Abstract.-

The thesis is divided into three sections:-

(I) The thermal decomposition of some "diazoperbromides".

The bis-diazoperbromide derived from 2-nitrobenzidine decomposes in hot glacial acetic acid to give 2:4:4'-tribromo- and 4:4'-dibromo-2-nitrodiphenyl. The tribromo-compound appears to be formed by an intramolecular mechanism.

(II) The unsuccessful attempts of preparing both 4:5-dimethyl- and 4:5:9-trimethyl-phenanthridine could be due to the steric effects of the methyl groups in the blocking positions.

2-Amino-6:6'-ditolyl (+)-camphor-10-sulphonate showed mutarotation and yielded an inactive base on decomposition.

Attempts were made to resolve 6-(methylphenyl)-phenyl-6'-methyl-2-trimethylammonium iodide, but, in each case an inactive iodide was obtained after decomposition of the active salt.

(III) 5:5'-Di*iso*quinolyl (+)-camphor-10-sulphonate could not be resolved, neither did it mutarotate; although its (+)-tartrate showed mutarotation in one occasion, there was no confirmed evidence of mutarotation of the tartrate; but comparison with similar salt of inactive base (2:2'-dipyridyl) gave an indication that the base might be capable of optical activity.

# STUDIES IN THE CHEMISTRY OF DIARYLS.

Thesis presented by **SHIU MAY LOH** in
requirement for the Degree of Doctor of Philosophy
in The University of London.

---

The author wishes to express her thanks to Professor E. E. Turner, F.R.S. for his continued help and encouragement, to Dr. D. M. Hall for valuable disscussion, and to Dr. M. M. Harris for the part she has played in the furtherance of these studies.

# CONTENTS.

## PART I.

The Thermal Decomposition of Some "Diazoperbromides".

## PART II.

Studies in the phenanthridines; and Synthetic work and Stereochemical Examination of 2-Amino-6:6'-ditolyl and 6-(methylphenyl)-phenyl-6'-methyl-2-trimethyl-ammonium iodide.

## PART III.

The temperature effect upon 5:5'-di*iso*quinolyl(+)-camphorsulphonate in chloroform solution.

## INTRODUCTION - SCETION I.

The diazonium halides combine by addition with two atoms of chlorine, bromine, or iodine which may be the same as or different from each other. In this way there are formed stable crystalline compounds which possess the constitution $\text{ArN}(\vdots\text{N})\cdot(\text{XX}'\text{X}'')$. The perbromides are the most easily obtained members of the group and were first prepared by Griess (Annalen, 1864, 137, 50; Phil. Trans., 1864, 154, 673), who added a solution of bromine in hydrobromic acid to aqueous solution of benzenediazonium nitrate. The brownish-red oil which separates under these conditions crystallises on removal from the mother-liquor and removal of excess bromine by ether. Large yellow plates crystallise from ether and the perbromide is stable while kept dry, but it is decomposed by water. Hantzsch (Ber., 1895, 28, 2754) pointed out the close analogy of the diazoperhalides, and the perhalides of the alkali metals, and he also prepared nine out of the ten possible combinations of chlorine, bromine, and iodine:-

| | | |
|---|---|---|
| $ArN_2 \cdot I_3$ | $ArN_2 \cdot Br_3$ | $(ArN \cdot Cl_3)$ |
| $I_2Br$ | $Br_2Cl$ | $ArN_2 \cdot Cl_2Br$ |
| $I_2Cl$ | $Br_2I$ | $Cl_2I$ |
| | $BrClI$ | |

The colour of these compounds varies from almost black for the periodide to yellow for the chloroiodide.

Chattaway (J., 1909, 95, 862; *ibid*., 1915, 107, 105) advanced the thesis that the diazo-perbromides have the constitution of N-tribromoaryhydrazines, $Ar \cdot NBr \cdot NBr_2$, because they can be obtained by the action of bromine on arylhydrazines, and are widely different from the ammonium perhalides, but the arguments advanced by Hantzsch (ibid., 1915, 48, 1344) and by Forster (J., 1915, 107, 115) leave no room for doubt that the perhalides are true diazonium compounds. Substances of the constitution proposed by Chattaway probably cannot exist, for bromine will not add to the double bond in benzene diazocyanide to form a cyanodibromophenydrazine, but ejects the cyano-group, forming first the diazonium bromide if sufficient bromine is present.

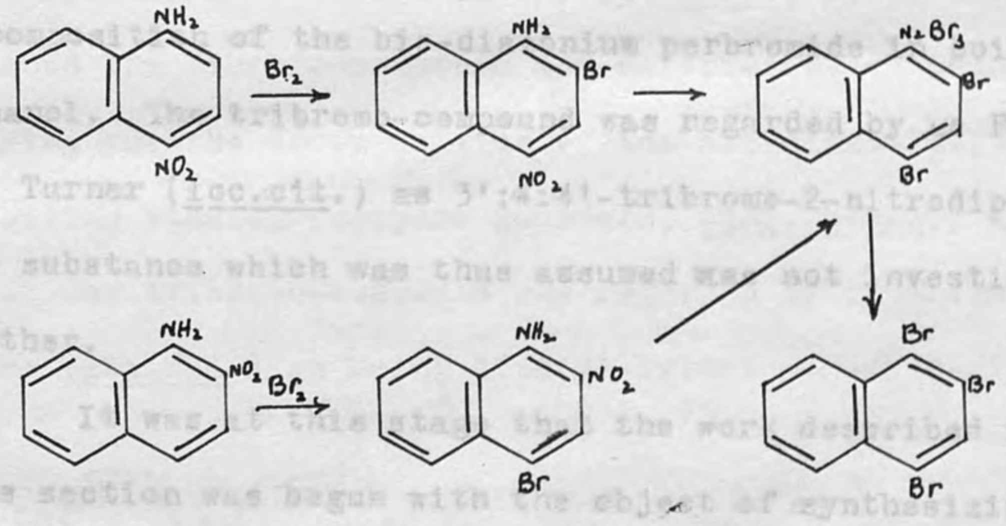
Of obvious relevance to this question is the recent observation that a vibration frequency around

2260 $cm^{-1}$ is characteristic of $R \cdot N_2^+$ cation (Aroey, Le Fevre and Werner, J., 1955, 276). Aroney and Le Fevre (*loc.cit.*, p.1630) have therefore, prepared the "diazo-perbromides" from *p*-tolidine, *p*-chloro-aniline, and β-naphthylamine, and recorded their absorption spectra over the range 3250-1350 $cm^{-1}$ and hence concluded that the perbromide contains the $R \cdot N_2^+$ group.

The diazonium perbromides give up two atoms of bromine with ease, and will saturate ethylenic links, as in cinnamic acid (Bulow and Schmachtenburg, *Ber.*, 1908, *41*, 2067). They differ from the diazonium salts in that when boiled with alcohol they afford the bromohydrocarbon instead of the hydrocarbon (Saunder, *Amer. Chem. J.*, 1891, *13*, 486). The bromohydrocarbons are also obtained by thermal decomposition of the perbromides in solvents such as glacial acetic acid. Occasionally when acetic acid is used the bromine formed brominates the bromo compound and when alcohol is used some ether $Ar \cdot OC_2H_5$ may be produced, but the method is excellent on the small acale, since normally few by-products are formed, in particular no $Ar \cdot OH$.

Consden and Kenyon (J., 1935, 1596) showed that when bromine in sufficient excess acts on 1:4- or

2:1-nitronaphthylamine both the amino- and the nitro-groups are replaced by bromine through the intermediary of the diazoperbromide. The bromine replaces the nitro-group, the nitrous acid thus set free diazotises the amino group which is converted into the perbromide, which then replaces the diazo group by bromine the final product being 1:2:4-tribromonaphthalene:-



Still higher perhalides can be formed. Chattaway (loc.cit.) showed that the brown oil which separates in the preparation of the perbromide contains no fewer than nine atoms of bromine, but they can only be retained in combination if the bromine vapour is prevented from escaping.

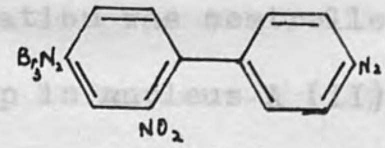
Le Fevre and Turner (J., 1926, 2041) observed that the bis-diazonium perbromide derived from 2-nitrobenzidine behaved abnormally when allowed to decompose in hot glacial acetic acid, the product most easily isolated being a tribromo-nitrodiphenyl, m.p. 195-196°, instead of the expected 4:4'-dibromo-2-nitrodiphenyl, m.p. 124°. Shaw and Turner (loc.cit., 1923, 285) obtained the dibromo- and no tribromo-compound by carrying out the decomposition of the bis-diazonium perbromide in boiling ethanol. The tribromo-compound was regarded by Le Fevre and Turner (loc.cit.) as 3':4:4'-tribromo-2-nitrodiphenyl. The substance which was thus assumed was not investigated further.

It was at this stage that the work described in this section was begun with the object of synthesizing 3':4:4'-tribromo-2-nitrodiphenyl and thus either confirming or disproving the postulated structure of the tribromo-nitrodiphenyl obtained from decomposition the of tetrazoniumperbromide derived from 2-nitrobenzidine in glacial acetic acid.

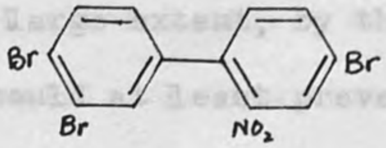
Further work on similar thermal decomposition of some diazoperbromides was envisaged.

## DISCUSSION - SECTION I.

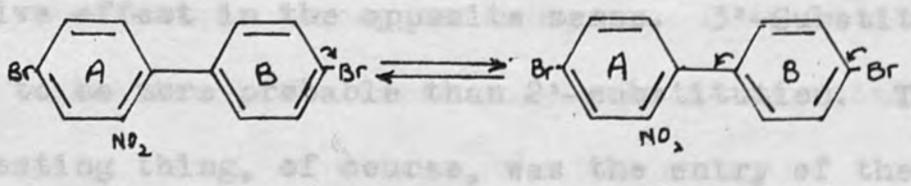
It was observed by Le Fevre and Turner (J., 1926, 2041) that the bis-diazoniumperbromide (1) derived from 2-nitrobenzidine behaved abnormally when allowed to decompose in hot glacial acetic acid, the product most easily isolated being a tribromonitrodiphenyl, m.p. 195-196°, instead of the expected 4:4'-dibromo-2-nitrodiphenyl (11) m.p. 124°. Shaw and Turner (loc.cit., 1932, 285) obtained the dibromo-compound and no tribromo-compound by carrying out the decomposition of the bis-diazoniumperbromide in boiling ethanol (compare Saunders, Amer.Chem.J., 1891, 13, 486). The tribromo-compound was regarded by Le Fevre and Turner (loc.cit.) as being 3':4:4'-tribromo-2-nitrodiphenyl



(I)



(III)



(II)

(111) since (a) it seemed inconceivab-le that the third bromine atom had entered the nucleus bearing the nitro-group.

It might be objected that, in the perbromide displacement on 2-nitrobenzidine, the third bromine atom could enter the same nucleus bearing the nitro-group. Against this objection, however, were at least two facts:-

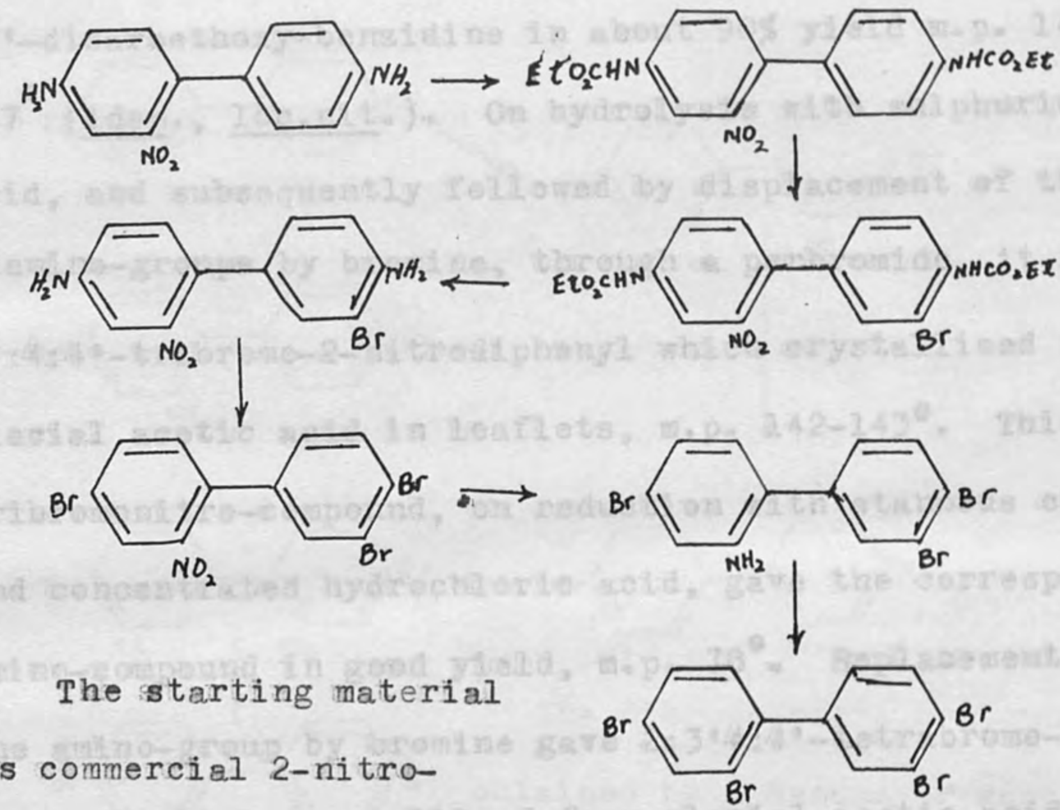
(i) the difficulty of introducing a third substituent into one nucleus of diphenyl compounds other than hydroxyl- and amino-dervatives.

(ii) the independence of the nuclei (ibid., loc.cit., 1928, 246; Burton and Kenner, loc.cit., 1921, 121, 489); the nitro-groups present in one nucleus cannot effect the activation of halogen atoms or nitro-group in the other nucleus.

(b) by analogy with the nitration of 4:4'-dibromo-2-nitrodiphenyl of Shaw and Turner (loc.cit.), the nitration was controlled, to a large extent, by the nitro-group in nucleus A (II) which could at least prevent electron displacements from nucleus A to B and might exert a small positive effect in the opposite sense. 3'-Substitution seems to be more probable than 2'-substitution. The most interesting thing, of course, was the entry of the third bromine atom into what would be regarded as a non-reactive system.

The problem was therfore examined afresh, the first essential being to establish the orientation of the tribromo-nitro-compound. An attempt was made to reduce the tribromonitro-compound by means of iron filings and aqueous alcohol on a boiling water bath for two hours. After the usual procedure the crude solid which was thus obtained could neither be purified nor did it melt below 300°. However, on reduction with stannous chloride and concentrated hydrochloric acid in glacial acetic acid, it gave a corresponding amino-compound which after being crystallised several times from alcohol and then benzene melted at 154°. The replacement of the amino-group in this compound by bromine, via a diazoniumperbromide followed by decomposition in hot glacial acetic acid, gave a tetrabromodiphenyl, crystallising from the same solvent in fine white needles, m.p. 273°, quite different from 2:3':4:4'-tetrabromodiphenyl, m.p. 124-125°, obtained by two syntheses. The first one could be represented as follows:-

Scheme (I)

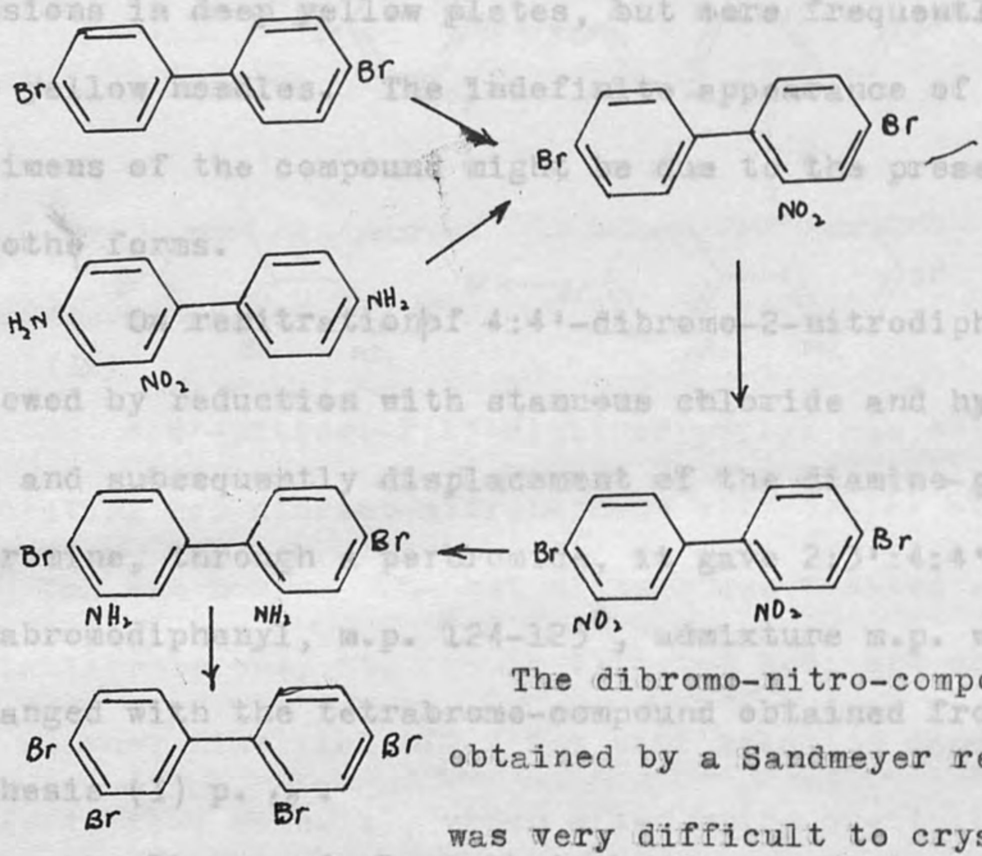


The starting material was commercial 2-nitrobenzidine which, after crystallisation from litres and litres of water gave bright-red needles, m.p. 143°. This was converted into 2-nitro-NN'-dicarbethoxy-benzidine, by boiling with diethylaniline and ethyl chloroformate in ethyl alcohol as described by Lesslie and Turner (loc.cit., 1933, 1589) in almost theoretical yield, m.p. 190-192°, after being once recrystallisated from ethyl alcohol.

Bromination of the diurethane by bromine in the presence of glacial acetic acid gave 3-bromo-2-nitro-NN'-dicarbethoxy-benzidine in about 90% yield m.p. 145-147° (idem., loc.cit.). On hydrolysis with sulphuric acid, and subsequently followed by displacement of the diamino-groups by bromine, through a perbromide, it formed 3':4:4'-tribromo-2-nitrodiphenyl which crystallised from glacial acetic acid in leaflets, m.p. 142-143°. This tribromonitro-compound, on reduction with stannous chloride and concentrated hydrochloric acid, gave the corresponding amino-compound in good yield, m.p. 78°. Replacement of the amino-group by bromine gave 2:3'4:4'-tetrabromo-diphenyl which crystallised from glacial acetic acid, m.p. 124-125°.

In the second synthesis, 2-nitro-4:4'-dibromo-diphenyl, m.p. 124° was obtained either by mononitration of the commercial 4:4'-dibromodiphenyl, a Sandmeyer reaction on recrystallised commercial 2-nitrobenzidine or by decomposition of the bis-diazonium perbromide derived from 2-nitrobenzidine in boiling absolute ethyl alcohol.

Scheme (II)

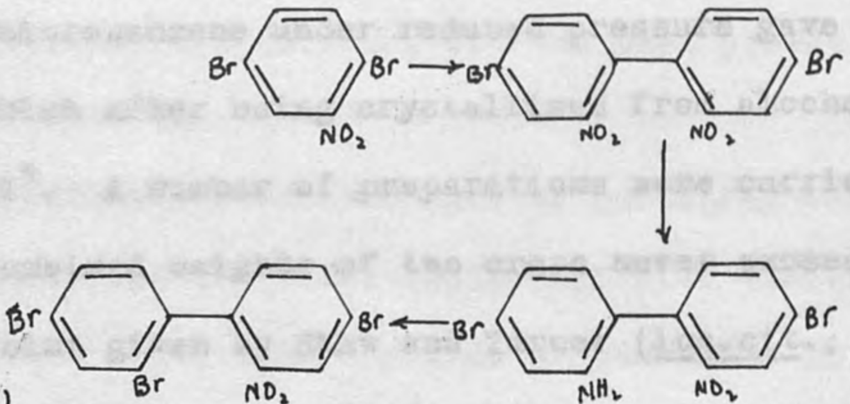


The dibromo-nitro-compound obtained by a Sandmeyer reaction was very difficult to crystallise; only after several recrystallisations from aqueous alcohol with a little charcoal, it melted at 124° and the yield was, therefore, very low. Among all the methods for the preparation of 4:4'-dibromo-2-nitrodiphenyl, the mononitration of 4:4'-dibromodiphenyl was always eligible as it was most satisfactory. This was not only simple in procedure but also gave a fairly pure product which could be easily crystallised from aqueous alcohol and the yield was also reasonably good.

The nitro-compound crystallised on certain occasions in deep yellow plates, but more frequently in pale yellow needles. The indefinite appearance of most specimens of the compound might be due to the presence of both forms.

On renitration of 4:4'-dibromo-2-nitrodiphenyl, followed by reduction with stannous chloride and hydrochloric acid and subsequently displacement of the diamino-groups by bromine, through a perbromide, it gave 2:3':4:4'-tetrabromodiphenyl, m.p. $124-125^{\circ}$, admixture m.p. was unchanged with the tetrabromo-compound obtained from synthesis (I) p. 10.

It seemed clear that the compound, m.p. $195-196^{\circ}$, must be 2':4:4'-tribromo-2-nitrodiphenyl (IV). However, this has been proved by performing the operation shown below:-



(IV)

4:4'-Dibromo-2:2'-dinitrodiphenyl was obtained by heating 2:5-dibromo-nitrobenzene with copper bronze at 240° for two hours. The hot mixture was treated with o-dichlorobenzene, the liquid filtered hot; and most of the solvent distilled off. The cool solution deposited a crystalline material, which after being crystallised first from glacial acetic acid and then from n-butyl alcohol, it formed pale yellow octahedra, m.p. 152°, and was unaffected by further crystallisation from ethyl alcohol.

Repetition of the above Ullmann reaction by using small amounts of boiling o-dichlorobenzene for extraction of the hot mixture; obtained by heating 2:5-dibromo-nitrobenzene with copper bronze at 240° for two hours; gave crystals on cooling, which after being recrystallised from ethanol in plates had m.p. 152°. Distillation of the o-dichlorobenzene under reduced pressure gave a brown residue which after being crystallised from alcohol melted at 138-141°. A number of preparations were carried out yet the combined weights of two crops never exceeded 40%. Melting point given by Shaw and Turner (loc.cit.) was 150°.

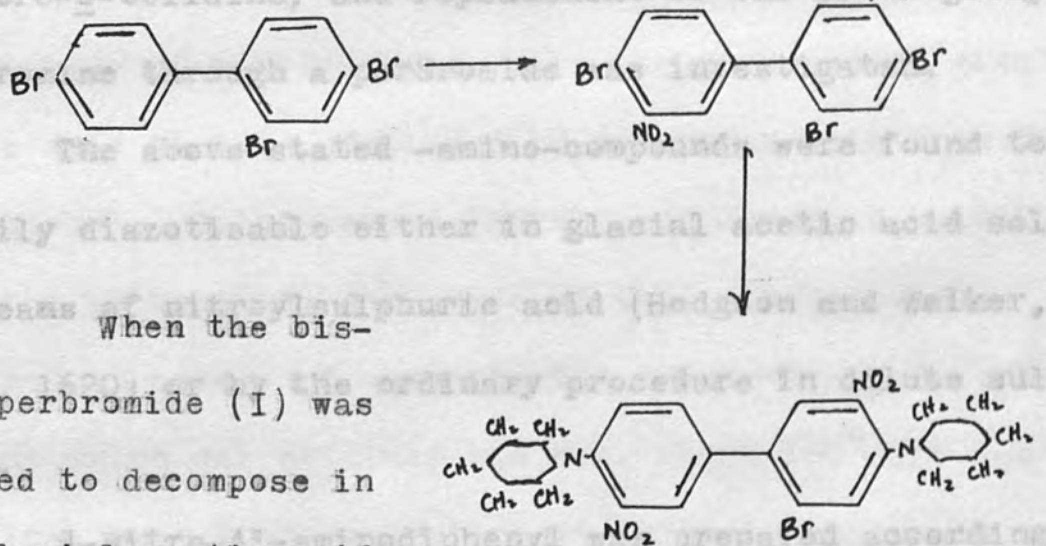
Considerable difficulty was encountered in the partial reduction of the foregoing dinitro-compound, by means of alkali sulphide. In the first preparation of 2-amino-4:4'-dibromo-2'-nitrodiphenyl, an ethanolic solution of 4:4'-dibromo-2:2'-dinitrodiphenyl (10 g.) was added to a hot well-stirred solution containing sulphur (1.6 g.), sodium sulphide ($+9H_2O$) (9.0 g.), and water (12 ml.). The solution was boiled for an hour, boiling water being added from time to time to maintain the volume. The solution was cooled and the orange-coloured precipitate filtered off and by extraction with dilute hydrochloric acid and precipitation with aqueous ammonia (d. 0.880) crude 2-amino-4:4'-dibromo-2'-nitrodiphenyl (1.9 g.; 20% yield) was obtained which after three crystallisations from ethanol melted at 103-104°.

Three subsequent preparations were carried out in a similar manner, using different proportions of sodium sulphide and sulphur, but the best yields ever obtained were 27%.

Attempts were also made by partially reducing the 4:4'-dibromo-2:2'-dinitrodiphenyl with ammonium sulphide and about 10-15% yields of the amino-nitro-compound were obtained. The idea of using ammonium sulphide instead of sodium sulphide was therefore discarded.

Replacement of the amino-group of 2-amino-4:4'-dibromo-2'-nitrodiphenyl by bromine through a perbromide method gave a product, identical with the compound of m.p. 195-196°, which was obtained from the decomposition of the bis-diazoperbromide derived from 2-nitrobenzidine; It was convertible in two stages, into 2:2':4:4'-tetrabromodiphenyl, m.p. 273°. The latter was also obtained by carrying out a benzidine rearrangement on 2:2'-dibromohydrazobenzene, followed by a diazonium perbromide replacement. It could not, however, be isolated from the mixture obtained by heating 2:4-dibromo-iodobenzene with copper powder.

An attempt to obtain 2':4:4'-tribromo-2-nitrodiphenyl by nitrating 2':4:4'-tribromodiphenyl under a number of different experimental conditions resulted in dinitration. The product would appear to be 2':4:4'-tribromo-3:5'-dinitrodiphenyl; after being crystallised from alcohol, m.p. 164-165°, since it reacted with hot piperidine to give a bromo-dipiperidino-dinitrodiphenyl, m.p. 146-147°.



When the bis-diazoperbromide (I) was allowed to decompose in hot glacial acetic acid containing one molecular proportion of cinnammic acid, acetanilide or aceto-p-toluidine, 4:4'-dibromo-2-nitrodiphenyl but no tribromo-nitrodiphenyl was isolated (compare Bulow and Schmachtenburg, Ber., 1908, 41, 2607).

Since it has been proved that the thermal decomposition of bis-diazonium perbromide derived from 2-nitrobenzidine in glacial acetic acid at 95° gives 2':4:4'-tribromo-2-nitrodiphenyl together with about twice its weight of 4:4'-dibromo-2-nitrodiphenyl, this let to synthesis of several other -amino-compounds, such as 4-nitro-4'-amino-, 2-nitro-4'-amino-, 4-bromo-4'-amino- 2-nitro-4-amino-diphenyl, 4-amino-veratole and 2-nitro-o-tolidine; and replacement of the amino-group by bromine through a perbromide was investigated.

The above stated -amino-compounds were found to be readily diazotisable either in glacial acetic acid solution by means of nitroylsulphuric acid (Hodgson and Walker, J., 1933, 1620) or by the ordinary procedure in dilute sulphuric acid.

4-Nitro-4'-aminodiphenyl was prepared according to Fittig (Annalen, 124, 278), by partial reduction with ammonium sulphide of 4:4'-dinitrodiphenyl, in red needles from alcohol, m.p. 199°.

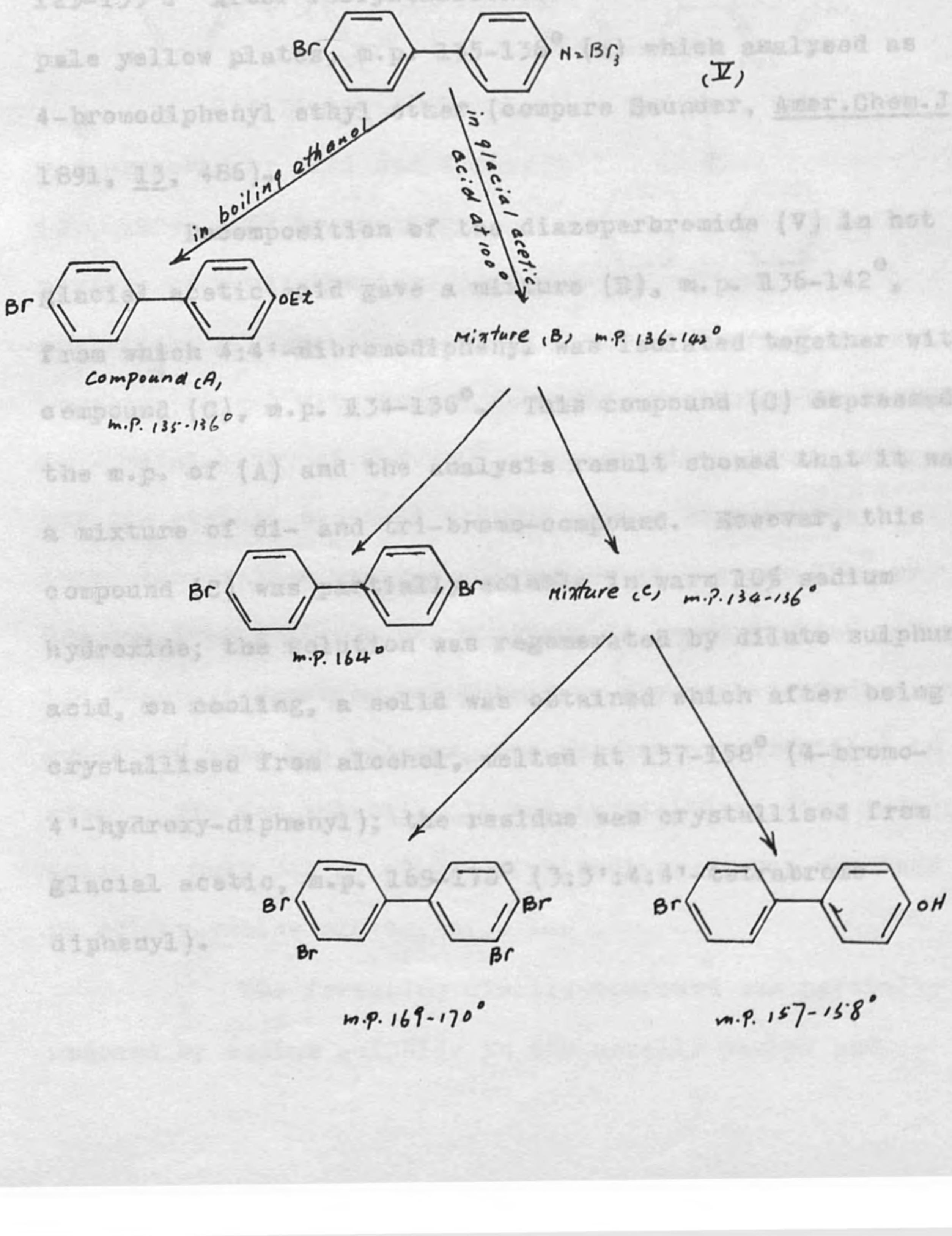
4-Nitro-4'-aminodiphenyl, under the conditions of perbromide displacement, did not give 4-nitro-4'-bromodiphenyl but a mixture of mono- and di-bromo- compound, m.p. 210-211°.

Partial reduction, by means of sodium sulphide on 2:4'-dinitrodiphenyl, 2-nitro-4'-aminodiphenyl was obtained in orange red needles from alcohol, m.p. 97-99° (Scherwood and Calvin, J.Amer.Chem.Soc., 1942, 64, 1350). This, under the conditions of the perbromide displacement, gave a mixture of mono- and dibromo-compound, m.p. 200-202°.

4-Bromo-4'-aminodiphenyl was obtained by bromination of 4-nitrodiphenyl in the presence of glacial acetic acid at 100°, followed by reduction with iron filings and alcohol, "West" method (Hartly and Jones, J., 1952, 1959). When the phthalimido-dervative of this substance was nitrated in excess of concentrated sulphuric acid. The product which was obtained had m.p. about 180° and was identical with 4-bromo-2-nitro-4'-aminodiphenyl. It was therefore assumed that both nitration and hydrolysis took place at the same time.

When the diazoperbromide derived from 4-bromo-4'-aminodiphenyl was allowed to decompose in hot glacial acetic acid, a mixture of mono- and di-bromo-compound, m.p. 136-142°, was obtained.

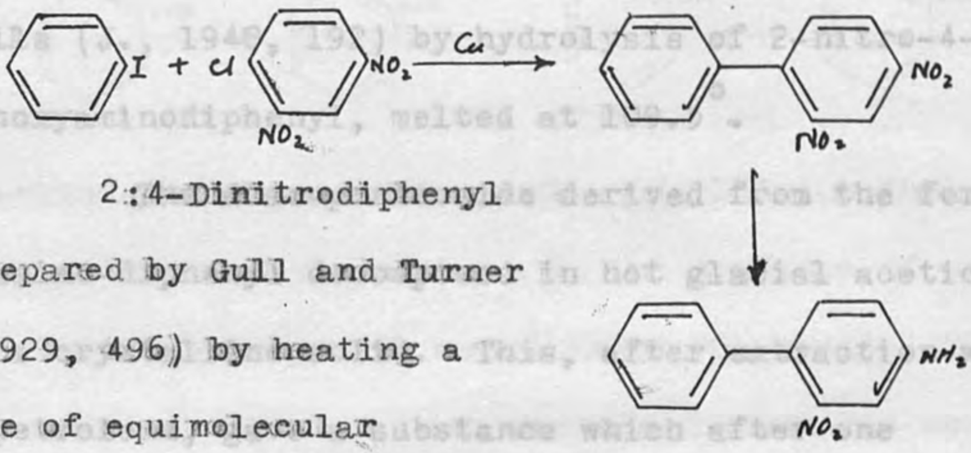
This experiment was repeated and the thermal decomposition of the diazo-perbromide of 4-bromo-4'-aminodiphenyl was studied more closely.



The diazoperbromide (V) was first decomposed in boiling ethanol and, on cooling, a solid was obtained which after first crystallisation from alcohol melted at 125-133°. After recrystallisation from alcohol, it formed pale yellow plates, m.p. 135-136° (A) which analysed as 4-bromodiphenyl ethyl ether (compare Saunder, Amer.Chem.J., 1891, 13, 486).

Decomposition of the diazoperbromide (V) in hot glacial acetic acid gave a mixture (B), m.p. 136-142°, from which 4:4'-dibromodiphenyl was isolated together with compound (C), m.p. 134-136°. This compound (C) depressed the m.p. of (A) and the analysis result showed that it was a mixture of di- and tri-bromo-compound. However, this compound (C) was partially soluble in warm 10% sodium hydroxide; the solution was regenerated by dilute sulphuric acid, on cooling, a solid was obtained which after being crystallised from alcohol, melted at 157-158° (4-bromo-4'-hydroxy-diphenyl); the residue was crystallised from glacial acetic, m.p. 169-170° (3:3':4:4'-tetrabromo-diphenyl).

2-Nitro-4-aminodiphenyl was prepared according to the following scheme:-



2:4-Dinitrodiphenyl was prepared by Gull and Turner (J., 1929, 496) by heating a mixture of equimolecular quantities of iodobenzene (21 g.) and 1-chloro-2:4-dinitrobenzene (20 g.) with copper in a wide-mouthed conical flask in a metal bath, at 210-230°. The reaction proceeded rapidly and the mixture was well stirred with a thermometer. The inner temperature was not allowed to rise above 230° or the reaction would be too vigorous to be controlled. After the vigorous reaction had subsided, the cooled product was extracted with hot benzene, and the extract distilled in steam. The non-volatile oil was crystallised from industrial spirit. Only 3-5 g. of 2:4-dinitrodiphenyl was obtained in golden-yellow plates, m.p. 110°.

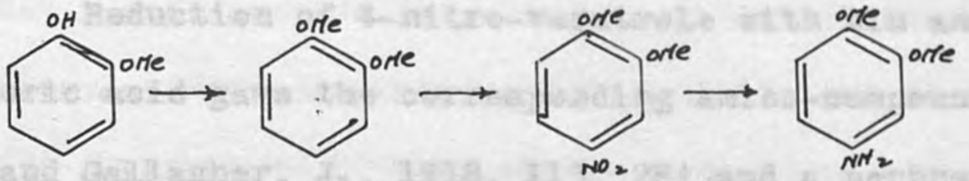
The foregoing dinitro-compound was partially reduced by sodium sulphide in the usually manner and

2-nitro-4-aminodiphenyl thus obtained was crystallised from aqueous alcohol in golden-yellow plates, m.p. 108-109°.

2-Nitro-4-aminodiphenyl obtained by Caldwell and Walls (J., 1948, 192) by hydrolysis of 2-nitro-4-carbethoxyaminodiphenyl, melted at 109.5°.

The diazoperbromide derived from the foregoing nitro-amino-diphenyl decomposed in hot glacial acetic acid giving a crystalline solid. This, after extraction with light petroleum, gave a substance which after one crystallisation from acetic acid and then aqueous alcohol had m.p. about 115°, and was unaffected by further crystallisation from the latter solvent as well as the former one. This might be assumed to be a mixture of dibromonitro- and tribromonitro-compound. Evaporation of the light petroleum gave a thick pale brown oil which eventually solidified. This was crystallised from alcohol in needles, m.p. 63-64°, and was assumed to be 2-nitro-4bromodiphenyl, although the analysis result (cf. p.62) was slightly low.

To prepare 4-amino-veratrole the following scheme was presented.



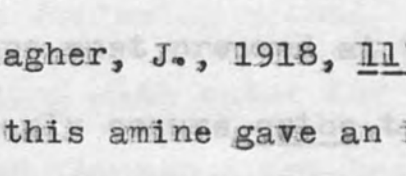
Perkin and Weizmann (J., 1906, 89, 1649) methylated catechol with dimethyl sulphate in the presence of methyl alcohol and caustic potash solution in 80% yield. The reaction was so vigorous that the methylation was complete in about three minutes.

Veratrole, under the conditions of nitration, gave 4-nitro-veratrole (Cardwell and Robinson, J., 1915, 117, 257) in good yield. Veratrole was very easily nitrated, but was not affected by moderately concentrated solution of nitric acid. Aqueous nitric acid containing only one part of nitric acid (d. 1.42) in ten parts of water nitrated the substance at room temperature quantitatively in two or three days, whilst more concentrated solutions naturally effect the substitution more readily. A 91% yield of 4-nitro-veratrole was obtained when vertrole (25 g.) was gradually added with careful cooling, to a mixture of nitric acid (20 ml., d. 1.42) and water (20 ml.). This product was fractionally crystallised, and found to be entirely free from any isomeric nitro-compound.

Reduction of 4-nitro-veratrole with tin and hydrochloric acid gave the corresponding amino-compound (Senier and Gallagher, J., 1918, 113, 28) and a perbromide displacement on this amine gave an intractable tar.

Mononitration of o-tolidine sulphate at 0° gave 2-nitro-o-tolidine (Lowenherz, Ber., 1892, 25, 1032) m.p. 156° from alcohol in red needles.

The bis-diazoperbromide derived from 2-nitro-o-tolidine decomposed in hot glacial acetic acid to give 2-nitro-4:4'-dibromo-3:3'-dimethyldiphenyl.



This result was unexpected since the 2'-position should be more reactive than the corresponding position in the methyl free compound.

The more general scope of the diazoperbromide decomposition reaction has been examined in a number of cases, with the following results:-

The bis-diazoperbromide derived from benzidine decomposed in boiling ethanol to give 4:4'-dibromodiphenyl, and in hot glacial acetic acid to give 2:2':4:4'-tetrabromodiphenyl. Here the decomposition of the two diazoperbromide groups must proceed at the same rate, and bromination clearly occurs <u>ortho</u> to the newly formed 4-Br-substituent.

The diazoperbromide derived from 4-aminodiphenyl decomposed in boiling ethanol to give 4-bromodiphenyl; and in hot glacial acetic acid to give 4:4'-dibromodiphenyl.

The diazoperbromide derived from 4-aminodiphenyl ether decomposed in hot glacial acetic acid to give 4:4'-dibromodiphenyl ether.

The diazoperbromide derived from 4-aminoantipyrine and 8-nitro-1-naphthylamine, decomposed in hot glacial acetic acid, only a trace of 4-bromo-antipyrine and 1-bromo-8-nitro-naphthalene was isolated respectively.

The diazoperbromide derived from 3-amino-2-naphthoic acid decomposed in hot glacial acetic acid and gave a mixture of monobromo- and dibromo-compound, m.p. 236-237°.

## EXPERIMENTAL - SECTION I.

### Purification of 2-nitrobenzidine.

The commercial 2-nitrobenzidine was purified according to the following method. The 2-nitrobenzidine (100 g.) was boiled with water for a few minutes and the solution filtered through a pre-heated Buchner funnel. The hot filtrate was poured on to ice. Bright-red crystals separated in a few minutes. The undissolved residue was re-boiled with water as before. This process was repeated several times until about 70-80 g. of 2-nitrobenzidine, m.p. 143°, was thus obtained. About a total of 30-40 litres of water were used for this purification.

### Perbromide displacement on 2-nitrobenzidine.

Le Fevre and Turner (J., 1926, 2041).

2-Nitrobenzidine (34.5 g., 2 mols) was dissolved in 48% hydrobromic acid (216 ml., 5.9 mols.) and water (432 ml.) by warming. The solution was cooled in a freezing mixture to -2°. It was bis-diazotised between -2° and 5° by the addition of sodium nitrite solution (22.5 g., 2.2 mols. in 45 ml. of water). The bis-diazo-solution was then treated with bromine (24 ml.) in 48% hydrobromic acid (150 ml.). The perbromide separated as an orange yellow thick paste. It was filtered off, washed with water, ethyl alcohol and dry ether, and dried in a vacuum over potassium hydroxide and then concentrated sulphuric acid. The dried perbromide was boiled with glacial acetic acid until bromine evolution ceased; and the resulting solution, on cooling, became a magma of crystals, which were recrystallised from glacial acetic acid, 2':4:4'-tribromo-2-nitrodiphenyl being obtained in yellow needles m.p. 195-196°.

This preparation was repeated a number of times and the yields varied from 24-33% and in one case it was obtained as high as 43%. It was, however, found that by decomposing the bis-diazonium perbromide in glacial acetic acid at 95°, a yield of 40% of tribromo- and 60% of dibromo-compound could be isolated.

A solution of 2-nitrobenzidine (11.5 g.) in a hot mixture of 48% of hydrobromic acid (72 ml.) and water (144 ml.) was cooled rapidly to about -2°. It was bis-diazotised under the surface at this temperature by the addition of sodium nitrite solution (7.5 g. in 18 ml. of water). The bis-diazo-solution was stirred between -2° and 0° for ten minutes to ensure completion of reaction and an almost clear solution obtained was filtered and treated gradually, while being stirred, with a mixture of bromine (8 ml.) and 48% hydrobromic acid (50 ml). After fifteen minutes, the orange-coloured bis-diazonium perbromide was filtered off, washed, with water, absolute ethanol, finally dry ether, and dried over solid potassium hydroxide and conc. sulphuric acid. Yield 35.5 g. (96.5%).

<u>Decomposition of the Bis-diazoperbromide</u>.

(a) <u>In glacial acetic acid at 95±3°</u>. 7.33 g. of the bis-diazoperbromide was added gradually to 40 ml. of glacial acetic acid kept at 95 3°. After the addition was completed, the solution was boiled until free from bromine. On cooling, a thick paste was obtained. Water was added to complete the separation of solid. The resulting paste was filtered, washed with water and dried at 100° and later in vacuum over sulphuric acid and solid potassium hydroxide. Yield 3.85 g. (Found: Br, 48.2 Calc. for tribromo-: 55.5 Calc. for dibromo-: 44.8%). By extraction twice with 50 ml.

of boiling light petroleum (b.p. 60-80°) this was freed from 4:4'-dibromo-2-nitrodiphenyl. Evaporation of the light petroleum extract gave 2.15 g. of almost pure dibromo-compound which after crystallisation from ethanol had m.p. 124°, alone or mixed with pure 4:4'-dibromo-2-nitrodiphenyl.

(b) In glacial acetic acid containing 4:4'-dibromo-2-nitrodiphenyl. The last reaction was repeated but with the initial addition of 3.57 g. (1 mol.) of 4:4'-dibromo-2-nitrodiphenyl. Yield of mixed products 7.42 g. i.e. 3.85+3.57 g..

(c) In glacial acetic acid containing cinnamic acid or acetanilide or p-aceto-toluidide. The bis-diazo-perbromide was added to glacial acetic acid (at 100°) containing one of these substances (1 mol. for each mol. of perbromide). Routine method of working up led in each case to isolation of 4:4'-dibromo-2-nitrodiphenyl. No tribromo-nitrodiphenyl could be isolated.

## Synthesis of 2:3':4:4'-tetrabromodiphenyl.

(a) 2:3':4:4'-Tetrabromodiphenyl was prepared according to Scheme (I) (p.9).

## Preparation of 2-nitro-NN'-dicarbethoxybenzidine.

Lesslie and Turner (J., 1933, 1589).

2-Nitro-NN'-dicarbethoxybenzidine was made according to the method of Lesslie and Turner. 79.8 G. of ethyl chloroformate were gradually added to a boiling solution of 70 g. of 2-nitrobenzidine and 92.5 g. of diethyl-aniline in 700 ml. of alcohol. Boiling was continued for 10 minutes after the vigorous reaction was complete. The solution was then diluted with water. The diurethane, which crystallised in theoretical yield, had m.p. 190-192° after recrystallisation from ethyl alcohol.

## Bromination of 2-nitro-NN'-dicarbethoxybenzidine.

The bromination was carried out exactly as described by Lesslie and Turner (loc.cit.) using bromine in presence of glacial acetic acid.

8.5 Ml. of bromine (1 mol. excess), dissolved in an equal volume of glacial acetic acid, was added to a hot (100°) solution of 32 g. of diurethane and 14.8 g.

of anhydrous sodium acetate in 436 ml. of glacial acetic acid. The mixture was boiled for ten minutes, and poured into a large bulk of water; the precipitated 3'-bromo-2-nitro-NN'-dicarbethoxybenzidine was filtered off and dried (34.5 g.; 90% yield) and crystallised from alcohol, whence it was obtained in 73% yield (25 g.) as yellow needles, m.p. 145-147°.

Hydrolysis of 3'-bromo-2-nitro-NN'-dicarbethoxybenzidine.

The hydrolysis was carried out as described by Lesslie and Turner (loc.cit.).

50 Ml. of water were cautiously added to a solution of 20 g. of 3'-bromo-2-nitro-NN'-dicarbethoxybenzidine in 100 g. of concentrated sulphuric acid. The temperature rose to 140-150°, and was maintained this for 10-15 minutes; hydrolysis was then complete. The solution was then poured into water, and concentrated aqueous ammonia added. A brick-red crystalline solid separated; it was filtered off and dried (10.6 g.; 78% yield). Pure 3'-bromo-2-nitrobenzidine was obtained, after one recrystallisation from alcohol, as needles of m.p. 155-156°.

### Preparation of 3':4:4'-tribromo-2-nitrodiphenyl.

A mixture of 6.2 g. of 3'-bromo-2-nitrobenzidine (2 mols.), 30 ml. of 48% hydrobromic acid and 60 ml. of water was bis-diazotised by the addition of 2.7 g. of sodium nitrite (2.2 mols.) in 8 ml. of water. The temperature was kept between -4° and 0° throughout the operation. Addition of the calculated bromine in 48% hydrobromic acid gave the yellow bis-diazonium perbromide. It was collected by filtration, washed with a little water, alcohol and dry ether, and finally dried in a vacuum over concentrated sulphuric acid. It was gradually added to glacial acetic acid kept at 100° and the solution was boiled until free from bromine. On cooling, the tribromonitro-compound separated. After being crystallised from glacial acetic acid, it formed leaflets, m.p. 141-142° (Found: Br, 55.0; $C_{12}H_6O_2NBr_3$ requires Br, 55.0%).

### Preparation of 2-amino-3':4:4'-tribromodiphenyl.

A solution of 4.4 g. of the preceding nitro-compound (1 mol.) in the least possible amount of hot glacial acetic acid was treated with just over the calculated quantity of 9 g. of stannous chloride (3.3 mols.) dissolved in 12 ml. of concentrated hydrochloric acid

(9 mols.). There was a vigorous reaction after each addition of the acetic acid solution, the contents of the flask boiled briskly. After the reaction was over, the mixture was then cooled, treated with excess of 10% sodium hydroxide solution and extracted with ether. The ether was evaporated off and the solid remaining was crystallised from ethanol. 2-Amino-3':4:4'-tribromodiphenyl (3.5 g.; 87% yield) was obtained as white needles, m.p. 78° (Found: Br, 58.8; $C_{12}H_8NBr_3$ requires Br, 59.0%).

Preparation of 2:3';4:4'-tetrabromodiphenyl.

A solution of 2.2 g. of 2-amino-3':4:4'-tribromodiphenyl in 20 ml. of glacial acetic acid was diazotised by addition of sodium nitrite in 20 ml. of concentrated sulphuric acid with the usual precautions. The mixture was poured on to crushed-ice with constant agitation; and the clear diazo-solution obtained by filtration was treated with the calculated quantity of bromine in 48% hydrobromic acid. The diazoperbromide precipitated was filtered off, washed and dried in vacuum. It was then gradually added to glacial acetic acid at 100° and the solution was boiled until free from bromine. On cooling, the tetrabromodiphenyl which separated was crystallised from glacial acetic acid; needles, m.p. 124-125° (a) (Found: Br, 67.50 $C_{12}H_8Br_4$ requires Br, 68.05%).

(b) 2:3':4:4'-Tetrabromodiphenyl was prepared according to scheme (II) (p.11).

## Nitration of 4:4'-dibromo-2-nitrodiphenyl.

Shaw and Turner (J., 1932, 293).

4:4'-Dibromo-2-nitrodiphenyl (preparation see p. 46) was nitrated according to method of Shaw and Turner. Dibromonitrodiphenyl was dissolved in two parts of warm nitric acid (*d.* 1.5). On cooling, 4:4'-dibromo-2:3'-dinitrodiphenyl separated in pale yellow needles, which, after being crystallised from benzene, melted at 148°.

## Reduction of 4:4'-dibromo-2:3'-dinitrodiphenyl.

Fittig (Annalen, 132, 207)

Schultz (*loc.cit.*, 174, 218).

The reduction was carried out as described by Fittig (*loc.cit.*) using zinc dust in presence of hydrochloric acid.

4:4'-Dibromo-2:3'-dintrodiphenyl (10 g.; 1 mol.) granulated zinc (12.7 g.; 7.4 atoms) were placed in a 250 ml.

flask fitted with an air condenser. Concentrated hydrochloric acid (21 ml.; 8.4 mols.) was then added in small portions. After the addition of the acid, the mixture was heated on a water bath for 1½ hours, then made alkaline with sodium hydroxide solution. A product was obtained which after crystallisation from alcohol melted at 88°.

## Preparation of 2:3':4:4'-tetrabromodiphenyl.

2:3'-Diamino-4:4'-dibromodiphenyl was bis-diazotised in hydrochloric acid and the bis-diazoperbromide precipitated in the usual way. It was decomposed in glacial acetic acid at 100°. The tetrabromodiphenyl obtained had m.p. 124-125° alone or when mixed with 2:3':4:4'-tetrabromodiphenyl.

## Synthesis of 2-nitro-2':4:4'-tribromodiphenyl and 2:2':4:4'-tetrabromodiphenyl.

(a) Both nitro-tribromo- and tetrabromodiphenyl were prepared according to the scheme p. 13.

### Preparation of 4:4'-dibromo-2:2'-dinitrodiphenyl.

Shaw and Turner (J., 1932, 293).

8.8 G. of copper bronze was gradually added with stirring to 20 g. of 2:5-dibromo-nitrobenzene contained in a hard glass tube immersed in a metal bath kept at 190-225°. The temperature of the reaction mixture was not allowed to exceed 225° and when the addition of the copper was complete, the reaction mixture was maintained at this temperature for one hour. The hot mixture was treated with 120 ml. of o-dichlorobenzene, the liquid filtered hot, and most of the solvent distilled off. The cool solution deposited 3.9 g. of crystalline material, which after being washed with light petroleum had m.p. 133°. After being crystallised from glacial acetic acid and then from n-butyl alcohol, it formed pale yellow octahedra, m.p. 152° and was unaffected by further crystallisation from ethyl alcohol.

In the subsequent preparations, 2:5-dibromonitrobenzene was heated with copper bronze at 225° as described above. The temperature was then allowed to drop to about 150° when the paste obtained was thoroughly extracted with boiling *o*-dichlorobenzene. The hot mixture was filtered through a pre-heated Buchner funnel and the precipitate was washed with a little boiling *o*-dichlorobenzene. The extracts were combined and the solid separated on cooling. The crude dibromo-dinitrodiphenyl was dried and crystallised from ethyl alcohol, m.p. 152°. On concentration of the filtrate by distillation of the *o*-dichlorobenzene a brown residue was obtained, which after being crystallised from alcohol had m.p. 138-140°. The combined weight of these two crops was about 5.7 g. (40%Theory).

Several melting points have been recorded for 4:4'-dibromo-2:2'-dinitrodiphenyl, varying from 138° (Ullmann, *Ber.*, 1901, *34*, 2181) to 150° ( Shaw and Turner, *loc.cit.*).

### Preparation of 2-amino-4:4'-dibromo-2'-nitrodiphenyl.

To a hot well-stirred solution, containing 1.6 g. (2 atoms) of sulphur, 9 g. (1.5 mols.) of sodium sulphide ($+9H_2O$) and 12 ml. of water, was added to an ethanolic solution of 10 g. (1 mol.) of 4:4'-dibromo-2:2'-dinitrodiphenyl. The dark reddish brown solution was boiled for an hour, adding boiling water from time to time to maintain the volume. After cooling, the orange-coloured precipitate was obtained, containing mononitro- and unchanged dinitro- compound, was filtered off, washed with water and repeatedly extracted with small quantities of boiling 2N-hydrochloric acid. The extracts were combined, cooled to 0°, and made alkaline with aqueous ammonia (d. 0.880). The re-precipitated base (1.9 g.; 20% yield) was crystallised three times from ethanol; needles; m.p. 103-104°.

Three subsequent preparations were carried out in a similar manner. In the second preparation 15 g. of 4:4'-dibromo-2:2'-dinitrodiphenyl, 2.4 g. of sulphur, 13.5 g. of sodium sulphide (+$9H_2O$), and 20 ml. of water were used and 2.4 g. (18% yield) of 2-amino-4:4'-dibromo-2'-nitrodiphenyl, m.p. 103-104°, was obtained.

In the third and fourth preparations, in which 20 g. of 4:4'-dibromo-2:2'-dinitrodiphenyl, 4.0 g. of sulphur, 22.5 g. of sodium sulphide (+$9H_2O$), and 30 ml. of water were used, 4.8 g. and 4.4 g. (27% and 24% yield) of 2-amino-4:4'-dibromo-2'-nitrodiphenyl, m.p. 103-104° were obtained.

Attempts were also made by partially reducing 4:4'-dibromo2:2'-dinitrodiphenyl with ammonium sulphide and about 10-15% yields of the amino-dibromo-nitro-compound were obtained. The idea of using ammonium sulphide was therefore discarded.
(Found: C, 39.8; H, 2.5; N, 7.7; Br, 42.7; $C_{12}H_8O_2N_2Br_2$ requires C, 40.0; H, 2.2; N, 7.6; Br, 43.0%).

### Preparation of 2':4:4'-tribromo-2-nitrodiphenyl.-

3.7 G. of 2'-amino-4:4'-dibromo-2-nitrodiphenyl was dissolved in 40 ml. of glacial acetic acid and the solution was cautiously added to a solution of 0.7 g. of sodium nitrite in 20 ml. of conc. sulphuric acid at 10-15°. The mixture was moderately stirred for 10 minutes and slowly poured onto ice. On addition of the calculated bromine in 48% hydrobromic acid, the orange-coloured diazonium perbromide separated as a paste. It was filtered, washed and dried. The perbromide was decomposed in 20 ml. of hot (100°) glacial acetic acid and the solution boiled till free from bromine. On cooling, crystals separated which were recrystallised from glacial acetic acid. 2':4:4'-Tribromo-2-nitrodiphenyl was obtained in yellow needles, m.p. 195-196°, undepressed by admixture with the tribromonitro-compound obtained from the perbromide displacement on 2-nitrobenzidine.

An attempte was also made by bromination of 2-nitro-4:4'-dibromodiphenyl in order to obtain the tribromonitro-compound. Either a solution of 3.57 g. of 2-nitro-4:4'-dibromodiphenyl (1 mol.) in a mixture of approximately 0.8 ml. of bromine (1.5 mols.) and 10 ml. of glacial acetic acid alone or with ferric chloride, was boiled under reflux for two hours. The resulting solution, on cooling, crystallised. The product was found to be unchanged starting material.

Preparation of 2-amino-2':4:4'-tribromodiphenyl.

Reduction of 10.9 g. (1 mol.) of the corresponding 2-nitro-compound with 18.7 g. (3.3 mols) of stannous chloride in 23 ml. (9 mols.) of concentrated hydrochloric acid - glacial acetic acid, followed by the normal procedure, gave a base, which after being crystallised twice from aqueous alcohol with charcoal, melted at 150-152° (Found: Br, 56.7; $C_{12}H_8N_2Br_3$ requires

Br, 59.1%). A third crystallisation either from alcohol or from glacial acetic acid had no affect on the melting point. However, boiling under reflux with 30 ml. of benzene, containing a little charcoal, for ten minutes, gave the pure 2-amino-2':4:4'-tribromodiphenyl as silvery rods, m.p. 154°. This, on heating, with one mol. of redistilled benzaldehyde at 100°, gave a benzal derivative, which, after being once crystallised from alcohol, had m.p. 229-230° (Found: Br, 48.3; $C_{19}H_{12}NBr_3$ requires Br, 48.5%).

A second preparation, in which 16.5 g. of nitro-compound was used, gave 5.8 g. (38% yield) of the <u>base</u> m.p. 150-152° and this, after being recrystallised from benzene with charcoal , gave 3.1 g. of pure 2-amino-2':4:4'-tribromodiphenyl, m.p. 154° (Found: Br, 58.8; $C_{12}H_8NBr_3$ requires Br, 59.1%).

An attempt was also made to reduce the 2-nitro-2':4:4'-tribromodiphenyl by means of iron filings (previously boiled with dilute hydrochloric acid), 30 ml. of water, and 11 g. of the nitro-compound was heated at 100° for two hours and frequently stirred. The iron residue was separated from the dilute mixture and extracted with alcohol. By distilling off the alcohol, a residue was obtained which could not be crystallised from common organic solvents. It did not melt below 300°.

Preparation of 2:2':4:4'-tetrabromodiphenyl.

The foregoing base was diazotised by the acetic - sulphuric acid method (cf.p.72) and the diazo-perbromide formed decomposed in hot glacial acetic acid in the usual way. The tetrabromo-compound crystallised from glacial acetic acid in white needles, m.p. 273° (Found: Br, 68.2, $C_{12}H_8Br_4$ requires Br, 68.05%).

(b) Synthesis of 2:2':4:4'-tetrabromodiphenyl.

Preparation of 3:3'-dibromohydroazobenzene.

This was carried out according to Gabriel (Ber., 1896, 29, 1407) by reduction of m-bromonitrobenzene with zinc dust.

40 G. of m-bromonitrobenzene was dissolved in 100 ml. of methyl alcohol in a 3-necked flask fitted with reflux condenser and a mechanical stirrer. 42 G. of sodium hydroxide dissolved in 100 ml. of water were then added and the mixture heated to boiling on a water bath. A total of 55-60 g. of zinc dust was added in small portions during half an hour. As the reaction proceeded the mixture became red in colour and the heating under reflux was continued for another 2-2½ hours until the red colour was discharged.

500 Ml. of hot industrial spirit was added and the whole contents of the flask were filtered while boiling hot through a pre-heated Buchner funnel; the flask was at once washed out with 25 ml. of hot spirit, and this was used to wash the excess of zinc dust on the funnel.

The filtrate was allowed to cool in the closed filter flask, which was placed in a freezing mixture in order to accelerate crystallisation. After an hour the almost colourless reaction product was thoroughly separated by filtration at the pump, and washed with 50% alcohol, to which a small quantity of aqueous sulphurous acid had been added, until the filtrate was no longer alkaline. By rapid recrystalline from a small volume of hot alcohol the dibromohydrazobenzene was obtained quite pure. Melting point 107-109°.

Benzidine rearrangement on 3:3'-dibromohydrazobenzene.

3:3'-Dibromohydrazobenzene (11.0 g.) dissolved in the minimum quantity of ether was added with shaking to 100 ml. of ice-cold, approximately 7N-hydrochloric acid. Crystals separated, after 50 ml. of concentrated hydrochloric acid had been added and the mixture had stood for half an hour. The hydrochloride was filtered at the pump, and washed, first with 7N-hydrochloric acid then with a little ether. Yield 7-8 g..

The dibromobenzidine hydrochloride was dissolved in hot water, cooled and a slight excess of 10% sodium hydroxide solution was added. The free base which separated in crystals was filtered off and washed with water till the filtrate was no longer alkaline. 2:2'-

Dibromobenzidine after being once recrystallised from alcohol, had m.p. 152°.

Preparation of 2:2':4:4'-tetrabromodiphenyl.

2:2'-Dibromobenzidine was bis-diazotised in hydrobromic acid and the bis-diazoperbromide prepared decomposed in hot glacial acetic acid in the usual manner. The tetrabromodiphenyl crystallised from the latter solvent in needles, m.p. 273° (Found: Br, 68.5%).

## Synthesis of 2:4:4'-tribromodiphenyl and its dinitro-cpd.

### Preparation of 2-nitro-4:4'-dibromodiphenyl.

The methods of (i) Shaw and Turner (J., 1932, 293), (ii) *idem.*, *ibid.*, (iii) Dennett and Turner (*loc.cit.*, 1926, 477) and (iv) Le Fevre and Turner (*loc.cit.*, 2044) were used.

(i) 20 G. of 4:4'-dibromodiphenyl was dissolved in 300 ml. of glacial acetic acid at 100° and 200 ml. of nitric acid (*d*.1.46) were added. The precipitate first formed redissolved, and after half an hour at 100° the solution was cooled; a stiff paste was then obtained, which was submitted to filtration. The yield of crude mononitro-compound was almost theoretical, and after three crystallisations from ethanol, 2-nitro-4:4'-dibromodiphenyl, m.p. 124° was obtained.

(ii) 2-Nitrobenzidine was bis-diazotised in hydrobromic acid, and the bis-diazonium perbromide precipitated in the usual manner. It was decomposed in hot absolute ethyl alcohol and gave 2-nitro-4:4'-dibromodiphenyl, m.p. 124°.

(iii) 2-Nitrobenzidine hydrobromide was ground into a fine paste with a little water and diazotised at -5°.

The solution was poured with vigorous shaking into a cold suspension of cuprous bromide in hydrobromic acid. After the vigorous reaction was over, the whole was heated at 100° for a short time and the gummy solid collected warmed with sodium hydroxide to remove phenolic substances. The yellow residue, after several crystallisations from alcohol and benzene, melted at 124°.

(iv) Restricted nitration of 4:4'-dibromodiphenyl. To a solution of 20 g. of the dibromo-compound in a mixture of 200 ml. of glacial acetic acid and 200 ml. of acetic anhydride at 85-90°, 10 g. of potassium nitrate in 30 ml. of concentrated sulphuric acid were added slowly. After being heated for a further 20 minutes, the solution was cooled; 3.2 g. of the dibromodiphenyl that separated was removed, and the residue ditlted with water. The resulting precipitate, 2-nitro-4:4'-dibromodiphenyl, melted at 110-115° after drying, and at 124° after several crystallisations from alcohol.

Preparation of 2-amino-4:4'-dibromodiphenyl.

17.8 G. of 2-nitro-4:4'-dibromodiphenyl was dissolved in the least possible amount of hot glacial acetic acid. The solution was added gradually to a hot clear solution of 37.3 g. of stannous chloride in 45 ml. of concentrated hydrochloric acid. There was a vigorous reaction after each addition of the acetic acid solution and the contents of the flask were boiled under reflux for a further 20 minutes. After the reaction was over, the mixture was poured into a beaker and allowed to cool, and a excess of 10% sodium hydroxide solution was added. The solid which separated was filtered off, washed with water and crystallised from either light petroleum (b.p. 60-80°) or from ethanol. 2-Amino-4:4'-dibromodiphenyl was obtained as white needles (9.0 g.; 55% yield), m.p. 130° (Found: Br, 48.7; $C_{12}H_9NBr_2$ requires Br, 48.9%).

Preparation of 2:4:4'-tribromodiphenyl.

1.7 G. of the foregoing base dissolved in 20 ml. of glacial acetic acid was diazotised by adding 0.5 g. of sodium nitrite in 20 ml. of conc. sulphuric acid at 15-20°. The mixture was then poured onto ice with constant agitation and filtered. The yellow diazonium perbromide was prepared and decomposed in hot glacial acetic acid in the usual way. The tribromodiphenyl obtained crystallised from ethanol in needles, m.p. 81°

(Found: Br, 61.5 $C_{12}H_7Br_3$ requires Br, 61.4%).

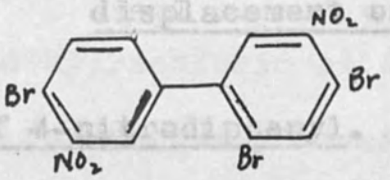
An attempt was also made to effect deamination of 2'-amino-2:4:4'-tribromodiphenyl by means of ethanol.

The base (7.1 g.) was heated with a mixture of concentrated sulphuric acid (20 g.) and water (40 ml.). The cool paste obtained was treated with ice and solid sodium nitrite (2.5 g.) at -5°; 20% oleum (9.4 ml.) was added, the temperature kept below 30°. The product was gradually added to boiling absolute ethyl alcohol (150 ml.), and the solution boiled under reflux for 2 hours. The solution was then diluted with a large excess of water, and extracted with ether. The extract was washed with alkali and then with water and dried over calcium chloride, and the solvent removed. The residue thus obtained could not be purified.

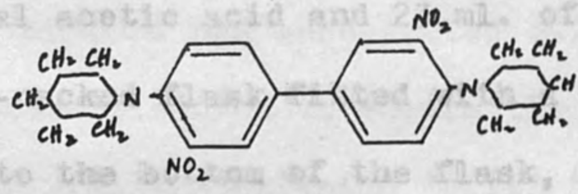
Nitration of 2:4:4'-tribromodiphenyl.

2:4:4'-Tribromodiphenyl was dissolved in 10 parts by weight of warm nitric acid (d. 1.5). On cooling, a solid separated which crystallised from ethanol in needles, m.p. 164-165° (Found: Br, 49.8 $C_{12}H_5N_2O_4Br_3$ requires Br, 49.9%). This is regarded as 2:4:4'-tribromo-

3':5-dinitrodiphenyl.



When heated with excess of piperidine for a few minutes it gave 2-bromo-3':5-dinitro-4:4'-dipiperidinodiphenyl,



orange red needles m.p. 145-146° from ethanol (Found: Br, 16.5 $C_{22}H_{25}N_4O_4Br$ requires Br, 16.4).

## Synthesis of 4-amino-4'-bromodiphenyl and perbromide displacement on it.

### Bromination of 4-nitrodiphenyl.

The method of Le Fevre and Turner (J., 1926, 2045) was used.

A mixture of 45 g. of 4-nitrodiphenyl, 85 ml. of glacial acetic acid and 23 ml. of bromine was placed in a two-necked flask fitted with a thermometer which reached to the bottom of the flask, and a reflux condenser. The flask was heated to a temperature of $100^{\circ}$ and was maintained at that temperature for 3½ hours (longer heating diminished the yield). The reaction mixture was then cooled and the solid separated. The crude 4-nitro-4'-bromodiphenyl which was collected by filtration then crystallised from about 300 ml. of glacial acetic acid as light brown needles, m.p. $170-172^{\circ}$ (78% yield). The product was sufficiently pure for use in the next stage.

### Preparation of 4-amino-4'-bromodiphenyl.

This was prepared by the "West" method (Hartly and Jones, loc.cit., 1952, 1959).

A mixture of 41.5 g. of 4-nitro-4'-bromodiphenyl, 29 g. of iron pin-dust, 250 ml. of ethyl alcohol and 15 ml. of concentrated hydrochloric acid was stirred under reflux on a boiling water bath for about 12 hours. The theoretical amount of 11 g. of sodium carbonate was added and stirring was continued for 30 minutes, whereafter a slight excess of dilute aqueous ammonia (*d*.0.880) was added. After the resulting mixture had been cooled quickly, ether was added and the whole filtered to ensure the complete removal of the amine. The precipitated ferric oxide was washed with more ether from the filtrate, and the warm alcoholic solution was poured into an equal volume of cold water to precipitate the amine. This was obtained as a grey powder, m.p. 143-144° (26.5 g.; 68.5% yield).

Several melting-points have been recorded for 4-amino-4'-bromodiphenyl, varying from 142-143° (Le Fevre and Turner, J., 1926, 2045), 145° corr. (Gelmo, *Ber.*, 1906, *39*, 4175) and 145-146° (Jones etc., *loc.cit.*).

### Perbromide displacement on 4-amino-4'-bromodiphenyl.

3.0 G. of the preceding base dissolved in 50 ml. of hot glacial acetic acid was diazotised by adding a solution of 1 g. of sodium nitrite in 40 ml. of conc. sulphuric acid at 15-20°. The diazoperbromide was prepared and decomposed in hot glacial acetic acid in the usual way. A product was obtained which could be crystallised from either alcohol or benzene or glacial acetic acid in needles, m.p. 136-142° (Found: Br, 58.8 Cal. for tribromo- 61.4. Cal. for dibromo- 51.3%). This was therefore assumed to be a mixture of dibromo- and tribromo- compound.

This experiment was repeated and 5 g. of the base was used. The perbromide thus obtained was decomposed as follows:-

(a) In boiling ethanol. The crude product after two crystallisations was obtained in shiny plates, m.p. 135-136° (A). This was regarded as 4-bromodiphenyl ethyl ether (Found: Br, 29.0 $C_{14}H_{13}OBr$ requires Br, 28.8%).

(b) In glacial acetic acid at 100°. Water was added to complete the separation of solid. The paste was filtered, washed with water, alcohol, dry ether, and dried over concentrated sulphuric acid and solid potassium hydroxide. By extracting thrice with boiling light petroleum (b.p. 60-80°) this was freed from 4:4'-dibromodiphenyl and gave a solid which after crystallisation from glacial acetic acid had m.p. 132-136$^{\circ}$. This was recrystallised from alcohol, m.p. 134-136$^{\circ}$ (C) and further recrystallisation had no change in melting point. The mixed melting point of (C) and (A) was 111-118$^{\circ}$ (Found: Br, 53.2; Cal. for bromo-hydroxy- Br, 32.1; Cal. for tribromo- Br, 61.4; Calc. for tetrabromo- Br, 68.0%). However, the mixture (C) was warmed with 10% sodium hydroxide solution and the liquid was filtered hot. The filtrate was cooled and regenerated by dilute sulphuric acid; on cooling, a solid obtained, after crystallisation from alcohol, melted at 157-158$^{\circ}$ (4-hydroxy-4'-bromodiphenyl) (compare Bell and Robinson, J., 1927, 1131). The residue was crystallised from glacial acetic acid, m.p. 169-170$^{\circ}$ (3:3';4:4'-tetrabromodiphenyl) (compare Roosmalen, Rec. trav. chim., 1934, 53, 359).

Evaporation of the light petroleum extract gave almost pure dibromo-compound which after crystallisation from alcohol or glacial acetic acid had m.p. 164$^{\circ}$, alone or mixed with pure 4:4'-dibromodiphenyl.

## Attempted perbromide displacement on 4-nitro-4'-amino- and 2-nitro-4'-amino-diphenyl respectively.

### Nitration of 4-nitrodiphenyl.

4-Nitrodiphenyl was nitrated according to Bell and Kenyon (J., 1926, 2707).

A mixture of 4-nitrodiphenyl (20 g.), fuming nitric acid (14 ml.; d. 1.5), and water (2 ml.), having been gently warmed for half an hour, was poured into water. The precipitate was collected by filtration and the crude mixture of dinitrodiphenyl (22.5 g.) was extracted thrice with boiling industrial spirit (100 ml.). 9 G. of undissolved residue was practically pure 4:4'-dinitrodiphenyl, and from the extract a mixture of about 10 g. of this substance and 2':4-dinitrodiphenyl was obtained. Separation of the latter was not attempted, the mixture being employed in the next stage of partial reduction.

### Partial reduction of 2':4-dinitrodiphenyl.

Walls (J., 1947, 72).

2':4-Dinitrodiphenyl (10 g.) was dissolved in boiling alcohol (150 ml.), and the solution was treated with sodium polysulphide prepared from flower of sulphur

(3 g.), sodium sulphide (11.7 g.) and water (40 ml.). After three hours' boiling under reflux the solution was left overnight and then poured into water. The rather sticky red precipitate was dissolved in hot N-hydrochloric acid (180 ml.) with a small amount of charcoal; on being cooled the solution was filled with white felted needles of the hydrochloride of 2-nitro-4'-aminodiphenyl, by-products remaining in solution. The salt was washed with cold dilute hydrochloric acid, dissolved in hot water, and the solution basified. The amine separated as a red oil which soon crystallised (4.2 g.). This product was pure enough for the purpose, but could be recrystallised from industrial spirit in red prisms, m.p. 98-99°.

<u>Attempted perbromide displacement on 2-nitro-4'-aminodiphenyl.</u>

The base was diazotised by the acetic - sulphuric acid method (cf. p.72), treated with the calc. amount of bromine in hydrobromic acid. The perbromide separated as a yellowish orange-coloured solid which was decomposed as follows:-

(a) <u>In boiling ethanol</u>. It gave 2-nitro-4'-bromodiphenyl, m.p. 65° undepressed with an authentic specimen.

(b) In glacial acetic acid at 100°. The product melted at 162-163°, after crystallisation from alcohol (Found: Br, 37.0. Calc. for monobromo- Br, 28.8. Calc. for dibromo- Br, 44.8%). This substance was therefore regarded as a mixture of mono- and di-bromo-compound.

Partial reduction of 4:4'-dinitrodiphenyl.

4:4'-Dinitrodiphenyl was partially reduced with sodium polysulfide solution by the method of Sherwood and Calvin (J.Amer.Chem.Soc., 1942, 64, 1350).

4:4'-Dinitrodiphenyl (12.2 g.) was dissolved in boiling ethyl alcohol. About 4 g. of sulphur was dissolved in a solution of sodium sulphide (12.5 g.) in water (100 ml.) while warm, and this polysulphide was added dropwise to the alcoholic solution. After boiling for a few minutes, the mixture was evaporated to dryness on the water bath. The residue was boiled with water (100 ml.). After cooling this was filtered and the filtrate containing the inorganic salts was discarded. The residue was extracted with hot 20% aqueous hydrochloric acid. On cooling light yellow crystals deposited. These were shaken with an excess of aqueous ammonia in the presence of a 1:1 mixture of toluene and benzene. The organic solvent layer, containing 4-nitro-4'-aminodiphenyl, was then separated and filtered. When concentrated, it yielded orange crystals, m.p. 200-202°.

### Attempted perbromide displacement on 4-nitro-4'-aminodiphenyl.

The procedure of obtaining a diazonium perbromide was as usual (cf. p. 72). When it was decomposed in hot glacial acetic acid in the usual way, it gave a product which after crystallisation from alcohol gave yellow needles, m.p. 210-211° (Found: Br, 39.9. Calc. for monobromo- 28.8; Calc. for dibromo- 44.8%). This substance was therefore regarded as a mixture of mono- and di-bromo-compound.

### Preparation of 4-bromo-4'-phthalimidodiphenyl.

Le Fevre and Turner (J., 1926, 254).

24.8 G. of 4-bromo-4'-aminodiphenyl was added in a small portions to boiling solution of 7.4 g. of phthalic anhydride in 12.5 ml. of tetrahydronaphthalene, the water formed being allowed to distil away, and boiled under reflux for a period of two hours; the 4-bromo-4'-

phthalimidodiphenyl which separated was collected, washed with cold benzene and crystallised from glacial acetic acid in pale yellow needles, m.p. 262°.

<u>Attempted nitration of 4-bromo-4'-phthalimidodiphenyl</u>.

4-Bromo-4'-phthalimidodiphenyl was nitrated in excess of concentrated sulphuric acid; a product was obtained which could not be purified further, m.p. about 180° undepressed with 4-bromo-4'-amino-2-nitrodiphenyl which was prepared according to the method of Le Fevre and Turner (loc.cit., 1926, 2044), by direct nitration of 4-bromo-4'-aminodiphenyl in the presence of excess of sulphuric acid. It was therefore assumed that both an attempted nitration and hydrolysis took place simultaneously. The perbromide displacement gave a gummy product from which no chemical individual could be isolated.

## Perbromide displacement on 2-nitro-4-aminodiphenyl.

### Preparation of 2:4-dinitrodiphenyl.

Gull and Turner (J., 1929, 496).

A mixture (equimolecular) of 21 g. of iodobenzene and 20 g. of 1-chloro-2:4-dinitrobenzene was heated in a wide-mouthed conical flask in a metal-bath, initially at 210°. 40 G. of copper bronze was added gradually, the mixture being well stirred with thermometer. The temperature of the mixture rose slowly to 225°, and reaction proceeded rapidly. After all the copper bronze had been added, heating was continued at 230° for 10 mins.. The cooled product was extracted with hot benzene, and the extracts were combined and distilled in steam. No diphenyl was detected. The non-volatile oil was crystallised from 200 ml. of hot industrial spirit. 2:4-Dinitrodiphenyl was then obtained (3-5 g.) in golden-yellow plates, m.p. 110°. A further quantity remained in the mother-liquor.

### Partial reduction of 2:4-dinitrodiphenyl.

Sodium sulphide (9.6 g.; 1 mol.), sulphur (2.5 g.; 2 mols.) and water (30 ml.) were boiled gently to obtain a clear solution. This was transferred to a

3-necked flask, fitted with a mechanical stirrer and reflux condenser on a boiling water bath. 2:4-Dinitrodiphenyl (10 g.; 1 mol.) dissolved in hot industrial spirit (200 ml.) was added during fifteen minutes, and after 1½ hours' refluxing, the mixture was cooled in an ice-salt bath and filtered. The solid obtained was extracted thrice with hot dilute sulphuric acid and white crystals of a sulphate separated, from which 2-nitro-4-aminodiphenyl was liberated by alkali; it crystallised from aqueous alcohol in gold yellow plates, m.p. 108-109°.

Caldwell and Walls (J., 1948, 192) gave 109.5°.

Diazoperbromide from 2-nitro-4-aminodiphenyl.

The foregoing base was diazotised in acetic - sulphuric acid (cf. p. 72), treated with the calculated bromine in hydrobromic acid and the perbromide separated as a yellow precipitate. This was washed, pressed and boiled with glacial acetic acid until bromine evolution ceased. On cooling, a semi-solid was obtained and water was added to complete the separation. The resulting thick brown oil was decanted, washed with water and dried in vacuum over sulphuric acid and solid KOH. The mixture was extracted thrice with boiling light petroleum (b.p. 60-80°); the undissolved residue could not be purified, and had m.p. 76-91°. From the extracts, solid was obtained which after being crystallised from industrial spirit had m.p. 63-64° (Found: Br, 27.9. Cal. for $C_{12}H_8NO_2Br$ Br, 28.7%). This substance was assumed to 2-amino-4-bromodiphenyl although the analysis result was slightly low.

Perbromide displacement on 4-aminodiphenyl.

Preparation of 4-aminodiphenyl.

4-Nitrodiphenyl (9.5 g.), dissolved in alcohol (100 ml.) were added slowly to a solution of stannous chloride (60 g.) in concentrated hydrochloric acid. The alcohol was removed after refluxing for one hour, and the base liberated with dilute sodium hydroxide. It crystallised from aqueous alcohol in leaflets, m.p. 50-52°.

Diazoperbromide from 4-aminodiphenyl.

The diazoperbromide, obtained in the usual way, was decomposed as follows:-

(a) In boiling ethanol. The product, after crystallisation from benzene, had m.p. 89° and was identical with 4-bromodiphenyl.

(b) In glacial acetic acid at 100°. The product melted at 164°, after crystallisation from methanol, and was identical with 4:4'-dibromodiphenyl.

Diazoperbromide from 4-aminodiphenyl ether.

The diazoperbromide was prepared in the normal manner. When it was decomposed in hot glacial acetic acid it gave 4:4'-dibromodiphenyl ether, which after being crystallised from ethanol had m.p. 60°.

Bis-diazoperbromide from benzidine.

Benzidine was bis-diazotised in aqueous hydrochloric acid and the bis-diazonium perbromide precipitated in the usual manner. This was decomposed as follows:-

(a) In boiling ethanol. The crude product after crystallisation from methanol had m.p. 164°, and was identical with 4:4'-dibromodiphenyl.

(b) In glacial acetic acid at 100°. The product, after crystallisation from glacial acetic acid, had m.p. 273° and was identical with 2:2':4:4'-tetrabromodiphenyl.

## Perbromide displacement on 2-nitro-o-tolidine.

### Preparation of 2-nitro-o-tolidine.

Lowenherz (Ber., 1892, 25, 1032).

A solution of o-tolidine (21.2 g.) in 100% sulphuric acid (172 ml.) was cooled in a freezing mixture till the temperature was below 0°. Finely ground potassium nitrate (10.3 g.) was added with careful stirring within half an hour, the temperature of the reaction mixture being kept between 2° to -5° until the whole of potassium nitrate had been added. After keeping for a further hour the mixture was poured into ice water. The sulphate was filtered off, ground to a stiff paste with water and excess of conc. aqueous ammonia added, with griding. Yield of base (22.2 g.) crystallised from toluene in red needles, m.p. 156°.

### Bis-diazoperbromide from 2-nitro-o-tolidine.

2-Nitro-o-tolidine was bis-diazotised in hydrochloric acid and the bis-diazoperbromide prepared in the usual manner. When it was decomposed in hot glacial acetic acid, it gave 4:4'-dibromo-2-nitro-3:3'-ditolyl which, after being crystallised from glacial acetic acid formed needles, m.p. 240-241° (Found: Br, 42.2 $C_{14}H_{11}O_2NBr_2$ requires Br, 41.6%).

## Attempted perbromide displacement on 4-amino-veratrole.

### Preparation of Veratrole.

Veratrole was prepared according to the method of Perkin and Weizmann (J., 1906, 89, 1649).

100 G. of catechol was dissolved in 200 ml. of methyl alcohol mixed with 175 g. of dimethyl sulphate and after cooling to -5°, a solution of 150 g. of caustic potash in 350 ml. of water was added all at once with caution. A vigorous action took place and the methylation was complete in about three minutes.

After diluting with water, the oil was extracted with ether, the ethereal solution well washed with water and dried over calcium chloride. Ether was first removed and the remainder was distilled off at 207-209°. The yield was 69% of the theoretical.

The previous suthors gave b.p. 205°.

### Nitration of veratrole.

Cardwell and Robinson (loc.cit., 1915, 107, 257).

A 95% yield of 4-nitro-veratrole was obtained when 25 g. of veratrole was gradually added with careful cooling to a mixture of 200 ml. of nitric acid (d.1.42) and

20 ml. of water. This product was fractionally crystallised, and found to be free from any isomeric nitro-compounds, m.p. 95-96°.

### Preparation of 4-amino-veratrole.

The method of Senier and Gallagher (loc.cit., 1918, 113, 28) was used.

10 G. of 4-nitro-veratrole was mixed with 16 g. of tin and, after the addition of a trace of graphite, 50 ml. of concentrated hydrochloric acid was added, and the mixture heated on a boiling water bath for about 2-4 hours. The yield of 4-amino-veratrole, isolated in the usual manner, was about 40% of the theoretical, m.p. 172-174°.

### Attempted perbromide displacement on 4-amino-veratrole.

4-Amino-veratrole was diazotised in dilute sulphuric acid and the diazoperbromide precipitated as an orange-yellow solid in the usual manner. On decomposition of the perbromide in glacial acetic acid, it was converted into an intractable, tar.

Attempted perbromide displacement on 3-amino-2-naphthoic acid.

The crude 3-amino-2-naphthoic acid which, after being once crystallised from aqueous alcohol formed pale yellow crystals, m.p. 215-217°, was diazotised by the acetic - sulphuric acid method (cf. p. 72) and the diazonium perbromide was obtained as yellow precipitate in the usual way.

Decomposition of diazoperbromide.

(a) In boiling ethanol. The product, after being twice crystallised from aqueous alcohol (charcoal) and then once from glacial acetic acid, had an indefinite m.p. 162-169°. This substance was soluble in warm 10% sodium hydroxide and sodium carbonate solution.

(b) In glacial acetic acid at 100°. Water was added to complete the separation of the solid. By extraction thrice with light petroleum (b.p. 60-80°), this gave a bromo-compound, which after being once crystallised from glacial acetic acid formed fine yellow needles, m.p. 218-220°, depressed by admixture with 3-bromo-2-naphthoic acid, m.p. 220°. It was recrystallised again from glacial acetic acid and the melting point rose to 236-237°; further recrystallisation had no affect on melting point (Found:

Br, 37.4. Calc. for dibromo- Br, 48.1; Calc. for monobromo- 31.6%). Evaporation of the light petroleum extract gave a product, which after being purified twice from aqueous alcohol and once from acetic acid, melted at 165-171° but the quantity was too small to be investigated further.

## Attempted perbromide displacement on 4-amino-antipyrine.

4-Amino-antipyrine was diazotised by the acetic - sulphuric acid method (cf. p. 72); the diazoperbromide was decomposed in boiling ethyl alcohol but nothing separated even on diluting with water. On decomposition in glacial acetic acid at 100° as usual, a sticky semi-solid slowly separated and water was added to complete the separation. The semi-solid was collected, washed with water and dried in a vacuum. By extraction with light petroleum or benzene or chloroform, it showed no improvement whatsoever and was therefore subjected to fractional crystallisation but only a trace of 4-bromo-antipyrine, m.p. 115-117° was obtained.

### Attempted perbromide displacement on 8-nitro-1-naphthylamine.

The commercial 8-nitro-1-naphthylamine, which, after being once recrystallised from light petroleum formed red crystals, m.p. 96-97° was diazotised in acetic - sulphuric acid (cf. p. 72). and the diazoperbromide precipitated in the usual manner as an orange yellow paste. Water was added to complete the separation. The precipitate was filtered off, washed with water and dried in a vacuum. By extraction twice with boiling light petroleum (b.p. 60-80°) the undissolved residue which had m.p. about 114°, could not be purified further by the common organic solvents. On concentration of the extract, only a trace of 8-nitro-1bromo-naphthalene was obtained, m.p. 97-99°.

General method of Diazotisation (Acetic - Sulphuric acid).

A solution of nitro-amine in hot glacial acetic acid (1 g. per 12 ml.) was rapidly cooled to room temperature and gradually stirred into a solution of sodium nitrite in concentrated sulphuric acid (1 g.per 7 ml.). The latter solution was prepared as follows; the finely powdered nitrite was added to the cooled acid with vigorous stirring, the temperature was raised to 70° until the nitrite had dissolved, and the solution was then cooled to room temperature and, if desired, filtered from sodium bisulphate. The diazotisation was conducted below 20°, and a 10% excess of sodium nitrite was used (compare the usual descriptions of diazotisation in concentrated sulphuric acid, in which 500% excess was often recommended). This diazo-solution was then poured into ice with constant agitation.

## INTRODUCTION - SECTION II.

Most of the work on phenanthridine was done between 1889 and 1905 by Pictet and his co-works, who developed a method of preparation (Pictet and Hubert, Ber., 1896, 26, 1182) in which acyl-o-xenylamines were dehydrated by fusion with zinc chloride.

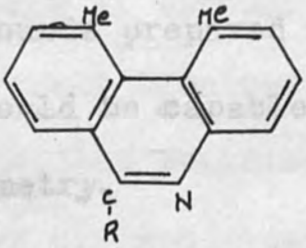
Over the next forty years several new syntheses of phenanthridine were described, but the number of substituted derivatives remained suprisingly small. It was not until the potential therapeutic interapeutic interest of this series was recognised in 1931 by Morgan and Walls (J., 1931, 2447) that systematic study resulted. The improved method of preparation of phenanthridines used by these workers proved to be of wide application, but a further seven years elapsed before the outstanding tryamocidal acivity of some phenanthridinium compounds became apparent (Browning, Mogan, Robb and Walls, J., Path. Bact., 1938, 46, 203).

The chemistry of phenanthridine has probably been studied less than that of any of the simple ring systems. The lack of interest in the past was no doubt due to the comparative inaccessibility of phenanthridine derivatives and to the fact that no natural products derived from phenanthridine were known. In recent years, however, interest in this series has been stimulated by the discovery that the lycorine and the chelidonine-sanguinarine alkaloids are derivatives of phenanthridine and by possibility of obtaining therapeutic agents.

The most generally applicable method for synthesizing substituted phenanthridines involves the cyclodehydration of acyl-*o*-xenylamines, and was due originally to Pictet and Hubert (*loc.cit.*), who heated a mixture of the anilide with zinc chloride at 250-300° C. until evolution of hydrogen chloride ceased.

Morgan and Walls (*loc.cit.*) avoided the disadvantages attending the use of zinc chloride; such as long heating, wasteful purification, and inapplicability to reactive substituents, by employing phosphor~~o~~us oxy-chlorides as the dehydrating agent. Where ring closure with phosphorus oxychloride alone proceeds with difficulty, the inclusion of a high-boiling solvent has often marked beneficial effects (Morgan and Walls, British patent, 1940, 273, 520; Walls, J., 1945, 294). The special suitability of nitrobenzene in this connection is probably associated also with its known ionizing properties.

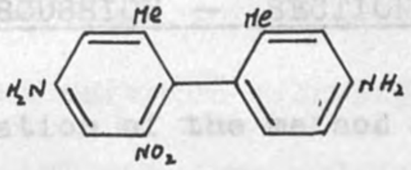
In view of the resistance to the formation of hydrocarbons of 4:5-dimethyl-phenanthrene type, as evidenced by the low yields obtained in their preparation, it was suprising to find in the literature that 4:5-dimethyl-



(I)

9-(*p*-nitro-phenyl-) phenanthridine (I, R=*p*-$C_6H_4NO_2$) was obtained in 80% yield (Ritchie, *J.Proc.Roy. Soc.N.S.W.*, 1945, *78*, 159), whereas 4:5-dimethyl-9-phenyl-phenanthridine (I, R=$C_6H_5$) was obtained as a gum (*ibid.*, *loc. cit.*). However, repetition of the preparations of Ritchie's substituted phenanthridines and also both 4:5:9-trimethyl- (I, R=$CH_3$) and 4:5-dimethyl-phenanthridine (I, R=H) were attempted.

An intermediate in the attempted synthesis of substituted phenanthridine (I) was 2-nitro-*m*-tolidine (II).

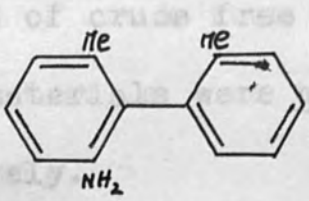


(II)

Because of the extensive study of the thermal decompositon of diazoperbromides carried out in the previous section, the diazonium perbromide of the compound (II) was also investigated.

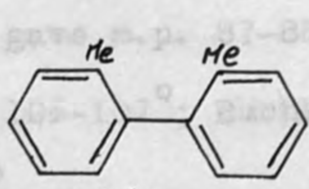
All the compounds prepared in the stages following 2-nitro-m-tolidine should be capable of optical activity due to molecular asymmetry.

2-Amino-6:6'-ditolyl (III) was not expected to be



(III)

very stable, optically, and the stability of its active salts was investigated. The 6-methylphenyl-6'-methyl-2-



(IV)

trimethyl-ammonium iodide (IV) was expected to be more stable than the amine (III) and its resolution was also studied.

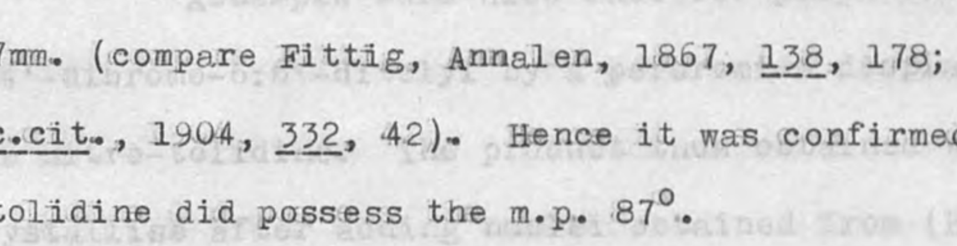
## DISCUSSION - SECTION II.

A modification of the method of Schultz and Rohde (C., 1902, II, 1447) was found for the preparation of m-tolidine, which, after crystallisation from water aqueous alcohol or benzene, melted at 87°. m-Nitrotoluene or m-azotoluene was reduced by means of zinc dust and aqueous caustic soda in presence of alcohol to 3:3'-dimethylhydrazobenzene. By direct treatment of the hydrazotoluene with hydrochloric acid, the tolidine hydrochloride that separated was filtered off and excess of ammonium hydroxide added. The yield of crude free base was about 50% and 75%; if the starting materials were m-nitrotoluene and m-azotoluene respectively.

The values given in the literature for the melting point of m-tolidine varied considerably. Schultz and Rohde (loc.cit.) gave m.p. 87-88°; Jacobson and Fabian (Ber., 28, 2553) 106-107°; Buchka and Schachebeck (Ber., 22, 838) 108-109°.

However, in view of the marked discrepancey in the m.p.'s, a portion of the prepared tolidine was heated with salicylaldehyde: this gave a disalicylidene derivative, m.p. 197-199°; another portion was deaminated by reducing its bis-diazonium chloride with 50% aqueous hypophosphorous acid. 2:2'-Ditolyl was thus obtained in 52% yield, m.p. 18°, undepressed m.p. with pure 2:2'-ditolyl, and b.p. 110-113°/6-7mm. (compare Fittig, Annalen, 1867, <u>138</u>, 178; Ullmann, <u>loc.cit.</u>, 1904, <u>332</u>, 42). Hence it was confirmed that <u>m</u>-tolidine did possess the m.p. 87°.

Nitration of <u>m</u>-tolidine between -5° and 0° with potassium nitrate (1 mol.) in presence of sulphuric acid gave a mono-nitro-compound (A), the constitution of which was proved by replacing two amino groups by bromine and subsequently heating with piperidine.



A Sandmeyer reaction on the nitro-compound (A) was accomplished with difficulty. The product obtained, (<u>x</u>)-nitro-4:4'-dibromo-6:6'-ditolyl, after crystallisation from aqueous alcohol, melted at 100-101° (B). This was gently heated for several minutes with piperidine or even heated under reflux for fifteen minutes. In both cases the nitro-dibromo-ditolyl was recovered unchanged and hence it was clear that the original compound was 2-nitro-m-tolidine.

Attempts were also made for prepar~~at~~ing 2-nitro-4:4'-dibromo-6:6'-ditolyl by a perbromide displacement on the nitro-tolidine. The product thus obtained would only crystallise after adding nuclei obtained from (B) and even so the yield was about 5%.

In order to prepare 2-nitro-6:6'-ditolyl, several attempts were made to deaminate the 2-nitro-m-tolidine by means of ethanol and hydroborofluoric acid before a successful one was found. Here again, 2-nitro-m-tolidine was deaminated by reducing its bis-diazonium chloride with 50% hypophosphorous acid.

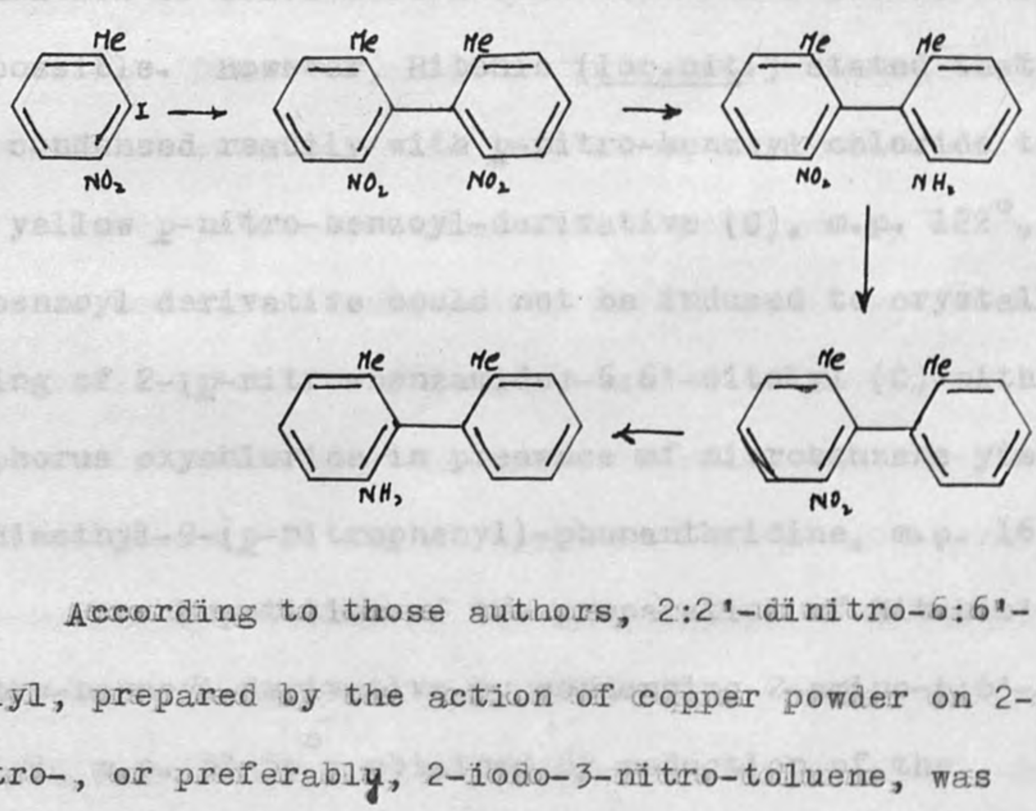
The hypophosphorous acid procedure was notable for its simplicity of operation. Ice-cold 50% aqueous hypophosphorous acid was added to the bis-diazonium solution of 2-nitro-m-tolidine (the molar ratio of hypophosphorous acid to diazonium salt was 15:1), and the reaction was allowed to proceed between -5° and 0°. Reduction was usually complete within 20-24 hours at about 0°.

The reduction product, after several crystallisations from aqueous alcohol, melted at 65°. Crystallisation of this was difficult because of its high solubility in all common organic solvents excepting water, it had a tendency to separate from mixed solvents, as an oil or gummy semi-solid. The best specimen obtained was in pale yellow plates. However, this difficulty could be avoided by distillation of the reduction product under reduced pressure, boiling point 188-204°/18-25mm.

The above 2-nitro-6:6'-ditolyl could be reduced by catalytic reduction using Adams's platinum in presence of alcohol, or by stannous chloride and concentrated hydrochloric acid in the presence of glacial acetic acid, to the corresponding amine, m.p. 54-56°, which was readily characterised by its formyl and acetyl derivatives, m.p. 124-126° and 131-133° respectively.

2-Nitro-6:6'-ditolyl used for the catalytic reduction should be purified to constant melting point. If not, not only longer hydrogenation was required, but also after evaporation of the solvent, the free amine separated as a sticky semi-solid which had to be purified by repeatedly converting into amine hydrochloride and regenerating by aqueous sodium hydroxide till a solid was obtained.

The properties of both above 2-nitro- and 2-amino-6:6'-ditolyl did not agree with those reported by Mascarelli and Angeletti (Gazz. chim. ital., 1938, <u>68</u>, 29) and Ritchie (<u>J.Proc.Roy.Soc.N.S.W.</u>, 1945, <u>78</u>, 156) who obtained them by a different synthesis as follows:-



According to those authors, 2:2'-dinitro-6:6'-ditolyl, prepared by the action of copper powder on 2-chloro-3-nitro-, or preferably, 2-iodo-3-nitro-toluene, was converted into 2'-amino-2-nitro-6:6'-ditolyl. This was deaminated by diazotisation and treatment with hypophosphorous acid to 2-nitro-6:6'-ditolyl, a pale yellow solid, m.p. 42-43° (Mascarelli and Angeletti, <u>loc.cit.</u>)

and m.p. 45° (Ritchie, loc.cit.). Reduction by stannous chloride and hydrochloric acid in presence of glacial acetic acid gave the base as a colourless oil boiling at 169-170°/20mm. which could not be induced to crystallise (Ritchie, loc.cit.), although Mascarelli and Angeletti (loc.cit.) described it as a pale yellow crystalline powder, m.p. 105°. The latter authors did not characterise their product by preparation of solid derivatives so further checks were not possible. However, Ritchie (loc.cit.) stated that the base condensed readily with *p*-nitro-benzoyl chloride to a pale yellow *p*-nitro-benzoyl-derivative (C), m.p. 122°, but the benzoyl derivative could not be induced to crystallise. Heating of 2-(*p*-nitro-benzamido)-6:6'-ditolyl (C) with phosphorus oxychloride in presence of nitrobenzene yielded 4:5-dimethyl-9-(*p*-nitrophenyl)-phenanthridine, m.p. 163°.

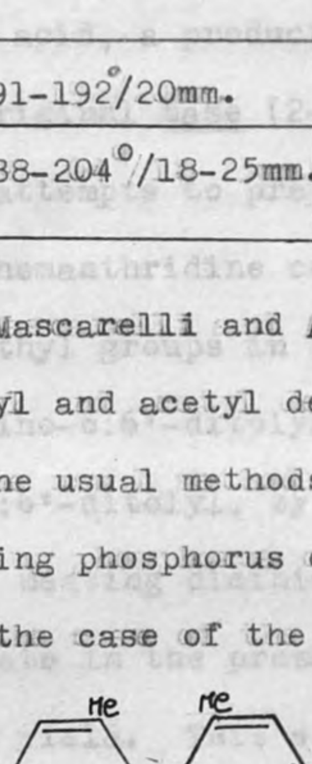
Repetition of the preparation of Ritchie's *p*-nitro-benzoyl-derivative by condensing 2-amino-6:6'-ditolyl, m.p. 54-56°; obtained by reduction of the corresponding nitro-compound which was prepared by deamination of 2-nitro-*m*-tolidine; with *p*-nitrobenzoyl chloride was done in the usual way. It was surprising to find that 2-(*p*-nitro-benzamido)-6:6'-ditolyl thus obtained melted at 160-161°. Could it then not be possible that Ritchie's cyclisation of *p*-nitro-benzoyl-derivative (C) with phosphorus oxychloride in the presence of nitrobenzene was actually a purification of the derivative itself? It would be thought that the 6'-methyl group and *p*-nitro-phenyl-group would retard cyclisation by virtue of their inductive effects, if the cyclisation had ever occurred; otherwise the unchanged amide might be recovered (compare, Morgen and Walls, J., 1931, 2447). Could it also not be possible that Ritchie's amine did not eventually solidfy after being once distilled under reduced pressure because the corresponding nitro-compound used was not absolutely pure? As it was seen in the preparations of both 2-nitro- and 2-amino-6:6'-ditolyl considerable difficulty was encountered on purification of the compounds; it was also stated that if an impure nitro-compound was used in the reduction, the corresponding amine obtained had to be purified by repeatedly converting into amine hydrochloride and regenerating by alkali, before a solid was obtained either by crystallisation from aqueous alcohol or by distillation under reduced pressure.

In view of the marked discrepancy in both m.ps. and b.ps. of 2-nitro- and 2-amino-6:6'-ditolyl, it might be easier to note the difference between them if they were tabled.

| | 2-nitro-6:6'-ditolyl | | 2-amino-6:6'-ditolyl | |
|---|---|---|---|---|
| | m.p. | b.p. | m.p. | b.p. |
| M.&A. | 42-43° | | 105° | |
| Ritchie | 45° | 191-192°/20mm. | | 169-170°/20mm. |
| Present Work | 65° | 188-204°/18-25mm. | 54-56° | 155-157°/10-11mm.<br>166-168°/15-16mm. |

(M.&A.) Mascarelli and Angeletti.

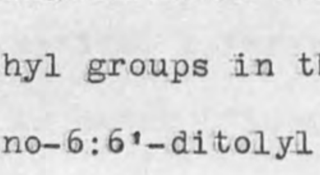
The formyl and acetyl derivatives of the base (B) were prepared by the usual methods and then subjected to the action of boiling phosphorus oxychloride in presence of nitrobenzene. In the case of the acetyl derivative ($R=CH_3$),



a product was obtained; after heating for four hours at 180°; which melted at 144-146° but the analysis did not agree with 4:5:9-trimethyl-phenanthridine.

The formyl derivative (R=H) was, however, converted into an intractable tar and a similar result was obtained when the reaction was carried out in boiling xylene or nitrobenzene with phosphorus oxychloride or a mixture of phosphorus oxychloride and phosphorus pentoxide; but at lower temperature either a tar was formed or there was no reaction. When the attempted cyclisation was carried out in polyphosphoric acid, a product was obtained and was found to be the original base (2-amino-6:6'-ditolyl). The unsuccessful attempts to prepare 4:5-dimethyl- and 4:5:9-trimethyl-phenanthridine could be due to the steric effects of the methyl groups in the 6:6'-positions.

2-Amino-6:6'-ditolyl was converted into 2-dimethylamino-6:6'-ditolyl, by boiling under reflux for two hours (longer heating diminished the yield) with excess of dimethyl sulphate in the presence of aqueous sodium hydroxide, in 60% yield. This was made to react with two parts by weight~~s~~ of methyl iodide and 6-methylphenyl-6'-methyl-2-trimethylammonium iodide was thus obtained.



A number of attempts were made to resolve this quaternary iodide, using silver (d)-camphor-10-

sulphonate and silver $\alpha$-bromo-(d)-camphor-10-sulphonate, but in each case an inactive iodide was obtained after decomposition of the active salts.

Mutarotation was observed on addition of (d)-camphor-10-sulphonate to the base, 2-amino-6:6'-ditolyl, in chloroform followed by polarimetric examination; but no mutarotation was observed with the tartrate. Decomposition of both salts gave an inactive base.

## EXPERIMENTAL - SECTION II.

### Synthesis of 6-methylphenyl-phenyl-6'-methyl-2-trimethylammonium iodide.

### Preparation of m-tolidine.

A modification method of Schultz and Rohde (C., 1902, II, 1447) was used.

m-Azotoluene (136.5 g.) was dissolved in alcohol (500 ml.) in a 3-necked flask fitted with reflux condenser and a mechanical stirrer. Sodium hydroxide (132 g.) dissolved in water (250 ml.) was then added and the mixture heated to boiling on a water bath. A total of 110 g. of zinc dust was added in small portions during half an hour. As the reaction proceeded the mixture became red in colour and the heating under reflux was continued for another 2-2½ hours until the red colour was cischarged.

The mixture was then decanted from the unreacted zinc dust into 2L. of 1:1 hydrochloric acid and the reaction flask rinsed with warm industrial spirit. Concentrated hydrochloric acid (300 ml.) was then added and the mixture shaken. The hydrochloride of the base separated out; this was filtered, washed with ether and finally purified by crystallisation from water in presence of charcoal. 2:2'-Dimethylbenzidine hydrochloride was obtained.

The combined ether washings from the different reactions were washed, dried, and the ether distilled off. The residue in the flask solidified and was crystallised once from industrial spirit. m-Azotoluene was obtained in orange red crystals, m.p. 54-55° and was re-used as starting material.

The free base was obtained from the hydrochloride by addition of 10% sodium hydroxide solution and warming. The base separated as a sticky solid which was washed with water, by decantation, several times and it finally solidified as hard light violet solid in 75% yield. This could be crystallised from water, aqueous alcohol, or benzene in shiny plates, m.p. 87°.

In some cases, m-nitrotoluene was used as a starting material; the procedure was carried out exactly as described above, only the heating under reflux on the boiling water bath was longer and the yield was about 50%.

When m-tolidine was boiled under reflux for a few minutes with salicyl-aldehyde in presence of ethyl alcohol; the disalicylidene derivative was obtained which after crystallisation from alcohol melted at 197-199°.

An attempt to prepare m-tolidine by heating 5-nitro-2-bromo-toluene with copper under various conditions, followed by a reduction was also made.

Preparation of 5-nitro-2-bromo-toluene.

A solution of 5-nitro-2-amino-toluene (25 g.) in a hot mixture of 48% hydrobromic acid (180 ml.) and water (360 ml.) was cooled rapidly to about -7°. It was diazotised under the surface at this temperature by the addition of sodium nitrite solution (19.0 g. in 40 ml. of water). The diazo-solution was stirred between -3° to -7° for a few minutes to ensure completion of reaction and the clear solution was treated gradually, while being stirred, with a mixture of bromine (20 ml.) and 48% hydrobromic acid (120 ml.). After 10-15 minutes, the yellow-coloured diazoperbromide was filtered off, washed with water, ethyl alcohol and dry ether, and dried over solid potassium hydroxide and condentrated sulphuric acid.

The perbromide was then added gradually to hot glacial acetic acid (100°) and heating continued till bromine evolution ceased; the resulting solution, on cooling, became a mass of crystals, which were recrystallised twice from light petroleum (b.p. 60-80°), 5-nitro-2-bromo-toluene being obtained in leaflets, m.p. 79° (Found: Br, 37.3, $C_7H_6NO_2Br$ requires Br, 37.0%).

Attempted preparation of 4:4'-dinitro-2:2'-ditolyl.

(a) 5-Nitro-2-bromo-toluene (20 g.) was heated with copper powder (20 g.) at 235° as described by Ullmann (Ber., 1935, 930) for the preparation of 6:6'-dinitro-2:2'-ditolyl. The hot mixture was treated with boiling industrial spirit, the liquid filtered hot, and most of the solvent distilled off. Water was added to the cool solution and a brown semi-solid separated out. After being first crystallised from aqueous alcohol (charcoal) and then light petroleum, it melted at 77-78°, alone or mixed with 5-nitro-2-bromo-toluene.

(b) Instead of using copper powder, activated copper bronze was used.

5-Nitro-2-bromo-toluene (20 g.) was heated in a boiling tube in a metal-bath, initially at 240°. The activated copper bronze (25 g.) was added gradually; the mixture was stirred with themometer. The temperature rose slowly to 248°. After all the copper had been added, heating was continued at 260° for an hour. The product was extracted with boiling industrial spirit, the liquid filtered through a pre-heated Buchner funnel and the solvent distilled off. A tarry substance was thus obtained which after being crystallised first from aqueous alcohol (charcoal) and then light petroleum, had m.p. 77-79°, alone or mixed with pure 5-nitro-2-bromo-toluene.

(c) A mixture of copper bronze (10 g.) and 5-nitro-2-bromo-toluene (10 g.) were boiled under reflux in nitrobenzene (50 ml.) for two hours. The hot solution was filtered and the solvent distilled off under reduced pressure. A solid was obtained which, after being once crystallised from light petroleum, formed leaflets, m.p. 79°, undepressed m.p. with 5-nitro-2-bromo-toluene.

(d) 5-Nitro-2-amino-toluene (15.5 g.; 1 mol.) was added slowly to concentrated sulphuric acid (36 ml.) and then the mixture cooled to 0°. Over a period of thirty minutes sodium nitrite (6.9 g.; 1 mol.)

was added, and stirring at 0° was continued for four hours. The mixture was then poured onto ice, stirred for another hour, and finally filtered.

A solution of pure cuprous chloride (49.5 g.; 4.95 mols.), ammonium hydroxide (130 ml.; d.0.880), and water (250 ml.) was poured into a 1L., three necked flask. Keeping the reducing solution at 25-30°, the diazo-solution was slowly added in a period of one and one-half to two hours. The mixture was slowly acidified with concentrated hydrochloric acid, completely dissolving the hydroxides. Filtering yielded an orange residue which was extracted with hot ethanol, and extract treated with charcoal. On repeated recrystallisation from alcohol light crystals were obtained; m.p. 168-170° (0.35 g.).

The preparation of 4:4'-dinitro-2:2'-ditolyl by an Ullmann reaction of 5-nitro-2-bromo-toluene or by diazo-coupling (Sherwood and Calvin, <u>J.Amer.Chem.Soc.</u>, 1942, <u>64</u>, 1351) was therefore discarded.

Several melting points have been recorded in the literature for <u>m</u>-tolidine, varying from 87-88° Schultz and Rohde, <u>loc.cit.</u>), to 108-109° (Buchka and Schachtebeck, <u>Ber.</u>, 1889, <u>22</u>, 838). In view of the marked discrepancy in the m.p's. 2:2'-ditolyl was therefore prepared by deamination of the m-tolidine. This proved that the latter did possess the m.p. 87°.

Preparation of 2:2'-ditolyl.

In a 500 ml. beaker was placed m-tolidine (10.6 g.), concentrated hydrochloric acid (d. 1.18; 37.5 g.) and water (12.5 ml.). The beaker was immersed in an ice-salt mixture and was fitted with an efficient stirrer. While a temperature of -5° to 0° was maintained, a solution of sodium nitrite (7.3 g.) in water (17.5 ml.) was slowly added from a dropping funnel. As the reaction proceeded, the mixture became more fluid and nitrite might then be added somewhat more rapidly; a quarter to half an hour was required for diazotisation.

While a temperature of -5° to 0° was maintained, 50% hypophosphorous acid (156 ml.) (precooled to 0°) was added to the diazonium solution in the course of ten to fifteen minutes. Moderate stirring and a temperature of -5° to 0° were continued for an additional hour; the beaker was then covered with a watch glass and placed in a refrigerator (at or close to 0°) for approximately 20 hours.

The reaction product consisted of a bright red oil and an aqueous solution, which was extracted with ether. The combined oil and ether extracts were washed with 20% aqueous sodium hydroxide, then with water and dried over potassium carbonate, and the ether distilled off. 2:2'-Ditolyl (5.7 g.; 52% Theory) was obtained by distillation under reduced pressure at 110-113°/5-6 mm., m.p. 18°, underpressed m.p. with pure 2:2'-ditolyl.

Ullmann and Meyer (Annalen, <u>332</u>, 42) gave b.p. 258°/737 mm., m.p. 17.8°.

<u>Preparation of 2-nitro-m-tolidine.</u>

<u>m</u>-Tolidine (42.5 g.) was dissolved in concentrated sulphuric acid (344 ml.) and cooled to -5°. Finely ground potassium nitrate (20.5 g.) was added with careful stirring within half an hour, the temperature being kept between -5° and 0°. After a further one and a half hours, the solution was poured into a large excess of ice-water (about 9L.). The sulphate that separated was filtered off; the moist salt was ground to a stiff paste with water, and excess of ammonium hydroxide (<u>d</u>.0.880) added, with grinding. The yield of free base

from the sulphate, after two recrystallisations from aqueous alcohol, m.p. 172-173°, in orange-red needles, was 35-38 g. (69-74 % Theory).

In two of the subsequent preparations, a reddish brown precipitate was obtained, after neutralization of the sulphate by aqueous ammonia (*d*.0.880). This, after being purified from aqueous alcohol, melted with decomposition at about 220°. The product was then boiled with benzene and filtered hot. The undissolved residue was discarded and only about 4-6 g. of crude 2-nitro-*m*-tolidine, m.p. 164-167°, was obtained on concentration of the benzene filtrate.

The reason for these unsatisfactory nitrations was probably because the temperature was not well controlled.

(Found: C, 64.5; H, 5.80; N, 16.4 $C_{14}H_{15}N_3O_2$ requires C, 64.9; H, 5.84; N, 16.8%).

### Preparation of 4:4'-dibfomo-2-nitro-6:6'-ditolyl.

(a) 2-Nitro-*m*-tolidine (12.9 g.; 1 mol.) was suspended in 48% hydrobromic acid (55 ml.) and water (20 ml.), and diazotised by adding an aqueous solution of sodium nitrite (7.2 g. in 15 ml. of water) between $-5^{\circ}$ and $0^{\circ}$. On completion of the addition, the cold solution of the bis-diazonium salt was slowly added with vigorous shaking to a cold suspension of cuprous bromide in hydrobromic acid. After the vigorous reaction was over, the whole was heated at $100^{\circ}$ for an hour and the gummy solid was collected and repeatedly washed with 10% sodium hydroxide to remove phenolic substance and then with water. The brownish yellow residue, after several crystallisations from alcohol, melted at $100-101^{\circ}$ (D) (Found: Br, 41.8; $C_{14}H_{11}NO_2Br_2$ requires Br, 41.6%). This was gently heated for several minutes with piperidine or even heated under reflux for fifteen minutes. In both cases the compound was recovered unchanged and it was therefore clear that the original nitro-compound was 2-nitro-_m_-tolidine.

(b) An attempt was made to prepare the 4:4'-dibromo-2-nitro-6:6'-ditolyl by a perbromide displacement on 2-nitro-_m_-tolidine. The bis-diazo-perbromide was obtained in the usual way and after decomposing in hot glacial acetic acid, a sticky semi-solid was obtained. This, after heating under reflux with charcoal and alcohol for 30 minutes, was filtered hot and the filtrate cooled. Nuclei, obtained from the product (D), were added and only then a small quantity of 4:4'-dibromo-2-nitro-6:6'-ditolyl slowly crystallised in yellow plates, m.p. 100-101°.

Preparation of 2-nitro-6:6'-ditolyl.

The following method generally gave about 20-30% yields, although occasionally 5-8% yields were inexplicably obtained.

2-Nitro-m-tolidine (25.7 g.; 2 mols.) was suspended in concentrated hydrochloric acid (75 ml.) and water (25 ml.); and an aqueous solution of sodium nitrite (14.5 g.; 2.04 mols.) slowly added with the usual precautions. The temperature of the reaction was maintained between -5° and 0°. On completion of the addition, the cold solution of the diazonium salt was slowly added with stirring to the solution of 50% hypophosphorous acid (312 ml.; 30 mols.) (precooled to 0°) in the course of 10-15 minutes. Moderated stirring and a temperature of -5° to 0° were continued for an additional hour; the container was then stoppered loosely and placed in a refrigerator for approximately twenty-four hours.

The reaction product consisted of a brown gummy solid floating on the aqueous phase. After separation of the solid, the aqueous solution was extracted with three 150 ml. portions of ether. The ether was distilled off. The combined solid and ether residue were washed with 20-30% aqueous sodium hydroxide, then with water, and dried over potassium carbonate. This, after several crystallisations from aqueous alcohol gave pale yellow plates, m.p. 65°.

Considerable difficulty was encountered on crystallisation of 2-nitro-6:6'-ditolyl from aqueous alcohol as it often separated as an oil or sticky semi-solid. This difficulty could however be avoided by distillation of the combined solid and ether residue, after washing with alkali and water, under reduced pressure.

| | | |
|---|---|---|
| 1st. | fraction | b.p. 188-204°/18-25 mm. |
| 2nd. | " | b.p. was difficult to record and some decomposition occured during the distillation of this fraction. |

The first fraction was solidified eventually and had m.p. 65°.

The second fraction was dissolved in aqueous alcohol and boiled with charcoal for few minutes. The solution was filtered hot and the filtrate cooled. Nuclei, obtained from first fraction, were added and 2-nitro-6:6'-ditolyl slowly crystallised in plates, m.p. 64-65°.

A futther quantity sometimes might still remain in the residue. This was therefore boiled under reflux with small amounts of industrial spirit several times. The extracts were combined and most of the solvent distilled off. A small quantity of impure nitro-ditolyl was occasionally obtained.

(Found: C, 73.4; H, 5.8; $C_{14}H_{13}NO_2$ requires C, 74.0; H, 5.8%).

Attempts were also made for the deamination of 2-nitro-m-tolidine before a successful one was found.

(a) The base (13 g.) was heated with a mixture of concentrated sulphuric acid (75 g.) and water (40 ml.). The cool paste obtained was treated with ice and solid sodium nitrite (10 g.) at -5°; 20% oleum (30 ml.) was added, the temperature being kept below 20°. The product was gradually added to boiling ethanol (500 ml.), and the solution boiled under reflux for 2 hours. The solution was diluted with a large excess of water, and extracted with ether. The extract was washed with alkali and with water and dried over calcium chloride, and the solvent removed. The residue thus obtained could not be purified.

(b) The base (13 g.) was heated with concentrated hydrochloric acid (40 ml.) for 20 minutes on the water bath, i.e. until it was completely converted into the hydrochloride. The paste was cooled, ice added and a solution of sodium nitrite (10 g.) in water (20 ml.) stirred in (10 minutes, addition under surface), ice being added as required. The diazo-solution was filtered, and hydroborofluoric acid added. The diazo-borofluoride that separated after standing over night in a refrigerator, was filtered off and dried in a vacuum over sulphuric acid. It was added gradually to a boiling mixture of 10 parts of absolute ethanol and 2 parts of concentrated sulphuric acid, and the solution then boiled for 10 minutes, treated with excess of brine, and worked up as in (a). The residue obtained could not be purified.

Preparation of 2-amino-6:6'-ditolyl.

(a) The corresponding nitro-compound (2-nitro-6:6'-ditolyl) used in the reduction was prepared as pure as possible by recrystallisation to constant melting point.

For the reduction of 2-nitro-6:6'-ditolyl (5.7 g.; 1 mol.), the platinum oxide (0.05 g.) (prepared according to Voorhees and Adams, J.Amer.Chem.Soc., 1922, 1402), and absolute ethyl alcohol (100 ml.) to be used were placed in a reaction bottle and reduced with hydrogen in a hydrogenator at 2.5 to 3 atm. for about an hour. After filtration of the catalyst, the alcohol was evaporated to dryness. The solid thus obtained on cooling was crystallised from alcohol; colourless needles, m.p. 54-56° (4.1 g.).

If the used 2-nitro-6:6'-ditolyl was impure; after filtration of the catalyst, the solvent was evaporated to a volume of about 15 ml., dilute hydrochloric acid was added, a small amount of tarry material filtered off, and the filtrate made alkaline with aqueous ammonia. The free amine which separated as a gum was redissolved in hydrochloric acid and precipitated as the amine hydrochloride by the action of concentrated hydrochloric acid. By repeating this procedure once more the base separated as a solid. The free base was then purified as before.

(b) The above reduction was carried out using platinum oxide as catalyst. The method gave satisfactory yields but was not suitable for large scale work. A reduction by means of stannous chloride and concentrated hydrochloric acid was therefore used.

A solution of 2-nitro-6:6'-ditolyl (15 g.) in hot glacial acetic acid (180 ml.) was treated with just over the calculated quantity of stannous chloride (80 g.) dissolved in concentrated hydrochloric acid (90 ml.). The mixture was boiled under reflux for an hour and then cooled, treated with excess of aqueous sodium hydroxide, and extracted with ether. The extract gave 2-amino-6:6'-ditolyl, which distilled at 166-168°/15-16 mm.; 155-157°/10-11 mm. and solidified eventually. It melted at 54-56°. (Found: C, 84.9; H, 7.1; N, 7.2; $C_{14}H_{15}N$ requires C, 84.7; H, 7.3; N, 7.1%).

2-Amino-6:6'-ditolyl condensed with p-nitrobenzoylchloride.

A mixture of 2-amino-6:6'-ditolyl (1 mol.) was heated with p-nitrobenzoyl chloride (1 mol.) in a sealed tube at 100° for 30 minutes; this was cooled, made alkaline and filtered. The crude 2-(p-nitrobenzamido)-6:6'-ditolyl, after washing with water, crystallised twice from aqueous alcohol in pale yellow plates, m.p. 160-161°. (Found: C, 72.2; H, 5.2; $C_{21}H_{18}N_2O_3$ requires C, 72.8; H, 5.2%).

Formyl derivative of 2-amino-6:6'-ditolyl.

This was prepared by heating under reflux of 2-amino-6:6'-ditolyl (2 g.) with formic acid (10 ml.) for 15 minutes and diluting the hot solution with cold water. It was cooled in ice, but no solid separated so the solution was saturated with salt. The salted product was filtered, washed with cold water and crystallised from light petroleum (b.p. 60-80°) as cream crystals, m.p. 124-126° (Found: C, 80.0; H, 6.2; N, 6.2; $C_{15}H_{15}NO$ requires C, 79.5; H, 6.6; N, 6.2%).

Attempted preparation of 4:5-dimethyl-phenanthridine.

(a) A mixture of phosphorus oxychloride (20 ml.), 2-formamido-6:6'-ditolyl (4 g.) and nitrobenzene (20 ml.) or xylene (20 ml.) were placed in a 100 ml. flask. The solution was heated between 190° and 200° with efficient stirring. After two hours, excess of reagents were distilled off under reduced pressure, and an intractable tar was obtained.

(b) In stead of phosphorus oxychloride, a mixture of phosphorus oxychloride and phosphorus pentoxide was used in this reaction as in (a). At 115-125°, there was no reaction; at 150-170°, a tar was obtained.

(c) In a 50 ml. flask were placed polyphosphoric acid (20 ml.) and 2-formamido-6:6'-ditolyl (2.5 g.) The solution was heated at 140-160° with efficient stirring for one and a half hours. The reaction mixture was decomposed with ice, and the solid that separated was neutralized with aqueous ammonia. This was filtered off and found to 2-amino-6:6'-ditolyl.

## Preparation of acetyl derivative of 2-amino-6:6'-ditolyl.

The acetyl derivative of 2-amino-6:6'-ditolyl was prepared by heating under reflux the base (2 g.) and redistilled acetic anhydride (2.5 mols.) for 10-15 minutes. The crude 2-acetamido-6:6'-ditolyl, after usual procedure, crystallised from light petroleum (b.p. 60-80°) in white needles, m.p. 131-133° (Found: C, 80.2; H, 7.2; N, 5.9; $C_{16}H_{17}NO$ requires C, 80.3; H, 7.1; N, 5.9%).

## Attempted preparation of 4:5:9-trimethyl-phenanthridine.

A mixture of 2-acetamido-6:6'-ditolyl (5 g.), phosphorus oxychloride (10 g.) and nitrobenzene (20 ml.) was boiled. Vigorous evolution of hydrogen chloride occurred. After 4 hours, excess of reagents was distilled off and the residual gum was extracted repeatedly with N-sulphuric acid (about 200 ml.). Neutralisation of the extract gave a small amount of grey flocculent precipitate which, on repeated crystallisations from benzene, gave a trace of white crystalline powder, that melted at 144-146° (Found: C, 56.4; H, 6.6; $C_{16}H_{15}N$ requires C, 86.6; H, 6.8%). Hence it cann't be the required trimethyl-phenanthridine.

## Methylation of 2-amino-6:6'-ditolyl.

The base (2 g.) dissolved in benzene (25 ml.) and sodium hydroxide (30 g.) in water (60 ml.), contained in a two-necked flask of 250 ml. capacity, fitted with a reflux condenser and a tap funnel, was heated to boiling on a water bath. Dimethyl sulphate (10 ml.) was then added from the tap funnel in small portions, each portion being allowed to react before adding the next. After 1½ to 2 hours (longer heating diminished the yield), another portion of alkali was added to destroy excess of dimethyl sulphate. After cooling, two layers were separated and the aqueous alkaline layer was then extracted twice with ether. The extracts were combined with the upper layer, washed with water and dried over anhydrous potassium carbonate.

The solution was filtered and both ether and benzene were removed from filtrate by distillation. The residue was distilled under reduced pressure and gave 2-dimethylamino-6:6'-ditolyl (1.4 g.; 61% yield), at 146-148°/7 mm.

(Found: C, 84.8; H, 8.4; $C_{16}H_{19}N$ requires C, 85.2; H, 8.4%).

Attempts were also made to effect methylation of 2-amino-6:6'-ditolyl before a successful one was found.

(a) A mixture of 2-amino-6:6'-ditolyl (3 g.) and water (6 ml.) was shaken for 10 minutes with three lots (3, 4 and 4 ml.) of dimethyl sulphate, being made alkaline with 10% sodium hydroxide between the addition. The final mixture was then heated at 100° for 15 minutes, cooled, made alkaline, and extracted with ether. Ether was distilled off. The ether residue was either distilled under reduced pressure or crystallised from aqueous alcohol it melted at 54-56°, undepressed m.p. of 2-amino-6:6'-ditolyl.

(b) The base (4 g.) was dissolved in methyl alcohol (12 ml.) with dimethyl sulphate (10 ml.) and after cooling to 0°, a solution of sodium hydroxide (15 g.) in water (25 ml.) was added all at once. After standing for ½ hour, an oil separated which was extracted with ether. On removing the solvent, a semi-solid residue was obtained which after crystallisation from aqueous alcohol, melted at 54-56°, undepressed m.p. of 2-amino-6:6'-ditolyl.

## Preparation of 6-methylphenyl-phenyl-6'-methyl-2-trimethyl-ammonium iodide.

A mixture of the foregoing dimethyl base and two parts by weight of methyl iodide was allowed to stand for 10 minutes (if the reaction had not occurred by then, scratching was necessary). The mixture would set solid. The solid product was freed from methyl iodide by evaporation and the residue dissolved in boiling water, any acidity being removed by aqueous ammonia, and liquid rapidly filtered at about 50°. The cold aqueous solution deposited the quaternary iodide as fine white needles (57-65% yield); spontaneous evaporation produced well-defined long needles. After crystallisation from water, the iodide had m.p. 177-178°. (Found: C, 55.8; H, 6.1; I, 34.1; $C_{17}H_{22}NI$ requires C, 55.3; H, 6.1; I, 34.4%).

### Attempt to prepare a salt of 6-(methylphenyl)-phenyl-6'-methyl-2-trimethyl-ammonium iodide with silver (d)-camphor-10-sulphonate.

dl-Quaternary iodide (1.83 g.) and the equiv. silver d-camphor-10-sulphonate were boiled under reflux in 50% aqueous ethyl alcohol (80 ml.) for 30 minutes. The filtered solution was evaporated, the residue freed from water by repeated evaporation with small quantities of benzene and dissolved in boiling ethyl acetate (10 ml.) and the filtered solution treated with light petroleum (b.p. 60-80°) (6 ml.). 0.17 G. of crystals (A), m.p. 60-62° were obtained, having $[\alpha]_{5461}$ +24.6° in ethyl alcohol.

Addition of light petroleum (b.p. 60-80°) (6 ml) to the mother liquor fine needles began to separate after a few hours in the refrigerator (at 4°). 0.91 G of crystals (B), m.p. 60-62° were obtained, having $[\alpha]_{5461}$ +27.4° in ethyl alcohol. The combined weight of A and B, 1.08 g., is 91.9% of the possible dd-salt, assuming no complication. Salt B was dissolved in hot benzene, the solution filtered, and then treated with light petroleum (b.p. 60-80°) (14 ml.). The camphorsulphonate (0.56 g.) separated in needles, m.p. 60-62°, having $[\alpha]_{5461}$ +27.6° in ethyl alcohol.

Further crystallisation had no effect on m.p. or sp. rotation (Found: C, 62.7; H, 6.6; $C_{27}H_{37}NO_4S$ requires C, 68.6, H, 7.8%).

### Attempted resolution of 6-(methylphenyl)-phenyl-6'-methyl-2-trimethyl-ammonium iodide, using silver $\alpha$-bromo-(d)-camphor-10-sulphonate.

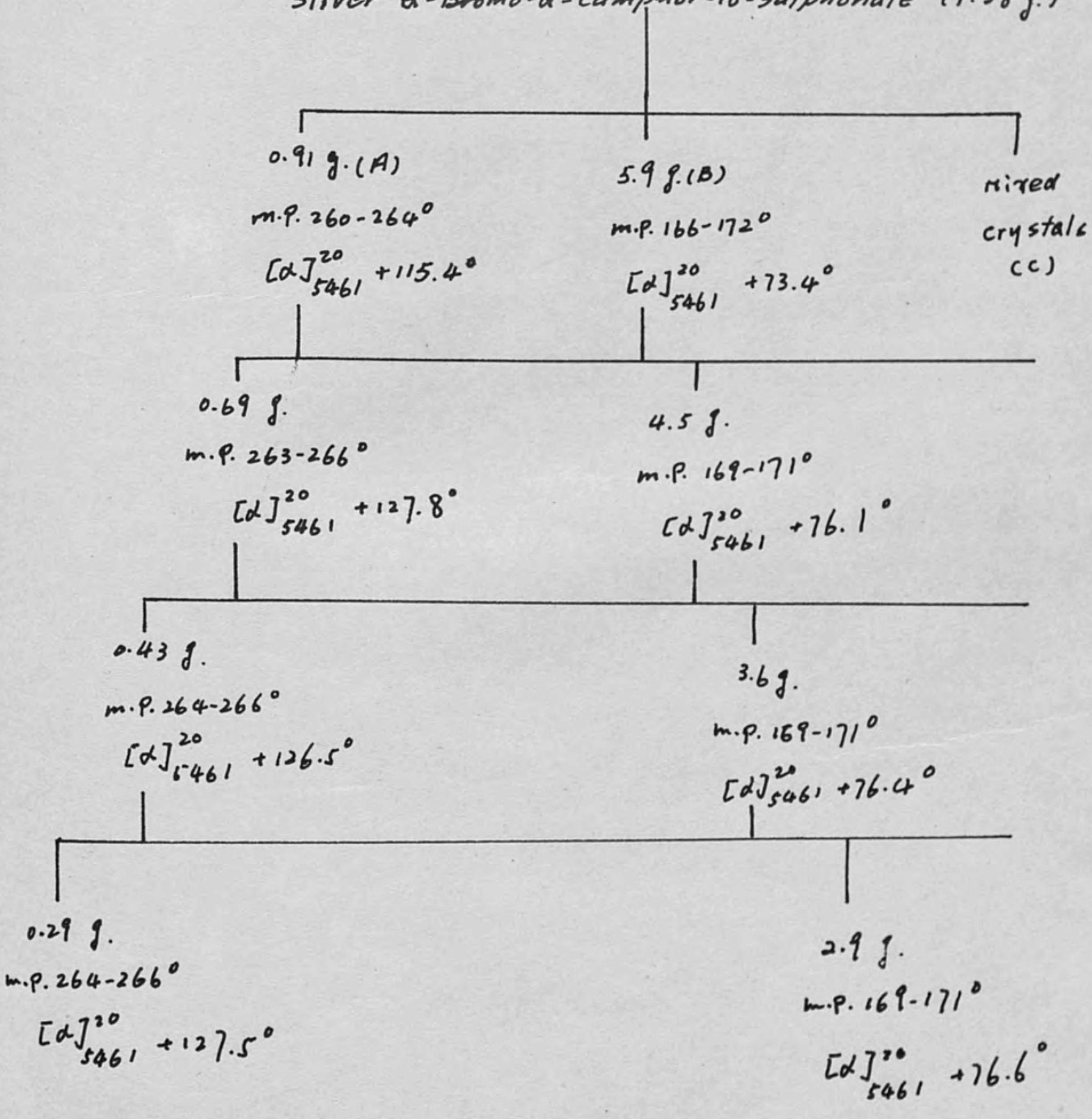
### Preliminary experiment.

dl-Quaternary iodide (0.93 g.) and silver $\alpha$-bromo-(d)-camphor-10-sulphonate (1.09 g.) were boiled under reglux in 50% aqueous ethyl alcohol for 30 minutes. The filtered solution was evaporated, the residue free from water by repeated evaporation with small quantities of benzene and dissolved in ethyl acetate (12 ml.). 0.36 G. of needles, m.p. 166-170° were obtained, having $[\alpha]_{5461}$ +74.6° in ethyl alcohol.

# CHART I.

dl-Quaternary iodide (7.90 g.) +

Silver α-Bromo-d-camphor-10-sulphonate (9.38 g.)



Attempted resolution of 7.9 g. of quaternary iodide.

(a) dl-Quaternary iodide (7.9 g.; 1 mol.) and silver α-bromo-(d)-camphor-10-sulphonate (9.38 g.; 1 mol.) were boiled under reflux in 50% aqueous ethyl alcohol (200 ml.) for 45 minutes. The filtered solution was evaporated, the residue freed from water by evaporation with small quantities of benzene and dissolved in ethyl acetate (80 ml.). Nuclei, obtained by cooling a small portion of the solution to below 0° and rubbing with a glass rod, were then added and the salt slowly crystallised in needles. Filtration gave 0.91 g. of crystals (A), m.p. 260-264° (decomp.), having $[\alpha]_{5461}$ +115.5° in ethyl alcohol. These crystals (A) would not redissolved in ethyl acetate, but could be obtained as long silky needles by recrystallizing from ethyl acetate -alcohol mixture. These needles had m.p. 264-266° (decomp.) and a specific rotation $[\alpha]_{5461}$ +127.8°. No significant change in specific rotation with recrystallization was obtained in the Chart I.

Found for CROP A $[\alpha]_{5461}$ +127.5°: C, 36.6; H, 5.8% does not correspond to any reasonable formula.

The filtrate was evaporated to 25 ml., and the crystals began to separate in fine needles, after stand in the refrigerator (at 4°) overnight. 5.9 G. of the salt (B) was then obtained m.p. 166-172°, having $[\alpha]_{5461}$ + 73.4° in $C_2H_5OH$. On recrystallisation from a mixture solvent of ethyl acetate - alcohol (see Chart I for details) the sepecific rotation of the salt gradually fell until after three recrystallisations, it was constant at $[\alpha]_{5461}$ + 77.8° in $C_2H_5OH$.

Found for CROP B $[\alpha]_{5461}$ +77.8°: C, 58.2; H, 6.5; S, 5.9; $C_{27}H_{36}NO_4BrS$ (1 mol. acid and 1 mol. base) requires C, 58.6; H, 6.5; S, 5.8%.

Further evaporation of the mother liquor of CROP B yielded only successive small quantities of fine needles, together with a sticky glassy solid (C). Decomposition of the CROPS A, B and C with cold conc. aq. solution of potassium iodide respectively gave an inactive base. This experiment was repeated to see if these results were reproducible.

Attempted resolution of 8.24 g. of quaternary iodide.

(b) The dl-iodide (8.24 g.) and the equiv. silver -bromo-(d)-camphor-10-sulphonate were caused to reacted as in (a). The mixed bromocamphorsulphonates were crystallised from ethyl acetate (30 ml.). The crude salt separated (6.1 g.), m.p. 169-172°, in white fine needles, and had $[\alpha]_{5461}$ +68.0° in chloroform.

The filtrate was evaporated to 15 ml. yield only successive small quantities of white needles (D) (about 0.1 g.), m.p. 169-172°. The combined weight of C and D, 6.2 g., is 92% of the possible dd-salt, assuming no complication.

Salt C was dissolved in a hot mixture solvent of ethyl acetate (45 ml.) and ethyl alcohol (3 ml.), the solution filtered, and left in the refrigerator (at 4°) for two days. The bromocamphorsulphonate (2.9 g.) separated in needles, m.p. 172-175°, having $[\alpha]_{5461}$ +74.3° in chloroform. It was crystallised from ethyl acetate - alcohol, and the 1.6 g. of optically pure dd-salt obtained had m.p. 173-175°, having $[\alpha]_{5461}$ +74.9° in chloroform. Further crystn. had no effect on m.p. or sp. rotation (Found: S, 5.6; Br, 14.7; $C_{27}H_{36}NO_4BrS$ (1 mol. acid and 1 mol. base) requires S, 5.8; Br, 14.5%). Decomposition of the salt with a cold conc. aq. solution of potassium iodide gave an inactive ~~base.~~ iodide.

All rotations were determined using 2 dcm. polarimeter tube unless otherwise state. For work in which temperature control was required, a polarimeter tube fitted with a metal jacket was employed. The temperature was maintained at a constant value by rapidly pumping water from an electrically heated thermostat through the jacket. Calibrated thermometers were placed in the inlet and outlet circuits of the system. The solution in the polarimeter tube was maintained at a constant temperature $\pm 0.1^{\circ}$.

In the experiments carried out at a lower temperature, water was circulated through the jacket from a lagged refrigerator unit supplied with a temperature control. The temperature was maintained at constant $\pm 0.1^{\circ}$.

The mercury green line $\alpha_{5461}$ was used throughout. Where chloroform and ethyl alcohol were required for polarimetric examination, the commerical "B.P." products were used.

### Attempt to prepare A tartrate of 2-amino-6:6'-ditolyl.

The base (0.985 g.; 1 mol.) and (d)-tartaric acid (0.750 g.; 1 mol.) were dissolved in boiling ethyl alcohol (20 ml.). The solution was filtered hot and on cooling the colourless crystalline solid which deposited was filtered off, washed and dried in vacuum. The yield 0.64 g. represents 36.8% of the total solid taken. M.P. 150-152°.

The crystalline solid (0.2408 g.) was dissolved in ethyl alcohol which had been stood in the thermostat and the solution made up to 20 ml.. The salt dissolved almost instantaneously. The observed rotation $\alpha_{5461} = 0.06^{\circ}$ did not change within two hours.

Found: C, 58.3; H, 4.7; $C_{18}H_{21}NO_6$ (1 mol. acid and 1 mol. base) requires C, 62.3; H, 6.0%.

<u>Preparation of 2-amino-6:6'-ditolyl camphor-10-sulphonate.</u>

2-Amino-6:6'-ditolyl (0.985 g.; 1 mol.) and (d)-camphor-10-sulphonate (1.260 g.; 1 mol.) were dissolved in boiling ethyl alcohol (30 ml.)(which had been stood in the thermostat). The solution was filtered while hot, and the filtrate evaporated to about 20 ml.. The crystalline solid which separated was filtrated off, washed with ethyl alcohol and dried in vacuum. The yield 0.65 g. represents 29.4% of the total weight of solid taken. M.P. 176-178°.

(Found: C, 67.3; H, 7.0; $C_{24}H_{31}NO_4S$ requires C, 67.1; H,7.2%)

## Investigation of 2-amino-6:6'-ditolyl d-camphor-10-sulphonate.

The salt (0.2474 g.) was dissolved in chloroform (20 ml.)(which had been stood in the thermostat), and the solution examined polarimetrically at 25°. Readings of the observed angle with time were recorded (Table 1.). A log. plot. of the results was made (fig.1) and a value of k 0.0155 $hr.^{-1}$ was obtained whence the half life is 20 hours.

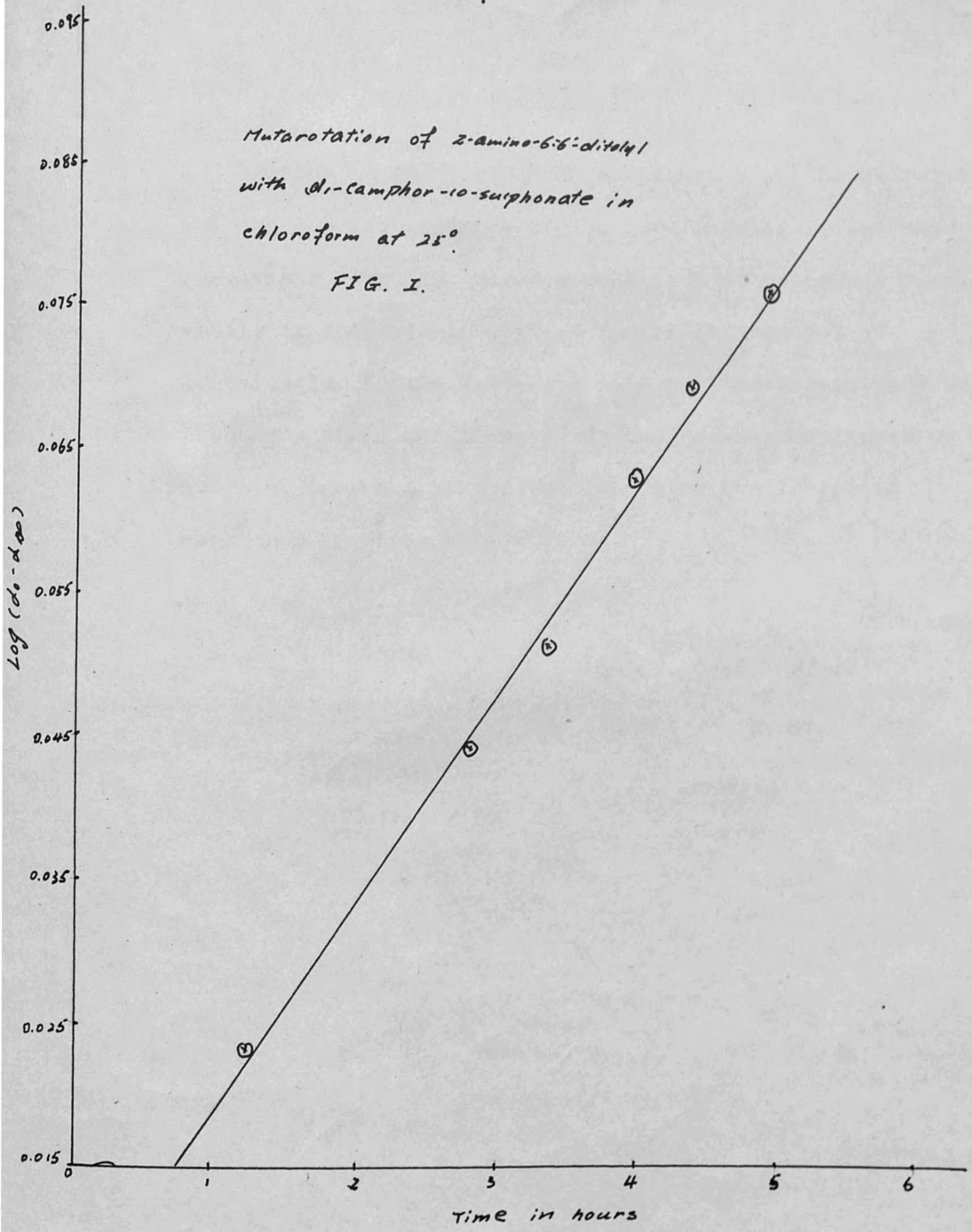
A solution of (d)-camphor-10-sulphonate salt (0.34 g.) in ice-cold chloroform (20 ml.) was shaken thrice with 10% sodium hydroxide solution at 0° and then once with water. After separation, the air was blown through the chloroform solution to dryness and a solid (0.14 g.) was thus obtained and dired in vacuum.

The solid (0.14 g.) was dissolved in chloroform and was made up to 20 ml.. The solution was examined polarimetrically at 25°. $\alpha_{5461} = 0.00°$. The base is optically inactive.

## Rate of Mutarotation of 2-amino-6:6'-ditolyl - (d)-camphor-10-sulphonate in chloroform at 25°.

Table 1.

| Time (hours) | $\alpha^{25}_{5461}$ | $(\alpha_t - \alpha_\infty)$ | $\log_{10}(\alpha_t - \alpha_\infty)$ | k hrs.$^{-1}$ |
|---|---|---|---|---|
| 0.00 | + 0.82 | 1.26 | 0.000 | - |
| 0.10 | + 0.82 | 1.26 | 0.000 | - |
| 1.42 | + 0.76 | 1.20 | 0.212 | 0.0150 |
| 2.80 | + 0.70 | 1.14 | 0.435 | 0.0155 |
| 3.35 | + 0.68 | 1.12 | 0.512 | 0.0150 |
| 3.95 | + 0.65 | 1.09 | 0.630 | 0.0159 |
| 4.30 | + 0.63 | 1.07 | 0.710 | 0.0165 |
| 4.97 | + 0.62 | 1.06 | 0.751 | 0.0151 |
| 72.77 | - 0.44 | 0.00 | 1.004 | - |
| $\infty$ | - 0.44 | 0.00 | 1.004 | - |

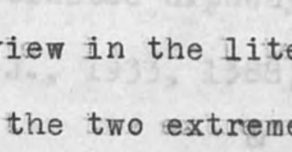


Mutarotation of 2-amino-6:6'-ditolyl with dl-camphor-10-sulphonate in chloroform at 25°.

FIG. I.

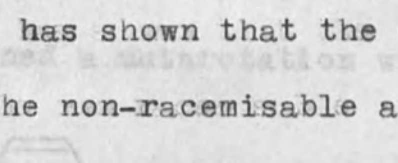
## INTRODUCTION - SECTION III.

Review in the literature has shown that the difference between the two extremes of the non-racemisable and non-resolvable, was discovered a multitude of compounds varying widely in optical stability. The minimum amount of substitution in the 2:2'- and 6:6'-positions necessary to produce optically active substances, was investigated by Lesslie, Shaw and Turner, who obtained the following compounds in their active forms:-



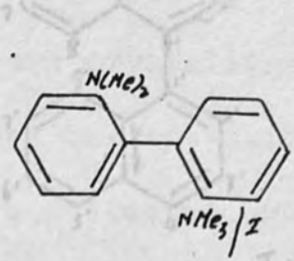
Lesslie and Turner

J. 1932, 2394



*idem.*, *ibid.*

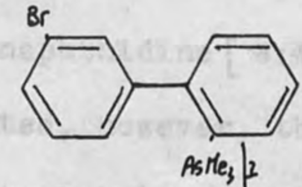
P. 2071.



Shaw and Turner

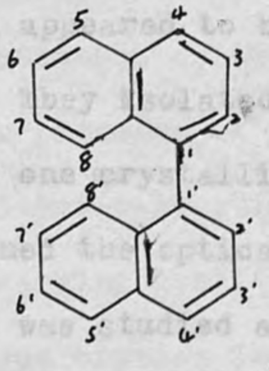
*ibid.*, 1933, 135.

The only known case of optical activity in a monosubstituted diphenyl was reported when Lesslie and Turner (J., 1933, 1588) obtained a mutarotation with 3'-



bromodiphenyl-2-trimethyl-arsonium iodide with (d)-camphor sulphonic acid. Other cases of optically active disubstituted diphenyls were reported. Among these the dinaphthyls, diquinolys and diisoquinolyls could also be resolved.

Free rotation of the interannular bond in 1:1-dinaphthyl (I) is hindered, although two of four blocking positions (2 and 2') remain filled with hydrogen atoms



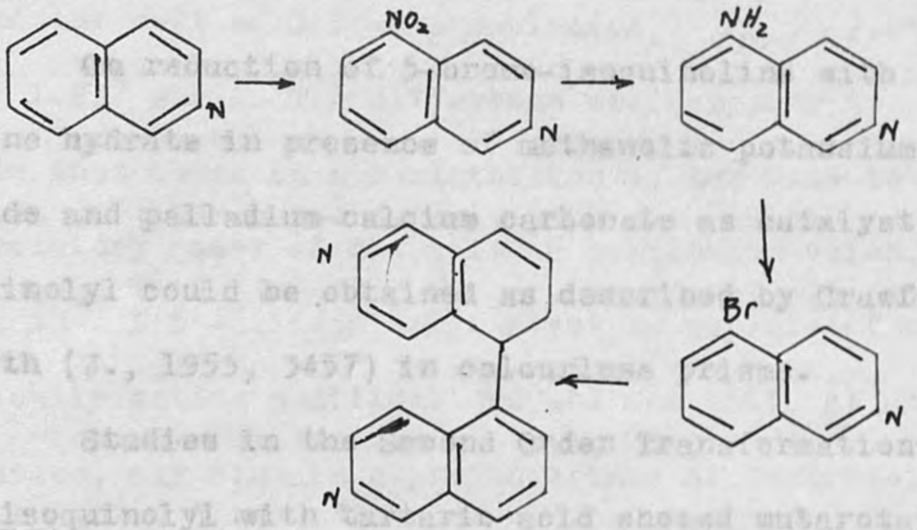
(I)

1:1-dinaphthyl-5:5'-dicarboxylic acid has been resolved into its optical isomers (Bell and Morgan, J., 1954, 716). The mechanical obstruction to free rotation must be very slight. In one planar position it amounts only to the overlap of the van der Waals envelopes of the pairs of hydrogen atoms on the 2:8' and 2':8 carbon atoms. The failure to resolve naphthidine [4:4'-diamino-derivative of (I)] was unexpected, however, the very similar compounds, 4:4'- and 5:5'-diquinolyl (I, with N in the positions 4:4' and 5:5'- respectively) were resolved by Crawford and Smyth (*ibid.*, 1952, 4133). Further resolutions of these types of compounds have now been achieved e.g. 1:1'-, 4:4'-, 5:5'- and 8:8'-di*iso*quinolyl (I, with N in the positions 2:2', 3:3', 6:6' and 7:7' respectively), but the first were not isolated (*idem.*, *ibid.*, 1955, 3464).

The result of 5:5'-di*iso*quinolyl by Crawford and Smyth (*loc.cit.*) appeared to be an asymmetric transformation since they isolated about 70% of the optically active tartrate from one crystallisation which they decomposed and obtained the optically active 5:5'-di*iso*quinolyl. This work was studied again in order to observe the mutarotation of the salts and the effect of the temperature on their optical activities.

## DISCUSSION - SECTION III.

To prepare 5:5'-diisoquinolyl the following synthesis was presented.



According to Le Fevre and Le Fevre (J., 1935, 1475) 5-nitro-isoquinolyl was obtained in a reasonable yield. This could be reduced with Raney nickel as catalyst in a hydrogenator or by stannous chloride and concentrated hydrochloric acid in presence of ethanol. In both methods, about 60% yield of 5-amino-isoquinoline were obtained.

In spite of varying conditions and different proportions of cuprous bromide in hydrobromic acid used in the Sandmeyer Reaction on 5-amino-isoquinoline in order to obtain 5-bromo-isoquinoline, considerable difficulties were encountered and the best yield obtained was 34%.

Attempts were also made for preparing 5-bromoisoquinoline via a perbromide displacement on the corresponding amine, but no bromoisoquinoline was ever isolated.

On reduction of 5-bromo-isoquinoline with hydrazine hydrate in presence of methanolic potassium hydroxide and palladium-calcium carbonate as catalyst, 5:5'-di<u>iso</u>quinolyl could be obtained as described by Crawford and Smyth (J., 1955, 3457) in colourless prisms.

Studies in the Second Order Transformation of 5:5'-di<u>iso</u>quinolyl with tartaric acid showed mutarotation from $\alpha_{5461}^{25}$ 1.05° after 2.5 minutes to $\alpha_{5461}^{25}$ 0.06° after 109 minutes one occasion. No mutarotation was observed on repetition of this transformation; and decomposition of the tartrate by cold ammonium hydroxide as described by Crawford and Smyth (<u>loc.cit.</u>) gave an inactive base. The cause of obtaining an inactive salt might be due to cooling too rapidly or long heating, since the salt became gummy at ordinary temperature.

As there was no confirmed evidence of mutarotation of the tartrate, (d)-camphor-10-sulphonate and the <u>base</u> in chloroform was compared, under identical conditions, with the rotations of the sulphonate of an inactive base, 2:2'-dipyridyl.

It will be observed that whereas the rotations of the salt of the inactive base are $\alpha^{5}_{5461}$ 1.19, $\alpha^{20}_{5461}$ 1.13° etc. and the salt of 5:5'-di*iso*quinolyl, $\alpha^{5}_{5461}$ 2.04°, $\alpha^{20}_{5461}$ 1.93° etc.. The difference would appear to indicate that there is a contribution by the base to the total rotatory power of the salt, a conclusion which, implies that 5:5'-di*iso*quinolyl might be capable of existing in optically active modifications and the salt, at any rate in solution, may contain a preponderance of dextrorotatory form.

# EXPERIMENTAL - SECTION III.

## Synthesis of 5:5'-Diisoquinolyl.

Crawford and Smyth, J., 1954, 3465.

### Preparation of 5-nitroisoquinoline.

Le Fevre and Le Fevre (J., 1935, 1475).

Isoquinoline (43 g.; 1 mol.) was dissolved in concentrated sulphuric acid (108.7 g.; d 1.84; 3.3 mols.) directly; considerable heat was evolved and the solution was cooled to 0° in an ice-salt mixture bath, stirred, and potassium nitrate (35 g.; 1.05 mols.), in concentrated sulphuric acid (200 ml.; d. 1.84) dropped in during two hours at 0°. After adding potassium nitrate, the mixture was kept below 50° for six hours with stirring. The reaction mixture was then slowly poured onto crushed-ice and carefully neutralised by aqueous ammonia (d. 0.880). The greenish yellow precipitate which separated after standing for 30 minutes was filtered off, washed with water and dried. It crystallised from aqueous alcohol with a little charcoal in yellow needles, m.p. 109-111°.

This preparation was repeated several times, and the yield varied from 45-63%, and in one case was obtained as high as 84.8%.

Preparation of 5-amino-isoquinoline.

(a) Craig and Cass (J.Amer.Chem.Soc., 1942, 64, 783).

5-Nitro-isoquinoline (8.7 g.) dissolved in absolute ethyl alcohol (150 ml.) was hydrogenated over Raney nickel (3 g.) under 3 atm. of hydrogen in three hours. After filtration of the catalyst, the alcohol was evaporated. The residue was re-dissolved in warm chloroform solution; the solution evaporated to incipient precipitation and poured into ligroin. 5-Amino-isoquinoline was obtained (4.6 g.; 64% Theory) as slightly yellowish crystals of m.p. 126-128°.

(b) The above reduction was carried out using Raney nickel as catalyst. This method gave satisfactory yields but was not suitable for large scale work. A reduction by means of stannous chloride and concentrated hydrochloric acid in presence of industrial spirit was therefore used.

Stannous chloride (150 g.) and hydrochloric acid (180 ml.; d. 1.18) were boiled gently to obtain a clear solution. This was placed in a one-litre 2-necked flask (fitted with a reflux condenser and a tap funnel) in a boiling water bath. 5-Nitro-isoquinoline (34.8 g.) dissolved in hot industrial spirit (250 ml.) was then added portionwise with shaking from the funnel, after a minutes or so the reaction became quite vigorous and in some cases cooling was necessary. After adding the ethanol solution, the reaction flask was shaken from time to time and heated was continued for another half an hour.

After this time the solution was cooled and stood over night. The amino-isoquinoline chloride was filtered off and crystallised from hot water.

The free base was obtained from the hydrochloride by the addition of 10% sodium hydroxide solution and extracting with ether. The residue, after removing of ether, was dissolved in boiling chloroform with a little charcoal, the solution filtered hot and poured into ligroin. The pure amino-isoquinoline was obtained in 60% yield (17.3 g.) and had m.p. 125-127°.

All the amino-compounds obtained from the different preparations were pure enough for the subsequent experiment after being once crystallised from chloroform-ligroin.

Preparation of 5-bromo-isoquinoline.

5-Amino-isoquinoline (25 g.; 1 mol.) was dissolved in 48% hydrobromic acid (100 ml., d. 1.48) and water (100 ml.) by warming and then cooled to -5° in an ice-salt mixture bath. A solution of sodium nitrite (15 g.; 1.1 mols.) in water (30 ml.) was added at such a rate that the temperature was not allowed to rise above -3°. The mixture was vigorously stirred for five minutes after the addition of sodium nitrite was complete.

It was slowly run into a cold solution of cuprous bromide (27 g.; 1.2 mols.) in 48% hydrobromic acid (50 ml.). A vigorous reaction set in and after standing at room temperature for ten minutes the reaction mixture was warmed on a boiling water bath until no more nitrogen was evolved and the solid was filtered off. This was washed thrice with warmed 10% sodium hydroxide and then with aqueous ammonia for several times to remove the excess of copper and finally extracted with boiling benzene. On removal of the benzene, a solid (12.2 g., 34% Theory) was obtained which after being twice crystallised from industrial spirit with a little charcoal formed brownish yellow needles, m.p. 82-83°.

Claus and Hoffmann (J.Prakt.Chem., , II, 47, 262) gave m.p. 80.5°.

An attempt to prepare 5-bromo-isoquinoline through a perbromide was made. 5-Amino-isoquinoline was diazotised, and to the diazo-solution a mixture of bromine in hydrobromic acid was added. A bulky, orange yellow precipitate of the perbromide formed at once but after standing for ten minutes it became an orange red oil which would not solidify on removal from the mother liquor and removal of excess bromine by ether or glacial acetic acid or alcohol.

In one of the attempts, the perbromide was filtered off as soon as it was formed and decomposed in hot glacial acetic acid in the usual way. Water was added yet no precipitate or oil was ever obtained.

## Preparation of 5:5'-diisoquinolyl.

Crawford and Smyth (J., 1954, 3465).

90% Hydrazine hydrate (10 ml.) was added slowly during 30 minutes to a boiling mixture of 5-bromoisoquinoline (10 g.), 1% palladium - calcium carbonate (10 g.) (preparation see next page), and 5% methanolic potassium hydroxide (500 ml.) contained in a three-necked flask of two litres capacity which was fitted with a stirrer, a tap-funnel and a reflux condenser. A similar amount of hydrazine hydrate was added after another 30 minutes. Heating under reflux with stirring was continued for 8 hours. The hot liquid was then filtered, the residue was washed with boiling methanol, and the filtrate and washings were evaporated to small bulk with additions of water. A dark oil separated which solidified on cooling. This solid, dissolved in dilute hydrochloric acid (100 ml.), was decolourised by shaking with animal charcoal for an hour and then reprecipitated with ammonia solution. Two recrystallisation from benzene - light petroleum gave 5:5'-di*iso*quinolyl (2.2 g.) as colourless prisms, m.p. 159-160°.

## Preparation of palladium - calcium carbonate catalyst.

Precipitated calcium carbonate (50 g.) was prepared by mixing hot solutions of appropriate quantities of A.R. calcium chloride and A.R. sodium carbonate. The calcium carbonate was suspended in water and a solution containing palladium chloride (1 g.) was added. The suspension was warmed until all the palladium was precipitated as the hydroxide upon the calcium carbonate, i.e., until the supernatant liquid was colourless. The precipitate was washed several times with distilled water by decantation, filtered with suction and washed until the washings were chloride-free, and dried. The dry palladium - calcium carbonate was kept in a tightly-stoppered bottle until required for use.

## Second Order Asymmetric Transformation of 5:5'-diisoquinolyl with (d)-tartaric acid in ethyl alcohol at 25°.

Solutions of 5:5'-di*iso*quinolyl (0.2563 g.; 1 mol.) and (d)-tartaric acid (0.3002 g.; 2 mols.) in ethanol (about 16 ml.), filtered and evaporated down to 5 ml. and stood overnight in a refrigerator at 4°. The crystals were filtered off quickly (Crawford and Smyth, *loc.cit.* stated that they went gummy at ordinary temp.) dissolved in ethanol (16 ml.) and the filtered solution immediately looked at in the polarimeter at 25°. (~~Did not know the quantity that crystallised, as didn't wait to weigh it, guess tartrate i% was about 2/3 total~~).

Readings of the observed angle with time were recorded (Table 2). A graph was made with time against $\alpha_{5461}$ (Fig. 2) and a value of $k = 0.0224$ mins.$^{-1}$ was obtained whence the half life is 1.34 mins..

Two subsequent preparations of the tartrate were carried out in the similar manner.

(a) 5:5'-Di*iso*quinolyl (1.1281 g.; 1 mol.) and (d)-tartaric acid (1.501 g.; 2 mols.) were dissolved in boiling ethanol (30 ml.), filtered hot and cooled in an ice-water. A tartrate (1.63 g.) crystallised. No mutarotation was observed even after two recrystallisations of the tartrate from ethanol.

(b) Same quantities of the *base* and *acid* were used as in (a), only they were dissolved in hot ethanol (25 ml.). The solution was filtered hot and cooled to 4°. The yellow crystals, which became gummy at room temperature was filtered quickly and dired in vacuum. The yield of 1.46 g. represented 52.5% of the total solid taken. No mutarotation was observed in ethyl alcohol.

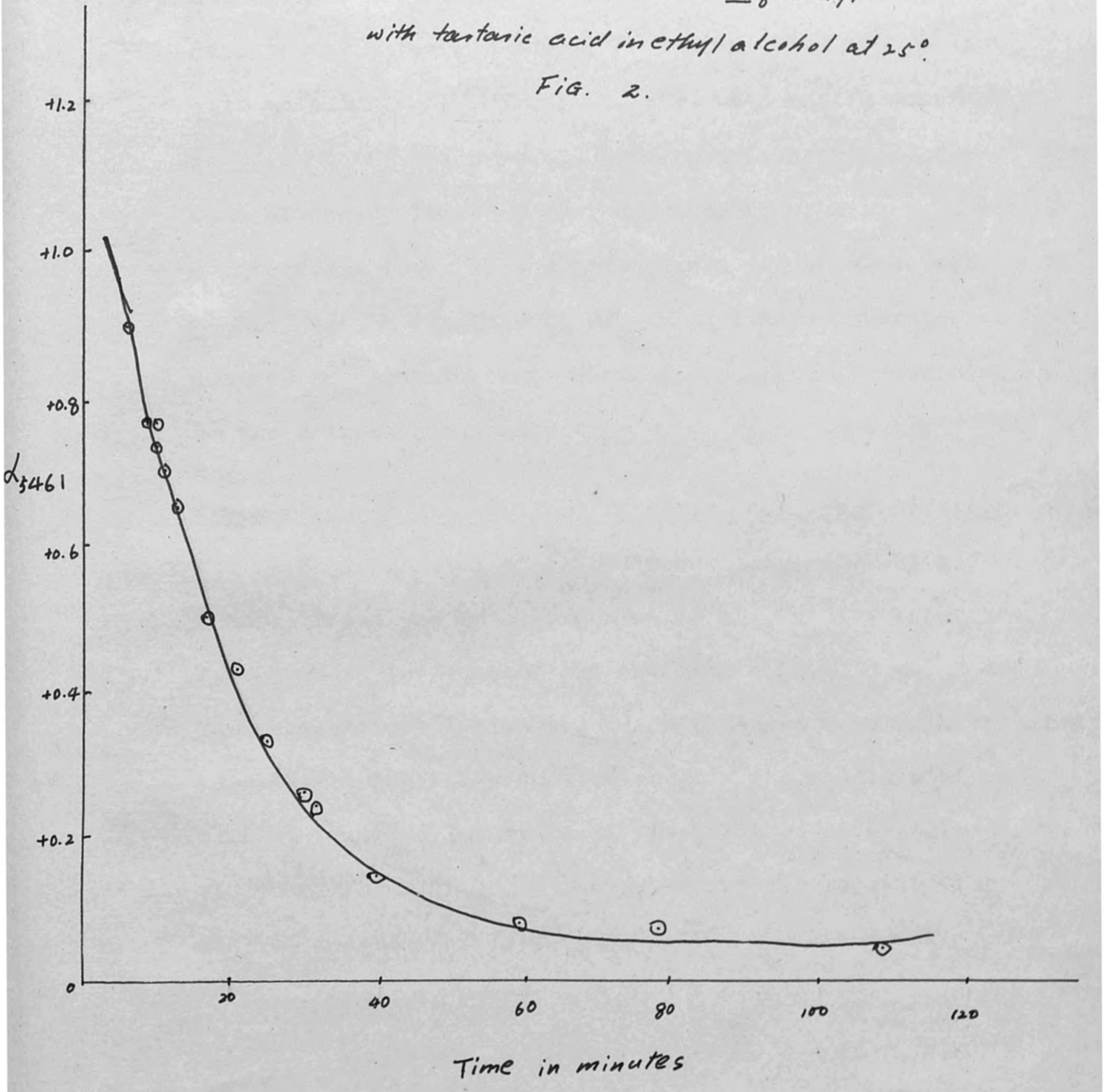
Decomposition of the salt in cold aqueous ammonia as described by Crawford and Smyth (*loc.cit.*) gave an inactive base.

## Rate of Mutarotation of 5:5'diisoquinolyl with (d)-tartaric acid in ethyl alcohol at 25°.

Table 2.

| Time (mins.) | $\alpha_{5461}$ | $\log \alpha_{5461}$ | $\log(\alpha_0 - \alpha_\infty)$ | k $mins.^{-1}$ |
|---|---|---|---|---|
| 0.00 | 1.05 | 0.0212 | - | - |
| 0.75 | 1.01 | 0.0043 | 0.0169 | 0.0225 |
| 6.00 | 0.77 | 1.8865 | 0.1347 | 0.0228 |
| 7.00 | 0.73 | 1.8633 | 0.1579 | 0.0226 |
| 8.00 | 0.70 | 1.8451 | 0.1761 | 0.0221 |
| 10.00 | 0.65 | 1.8129 | 0.2083 | 0.0208 |
| 13.50 | 0.50 | 1.6990 | 0.3322 | 0.0246 |
| 17.50 | 0.43 | 1.6335 | 0.3877 | 0.0216 |
| 20.50 | 0.35 | 1.5441 | 0.4771 | 0.0233 |
| 21.50 | 0.34 | 1.5315 | 0.4897 | 0.0226 |
| 27.50 | 0.26 | 1.4150 | 0.6062 | 0.0221 |
| 28.50 | 0.25 | 1.3979 | 0.6233 | 0.0218 |
| 106.50 | 0.06 | 2.7789 | 1.2430 | - |
| ∞ | 0.06 | | | |

Mutarotation of 5:5'- Diisoquinolyl
with tartaric acid in ethyl alcohol at 25°.
FIG. 2.



The measurment of variation of rotation with temperature was carried out in a well-lagged 2 dcm.-tube round which water was pumped at a brisk rate from a tank with an adjustable thermostat. The temperature recorded is that of the thermostat. Polarimetric readings were made at steady temperatures, mounting from point to point up the range shown in the graph; then the solution was cooled, taking readings at decending intervals of temperature down to the lowest point recorded, and finally returning to the original temperature.

### Preparation of 5:5'-diisoquinolyl in chloroform solution.

To a solution of 5·5'-di*iso*quinolyl (0.1025 g.; 1 mol.) dissolved in chloroform (16 ml.) at the temperature, T, was added (d)-camphor -10-sulphonate (0.1858 g.; 2 mols.). The resoluting solution was quickly poured into a polarimeter tube thermostatically controlled at T and readings ~~of~~ made at recorded.intervals of time, but no mutarotation was observed at 18.7$^{\circ}$. The procedure was repeated for several values of T (Fig. 3A).

Table 3 A.

| Time after wetting (in mins.) | Rdg. $\alpha_{5461}$ | Temp. °C |
|---|---|---|
| 3.4 | 1.93° | 18.7° |
| 4.0 | 1.92° | " |
| 4.7 | 1.92° | " |
| 5.5 | 1.92° | " |
| 15.0 | 1.92° | " |
| | 1.94° | 23.6° |
| | 1.91° | 26.3° |
| | 1.89° | 29.3° |
| | 1.91° | 29.9° |
| | 1.85° | 38.3° |
| | 1.82° | 44.0° |
| | 2.04° | 5.2° |

## Preparation of 2:2'-dipyridyl in chloroform solution.

A solution of the base (0.0625 g.; 1 mol.) and (d)-camphor-10-sulphonate (0.1858 g.; 2 mols.) in chloroform was made as described for the proceeding preparation and the same procedure was carried out (Fig. 3B). No mutarotation was observed.

Table 3B.

| Temp. (°C) | Rdg. $\alpha_{5461}$ |
|---|---|
| 5.0 | 1.19 |
| 14.5 | 1.18 |
| 20.9 | 1.13 |
| 27.0 | 1.11 |
| 29.9 | 1.08 |
| 40.7 | 0.99 |

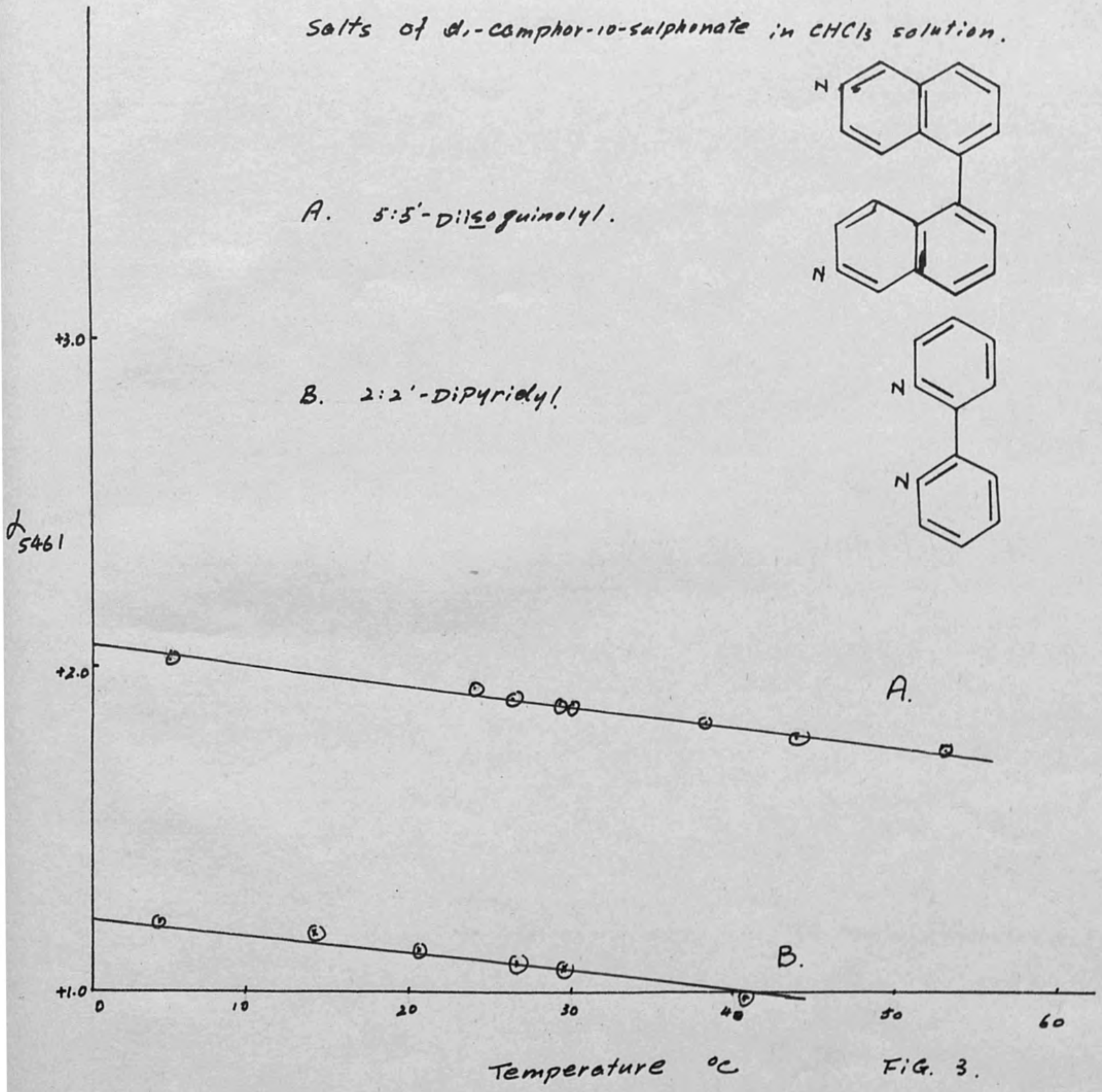

Salts of d,-camphor-10-sulphonate in CHCl3 solution.
A. 5:5'-DiIsoquinolyl.
B. 2:2'-Dipyridyl
N
N
N
N
α5461
+3.0
+2.0
+1.0
0
10
20
30
40
50
60
A.
B.
Temperature °C

FIG. 3.

# ORIENTATION EFFECTS IN THE DIPHENYL SERIES. PART XIV. THE THERMAL DECOMPOSITION OF SOME "DIAZOPERBROMIDES"

BY

SHIU MAY LOH

AND

E. E. TURNER

Preprinted from the
Journal of the Chemical Society, April, 1955, pages 1274—1277.

# *Orientation Effects in the Diphenyl Series. Part XIV.**

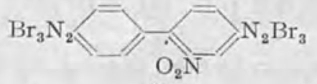
## *The Thermal Decomposition of Some "Diazoperbromides."*

By Shiu May Loh and E. E. Turner.

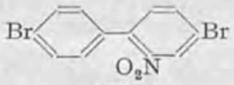
[Reprint Order No. 5982.]

The bisdiazonium perbromide derived from 2-nitrobenzidine decomposes in hot glacial acetic acid to give 2′ : 4 : 4′-tribromo- and 4 : 4′-dibromo-2-nitrodiphenyl. The tribromo-compound appears to be formed by an intramolecular mechanism.

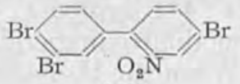
It was observed by Le Fèvre and Turner (*J.*, 1926, 2041) that the bisdiazonium perbromide (I) derived from 2-nitrobenzidine behaved abnormally when allowed to decompose in hot glacial acetic acid, the product most easily isolated being a tribromonitrodiphenyl, m. p. 195—196°, instead of the expected 4 : 4′-dibromo-2-nitrodiphenyl (II), m. p. 124°. Shaw and Turner (*J.*, 1932, 285) obtained the dibromo-compound and no tribromo-compound by carrying out the decomposition in boiling ethanol (cf. Saunders, *Amer. Chem. J.*, 1891, **13**, 496). The tribromo-compound was regarded by Le Fèvre and Turner as being 3′ : 4 : 4′-tribromo-2-nitrodiphenyl (III) since (*a*) it seemed inconceivable that the third bromine atom had entered the nucleus bearing the nitro-group and (*b*) by analogy with the nitration of 4 : 4′-dibromo-2-nitrodiphenyl, 3′-substitution seemed to be more probable than 2′-substitution. The most interesting thing, of course, was the entry of the third bromine atom into what would be regarded as a non-reactive system.



(I)



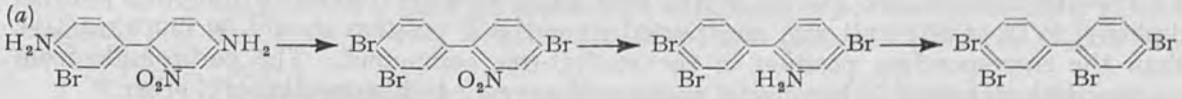
(II)



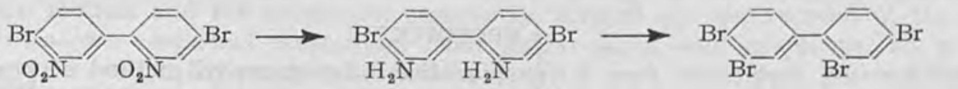
(III)

Reduction of the tribromo-compound gave a tribromo-aminodiphenyl, m. p. 154°, and replacement of the amino-group in this compound by bromine gave a tetrabromodiphenyl, m. p. 273°, different from 2 : 3′ : 4 : 4′-tetrabromodiphenyl, m. p. 124—125°, which was obtained from 3-bromo-2′-nitrobenzidine or from 2 : 3′-diamino-4 : 4′-dibromodiphenyl by routes *a* and *b*;

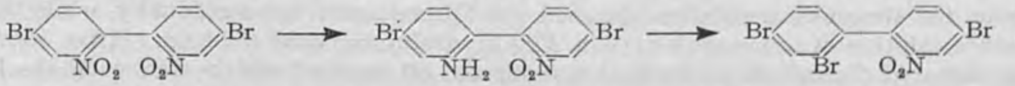
(*a*)



(*b*)



It thus seemed clear that the compound, m. p. 195—196°, must be 2′ : 4 : 4′-tribromo-2-nitrodiphenyl (IV). This has been proved by performing the operations shown below:



(IV)

The product was identical with the compound of m. p. 195—196° and was convertible in two stages into 2 : 2′ : 4 : 4′-tetrabromodiphenyl, m. p. 273°. The latter was also obtained by carrying out a benzidine rearrangement on 2 : 2′-dibromohydrazobenzene, followed by a diazonium perbromide replacement. It could not, however, be isolated from the mixture obtained by heating 2 : 4-dibromoiodobenzene with copper powder.

---

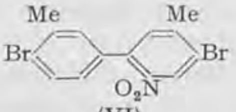
* Part XIII, *J.*, 1937, 266.

The decomposition of the bisdiazonium perbromide derived from 2-nitrobenzidine proceeds with some tar formation in boiling glacial acetic acid but has now been found to give an easily worked product when the decomposition in acetic acid is carried out at 95°. This has enabled us to make a more complete study of the decomposition, which under these conditions gives the tribromonitro-compound together with about twice its weight of 4 : 4′-dibromo-2-nitrodiphenyl. This is of some importance, as it supports the suggestion that the dibromo-compound, as such, is not the precursor of the tribromo-compound. This suggestion became more acceptable when we found that decomposition of the bisdiazonium perbromide in acetic acid in presence of one molecular proportion of the dibromo-compound gave the same yield of tribromo-compound as was obtained in absence of the dibromo-compound. Incidentally, we had already tried but failed to effect the bromination of the dibromonitro-compound by the action of bromine in boiling acetic acid solution.

It seems reasonable to conclude that in the decomposition of the bisdiazonium perbromide derived from 2-nitrobenzidine the diazonium group attached to the ring containing the nitro-group is (perhaps unexpectedly) less stable than the other diazonium group, so that bromination leading to the tribromonitro-compound occurs while the ring not containing the nitro-group retains the (*meta*-directing) diazonium grouping. Only in this way can one account for the 2′-bromination. The hitherto unknown 2 : 4 : 4′-tribromodiphenyl has been prepared from 4 : 4′-dibromo-2-nitrodiphenyl, in two stages. An attempt to obtain 2′ : 4 : 4′-tribromo-2-nitrodiphenyl by nitrating it under a number of different experimental conditions resulted in dinitration. The product appears to be 2′ : 4 : 4′-tribromo-3 : 5′-dinitrodiphenyl (V), since it reacts with hot piperidine to give a bromodinitrodipiperidinodiphenyl.

When the bisdiazonium perbromide was allowed to decompose in heated glacial acetic acid containing one molecular proportion of cinnamic acid or acetanilide or aceto-*p*-toluidide, 4 : 4′-dibromo-2-nitrodiphenyl but no tribromonitrodiphenyl was formed (cf. Bülow and Schmachtenburg, *Ber.*, 1908, **41**, 2607).

(V)



(VI)

The more general scope of the diazonium perbromide decomposition reaction has been examined in a number of cases : the perbromide derived from benzidine decomposed in boiling ethanol to give 4 : 4′-dibromodiphenyl, and in hot glacial acetic acid to give 2 : 2′ : 4 : 4′-tetrabromodiphenyl. That from 4-aminodiphenyl in boiling ethanol gave 4-bromodiphenyl, and in hot glacial acetic acid gave 4 : 4′-dibromodiphenyl. That from 2-nitro-*o*-tolidine in hot glacial acetic acid gave 4 : 4′-dibromo-3 : 3′-dimethyl-2-nitrodiphenyl (VI); this result was unexpected since the 2′-position should be more reactive than the corresponding position in the methyl-free compound. The perbromide from 4-aminodiphenyl ether in hot glacial acetic acid gave 4 : 4′-dibromodiphenyl ether.

## EXPERIMENTAL

*Bisdiazonium Perbromide from 2-Nitrobenzidine.*—An improved method of preparing this compound was as follows : A solution of 2-nitrobenzidine (11·5 g.) in a hot mixture of 47% hydrobromic acid (72 g.) and water (144 c.c.) was cooled rapidly to about −2°. A solution of sodium nitrite (7·5 g.) in water (18 c.c.) was rapidly stirred into the paste, under the surface. After 10 min. the almost clear solution obtained was filtered and treated gradually, while being stirred, with a solution of bromine (8 c.c.) in 47% hydrobromic acid (50 c.c.). After 15 min. the orange-coloured diazonium perbromide was filtered off, washed with water, with absolute ethanol, and with dry ether and dried in a vacuum over solid potassium hydroxide and concentrated sulphuric acid (yield, 35·5 g., 96·5%).

*Decomposition of the Bisdiazonium Perbromide.*—(a) *In glacial acetic acid at* 95° ± 3°. The perbromide (7·33 g.) was added gradually to glacial acetic acid (40 c.c.) kept at 95° ± 3°. Then the solution was boiled until free from bromine. On cooling, a thick paste was obtained. Water was added to complete the separation of solid. The resulting paste was filtered off, washed with water, and dried at 100° and later in a vacuum (over $H_2SO_4$ and KOH) (yield, 3·85 g.) (Found : Br, 48·2. Calc. for $C_{12}H_6O_2NBr_3$ : Br, 55·5. Calc. for $C_{12}H_7O_2NBr_2$ : Br, 44·8%). By extracting twice with 50 c.c. of boiling light petroleum (b. p. 60—80°) this was freed from 4 : 4′-dibromo-2-nitrodiphenyl and gave 1·7 g. of 2′ : 4 : 4′-tribromo-2-nitrodiphenyl. Evaporation of the light petroleum extract gave 2·15 g. of almost pure dibromo-compound, which after crystallisation from ethanol had m. p. 124°, alone or mixed with 4 : 4′dibromo-2-nitrodiphenyl.

(b) *In glacial acetic acid containing* 4 : 4′-*dibromo-2-nitrodiphenyl.* The last experiment was repeated but with the initial addition of 3·57 g. (1 mol.) of 4 : 4′-dibromo-2-nitrodiphenyl. The yield of mixed products was 7·42 g., *i.e.*, 3·85 + 3·57 g.

(c) *In glacial acetic acid containing cinnamic acid or acetanilide or aceto*-p-*toluidide.* The perbromide was added to glacial acetic acid (at 100°) containing one of these substances (1 mol. for each mol. of perbromide). Routine methods led in each case to the isolation of 4 : 4′-dibromo-2-nitrodiphenyl, but no tribromonitrodiphenyl.

3′ : 4 : 4′-*Tribromo-2-nitrodiphenyl.*—3-Bromo-2′-nitrobenzidine (Lesslie and Turner, *J.*, 1933, 1590) was diazotised in hydrobromic acid solution at −4°. Addition of bromine in hydrobromic acid gave the yellow bisdiazonium perbromide. This was filtered off, washed with water, and dried in a vacuum. It was added gradually to glacial acetic acid kept at 100—110°. The solution was freed from bromine by boiling. On cooling, the *tribromonitro-compound* separated. After being crystallised from glacial acetic acid it formed leaflets, m. p. 141—142° (Found : Br, 55·0. $C_{12}H_6O_2NBr_3$ requires Br, 55·0%).

2-*Amino*-3′ : 4 : 4′-*tribromodiphenyl.*—A solution of the preceding nitro-compound in hot glacial acetic acid was treated with just over the calculated quantity of stannous chloride dissolved in concentrated hydrochloric acid. The mixture was boiled for a few minutes and then cooled, treated with excess of aqueous sodium hydroxide, and extracted with ether. The extract gave 2-*amino*-3′ : 4 : 4′-*tribromodiphenyl*, which crystallised from ethanol in needles, m. p. 78° (Found : Br, 58·8. $C_{12}H_8NBr_3$ requires Br, 59·0%).

2 : 3′ : 4 : 4′-*Tetrabromodiphenyl.*—(*a*) A solution of the aminotribromodiphenyl in glacial acetic acid was added gradually to a solution of sodium nitrite in concentrated sulphuric acid at 0°. The mixture was poured on ice and the solution obtained by filtration treated with bromine–hydrobromic acid. The precipitated perbromide was filtered off, washed, and dried in a vacuum ($H_2SO_4$). It was then gradually added to glacial acetic acid at 100°. The solution was freed from bromine by boiling and then cooled. The *tetrabromodiphenyl* which separated was crystallised from glacial acetic acid and formed needles, m. p. 124—125° (Found : Br, 67·5. $C_{12}H_6Br_4$ requires Br, 68·1%).

(*b*) 2 : 3′-Diamino-4 : 4′-dibromodiphenyl was diazotised in hydrochloric acid, and the bisdiazonium perbromide was precipitated in the usual way. It was decomposed in glacial acetic acid at 100°. The tetrabromodiphenyl obtained had m. p. 124—125° alone or when mixed with the product from (*a*).

2-*Amino*-2′ : 4 : 4′-*tribromodiphenyl.*—Reduction of the corresponding 2-nitro-compound, m. p. 195—196°, with stannous chloride in concentrated hydrochloric acid–glacial acetic acid, followed by normal procedure, gave the *base*, which after being crystallised from dilute alcohol (charcoal) and then from benzene formed rods, m. p. 154° (Found : Br, 58·8. $C_{12}H_8NBr_3$ requires Br, 59·1%).

2 : 2′ : 4 : 4′-*Tetrabromodiphenyl.*—(*a*) The foregoing base was diazotised by the acetic–sulphuric acid method and the diazonium perbromide formed and decomposed in the usual way. The *tetrabromo-compound* crystallised from glacial acetic acid as prisms, m. p. 273° (Found : Br, 68·2. $C_{12}H_6Br_4$ requires Br, 68·05%).

(*b*) 2 : 2′-Dibromobenzidine was diazotised and the bisdiazonium perbromide prepared, and then decomposed in hot glacial acetic acid. The tetrabromodiphenyl crystallised from the latter solvent in needles, m. p. 273° (Found : Br, 68·5%).

2-*Amino*-4 : 4′-*dibromo*-2′-*nitrodiphenyl.*—To a hot, well-stirred solution containing sulphur (1·6 g.), sodium sulphide (+$9H_2O$) (9·0 g.), and water (12 c.c.), was added an ethanolic solution of 4 : 4′-dibromo-2 : 2′-dinitrodiphenyl (10 g.). The solution was boiled for an hour, boiling water being added from time to time to maintain the volume. The solution was cooled and the orange-coloured precipitate filtered off. By extraction with dilute hydrochloric acid and precipitation with dilute aqueous ammonia and finally crystallisation from ethanol, 2-*amino*-4 : 4′-*dibromo*-2′-*nitrodiphenyl* was obtained as needles, m. p. 103—104° (Found : C, 39·8; H, 2·5; N, 7·7; Br, 42·7. $C_{12}H_8O_2N_2Br_2$ requires C, 40·0; H, 2·2; N, 7·6; Br, 43·0%).

2′ : 4 : 4′-*Tribromo-2-nitrodiphenyl.*—The foregoing base was diazotised by the acetic–sulphuric acid process. The diazonium perbromide was prepared, and decomposed in hot glacial acetic acid. The tribromonitrodiphenyl obtained had m. p. 195—196°, alone or when mixed with the product from 2-nitrobenzidine.

*2-Amino-*4 : *4′-dibromodiphenyl.*—4 : 4′-Dibromo-2-nitrodiphenyl was reduced in hot acetic–hydrochloric acid solution with stannous chloride. The cooled mixture was added to excess of dilute aqueous sodium hydroxide. The solid which separated was filtered off, washed with water, and crystallised from light petroleum (b. p. 60—80°) or from ethanol. The *2-amino-*4 : *4′-dibromodiphenyl* formed needles, m. p. 130° (Found : Br, 48·7. $C_{12}H_9NBr_2$ requires Br, 48·9%).

2 : 4 : *4′-Tribromodiphenyl.*—The foregoing base was diazotised by the acetic–sulphuric acid method. The diazonium perbromide was prepared and decomposed in hot acetic acid. The *tribromodiphenyl* obtained crystallised from ethanol in needles, m. p. 81° (Found : Br, 61·5. $C_{12}H_7Br_3$ requires Br, 61·4%).

*Nitration of* 2 : 4 : *4′-Tribromodiphenyl.*—The tribromo-compound was dissolved in 10 parts of warm nitric acid (*d* 1·5). On cooling, a solid separated and this crystallised from ethanol in needles, m. p. 164—165° (Found : Br, 49·8. $C_{12}H_5O_4N_2Br_3$ requires Br, 49·9%). This is regarded as 2 : 4 : *4′-tribromo-3′* : *5-dinitrodiphenyl.* When heated with excess of piperidine for a few minutes it gave *2-bromo-3′* : *5-dinitro-4* : *4′-dipiperidinodiphenyl*( ?), orange-red needles, m. p. 145—146°, from ethanol (Found : Br, 16·4. $C_{22}H_{25}O_4N_4Br$ requires Br, 16·4%).

2 : *4-Dibromoiodobenzene.*—2 : 4-Dibromoaniline hydrochloride (29 g.) was diazotised in aqueous hydrochloric acid by aqueous sodium nitrite. The diazonium solution was added to potassium iodide solution and the solid which separated was steam-distilled from aqueous sodium hydroxide (yield, 27 g.). The dibromoiodobenzene crystallised from ethanol in needles, m. p. 45—46° (3·414 mg. gave 5·847 mg. of AgBr + AgI. Calc. for $C_6H_3Br_2I$ : 5·759 mg.).

*Bisdiazonium Perbromide from Benzidine.*—Benzidine was diazotised in aqueous hydrochloric acid and the bisdiazonium perbromide precipitated in the usual manner, then decomposed as follows : (a) *In boiling ethanol.* The crude product after crystallisation from methanol had m. p. 164° and was identical with 4 : 4′-dibromodiphenyl. (b) *In glacial acetic acid at* 100°. The product, after crystallisation from glacial acetic acid, had m. p. 273° and was identical with 2 : 2′ : 4 : 4′-tetrabromodiphenyl.

*Diazonium Perbromide from 4-Aminodiphenyl.*—The perbromide, obtained in the usual way, was decomposed as follows : (a) *In boiling ethanol.* The product, after being crystallised from benzene, had m. p. 89° and was identical with 4-bromodiphenyl. (b) *In glacial acetic acid at* 100°. The product melted at 164°, after crystallisation from methanol, and was identical with 4 : 4′-dibromodiphenyl.

*Bisdiazonium Perbromide from 2-Nitro-*o*-tolidine.*—2-Nitro-*o*-tolidine was diazotised in hydrochloric acid and the bisdiazonium perbromide prepared in the usual manner. When it was decomposed in hot glacial acetic acid it gave 4 : *4′-dibromo-3* : *3′-dimethyl-2-nitrodiphenyl* which, after being crystallised from glacial acetic acid, formed needles, m. p. 240—241° (Found : Br, 42·2. $C_{14}H_{11}O_2NBr_2$ requires Br, 41·6%).

*Diazonium Perbromide from 4-Aminodiphenyl Ether.*—This was prepared in the normal manner. When decomposed in hot glacial acetic acid it gave 4 : 4′-dibromodiphenyl ether, which after being crystallised from ethanol had m. p. 60°.

BEDFORD COLLEGE, UNIVERSITY OF LONDON.

[*Received, December 20th*, 1954.]

PRINTED IN GREAT BRITAIN BY RICHARD CLAY AND COMPANY, LTD.,
BUNGAY, SUFFOLK.

The work carried out in Section II was according to the following Scheme:-