$ oxidation of the corresponding aldehyde. In order to characterise the acid the methyl ester was prepared.



1 g. 3:4-dibromo-5-nitrobenzoic acid.

25 c.c. methyl alcohol

10 drops H_2SO_4 (conc.).

The above mixture was refluxed for 3 hours, cooled and water added. The white flocculent precipitate which resulted was recrystallised from aqueous acetone.

Yield = 0. 4 g. m.p. = 106°C. - White needles.

Analysis:- N fd = 3.3%

$C_8H_5O_4NBr_2$ requires N = 4.1%.

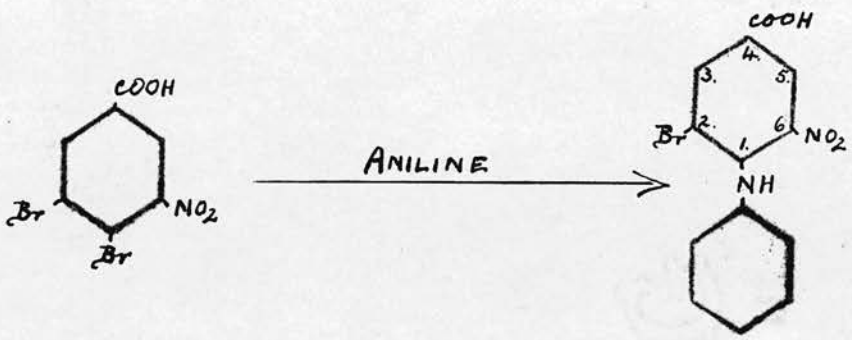
Although the yield of the acid was not large it was very much higher than that obtained when the following reangnts were used(a) Potassium permanganate

(b) Alkaline $KMnO_4$

(c) 1.2 HNO_3 in sealed tube.

VII. 2-Bromo-6-nitro-4-carboxydiphenylamine.

Cf. [Lindemann and Wessel, Ber. (1925) 58, 1221].



20 g. 3:4-dibromo-5-nitrobenzoic acid.

Excess aniline.

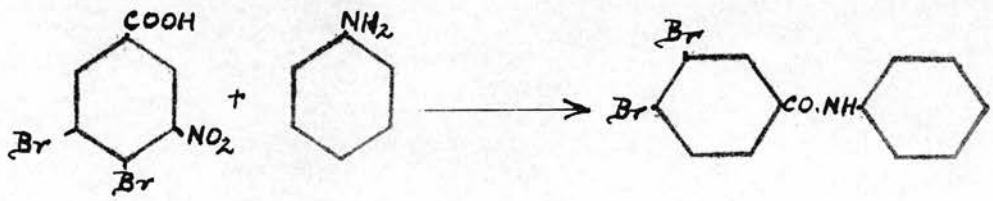
The mixture of excess aniline and the above acid was heated over a naked flame for 40-50 minutes, HCl (conc.) was added to remove the excess aniline and the mixture poured into H_2O to remove aniline HCl. The golden-yellow solid obtained was recrystallised from benzene.

Yield = Quantitative. m.p. = 207-8°C. -sublimes in lustrous plates.

Analysis:- Found C, 46.3; H, 2.8; Br 23.7.

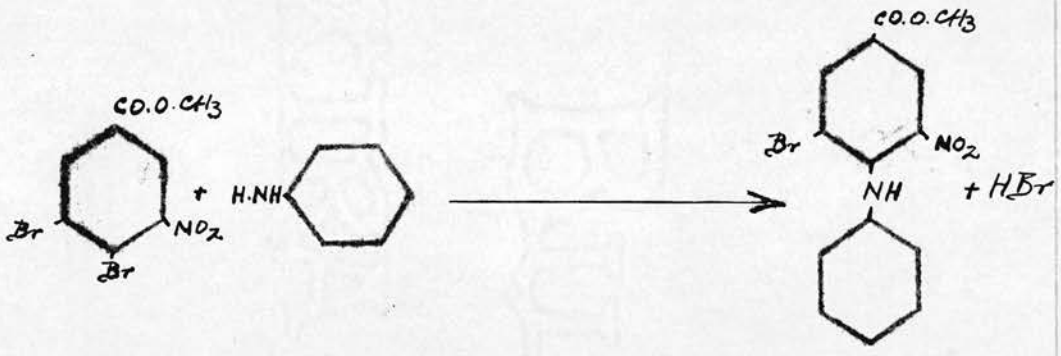
$C_{13}H_9O_4N_2Br$ requires C, 46.3; H, 2.7; Br 23.7%

This acid was found to be insoluble in NaOH. The faint possibility of anilide formation was eliminated however by the Br analysis. If the following reaction had occurred:-



Then the % of Br would have been 40%.

VIII A. Methyl ester of 2-Bromo-6-nitro-4-carboxydiphenylamine.



1 g. 3:4 dibromo-5-nitro-methyl benzoate.

X S aniline.

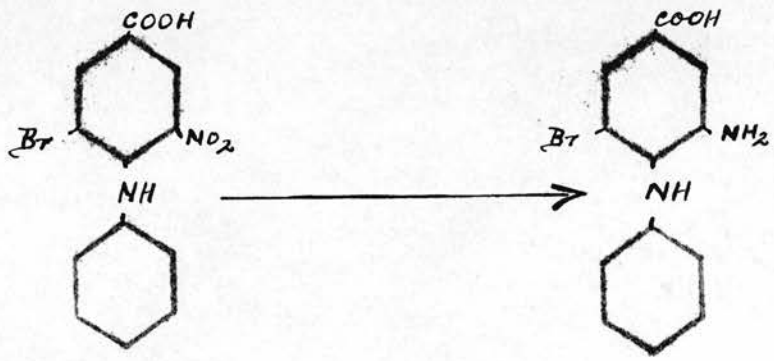
The above compounds were heated on a water-bath for 48 hours. HCl (conc.) was added to destroy X S aniline and the solid was poured into water to remove aniline hydrochloride. The resulting solid was recrystallised from benzene.

Yield = 0.2 g. m.p. 151-2°C. - brown prisms.

Analysis:- N fd = 8.4%

$C_{14}H_{11}O_4N_2Br$ requires N = 8.0%.

VIII. 2-Bromo-6-amino-4-carboxydiphenylamine.



6 g. 2-Bromo-6-nitro-4-carboxydiphenylamine.

18 g. sodium sulphide (crystalline).

25 c.c. H_2O.

A mixture of the above compounds was heated on a water-bath for 24 hours, the liquid cooled and the amine [+ sulphur] precipitated by carefully adding glacial acetic acid. The precipitate was dissolved in hot sodium carbonate solution, the sulphur filtered off, and the amine re-precipitated from the wine-coloured solution by glacial acetic acid. Recrystallisation was effected from alcohol.

Yield = 4.5 g. [83%] m.p. 244-5°C. -sublimes in colourless plates.

Analysis: N fd = 9.2%.

$C_{13}H_{11}O_2N_2Br$ requires N = 9.1%.

The following colour tests were carried out on the newly-formed amine:

With acid $FeCl_3$ ⟶ Wine colour

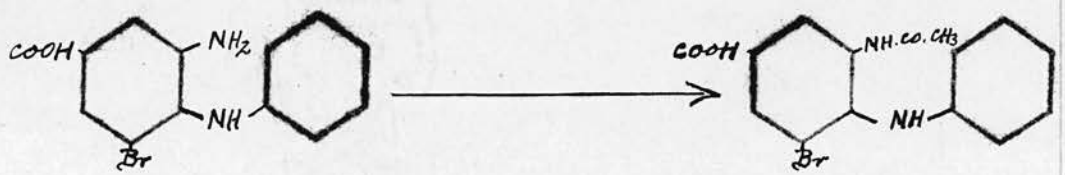
With H_2SO_4 (conc.) ⟶ Wine colour

Chloranil Test $\xrightarrow{\text{Heating}}$ Light-red.

Cf. [Frehden and Goldschmidt - Mikrochimica Acta, (1937), I, 347.]

VIII. A/

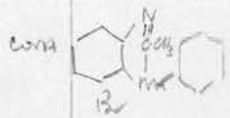
VIII. A. Acetyl-derivative of 2-bromo-6-amino-4-carboxydiphenylamine.



0.2 g. 2-bromo-6-amino-4-carboxydiphenylamine.

1 c.c. water.

12 drops acetic anhydride.



$C_{15}H_{11}O_2N_2Br$

N_1 8·46 %.

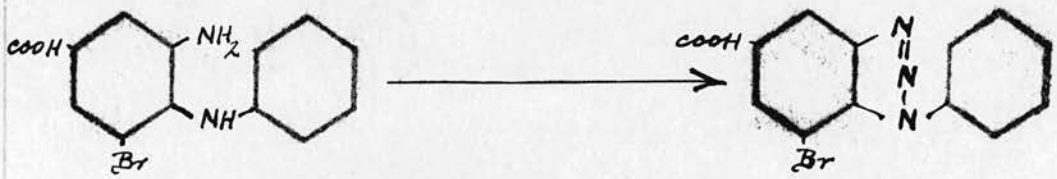
The above compounds were shaken together for 10-15 minutes and the resulting dark-brown oily solid recrystallised from aqueous methyl alcohol.

Yield = Quantitative m.p. 163-4°C. - white needles.

Analysis:- N fd = 8.15%.

$C_{15}H_{14}O_3N_2Br$ requires N = 8.00%.

IX. 7-Bromo-5-carboxy-1-phenylbenztriazole.



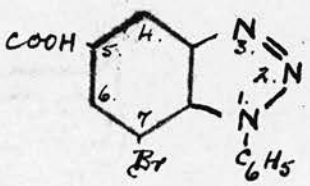
4.5 g. 2-bromo-6-amino-4-carboxydiphenylamine.

1.8 g. sodium carbonate in 50 c.c. water.

2.3 g. sodium nitrite dissolved in minimum of water.

X S 10% H_2SO_4

The nomenclature is explained by the following diagram:



The free amine was dissolved in the sodium carbonate solution and the sodium nitrite solution then added slowly. The entire mixture was then added dropwise with continual stirring to excess ice-cooled 10% H_2SO_4. The stirring was continued for 10-15 minutes after the complete addition of the sodium carbonate solution, and the mixture allowed to stand at room temperature for 2 hours. The resulting pale yellow solid was filtered and crystallised from aqueous methyl alcohol as a light-brown powder.

Yield = Quantitative m.p. = 215-7°C. - sublimes in white needles and cubes.

Analysis: N fd = 13.3%

$C_{13}H_8N_3Br$ requires N = 13.2%

Colour test With H_2SO_4 (conc.) + HNO_3 (conc.)

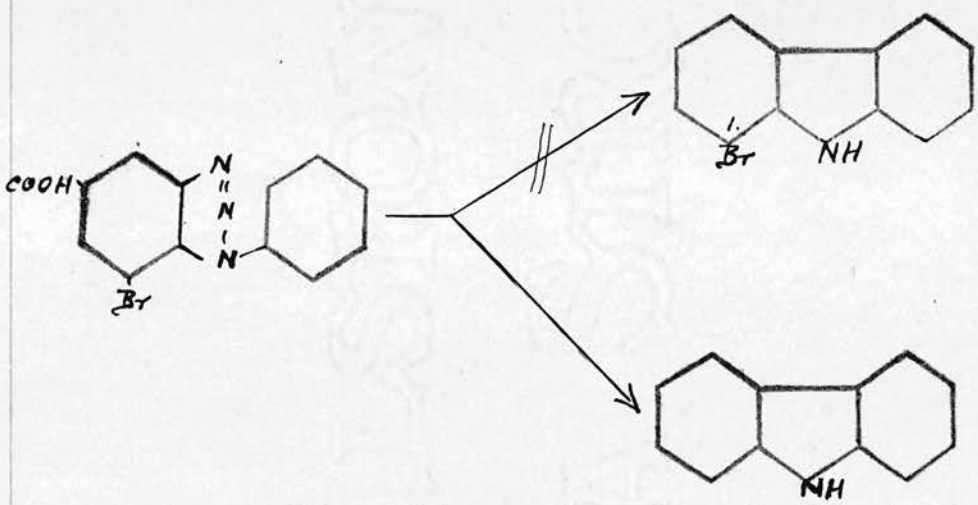
↓

Remains original brown colour.

The significance of this test is clear from the following/

following experiment.

X. Attempted preparation of 1-Bromocarbazole.



1·5 g. 7-bromo-5-carboxy-1-phenyltriazole.

3 g. freshly-prepared quicklime.

A finely ground mixture of the above compounds in a small distilling flask was placed in a metal bath which was gradually heated to 360°C. Between 320-360°C. a yellowish brown oil distilled over, and in addition large white flakes of sublimate formed on the upper parts of the distilling flask. A micro-extraction of the solidified oil, with light petroleum (100-120°) yielded a light brown crystalline solid which gave colourless plates on sublimation.

Yield = 0.1 g. m.p. 220-230°C.

Analysis: Analysis of the product of the micro-extraction showed that no Br was present.

Colour test: With H_2SO_4 (conc.) + HNO_3 (conc.)

↓

Deep green colour obtained.

This colour reaction is in direct contrast to the one carried out in similar conditions with the substituted benztriazole compound. Moreover the light petroleum extract of the supposed 1-bromo-carbazole gave the characteristic violet fluoresence of carbazole in ordinary and U.V. light. A mixed melting point with pure carbazole gave a gradual melting from 220-230°C. as in the case of the product of the final reaction. It was therefore concluded from these observations that the drastic conditions employed for the conversion of the substituted bentriazole compound removed both carbon dioxide and bromine to yield carbazole.

Experiments were carried out heating the benztriazole compound with

A. calcium carbonate

B. soda-lime.

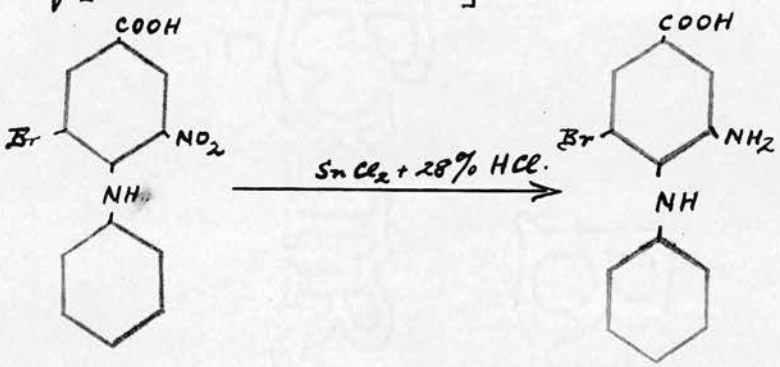
in a sealed tube in a copper block and in an asbestos furnace in an atmosphere of CO_2.

In each case a sublimate of white plates in minute quantity and with m.ps. between 220-232°C. resulted, and in each case, on treating with the sublimate with/

with 1 drop H_2SO_4 (conc.) + 1 drop HNO_3 (conc.) the deep-green colour, characteristic of carbazole itself, was formed.

Unexpected results were recorded when the 2-bromo-6-nitro-4-carboxydiphenylamine were reduced with stannous chloride and 28% HCl.

cf [J.C.S. (1932), 2188.]



10 g. 2-bromo-6-nitro-4-carboxydiphenylamine.

300 c.c. methyl alcohol.

6 g. stannous chloride.

300 c.c. 28% HCl.

The nitro-compound was dissolved in the methyl alcohol and the mixture brought to the boiling point. The solid $SnCl_2$ dissolved in the 28% HCl was added in small portions, the mixture was refluxed for 20-25 minutes and a dark-brown crystalline solid separated. On cooling NaOH (conc.) was added until the yellow precipitate of stannous oxide which first forms, dissolves. The remaining solid was recrystallised/

recrystallised from methyl alcohol (twice) and finally purified by extraction with light petroleum (100-120°).

Yield = 4 g. [50%] m.p. = 152-3°C. sublimes in orange-red prisms.

Analysis: Found C, 49.5; H, 3.2

$C_{13}H_{11}O_2N_2Br$ requires C, 50.8; H, 3.58%.

Colour tests. With H_2SO_4 (conc.) + HNO_3 (conc.) ↓ Deep red colour which disappears on heating.

With acid $FeCl_3$ ⟶ no colour.

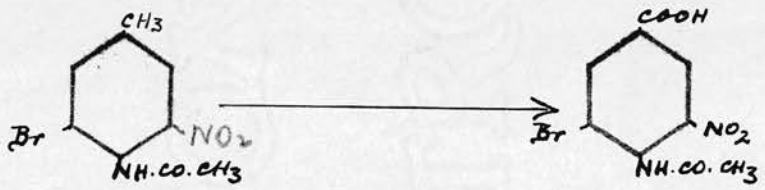
Attempts to prepare acetyl- and benzal -derivatives of this amine were unsuccessful. Similarly, attempts to convert this amine into the corresponding triazole compound by the methods of Plant and Tomlinson [J.C.S. (1932), 2188] and Lindemann and Wessel [Ber. (1925), 58, 1221], were also unsuccessful.

During the course of the foregoing synthesis the following acids were prepared. No mention is made of them in the literature. They are in no way necessary to the main synthesis although at one time it was thought they might be used as intermediates. They are:

I. 3-bromo-5-nitro-4-acetaminobenzoic acid.

II. 3-bromo-5-nitro-4-aminobenzoic acid.

I. 3-Bromo-5-nitro-4-acetamidobenzoic acid.



See p. 30.

10 g. 3-bromo-5-nitro-4-acetamidotoluene.

18 g. $KMnO_4$ (finely powdered).

500 c.c. water.

The finely-powdered $KMnO_4$ was added slowly to the suspension of bromo-nitro-acetamidotoluene in water. The mixture was heated in a boiling water-bath for 2½ hours by which time the potassium permanganate was decolourised. The mixture was filtered hot, thus removing the manganese dioxide formed and sulphurous acid was added to the filtrate to destroy the last traces of MnO_2 and unchanged $KMnO_4$. The light-yellow solid was recrystallised from alcohol three times.

Yield = 2.5 g. [20%]. m.p. = 248-9°C. sublimes in rosettes of needles.

Analysis:- N fd = 10.2%.

$C_9H_7O_5N_2Br$ requires N= 9.2%.

The small amount of acid may be due to decomposition of/

of the acid after its formation as, on acidifying the filtrate with H_2SO_3 effervescence was observed indicating the presence of carbonate.

Cohen and Dutt [J.C.S. (1914), 105, 510], found this method of oxidation abortive in their experiments on the oxidation of mixed dibromo-toluenes. Modifications of the permanganate oxidation were carried out without improving on the 20% yield already quoted.

[A.] Alkaline $KMnO_4$ NaOH was used so that the acid passed into the filtrate as the sodium salt. Acidification with HCl (conc.) gave the acid as before.

Yield = 2 g.

[B.] Calcium permanganate was used in similar proportions as the potassium permanganate. It was thought that $Ca(OH)_2$, being a much weaker base than KOH, would help the acid formation.

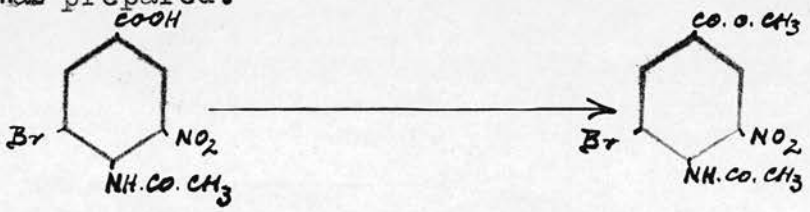
A similar yield to [A.] was recorded.

[C.] Acetone, specially purified by refluxing with $KMnO_4$ for 1 hour, and redistilling, was used as solvent instead of water. Using similar quantities of $KMnO_4$ and 3-bromo-5-nitro-4-acetamidotoluene as in A., under similar experimental conditions, unchanged compound was obtained.

I.-A. Methyl ester of 3-Bromo-5-nitro-4-acetamidobenzoic acid.

I.-A. Methyl ester of 3-Bromo-5-nitro-4-acetamidobenzoic Acid.

To confirm the presence of the carboxy-group the methyl ester was prepared.



0.5 g. 3-bromo-5-nitro-4-acetamidobenzoic acid.

10 c.c. methyl alcohol.

4 drops H_2SO_4 (conc.).

The above mixture was refluxed for 1 hour, cooled and the ester precipitated by the addition of water. The pale yellow solid formed was recrystallised from methyl alcohol.

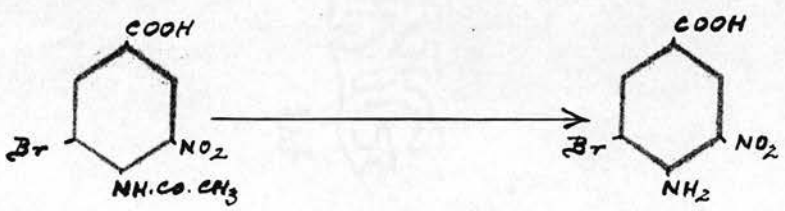
Yield = Quantitative m.p. = 203°C.

Sublimes in rosettes of needles.

Analysis: N fd = 9.3%.

$C_{10}H_9O_5N_2Br$ requires N= 8.8%.

II. 3-Bromo-5-nitro-4-aminobenzoic acid.



0.5 g./

0.5 g. 3-bromo-5-nitro-4-acetamidobenzoic acid.

10 c.c. water.

10 c.c. H_2SO_4 (conc.).

The above mixture was refluxed for 1 hour, poured into 50 c.c. water, the light-brown solid obtained being recrystallised from aqueous alcohol.

Yield = 0. 2 g. [50%]. m.p. =275-6°C. Needles.

Analysis: N fd = 11.2%.

$C_7H_5O_4N_2Br$ requires N = 10.7%.

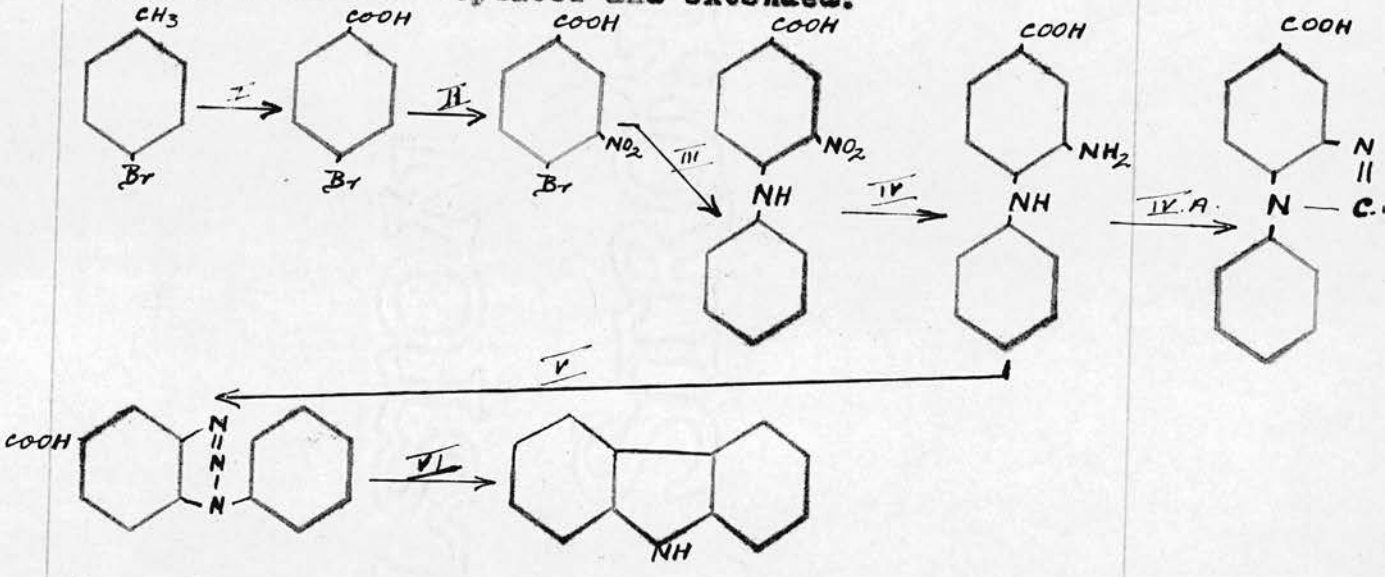
During the latter part of the synthesis of 1-bromocarbazole it was decided to repeat Ullmann's work [Ann. (1904), 332, 82] on a simpler preparation, namely that of carbazole from 2-amino-4-carboxydiphenylamine, the reason being three-fold:

1. Practice would be gained in the correct procedure to adopt for the reduction, diazotisation and conversion of the substituted benztriazole compound into the corresponding carbazole.

2. On treating the 2-bromo-6-amino-4-carboxydiphenylamine with $SnCl_2$ HCl, the product did not analyse correctly for the amine (pp43-4) which should normally be formed, nor would this product yield a triazole compound on the appropriate treatment.

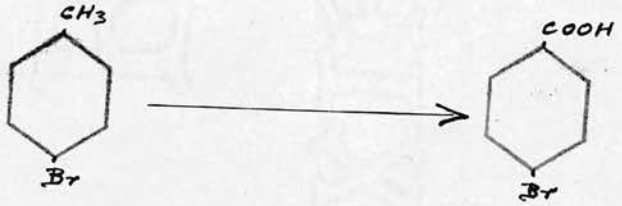
3. Suitable apparatus was found to be necessary (see pp41-2) Ullmann's work [Ann. (1904), 332, 82]/

82 was therefore repeated and extended.



I. p-Bromobenzoic acid.

[Conn and Lowry, Chem. Abstr. (1926), 20, 3396].



10 g. p-bromotoluene.

20 g. $KMnO_4$ finely powdered.

500 c.c. water.

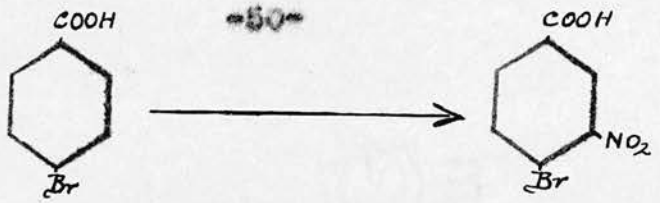
Experimental procedure as in above abstract.

Yield = 2 g. [20%]. m.p. = 254°C. (alcohol).

lit. m.p. = 254°C.

II. 4-Bromo-3-nitro-benzoic acid.

[Hübner, Ann. (1884), 222, 177)]



1 g. p-bromobenzoic acid.

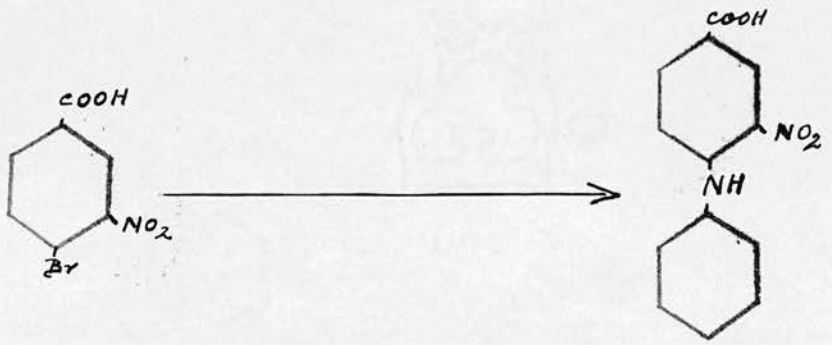
10 c.c. fuming nitric acid.

Hübner's procedure was modified as follows:
The above compounds were heated gradually until a solution was formed. On allowing to stand overnight the acid separated out in white prisms. With half the amount of fuming HNO_3 quoted above the acid separated out in 1-2 hours.

Yield = 0.75 g. [62%] m.p. = 199°C. (lit.)
(Alcohol).

III. 2-Nitro-4-carboxydiphenylamine.

Cf. [Lindemann and Wessel, Ber. (1925), 58, 1221].



0.75 g. 4-bromo-3-nitrobenzoic acid.

X S aniline.

This condensation was effected by heating the above compounds in an open vessel on a water-bath for

24/

24 hours. After the excess aniline had been removed with HCl (conc.), the reddish-brown residue was crystallised from a mixture of ethyl alcohol and glacial acetic acid.

Yield = 0.6 g. [90%]. m.p. = 260-1°C. sublimes in light-brown prisms.

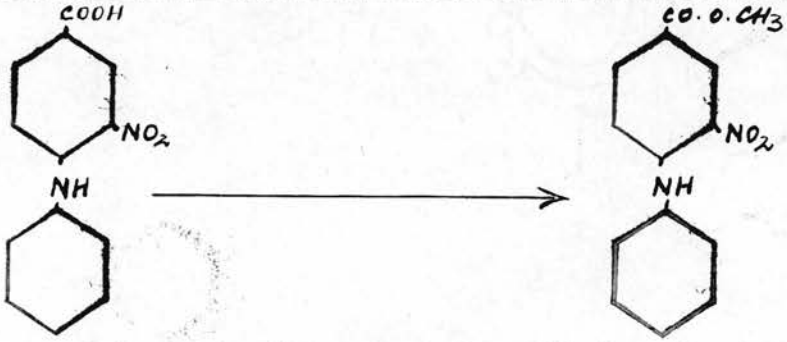
lit.m.p. = 260-1°C.

Analysis: N fd = 10.63%.

$C_{13}H_{10}O_4N_2$ requires N = 10.85%.

The acid exhibits, as does 2-bromo-6-nitro-4-carboxy-diphenylamine, the peculiar property of insolubility in alkali.

III. A. Methyl ester of 2-nitro-4-carboxydiphenylamine.



0.5 g. 2-nitro-4-carboxydiphenylamine.

50 c.c. methyl alcohol.

10 drops H_2SO_4 (conc.),

The above compounds are refluxed for 5 hours, cooled and/

and the ester precipitated by the addition of water. Recrystallisation is effected from aqueous acetone.

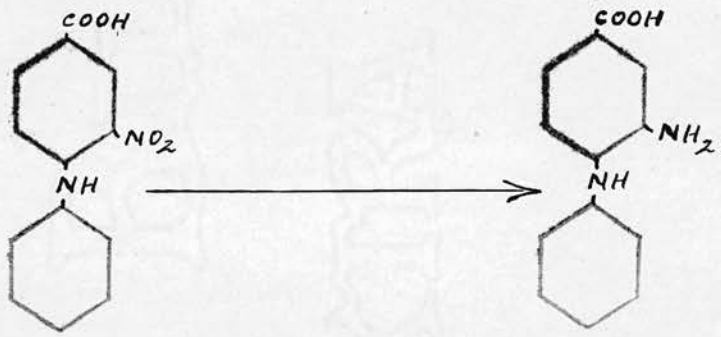
Yield = 0.2 g. m.p. = 130°C. Yellow needles.

Analysis: N fd = 9.6%.

$C_{14}H_{12}O_4N_2$ requires N = 10.28%.

IV. 2-Amino-4-carboxydiphenylamine.

Cf. [Schöpff, Ber, (1889), 22, 3286].



0.4 g. 2-nitro-4-carboxydiphenylamine.

1.5 g. sodium sulphide (crystalline).

5 c.c. water.

1 c.c. alcohol.

The experimental procedure was greatly modified from that in the quoted reference. The above compounds were refluxed in a water-bath for 2 hours. The deep-red colour of the original solution became light yellow, the solution was cooled and glacial acetic acid slowly. The resulting solid, which contained/

contained the amine along with sulphur, was heated to boiling with sodium carbonate solution, hot filtered and the amine re-precipitated by the addition of more glacial acetic acid. Recrystallisation was effected from methyl alcohol.

Yield - 0.2 g. [57%]. m.p. = 153°C. (lit.).

The experiment was repeated and a greatly improved yield resulted as refluxing was continued in this instance for 6 hours.

5 g. 2-nitro-4-carboxydiphenylamine.

20 g. sodium sulphide (crystalline).

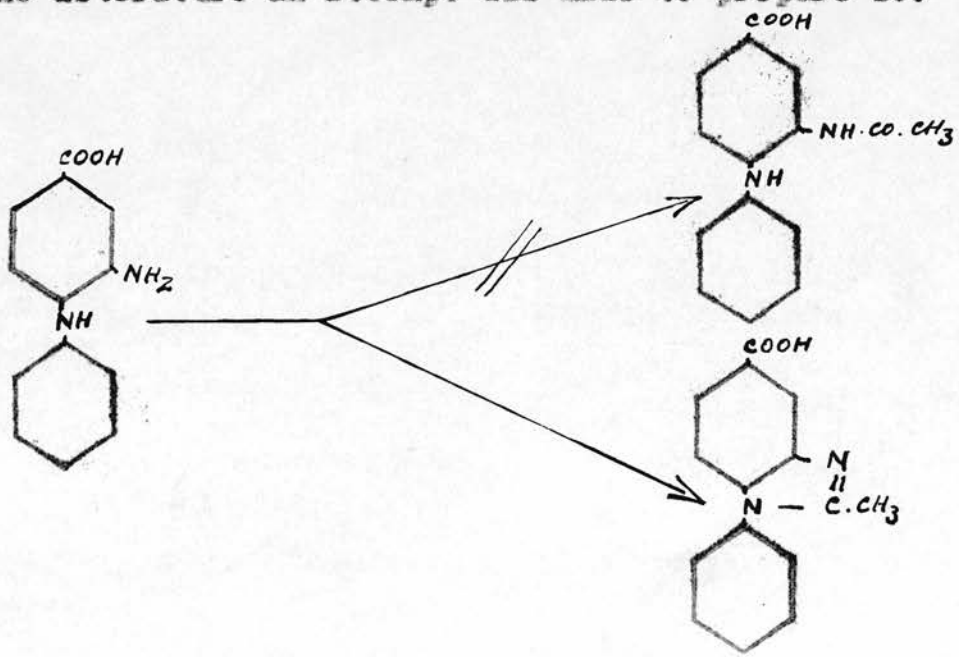
50 c.c. water.

10 c.c. alcohol.

Yield = 3.5 g. [78%]. m.p. = 153°C. (lit.).

IV. A. Acetylation of 2-amino-4-carboxydiphenylamine.

As no acetyl derivative of this compound is listed in the literature an attempt was made to prepare it.



0.3 g. 2-amino-4-carboxydiphenylamine.

1 c.c. water.

12 drops acetic anhydride.

The above mixture was shaken for 10-15 minutes and the solid recrystallised from a mixture of methyl alcohol and glacial acetic acid. Final purification was effected by sublimation.

Yield = 0. 12 g. m.p. = 293-294°C.
sublimes in white prisms and tetrahedra.

Analysis: N fd = 11.24%

$C_{15}H_{14}O_3N_2$ requires N = 10.37%.

This formula is based on the assumption that the compound is the acetyl derivative.

An alternative possibility is that the compound being an ortho-diamine may yield a benzimidazole derivative.

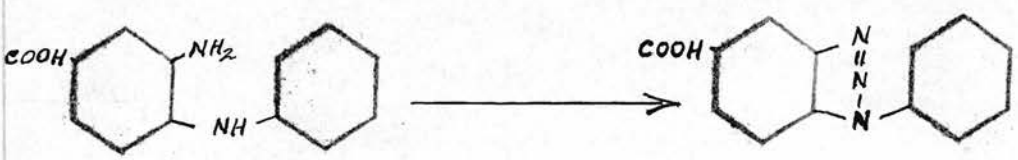
On this assumption

$C_{15}H_{12}O_2N_2$ requires N = 11.1% N fd = 11.24% .

This definitely indicates the formation of the 4-carboxy-benzimidazole compound.

V. 5-Carboxy-1-phenylbenztriazole.

[Ullmann, Ann. (1904), 332, 86].



1 g. 2-amino-4-carboxydiphenylamine.

0.5 c.c. Na_2CO_3 in 30 c.c. water.

0.5 g. $NaNO_2$ dissolved in minimum of water.

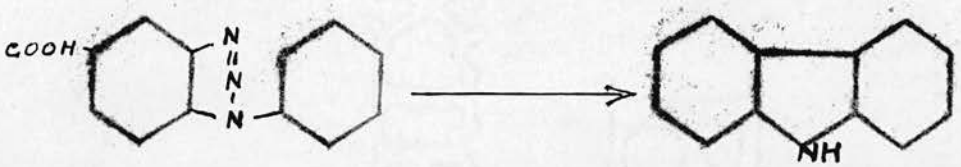
X S 10% H_2SO_4.

Experimental procedure as in above reference.

Yield = 0.7 g. [70%]. m.p. = 282°C.-white needles.

lit. m.p. = 272°C.

VI. Carbazole.



The benztriazole compound so formed was converted to carbazole according to the instruction of Ullmann [Ann. (1904), 332, 82].

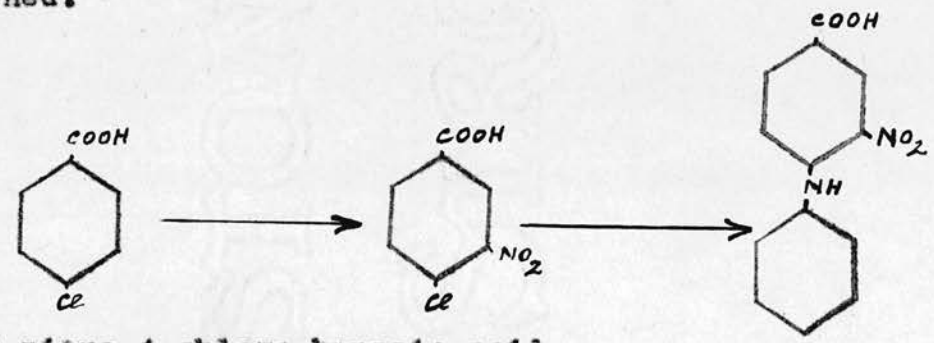
Yield = 0.05 g. [10%]. m.p. 232-37°C.

A mixed m.p. with pure carbazole gave no depression of the melting point. The compound is therefore carbazole.

During the course of these experiments two further methods were developed for the preparation of/

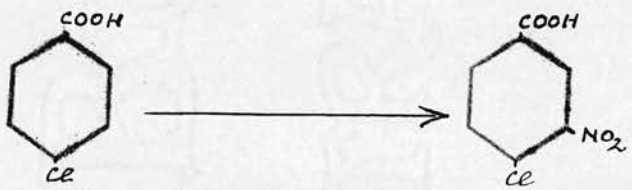
of 2-nitro-4-carboxydiphenylamine, good yields being obtained.

A.



I. 3-nitro-4-chloro-benzoic acid.

[Hübner, Z. (1866), 615].



10 g. p-chloro-benzoic acid.

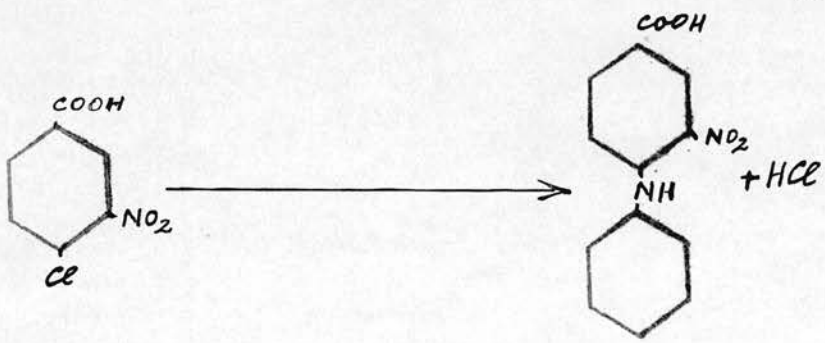
100 c.c. fuming nitric acid.

Procedure is as in reference quoted above.

Yield = 11 g. [92%]. m.p. 180-2°C (lit.).

II. 2-nitro-4-carboxylic diphenylamine.

Cf. [Lindemann and Wessel Ber. (1925), 58, 1221].



11 g./

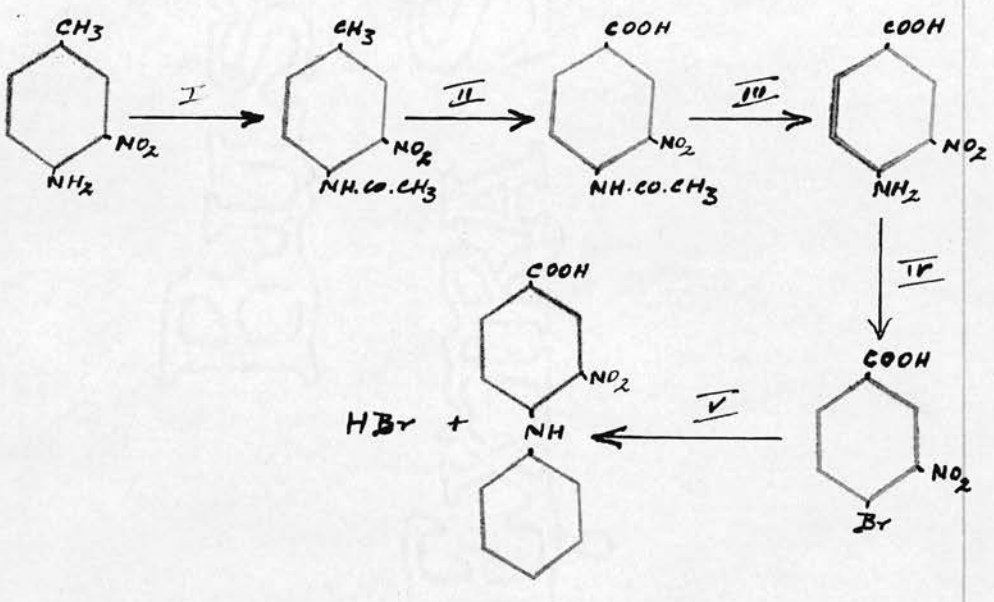
11 g. 3-nitro-4-chlorobenzoic acid.

X S. aniline.

Procedure is similar to that already described for the condensation of p-bromobenzoic acid and aniline.

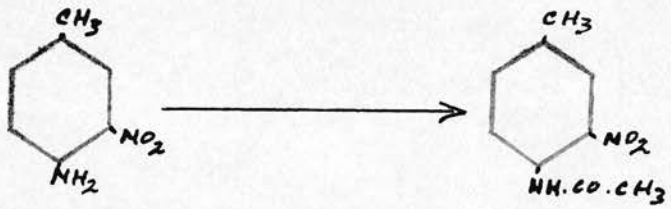
Yield = 13 g. [85%]. m.p. = 180-2°C. (lit.).

B.



I. 2-Nitro-4-acetamidotoluene.

Cf. [Ehrlich, Ber, (1882), 15, 2009].



20 g. m-nitro-p-toluidine.

40 c.c. acetic anhydride.

0.8 c.c. conc. H_2SO_4.

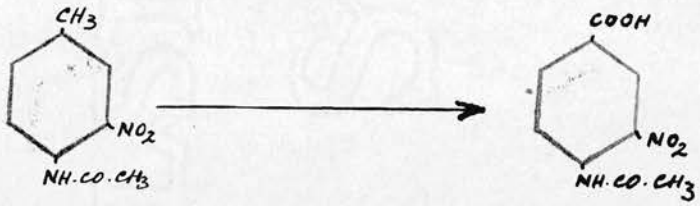
procedure as in above reference.

Yield = Quantitative. m.p. = 95-96°C. (alcohol).

lit.m.p. = 96°C.

II. 3-Nitro-4-acetamidobenzoic acid.

Cf.[Ullmann and Mauthner, Ber. (1903), 36, 3032.]



25 g. 3-nitro-4-acetamidotoluene.

50 g. finely powdered $KMnO_4$.

750 c.c. water.

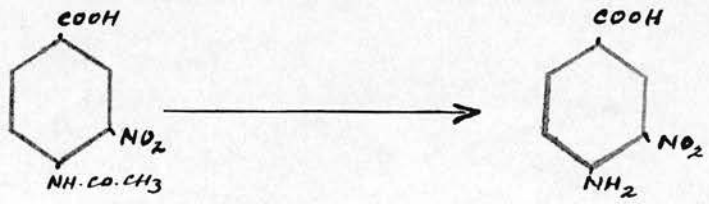
Experimental procedure as in reference quoted above.

Yield = 22 g. [80%] m.p. = 224-5°C.

lit. m.p. = 220°C.

III. 3-Nitro-4-aminobenzoic acid.

Cf.[Ullmann and Mauthner, Ber. (1903), 36, 4032].



22 g./

22 g. 3-nitro-4-acetamidobenzoic acid.

220 c.c. 50% H_2SO_4.

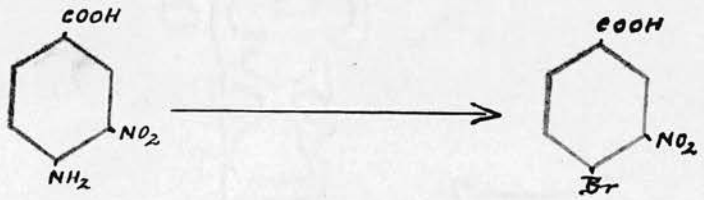
Experimental procedure as in reference quoted above.

Yield = 15 g. [85%]. m.p. = 278-280°C.

lit.m.p.= 284°C.

IV. 4-Bromo-3-nitrobenzoic acid.

Cf. [Cohen and Dutt, J.C.S. (1914), 105, 510].



A
15 g. 3-nitro4-aminobenzoic acid in 150 c.c. glacial acetic acid.

10 c.c. HCl conc.

15 g. $NaNO_2$.

B
45 g. copper sulphate in aqueous solution.

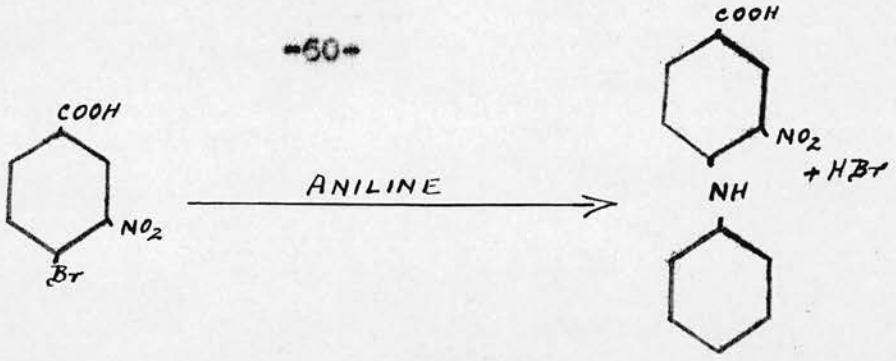
24 g. potassium bromide in aqueous solution.

[B] is saturated with SO_2 to yield the required quantity of CuBr. Solution of [A] is added to a solution of the cuprous bromide thus formed in hydrobromic acid as in the reference quoted.

Yield = 12.5 g. [65%]. m.p. = 199°C (alcohol).

V. 2-nitro-4-carboxydiphenylamine.

Cf. [Lindemann and Wessel Ber,(1925), 58, 1221].



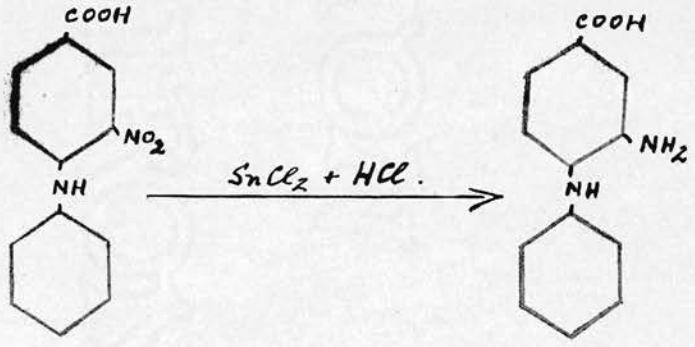
12.5 g. 3-Nitro-4-bromobenzoic acid.

X S aniline.

The procedure followed that in the reference quoted except that heating was carried out for 15-20 minutes over a naked flame instead of 2 hours in a water-bath.

Yield = 12 g. [90%] m.p. = 260-1°C.(lit.)

Further unexpected results were obtained by a stannous chloride - HCl reduction of 2-nitro-4-carboxydiphenyl-amine [Cf.pp.43-4].



5 g./

5 g. 2-nitro-4-carboxydiphenylamine

50 c.c. methyl alcohol

5 g. stannous chloride

175 c.c. HCl (conc.).

The nitro compound was dissolved in the hot methyl alcohol and a warm solution of the $SnCl_2$ in HCl added slowly over a period of 30 minutes. The mixture was refluxed for a further period of 2½ hours, during which time the solution became darker in colour. The solution, on cooling, was treated with excess NaOH (30%). This dissolved the salt which is first precipitated on the addition of alkali. The remaining brown solid was crystallised from methyl alcohol and finally from light petroleum (100-120°).

Yield = 2.45 g. [58%] m.p. = 129°C.
Sublimes in light yellow prisms.

Analysis: Found, C, 65.03; H, 4.9

$C_{13}H_{12}O_2N_2$ requires C, 68.4 ; H, 5.26%.

From 2.148 mg. there was a residue of 0.11 mg.

Colour tests: With $FeCl_3$ ⟶ Deep blue colour, characteristic of the diphenylamine nucleus.

With Chloranil → No colour change.

[Cf. Frehden and Goldschmidt, Mikrochimica Acta, (1937), 1, 347].

In addition the compound formed no methyl ester or benzal derivative.

Acetylation of product of $SnCl_2$-HCl reduction of 2-nitro-4-carboxydiphenylamine.

In order to identify the product as an amine acetylation was carried out as follows:

0.2 g. $SnCl_2$-HCl reduction product of 2-nitro-4-carboxy-diphenylamine [X].

1 c.c. water

12 drops acetic anhydride.

The above compounds were mixed and shaken together for 10-15 minutes. The solid which had undergone a colour change from dark to light red was filtered and recrystallised from a mixture of methyl alcohol and glacial acetic acid.

Yield = Quantitative m.p. 264-5°C. Sublimes in rosettes of orange-red needles.

Analysis: N fd = 11.3%.

$C_{15}H_{14}O_3N_2$ requires N = 10.4%.

This assumed that the acetyl derivative has been formed during the reaction. But, as in the case of the true 2-amino-4-carboxydiphenylamine obtained by reduction of the corresponding nitro-compound by the sodium sulphide method already described, the 4-carboxybenz-imidazole compound was formed. Thus:

N fd = 11.3%.

$C_{15}H_{13}O_2N_2$ requires N = 11.1%.

Attempted preparation of the azimido-compound of this $SnCl_2$-HCl reduction product.

1.4 g. reduction product [X] in 60 c.c. glacial acetic acid.

0.65 g. sodium nitrite [1.5 mols.] in minimum of water.

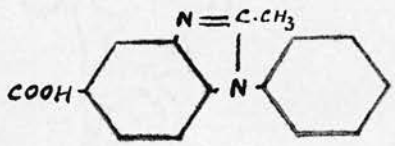
10 c.c. HCl (dil.).

The HCl (dil.) and sodium nitrite solution were added slowly with stirring to a suspension of the reduction compound in glacial acetic acid, the solid becoming lighter brown in colour. Filtration and recrystallisation from glacial acetic acid and alcohol yielded a compound with a melting point identical with that of the acetylation product viz. 264-5°C. A mixed melting point with it gave no depression. As the compound X had stood in the glacial acetic acid for some 2 hours and as this was unlikely to yield the acetyl derivative it was strongly suspected that the benzimidazole compound was formed. If the compound were the acetyl derivative hydrolysis with 50% H_2SO_4 would yield the free amine very easily but, if the imidazole compound is present then 50% H_2SO_4 hydrolysis will give an unchanged compound. Boiling with 50% H_2SO_4 for ¾ hour yielded the unchanged/

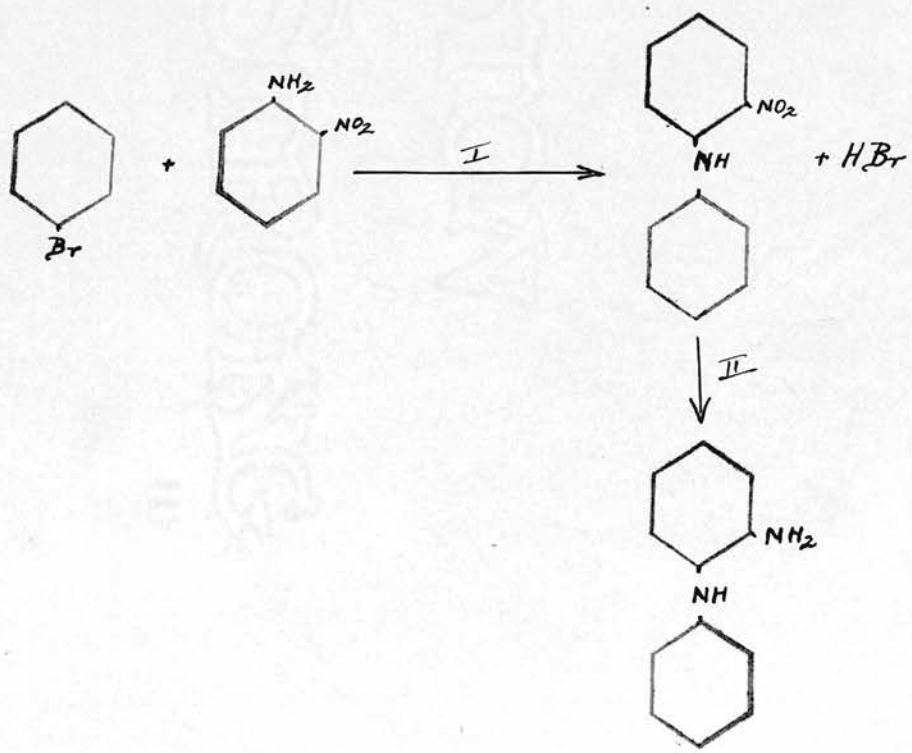
unchanged compound. ∴ The presence of the imidazole compound is confirmed.

Yield = 0.7 g. [50%]. m.p. = 264-5°C.

Product of $SnCl_2$-HCl reduction of 2-nitro-4-carboxy-diphenylamine.

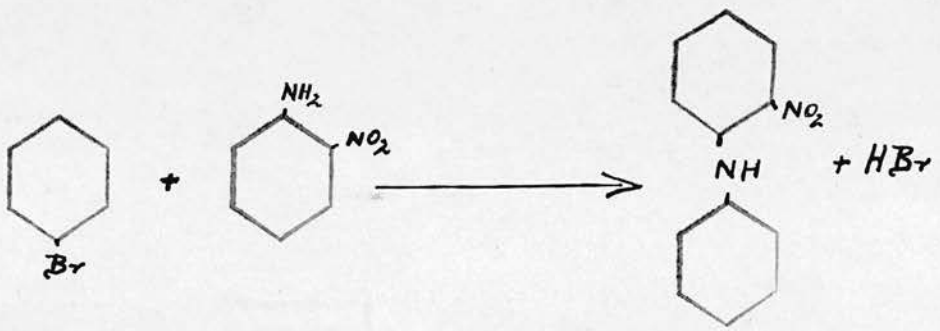


In view of these results it was decided to prepare o-aminodiphenylamine for the purpose of comparing its properties with those of the 6-bromo-2-amino-4-carboxydiphenylamine and the 2-amino-4-carboxy-diphenylamine already prepared.



I. o-Nitro-diphenylamine.

[Cf. Hickinbottom, p. 271].



30 g. o-nitraniline.

10.5 g. potassium carbonate.

125 c.c. bromobenzene.

0.1 g. cuprous iodide.

Experimental procedure was as in reference quoted above.

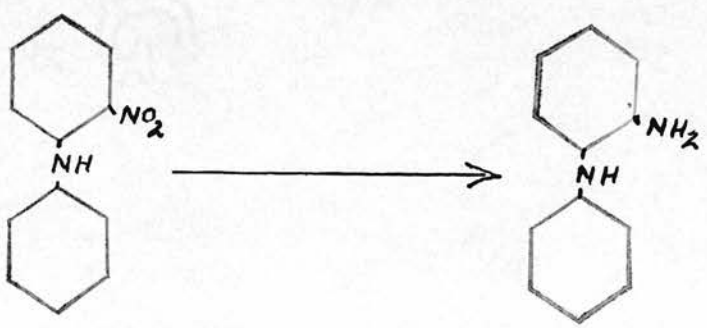
Yield = 9 g. [45%]. m.p. = 74-5°C.

lit. m.p. = 75°C.

A mixed m.p. with o-nitraniline gave a depression of 25-30 degrees.

II. o-Aminodiphenylamine.

[Cf. Kehrmann and Havas, Ber. (1913), 46, 341].



3 g. o-Nitrodiphenylamine.

30 c.c. alcohol.

12 g. stannous chloride.

30 g. fuming HCl.

The experimental procedure was, in the main, similar to that quoted in the above reference. Certain modifications were however employed as follows:

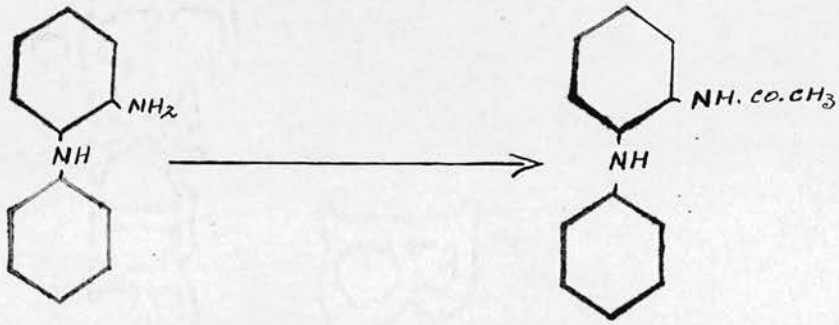
As the double tin salt did not separate out at the required point the solution was made alkaline with 33% KOH. A white precipitate first of all formed, changed to a temporary emulsion and finally a brown amorphous powder separated. Filtration and further boiling with KOH resulted in the formation of a brown oil which was separated from the remaining tin salt by ether extraction. The ether was removed on a steam-bath and addition of 10 c.c. light petroleum (60-80°), resulted in the formation of a brown solid which was recrystallised from water.

Yield = 0.48 g. [20%]. m.p.=79-80°C. (lit.) white needles.

Colour test: Chloranil test ⟶ Dirty green ↓ cherry red on standing for 1 hour.

Acetyl derivative of o-aminodiphenylamine.

Cf.[Wolff, Ann., (1912), 394, 65].



0.2 g. o-Aminodiphenylamine.

12 drops acetic anhydride.

1 c.c. water.

The above mixture was shaken for 10-15 minutes and the resulting solid recrystallised from hot water.

Yield = Quantitative m.p. = 121°C. (lit.)

white needles.

The compound is therefore a simple acetamido- and not a benzimidazole derivative.

Note 1. This method is a modification of the reference quoted above.

2. The acetyl derivative also resulted after the following procedure:

0.3 g. o-Aminodiphenylamine

1 c.c. acetic anhydride

1 drop H_2SO_4 (conc.).

The mixture was heated for 2 minutes over a naked flame and the resulting oily, solid recrystallised from/

from aqueous methyl alcohol.

Yield = Quantitative m.p. = 121°C. (lit.)

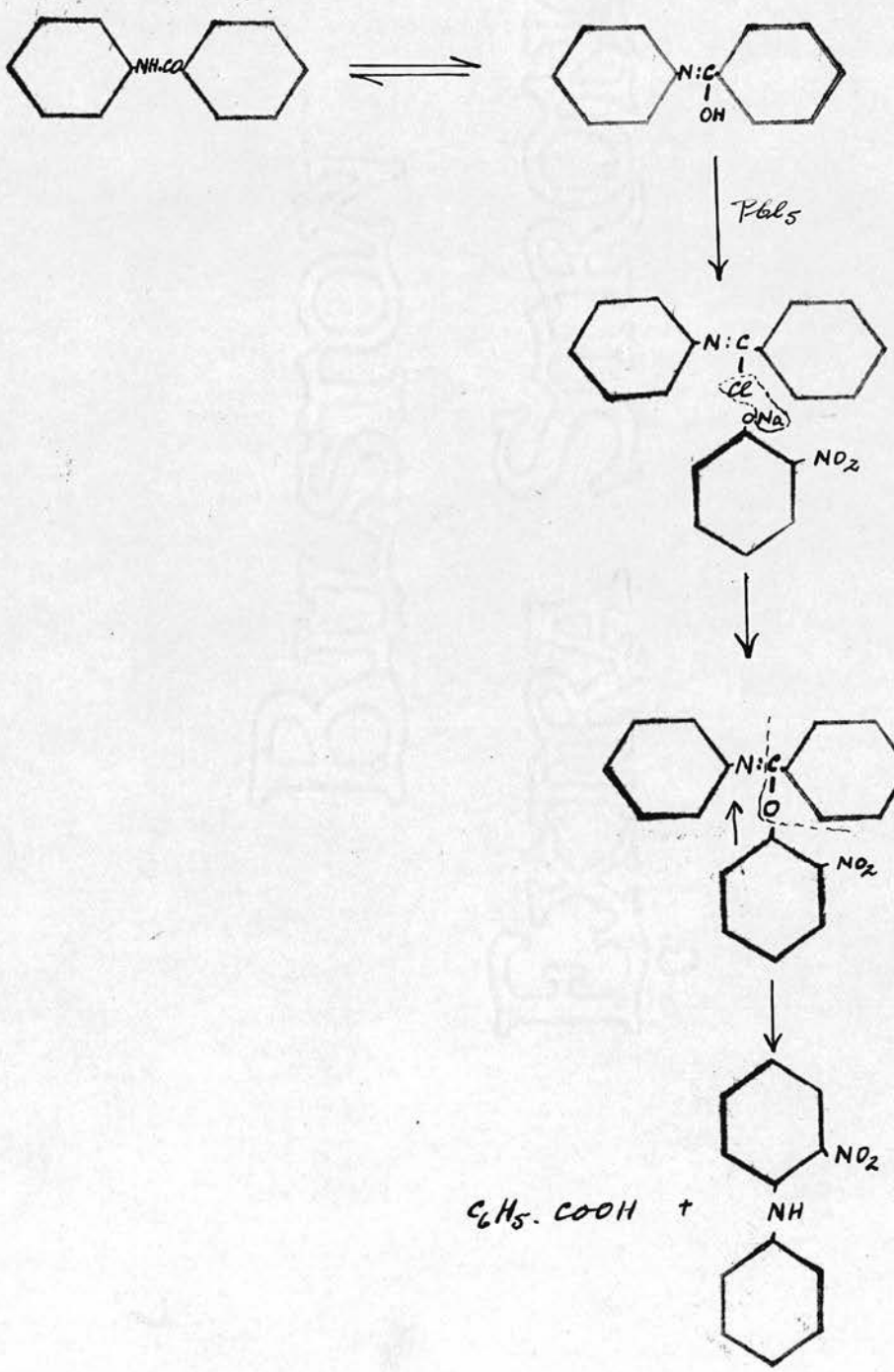
3. Boiling with glacial acetic acid in an attempt to acetylate, yielded unchanged o-amino-diphenylamine.

4. No benzal derivative resulted on treatment with benzaldehyde. The following table summarises the behaviour of the 2-amino-, 2-amino-4-carboxy-, and the 6-bromo-2-amino-4-carboxydiphenylamine:

Property	2-amino-diphenylamine	2-amino-4-carboxy-diphenylamine.	6-bromo-2-amino-4-carboxydiphenyl-amine.
m.p.	79-80°C. (lit.)	153°C. (lit.)	244-5°C.
Microscopic appear-ance.	White needles	White prisms	Colourless plates
Sublimation	Negative	Positive	Positive
Formation of Benzal derivative	Negative	Negative	Negative
Reaction with $(CH_3CO)_2O$ + H_2O	Acetyl derivative formed m.p. 121°C. (lit.).	Benzimidazole compd. formed m.p. 264-5°C.	Acetyl derivative formed m.p. = 163-4°C.
Reaction with glacial acetic acid	Nil	Benzimidazole compd. formed	Nil
Solubility in 2N NaOH	Insol. in the cold. Forms an oil on heat-ing.	Insol. in hot or cold.	Insol. in hot or cold.
Chloranil test	Dirty green Cherry red	No colour change	Remains original light-green in the cold. Light-red on heating.
Acid $FeCl_3$ test	No colour	Deep blue colour	Wine colour.

It was hoped to prepare a number of substituted diphenylamines by the method of Chapman [J.C.S. (1922), 1676; ibid, (1926), 2296], which could ultimately be converted to substituted carbazoles.

1. o-nitrodiphenylamine.



A. N-Phenylbenzimido-o-nitrophenyl ether.

20 g. Benzanilide

21 g. PCl_5

50 c.c. toluene [sodium dried].

The above mixture was heated in boiling water for 1 hour. The toluene and $POCl_3$ were removed under reduced pressure on a water bath, the final traces of $POCl_3$ being removed under vacuo in a metal bath at 220°C. 100 c.c. of Grignard ether was then added and the mixture refluxed. It was assumed that 90% of the iminochloride was removed. This ethereal solution was therefore added to 120 c.c. dried alcohol containing slightly more than the theoretical amount of sodium and three times as much o-nitrophenol, and the mixture allowed to stand in an open vessel overnight. The ether and most of the alcohol were distilled off, the residue poured into water and the oil which solidified, dissolved in hot alcohol. The first batch of precipitate was crystallised from a mixture of glacial acetic acid and alcohol m.p. = 116°C. (lit.). The solution on cooling gave a mixture of o-nitrophenol and the imino-ether. Steam distillation removed the nitrophenol and recrystallisation of the residue from a mixture/

mixture of glacial acetic acid and alcohol yielded more imino-ether m.p. = 116°C (lit.).

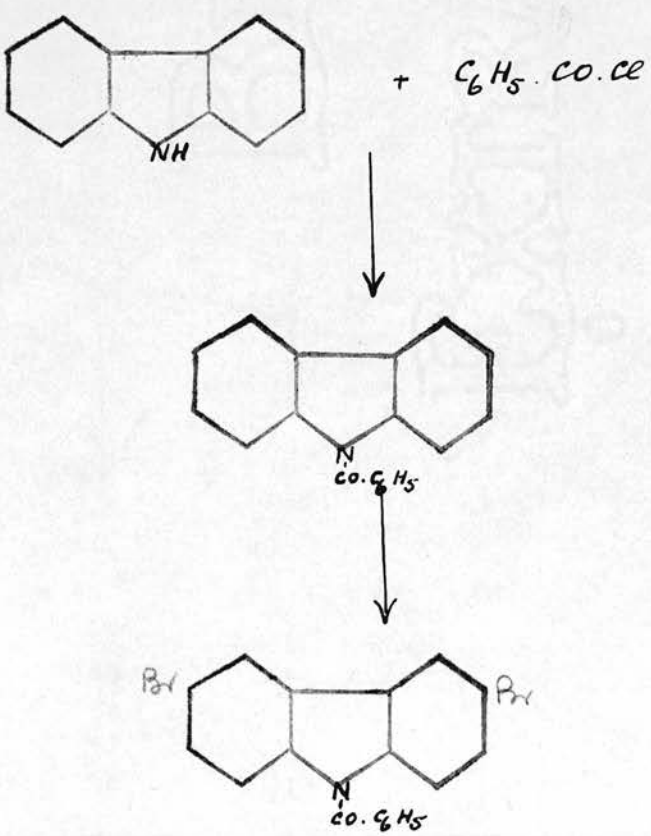
Total yield = 5 g. [15%]. m.p. = 116°C. (lit.). Owing to the unsatisfactory results obtained, after repeated attempts, to prepare o-nitrodiphenylamine, efforts to prepare other substituted diphenylamines by this process were abandoned.

Debromination of Carbazole Compounds.

1. 3:6-Dibromo-9-benzoylcarbazole.

A. 9-benzoylcarbazole was first of all prepared by the method of G. Mazzara [Ber, (1891), 24, 276].

B. Bromination of the 9-benzoylcarbazole Cf. Mazzara and Leonardi, [G, (1892), 22, II, 572] was carried out in the following manner:



5 g. 9-benzoylcarbazole.

30 c.c. chloroform

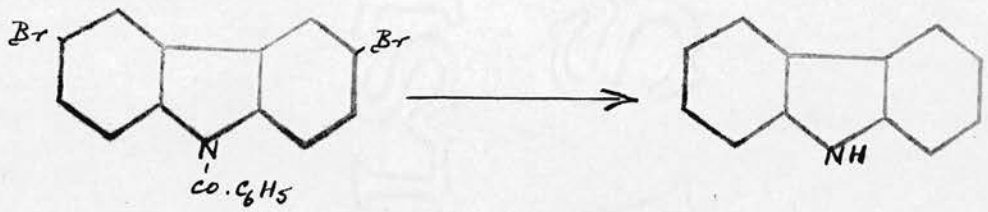
6 g. bromine 2 molec. props.

The bromine was added dropwise to the chloroform solution of the benzoylcarbazole, the mixture left standing for 2 hours, and the brown solid which separated crystallised from glacial acetic acid.

Yield = 5 g. [66%]. m.p. = 213-5°C.

lit. m.p. = 215-6°C.

C. Debromination.



2 g. 3:6-dibromo-9-benzoylcarbazole.

0.8 g. cuprous cyanide.

10 c.c. pyridine.

3 c.c. water.

The above mixture was heated in a sealed tube for 20 hours at 300°C. Ammonia was added to the contents of the tube to remove the copper, the precipitate was filtered and purified by sublimation.

Yield = 0.4 g. [50%]. m.p. = 240-3°C.

The/

The substance was identified as carbazole by

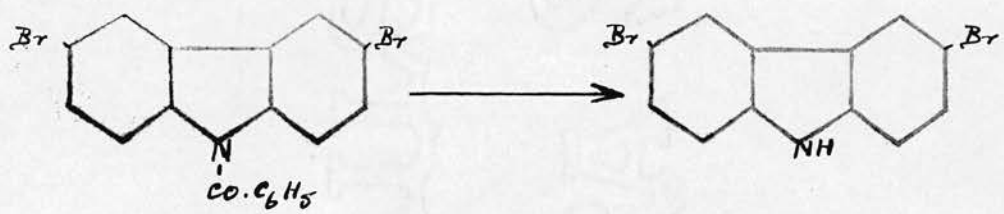
(i) A mixed melting-point with pure carbazole, in which no depression was observed.

(ii) Picrate orange-red needles were obtained m.p. = 181-3°C. Carbazole picrate = 183°C.

The drastic experimental conditions have apparently hydrolysed off the benzoyl group in addition to debrominating the compound.

2. A. 3:6-Dibromo-carbazole.

Cf. [Mazzara and Leonardi, G.(1892), 22, II, 573].



3 g. 3:6-dibromo-9-benzoylcarbazole.

50 c.c. 5% alcoholic potash.

The above mixture was refluxed for 2 hours on a water-bath, poured into 50 c.c. water and the resulting solid recrystallised from alcohol.

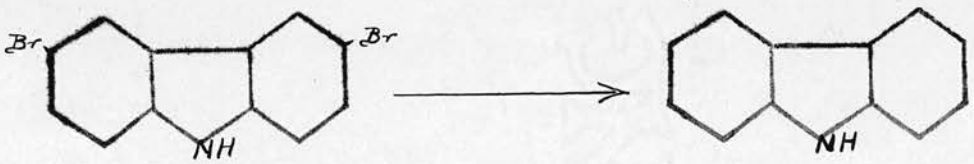
Yield = 2 g. [88%]. m.p. = 210-2°C.

lit. m.p. = 212-3°C.

As the m.ps. of the starting material 215-6°C and the/

the product 212-3°C. were so close a mixed melting point was carried out and gave a depression of 30-40°C.

B. Debromination.



1 g. 3:6-dibromocarbazole.

0.6 g. cuprous cyanide.

5 c.c. pyridine.

2 c.c. water.

The above mixture was heated in a sealed tube for 20 hours at 300°C. Subsequent procedure was as in the previous debromination, including purification by sublimation.

Yield = 0.15 g. [30%]. m.p. = 240-5°C.

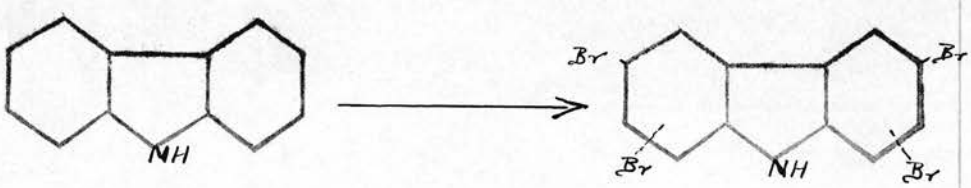
The compound was again identified as carbazole by

(i) mixed m.p. with pure carbazole no depression

(ii) a picrate gave orange-red needles m.p. = 181-3°C.

3. Tetra-bromo-carbazole.

Cf. [Lindemann and Mühlhaus, Ber., (1925), 58, 2375].



5 g. carbazole.

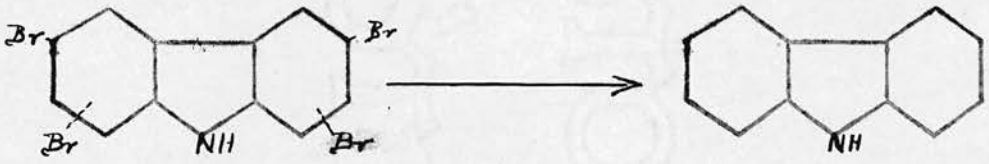
15 g. bromine [5 molec. proportions].

The carbazole was added to the bromine in small portions, the mixture allowed to stand for 1 hour, and the excess bromine removed by placing on a steam-bath for ½ hour. The product was crystallised from benzene.

Yield = 2 g. [15%]. m.p. = 218-9°C. sublimes in needles.

lit. m.p. = 220°C.

Debromination.



0.75 g. tetrabromocarbazole.

0.6 g. cuprous cyanide.

5 c.c. pyridine.

1 c.c. water.

The above mixture was heated in a sealed tube at 220°C. for 20 hours. Subsequent procedure as before. Purification of the solid was effected by sublimation.

Yield = 0.22 g. [90%] m.p. = 240-58C.

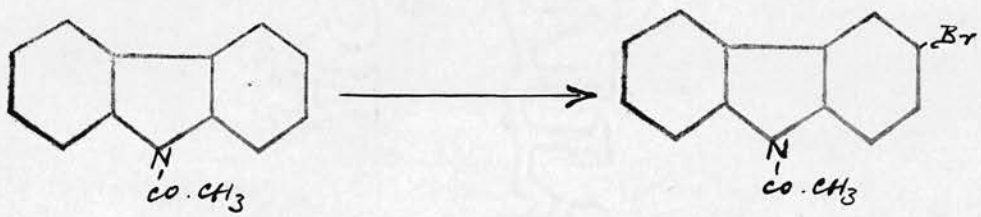
The/

The carbazole was identified as before. On attempting to prepare tetra-bromocarbazole by the method of Votoček [Ch. Z., (1896), Rep. 20, 190] a mixture of bromocarbazoles was obtained.

m.p. = 270-90°C. on sublimation.

4. 3-Bromo-9-acetylcarbazole.

Bromination was effected as follows:- [Boëseken R. (1921). 31. 350].



5 g. 9-acetylcarbazole.

100 c.c. glacial acetic acid.

4 g. bromine in 20 c.c. glacial acetic acid.

The 9-acetylcarbazole was dissolved in the 100 c.c. glacial acetic acid and the bromine in glacial acetic acid was added dropwise with stirring. The mixture was allowed to stand for 7 hours, when all the bromine was used up and a red → blue colour change had taken place in the solution. Any remaining solid was filtered off, the filtrate being poured into water and the dark-green oily solid crystallised from/

from alcohol,, a small quantity of ether being also added and allowed to evaporate at room temperature.

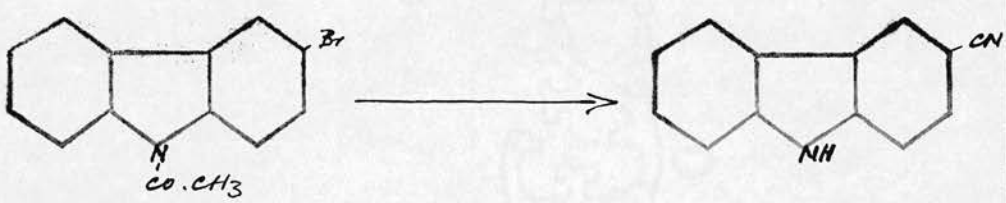
Yield = 2 g. [30%]. m.p. = 127°C. Needles.

lit.m.p. = 128°C.

The method of preparation advocated by Ciamician and Silber [C, (1882), 12, 276] was found to yield a mixture of mono- and di-bromo-acetylcarbazole. It is advocated in this reference that the 9-acetylcarbazole be heated in CS_2 along with bromine in CS_2 for as short a time as 5 minutes. On repeating this procedure and purifying the product by sublimation a white crystalline solid m.p. 180-90°C. resulted. This was probably dibromo-acetylcarbazole.

m.p. = 189-190°C. (lit.).

C. Debromination.



1.2 g. 3-bromo-9-acetylcarbazole.

0.41 g. cuprous cyanide [1.1 molec. props.].

5 c.c. pyridine

2 c.c. water.

The above mixture was heated for 14 hours at 300°C. in a sealed tube. Conc. ammonia was added to the resulting solution and the precipitate boiled for 5 minutes with a few drops of HCl (dil.) in order to remove all traces of copper. Purification was effected by sublimation.

Yield = 0.2 g. [30%]. m.p. = 198-200°C.

Analysis: N fd = 14.4%.

$C_{13}H_8N_2$ requires N = 14.58%.

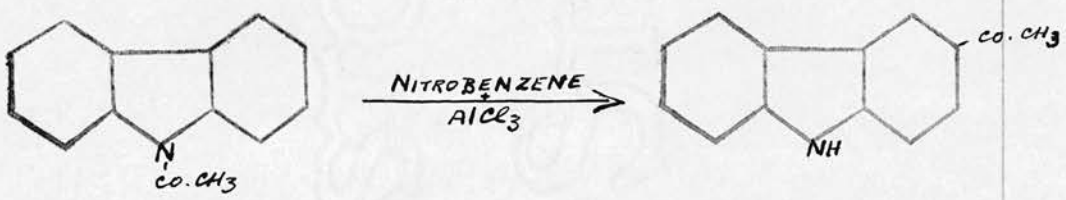
This assumes that carbazole nitrile has been formed. These debromination reactions though "abnormal" are not peculiar to substituted carbazole compounds. The following results were obtained by Dr Neil Campbell and Miss Muir in this Department. In each case the compound was heated with the correct molecular proportion of cuprous cyanide i.e. 1 molec. proportion CuCN for each Br atom to be removed in pyridine in a sealed tube for 20 hours at 280-300°C.

Compound	Product
1-Bromonaphthalene	1-Naphthoamide.
2-Iodonaphthalene	1-Naphthoic acid.
4-Bromoacenaphthene	Acenaphthene
9-Bromophenanthrene	Phenanthrene
2:7 Dibromofluorene	Fluorene
9:10 Dibromoanthracene	Anthracene
4-Bromofluoranthene	Fluoranthene
Dibromofluoranthene	Fluoranthene
10 Bromo-1:2 benz-anthracene	10 cyano-1:2 benzanthracene

It was considered that this debromination reaction would be useful both for determining the structure of compounds and also for their identification. Such debrominations may prove of use in synthetic work and their possibilities are being investigated.

e.g. 3-Bromo-6-acetylcarbazole.

[Plant, Rodgers and Williams, J.C.S. (1935), 741].



Attempts were made to prepare this compound by both the methods described in the above reference.

A. 3-acetylcarbazole.

(i) 14 g. 9-acetylcarbazole.

120 c.c. nitrobenzene.

10 g. aluminium chloride.

Experimental procedure is as in the above reference.

Yield = 9 g. [64%]. m.p. = 160-2°C. softens 156°C.

lit.m.p. = 162°C. softens 157°C.

B. Bromination of 3-acetylcarbazole.

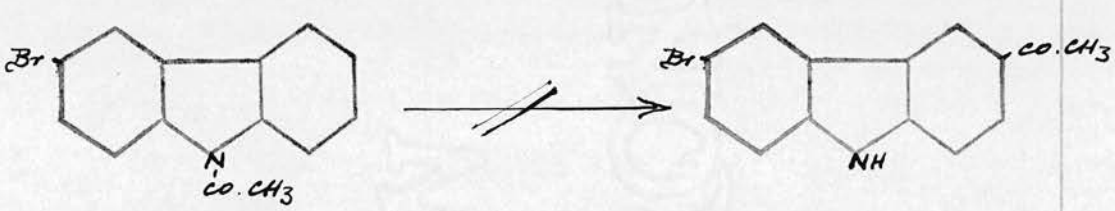
9 g. 3-acetylcarbazole.

7 g. bromine in 45 c.c. glacial acetic acid.

Procedure was as in the reference quoted. The resulting/

resulting product was a dark-brown amorphous solid with a m.p. = 150-180°C. and was obviously a mixture.

(ii) 3-bromo-6-acetylcarbazole.



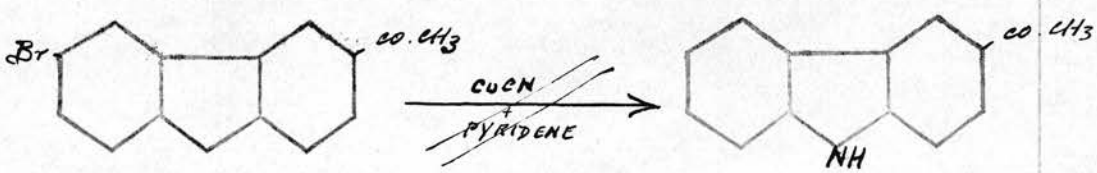
5 g. 3-bromo-9-acetylcarbazole

2.75 g. aluminium chloride

2.6 g. acetyl bromide

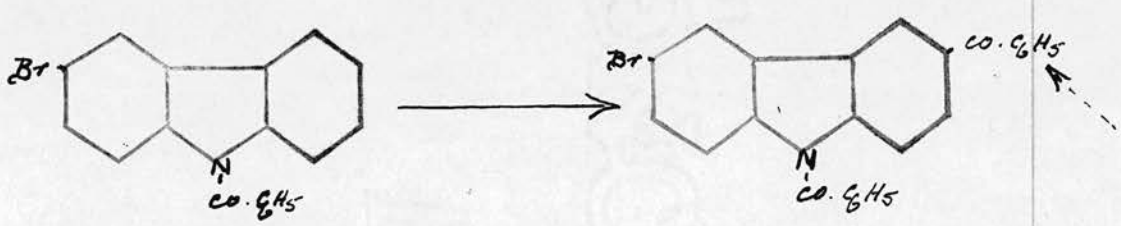
250 c.c. carbon disulphide.

Procedure is as in the reference quoted above but the reaction yielded the unchanged compounds.
It was hoped to remove the bromine by CuCN and pyridine as in the foregoing experiments, and obtain an acetylcarbazole the position of the acetyl group being also proved. Repeated re-crystallisations from methyl alcohol however failed to raise the melting point or decrease the range over which the presumed mixture melted. Repeated attempts gave similar results, a mixture of compounds being obtained.



6-Bromo-3:9-dibenzoylcarbazole.

[Plant, Rogers and Williams, J.C.S. (1935), 741-4].



3 g. 3-bromo-9-benzoylcarbazole.

6 g. aluminium chloride

25 c.c. carbon disulphide.

2 g. benzoyl chloride.

A. An attempt was made to prepare a bromo-dibenzoylcarbazole as in the reference quoted above. The attempt was unsuccessful as a white crystalline compound m.p. = 122°C. was obtained and identified as benzoic acid by a mixed melting point.

B. The Perrier Modification of the Friedel-Crafts Reaction [Bulletin de la Société chimique de Paris 1904, 3 , 31, 859] yielded the original 3-bromo-9-benzoylcarbazole. Similar attempts were made with 3-bromo-9-acetylcarbazole, using methods [A] and [B] but the original compound was obtained in each case. Further attempts in this field were therefore abandoned.

Attempted/

Attempted Preparation of substituted Carbazoles from substituted benzene compounds.

Cf. [Ullmann, Ann. (1904), 332, 82 et seq.].

The general procedure may be summarised as follows:

A. Condensation : This may be effected by heating the benzene compounds together

(i) over a naked flame

(ii) in a water-bath

with or without a condensing agent.

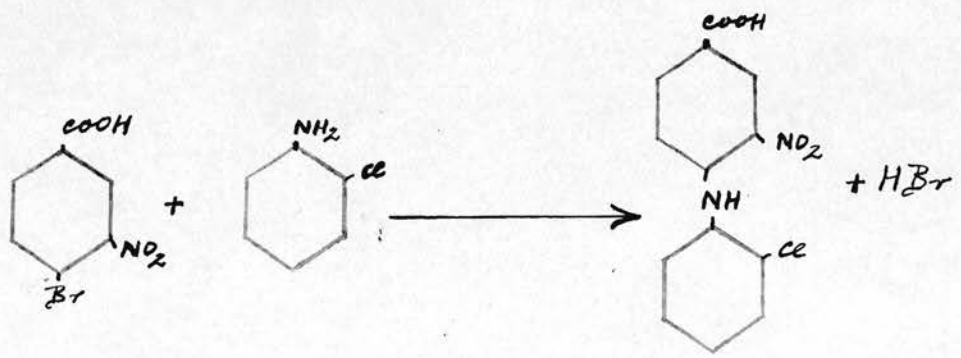
B. Reduction : The condensation product is reduced by aqueous or alcoholic sodium sulphide.

C. Diazotisation : The reduced compound is diazotised as in the above reference.

D. Conversion of the benz-triazole compound thus obtained into the corresponding substituted carbazole.

A. 1-Chloro-carbazole.

2'-chloro-6-nitro-4-carboxydiphenylamine.



10 g. 4-bromo-3-nitrobenzoic acid.

Excess o-chloroaniline

3 g. potassium carbonate

A trace of copper bronze.

The above mixture was heated over a naked flame for 40-45 minutes. On cooling HCl (conc.) was added to destroy excess chloroaniline, the resulting solid boiled several times with water in order to remove chloroaniline hydrochloride and filtered hot. The golden-yellow solid was recrystallised from a mixture of methyl alcohol and glacial acetic acid. It was very sparingly soluble in methyl alcohol, ethyl alcohol, benzene and light petroleum.

Yield = 6.5 g. [83%]. m.p. = 240-1°C. sublimes in yellow needles.

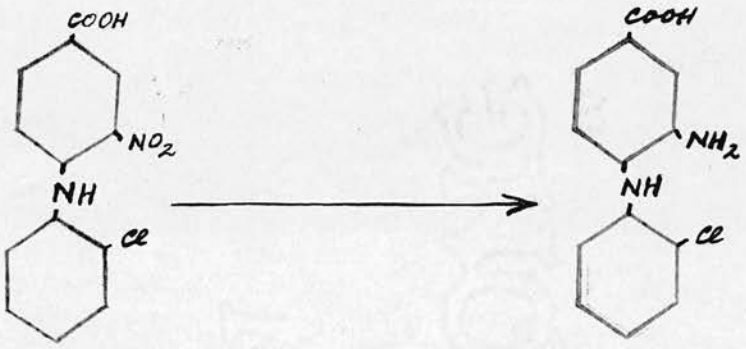
Analysis: C fd = 54.9% H fd = 3.26%

$C_{13}H_9O_4N_2Cl$ requires C = 53.3% requires H = 3.1%.

The compound probably still contained traces of chloroaniline hydrochloride despite the fact that it gave a sharp melting-point.

B. 2'chloro-2-amino-4-carboxydiphenylamine. /

B. 2'Chloro-2-amino-4-carboxydiphenylamine.



5 g. 2'chloro-2-nitro-4-carboxydiphenylamine.

18 g. sodium sulphide.

5 g. sulphur (powdered).

25 c.c. water.

The sodium sulphide and sulphur were dissolved in the water by boiling for 10-15 minutes. The Na_2S_2 thus formed was the actual reducing agent and to it in small portions the substituted nitrodiphenylamine was added. The mixture was heated in a boiling water-bath for 18 hours. On cooling, glacial acetic acid was added until the red solution was acid. The precipitate obtained was boiled for 5-10 minutes with Na_2CO_3 solution, filtered hot and the free sulphur thus removed. On carefully re-acidifying the cooled filtrate with glacial acetic acid the resulting solid was recrystallised from hot water and a small amount of alcohol. A final purification was effected from light/

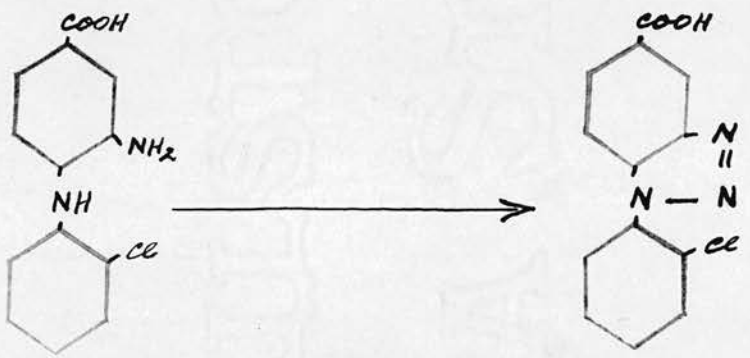
light petroleum b.p. (100-120°). It was very soluble in both methyl and ethyl alcohol but sparingly soluble both in light petroleum and benzene.

Yield = 2.4 g. [53%]. m.p. = 175-7°C - white needles.

Analysis: C fd = 57.9% H fd = 4.4%.

$C_{13}H_{11}O_2N_2Cl$ requires C = 59.4% requires H = 4.2%.

C. 5-Carboxy-1-o-chlorophenylbenztriazole.



2 g. 2'-chloro-2-amino-4-carboxydiphenylamine.

1 g. Na_2CO_3 dissolved in 50 c.c. water.

1 g. $NaNO_2$ in minimum amount of water.

X S 10% H_2SO_4.

The reduced diphenylamine was dissolved in the Na_2CO_3 solution, the sodium nitrite solution added slowly and the mixture added dropwise with stirring to ice-cooled excess 10% H_2SO_4. The resulting pale pink solid was purified by extraction with light/

light petroleum b.p. = 100-120°C.

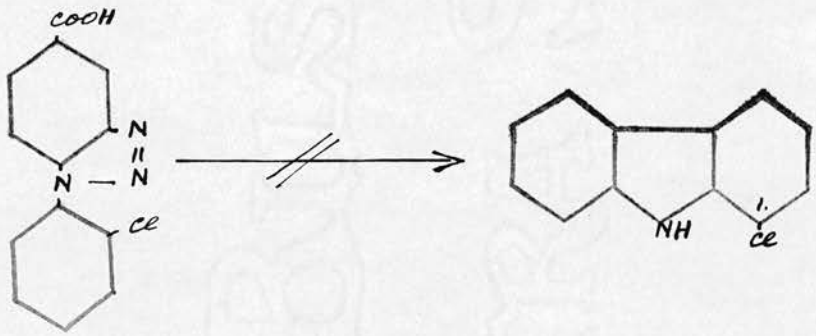
Yield = Quantitative m.p. = 207-8°C. - white prisms - sublime.

It is sparingly soluble in light petroleum but very soluble in both methyl and ethyl alcohol.

Analysis: N fd - 15.29%.

$C_{13}H_8O_2N_3Cl$ requires N= 15.3%.

D. Attempted Preparation of 1-Chlorocarbazole.



0.8 g. 5-carboxy-o-chlorophenylbenztriazole.

1.6 g. freshly prepared quicklime.

The above mixture was mixed thoroughly in a mortar, placed in a 10 c.c. distilling flask and heated at 360°C. for 4-5 hours in a metal bath. This procedure was followed by heating the flask over a naked flame for ½ hour when white flakes of sublimate appeared on the upper parts of the flask and/

and a dark-brown oil solidified in the outlet tube of the distilling flask. This solid was purified by a micro-extraction with light petroleum b.p. - 100-120°C.

Yield = 0.13 g [23%]. m.p. = 225-230°C. colourless plates.

Analysis: C fd = 85.1% H fd = 5.2%.

$C_{12}H_8NCl$ requires C = 71.4% requires H = 3.97%

If carbazole had resulted then

$C_{12}H_9N$ requires C = 86.2% requires H = 5.38%.

The final compound obtained was therefore carbazole.

Colour test: 1 drop H_2SO_4 (conc.)+1 drop HNO_3 (conc.) added to the product ⟶ deep green colour produced.

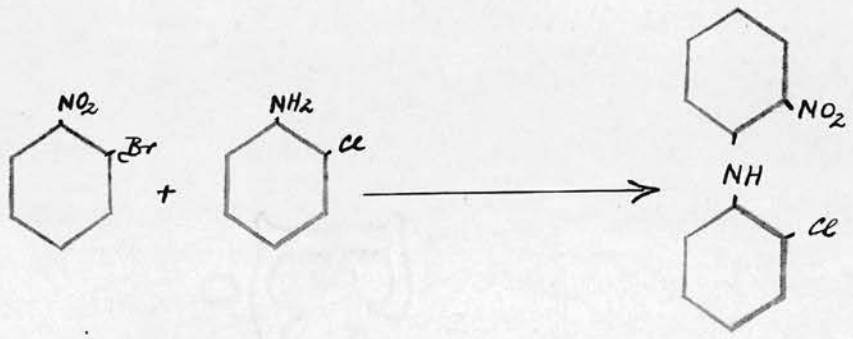
A similar test with the triazole compound gave no colour and so the presence of the carbazole nucleus was concluded.

Attempts to convert the 5-carboxy-o-chlorophenyl-benztriazole to 1-chlorocarbazole by heating the former (i) by itself in an asbestos furnace in an atmosphere of CO_2

(ii) with soda-lime

proved unsuccessful, unchanged compound being obtained in each case.

2'-Chloro-2-nitrodiphenylamine.



3 g. o-Bromo-nitrobenzene.

X S o-chloroaniline

1 g. potassium carbonate.

A trace of copper bronze.

The above mixture was heated on an oil-bath for 15 hours, at 160-170°C., cooled and HCl (conc.) added to destroy X S chloroaniline. The black oily, solid was purified firstly by extraction with light petroleum b.p. 100-120°C. and then by recrystallisation from alcohol.

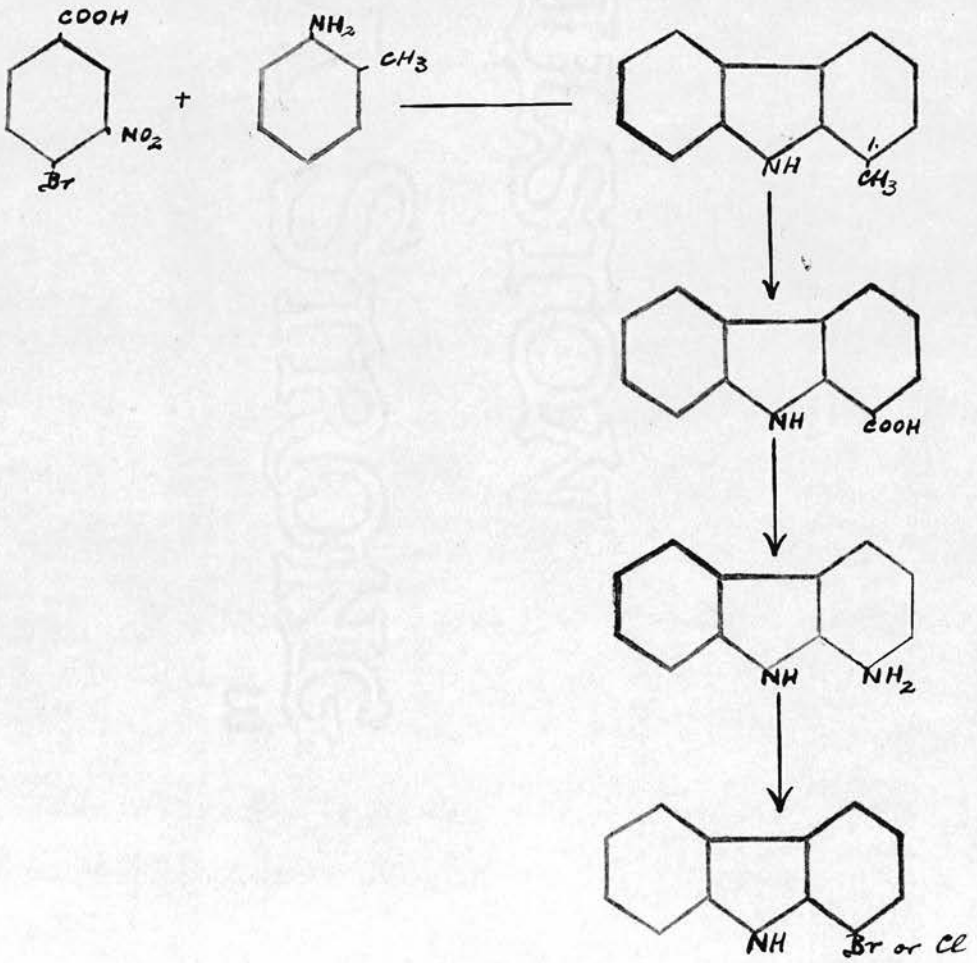
Yield = 1.1 g. [29%]. m.p. = 114°C. - red prisms.

Analysis: C fd = 58.06% H fd = 3.5%

$C_{12}H_9O_2N_2Cl$ requires C = 57.9% requires H= 3.6%.

It was originally intended to attempt the preparation of 1-chlorocarbazole from this product but the yield was/

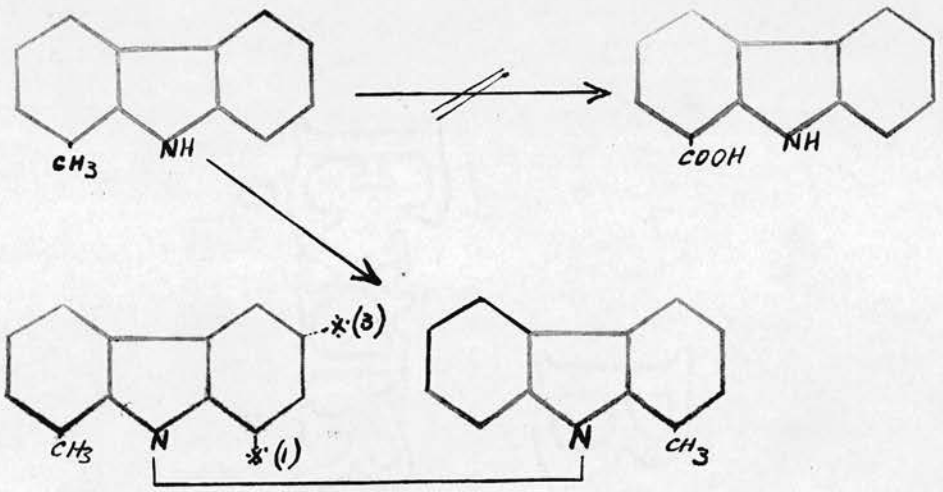
was very much inferior to the 2'-chloro-2-nitro-4-carboxydiphenylamine and so the attempt was abandoned. An attempt to prepare 1-bromo-carbazole by using X S o-bromoaniline instead of o-chloroaniline as in the above condensation proved unsuccessful as the condensation yielded a charred mass. The method devised by Ullmann [Ann, (1904), 332, 84] for the preparation of 1-methylcarbazole was considered to be a means whereby other 1-derivatives could be prepared. The following scheme was therefore attempted:-



1-Methylcarbazole was therefore prepared as in the above reference.

V. Attempted preparation of 1-carboxycarbazole.

[Perkin and Tucker, J.C.S. (1921), 216].



0.5 g. 1-methylcarbazole

1 g. powdered $KMnO_4$

15 c.c. acetone.

A. In this first attempt to oxidise 1-methylcarbazole, acetone purified by boiling with $KMnO_4$ for 3 hours and distilling, was used in conjunction with powdered $KMnO_4$. The above mixture was refluxed on a water-bath for 3 hours, filtered hot and the filtrate acidified with sulphurous acid. The pale yellow solid which separated was purified by extraction with light petroleum b.p. = 100-120°C.

Yield = 0.3 g. m.p. = 135-155°C.

Analysis: C fd = 85.2% H fd = 4.98%

$C_{26}H_{20}N_2$ requires C = 86.7% requires H = 5.5%.

On the assumption that the carboxy-acid was formed

$C_{13}H_9O_2N$ requires C, 53.9 ; H, 4.2%.

The product was found to be insoluble in NaOH [Perkin and Tucker J.C.S. (1921), 216] found however that oxidation of carbazole with acetone $KMnO_4$ yielded a mixture of dicarbazyls. Hence a mixture of methyl-dicarbazyls may be expected in this case. 1:1' and 3:3' methyl dicarbazyls can also be formed and are indicated by * (1) and * (3). The analysis, although not satisfactory, bore out this assumption as 1-carboxycarbazole would have a much lower C and H content.

B. 0.5 g. 1-methylcarbazole.

10 c.c. 1.2 nitric acid.

The above mixture was heated in a sealed tube for 7-8 hours at 150-60°C. The dark-yellow product was recrystallised from glacial acetic acid.

Yield = 0.2 g. m.p. = 240-60°C.

Analysis: N fd = 14.7%.

If 1-carboxycarbazole was the product

Then $C_{13}H_9O_2N$ requires N = 6.6%

If a mixture of dicarbazyls had been formed

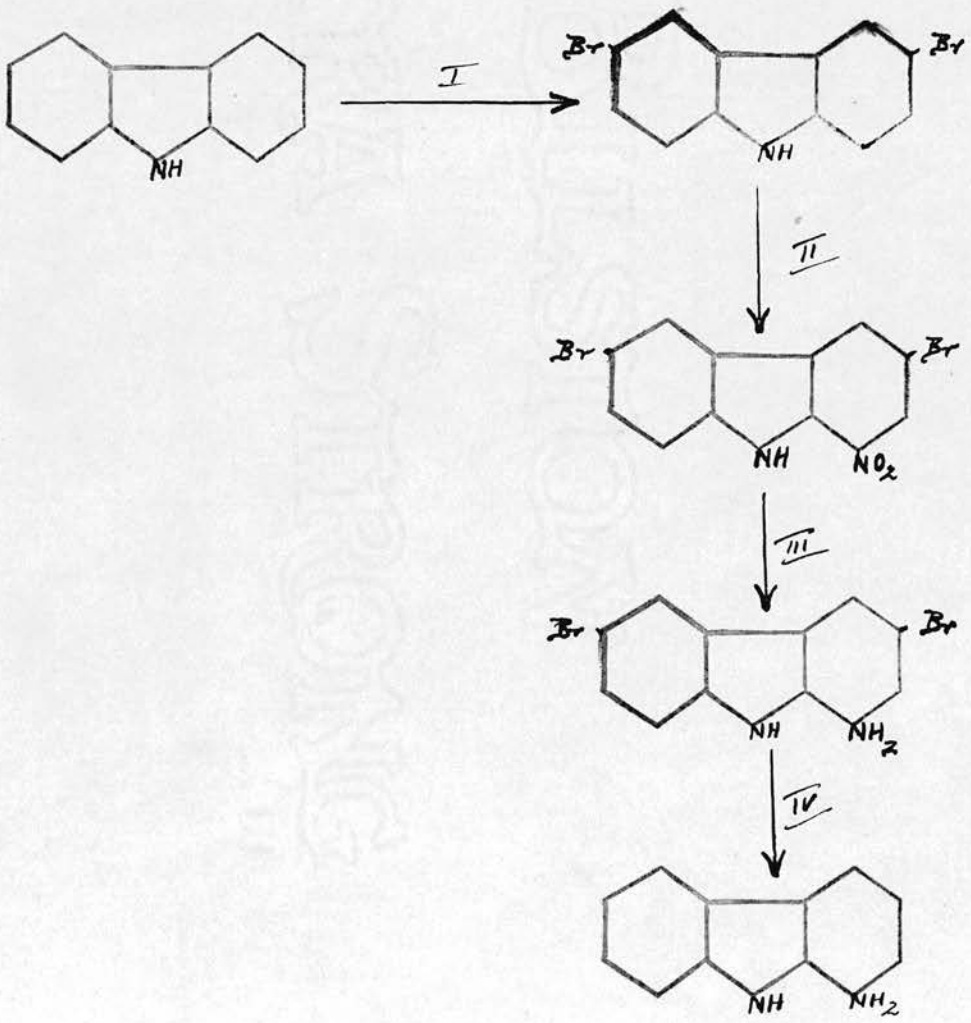
Then $C_{26}H_{22}N_2$ requires N = 7.7%.

Mono-nitro-methylcarbazole $C_{13}H_{10}O_2$ requires N = 12.3%.

Dinitro-methylcarbazole $C_{13}H_9O_4N_3$ requires N = 15.5%.

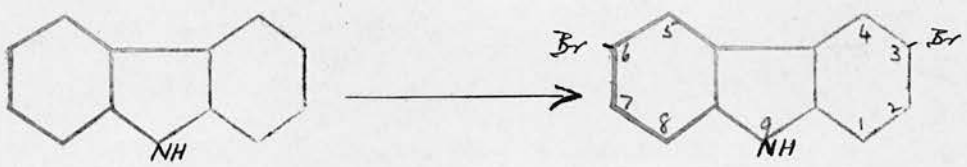
It is obvious from the analysis that nitration has taken place, in all probability a mixture of mono- and dinitro-methylcarbazoles or dinitro-methyldicarbazyls being formed.
Further attempts to prepare 1-derivatives from 1-methylcarbazole were therefore abandoned.

Preparation of 1-Aminocarbazole.



I. 3:6-Dibromocarbazole.

[Lindemann and Mühlhaus, Ber., (1925), 58, 2371].



50 g. carbazole

1. 600 c.c. CS_2

2. 31 c.c. bromine
   150 c.c. CS_2

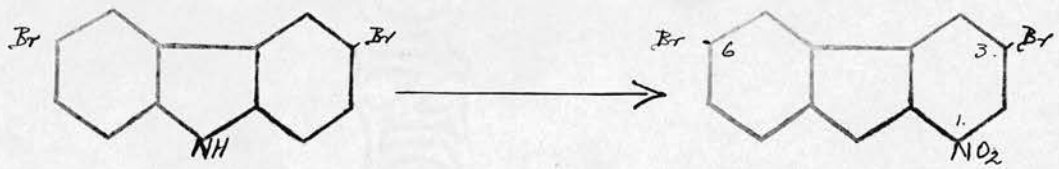
Solution 2 was added dropwise to a boiling suspension of 1. Experimental procedure followed that in above reference.

Yield - 54 g. [57%]. m.p. = 211°C (alcohol)

lit. m.p. = 213°C.

II. 3:6-Dibromo-1-nitrocarbazole.

[Ber., (1925), 58, 2371].



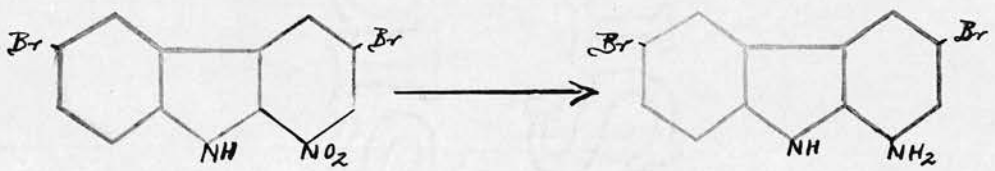
1. 42 g. 3:6-dibromocarbazole
   500 c.c. glacial acetic acid.

2. 8.5 c.c. conc. HNO_3
85 c.c. glacial acetic acid.

2 was added to a hot suspension of 1. Further procedure was similar to reference quoted.

Yield = 42 g. [90%]. m.p. = 260°C. (lit.).

III. 3:6-Dibromo-1-aminocarbazole.



10 g. 3:6-dibromo-1-nitrocarbazole.
50 g. Na_2S (crystalline)
10 g. sulphur (powdered)
500 c.c. alcohol.
100 c.c. water.

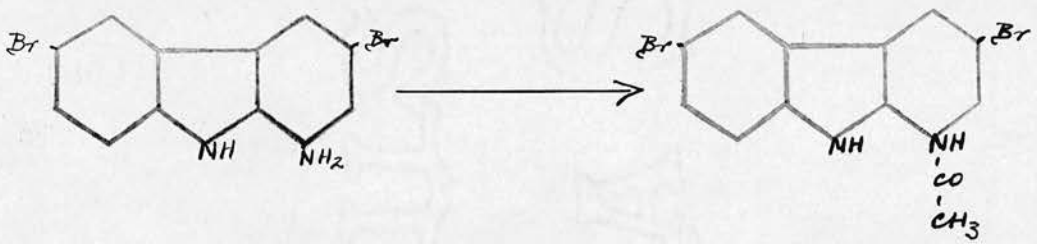
The Na_2S and S were dissolved by boiling in 100 c.c. water. The hot solution of Na_2S_2 was added to a boiling suspension of the 3:6-dibromo-1-nitrocarbazole in alcohol and the mixture refluxed for 1 hour, after which it was poured into water. The yellow solid obtained was purified by extraction with chloroform, this procedure being slightly different from the quoted reference as there, ordinary recrystallisation from chloroform was practised. The authors do not/

not quote a yield however.

Yield = 4.75 g. [54%]. m.p. = 190-2°C.

lit.m.p. = 192°C.

This procedure was repeated four times with similar results. As Lindemann and Mühlhaus [Ber. (1925), 58, 2371] quote no melting point for the monoacetyl derivative of 3:6-dibromo-1-aminocarbazole their acetylation procedure was repeated with slight modifications as follows:-



0.2 g. 3:6-dibromo-1-aminocarbazole

1 c.c. H_2O

12 drops acetic anhydride.

The above mixture was ground together thoroughly in a small mortar, the product being crystallised from alcohol.

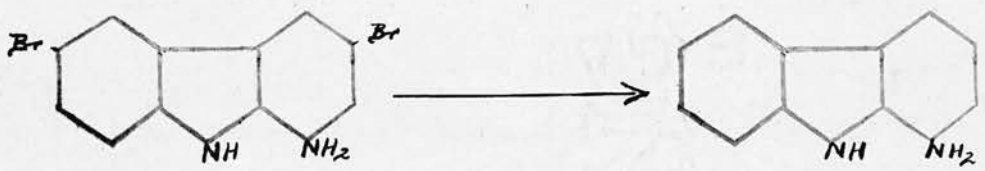
Yield = Quantitative m.p. = 262-4°C.

The compound sublimed in small white lustrous plates

Analysis: N fd = 7.32%.

$C_{14}H_{10}ON_2Br_2$ requires N= 7.3%.

IV. 1-Aminocarbazole.



10 g. 3:6-Dibromo-1-aminocarbazole.

40 g. hydriodic acid. [sp. gr. 1.94].

3.5 g. red phosphorus.

The above mixture was refluxed for 4 hours, 25 c.c. hot water added, and the mixture filtered hot. A saturated solution of sodium acetate was added until the filtrate became alkaline to litmus. The white solid obtained was recrystallised from benzene.

Yield = 1.7 g. [34%]. m.p. = 193-5°C. - white needles.

lit. m.p. = 195°C.

Analysis: N fd = 15.3%.

$C_{12}H_{10}N_2$ requires N = 15.38%.

Picrates of (i) 3:6-Dibromo-1-aminocarbazole and

(ii) 1-aminocarbazole

were prepared in the usual way.

(i) on crystallisation from alcohol gave an orange-red solid m.p. = 205-7°C. Sublimes in yellow needles.

Analysis: N fd = 11.2%.

$C_{18}H_{11}O_7N_5Br$ requires N= 12.3%.

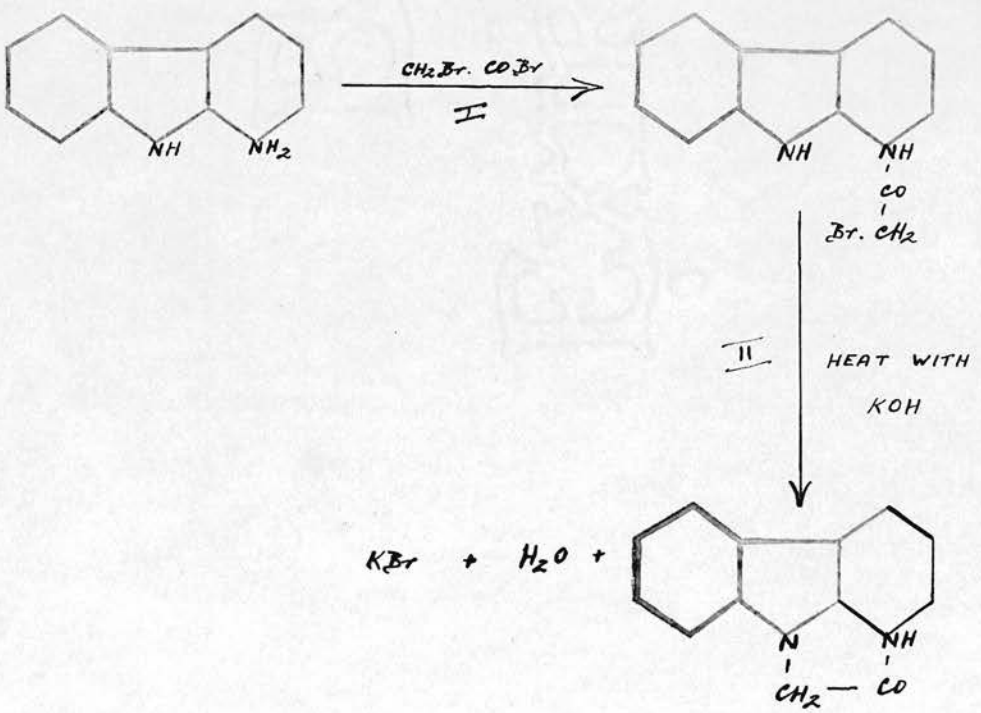
(ii)/

(ii) on crystallisation from alcohol yielded a pale green solid m.p. = 195-7°C. Yellow prisms. A mixed m.p. with 1-aminocarbazole gave a 30-40 degree depression.

Analysis: N fd = 14.6%.

$C_{18}H_{13}O_7N_5$ requires N = 17.00%

As the analysis figures for 1-aminocarbazole picrate were very unsatisfactory it was decided to confirm the presence of the amino-group by forming a ring compound in the following manner:-



I. 1-ω-Bromacetamidocarbazole.

A. 1 g. 1-aminocarbazole in 25 c.c. benzene.

B. 0.5 c.c. bromoacetylbromide in 5 c.c. benzene.

[B] was added to a hot solution of [A] and the mixture refluxed for 30-35 minutes. The resulting solution was allowed to stand overnight, the black residue filtered off and discarded, and the filtrate reduced at ordinary temperature to half its volume. A pale green solid separated.

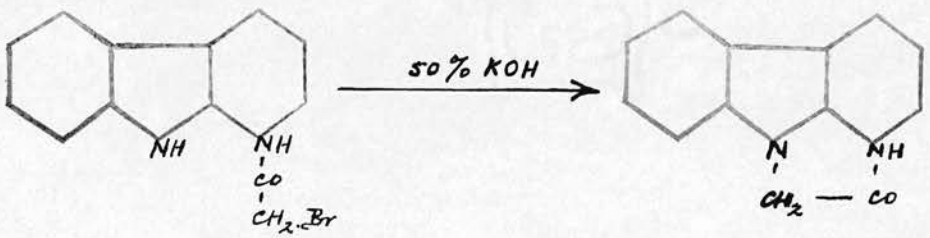
Yield = 0.75 g. [47%]. m.p. = 188°C. -white prisms.

A mixed m.p. with 1-aminocarbazole gave a 30-35 degree depression.

Analysis: Br fd = 26.1%.

$C_{14}H_{11}ON_2Br$ requires Br = 26.4%.

II. Formation of 1:9-[3'Keto-piperazino]-carbazole.



0.5 g. 1- -Bromacetamidocarbazole

1 c.c. 50% KOH

20 c.c. alcohol.

The/

The above mixture was refluxed for 30 minutes, allowed to stand overnight and the KBr filtered off. 10 c.c. water were added to the filtrate and the emulsion poured into 50 c.c. HCl [1:1]. The resulting dark-grey solid was ground up with

(i) water

(ii) methyl alcohol,

final purification being effected from xylene. The xylene solution gave a brilliant pale green fluoresence.

Yield = 0.1 g. [27%]. m.p. = 247-52°C.

Sublimes in white prisms.

Analysis: N fd = 11.9%.

$C_{14}H_{10}ON_2$ requires N = 12.55%.

Although this analysis was slightly low it established the fact that ring closure took place. The very small quantity of material precluded further purification.

Selenic Acid and Colourations with substituted Carbazole Compounds.

The following procedure was found to be satisfactory. A few drops of sulphuric acid (conc.) were placed in a small test-tube and a small drop of selenic acid added. A trace of the compound was then added and the test-tube shaken. The colouration generally developed after a few seconds.

Compound	Colour
Pyrrole	Brown
Indole	Magenta
Carbazole	Emerald green
3:6-Dibromocarbazole	Dark green
3:6-Di-iodocarbazole.	Bluish-green
3-Bromocarbazole	Emerald green
1-Methylcarbazole	Dark green
Tetrabromocarbazole	+ Emerald green
Diphenylamine	Blue on heating
1-Aminodiphenylamine	Violet
1-Nitrodiphenylamine	Violet
1-Nitrocarbazole	Brown
Fluorene	+++ Green $\xrightarrow{\text{Heat}}$ Blue.
Pyridine	Nil
Indazole	Nil

+ Due to impurity. The compound was purified by shaking with ether to remove carbazole. The purified compound gave no colouration.

+++ Colouration given with H_2SO_4 (conc.) alone.

Fluorescence of Substituted Carbazoles

Compound	Solid	Solution	Intensity
Carbazole	Violet	Violet [Alc.]	Brilliant
3:6-Dibromocarbazole	Yellow-orange	Nil [Ether]	"
Tribromocarbazole	Red-orange	Nil [Ether]	"
1-Bromocarbazole	Nil	Violet [Alc.]	"
3:6-Di-iodocarbazole	Brown	Nil [Ether]	Dull
3:6-Dibromo-1-amino-carbazole	Nil	Nil [$CHCl_3$]	-
Tetrabromocarbazole	Deep-orange-red	Nil [Ether]	Brilliant

Both the colour and fluorescence tests were useful in that they provided a means of detecting minute traces of carbazole as impurity.

DISCUSSION OF EXPERIMENTAL RESULTS

Substituted 1-nitrocarbazoles.

In the course of this research many of the preparative methods quoted in the literature have been modified, purer products and higher yields being obtained as a result.

For instance, [Rec. trav. chim. (1912), 31, 350] in preparing 9-acetylcarbazole, boiled a mixture of carbazole and acetic anhydride with "a few drops of H_2SO_4 conc." for 1 hour. This method was greatly simplified by boiling the carbazole with an acetic anhydride - sulphuric acid conc. mixture 0.4 c.c. H_2SO_4 (conc.) per 20 c.c. acetic anhydride for five minutes, the relative proportion of sulphuric acid (conc.) and the time of heating being arrived at by a process of trial and error. To nitrate the 9-acetylcarbazole so that one nitro-group entered the molecule and occupied the 1-position, Menke's reagent was used. By analogy with the results obtained by [Menke Rec. trav. chim. (1925), 44, 171] in which ortho-nitroacetanilide resulted from the nitration of acetanilide, the nitro-group might be expected to occupy the 1-position which is ortho to the imino-group in the carbazole molecule. A very high-melting crystalline/

crystalline solid resulted however and in poor yield so that this method of preparation for 1-nitro-9-acetylcarbazole must be considered unsatisfactory. By reversing the process and acetylating the 1-nitrocarbazole prepared as in [J.C.S. (1931), 3283], a solid of similar microscopic and macroscopic appearance resulted. Similar to the products obtained by Menke's method, it did not melt below 300°C., the yield being very small indeed.

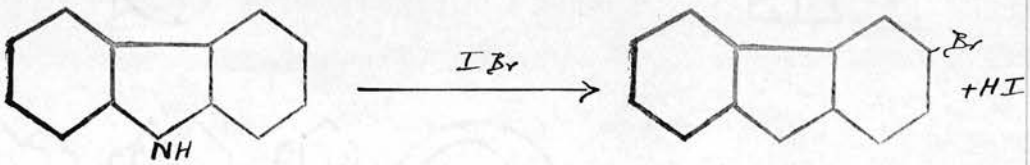
In contrast to these unsatisfactory results a dinitro-9-acetyl-carbazole, the nitro-groups probably occupying the 3:6 positions, was prepared in good yield using concentrated nitric acid as the nitrating agent.

Mono-Halogenated carbazole compounds.

3-Bromocarbazole.

The methods employed for the preparation of this compound as in [Vaubel Z. ang. (1901), 14, 784] and [Ciamician and Silber G, (1882), 12, 276] are both tedious and give poor yields. A simpler and more direct method of bromination was desirable and the brominating reagent used in the preparation of 4-bromo--naphthol and -bromonaphthalene by [Militzer J.A.C.S., (1938) 60, 256] was tried. This reagent, iodine bromide/

bromide, had also been applied successfully to the hydrocarbon fluoranthene [Gerty - Thesis, Edinburgh, 1939]. Two molecular proportions of iodine bromide were necessary as can be seen from the equations:

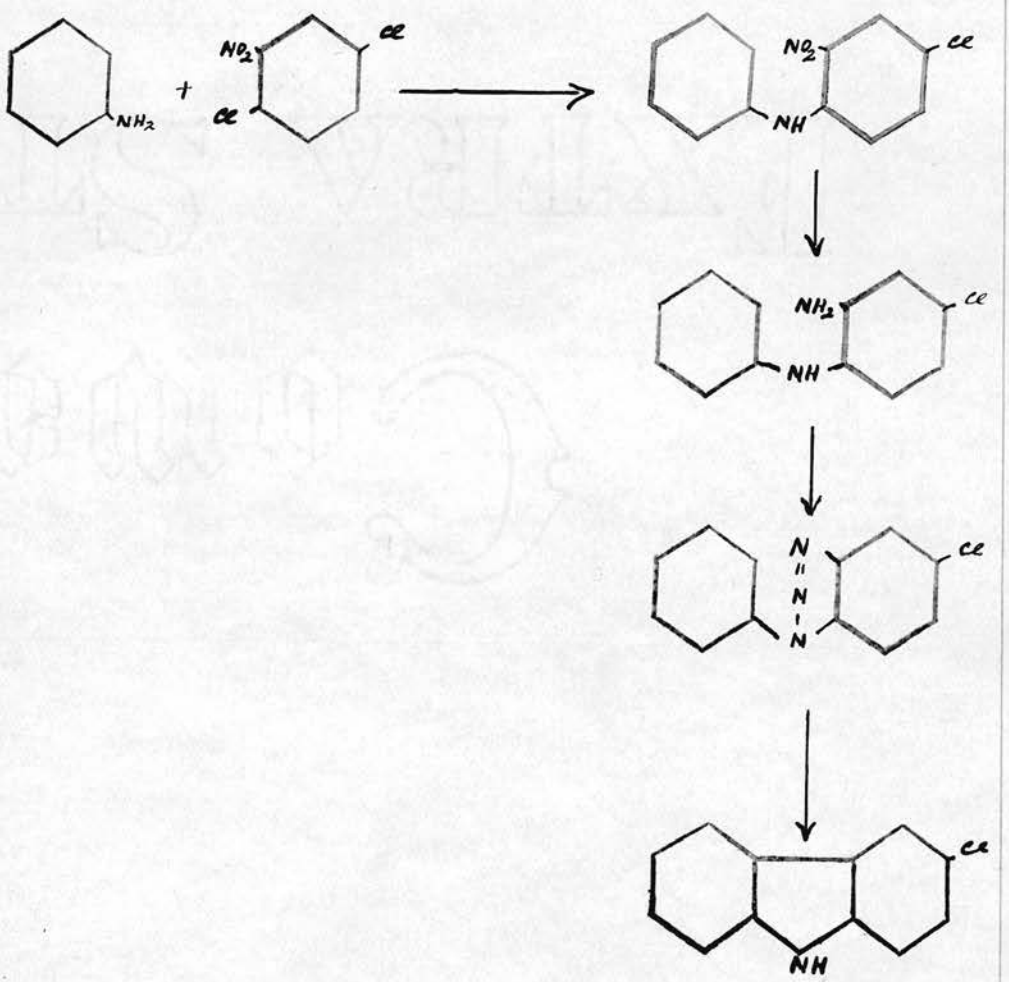


$$HI + IBr \longrightarrow I_2 + HBr$$

and a very pure product resulted, in 11% yield. It has been found in this instance a very satisfactory mild brominating agent for substitution on the aromatic ring.

3-chloro-carbazole.

The preparation of this compound, to a much greater degree than the corresponding bromo-derivative, has been characterised by laborious experimental procedure. For example, [Ullmann, Ber. (1904), 332, 93] prepared it by condensing aniline and 1:4-dichloro-2-nitrobenzene, reducing the condensation product, diazotising the reduced product and finally converting the benztriazole compound thus formed into 3-chloro-carbazole, the yield of the final product being approx. 50%.



This appears to be the standard method for the preparation of mono-chlorocarbazoles as 2-chlorocarbazole was similarly obtained by [Ullmann Ber. (1898), 31, 1697] using aniline and an appropriately substituted benzene compound. Phenyl-iodo-dichloride, which was successfully utilised as a chlorinating agent by [Garvey, Halley and Allen J.A.C.S., (1937), 59, 1827], proved highly/

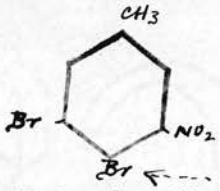
highly successful in its application to carbazole. A product of high purity and in 70% yield resulted and must be considered a much more suitable and economical method than that of Ullmann.

Attempted synthesis of 1-bromocarbazole.

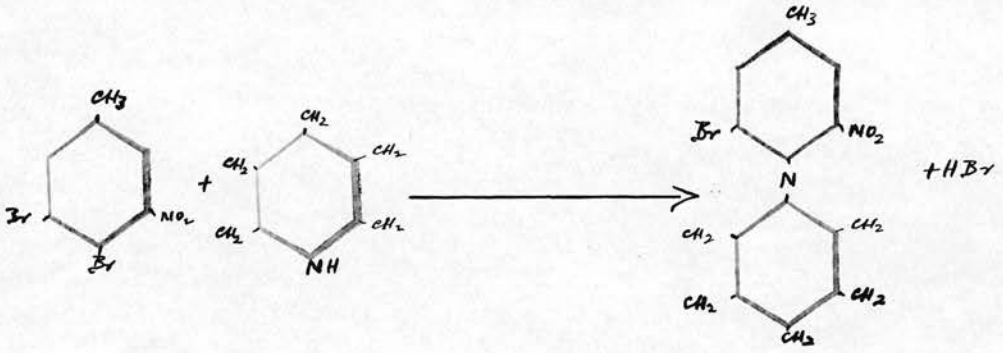
As has already been pointed out see [pp 16-7] 1-derivatives of carbazole have proved very difficult to prepare, the 1-bromocarbazole being among those not yet synthesised. The significance of succeeding in such a project from the point of view of proving the structure of poly-bromocarbazoles has also been emphasised see [p. 18]. Para-toluidine, a cheap and easily prepared compound, was the starting material employed. Acetylation, bromination and nitration of the starting material gave compounds of high purity and good yield. The 3-bromo-5-nitro-4-acetamido-toluene thus formed was hydrolysed to the free amine by a 1:1 mixture of alcohol and hydrochloric acid (conc.), this method giving a higher yield than hydrolysis with 50% sulphuric acid. For a similar reason conversion of the amino-group into a bromine group was effected by the method of Cohen and Dutt [J.C.S. (1914), 105, 510] in preference to that of Hodgson and Walker [J.C.S., (1933)]//

(1933), 1620 .

In the 3:4-dibromo-5-nitrotoluene thus prepared the bromine atom in the para-position ought to be reactive owing to the activating influence of the adjacent $-N\overset{=O}{\underset{=O}{}}$ group.



This was indeed found to be the case. On heating the compound with piperidine a water soluble, crystalline compound, identified by melting point as piperidine hydrobromide, resulted.



It was rather surprising therefore to find that no condensation product could be obtained with aniline Cf. [Lindemann and Wessel (1925), 58, 1221]. Modifications of the experimental procedure from that quoted in the above reference were attempted, including the use of (i) aluminium chloride (ii) sodium acetate and alcohol (iii) sodium hydroxide and alcohol and (iv) copper/

copper bronze, as condensing agents, but all attempts were unsuccessful.

It was finally decided to oxidise the methyl group in the 3:4-dibromo-5-nitrotoluene to a carboxy group, in order to obtain a compound of greater reactivity. It was also observed that condensations of substituted benzoic acids and aniline had been accomplished successfully by [Ullmann Ann. (1904), 332, 86] and Schöpff [Ber, (1889), 22, 3286]. In this instance condensation of 3:4-dibromo-5-nitrobenzoic acid and aniline was very satisfactory, the condensation product being obtained pure in almost quantitative yield. It was found to be insoluble in sodium hydroxide, an extremely unusual occurrence where there is a -COOH group present. This is probably due to the formation of an insoluble sodium salt as the solid changes colour from golden-brown to red. Condensation of the methyl ester of 3:4-dibromo-5-nitrobenzoic acid and aniline also proved successful although the yield was not so high in this case.

2-Bromo-6-nitro-4-carboxydiphenylamine was reduced to the corresponding amine by aqueous sodium sulphide the product being obtained in analytical purity and in good yield. The amine gave a light red/

red colour on subjecting it to the chloranil test [Frehden and Goldschmidt, Mikrochamica Acta, (1937), I, 347], which is a positive result as amines give either violet, blue or red colourations. It is not specific however, as phenols also give colourations. The mono-acetyl derivative of the amine was very easily prepared by shaking with water and acetic anhydride. Diazotisation according to [Ullmann Ann(1904), 332, 84] gave the corresponding benztriazole compound in quantitative yield and analytical purity. By analogy with the benztriazole compound in the above reference, the 7-bromo-5-carboxy-1-phenylbenztriazole was confidently expected to yield 1-bromocarbazole. Distillation of a freshly-prepared quicklime - benztriazole mixture yielded the best results. The rigorous experimental conditions however, removed the Br atom from the nucleus in addition to splitting off carbon dioxide. A mixed melting point with pure carbazole confirmed that the product of the reaction was carbazole after analysis had shown that bromine was not present. The characteristic violet fluorescence of carbazole, both in ordinary and ultra-violet light, was also clearly observed in a light petroleum extraction of the reaction product.

Several other methods were attempted in order

to/

to bring about a successful conversion of the substituted benztriazole to 1-bromocarbazole including -

(i) Heating the benztriazole alone in a sealed tube and also in a combustion tube in an atmosphere of carbon dioxide

(ii) Heating the benztriazole with soda-lime and calcium carbonate, separately, both in sealed tubes and combustion tubes.

Negative results were obtained in each case. In all these experiments the high temperature required caused decompesition to occur. On the basis of these experiments it was therefore reluctantly concluded that the synthesis of 1-bromo-carbazole by the Graebe-Ullmann method was not possible.

During the course of the foregoing attempted synthesis two subsidiary reactions of interest were carried out and resulted in the preparation of two acids not at present described in the literature.

A. The first of these was prepared by the potassium permanganate oxidation of 3-bromo-5-nitro-4-acetamido-toluene. 3-Bromo-5-nitro-4-acetamidobenzoic acid was obtained in poor yield [20%] and modifications of the oxidation entailing the use of (i) calcium permanganate (ii) acetone and (iii) alkaline permanganate failed to give an improved yield.

Difficulty was also experienced in purifying it.

In/

In their attempts to oxidise some mixed dibromotoluenes Cohen and Dutt [J.C.S. (1914), 510] found this method abortive.

B. The second acid was prepared by hydrolysing the 3-bromo-5-nitro-4-acetamidobenzoic acid with 50% sulphuric acid. The free amino acid thus formed was obtained in 50% yield and in analytical purity.

A final point of interest connected with the 1-bromocarbazole synthesis was the formation of an orange-red, sharp melting solid from a stannous chloride - hydrochloric acid reduction of 2-bromo-6-nitro-4-carboxydiphenylamine Cf. [Plant and Tomlinson J.C.S. (1932), 2188]. Its behaviour can be summarised as follows:

(i) It melted sharply between 152-3°C. which is approximately 100°C. below that of the true amine.

(ii) On the assumption that the corresponding amine had been formed the carbon content was found to be 1.3% low and the H content 0.38% low.

(iii) It did not form acetyl or benzal derivatives and all attempts to effect a diazotisation to the corresponding benztriazole compound were unsuccessful.

(iv) With H_2SO_4 (conc.) and HNO_3 (conc.) a deep red colouration resulted but it disappeared on heating.

(v)/

(v) It gave no colour with chloranil.

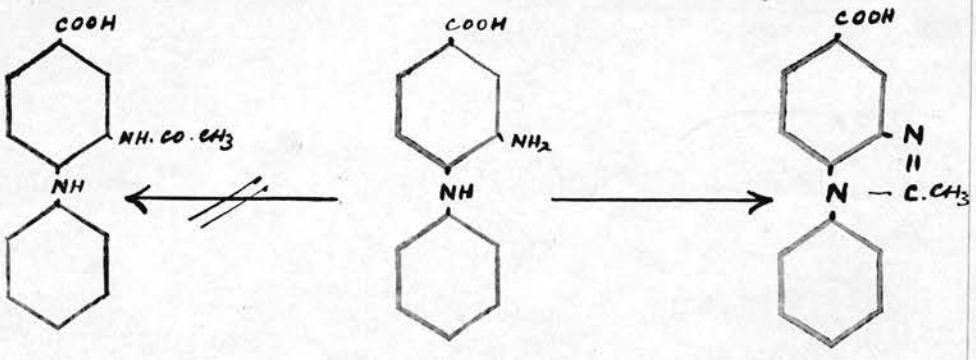
Adequate explanation of these phenomena was found impossible. It did not appear to be a true amine.

Repetition, Modification and Extension of the work of Ullmann [Ann. (1904), 332, 84].

During the attempted 1-Bromocarbazole synthesis it was often difficult to find the best method of condensation, reduction or diazotisation. Simultaneously with these experiments therefore, Ullmann's work on analogous compounds was repeated and proved of great value in affording opportunities for acquiring the necessary technique in these rather "tricky" syntheses. In the first of his preparations viz. carbazole, Ullmann refers to the work of Schöpff [Ber, (1889), 22, 3286], in which the preparative methods of the various intermediates culminating in the formation of 5-carboxy-1-phenylbenztriazole, is described. The various stages, consisting of oxidising p-bromo-toluene, nitrating the p-bromobenzoic acid formed and condensing the product with aniline, was repeated , the products at each stage being obtained in very good yield and state of purity. The condensation product, 6-nitro-4-carboxydiphenylamine was obtained pure in excellent yield, but exhibited/

exhibited the unusual property of insolubility in NaOH, behaviour which is analogous to the 2-bromo-6-nitro-4-carboxydiphenylamine already discussed. Proof of the existence of the -COOH group was forthcoming when the methyl ester was prepared. It is probable that the insoluble sodium salt of the acid has again been found.

Reduction to 2-amino-4-carboxydiphenylamine was effected with alcoholic Na_2S but attempted acetylation of the amine producted the benzimidazole compound:



It therefore appeared that the reaction could not be regulated to yield the simple acetyl derivative. Conversion into the corresponding benztriazole compound and thence to carbazole was completed successfully, the final stage yielding the best result when the triazole derivative mixed thoroughly with freshly-prepared quicklime, was distilled. Two subsidiary points of interest/

interest emerged from the foregoing experiments:

1. A. Two further methods were developed for the preparation of the condensation product 6-nitro-4-carboxydiphenylamine. One of these merely consisted of showing that p-chlorobenzoic acid could be nitrated and coupled with aniline to give the condensation product in as high a yield as its bromo-analogue.

   B. The second preparative method utilised m-nitro-p-toluidine as the starting material. Its acetyl derivative was oxidised and the product hydrolysed, both reactions giving almost quantitative yields. [Ullmann and Mauthner, Ber., (1903), 36, 4032]. The method used by Cohen and Dutt, [J.C.S. (1914), 510] yielded m-nitro-p-bromobenzoic acid, which was condensed with aniline [Cf. Schöpff, (1889), 22, 3286].

2. Reduction of the 6-nitro-4-carboxydiphenylamine with stannous chloride and HCl produced a sharp-melting crystalline compound which behaved in an anomalous fashion.

   (i) It melted at 129°C. sharply but analysis on the assumption that the corresponding amine had been formed showed that the carbon content was 3.3% low and H content 0.36% low. A residue of 0.11 mg. in 2.148 mg. of substance was found however and is probably due to a tin double salt.

(ii)/

(ii) The compound gave no colouration with the chloranil test but treatment with water and acetic anhydride yielded the benzimidazole compound. Its reaction to chloranil would seem to indicate that it is not a true amine but its behaviour to the above acetylating mixture gives a similar result. to that given by the true amine.

(iii) An attempt to prepare the azimidocompound by dropping HCl and a solution of $NaNO_2$ into a glacial acetic acid suspension of this reduction product also resulted in the formation of the benzimidazole compound however. From this it appears that standing in glacial acetic acid is sufficient to effect the conversion. Confirmation of the presence of the benzimidazole derivative was given by hydrolysis with 50% H_2SO_4, a reaction which yielded the unchanged compound. Had the acetyl derivative been formed hydrolysis to the free amine would have taken place with ease.

A comparison between 6-amino-diphenylamine, 6-amino-4-carboxydiphenylamine and 2-bromo-6-amino-4-carboxydiphenylamine did not show any marked differences in chemical properties. All three amines, on boiling with two molecular proportions of benzaldehyde, gave no benzal derivatives but all three gave deep red colouration with chloranil. The only

chemical difference noted was the effect of an acetylating mixture of water and acetic anhydride, the 6-amino- and 2-bromo-6-amino-4-carboxydiphenylamines yielding monoacetyl-derivatives whilst the 6-amino-4-carboxydiphenylamine gave the benzimidazole compound in good yield. The peculiar property of insolubility in alkali exhibited by both the amines containing the carboxy group has already been mentioned [see p.69]. In order to make a general comparison of the chemical behaviour of substituted diphenylamines, a large number of such compounds would require to be prepared. It was therefore decided to repeat the work of Chapman [J.C.S. (1922), 1676, ibid, (1927), 1743], in which a simple method for the preparation of substituted diphenylamines in good yield, is outlined.

It was also hoped that the substituted diphenylamines thus prepared could be converted to the corresponding carbazole compounds. In order to test the method it was decided to prepare o-nitrodiphenylamine, the first stage in the process being the formation of N-phenylbenzimino-o-nitrophenyl ether. Repeated attempts to obtain this compound in good yield were unsuccessful despite the fact that the most rigorous precautions to exclude moisture were taken. The imino-chloride was invariably mixed with a large percentage/

percentage of unchanged benzanilide and as these results were so unsatisfactory attempts to prepare other substituted diphenylamines by this method were abandoned.

Debromination of carbazole compounds.

During the course of this research it was found that bromine atoms could be removed from the carbazole nucleus by heating the compound with cuprous cyanide, pyridine and a little water, in a sealed tube. The rigorous conditions employed in the experiments described also resulted in the hydrolysis of acetyl and benzoyl groups which were loosely bound to the nucleus in the 9-position but in the case of tetrabromo-carbazole a 90% yield of carbazole was obtained which was considered highly satisfactory. The abnormality of the reaction can be gauged from the fact that nitriles, amides and carboxylic acids were, in some cases, obtained as final products but in the majority of the cases quoted, the hydrocarbon resulted. The mechanism of the reaction is not known and a complete investigation of the problem is being made. One concluding point of interest was that in all the experiments carried out, the formation of copper bronze was observed. This debromination reaction, when regulated so that either cyanide, amide carboxylic acid or hydrocarbon can be obtained at will, ought to prove of importance in determining the identity

and/

and elucidating the structure of compounds. In this connection several attempts to prepare 3-bromo-6-acetyl-carbazole were made unsuccessfully. [Plant, Rodgers and Williams, J.C.S. (1935), 741]. It was hoped to remove the Br atom only, from this compound and prove the position of the acetyl group in the resulting acetyl-carbazole.

Further attempts to prepare 1-carbazole derivatives.

From a previous study of Ullmann's work [Ann. (1904), 332, 82] it was realised that condensations of substituted benzene compounds, followed by reduction, diazotisation and conversion to 1-substituted carbazole derivatives, was theoretically possible. An attempt was therefore made to prepare 1-chlorocarbazole by condensing 4-bromo-3-nitrobenzoic acid and ortho-chloroaniline. Despite the fact that the condensation and reduced condensation products were not analytically pure a triazole compound was prepared which analysed correctly for nitrogen content. Efforts to effect a conversion to 1-chlorocarbazole were however unsuccessful, the rigorous experimental conditions necessary, causing the chlorine atom to be eliminated from the nucleus in an analogous fashion to the removal of bromine in the attempted conversion of 7-bromo-5-carboxy-1-phenyl-benztriazole to 1-bromocarbazole. The product of conversion/

conversion was carbazole. A condensation of o-bromo-nitrobenzene and o-chloro-aniline proved successful in that a product in analytical purity resulted but the yield was much smaller than in the previous condensation so that this possible method of preparation of 1-chloro-carbazole was not continued further.

Extension of Ullmann's method for the preparation of 1-methylcarbazole [loc. cit.] suggested a rational line of attack for preparing other 1-derivatives. It was thought that oxidation of this compound would yield carbazole-1-carboxylic acid but a mixture of methyl-dicarbazyls was obtained instead [Cf. Perkin and Tucker, J.C.S. (1921), 216]. The employment of 1 nitric acid (d, 1.2) as an oxidising agent in this case proved of no avail, nitration taking place instead. From the analysis figures quoted it appears that a mixture of either dinitro-methylcarbazole or dinitro-di-methyldicarbazyls has resulted. Had the oxidation yielded 1-carboxycarbazole, the 1-amino, and from it the 1-bromo or 1-chlorocarbazoles could have been prepared.

A final effort to prepare a 1-derivative of carbazole was crowned with success. The work of Lindemann and Mühlhaus, in preparing 3:6-dibromo-1-aminocarbazole, was repeated [Ber, (1925), 58, 2371] and/

and, with the aid of a debromination reaction, using hydriodic acid, the 1-amino derivative resulted. The preliminary experiments in the above reference were repeated with almost identical results the only change in procedure being that the crude 3:6-dibromo-1-aminocarbazole was extracted with chloroform in order to obtain the best results. The workers in the quoted reference recrystallised their product from chloroform but do not quote their yield which was found by this slight modification to be 54%. From the hydriodic acid debromination a 40% yield of 1-aminocarbazole resulted and therefore afforded the best method so far devised for the preparation of this compound. In order to confirm the presence of the amino-group a keto-piperazine was prepared as already described [see p. 99.]

A summary of the yields obtained in the preparation of 1-aminocarbazole showed at a glance the efficiency of the methods employed.

Carbazole —57%→ 3:6-Dibromocarbazole

↓ 90%

3:6-Dibromo-1-nitrocarbazole

↓ 54%

3:6-Dibromo-1-aminocarbazole

↓ 34%

1-Aminocarbazole.

The selenic acid in sulphuric acid (conc.) tests were of interest as Levine [J. Lab. clin. med. (1926), 11, 809] carried out tests with selenious acid in sulphuric acid (conc.) on phenols. Mecke performed similar tests on alkaloids and Levine concluded that these tests were specific for phenols or alkaloids containing phenolic groups. The tests carried out in this research show Levine's conclusion to be erroneous.

SUMMARY.

The application of Menke's reagent for the purpose of preparing 1-nitro and 1-nitro-substituted carbazoles was not satisfactory as the percentage of the 3-isomer was very high in all cases.

Iodine bromide and phenyliodochloride were utilised successfully in the preparation of 3-bromo- and 3-chlorocarbazole respectively. In both cases a high yield resulted and the products were analytically pure. As mild halogenating agents therefore they were much more suitable than other methods described in the literature.

Attempts to synthesise 1-bromo- and 1-chlorocarbazole by the Graebe-Ullmann method [see p.29] proved unsuccessful as the rigorous experimental conditions employed in converting the substituted benztriazole compound into the 1-substituted carbazole removed the halogen atom in addition to carbon dioxide.

The preparation of 1-carboxycarbazole by the oxidation of 1-methylcarbazole was unsuccessful, a mixture of methyl-dicarbazyls resulting instead.

1-Aminocarbazole was successfully obtained by debrominating 3:6-dibromo-1-aminocarbazole which was in turn prepared by the methods of Lindemann and Mühlhaus/

Mühlhaus [Ber. (1925), 58, 2371]. The percentage yield of the latter compound was appreciably increased by using different means of purification and the 40% yield of 1-aminocarbazole was very much higher than any previously recorded in the literature.

Debromination experiments on carbazole compounds were carried out by heating them in sealed tubes with cuprous cyanide and pyridine. Carbazole was obtained in each instance except with 3-bromo-9-acetylcarbazole when carbazole 3-nitrile resulted.

POSTSCRIPT

The author wishes to record his most sincere thanks to Dr Neil Campbell for the encouragement and advice which he has given during the course of this research. His numerous suggestions were invariably instrumental in providing the solution to the many problems encountered, and make# acknowledgment of this help difficult to express adequately.

BIBLIOGRAPHY.

Graebe and Glaser	Ber. (1872), 5, 12.
" "	Ann. (1872), 163, 343.
Graebe	Ann. (1873), 167, 125.
Graebe and Ullmann	Ann. (1896), 291, 16.
Akt. Ges. für Teer und Erdöl industrie	D.R.P. (1899), 111, 359, Kl. 121.
Frankhänel	D.R.P. (1909), 226, 112 Kl 120.
Loebisch and Schoop	M (1886), 7, 611.
Bernthsen	Ber. (1886), 19, 3255.
Ackermann	D.R.P. (1909), 222, 879, Kl 12 p.
Von Braun, Heider and Neumann	Ber. (1916), 49, 2618.
Ullmann	Ber. (1898), 31, 1697.
Tucker and Stevens	J.C.S. (1923), 2146.
Padoa and Chiaves	R.A.L. (1908), 5, 16, II, 762.
Tucker	J.C.S. (1926), 546.
Ullmann	Ann. (1904), 332, 84.
Graebe and Adlerskron	Ann.(1880), 202, 23.
Oddo	G. (1911), 41, I, 255.
Gilbert Morgan	J.C.S. (1931), 3283.
F. Lindemann	Ber. (1924), 57, 1316, 555.
P. Ziersch	Ber. (1909), 42, 3798.

P. Ziedler	Ann. (1878), 191, 304.
Suida	Ber. (1879), 12, 1403.
Schott	D.R.P. (1901), 134, 983, Kl 12 p.
Borsche, Witte and Bothe	Ann. (1908), 359, 74.
J. Böeseken	Rec. trav. chim. (1912), 31, 350.
Mazzara	Ber. (1891), 24, 278.
Plant and Rodgers	J.C.S. (1936), 40.
Plant and Tomlinson	J.C.S. (1932), 2188.
Plant and Williams	J.C.S. (1934), 1142.
Plant, Rodgers and Williams	J.C.S. (1935), 741.
Lindemann and Wessel	Ber. (1925), 58, 1221.
Lindemann and Mühlhaus	Ber. (1925), 58, 2371.
Votocek	Ch. 1896, I. Rep. 20, 190.
R. Salvadori	G. (1896), 238.
W. Will	Zeit. ang. Chem. (1901), 748.
Perkin and Tucker	J.C.S. (1921), 216.
Plant and Briscoe	J.C.S. (1928), 1990.
L.H. Gerty	Thesis, Edinburgh.
Menke	Rec. trav. chim. (1925), 44, 141, 269.
Vaubel	Z. ang. (1901), 14, 784.
Ciamician and Silber	G. (1882), 12, 276.
Militzer	J.A.C.S. (1938), 60, 256.

Garvey, Halley and Allen	J.A.C.S. (1937), 59, 1827.
Kaufmann	Ber. (1909), 42, 3481.
	Org. Synthesis, 6, 8-9.
Wroblewsky	Ann. (1872), 168, 153.
"	Ann. (1878), 192, 202.
Cohen and Dutt	J.C.S. (1914), 105, 510.
Frehden and Goldschmidt	Mikrochimica Acta, (1937), I, 347.
Hübner	Ann. (1884), 222, 177.
"	Z. (1866), 615.
Ehrlich	Ber. (1882), 15, 2009.
Ullmann and Mauthner	Ber. (1903), 36, 4032.
Schöpff	Ber. (1889), 22, 3286.
Hickinbottom	Page 271.
Kehrmann and Havas	Ber. (1913), 46, 341.
Wolff	Ann. (1912), 394, 65.
Hodgson and Walker	J.C.S. (1933), 1620.
Conn and Lowry	Chem. A., (1926), 20, 3396.
Mazzara and Leonardi	G, (1892), 22 II, 572.
M.C. Perrier	Bulletin de la Societe chimique de Paris (1904), 22 II, 572.
~~M.C.-Perrier~~ Chapman	J.C.S. (1922), 1676.
"	J.C.S. (1926), 2296.
Kofler	Mikrochemie (1934), 15, 242.
Blanksma	C. (1922), II, 1965.
Tucker	J.C.S. (1923), 2140.
Levine	J. Lab. clin. Med. (1926), 11, 809.