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A.

Thesis for the degree of Doctor of Philosophy in
the University of Durham, presented by
OLIVER STEPHENSON, B.Sc., A.I.C.,
of Bede College, Durham.

PART I.

REACTIONS OF THE DIAZOCYANIDES.

PART II.

THE PREPARATION OF CINNOLINE DERIVATIVES.



B.

The experimental work described in this thesis was carried out in the laboratories of the Durham Colleges under the supervision of Dr. W.A. Waters, during the session 1938-1939, and Dr. J.C.E. Simpson, during the session 1939-1940.

A summary of the work described has been published in the Journal of the Chemical Society in two papers -

- (a) DECOMPOSITION REACTIONS OF THE AROMATIC DIAZO-COMPOUNDS. PART VIII. THE DIAZOCYANIDES.

By Oliver Stephenson and William A. Waters.

J.C.S. 1939, 1796 - 1804.

- (b) CINNOLINES. PART I. SOME NEW EXAMPLES.

By James C.E. Simpson and Oliver Stephenson.

J.C.S. 1942, 353 - 358.

C.

Grateful thanks are due to Dr. W.A. Waters, and
Dr. J.C.E. Simpson, for their helpful guidance and
encouragement during the carrying out of the experimental
work described in this thesis.

P A R T I.

REACTIONS OF THE DIAZOCYANIDES.

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SECTION I.HISTORICAL INTRODUCTION.

At Marburg in 1858, Peter Griess¹ prepared the first aromatic diazo compound from picramic acid in the course of an investigation suggested by Kolbe. Even at this early date, some knowledge of the action of nitrous acid on the amino-group was already in existence, and it was known that amino-benzoic acid could be converted to hydroxybenzoic acid by the action of warm nitrous acid. Griess however carried out his experiments on picramic acid in cold alcoholic solution and obtained a substance which had none of the properties of hydroxy-picramic acid.

This discovery of Griess' attracted wide attention, and the properties and main reactions of the diazo-compounds were widely explored, and by 1863, azo-dyestuffs obtained from them, were being manufactured.

Griess' original method of preparation of these compounds involved the treatment of a cold alcoholic solution of the amine with nitrous fumes, but this cumbersome method was soon superseded by others, a brief survey of which is given in the following table.²

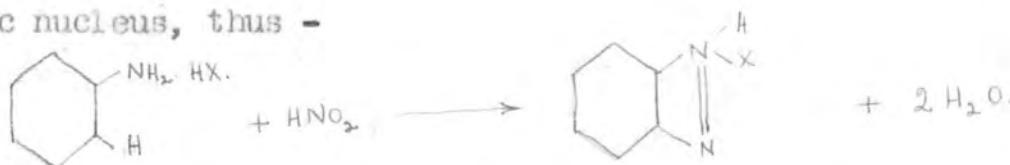
In general characteristics however, all the methods are the same in that they ultimately treat the amine salt with cold nitrous acid, according to the equation -



T A B L E I.

REACTION TECHNIQUE	SPHERE OF EMPLOYMENT
1. A solution of a metallic nitrate is added to a cold solution of the amine in mineral acid $\text{Ar-NH}_2 + 2\text{HX} + \text{NaNO}_2 \longrightarrow \text{Ar-N}_2\text{X} + \text{NaX} + 2\text{H}_2\text{O}$ The DIRECT method.	(a) Strongly basic amines giving salts readily soluble in aqueous mineral acids. (b) Amines sulphonated sufficiently to be soluble in acid solution.
2. Mixed alkaline solutions of a metallic nitrate and a salt of a sulphonated or carboxylated amine are run into an excess of cold mineral acid $\text{Ar}-\text{NH}_2-\text{SO}_3\text{Na} + \text{NaNO}_2 + 3\text{HX} \longrightarrow \text{Ar}-\text{N}_2\text{X}-\text{SO}_3\text{H} + 2\text{NaX} + 2\text{H}_2\text{O}$. The INVERTED method.	(a) Amino-acids such as sulphamic acid, amino-benzoic acid, naphthionic acid. (b) Some weakly basic amines e.g. p. nitroaniline.
3. The amine is dissolved in a concentrated acid (sulphuric, phosphoric, glacial acetic) and diazotised with nitrosyl sulphuric acid. $\text{Ar-NH}_2 + \text{NaHSO}_4 \longrightarrow \text{Ar-N}_2\text{HSO}_4 + \text{H}_2\text{O}$	For weakly basic amines
4. The amine is dissolved in nitric acid and metabisulphite added. WITT'S method.	For weakly basic amines which are not easily oxidised or nitrated.
5. The amine salt is suspended or dissolved in a little water or alcohol and treated with nitrogen trioxide GRIESS' method.	For affecting diazotisation so that the solid diazo-salts may be subsequently isolated.
6. The amine salt is dissolved in water, acids or alcohol, or suspended in an inert solvent and treated with an alkyl nitrite $\text{Ar-NH}_2\text{-HX} + \text{Alk-NO} \longrightarrow \text{Ar-N}_2\text{X} + \text{Alk-OH} + \text{H}_2\text{O}$ KNOEVENAGEL'S method.	

Griess called his new compounds the "diazo-compounds" because he believed that they owed their genesis to the replacement of two atoms of hydrogen by two atoms of nitrogen in the aromatic nucleus, thus -



This idea was shown to be false however, when pentasubstituted anilines were found to diazobise without loss of a substituent.³

We know now that the characteristic group of the aromatic diazo-compounds consists of two nitrogen atoms which have replaced one hydrogen atom in the aromatic nucleus. The group can show both basic and acidic properties in that salts of the general formula $[Ar.N_2^+] X^-$ are formed with acids, and of the formula $[Ar.N_2.O^-] Na^+$ with bases. In addition there are non-ionic derivations such as the diazo-cyanides $Ar.N_2.CN$, which can not be placed in either of the previous categories.

GENERAL PROPERTIES OF DIAZO-CYANIDES.

When cyanides in aqueous solution act on diazo salts which are free from sulphonic or carboxylic groups, coloured diazo-cyanides are precipitated -



The reaction differs from the normal coupling reaction in that the solution must remain acid until combination is complete (cf - pages 9-10).

The first mention of this reaction was in 1865 when Kunze and Hubner⁴ brought diazo-compounds into reaction with potassium cyanide, and in 1876, Griess⁵ made some investigations. It was in this latter year that Gabriel⁶ isolated the double cyanide of benzene diazocyanide - $C_6H_5\text{N=N.CN; HCN}$, by adding cold diazotised aniline to an excess of a cold concentrated solution of potassium cyanide, obtaining the above compound in fine yellow needles (m.p. 70°) from petrol. A corresponding compound was prepared from p. Chlor aniline.

The first free diazocyanide was obtained nearly twenty years later by Hantzsch and Schultze⁷, by reversing Gabriel's process and adding the cyanide solution to the diazo solution in hydrochloric acid at -5°C . They found that a more stable isomer was formed when the reaction was carried out above this temperature. Further investigation showed that almost all diazocyanides could be isolated in two forms, one labile (syn- or cis-); the other stable (anti- or trans-).

The following table illustrates the main differences between the labile and stable isomeric diazocyanides derived from p. chloraniline.

T A B L E II.

Comparison of the syn-and anti-diazocyanides derived from p. chloraniline.

	LABILE (SYN-) diazocyanide	STABLE (ANTI-) diazocyanide
<u>Crystal form</u>	Yellow or brown needles	Highly crystalline red or red-brown prismatic needles.
<u>Melting Point</u>	29°	$105-6^{\circ}$

<u>Alkaline B-naphthol</u>	Couples partially in alcoholic solution	Does not couple
<u>Active copper</u>	Yields the nitrile only in 1% yield in alcoholic solution along with 20% of the hydrogen substi- tution product. In acetone it gives about 10% nitrile and about 5% of the hydrogen substitution product. In non-ionising solvents decompositions involve free radicals. TARS are major products in all cases.	Unattacked in absence of light.
<u>Organic Solvents.</u>	In tautomeric equilibrium with diazonium cyanide in ionising solvent. Neutral solutions yield self-coupling products. In non-ionising solvents isomerise to anti- diazocyanides even in absence of light.	Thermally stable Converted photo- chemically to iso- meric reactive syn- cyanides in ionising solvents.
<u>Stability of dry solid.</u>	Darkens rapidly in light with some tar formation. Can be kept for long periods in cold in absence of light.	Simpler members are so stable that they can be distilled in steam.
<u>Alkaline Alcoholic Solution.</u>	Yields the diazo-imido ether, $\text{Ar-N}_2\cdot\text{C}(\text{NH})=\text{O}\cdot\text{Et}$	Yields the same diazo-imido ether.
	Di-ortho syn- and methylated syn-diazo cyanides decompose to give N_2 and the nitrile.	No decomposition. Gives the diazo-imido ether.
<u>Sulphinic Acids</u>	Yields colourless, stable additions products of the type. $\begin{array}{c} \text{Ph. N} - \text{N. CN} \\ \qquad \backslash \\ \text{So}_2 \cdot \text{Ph. H} \end{array}$ <p>Azo-benzene too gives a</p>	Same.

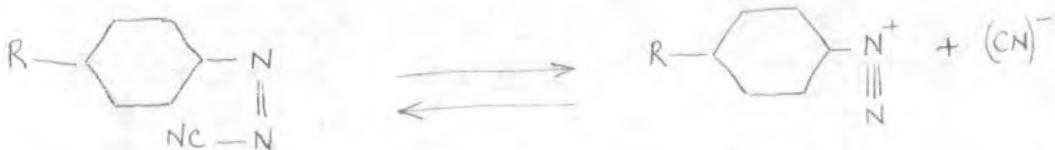
	similar compound	
<u>Hydrolysis</u>	Diazo-carbamide formed by boiling with weak acids. Further boiling with alkali yields the salt of the diazobenzene carboxylic acid.	Same.
<u>Condensation with P. Toluidine etc.</u>	Yield diazo-guan- idines. Ar.N ₂ . C = NH I NH. Tol.	Same.

SECTION 2.IONISATION OF DIAZO CYANIDES.

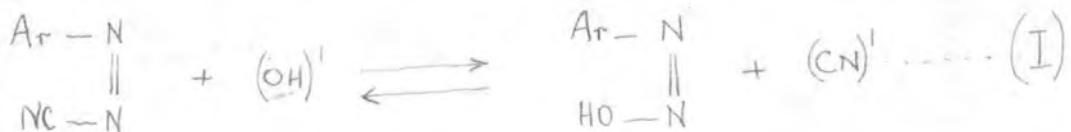
Hantzsch considered that the non-ionic diazocyanides were to be classed as azo-compounds, and believed that there should also be capable of existence diazonium cyanides, which would be true salts analogous to the diazonium chlorides. From p. anisidine he actually prepared three isomeric compounds - syn- anti- , and diazonium- cyanides (see p. 19)

The experimental work described in this thesis has done much to amplify this view. Thus, in the laboratory, we have found⁹ (see Experimental Section p. 88) that freshly prepared solutions of syn-diazocyanides in dilute alcohol, on treatment with silver nitrate in the same solvent, gave rapid precipitation of silver cyanide and left an almost colourless solution of the diazonium nitrate which coupled immediately with alkaline B-naphthol. Other metallic salts were found to behave similarly though the reaction was more complex, double cyanides being probably formed. The anti-diazocyanides being probably formed. The anti-diazocyanides did not behave thus and did not yield conducting solutions. (compare refs. 10 and 11).

This rapid precipitation of silver cyanide from syn-diazocyanides can be attributed to the fact that in ionising solvents they are in tautomeric equilibrium with the unstable diazonium cyanide, (cf. Hantzsch¹²)



and can not be due to hydrolysis



since we found that the reaction was not inhibited by additions of nitric acid.

These acidified alcoholic solutions of syn-diazocyanides were remarkably stable⁹, and gave quantitative precipitates of silver cyanide even after being kept for a considerable time.

On the other hand, neutral solutions of syn-diazocyanides in aqueous alcohol darkened rapidly on keeping for a few minutes, and then did not give quantitative precipitation of silver cyanide upon treatment with alcoholic silver nitrate. The filtrates from acidified solutions coupled instantly, but the coloured filtrates from the neutral solutions which had been allowed to stand, only coupled to a slight extent.

The amount of potential cyanide in a neutral solution decreased in about 30 minutes to a steady value which was not less than 50% of the amount of active cyanide group initially present, (see Table XV. p. 89), and the percentage of silver cyanide finally obtainable was not altered either by keeping the mixture of diazocyanide and silver nitrate for some hours before filtering, or by acidifying the mixture after the reaction in neutral solution had proceeded for some hours.

This indicates that neutral alcoholic solutions of syn-diazocyanides decompose on keeping to give products containing altered or non-ionisable cyanide groups, and can not be due to the occurrence of a tautomeric change (I), since this would not alter the total amount of silver cyanide which would be formed.

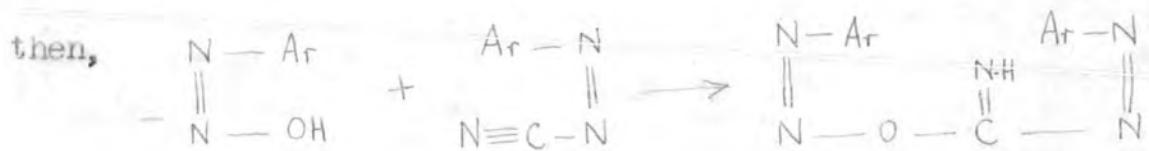
One possible product was, of course, the anti-diazocyanide, but this was evidently not the major product, since if the fall in the quantity of ionisable cyanide were solely due to the formation of anti-diazocyanide, the solution should eventually give no precipitate with silver nitrate. Moreover, alcoholic solutions of syn-diazocyanides which had been kept for some time did not yield anti-diazocyanides in any quantity if evaporated or if extracted with benzene. Free hydrogen cyanide distilled with the alcohol, and the residue was a dark tar.

It may be concluded therefore, that the moderately rapid decomposition which occurs in neutral solutions of syn-diazo-cyanides in alcohol, is due to hydrolysis and self-coupling, and one can understand why Hantzsch and his colleagues found that the syn-diazo cyanides had to be prepared by adding potassium cyanide solution to a cold acid solution or a diazonium salt, and not by adding a diazonium salt solution to an excess of an alkaline solution of potassium cyanide.

In 1919, Heller and Meyer¹³ had stressed the importance of keeping the diazo solution acidic during the addition of the potassium cyanide. They ran benzene diazonium chloride into an

excess of cold alkaline potassium cyanide and obtained a sparingly soluble, unstable red salt of the type —

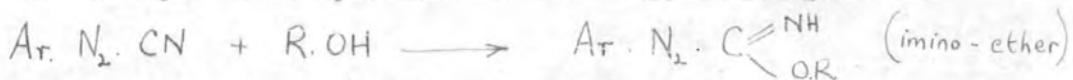
$\text{Ar}-\text{N}_2-\text{C}\begin{array}{l} \diagup \text{NH} \\ \diagdown \text{O. N}_2 \end{array} \text{Ar}$, which is apparently formed by addition of the normal diazotate to the diazocyanide following a partial hydrolysis of the diazocyanide —



or, in brief, $2 \cdot \text{Ar. N}_2\text{CN} + \text{H}_2\text{O} = \text{Ar. N}_2\text{O. C}(\text{NH}). \text{N}_2\text{Ar} + \text{HCN}$, whence 2 molecules of syn-diazocyanide should yield 1 molecule of free hydrogen cyanide.

This view of Heller and Meyer's was supported by our own work, just mentioned, on the precipitation of silver cyanide from alcoholic solutions of syn-diazocyanides, by addition of silver nitrate.

The great facility with which the cyano-group of the syn-diazocyanides would condense with compounds of the type R.OH and $\text{R}''\text{. NH}$ had been demonstrated by Hantzsch and Schultze¹⁴, who found that in the presence of a trace of alkali, alcoholic solutions of syn-diazocyanides reacted as follows —



'Gabriel's Compound', $\text{Ar. N}_2\text{CN}$; HCN , mentioned previously, was also thought to be of this type, viz. $\text{Ar. N}_2\text{C}\begin{array}{l} \diagup \text{NH} \\ \diagdown \text{CN} \end{array}$

Hantzsch also found that these same addition compounds could be made from the anti-diazocyanides and said that they must belong to the anti-series, but we have no further evidence that this is true.

SECTION 3.

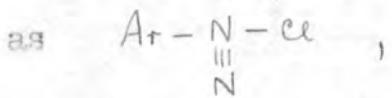
STRUCTURE of the DIAZOCYANIDES.

In order to give a comprehensive account of the structures which have been proposed for the diazocyanides, it is necessary to give a brief résumé of the structures proposed for the diazo compounds generally.

In 1866, Kekulé,¹⁵, showed that Griess' original idea that the diazo compounds were formed by replacement of the two atoms of hydrogen in the aromatic nucleus by two atoms of nitrogen was incorrect, because, as he pointed out, a mono-substituted benzene derivative remained in all reactions involving loss of the diazo nitrogen.

This was clinched later when it was shown that penta-substituted anilines could be diazobised without loss of a substituent.³ Hence, Kekulé suggested the formula $\text{Ar-N}=\text{N-Cl}$ for the diazo salt.

Three years later, Blomstrand, considering that the salt was analogous to an ammonium salt, wrote the formula



and his idea was supported by Strecker and Römer,¹⁶, on the ground that the unstable diazo compounds were unlike the stable azo-compounds whose formula was R-N=N-R .

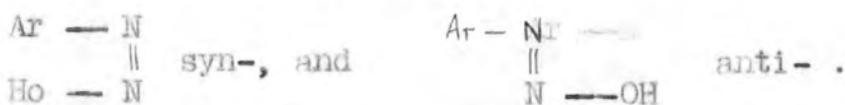
Kekulé's formula was generally accepted however, and for a time interest focussed on the practical use of the compounds rather than on their structure. In 1892 however, the question of constitution was again raised by H. von

Pechmann¹⁷, who found that toluene diazohydroxide reacted with benzoyl chloride to give nitroso toluanilide, $\text{C}_6\text{H}_4\cdot\text{N}(\text{No})\cdot\text{CO}\cdot\text{Ar}$, and hence he proposed the nitrosamine formula, $\text{Ar}\cdot\text{NH}\cdot\text{NO}$.

Two years later, the problem entered a new stage with the discovery of two isomeric potassium diazotates, $\text{Ph}\cdot\text{N} = \text{N}\cdot\text{OK}$. The first suggestion to account for the isomerism was that one salt was derived from the diazohydroxide, $\text{Ph}\cdot\text{N} = \text{N}\cdot\text{OH}$, and the other from the nitrosamine, $\text{Ph}\cdot\text{NH}\cdot\text{NO}$. In the same year, Hantzsch¹⁸, fresh from his triumphant suggestion that the isomeric oximes were geometrical and not structural isomers, extended this proposal to the isomeric diazotates and iso-diazotates. Hantzsch and Werner had shown that the oximes existed in two stereoisomerides made possible by the immobile $\text{C} - \text{N}$ bond, thus -



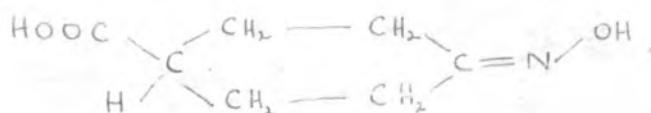
and he said that the normal and iso-diazo compounds must be derived from two isomeric diazo hydroxides, which he called the "Syn-" and "anti-" forms, thus -



The syn- molecule, rendered unstable by internal strain, was said to correspond to the normal diazo compounds, and the more stable anti- form to the iso-diazo compounds.

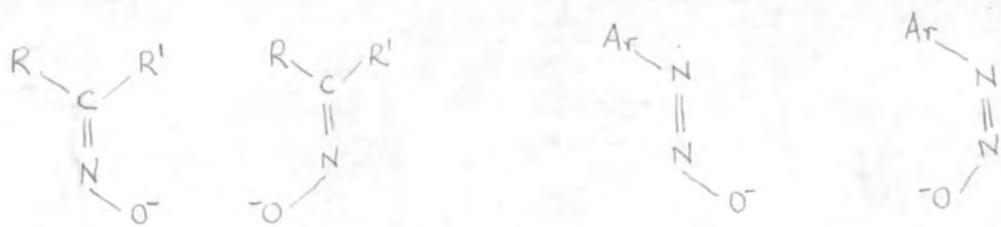
A prolonged controversy embracing this problem took place between Hantzsch and Bamberger until 1910, and led to a much clearer understanding of the conceptions of tautomerism and stereoisomerism. Further, Hantzsch, for the first time in the history of organic chemistry, used physico-chemical measurements for elucidating the structure of organic molecules, and thus some of the experimental work that he published at this time formed an important milestone in the development of organic chemistry. During the course of the controversy Hantzsch modified his views on several important points, and eventually, from the experimental material to which both parties had contributed, built up a self-consistent theory which has gained general assent.

Hantzsch's view that the isomerism of the oximes and diazo-compounds was geometrical, had much to recommend it. Without doubt we know that such isomerism exists with the unsymmetrical oximes for Mills and Bain¹⁹, have resolved the oxime of cyclohexanone carboxylic acid -

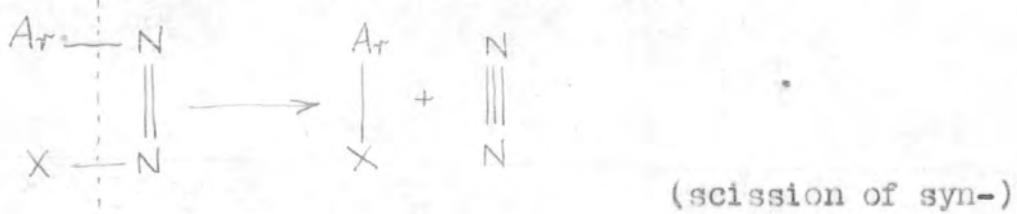


into two optically active forms. This could only occur if the molecule were rendered assymmetric by the oxime-hydroxyl group occupying a different place from that of -H and -COOH.

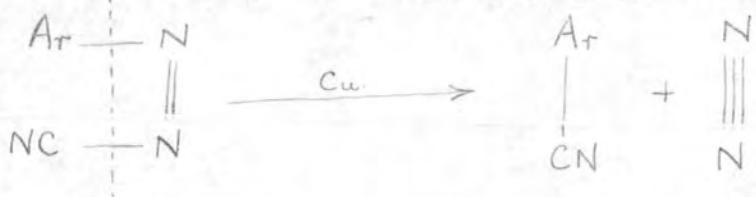
Further, they retain their difference as anions, so the analogy with the diazotate and iso-diazotate is complete.



Hantzschi had found that the unstable (syn-) diazo-compounds coupled with alkaline *B-naphthol*, whereas the stable (anti-) diazo compounds did not, and this reaction was taken as the easiest way of differentiation between the two series. Hantzschi also pointed out that the two forms differed in their manner of decomposition -



In solution the unstable form only was decomposed by copper powder, yielding the aromatic nitrile with evolution of nitrogen: Hantzschi said that this must be the syn- form and illustrated this by the following diagram -



An example of decompositions typical of the anti-diazo compounds was provided by the oxidation of benzene iso-diazotate to nitrosobenzene, which Hantzschi represented as -

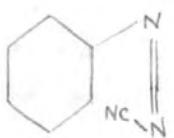


Hantzsch's assumption that the labile form had the syn-structure was based on analogy with the majority of geometrically isomeric ethylenic compounds such as maleic and fumaric acids, where the trans-isomer was the more stable.

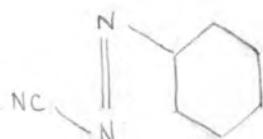
However, even in the ethylenic series there are anomalies, such as the fact that cis-dichlorethylene is more stable than trans-²⁰.

Another of Hantzsch's arguments was based on the fact that less stable diazocyanides only, yielded the nitrile with copper powder. He assumed that if two groups lay on the same side of a double-bond, they would be eliminated more readily, and he made the argument more striking by assuming that the angles between the double-bond uniting the nitrogen atoms, and the single bonds linking the aryl and hydroxyl groups, were each less than 90°.

Thus he represented the two isomers as below and said it was clearly the cis-form which would lose nitrogen more readily.



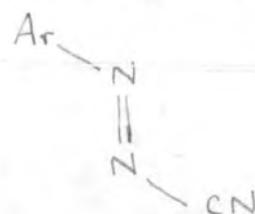
cis-



trans-

However, Hantzsch's assumptions about the angles was

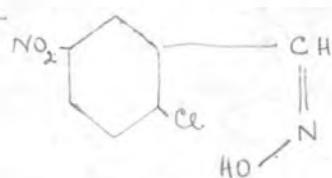
However, Hantzsch's assumptions about the angles was extremely improbable and unsupported by any evidence, since the three valencies of a trivalent nitrogen atom are arranged in space much as the three valencies of a carbon atom, so that the angle is more likely to be 125° rather than just under 90° . For this reason, the purely steric interference implied by Hantzsch's formulae is unlikely, and the 2 isomers are more accurately represented by formulae such as the following -



The fallacy of Hantzsch's geometrical theory of the relative reactivity of cis- and trans- isomers has been shown in the case of the oximes, it having been proved that the acetyl derivative of the trans-aldoxime loses acetic acid with alkali to give the nitrile, whereas the syn-aldoxime acetyl derivative was merely hydrolysed by alkali to the free oxime - just the opposite to Hantzsch's Statement.



e.g. Thus Brady and Bishop²¹, in 1925 showed that the syn-oxime of 2-chloro-5-nitro-benzaldehyde readily gave the nitrile, whereas the anti-oxime did not.



Similarly, in ethylenic geometrical isomers, trans-elimination usually takes place more readily than cis-.

As a second point, Hantzsch pointed out that certain normal diazotates containing a thiol group in the ortho-position underwent ring-closure with alkali, instead of iso-diazotate formation.³²



Here again however, the argument was incomplete because in these cases only one of the two possible isomers could be obtained, and hence it was impossible to compare the relative ease of ring-closure of the two forms.

It was fundamental to Hantzsch's theory that the decomposition reactions of the diazonium compounds should take place indirectly through the intermediate formation of the syn-diazo compound; he explained this by the following scheme³³ -



His theory thus explained why the labile and not the stable form was the invariable first product of the reaction, and further, how diazonium salts could resemble ammonium salts in the salt-forming power of their pentavalent N-atom, yet differ in the manner of their decomposition.

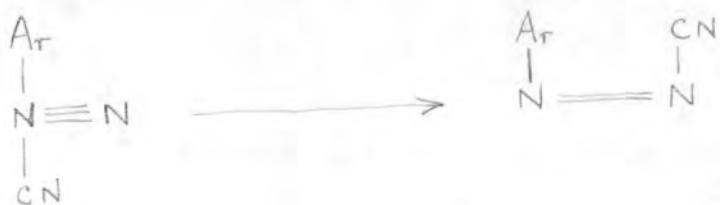
The stability of ammonium salts depends on the nature of the acid radical, whereas Cain and others³⁴ have found that

the rates of decomposition of benzene diazonium chloride, bromide, sulphate and nitrate were all practically the same. This is an argument against Hantzsch's theory as it shows that the diazonium cation can decompose in aqueous solution.

The physical properties and reactions of the diazocyanides showed that they were typical covalent compounds. They were coloured, insoluble in water, soluble in organic solvents and their solutions were non-conductors, hence Hantzsch said that they were syn- and anti- diazo- compounds, formed according to the general principles of his theory.



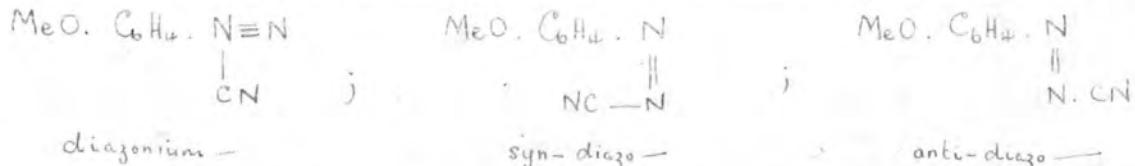
Accordingly, Hantzsch said it was to be expected that colourless, highly ionised, diazonium cyanides should be capable of existence. A clue to their existence was discovered when he found that many diazonium chlorides on treatment with silver cyanide, gave, in addition to the yellow insoluble diazocyanide, a soluble, colourless double cyanide with silver cyanide.¹⁰ Alkali cyanides could not be used for this reaction since the hydroxyl (OH) ions present caused isomerisation of diazonium to diazo-cyanide -



Hydrocyanic acid was such a weak acid that it was difficult to find a case where a solid diazonium cyanide could be isolated. However, in 1901, Hantzsch²⁵ discovered one example, and so far it has proved to be unique.

He evaporated p. anisel diazonium hydroxide with excess of HCN in vacuo at room temperature, and obtained a double cyanide of the constitution, $\text{MeO.C}_6\text{H}_4.\text{N}_2.\text{CN}; \text{HCN}; \text{H}_2\text{O}$. It had the properties of a diazonium salt, being a colourless, crystalline solid, highly ionised in aqueous solution, and giving the typical yellow colour of diazo-cyanide on treatment with alkali.

In this one case therefore, Hantzsch could point to a complete family of three isomers as demanded by his theory -



This achievement afforded strong support for the stereochemical theory, but unfortunately there is little chance of isolating many more solid diazonium cyanides.

The experimental work of this thesis however (p. 88 —) strengthens Hantzsch's main contentions, but modifies them in some respects. (p. 7 —).

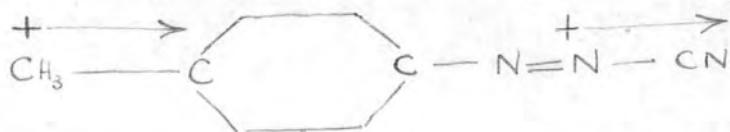
Hydrocyanic acid occupies an anomalous place among the acids, and its structure has only in recent years received a

satisfactory explanation on the electronic theory.²⁶ Acids stronger than hydrocyanic only give the stable diazonium salt, and weaker ones only yield the diazo-compounds.

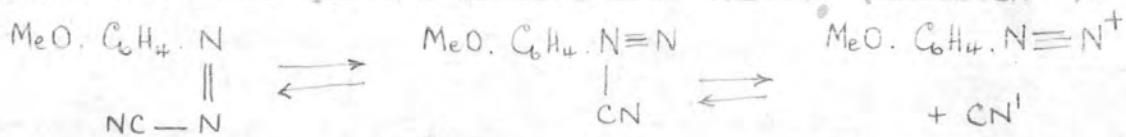
Thus in p. chlorobenzene diazocyanide, the chlorine atom tends to attract electrons from the - CN group, thus strengthening the covalent bond N—CN, and retarding ionisation as shown -



With a positive group in the nucleus, the opposite occurs and tendency to ionise is increased, thus -



e.g. when the diazo-cyanides of p-anisole or ϕ - cumene are dissolved in water, the equilibrium concentration of diazonium cyanide can reach quite a considerable value. (Hantzsch²⁵).



Our own experimental work showed that treatment of diazotised toluidines with potassium cyanide yielded unstable tarry products, whereas 4-chloro-o-toluidine and 5-chloro-o-toluidine both gave well-defined syn- and anti- diazocyanides. (See Experimental Section - pages 86-7)

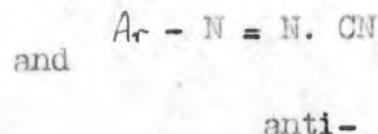
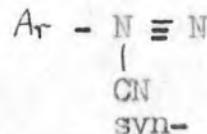
The most weakly negative substituents influence the equilibrium so greatly in favour of the diazo-forms that, in

general, only syn- and anti- diazocyanides can be isolated. In the following table, (Hantzsch, loc. cit.) certain diazo-cyanides are compared from the point of view of their tendency to ionise to the diazonium form.

T A B L E III.
IONISATION OF CERTAIN DIAZO-CYANIDES.

SOLID SYN-DIAZOCYANIDE	NORMAL DIAZOCYANIDE SOLUTION	NORMAL DIAZO-HYDROXIDE SOLUTION (Diazonium hydroxide)
(a) $(\text{CH}_3)_3\text{C}_6\text{H}_2\cdot \text{N}_2\cdot \text{CN}$ (b) p. $\text{CH}_3\text{O}\cdot \text{C}_6\text{H}_4\cdot \text{N}_2\cdot \text{CN}$ Easily soluble in acid solution	Almost completely isomerised and ionised to the diazonium cyanide	$(\text{CH}_3)_3\text{C}_6\text{H}_2\cdot \text{N}_2\cdot \text{OH}$ p. $\text{CH}_3\text{O}\cdot \text{C}_6\text{H}_4\cdot \text{N}_2\cdot \text{OH}$ $K =$ extremely large.
$\begin{array}{c} \text{C}_6\text{H}_5 - \text{N} \\ \\ \text{NC} - \text{N} \end{array}$	Probably exists for greater part as diazonium cyanide	$\text{C}_6\text{H}_5\cdot \text{N}_2\cdot \text{OH}$ $K = 0.123$
p. Br. $\text{C}_6\text{H}_4\cdot \text{N}_2\cdot \text{CN}$ Dissolves slowly in hydrochloric acid.	Perhaps 50% as diazonium and 50% as syn-diazo.	p. Br. $\text{C}_6\text{H}_4\cdot \text{N}_2\cdot \text{OH}$ $K = 0.0149$
2:4-B ₂ . C ₆ H ₃ . N ₂ . CN Difficulty soluble in hydrochloric acid.	Small amount of diazonium - Greater part as syn-diazo.	2:4-B ₂ . C ₆ H ₃ . N ₂ . OH $K = 0.0136$
2:4:6-B ₃ . C ₆ H ₂ . N ₂ . CN Insoluble in hydrochloric acid	Probably only exists as Syn-diazo. Not much investigated on account of its insolubility.	2:4:6-B ₃ . C ₆ H ₂ . N ₂ . OH $K = 0.0014$

From 1895-7, Bamberger²⁷ and Blomstrand²⁸ had worked on the idea that the syn-diazocyanide was a diazonium cyanide, and the anti-a diazocyanide as shown -



but this theory was disproved by Hantzsch's discovery of the three isomerides of p. anisidine diazocyanide.

Orton,²⁹ suggested that the syn-diazocyanide was an isocyanide of anti-structure, thus -



This view of Orton's would however, seem to be disproved by the observation of Hantzsch and Schultze¹⁴, that both the syn- and anti- series gave rise to the same diazobenzene carboxylic acid, Ar. N=N. COOH. According to the stereochemical theory however, the labile syn-compound might pass into the more stable anti-diazocyanide before hydrolysis.

Hantzsch offered no other proof against Orton's idea, he merely stated that neither was an isocyanide. Orton's view was definitely disproved in 1938 by Le Fèvre and Vine³⁰, who made measurements of the dipole moments of several diazocyanides and proved -

(1) that both syn- and anti- compounds were nitriles and not isonitriles, and

(2) that Hantzsch was correct in assigning the anti-diazo structure $R - \text{C}_6\text{H}_4 - \text{N} \equiv \text{N} \cdot \text{CN}$, to the stable isomers.

Orton's suggestion was disproved by the fact that there was not even approximately a constant difference in dipole moments between all pairs of isomeric diazocyanides, independent of the nature and position of the substituents, R.

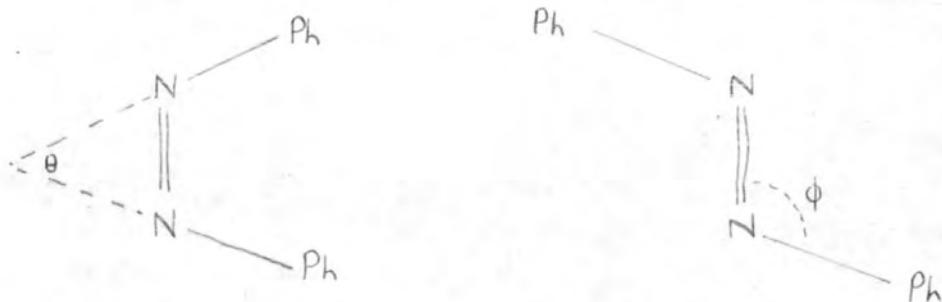
The following results were obtained by Le Fèvre and Vine -

T A B L E IV.
DIPOLE MOMENTS OF ISOMERIC DIAZOCYANIDES.

MATURE and POSITION of SUBSTITUENT	DIPOLE MOMENT (D*)
CIS -	TRANS-
4 - CHLORO -	2.93
4 - BROMO -	2.91
4 - NITRO -	2.04
3 - BROMO -	3.79
2.4.6 - TRIHOMO	2.50

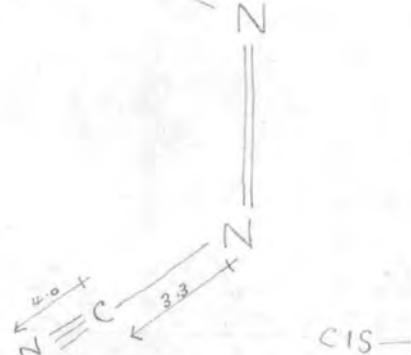
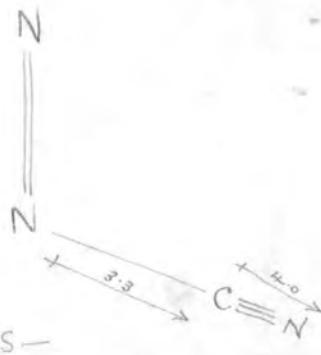
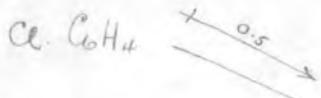
* Denbye Units = E.S.U. $\times 10^{-18}$

The moment of cis-azobenzene has been found to be 3.0.³¹



The angle ϕ in transazobenzene has been found to be ca. 130° by crystal analysis, which makes the angle θ , in cis-azobenzene, about 80° . Hence, since $2\mu \cos \frac{1}{2}\theta = 3.0$, then the $C_6H_4 \longrightarrow N_2$ link moment is ca. 3.0.

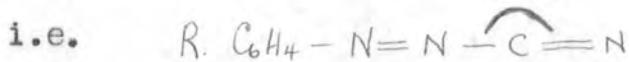
The following sketches represent cis- and trans-p.chlorodiazocyanide.



26.

The $\text{C}_6\text{H}_5 \rightarrow \text{Hal}$. moment is ca. 1.5, and the resultant of the p-Hal- $\text{C}_6\text{H}_4-\text{N}_2-$ group will be ca. 0.5, directed towards the azo-group as shown. The moment associated with the $-\text{C}\equiv\text{N}$ group itself (c.4.0) will be much greater than any opposing $\text{N}_2 \leftarrow \text{CN}$ moment, and the resultant will be directed away from the azo-group. Thus, the moment of the stable- is decidedly greater than the moment of the labile form, and this agrees with Hantzsch's configurations.

(NOTE - (Stephenson and Waters⁹) - Both syn- and anti-forms of the diazocyanides are much more stable than the corresponding diazohydroxides, and this can be attributed to the fact that the conjugation of the $\text{C}\equiv\text{N}$ and $\text{N}=\text{N}$ groupings makes the whole molecule one concordant resonance system, comparable with azobenzene. In accordance with this view, it is found that the dipole moment of the group $\text{N}=\text{N}-\text{C}\equiv\text{N}$ (3.3 D), is appreciably less than that of the nitrile group $\text{C}\equiv\text{N}$ (4.0 D), just as one would expect if there were some mesomeric electron transference from the CN group to the adjacent C-N link,



Early physical measurements provided no definite evidence on the question of the structure of the isomeric diazocyanides. Stewart³², had suggested that of two geometrical isomerides, the more symmetrical showed the greater power of absorbing light, but no such generalisation could be applied to azo- and diazo-compounds, for although in the 2.4.6. - tribromo derivative the trans- form had the greater absorption in both the visible and near ultraviolet region³³, yet in potassium - 2 - chloro-benzene-diazo sulphonate³³, and 4 - bromo- benzene diazocyanide as well as azo-benzene, the stable form absorbed more in the ultra-violet but less in the visible, than the labile isomer.

Brühl³⁴, found that syn- and anti- 2.4 - dibromo benzene diazocyanide had molecular refractions for the Na_D line of 56.59 and 58.64 respectively in benzene solution, which was in accordance with the general observation that the trans-isomer of a given pair had the greater molecular refraction.

Le Fèvre and Vine³⁰, have verified this conclusion for several pairs of diazocyanides, the trans- (stable) isomers had the higher molecular refraction in each case, as shown in Table V.

TABLE V.

MOLECULAR REFRACTIONS OF CERTAIN PAIRS OF DIAZO-CYANIDES.

DIAZO-CYANIDE	CIS-	TRANS-
4- CHLORO	46.1	48.0
4- BROMO	49.9	52.3
4- NITRO	44.7	48.6
2- BROMO	47.2	51.6
2.4.6 - TRIBROMO	64.0	68.0

SECTION 4.ISOMERIC CHANGE OF THE DIAZOCYANIDES.

The early work on the isomeric change of the diazo-cyanides was carried out chiefly by Hantzsch who prepared various substituted diazocyanides with a view to investigating the effect of different radicals on the stability of the syn-diazocyanides. The bulk of his work was qualitative only, and hence many of his conclusions were mainly speculative.¹⁰

He correctly concluded that all negative groups in the benzene nucleus tend to stabilise the syn-form. He found, for instance, that the simplest diazocyanide - benzene diazo-cyanide, $C_6H_5\cdot N_2\cdot CN$ could not be obtained free, but only in the form of its double-salt with hydrocyanic acid, — $C_6H_5\cdot N_2\cdot CN; HCN$.

We have verified this fact experimentally too, since we found that diazotised toluidines only gave oily tars on treatment with potassium cyanide solution at $-5^{\circ}C$, whereas several chlorinated toluidines gave well-defined, crystalline, syn- and anti- diazocyanides.

Hantzsch put the stabilising effect of the negative groups in the following order -

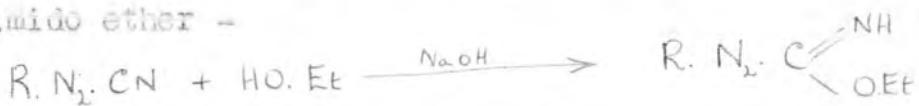


He also pointed out that the greater stability of the richly halogenated syn- diazocyanides was shown by the fact that the intramolecular decomposition into nitrile and nitrogen

was more difficult with increase in halogen content in the ortho- or para- position.

E.g. in Gattermann's reaction, copper powder acted almost explosively on p.chlorosyn-diazocyanide at ordinary temperature, moderately on p. bromo-, slightly on the dibromo-, and scarcely had any effect on the tribromo-syn- diazocyanide. The halogenated anti-diazocyanides also showed the same retarding influence of the halogen on reactivity, especially in addition reactions with water, alcohol, or the - CN group.

Hantzsch¹⁰, found that di-ortho syn-diazocyanides isomerised only with difficulty to the anti-diazocyanides, and also coupled with difficulty with alkaline β - naphthol in alcoholic solution. Also, in alkaline alcoholic solution, di-ortho syn- diazo cyanides did not yield the corresponding diazo-imido ether -



but decomposed with evolution of nitrogen.

Hantzsch next studied the effect of the alkyl radicle on the stability of the diazocyanides and found that the effect was opposite to that of the halogens. They coupled instantaneously with alkaline β - naphthol and, like the di-ortho halogenated syn-diazo cyanides, gave brisk nitrogen evolution in alkaline-alcoholic solution without yielding the diazo-imido ether.

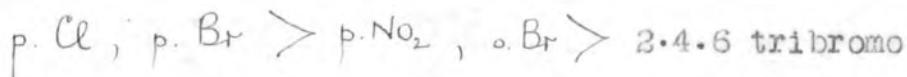
Hantzsch compared the diazocyanides, diazosulphonates

and diazotates from the point of view of stability, and suggested that the relatively large stability of the diazo-cyanides was due to the direct linking of the two nitrogen atoms to a carbon atom - (- N = N - CN), pointing out that the diazocyanides were not self-explosive, whereas several diazo sulphonates deflagrated in the dry state.

(Compare Stephenson and Waters, this thesis, p. 26)

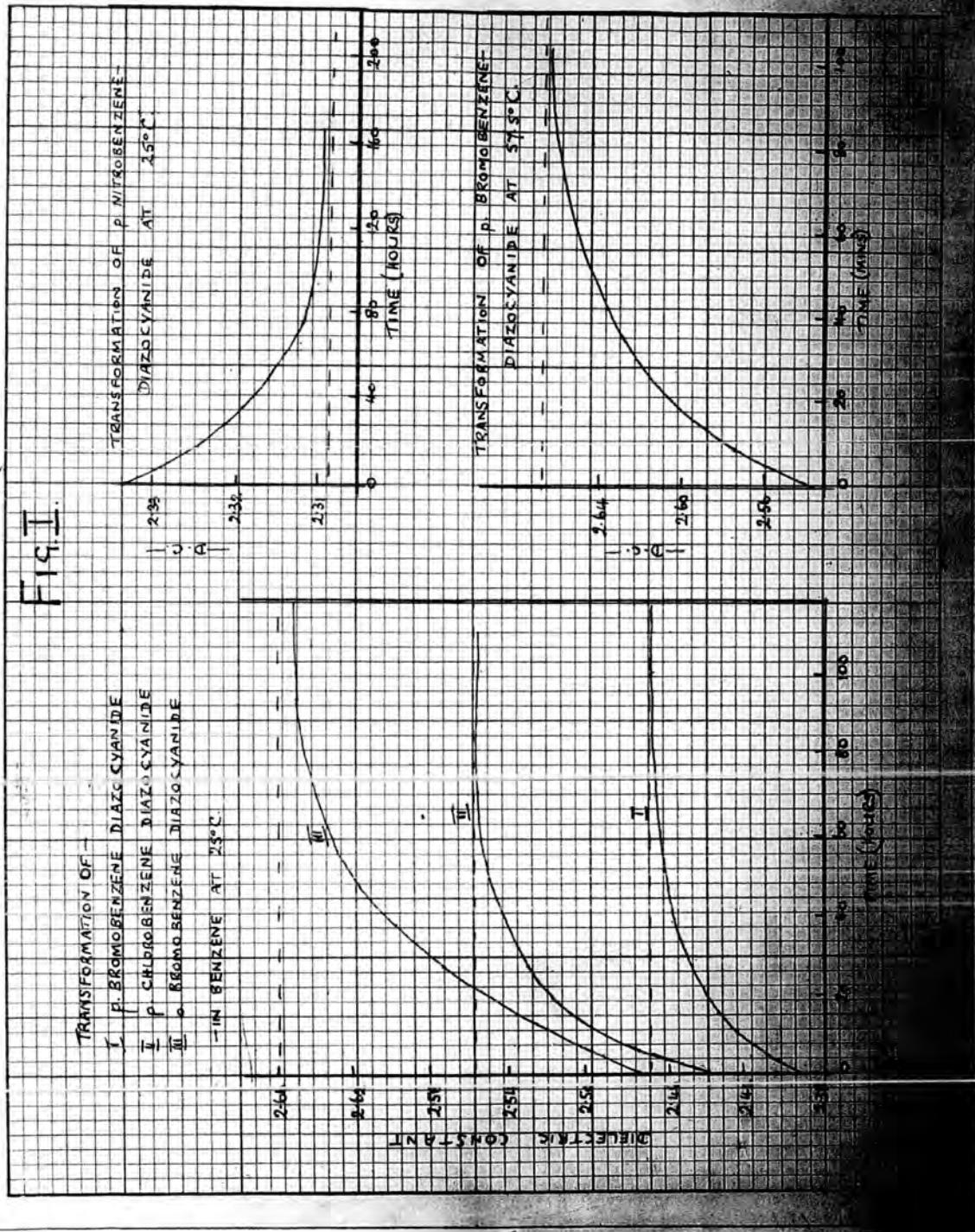
THERMAL ISOMERISATION.

In 1938, Le Fevre and Vine,³⁰, rounded off the earlier work of Hantzsch by making quantitative measurements on the rate of thermal isomerisation of the diazo-cyanides. They found that the rates of isomerisation were in the following order -



The cis \rightarrow trans transformation was followed in benzene by dielectric constant measurements. The solutions were kept in brown glass bottles and, at the concentrations used (1- 5%), the photochemical effect was very slight. The following graphs, Fig. I p.31 were obtained by Le Fevre and Vine. The cis \rightarrow trans change went to completion following the unimolecular law; curves were calculated from the equation $\frac{dx}{dt} = k(a-x)$, best values of k being chosen.

FIG. I.



The following table shows the velocity constants obtained by Le Fevre and Vine for certain derivatives.

T A B L E V I.

VELOCITY CONSTANTS FOR THE CIS → TRANS CHANGE FOR
SOME DIAZOCYANIDES.

DERIVATIVE	$k_{25^\circ} \text{ hr}^{-1}$	$k_{55^\circ} \text{ hr}^{-1}$
p. CHLORO-	•058	—
p. BROMO-	•058	2.08
p. NITRO-	•026	—
o. BROMO-	•028	—
2.4.6. TRIBROMO-	not appreciable	0.11

Hartley obtained similar curves for the p.bromo derivative at 25° and 55° using a photometric method and solutions at much greater dilution.

Dielectric Constant measurements at two temperatures on the p. bromo derivative by Le Fevre and Vine showed that the energy of activation was 21.6 (Hartley found 23.0) kg. cals. and Hartley obtained a value of 23.0 kg. cals. for the transformation of cis → trans azobenzene, therefore in each case ^{the transformation probably} takes place by the same mechanism.

Le Fevre and Vine also found that a pure dry sample of p. bromo syn- diazocyanide could be kept unchanged at 0° for two months, and that the cis → trans transformation occurred photochemically under the action of light both on the solid and in solution.

PHOTOCHEMICAL ISOMERISATION.

Ciusa³⁵ found that isomerisation of the cis- 2.4.6. tribromo diazocyanide was brought about by sunlight in benzene solution and Hartley found that the effect was reversible.

Hartley, investigating azobenzene, found that trans-azobenzene in solution was partly converted to the cis- form (which absorbed more light in the blue end of the visible spectrum), and he used this property to find the amount of cis- azobenzene in an equilibrium mixture. Next, he made up cis- and trans- p. bromobenzene diazo cyanide in identical concentration in benzene and found again that the cis-form had the greater absorption. Both samples were then exposed to daylight and both reached the same intermediate absorption corresponding to 20% of the cis- compound.

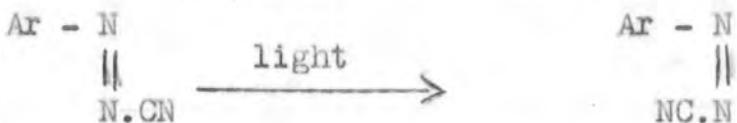
Conclusive evidence for the photochemical transformation of anti- diazocyanides to syn- diazocyanides is described in pages 91 — 96 of the experimental section of this thesis.

We found that when silver nitrate solution was added to solutions of anti-diazocyanides in ethyl alcohol, the originally clear solution went turbid on exposure to light and eventually all the anti-diazo cyanide was decomposed leaving a practically clear solution of a diazonium salt; after a time some reduction of the silver salt also took place.

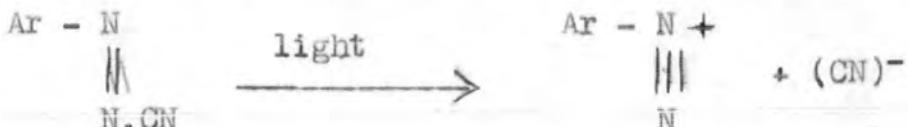
Now, precipitation of silver cyanide is a reaction typical of solutions of syn- diazocyanides in ionising solvents, and is also a reaction of the diazonium cyanides, (cf. p.^s 7 — 9 of

this thesis), therefore this photochemical change in acetone or alcohol may be either -

(1) Direct isomerisation of trans \rightarrow cis diazocyanide



OR, (2) Ionisation of trans-diazocyanide to diazonium cyanide,



On Hartley's evidence that the change takes place in benzene solution, (1) is the more likely course of the reaction.

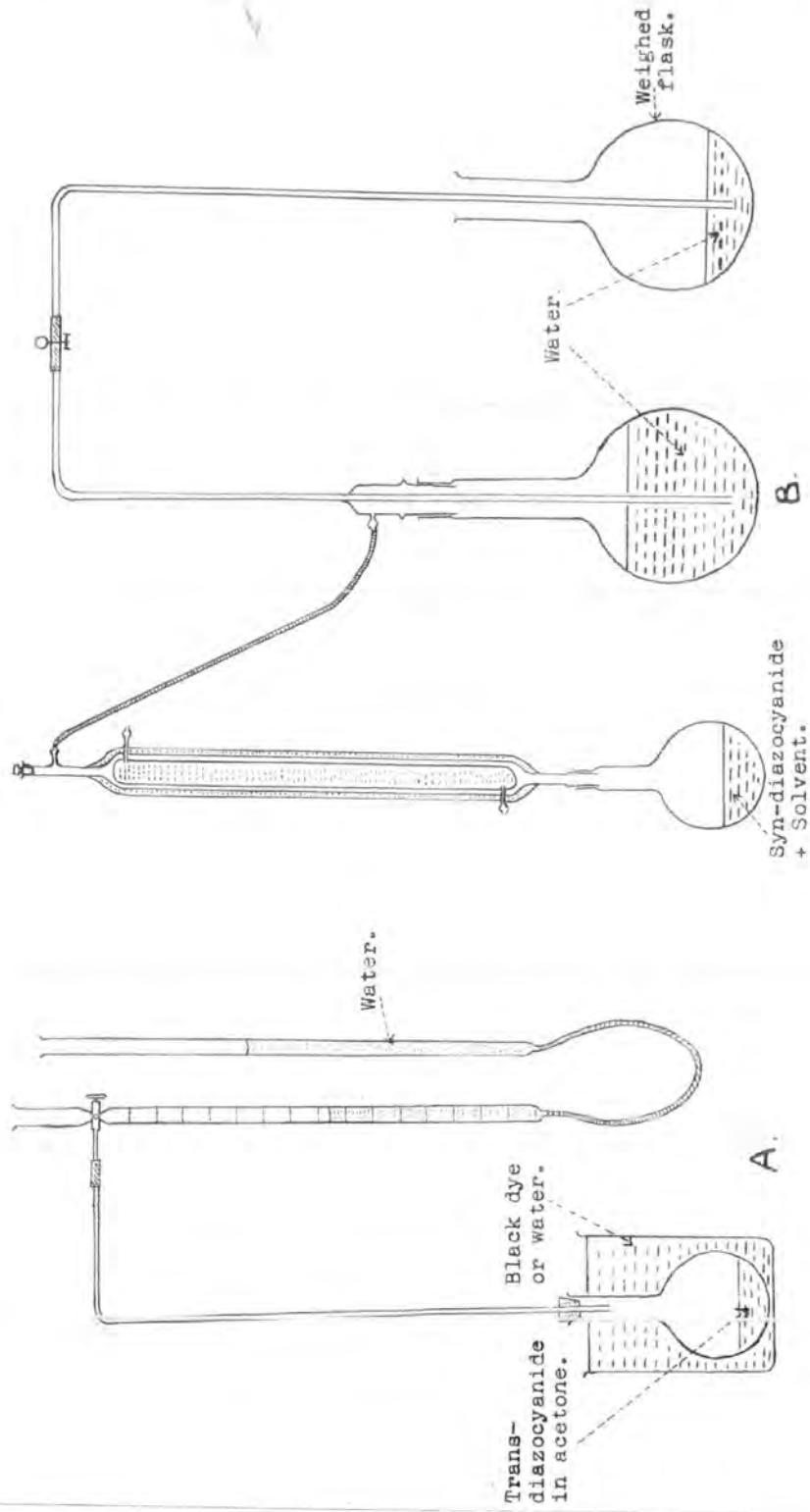
We started with a solution of pure anti-diazocyanide and, by exposing it to sunlight, found that the photochemical change reached an equilibrium value which, for substances as yet examined, was overwhelmingly in favour of the anti-form, since solutions of anti- which had been exposed to strong sunlight for a considerable time, gave only a faint turbidity on treatment with silver nitrate solution.

Further, we found that solutions of anti-diazocyanides in alcohol or acetone underwent complicated changes on prolonged exposure to light. Solutions of anti-diazocyanides in acetone or alcohol were exposed to light in closed vessels (Fig. II A p 344) and darkened considerably with evolution of nitrogen, showing that a slow decomposition occurred similar to that noted when solutions of syn-diazocyanides were kept. On the other hand, identical

DECOMPOSITION OF TRANS-
DIAZOCYANIDE IN ACETONE.
OF SYN-DIAZOCYANIDES.

Fig. II

MEASUREMENT OF N_2 EVOLVED IN DECOMPOSITION
OF SYN-DIAZOCYANIDES.



solutions protected from light by immersion in a bath of black dye, were practically unaltered. The nitrogen evolved was measured in each case and the results are shown graphically in FIGURES. III., IV., & V., p^s 35(a), 35(b) & 35(c).

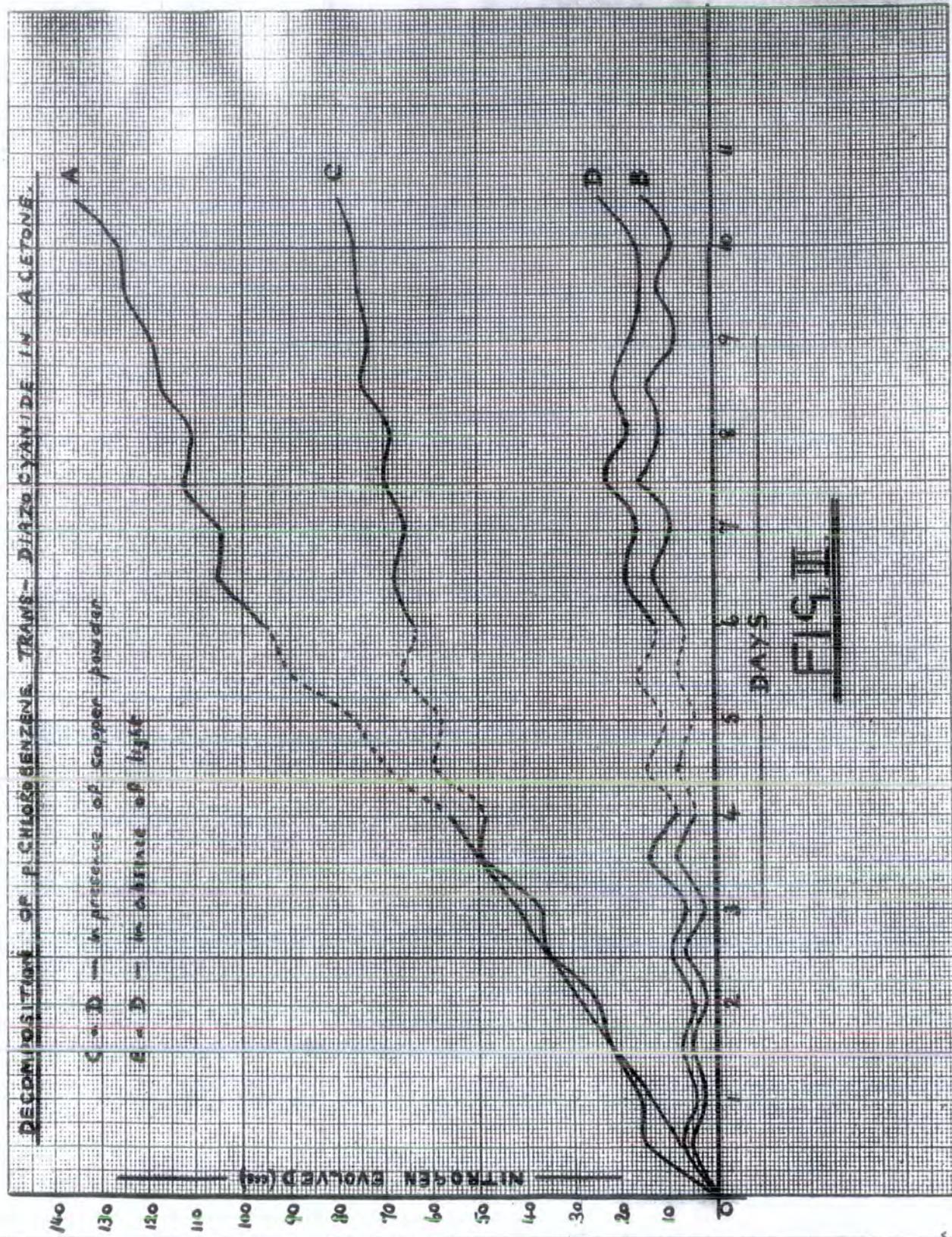
The essential decomposition products resulting from the photochemical decomposition of the anti- diazocyanides in alcohol and acetone were identical with those obtained by the thermal decomposition of the syn- diazo-cyanides (see the Experimental section of this thesis, p^s q₁ — q₆).

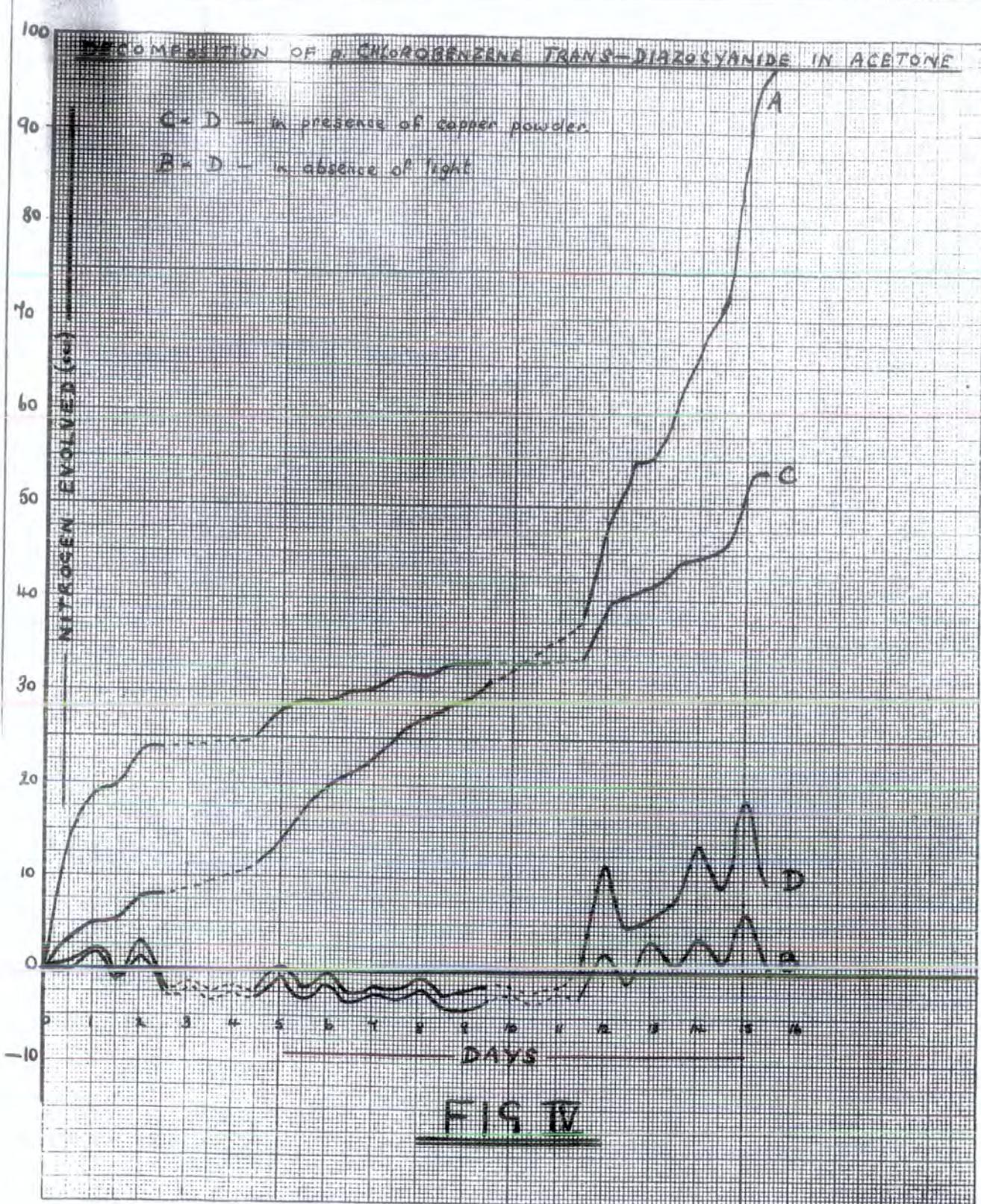
The figures also indicate the effect of adding copper powder as a catalyst, but although it undoubtedly influences the course of the decomposition of the syn- diazocyanides, since the final decomposition products were not the same in each case; it had no obvious direct action on the decomposition of the anti- diazocyanides.

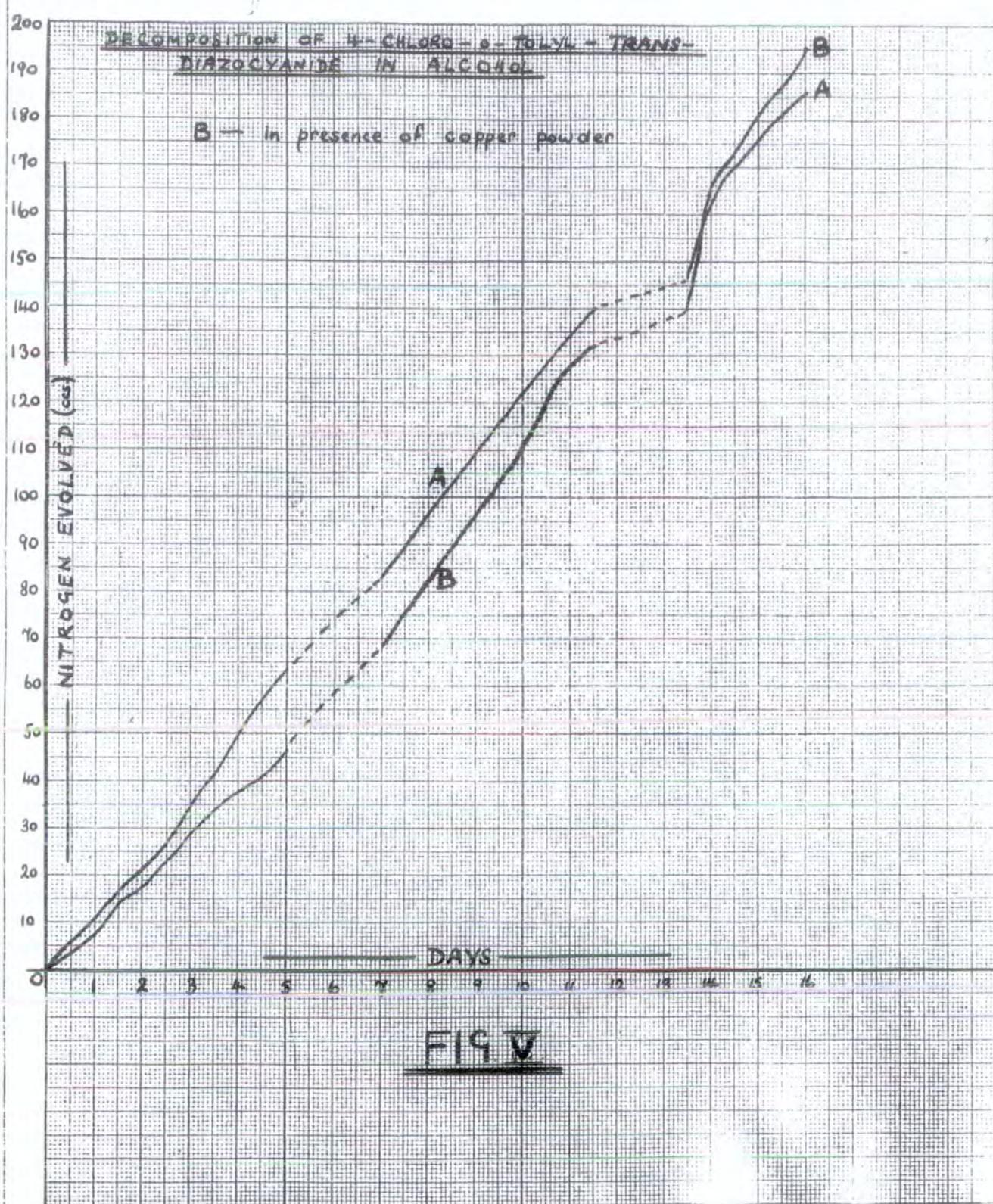
Under non- ionising solvents such as benzene or carbon tetra chloride, evolution of nitrogen did not occur, because the anti-diazocyanides could be recovered practically quantitatively from their solutions, even after exposure to light, merely by evaporation of the solvent.

The reverse change, cis → trans, did not seem to be a photochemical reaction although the solid cis- compounds always darkened rapidly on exposure to light.

We found, like Le Fevre and Vine, that the dry solids did not isomerise in the dark when kept cool, but all solutions rapidly underwent changes. The isomerisation of the syn → anti forms





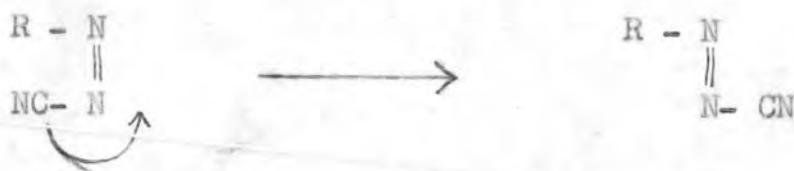


was quantitative only in non-ionising solvents such as benzene and carbon tetrachloride, even in the absence of light. Even in ether there was some side-reaction, and in alcohol and acetone, syn-diazocyanides darkened rapidly and gradually evolved nitrogen to about 20 - 40% of the total diazo-group present. The residual product from these solvents was a tar, together with free hydrogen cyanide and very little, (if any), anti-diazocyanide.

This difference in behaviour of the syn-diazocyanide in ionising and non-ionising solvents is due to the fact that it is in tautomeric equilibrium with the unstable salt, the diazonium cyanide, in ionising solvents. cf. Hantzsch^{12, 11.} and pages 7-10 of this thesis.



With regard to the cis \rightleftharpoons trans change for the diazocyanides, another question arises. The change may take place by the intramolecular switch of a group by rotation, e.g.



or, the molecule may split up into two pieces which then re-unite.

Our experimental work shows that syn-diazo-cyanides are converted to the trans-isomers in non-ionising solvents in 100% yield, therefore the evidence is against the second theory, for, if the molecule did split up into two parts when isomerising,

these parts would very probably react to some extent with the solvent.

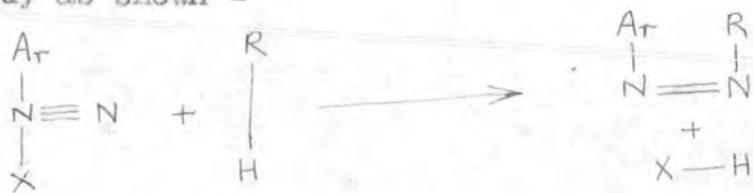
In the presence of copper however, the split evidently does occur, for, when carbon tetrachloride was used as solvent, the aryl chloride, R. C₆H₄. Cl, was formed from the diazocyanide, R. C₆H₄. N₂. CN, in 10-20% yield. Hydrogen cyanide was also formed and aqueous extracts of the reaction products regularly contained both cupric and chloride ions.

SECTION 5.

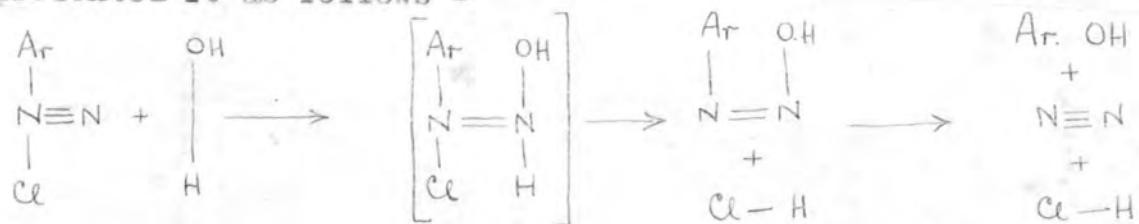
THEORIES ON THE DECOMPOSITION OF THE
DIAZO - COMPOUNDS.

Hantzschi's Theories. -

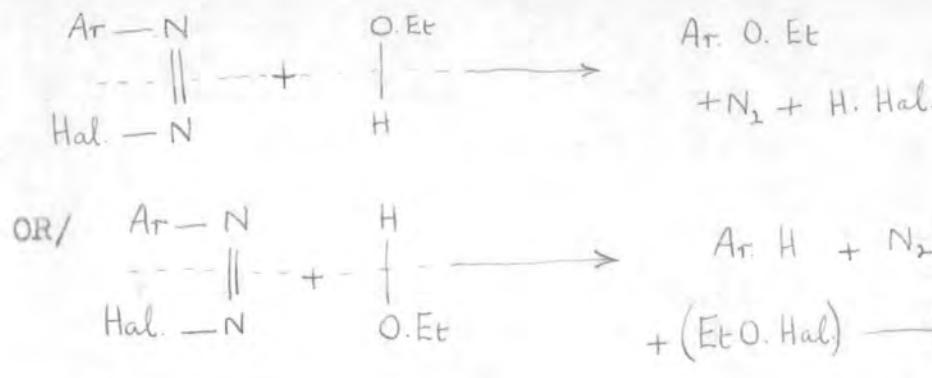
Hantzschi²³, said that only the syn- form of the diazo compounds was active and insisted that all the reactions of the diazo- compounds must involve the intermediate formation of the syn- body as shown -



He later admitted that there were exceptions, especially in the decomposition of the diazonium salts in acid solution - This,, he said, was a special case of his general theory, and he represented it as follows -



Hantzschi and Jochem³⁶, decomposed a series of diazonium salts in methyl and ethyl alcohols, and concluded that, as the molecular weight of the alcohol increased, and the number of negative groups in the benzene nucleus increased, the yield of aryl hydride increased, and that of the aryl ether diminished. He represented all these changes as taking place via the syn- diazo structure, thus -

PRAY'S WORK.

In 1926 however, Pray,³⁷ studied the rate of decomposition of benzene diazonium salts in water and in a series of aliphatic alcohols and acids. For the alcohol series, reaction velocities as measured by rate of nitrogen evolution, were all of the same order, and were practically identical for lower members.

Similar results were obtained for aliphatic acids, as the following table shows -

TABLE VII.RATES OF DECOMPOSITION OF BENZENE DIAZONIUM CHLORIDE IN VARIOUS ALCOHOLS AND ACIDS.

$$k' = 0.4343 k \times 10$$

SOLVENT	k' at 20°C	k' at 30°C .	k' at 40°C .
Methyl alcohol	11.3	53.5	227
Ethyl alcohol	11.3	53.5	218
n. propyl alcohol		52.0	204.2
n. butyl alcohol		50.0	201
iso-butyl alcohol		54.0	208
Amyl alcohol		46.3	-
Formic acid		18.6	73.1
Acetic acid		18.7	82.0
Propionic acid		18.9	82.0
Butyric acid		23.0	102.0
Water		25.0	107.0

Now, Hantzsch and Jochem showed that the reactions between benzene diazonium chloride and methyl and ethyl alcohols

differed qualitatively as shown -



yet the observed rate of reaction was identical in both cases. The initial rate - determining process could not therefore have been, as Hantzsch imagined, the rate of decomposition of the addition compound with the syn-diazo structure, for this would have depended on the nature of the alcohol, R.OH.

Waring and Abrams³⁸ in 1941, decomposed benzene diazonium chloride in various amyl alcohols to see if the rate of decomposition was affected by the presence of branched chains in the solvent molecule or by increased viscosity in the solvent. They found that the rate of decomposition was practically the same in isoamyl, active amyl, and tertiary amyl alcohols, and also that addition of salts or variations in the surface of the reaction vessel had no catalytic effect on the decomposition. Further, they calculated that the activation energy for the decomposition was about 10^4 cals/mol. too high for a simple ionic mechanism.

As far back as 1895, Kuhlung³⁹, had noticed that the sodium salt of diazotised p. nitraniline reacted with toluene to give a compound, proved by Kleigh and Huber⁴⁰, to be 4 - nitro - 2' - methyl diphenyl.

Further, Gomberg and co-workers⁴¹, found that, by stirring a moderately concentrated aqueous solution of sodium diazotate in

the cold with a neutral aromatic liquid, nitrogen was evolved, and a biaryl formed in yields varying from 5- 40%



The most characteristic feature of the reaction was, that in the formation of the biaryl, the ordinary laws which governed aromatic substitution were not obeyed, e.g. with benzene diazohydroxide, toluene yielded 2- and 4- methyl diphenyl; bromobenzene gave 2- and 4- bromodiphenyl; benzonitrile gave 4- cyano diphenyl, and nitro benzene gave 4- nitro- diphenyl.

As an extension of the Gomberg reaction, Grive and Hey⁴², decomposed the diazohydroxide in equimolecular quantities of a mixture of toluene and nitrobenzene, and obtained isomeric nitro-diphenyls four times as great as the yield of isomeric methyl diphenyls, thus showing that substitution took place in ortho- and para- positions much quicker with a meta-directive group already present in the nucleus, than when an ortho- para- directive group was present.

During the last few years, considerable evidence has been brought forward for a free-radical mechanism in the decomposition of the diazo-compounds, the chief workers in this field of research being Hey and Waters.

Grive and Hey,⁴³ decomposed nitroso - acetanilide,



with benzene diazo acetate, $\text{C}_6\text{H}_5\text{.N=N.O.CO.CH}_3$), in a series of aromatic solvents, and found that the rates of decomposition, as

measured by nitrogen evolved, were independent, or nearly so, of the aromatic solvent. The decomposition was uni-molecular in type, and Butterworth and Hey,⁴⁴ obtained similar results for non-aromatic solvents.

The following table shows the results obtained by Grise and Hey.

42, 43

TABLE VIII

DECOMPOSITION OF BENZENE DIAZOACETATE IN VARIOUS SOLVENTS.

SOLVENT	PRODUCTS.
BENZENE	N ₂ evolved quantitatively and diphenyl obtained in 80% yield.
TOLUENE	N ₂ , CH ₃ CHO, CH ₃ COOH, Methyl diphenyls.
m. XYLENE	N ₂ , CH ₃ CHO, CH ₃ COOH 2-4. dimethyl diphenyl.
ETHYL BENZOATE	Ethyl diphenyl carboxylates
BENZALDEHYDE	Diphenyl-4-aldehyde.

In most cases it was found that ortho- para- substitution was the general rule, but in reactions between 4-nitroso-acetamide diphenyl and both chloro- and bromo-benzenes, it was found that substitution of the diphenyl group took place at all three positions in the halogenobenzene nucleus, giving the 2-, 3- and 4-halogeno-p-terphenyls⁴⁵, which agrees with the previous observation of Hey's⁴³ that the reaction between diazobenzene hydroxide and ethyl benzoate gave 2-, 3- and 4-diphenyl carboxylic esters.

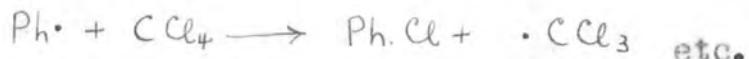
These results and many others have been incorporated satisfactorily into a reaction involving the slow formation of

free aryl radicals from the diazo compound, or, more probably, from its wholly covalent tautomer.⁴⁵

e.g. (1) the slow reaction -



(2) The fast reactions -



Under these circumstances, the reaction velocity, measured by the rate of evolution of nitrogen, becomes the rate of formation of free aryl radicals, and this would be a unimolecular reaction independent, or practically so, of the second component which is present in large excess and merely acts as a medium for the decomposition. The subsequent fate of the phenyl radical, whether it is converted into benzene, a phenyl alkyl ether, or some more complicated molecule, will therefore have no bearing on the initial rate-determining stage.

REACTION OF DIAZONIUM CHLORIDES WITH PYRIDINE.

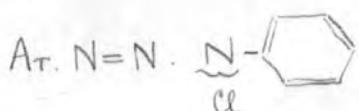
Möhlau and Berger⁴⁷ observed that 3- and 4- phenyl pyridines were formed when dry benzene diazonium chloride was decomposed in pyridine. This interesting reaction was investigated more fully by Hey and his colleagues in 1940. Their method consisted of the slow addition of an aqueous diazonium salt to an excess of pyridine at 20° - 70°C. (depending on the amine). A brisk reaction took place and yields of 20-80% of mixtures of α-, β- and γ-aryl pyridines were obtained. They found that addition of pyridine

to the diazonium solution gave a much less smooth reaction with a good deal of tar formation.

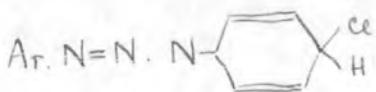
With regard to the mechanism of this reaction the following points are worth noting -

- (1) Addition of pyridine to aqueous p. nitrobenzene diazonium chloride gave no reaction until the base was in excess of the total acid (free and combined) present, after which further addition of pyridine gave a vigorous reaction.
- (2) Pyridine was added to p. nitrobenzene diazonium chloride in just sufficient amount to form an intermediate compound of the type $\text{NO}_2\text{C}_6\text{H}_4\text{N}=\text{N}\cdot\text{N.C}_6\text{H}_5\}$ Cl' , and the resulting mixture stirred with excess of benzene, yielded p. nitrodiphenyl but no p. nitrophenyl pyridine.
- (3) It was found that aqueous diazonium salts did not react with solutions of quaternary pyridinium salts to yield aryl pyridines e.g. diazotised p. nitraniline only yielded p. iodo-nitrobenzene with aqueous pyridine methiodide.

The reaction was repeated with nitroso-acylaryl amines in pyridine and again, α - , β - , and γ - aryl pyridines were formed, pointing to a non-ionic mechanism for the reaction, since an ionic mechanism would be expected to give an aryl pyridinium chloride, or, by a subsequent migration, the α - and γ - isomerides only. It is probable that an addition compound such as (A) or (B) was first formed

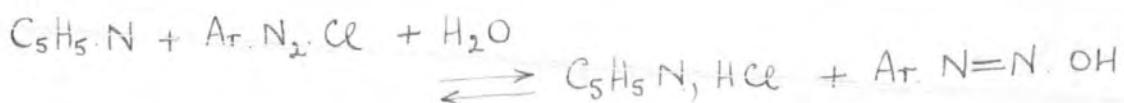


(A)



(B)

which subsequently decomposed into radicals which reacted with free pyridine, but it is also possible that, as in the Gomberg reaction, the active agent may be the diazohydroxide produced thus -



The yields in this reaction were better than those in the Gomberg reaction, because here the medium was homogenous; it is probable however, that in both these reactions, a free-radical mechanism is responsible, for in both reactions the normal polar directive influences either of the benzene or pyridine nuclei are not operating.

Waters,⁴⁸ studied further decompositions of benzene diazoacetate and obtained further evidence for the free-radical decomposition mechanism. In hydrogen-containing solvents he found that benzene was invariably a reaction product, and in halogen-containing solvents the corresponding aryl halide was formed. This was explained by the non-ionic reactions -



(Haworth and Hey⁴⁵, pointed out that the diazoacetates (nitroso acylarylamines) reacted with hydrocarbons in either of two ways -



reaction (1) predominating when R = aryl, and reaction (11) when R = aliphyl.)

Also, with acetic anhydride as solvent, carbon dioxide was produced and this was attributed to the transient formation of the neutral acetate radical -



Further evidence for this non-ionic fission of benzene diazoacetate was provided by the fact that, in non-ionic solvents, in presence of excess chalk to keep the solution neutral, the metals Fe, Zn, Cu, Pb, and Sb were attacked, yielding their acetates.

Waters,⁴⁹ next investigated the reactions of the diazo-hydroxides and found that they showed complete analogy to the diazoacetates. Decomposition in carbon disulphide yielded diphenyl disulphide, Ph - S - S - Ph, and in cyclo hexane yielded benzene.

Waters⁴⁹ then found that the reactions of the diazonium chlorides were of the same type as those mentioned for diazo-hydroxides and diazo-acetates e.g. decomposition of solid benzene diazonium chloride in acetone yielded chloro benzene and hydro-chloric acid, and in the presence of chalk the products were

chloracetone and benzene. Decompositions in halogen-containing solvents yielded the corresponding aryl halides as previously.

In acetone in presence of chalk, the benzene diazonium chloride attacked the metals Hg, Sb, Bi, Pb, Sn, Ni, Fe, Cu and Ag, yielding their chlorides, and the first two metals gave in addition, phenyl mercuric chloride, Ph-Hg-Cl₂, and triphenyl antimony dichloride, Ph₃-Sb-Cl₂, respectively.

Since the diazonium chloride did not decompose in any solvents below 50°C, it seemed probable that it was first converted on warming into its unstable covalent tautomer -



and this decomposed spontaneously into N₂, Ph· and atomic chlorine. This theory will explain all the previous experimental results which are here summarised -

(1) Formation of benzene in acetone or alcohol -



(2) Formation of hydrochloric acid in all reactions -



(3) Formation of chlorobenzene -



(4) Chlorination of acetone by neutral atomic chlorine



(5) The attack on metals by neutral atomic chlorine, and on others by free alkyl radicals, e.g. formation of Ph. Hg. Cl and $\text{Ph}_3\cdot \text{Sb}\cdot \text{Cl}_2$ showed that the attacking phenyl radical must have had strong electrophilic character.

Further, Waters⁵⁰ studied the effect of 38 metals on a suspension of benzene diazonium chloride in acetone. He found that catalytic reaction often occurred at room-temperature or lower, and concluded that the covalent tautomer $\text{Ph}\cdot \text{N}=\text{N}\cdot \text{Cl}$ must have been formed, since in aqueous solution, where benzene diazonium chloride existed as (PhN_2^+) Cl^- , copper was practically the only metallic catalyst for its decomposition. It is possible that the metals are catalytic in action due to their being electron-donors -



Small amounts of diphenyl were isolated in many cases, even in the absence of metals, probably due to the secondary reaction -



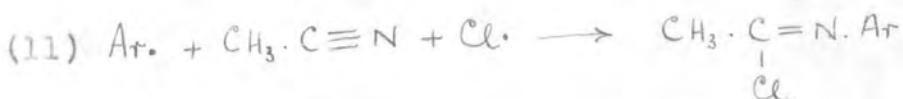
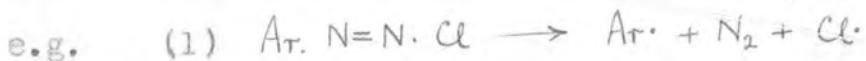
this idea being supported by the fact that the yield of diphenyl which was usually about 5% went up to 25% when benzene was added to the reaction mixture. Also, the fact that α - and β -phenyl naphthalenes were formed when benzene diazonium chloride was decomposed in solutions of naphthalene in acetone, lent further support to the theory that the decomposition was non-ionic.

Other reactions of neutral phenyl radicals formed from

diazo-compounds were investigated by Hanby and Waters⁵¹ who decomposed benzene diazonium chloride in acetonitrile and obtained -

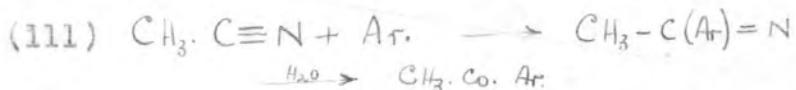
- (a) benzene
- (b) chlorobenzene
- (c) acetanilide
- (d) acetophenone.

(a) and (b) are normal reactions like the previous ones mentioned, but (c) and (d) are addition processes involving free-radicals -



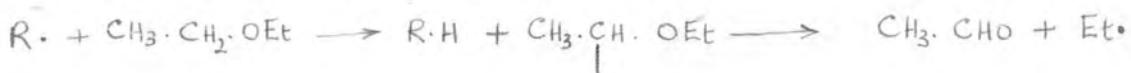
which on hydrolysis yields acetanilide.

Acetophenone is formed by the following reaction -



Further, reactions (b), (c) and (d) were suppressed by addition of zinc, which was to be expected, since the metal would unite with chlorine.

Acetaldehyde was always evolved in decompositions of benzene diazonium chloride in ether or alcohol, and this can be explained by the following scheme -

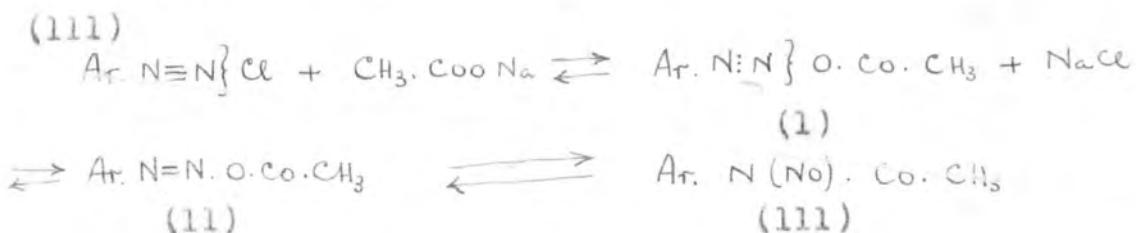


Further examples of this addition of free radicals to unsaturated compounds were found by Meerwein, Büchner and Van Emster,⁵² who showed that the free radicals Ph. and Cl[·] (from benzene diazonium

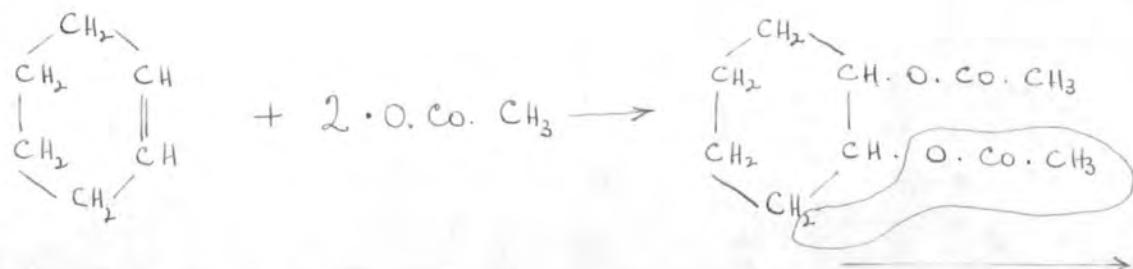
chloride in aqueous acetone or pyridine in presence of sodium acetate), added on to such unsaturated compounds as methyl cinnamate, methyl fumarate, and phenyl propionic acid.

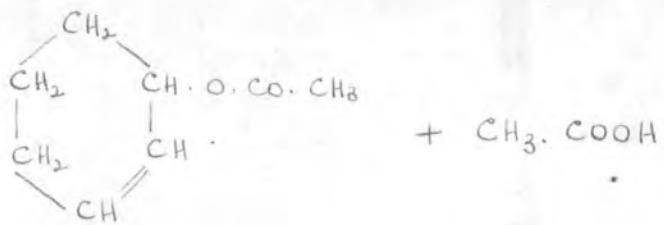
These reactions may be regarded as involving free aryl radicals and chlorine atoms, which thus show additive properties towards unsaturated organic molecules, as well as to metals.

The sodium acetate may serve to convert the diazonium chloride into the corresponding acetate (1), which can readily pass into the covalent acetyl derivative of the diazohydroxide (11), which is probably the active agent responsible for the production of free radicals in these reactions as well as in those of the nitrosoacyl arylamines



Further, Waters⁵³ found that benzene diazo acetate and benzene diazonium chloride reacted with cyclohexene to give Δ^1 -cyclohexenyl acetate and Δ^2 -cyclohexenyl chloride respectively. This reaction can be explained by the following scheme involving interaction of cyclohexene with free acetate radicals or atomic chlorine.





To summarise, the decomposition of aromatic diazo-compounds in AQUEOUS solution can be classified into three distinct groups:⁶⁴

TYPE 1.

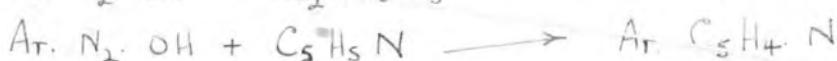
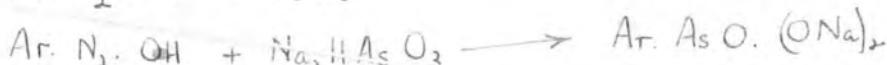
Decompositions in acid solution, leading to the formation of phenols:



This is definitely a decomposition of a diazonium kation, since the rate of evolution of nitrogen is independent of the nature of the radical X.²⁴

TYPE 2.

Non-ionic decompositions of aryl diazo-hydroxides, Ar-N₂-OH, which can exist in neutral or slightly alkaline solutions, e.g.,^{42a, 43, 45, 49}



TYPE 3.

Reactions such as $\text{Ar. N}_2\text{Hal} \rightarrow \text{Ar. Hal} + \text{N}_2$ which can occur in acid solution and usually need a special catalyst, such as a cuprous salt (Sandmeyer reaction) or metallic copper (Gattermann reaction). Reactions of this type occur under conditions where diazonium kations and not covalent diazo-hydrox-

ides must be involved, yet they have many characteristics in common with reactions of Type 2. It is suggested that these reactions are non-ionic decompositions of diazonium kations, brought about by a single-electron transferrence from a catalyst.⁶⁴ (see pages 82-85.)

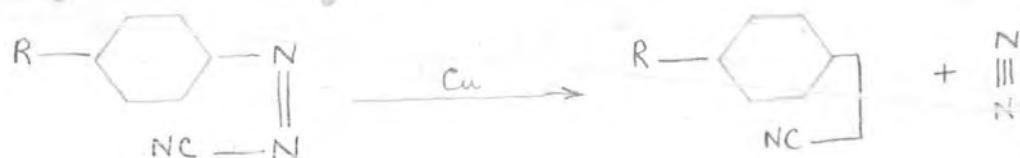
SECTION 6.

DECOMPOSITION REACTIONS OF THE SYN- DIAZOCYANIDES.

We investigated the decomposition of the diazocyanides in ionising and non-ionising solvents to see to what extent the theories postulated for the mechanisms of decompositions of diazo-acetates, diazo hydroxides and diazonium chlorides can be generalised.

Hantzsch and Schultze⁷ stated that alcoholic solutions of syn-diazocyanides could be catalytically decomposed by addition of copper powder, nitrogen being evolved and an aromatic nitrile formed.

They depicted the reaction as a fission of a molecule of nitrogen followed immediately by the union of 2 vicinal radicals, a scheme subsequently adopted by Hantzsch for all decompositions of diazo-compounds.



However, these workers attached no significance to the fact that nitrile formation was in no way quantitative neither did they investigate the decomposition in non-ionising solvents.

With several syn-diazocyanides we have found in all cases that copper-catalysed decompositions in ionising solvents yielded only a small percentage of nitrile, the bulk of the product being a black non-volatile tar, indicating that the solvent played an integral part in the decomposition.

We obtained the following general results -

- (a) Moist specimens of syn-diazocyanides, in absence of light

at room temperature, gave off hydrogen cyanide and left a complex tarry residue from which only a little anti-diazocyanide could be isolated by extraction with solvents or by steam distillation.

(b) The syn-diazocyanides were insoluble in water or in dilute acids, but decompositions were carried out in suspension in these media. The decomposition was not photochemical since it proceeded in absence of light with evolution of nitrogen. The solid diazo-cyanide darkened rapidly leaving a dark brown tarry residue, which on steam-distillation, yielded only a trace of anti-diazocyanide. The bulk of the product was a complex non-volatile tar.

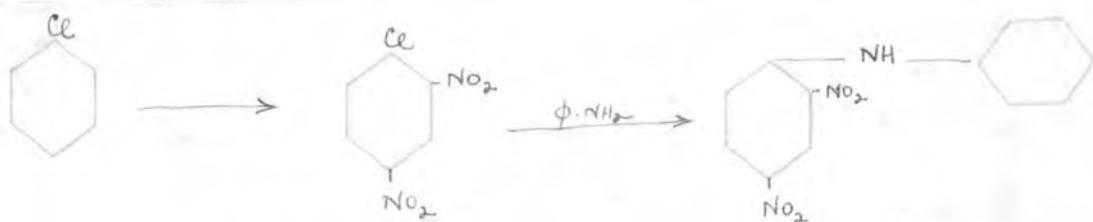
(c) The syn-diazocyanides were easily soluble in alcohol and began decomposing slowly in the cold, the solution darkening rapidly. The decomposition was carried out in the apparatus shown, (Fig. II_B, p 346), the nitrogen evolved being measured by displacement of water.

Decomposition was accelerated by warming and about 40% of the diazo-group was evolved as nitrogen (see Table IX. p. 59) At the end of the reaction the solvent was distilled off and found to contain (a) free hydrogen cyanide, detected by silver nitrate solution, and (b) acetaldehyde, which was isolated as its 2,4. dinitro phenyl hydrazone, the m.p. of which was checked by admixture with an authentic specimen.

Steam-distillation of the tarry residue yielded only a trace of anti-diazocyanide in all cases, yet Hantzsch⁷ had said that the syn-diazocyanide isomerised smoothly to the anti- in

alcoholic solution. The only other volatile product was the hydrogen-substitution product which was formed in yields up to 22%, and this after purification was usually identified by conversion to a solid nitration product. Chloro benzene, obtained from decompositions of 2- and 4- chloro benzene syn-diazocyanide, was always identified by nitration to 2.4. - dinitro chlor benzene and subsequent condensation of this product with aniline in methyl alcohol to give 2.4. dinitro diphenyl amine m.p. 154 - 5°

i.e.

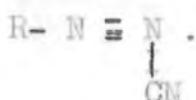


(d) The syn-diazocyanides were very soluble in acetone and decomposed slowly in this solvent at room temperature. The solution darkened rapidly and evolved nitrogen slowly. Only about 20% of the diazo-group was evolved as nitrogen, the only other simple product being hydrogen cyanide. After removal of the solvent only a trace of anti-diazo cyanide could be isolated by steam-distillation of the residue, and the main product again was a non-volatile tar which sometimes formed as much as 90% of the yield.

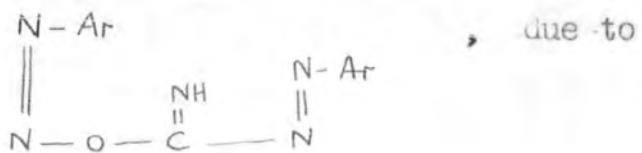
(e) A decomposition of P. chlorobenzene syn-diazo cyanide was carried out in methyl acetate solution. The decomposition was similar to that in alcohol or acetone, the only simple products being hydrogen cyanide and the anti-diazo cyanide. In this case

however, no quantitative measurements were made.

Since the syn-diazocyanides are in tautomeric equilibrium with diazonium cyanides, we can not be sure whether their decompositions in ionising solvents are decompositions of the diazo cyanides, $R-N = N \cdot CN$, or of the diazonium cyanides,



Our investigation of the reaction of syn-diazocyanides with silver nitrate ($pK_1 = 9$), has shown that neutral solutions of syn-diazocyanides in ionising solvents decompose to yield products of the type



, due to

hydrolysis and self-coupling. Therefore, since neutral solutions of the syn-diazo cyanides in ionising solvents can soon change in this way, their ultimate thermal decomposition reactions, in which nitrogen is evolved, are not necessarily decomposition reactions of the syn-diazocyanides themselves.

COPPER CATALYSED DECOMPOSITIONS OF THE SYN-DIAZOCYANIDES IN IONISING SOLVENTS.

(a) In ALCOHOL.

In alcoholic solution, the decomposition of the syn-diazo-cyanides was catalysed vigorously by addition of copper powder, and the reaction had to be controlled by cooling. The total nitrogen

evolved (about 55%) was greater than without copper (See Table IX. p. 59). At the end of the reaction the solvent was distilled off and found to contain an excess of hydrogen cyanide (detected by addition of alcoholic silver nitrate) and an excess of acet-aldehyde, which was detected by smell and characterised by the formation of its 2,4-dinitro phenyl-hydrazone m.p. and mixed m.p. 162° C.

About 20 - 25% of the hydrogen-substitution product was obtained by steam-distillation of the tarry residue, and was identified usually by conversion to a solid nitration product. Only about 1% of nitrile was formed, and this was identified by alkaline hydrolysis to the corresponding acid e.g.



The bulk of the product was a hard, black, porous, non-volatile tar, from which very little, if any, anti-diazocyanide could be isolated by steam-distillation.

In all these decompositions of the syn-diazocyanide in alcoholic solution, there was no evidence of any chemical attack on the copper, as the aqueous extracts after steam-distillation of the tar contained no copper salts.

(b) In ACETONE.

The copper-catalysed decomposition of the syn-diazocyanides in acetone was very vigorous and always had to be controlled by cooling. In this case, over 50% of the diazo group was evolved

as nitrogen. The yield of nitrile was much more (10%), and the yield of hydrogen substitution product much less (5%), than was the case in alcohol.

A good deal of non-volatile tar was always formed, and the solvent, distilled off, was found to contain no hydrogen cyanide or other simple product. Very little anti-diazocyanide could be isolated from the tar, and there was no evidence of any chemical attack on the copper.

The metals mercury, antimony and zinc were tried as catalysts on the decomposition of the syn-diazocyanides in acetone and alcohol, since these metals had been active catalysts in the decomposition of other diazo compounds. In this case however, none of these metals had any catalytic effect whatever, and the products of the decompositions were the same as those obtained in the absence of any metallic catalyst.

The following table summarises the results obtained in the decomposition of the syn-diazo cyanides in acetone and alcohol. Data for decompositions in ether are added for the sake of comparison.

TABLE IX.

DUCTS FORMED IN THE DECOMPOSITION OF THE SYN- DIAZOCYANIDES in ACETONE,
COHOL, and ETHER, with and without addition of copper powder.

SUBSTANCES	PRODUCTS VOLVED	FORMED SUBSTITUTION PRODUCT	TAR MITOGEN IN TAR	
			PRO-	DUCT FORMED
2- CHLORO-	NONE	ALCOHOL $\text{CH}_3 \cdot \text{CHO}$	36	NONE 32 60 -
5-CHLORO-o-TOLYL-	NONE	ALCOHOL Trace of Trans-	39	NONE 17.5 41 -
5-CHLORO-o-TOLYL-	COPPER	ALCOHOL $\text{CH}_3 \cdot \text{CHO}$	56	c. 0 39 53 13.9
2- CHLORO-	COPPER	ALCOHOL HCN	51	0.5 22 55 14.3
4- BROMO-	NONE	ACETONE 35% Trans-HCN	35	NONE NONE 73 -
5-CHLORO-o-TOLYL	NONE	ACETONE 5% Trans-HCN	31.	NONE NONE 95 -
2-CHLORO-	COPPER	ACETONE	46	10 4 46 12.7
4-CHLORO-o-TOLYL	COPPER	ACETONE	67	9 6 58 10.9
4-CHLORO-o-TOLYL	COPPER	ACETONE	?	10.5 0.5? - -
4-CHLORO-	COPPER	ETHER	-	- - 51 12.7
4-Bromo-	COPPER	ETHER	CH_3CHO	- 3 6 60 12.4
2-CHLORO-	COPPER	ETHER AND	40	2 6 - 16.9
4-CHLORO-o-TOLYL	COPPER	ETHER HCN	67	4 9 66 15.3
5-CHLORO-o-TOLYL	COPPER	ETHER	-	2 14 46 14.0

SECTION 7.THE EXPERIMENTAL EVIDENCE FOR THE NON-POLAR DECOMPOSITIONS OF
THE SYN- DIAZOCYANIDES.

Solutions of syn- diazo cyanides in the non-ionising solvents carbon tetrachloride, benzene, cyclohexane and ether, did not lose nitrogen on warming, but changed over to the stable anti- diazocyanides in almost quantitative yield.

In the presence of a little moisture however, some tar-formation always took place, even in these solvents.

Copper catalysed decompositions.(a) In DIETHYL ETHER.

Decompositions of the syn- diazo cyanides in diethyl ether with copper powder were peculiar. The initial decomposition was vigorous, and, even after refluxing the mixture for some hours, decomposition continued slowly for several days afterwards, and on evaporation to dryness, the residues often decomposed explosively. Since this was not noted in the absence of copper, it was probably due to the action of copper powder on the molten syn- diazocyanide, and obviously the decomposition of the syn- diazocyanide was very slow at the boiling point of ether.

The solvent, removed by distillation, always contained an excess of hydrogen cyanide and acetaldehyde, and formation of the latter compound can be best explained by assuming an attack on the ether by free radicals formed in the reaction, a mechanism which is discussed on page 64. Steam-distillation of the residue yielded up to 3% of the aromatic nitrile, mixed

however, with a larger quantity (up to 10%) of the hydrogen substitution product, $C_6 H_5 . R.$ Only traces of anti-diazocyanide could be isolated, but again, the bulk of the product was a non-volatile tar. The copper catalyst was not attacked, and metals silver, mercury, lead, iron and zinc had no catalytic effect.

(b) In BENZENE.

Copper-catalysed decompositions of the syn-diazo cyanides in benzene were much less vigorous than those in acetone or alcohol, and it was often necessary to warm the mixture to start the reaction.

About 30 - 50% of the diazo-group was eliminated as nitrogen, and the solvent, removed by distillation, always contained hydrogen cyanide. From the complex tarry residues, a small quantity (up to 2%) of the unsymmetrical diaryl, $R.C_6 H_4 . Ph.$) was isolated along with a little anti-diazo cyanide by steam distillation. The diaryls were identified by mixed melting points with authentic specimens or, in some cases, by conversion to a crystalline mono-nitration product. In some cases traces of nitrile, $R.C_6 H_4 . CN$, were isolated, but it is possible here that the starting materials were not perfectly dry. There was no evidence of any chemical attack on the copper.

The decomposition in benzene was studied using the purified syn-diazo cyanides from o- and p-chloraniline, p-bromaniline and 4- and 5-chloro-ortho toluidines. Diaryls were obtained from the first three of these, by steam-distillation

of the tarry residues. No diaryls were obtained from the latter two syn-diazo cyanides, but possibly they could have been isolated by vacuum distillation.

The metals silver, mercury, iron, lead and zinc were tried as catalysts but only iron showed any catalytic activity, yielding a trace of 4-chloro diphenyl when the syn-diazo cyanide obtained from p.chloraniline was used.

Although no quantitative measurements were made in this case, it was obvious that iron was far inferior to copper powder as a catalyst. (See p. -131)

The formation of diaryls in this reaction provides strong evidence for the attack on benzene by free aryl radicals (see p. 65).

(c) In CARBON TETRA CHLORIDE.

Copper catalysed decompositions of the syn-diazo cyanides in carbon tetra chloride were similar to those in benzene, as it was often necessary to warm the mixture to start the reaction, and again, about 30 - 50% of the diazo group was eliminated as nitrogen.

The aryl chloride, R. C₆H₄. Cl, was formed in 10 - 20% yield from all five syn-diazo cyanides used in these experiments, and was identified, in the case of liquids, by oxidation or nitration to known products, and in the case of solids, e.g.  Br, by mixed melting point with an authentic specimen.

Formation of the aryl chloride is conclusive proof that

the solvent had been attacked, and the mechanism of this reaction is discussed on pages 65-66.

Hydrogen cyanide was formed when the syn-diazo cyanide was not perfectly dry and aqueous-extracts of the reaction products, after steam-distillation of the tars, always contained an excess of cupric and chloride ions - further proof that the solvent had taken an integral part in the decomposition. In one experiment, an excess of chalk was added to the reaction mixture to keep the solution neutral, but here again cupric and chloride ions were detected along with calcium ions in the aqueous extract, showing that attack on the copper was not due to the formation of chloride ions, but rather to formation of neutral atomic chlorine.

The metals silver, mercury, iron, lead and zinc, had no catalytic effect on the decomposition.

SECTION 8.DISCUSSION OF THE MECHANISMS OF THE COPPER-CATALYSED DECOMPOSITIONS
OF THE SYN- DIAZOCYANIDES IN NON-IONISING SOLVENTS.

Two alternate mechanisms are possible for the decomposition of the diazo cyanides -

(1) Hantzsch's mechanism



(2) The Free-Radical mechanism -



All of our results support the free radical mechanism for the decomposition, and show that one can ascribe to the copper-catalysed decompositions of the syn- diazocyanides in non-ionising solvents a non-ionic mechanism, and suppose that they decompose in presence of metallic copper into nitrogen and two free neutral radicals, which do not unite together instantly as Hantzsch supposed, but react in a complex manner with vicinal solvent molecules.

Thus, in ETHER, the following reactions may take place -



These two reactions show why hydrogen cyanide and acetaldehyde are always produced in all decompositions of the

syn- diazocyanides in ether.

Nitrile formation may occur by direct combination between free phenyl and cyanide radicals -



The reaction, $\text{Ph}\cdot + \text{Ph}\cdot \longrightarrow \text{Ph}\cdot \text{Ph}$ does not take place, since the chances of collision between two phenyl radicals are much less than the chances of collision between the radicals $\text{Ph}\cdot$ and $\text{CN}\cdot$ which are liberated close together.

In BENZENE, diphenyl formation may take place as the result of attack on the solvent by free phenyl radicals, thus -

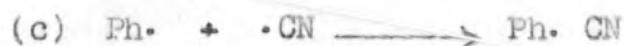


(cf. Hey^{42, 43})

Hydrogen cyanide formation takes place by a similar reaction between free cyanide radicals and the solvent -

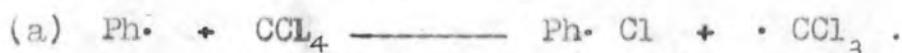


and nitrile formation by either of the two reactions -



the latter being a secondary reaction following the formation of free hydrogen cyanide.

In CARBON TETRACHLORIDE, the aryl chloride may be formed by reaction between free phenyl radicals and the solvent -



It is noteworthy that nitrile formation, which in this case can NOT take place by reaction between cyanide radicals and solvent, is practically suppressed. Thus, it seems likely that nitrile formation by reaction between free phenyl and cyanide radicals, if occurring at all, must take place only to a very small extent. This is to be expected of course, since, with a large excess of solvent, the chances of collision between phenyl radicals and solvent molecules are much greater than the chances of collision between phenyl and cyanide radicals.

The formation of copper and chloride ions in this reaction was probably due to attack on the copper by the $\cdot \text{CCl}_3$ radical formed in reaction (a).

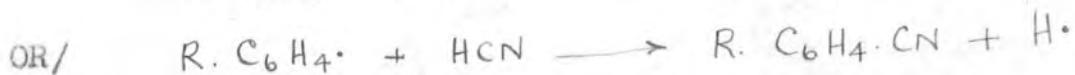


In all reactions in hydrogen-containing solvents, the free cyanide radical yields hydrogen cyanide by the following reaction -



and it evidently does not attack the copper.

Another important fact in support of the non-ionic theory of the decomposition of covalent aromatic diazo-compounds, was that aromatic nitrile formation, (the Gattermann reaction), which may occur by either of the following reactions -



was by no means one of the principal resultant chemical changes.

The final conclusion is, therefore, that the non-ionic decompositions discovered with the diazoacetates⁴⁸,^{42a}, and presumed to occur with the diazohydroxides and diazonium chlorides⁴⁹, proceed in an exactly similar manner with these syn-diazo cyanides in the complete absence of water or of any ionising solvent.

This still further substantiates the theory of free-radical fission of the aromatic diazo-compounds, and makes it quite evident that this decomposition is characteristic of the covalent diazo-compounds, and not of the diazonium cation.

Moreover, it is also evident that the two radicals which result from the scission of the azo-group as nitrogen gas, do not unite at once, even with the syn-diazo-compounds, but react in a complex manner with vicinal solvent molecules.

Hantzschi's mechanism for the decomposition of the aromatic diazo compounds VIZ:-



has therefore, no foundation in experimental fact.

SECTION 9.

INVESTIGATION of the TARS formed in the decomposition of the syn-diazocyanides.

We investigated the tars resulting from the decomposition of the syn-diazocyanides to see whether they were formed by azo-coupling -



or, by complex free - radical coupling -



i.e. It was necessary to find out whether tar formation was a reaction following or preceding the elimination of the nitrogen.

These tars always constituted the major portion of the resultant product. Those obtained from decompositions carried out in acetone or alcohol, in absence of copper, were dark-brown, pitch-like materials, which easily softened on warming. Those obtained from all decompositions where copper was used as catalyst were hard, black, porous, cokey materials, which could easily be dried and powdered. They did not tend to soften on warming, and dissolved only with difficulty in warm, concentrated sulphuric acid, which seems to indicate that they are not polyazo compounds, since azo-compounds and complex azo-dyes are easily soluble in strong sulphuric acid.

These latter tars could not be separated from the finely divided copper particles, hence they were analysed for nitrogen by the Kjeldahl method, and the copper estimated in the resulting liquid by acidification with acetic acid followed by addition of excess of potassium iodide solution, and, titration of the liberated iodine with hypo. This gave the nitrogen content of the tars for copper-free material (see Experimental Section, pp. 133-5)

TABLE X.

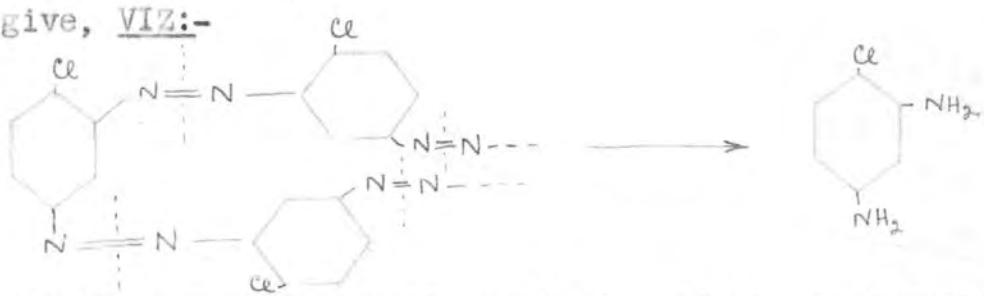
Nitrogen content of the TARS from copper-catalysed decompositions.

<u>SYN- DIAZO COMPOUND</u>	<u>SOLVENT</u>	<u>% of N in TAR</u>
2- CHLORO- 5-CHLORO-o- TOLYL-	ALCOHOL " "	14.3 13.9
2- CHLORO- 4-CHLORO-o- TOLYL-	ACETONE " "	12.7 10.9
4- CHLORO-	CYCLO HEXANE	17.5
4- CHLORO- 4- BROMO- 2- CHLORO- 4-CHLORO-o- TOLYL- 5-CHLORO-o- TOLYL-	ETHER " " " " " " " "	12.7 12.4 16.9 15.3 14.0
2- CHLORO- 2- CHLORO- 4- BROMO- 5- CHLORO-o- TOLYL-	BENZENE " " " " " "	13.8 13.0 10.5 10.1
2- CHLORO- 2- CHLORO- 4- CHLORO-o- TOLYL- 5- CHLORO-o- TOLYL-	CARBON TETRACHLORIDE " " "	10.2 10.4 7.5 10.2

These tars may be regarded as the end-products of complicated chain-reaction processes, and not as poly-azo compounds produced by chain-coupling reactions, since the tars have been found to contain only about 10% of nitrogen per aryl group, and not two nitrogen atoms which the structure, $\text{Ar}_2\text{N}_2[\text{C}_6\text{H}_3 \cdot \text{X} \cdot \text{N}_2]_n$. Ar, would require.

Hence tar formation must follow loss of nitrogen.

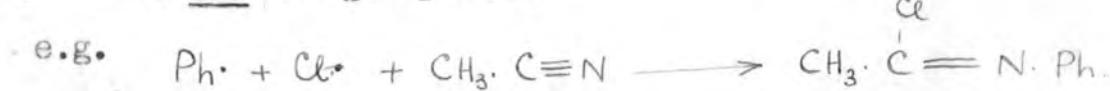
Further, after vigorous reduction with zinc and hydrochloric acid, or with stannous chloride, the tars did not yield detectable quantities of diamines, which polyazo compounds would be expected to give, VIZ:-



though they did give small quantities of the corresponding monoamines, probably due to the reduction of some anti-diazo-cyanide in the tar. On boiling with caustic soda, the tars dissolved and gave off some ammonia, probably due to the hydrolysis of anti-diazo cyanide and/or nitrile.

The tars were insoluble in the solvents used for the decomposition since they separated out from the reaction mixtures.

Hanby and Waters⁵¹, have shown that aryl groups can add on to the — C ≡ N group —





and this would indicate that these tars may be partly polyphenyl,

e.g. $\text{R. C}_6\text{H}_4 \cdot [\text{C}_6\text{H}_3 \cdot \text{X}]_n \cdot \text{Ar}$, where $\text{X} = \text{CN}$,

or $- \text{N} = \text{N} \cdot \text{CN}$ (anti), and partly polyamine,

e.g. $\text{R. C}_6\text{H}_4 \cdot \text{C} \cdot \text{N} \cdot \text{Ar}$

OR/ $\text{Ar. N} \underset{|}{[\text{C}_6\text{H}_3 \cdot \text{X}]} \cdot \text{N} -$

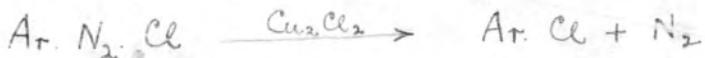
SECTION 10.

THE ACTION OF COPPER AND ITS COMPOUNDS ON THE DECOMPOSITIONS OF THE DIAZO-COMPOUNDS.

Copper and its compounds play such an important part in the decomposition reactions of the diazo-compounds, including the diazo-cyanides, that it is worth while here to discuss briefly some of the more important copper - catalysed reactions.

USE OF COPPER SALTS.

In 1884, Sandmeyer⁵⁴ attempted to prepare phenyl acetylene by bubbling acetylene into a solution of benzene diazonium chloride and cuprous chloride in hydrochloric acid, and obtained instead, chlorobenzene in almost quantitative yield. Further investigation showed him that cuprous chloride was the active agent in the decomposition, thus -



The Sandmeyer reaction, as it is called, is now widely used in organic syntheses, and some of its applications are summarised in Table XI.

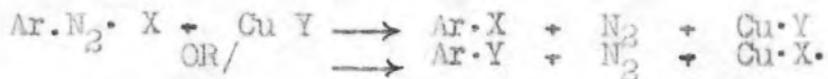
TABLE XI.

APPLICABILITY OF THE SANDMEYER REACTION.

PREPARATION	METHOD
1. Aryl halides - $\text{Ph-N}_2 \cdot \text{X} + \text{Cu X} \longrightarrow$ $\text{Ph-X} + \text{N}_2 + \text{Cu X}$ where X = Cl or Br	Cold acid diazonium solution added to a solution of the cuprous salt
2. Nitriles - $\text{Ph-N}_2 \cdot \text{X} + 2\text{KCN} + \text{CuSO}_4 \longrightarrow$ $\text{Ph-CN} + \text{N}_2 + \text{Cu}(\text{CN})_2 + \text{K}_2\text{SO}_4$	Diazo solution added to hot solution of $\text{CuSO}_4 + \text{KCN}$
3. Thio cyanates	Concentrated solution of KCNS and paste of $\text{Cu}_2(\text{CNS})_2$ added to solution of diazonium sulphate.
4. Nitro - compounds. Only used for difficultly accessible compounds like β - nitro-naphthalene.	(a) Two equivalents of sodium nitrite added to solution of the amine in dilute nitric acid and solution poured on to finely divided cuprous oxide. (b) Diazo sulphate + fresh suspension of cupro-cupri-sulphite treated with an excess of sodium nitrite.
5. Azo - compounds. (Often obtained when one expects to get the aryl halide.)	Solution of cuprous chloride in hydrochloric acid added to the cold diazo solution. (The cuprous salt is oxidised to cupric).
6. Arsenic salts - e.g. phenyl arsenic acid (Cuprous oxide helps, but is not essential in this reaction.)	Cold diazobenzene nitrate neutralised with caustic soda and added to a mixture of sodium arsenite, caustic soda, and cuprous oxide.
7 (a) $4 \text{Ph-N}_2 \cdot \text{HSO}_4 + 2 \text{Cu}_2\text{C}_2 \longrightarrow$ $\text{C}_2\text{H}_2 + 4\text{N}_2 + 4\text{CuSO}_4$ $+ \text{Ph}_2\text{CH} \cdot \text{CH} \cdot \text{Ph}_2$ (b) $2 \text{Ph-N}_2 \cdot \text{HSO}_4 + \text{Cu}_2\text{C}_2 \longrightarrow$ $\text{C}_2\text{H}_2 + 2\text{N}_2 + \text{Ph-Ph} + 2\text{CuSO}_4$	Copper acetylide added to diazonium chloride solution, yields chlorobenzene, phenol, diphenyl, and tetraphenyl ethane.

In these preparations, (1) and (2) are the most widely used in the laboratory, the others being chiefly of theoretical interest.

Hantzsch and Elagden,⁵⁵ investigated this reaction to see whether the "diazonium halogen", or the halogen atom from the copper halide, united with the benzene nucleus to give the aryl halide i.e. they wanted to see which of the following reactions occurred -

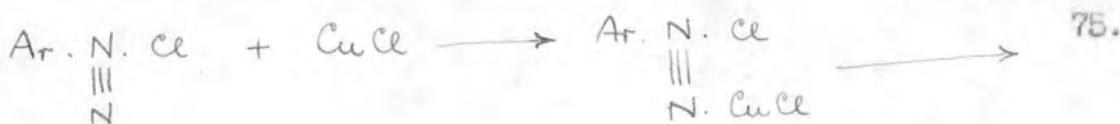


They found that, in indifferent solvents at a low temperature, the preponderant reaction was -



though complete interchange was impossible because the CuX formed attacked the Ar·N₂·X to give some Ar·X.

Thus, cuprous iodide gave some iodobenzene with diazonium chlorides or bromides, just as diazonium iodides yielded some chlorbenzene and bromobenzene with cuprous chloride or cuprous bromide respectively. They isolated double compounds between benzene diazonium chloride and cuprous bromide at low temperatures, and Waentig and Thomas,⁵⁶ isolated the corresponding chloro-compound. These latter workers said that the mechanism of the catalytic reaction was indicated by the following equations -



Lellmann and Remey⁵⁷, and also Sandmeyer, isolated intermediate, unstable, coloured double-salts of the type - $\begin{array}{c} \text{Ar} - \text{N} \\ || \\ \text{Br. N. ; Cu}_2\text{Br}_2 \end{array}$

These double copper salts were coloured red, orange, or yellow, not green or blue like inorganic copper salts, and are quite different from double salts of metals like zinc, tin, cadmium, antimony, bismuth or mercury, with diazonium compounds, which are colourless and decompose to give phenols.

Hantzsch and Elagden (loc.cit.) next studied the reaction between syn-diazo cyanides and copper halides. They found that the syn-diazo cyanides behaved quite differently from the diazonium halides since they gave no double salts with copper halides even in concentrated alcoholic solution, and were only decomposed very slowly by solid cuprous chloride. They attributed this comparative indifference to the "azo-benzene like" syn-structure of the diazo cyanide.

Hantzsch and Schultze¹⁴, had already found that the syn-diazo cyanides in alcoholic solution were readily decomposed by copper powder, and hence, Hantzsch concluded that the action of the

copper powder was catalytic, in contrast to the action of the copper halide which was not catalytic, but involved formation of a labile, active, intermediate double salt.

We did not investigate the reaction between diazo cyanides and cuprous salts except to show that the syn-diazocyanide of p. chloraniline was decomposed slowly in carbon tetrachloride by cuprous chloride to give a small amount of p. dichlorobenzene.

This problem however needs a much more thorough investigation before any definite conclusions can be formed, though it is certain that the syn-diazocyanides are much less reactive with cuprous salts than are the diazonium halides. It will also be very interesting to investigate the action of other salts on the syn-diazo cyanides, since we found, in test-tube experiments, that ferrous sulphate solution brought about extremely rapid decomposition of alcoholic solutions of the syn-diazo cyanides, and other salts had some obscure effect.

Hantzsch tried gold and mercurous chlorides in place of cuprous chloride, as catalysts in the decomposition of the diazo-compounds, but concluded that they were inactive.

Korezynski, Mrozinsky and Vielau⁵⁸, searched for other suitable catalysts, using salts of metals whose atomic weights were near that of copper,—iron, cobalt, nickel, and zinc, and extended their work to metals whose atomic weights were multiples

of the atomic weights of these metals. They found that cobalt and nickel compounds were sometimes good substitutes for copper compounds. The double cyanide of potassium and nickel gave yields of nitrile at 100° identical with those obtained using the corresponding copper salt, whereas the corresponding cobalt salt was inactive.

However, in contrast, they found that the compound, $(Ar.N_2 \cdot SCN)_2$; $Co(SCN)_2$, could be prepared by adding benzene diazonium chloride to a cold solution of cobalt thio cyanate, and, in this reaction, cobalt compounds gave higher yields than copper compounds, whilst nickel compounds were inactive.

The reaction, $Ar.N_2 \cdot Cl \rightarrow Ar.Cl$, was catalysed by nickelous chloride and cobaltous chloride, but the yields were only about 10%, and zinc and iron compounds had no catalytic activity.

Chromium, molybdenum, manganese and tin salts, showed very little activity, but tungsten with atomic weight about three times, and uranium with atomic weight about four times that of the above active elements, were again active.⁵⁹

Fry and Grote⁶⁰, studied the para-halogen amines and found that they gave the same yields of dihalogen benzenes when the diazonium solution was added to a hot or cold solution of $Cu X$ (where $X = Cl, Br$ or I).

They also found that cupric salts were practically as active as cuprous salts in cold solution.

USE OF METALLIC COPPER.

In 1890, Gattermann,⁶¹ found that the diazonium halides were decomposed in solution by copper powder, yielding the aryl halide with evolution of nitrogen - he believed that free copper was as active as copper ions. The following table shows some of the uses of the Gattermann reaction -

T A B L E XII.APPLICABILITY OF THE GATTERMANN REACTION.

REACTION	METHOD.
1. $\text{Ar.N}_2\cdot\text{X} \rightarrow \text{Ar X}$. $\text{X} = \text{F, Cl, Br, I, CN.}$	Copper powder added to the cold diazo solution.
2. $\text{Ar.N}_2\cdot\text{HSO}_4 + \text{KcNo} \rightarrow \text{Ar.N}\cdot\text{Co}^4 + \text{KHSO}_4 + \text{N}_2$	KcNo solution added to the diazonium sulphate then copper powder added.
3. Introduction of sulphinic acid (-SO ₂ -Hgp)	Diazo sulphate in excess of H ₂ SO ₄ . Saturated with SO ₂ in cold solution and copper powder added.* (Note 1.)
4. Dibenzoyl hydrazines R.N.(Co.Ar).N.(Co Ar).R	Aqueous suspension of benzoyl chloride and copper powder added to solution of diazo salt.
5. Diphenyl.	Copper powder added to alcoholic diazonium sulphate solution.* (Note 2.)
6. Sulphonic acids.	Diazonium salt heated with sulphuric acid and copper powder - yields only 20%.

FOOTNOTES -

NOTE 1. - Cuprous sulphide may be used in place of copper powder.

NOTE 2. - Cuprous oxide in ammonia may be used in place of copper powder e.g. o.nitro benzene diazonium chloride gives a good yield of 2.21 dinitro diphenyl with copper powder.

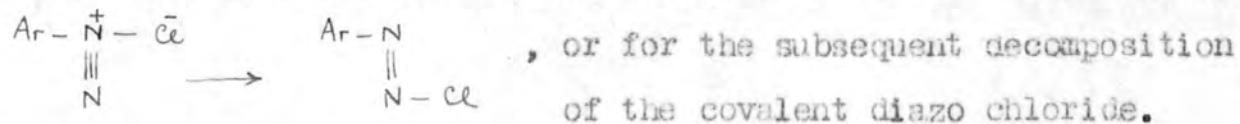
In both the Gattermann and Sandmeyer reactions, diphenyl compounds are often isolated as by-products. The mechanism of diphenyl formation has already been discussed (see p. 65), but, it is remarkable that copper puts up the yield tremendously (up to 70%) in aqueous solution.

In 1939, Waters⁵⁰, made a systematic study of the influence of 38 elements on the decomposition of benzene diazonium chloride in suspension in acetone, kept neutral by chalk. He found that, in general, 'metallic' elements yielded their chlorides, and aromatic compounds were formed by the metals - mercury, tin, arsenic, sulphur, antimony, selenium and tellurium.

He therefore concluded that free aryl radicals were produced in these reactions, and these only reacted with metals when stable, covalent, organometallic compounds were capable of existence.

Waters regards this general catalytic action of metals as a catalysis of the decomposition of the non-ionic diazochloride, $\text{Ph-N}=\text{N-Cl}$, and not as a decomposition of the diazonium kation $(\text{Ph-N}_2)^+$, for reactions of the latter would be possible in aqueous solution, in which circumstances copper is almost the unique catalyst.

No decomposition of the diazonium chloride took place in cold acetone in absence of metals, therefore it seems that the metals must be catalysts for the diazonium \longrightarrow diazo change



Possibly the metals act as electron-donors, bringing about liberation of free aryl radicals, thus -



To return to the Gattermann reaction -

In the decomposition of benzene diazonium chloride in acetone, Waters found that diphenyl was often a minor reaction product as was chlorbenzene. The yield of chlorbenzene increased when the reaction mixture was not kept neutral by chalk, its formation being ascribed, in the absence of metals, to the secondary reactions -

$\text{Ph} + \text{HCl} \longrightarrow \text{Ph-Cl} + \text{H}$ (in acid),
 and, $\text{Ph} + \text{CH}_3\text{Cl} \cdot \text{Co} \cdot \text{CH}_3 \longrightarrow \text{Ph-Cl} + \text{CH}_3 \cdot \text{Co} \cdot \text{CH}_3$ (in neutral solution), rather than to a direct combination between the free radicals.

As already mentioned, in dilute aqueous solution, copper has been found to be the only effective metallic catalyst for replacing the diazo-group by chlorine, bromine or pseudo-halogens. Even in acetone suspension, its effect was outstanding as the following table of results by Waters shows -

TABLE XIII.

YIELDS OF CHLORBENZENE OBTAINED IN THE DECOMPOSITION OF BENZENE DIAZONIUM CHLORIDE IN ACETONE.

CATALYST	Ti	V	Mn	Fe	Co	Ni	Cu	Zn
% OF CHLORBEN- ZENE.	+ trace	+	3	20	1	2	60	0

(It will be noted that, besides copper, iron was the only other metal which gave an appreciable yield of chlorbenzene. This is comparable with our observation that, in the decomposition

of syn- diazocyanides in benzene, iron was the only other metal besides copper, which gave any diphenyl derivative.

Hantzsch thought that the Gattermann reaction might have two alternative courses; one via an intermediate compound, and the other purely catalytic.

Saunders⁶², suggests, that the cuprous ions formed in the Gattermann reaction, do the work. This latter view has been proved incorrect by our experimental work which has shown that decomposition of syn- diazo cyanides in ionising solvents by addition of copper powder, gave nitrile-formation when no cuprous or cupric ions were formed.

Further, we took pure, dry, syn- diazocyanides, and decomposed them in dry organic solvents by addition of copper powder, and found that the metal was always an effective catalyst, even though no copper salts were formed.

Copper salts were only formed in halogenated solvents, and this can be ascribed to secondary reactions of the type -



Though the syn- diazo cyanides decomposed easily with copper powder in ether, ethyl acetate, ethyl alcohol, acetone and benzene, there was no sign of any chemical attack on the copper in these cases.

The metals, zinc, mercury, silver, antimony and lead, had no catalytic activity whatever.

With the possible exception of iron therefore, copper

was unique in its catalytic activity, but why this should be so is difficult to tell. Further investigation of this subject is obviously needed.

Recently, Hodgson⁶³ and his colleagues have suggested that the Sandmeyer reactions are essentially decompositions of complex diazonium salts of the type, $\text{Ar-N}_2^{\bullet}\text{-X-Cu}_2\text{X}_2$, in which the halide anions X, can be exchanged for others in the surrounding solution. They have not explained however, why cuprous salts decompose differently from other double diazonium salts formed by metals like zinc, cadmium, mercury, arsenic etc. e.g. $(\text{Ar-N}_2\text{Cl})_2\text{ZnCl}_2$; $(\text{Ar-N}_2\text{Cl})_2\text{SbCl}_3$.

Waters⁶⁴ has recently put forward a theory which does much to explain the almost unique action of cuprous salts in the Sandmeyer reaction. He suggests that the Sandmeyer and Gattermann reactions involve non-ionic decompositions of diazonium kations brought about by a single electron transference from a cuprous kation or from metallic copper. This hypothesis explains -

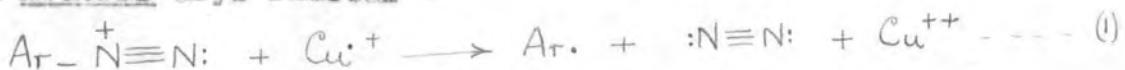
- (1) The unique character of cuprous salts as catalysts
- (2) The course of the principal side reactions without using special structural formulae for intermediate reaction complexes.

As Waters points out, a diazonium kation can only decompose to nitrogen gas and an aryl kation, thus -

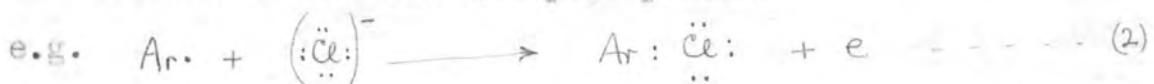


but with the addition of an extra electron provided by a reducing agent (e.g. a cuprous salt), the diazonium kation can give rise to

a neutral aryl radical -



In acid aqueous solution this neutral aryl radical will react with halide ions with consequent release of an electron if there is an electron-acceptor present



In the Sandmeyer reaction, the local halide anion concentration of the double salt will be very large, and the electron released in reaction (2) will be accepted by the cupric kation formed in reaction (1)



Therefore the whole cycle involving single electron transference can take place in the immediate locus of the complex salt.

This theory explains why cuprous salts are almost unique in promoting reactions of this type, since

(1) Metallic kations of constant valency, e.g. Na^+ , Zn^{++} , Al^{++} , cannot act as electron sources, neither can kations in their highest state of valency e.g. Cu^{++} , Fe^{++} , Au^{++} .

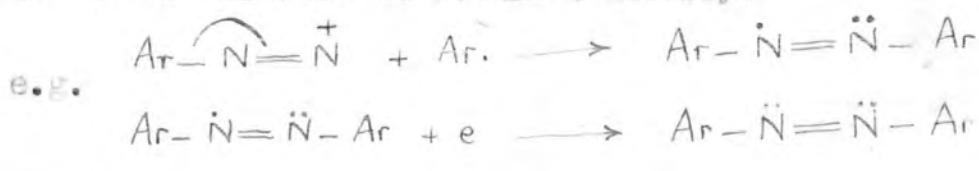
(2) The oxidation potential for the release of an electron from the kations of other transition elements is far too high for the change to occur easily in acid media

e.g. Mn^{++}	\longrightarrow	Mn^{++}	requires an oxidation potential
			of 1.5 V.
Co^{++}	\longrightarrow	Co^{++}	" " " 1.8 V.
Fe^{++}	\longrightarrow	Fe^{++}	" " " 0.75V.
Cu^+	\longrightarrow	Cu^{++}	" " " 0.2V.

The stannous kation with an oxidation potential of - 0.4 V. is too strong a reducing agent in acid solution and converts diazonium compounds to hydrazines. Arsenic, antimony, and bismuth in their trivalent state are too feeble reducing agents in acid solution, but in neutral solution, arsenic and antimony are oxidised more easily and react with aromatic diazo-compounds (cf. Waters⁴⁹) 1957, 121.

(3) Silver, lead, mercurous and thallous halides are insoluble in water and acids and hence are of no use in preparing aryl halides.

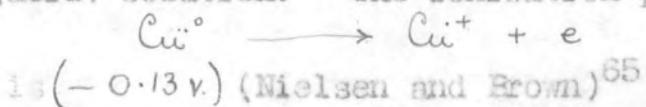
The formation of azo- compounds as by-products in the Sandmeyer reaction (Hantzsch and Blagden⁵⁵) can result from the reaction between diazonium kations and aryl kations, the primary product being a radical which must acquire an additional electron from some other molecule to attain stability.



Thus, formation of azo-compounds and also of diaryls, leads to permanent oxidation of some of the cuprous salt, but stabilisation of transient neutral radicals may in part be attained by complicated chain reactions leading to tar formation, such as we found in our investigation of the diazo cyanides (see p. 70-71)

The products in the Gattermann reaction are the same as in the Sandmeyer reaction, and the previous theory can be applied

here because a small amount of copper salt is always formed in aqueous (acid) solution. The ionisation potential for —



is very small in acid solution, so that the reduction potential for the initial stages of the Sandmeyer and Gattermann reactions, e.g. $\text{Cu}^+ + \text{Ar}-\overset{+}{\text{N}}\equiv\text{N}: \longrightarrow \text{Cu}^{++} + \text{Ar}^- + :\text{N}\equiv\text{N}:$ would be almost identical.

However, although many metals will react with diazochlorides in acetone, ethyl acetate or acetonitrile, our experimental work has shown that only copper seems to be effective as a promotor of the decomposition of the syn-diazocyanides in a number of solvents, thus showing that many problems concerning the critical potentials for initiating single electron transferences remain to be solved.

SECTION 11.EXPERIMENTAL SECTION.

Syn- diazocyanides were prepared from

- (a) p. chloraniline, (b) o. chloraniline, (c) p. bromaniline,
 - (d) 4- chloro-o- toluidine and, (e) 5- chloro-o- toluidine,
- by the following method -

PREPARATION OF SYN- DIAZOCYANIDES.

The base hydrochloride ($\frac{1}{10}$ gm. mol.) was finely powdered and dissolved in 25 cc. concentrated hydrochloric acid + a little water, cooled to 0°C and treated with 1/10th of a gm. mol. (7 gms.) of sodium nitrite. 20 cc. of absolute alcohol was added to prevent freezing and the mixture cooled to about -10°C .

A saturated solution of potassium cyanide (1/5th gm.mol.) was then run in slowly with vigorous stirring, the temperature being kept below -5°C . More acid was added if necessary to keep the solution acidic at the end of the reaction.

The orange coloured precipitate was filtered off, washed well with ice-cold water, and dried as far as possible by suction.

Damp reaction products were purified rapidly by dissolving in an ice-cold mixture of ether and light petroleum, shaking for ten minutes with fresh, anhydrous sodium sulphate, filtering, and blowing off the ether in a current of dry air.

Products were then dried overnight in a dark glass vacuum dessicator at 0°C .

PREPARATION OF ANTI- DIAZOCYANIDES.

Anti- diazocyanides were prepared by decomposing the dry syn-

compounds by warming in carbon tetrachloride, and filtering after addition of animal charcoal. The filtrates on concentrating and cooling yielded fairly pure specimens of anti-diazocyanides. Where necessary, further purification was carried out by crystallisation from 40-60 petroleum.

Dry specimens of syn-diazocyanides could be kept for several days in the dark, and almost indefinitely in the dark at 0°, but damp specimens gave off hydrogen cyanide on keeping and formed tarry products which smelt strongly of isocyanide and contained very little anti-diazocyanide.

We studied the reactions of the following diazocyanides. Those marked with an asterisk have not been described previously.

T A B L E XIV.

DIAZOCYANIDES USED IN OUR EXPERIMENTAL WORK.

<u>DIAZOCYANIDE</u>	<u>MELTING POINT.</u>	
	<u>SYN-</u>	<u>ANTI-</u>
(1) 4- CHLORO-	29°	105°
(2) 2- CHLORO-	49°	78°
(3) 4- BROMO-	43°	130°
(4) 2-METHYL - 5 - CHLORO-	49°	68°
(5) 2-METHYL - 4 - CHLORO-	60°	75°

The syn-diazocyanides were obtained as small orange-yellow needles, and the anti-as long red prismatic needles.

REACTION BETWEEN SYN- DIAZOCYANIDES AND SILVER NITRATE.

(1) QUALITATIVE -

Freshly prepared alcoholic solutions of the syn- diazocyanides of the bases (a) - (e), reacted immediately with alcoholic silver nitrate, precipitating silver cyanide and leaving practically colourless solutions of the diazonium nitrate which in chloride, coupled readily with alkaline β - naphthol.

After a short time the alcoholic solutions turned reddish-brown, and then would not couple. Acidified solutions however did not change colour on keeping.

(2) QUANTITATIVE -

In the following quantitative experiments, the syn- diazocyanide prepared from 5- chloro- o- toluidine was used. It was prepared in the usual manner, then dried overnight in a dark-glass vacuum dessicator at 0° .

SAMPLE I.

Using a 0.0189 molar solution of the syn- diazocyanide in absolute alcohol. 50 cc. of this solution was added at timed intervals to 100 cc. of alcoholic silver nitrate (50cc. of $10\frac{N}{10}$ AgNO_3 + 50cc. absolute alcohol). The silver cyanide formed was collected on a sintered glass Gooch, washed well with water and alcohol, dried in the air-oven at 120° , and weighed. The following results were obtained:-

TABLE XV.

<u>TIME FROM ZERO</u> <u>(Mins.)</u>	<u>WEIGHT OF</u> <u>SILVER CYANIDE</u>	<u>% OF CYANIDE</u> <u>REACTING.</u>
1.35	0.0866	68.3
4.5	0.0816	64.3
8.0	0.0738	58.1
11.5	0.0703	55.4
22.0	0.0636	50.1
40.0	0.0600	47.3
82.0	0.0615	48.4
187.0	0.0600	47.3

SAMPLE 2.

Sample 0.0147 molar

(A) NEUTRAL solution.

<u>TIME (mins.)</u>	<u>WEIGHT OF</u> <u>SILVER CYANIDE</u>	<u>% OF CYANIDE</u> <u>REACTING.</u>
3.7	0.0775	78.3
10.0	0.0693	70.0
24.0	0.0646	65.3
41.0	0.0628	63.5
60.0	0.0645	65.2
145.0	0.0639	64.6
285.0	0.0593	59.9
3 DAYS	0.0581	58.7

(B) ACIDIC solution.

Solution 0.0148 molar in absolute alcohol made $\frac{N}{2}$ with dilute nitric acid. The solution in this case was much paler than in (A), and addition of silver nitrate gave a much cleaner precipitate of silver cyanide.

TABLE XVI.

TIME (Mins.)	WEIGHT OF SILVER CYANIDE	% OF CYANIDE REACTING.
3.0	0.0929	93.9
5.5	0.0924	93.4
8.0	0.0923	93.3
20.0	0.0925	93.5
90.0	0.0916	93.6
228.0	0.0920	93.8
260.0	0.0928	93.8 α
3 DAYS	0.0750	75.5 β

In the above calculations the diazocyanide was assumed to be 100% pure, but evidently the purity of Sample 2 was c. 94% and that of Sample 1 still less.

The reactions with Sample 2 were carried out in a darkened room, except for α which had been exposed to sunlight for half an hour, and for β which had been exposed to light for two days.

These tables are all represented graphically in FIG. VI
p. 90(a).

REACTION BETWEEN ANTI-DIAZOCYANIDES AND SILVER NITRATE.

Alcoholic solutions of all the anti-diazocyanides gave no immediate precipitation when treated with alcoholic silver nitrate, but on exposure to light, silver cyanide gradually formed, and the solution became paler in colour. Eventually, reduction of the white silver cyanide precipitate occurred.

FIG. VI

95

ACID SOL^N

90

PRECIPITATION OF AgCN FROM ALCOHOLIC SOLUTIONS
OF 5-CHLORO-O-TOLYL SYN-DIAZOCYANIDE

85

80

75

70

65

60

55

50

45

% AgCN

-

-

-

-

-

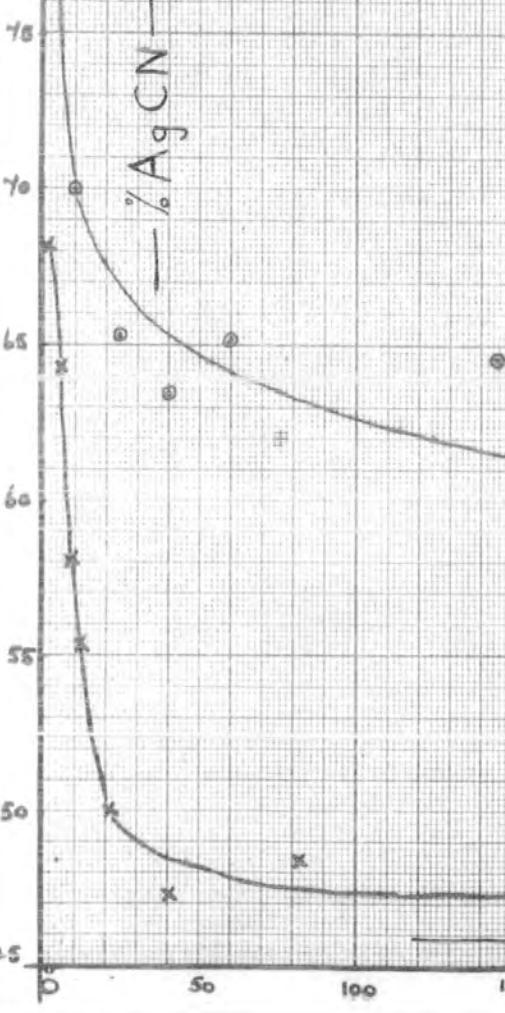
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TIME (MINS)

- NEUTRAL SOL^N- NEUTRAL SOL^N

DECOMPOSITION OF ANTI- DIAZOCYANIDES IN ACETONE AND ALCOHOL.

(A) Trans- 4-chlorobenzene diazocyanide in acetone.

10% solutions of the diazocyanide were allowed to decompose in the apparatus shown (Fig. II A p.^{34(a)}) in 4 flasks A - D, containing 50 cc. of solution and connected to nitrometers.

Flasks B and D were protected from the light by immersion in a bath of black dye, and flasks C and D each contained 3 gms. of copper powder.

To prevent water vapour from distilling back into the acetone solution, the nitrometer tap was kept closed except when readings were taken. Readings were taken twice daily, at 9 a.m. (M), and at 5 p.m. (A).

The readings obtained are shown in Table XVII and Table XVIII.

TABLE XVII.

Decomposition of Trans- 4-chlorobenzene diazocyanide in acetone - NITROGEN EVOLVED.

DAYS	TOTAL VOLUME AT N.T.P.				INCREASES IN VOLUME.			
	A	B	C	D	A	B	C	D
1	M 60.9	A 55.4	C 56.9	D 56.3	-	-	-	-
	A 68.5	M 61.5	A 72.4	M 63.4	7.6	6.2	15.5	7.1
2	M 75.1	A 57.8	M 72.2	A 59.9	14.2	8.4	15.3	3.6
	A 82.6	M 60.6	A 78.9	M 63.3	21.9	5.2	12.0	7.0
3	M 88.5	A 57.1	M 81.9	A 60.3	37.4	1.7	25.0	4.0
	A 96.5	M 61.6	A 92.9	M 65.5	35.0	6.2	36.0	9.2
4	M 102.2	A 57.6	M 93.2	A 61.6	41.3	3.2	36.3	5.3
	A 111.4	M 63.4	A 106.4	M 69.9	50.5	8.0	49.5	13.6
5	M 116.8	A 59.4	M 105.2	A 64.3	55.9	4.0	48.8	8.0
	A 126.6	M 62.3	A 120.9	M 68.7	95.7	6.9	64.0	12.4
7	M 166.6	A 68.2	M 125.1	A 74.8	105.7	12.8	68.2	18.5
	A 165.6	M 64.2	A 122.8	M 72.2	104.7	8.8	65.9	15.9
8	M 174.9	A 71.2	M 127.2	A 79.1	113.0	15.8	70.1	22.8
	A 171.9	M 65.7	A 126.3	M 74.6	111.0	10.3	69.4	18.3
9	M 178.1	A 69.1	M 131.7	A 77.6	117.3	13.7	74.8	21.3
	A 180.3	M 63.6	A 130.8	M 73.1	119.4	8.2	73.9	16.8
10	M 186.2	A 66.9	M 132.4	A 71.7	125.3	11.5	75.5	15.4
	A 187.4	M 64.0	A 133.0	M 73.0	126.5	8.6	76.1	16.7
11	M 192.1	A 70.3	M 136.1	A 80.0	136.3	14.9	79.2	23.7

The following second set of readings were obtained using the same sample of anti-diazocyanide.

TABLE XVIII.

1	56.4	54.5	52.8	53.4	-	-	-	-
2	M 59.4	54.0	67.5	53.8	3.0	-0.5	14.7	0.4
A	61.5	56.3	71.9	55.6	5.1	1.8	19.1	2.2
3	M 61.6	53.1	72.7	53.4	5.2	-1.4	19.9	-1.0
A	64.2	55.7	76.7	56.6	7.8	1.2	23.9	3.2
4	M 64.7	51.9	76.9	51.6	8.3	-2.6	24.1	-1.8
6	M 67.9	51.6	77.8	51.1	11.5	-2.9	35.0	-2.3
A	70.6	53.7	80.7	53.8	14.2	-0.8	27.9	0.4
7	M 73.6	51.4	81.9	51.2	17.2	-3.1	29.1	-2.2
A	76.4	52.8	81.5	52.8	20.0	-1.7	28.7	-0.6
8	M 77.5	50.9	82.5	50.7	21.1	-3.6	29.7	-2.7
A	79.4	51.7	83.0	52.8	27.2	-1.9	31.5	-0.6
9	M 82.0	51.5	84.8	51.6	25.6	-3.0	32.0	-1.8
A	83.6	52.6	84.3	52.8	27.2	-1.9	31.5	-0.6
10	M 84.7	50.6	85.6	50.7	28.3	-3.9	32.6	-2.7
A	85.5	50.6	85.8	51.1	29.1	-3.9	33.0	-2.3
11	M 87.6	51.3	85.9	51.9	31.2	-3.2	33.1	-1.5
13	M 96.8	51.7	86.5	53.7	40.4	-8.8	33.7	0.3
A	104.9	56.5	92.2	64.9	48.6	2.0	39.4	11.5
14	M 111.0	53.5	93.2	58.1	54.6	-1.0	40.4	4.7
A	111.6	57.9	94.3	59.2	55.2	3.4	41.5	5.8
15	M 118.1	55.1	96.7	60.7	61.7	0.6	43.9	7.3
A	124.1	58.0	96.9	67.1	67.7	3.5	44.1	13.7
16	M 128.7	55.4	98.4	68.3	72.3	0.9	45.6	8.9
A	149.2	60.8	106.1	71.9	92.8	6.5	53.3	18.5
17	M 153.3	54.9	106.5	63.0	96.9	0.4	53.7	9.6

The results are represented graphically in Figs III & IV p. 35(a) & 35(b)

The acetone was distilled off from each mixture directly into an excess of silver nitrate solution. In the case of the darkened mixtures, these were protected from light during the distillation. The silver cyanide formed was filtered into a sintered glass gooch, washed well with water then with alcohol, dried at 110° and weighed, the following results being obtained -

TABLE XIX.

	I.	WEIGHT OF SILVER CYANIDE	
		II.	
A Without copper in light	0.7522g	0.6815 g.	
B With copper in light	0.0063 g	0.0052 g.	
C Without copper in dark	0.0865 g	0.0220 g.	
D With copper in dark	NIL	N I L	

From residues C and D, the trans- diazocyanide was recovered unchanged by steam distillation, in almost quantitative yield.

The residue from A was a black, semi-crystalline tar, which on steam-distillation yielded only a trace of trans- diazocyanide and left a black, non-volatile, tarry residue.

Residue B was very different in appearance, being a jet-black, glossy tar. On steam-distillation it yielded some unchanged diazocyanide, and the white needles of the nitrile were noted in the condenser. It was found impossible to separate the nitrile and trans- diazocyanide by fractional crystallisation from dilute methyl alcohol, hence nitrile formation could not be definitely confirmed.

Decomposition of the TRANS- diazocyanide from 4- chloro-o-toluidine in ALCOHOL.

The previous experiments were repeated using the 4- chloro-o-tolyi trans- diazocyanide in 10% alcoholic solution. Experimental

details were the same as in the two previous experiments except that no decompositions were examined quantitatively in absence of light, it having been found that an alcoholic solution of trans- 4- chloro- o- toyl diazocyanide was unchanged on keeping in the dark for several weeks.

The following results were obtained -

T A B L E XX.

Decomposition of TRANS 2-chloro- 5- methyl-benzene diazo cyanide in alcohol - NITROGEN EVOLVED.

- A - 50cc of 10% alcoholic solution
- B - 50cc of 10% alcoholic solution +
1 gm. of copper powder.

T A B L E XIII.

DAYS	TOTAL VOLUMES AT N.T.P.		INCREASES IN VOLUME	
	A.	B.	A.	B.
1 M	55.1	55.0	-	-
A	60.8	58.5	5.7	3.5
2 M	65.1	63.0	10.0	7.0
A	72.1	68.8	17.0	13.8
3 M	76.4	72.1	21.3	17.1
A	83.5	78.7	38.4	33.7
4 M	90.1	83.6	35.0	26.6
A	96.7	89.3	41.6	34.3
5 M	103.9	93.7	48.8	38.7
A	111.1	99.9	56.0	44.9
6 M	118.5	108.6	63.4	47.6
8 M	137.9	123.7	88.8	68.7
A	144.7	130.9	89.6	75.9
9 M	151.8	138.0	96.7	83.0
A	157.6	144.3	102.5	89.3
10 M	164.7	151.3	109.6	96.3
A	170.6	157.8	115.5	102.8
11 M	177.5	165.6	122.4	110.6
A	182.9	172.0	127.8	117.0

TABLE XXI (Continued).

DAYS	TOTAL VOLUMES AT N.T.P.		INCREASES IN VOLUME.	
	A	B	A	B
12 M	190.3	180.8	135.2	125.8
	195.3	186.9	140.2	131.9
13 M	202.0	195.2	146.9	140.2
	220.1	221.2	165.0	166.2
15 M	225.2	227.5	170.1	172.5
	231.1	235.9	176.0	180.9
16 M	236.1	241.2	181.0	186.2
	241.0	250.2	185.9	195.2

These results are represented graphically in Fig. V p. 35(c).

The solvent was distilled off in each case. The solvent from A gave a colour with Schiff's reagent only after a minute's shaking, therefore very little aldehyde was present. The distillate gave no precipitate of silver cyanide with silver nitrate, and went turbid on dilution, a few drops of pale brown oil separating out. Steam distillation of the tarry residue yielded a little oil and no trans-diazocyanide.

The oil, extracted with ether, contained no nitrile, since, on boiling with caustic soda, no ammonia was evolved. The oil was identified as p. chloro toluene by oxidation with alkaline permanganate to p. chlorobenzoic acid m.p. 238° , the melting point being unchanged on admixture with an authentic specimen.

The solvent from B gave an immediate colour with Schiff's reagent, contained no cyanide, and yielded an oil on dilution.

The tarry residue on steam-distillation yielded more oil along with a trace of solid. The steam-distillate was extracted with

ether, the ether removed by distillation and the oily residue refluxed with aqueous caustic soda. A good deal of ammonia was evolved.

The alkaline solution was diluted and extracted with ether, yielding 0.3 gm. of an oil which was identified as p.chlorotoluene by oxidation with permanganate to p. chlorobenzoic acid m.p. 236° , as above.

The alkaline extract on acidification yielded 0.1 gm. of a white solid, m.p. 169° after crystallisation from dilute alcohol. This was identified as 2- methyl- 5- chloro- benzoic acid by mixed melting point with an authentic specimen.

. . . The products of the photochemical decomposition of TRANS- 4 chloro-o- toyl diazocyanide in alcohol are -

(a) Without copper -

The hydrocarbon, p. chlorotoluene, and a trace of aldehyde.

(b) With copper -

The hydro carbon, the nitrile, and acetaldehyde.

i.e. The photochemical decomposition of the tranz- diazocyanides yielded the same products as the thermal decomposition of the syn- diazocyanides.

DECOMPOSITION OF THE SYN- DIAZOCYANIDES IN VARIOUS SOLVENTS,
WITH AND WITHOUT ADDITION OF METALS.

The following results were obtained in decomposition reactions carried out on a larger scale with freshly prepared samples of syn- diazocyanides. The apparatus used is shown in Fig. II B. p. 34 (a).

Dry solutions of the syn- diazocyanides in the various solvents were warmed under reflux by immersion in water, until reaction set in.

The evolved nitrogen was collected by displacement of water and measured. The solvent was then distilled off and tested for volatile products, the residue was distilled in steam, the distillate examined, and the residual tar collected, dried, and analysed for its nitrogen by the Kjeldahl method, and subsequently for copper by thiosulphate titration.

DECOMPOSITIONS IN ETHYL ALCOHOL.

(1) In absence of metal:-

(a) 22 gm. of the syn- diazocyanide from 5- chloro- o- toluidine was dissolved in 450 cc. absolute alcohol. The mixture was warmed and a fairly vigorous nitrogen evolution began, but reaction stopped after about 15 minutes. The solution was allowed to stand for three days. The solvent was then distilled off and found to contain an excess of cyanide (by precipitation of silver cyanide). It gave an immediate colouration with Schiff's reagent and a copious precipitate with 2.4. dinitrophenyl hydrazine

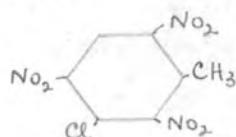
(m.p. 161° on recrystallisation from alcohol - mixed m.p. unchanged on admixture with a pure specimen of acetaldehyde 2·4. dinitro phenyl hydrazone). The alcohol distillate was diluted well with water and a pale-brown oil separated. This was extracted with chloroform, dried over calcium chloride and distilled directly, giving 1·8 gms. b.p. $158^{\circ} - 160^{\circ}$.

After removal of the alcohol the tarry residue was steam-distilled and yielded more pale-brown oil which was extracted with ether, dried over calcium chloride and distilled giving, 1·6 gms b.p. $160^{\circ} - 164^{\circ}$.

Total yield of oil = 3·4 gms. ($17\frac{1}{2}\%$)

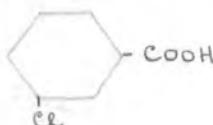
The oil was shown to be m. chloro toluene by two methods -

(i) Nitration. The oil ($\frac{1}{2}$ g.) was nitrated in 2 stages by fuming nitric acid (1cc) and concentrated sulphuric acid (1cc). The first stage yielded a mixture of nitration products which was further nitrated by warming on the water-bath to 90° with 1cc fuming nitric acid and 1 cc concentrated sulphuric acid. The nitration mixture was poured on to ice and the almost white solid filtered and crystallised from methyl alcohol in white needles m.p. 149° , corresponding to 3 chloro.2·4·6. trinitro toluene —



(ii) Oxidation:- $\frac{1}{2}$ gm. of the oil was oxidised by refluxing for 12 hours with a slight excess of alkaline permanganate. The solution was decolourised by passing SO_2 and the acid obtained

filtered, washed well with cold water and crystallised from aqueous meths in white needles m.p. 158-9°, corresponding to 3-chlorobenzoic acid. —



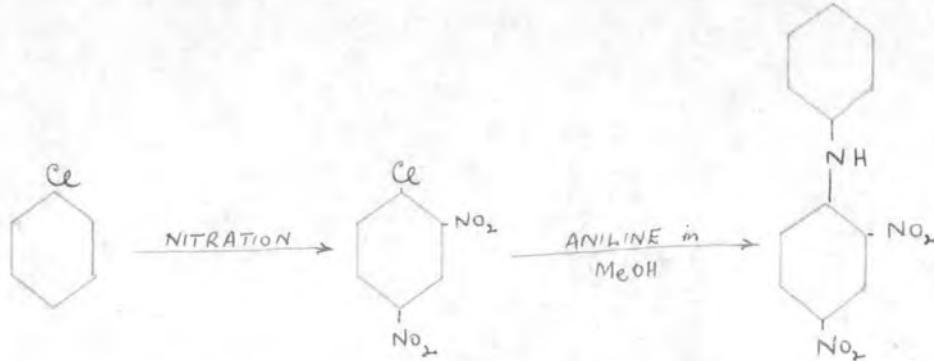
(b) 26 gm. of 2-chlorobenzene syn-diazocyanide were dissolved in 300cc of absolute alcohol. Nitrogen evolution began immediately and the reaction became vigorous on gentle warming. The reaction had practically ceased after half an hour and was completed by refluxing for a few minutes.

The solvent distilled off contained an excess of hydrogen cyanide and acetaldehyde (both identified as previously). The whole distillate was diluted well with water and a pale-brown oil separated overnight. Steam distillation of the tarry residue gave only a trace of chlorobenzene and a trace of the trans-diazocyanide (melting point 78°).

The diluted alcohol distillate, after extraction with chloroform, as previously, yielded 3.7 gms (22%) of chlorobenzene.

This was identified as follows -

1 gram of the oil was heated for 3 hours at 100° with 3 cc of conc. nitric acid and 3 cc of conc. sulphuric acid. The nitration mixture was cooled and poured on to ice, when a sticky solid (crude 2,4-dinitro chlorbenzene), separated. This was dissolved in 20cc methyl alcohol, a few drops of aniline added and the solution heated to boiling. On cooling, bright red needles of 2,4-dinitro diphenylamine separated, m.p. 154-155° (unchanged on admixture with an authentic specimen).



This method was always used for the identification of chlorobenzene.

(2) DECOMPOSITIONS IN ALCOHOL WITH COPPER POWDER AS CATALYST.

(a) 13 gms. of the syn- diazocyanide from 5- chloro- o-toluidine were dissolved in 300cc of absolute alcohol and 5 gms of copper powder added.

An immediate vigorous evolution of nitrogen occurred and the reaction had to be controlled by cooling. Nitrogen evolution was complete in about 3 minutes. The mixture was refluxed 5 minutes to complete the reaction, cooled to room temperature and the nitrogen evolved measured after levelling. The reaction mixture stood overnight and the solvent was distilled off and found to contain an excess of hydrogen cyanide and acetaldehyde (by the usual tests.)

The distillate was diluted well with water, allowed to stand overnight, and the oil which separated was extracted with chloroform.

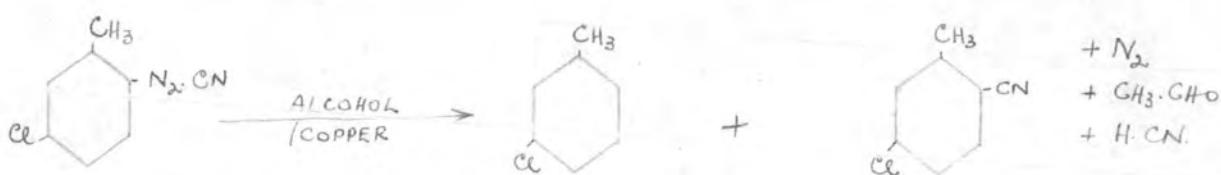
The chloroform extract was dried and distilled and yielded 2.2 gm. of an oil, bp. 150-160°, which was identified as m. chlorotoluene by oxidation with alkaline permanganate to m. chlorobenzoic acid, m.p. and m.m.p. - 157-158°.

The tarry residue left after removal of the alcohol was

steam-distilled, the steam-distillate extracted with ether, the extract dried over calcium chloride and the ether distilled off. This yielded an oily residue which was hydrolysed by refluxing with aqueous caustic soda until all ammonia was evolved. The alkaline extract was diluted and extracted with ether, and the ether extract after drying and distillation yielded 0.2 or 0.3 gm. of an unhydrolysable oil which was presumably m. chlorotoluene. The alkaline extract on acidification yielded 0.1 gms. of 5 chloro-o-toluic acid, m.p. and mixed m.p. — 172°

∴ Yields are -

- (1) 2.4 gm (29%) of m. chlorotoluene
- (2) 0.1 gm (c.1%) of 5-chloro-o-toluic nitrile.



(b) 21 gms. of 2-chlorobenzene-syn-diazocyanide were dissolved in 280cc of absolute alcohol and 5 gms. of copper powder added.

Nitrogen evolution began immediately, ^{became vigorous, and had to be} controlled by cooling. The reaction was complete in a few minutes.

The solvent distilled off contained excess of hydrogen cyanide and acetaldehyde (immediate colour with Schiff's reagent and 2.4-dinitro phenyl hydrazone m.p. and m.m.p. 161°).

The whole distillate was diluted well with water, stood overnight and was extracted with chloroform, yielding, after drying and distillation —

2.8 gms of oil b.p. 125-134°, identified as chlorobenzene

by nitration to crude 2,4-dinitrochlorobenzene and condensation of this with aniline to 2,4-dinitro-diphenylamine; no condensation of this with aniline to 2,4-dinitro-diphenylamine m.p. and m.m.p. 155°

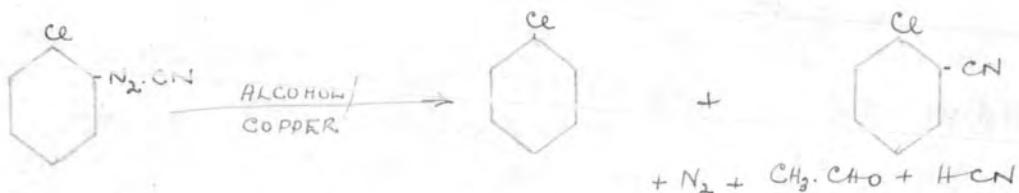
The tarry residue, steam-distilled, gave a few drops of oil and a trace of solid. Extraction of the steam distillate with ether, and hydrolysis as usual with caustic soda yielded -

0.25 gm. chlorobenzene, and 0.1 gm. of 2-chloro benzoic acid m.p. and m.m.p. 137°

∴ Yields are -

(i) 3.05 gm. chlorobenzene (22%)

(ii) 0.1 gm. 2-chlorobenzonitrile (c.0.5%)



In each of these cases, the aqueous residue after steam distillation, contained no copper ions and there was no evidence of any chemical attack on the copper, such as was found in decompositions in carbon tetrachloride. (p. 114-121)

(3) DECOMPOSITIONS IN ALCOHOL WITH OTHER METALS AS CATALYSTS.

(a) MERCURY -

4.5 gms. of 4-chloro-o-tolyl-syn-diazocyanide were dissolved in 75 cc of absolute alcohol, 20 gms. of mercury added and the mixture shaken well. Only a very slight nitrogen evolution was noticed. The mixture was warmed slightly but no further

reaction took place. The solvent was distilled off and gave positive tests with silver nitrate, Schiff's reagent, and 2.4. dinitrophenylhydrazine. The distillate on dilution yielded 0.5 gms. of p.chlorotoluene (identified by oxidation with alkaline permanganate to p.chlorobenzoic acid, m.p. and mixed m.p. 236°).

Steam-distillation of the tarry residue yielded no nitrile and the mercury metal was not attacked since it did not blacken on addition of concentrated ammonia solution.

(b) ZINC-

9 gms. of 4-chloro-o-tolyl-syn-diazocyanide was dissolved in 100 cc of absolute alcohol and 10 gms. of zinc dust added. Nitrogen evolution was only very slight, even on warming. The mixture stood overnight and the alcohol, distilled off, was found to contain hydrogen cyanide and acetaldehyde, and on dilution yielded 0.8 gms. of p.chlorotoluene which was identified as usual. Steam-distillation of the tarry residue yielded no nitrile, and the aqueous extract after steam-distillation contained no zinc salts.

(c) ANTIMONY-

Antimony metal had no catalytic effect on the decomposition of p.chlorobenzene-syn-diazocyanide in alcohol, though no quantitative measurements were made.

DECOMPOSITIONS IN ACETONE.(1) In the absence of metallic catalyst.

(a) 20 gms. of p. bromobenzene syn- diazocyanide were dissolved in 200 cc of dry acetone. Very little nitrogen was evolved, and the mixture was warmed and then allowed to stand overnight.

The solvent distilled off contained an excess of hydrogen cyanide and no other volatile products.

Steam-distillation of the tarry residue yielded 5 gms of the trans- diazocyanide m.p. 129-130° and no other volatile product. The residue in the flask was a hard, black, non-volatile tar from which no crystalline products could be isolated by extraction with petrol, alcohol or benzene.

(b) 20 gm. of 5-chloro - o - toyl - syn- diazocyanide were dissolved in 330 cc dry acetone and left standing for half an hour at room temperature. Only a very slight evolution of nitrogen took place, and the mixture was warmed for a few minutes to complete any reaction, and allowed to stand overnight. The solvent distilled off, contained an excess of hydrogen cyanide and no other volatile product.

Steam-distillation of the tarry residue yielded only about 1 gm. of the trans- diazocyanide m.p. 75° (after crystallisation from 40-60 petrol), and no crystalline products could be obtained from the tarry residue by extraction with petrol, benzene or ether.

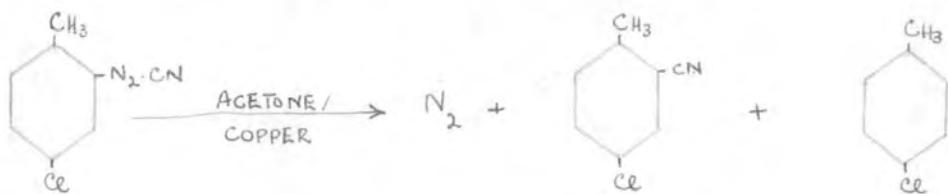
2. With copper as catalyst.

(a) 26 gms. of 4-chloro-o-tolyl-syn-diazocyanide were dissolved in 200 cc of dry acetone and about 5 gms. of copper powder added. There was no immediate reaction but soon a very vigorous nitrogen evolution took place and the reaction had to be controlled by cooling. The reaction stopped after half an hour and was completed by refluxing for a few minutes. The acetone was then distilled off and found to contain no hydrogen cyanide and no other volatile products. The brown tarry residue was steam-distilled and a little brown oil along with a pale yellow solid came over. The aqueous residue in the flask after the steam-distillation contained no copper or cyanide ions. The steam distillate was extracted with ether, concentrated and petrol added. Pale yellow needles m.p. 46° (2.5 gms) separated and were filtered off and identified as 2-methyl- 5-chloro benzonitrile by alkaline hydrolysis to 2-methyl-5-chlorobenzoic acid, m.p. and mixed m.p. 169° .

The ether-petrol filtrate was evaporated down and left 0.2 gm. of oil, which on alkaline hydrolysis yielded a further 0.1 gm of 2-methyl-5-chlorobenzoic acid, m.p. 169° and 0.1 gm of unhydrolysable oil which was identified by oxidation with alkaline permanganate to p.chlorobenzoic acid m.p. and mixed m.p. 236° .

∴ Yields are

- (1) 2.6 gm. (10.5%) 2-methyl-5-chloro benzonitrile
- (11) 0.1 gm. (0.5%) p. chlorotoluene.



(b) Experiment (a) was repeated as the isolation of p. chlorotoluene was considered unsatisfactory.

20 gm. of 4-chloro- o - tolyl-syn- diazocyanide were dissolved in 200 cc. of dry acetone and 5 gm. of copper powder added. Nitrogen evolution began immediately and became very vigorous so that the reaction had to be controlled by cooling. Reaction was completed later by warming for 10 minutes.

The solvent was distilled off and contained no volatile products. Steam-distillation of the tarry residue gave an oily solid which was extracted with ether, and the residue after removal of the ether was refluxed with aqueous caustic soda until all ammonia was evolved.

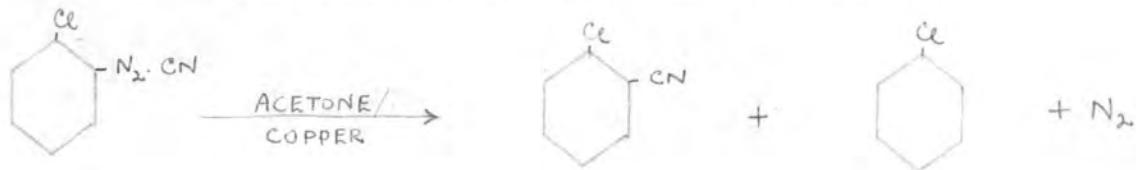
The alkaline extract was diluted and extracted with ether. Acidification of the aqueous fraction gave 1.7 gms. of an acid identified as 2-methyl-5-chlorobenzoic acid by m.p. and mixed m.p. 169°.

The ether extract yielded 0.8 gms. of oil b.p. 150-158°, identified as p. chlorotoluene by oxidation to p. chlorobenzoic acid, as previously. (m.p. and mixed m.p. 236°)

∴ Yields are (1) 1.7 gms. (9%) of 2-chloro-5-methyl benzonitrile
 (2) 0.8 gms. (6%) of p.chloro-toluene.

(c) 22 gms. of 2-chlorobenzene syn-diazocyanide were dissolved in 250 cc. of dry acetone and 5 gms. of copper powder added. Nitrogen was evolved immediately, the reaction became very vigorous and had to be controlled by cooling. Reaction was completed by refluxing for 5 minutes. The solvent was distilled off and contained no hydrogen cyanide or other volatile products. The remaining tarry residue was steam-distilled and yielded a little pale brown oil along with some pale yellow solid. The steam-distillate was extracted with ether, the ether distilled off, and the oily residue hydrolysed by boiling with aqueous caustic soda until all ammonia was evolved. Worked up in the usual way it yielded -

- (1) 2.1 gm. of 2-chlorobenzic acid, (10%), m.p. and mixed m.p. 137° .
- (ii) 0.6 gm. (4%) of chlorobenzene, identified by nitration and subsequent condensation with aniline in methyl alcohol to 2,4-dinitro-diphenylamine m.p. and mixed m.p. 155°



The copper was not attacked, since the aqueous extract after steam-distillation contained no copper salts.

- (d) 20 gm. of 4-chlorobenzene-syn-diazocyanide was dissolved in 200 cc. of dry acetone and 5 gm. of copper powder added. An immediate violent reaction took place and most of the reaction mixture was blown out of the flask before cooling could be applied.

The residue after removal of the solvent was steam-distilled and yielded some 4-chlorobenzonitrile m.p. 92° , after crystallisation from dilute alcohol, identified by alkaline hydrolysis to 4-chlorobenzoic acid m.p. and mixed m.p. 236° .

A trace of oil, smelling strongly of chlorobenzene, was also obtained but not identified for certain.

(3) DECOMPOSITIONS IN ACETONE WITH OTHER METALS AS CATALYSTS.

(a) ANTIMONY.

5 gm. of 4-chlorobenzene syn-diazocyanide were dissolved in 50 cc. of dry acetone and 2 gms. of antimony powder added. No apparent reaction took place in the cold or on warming. The solvent was distilled off and found to contain an excess of hydrogen cyanide but no other volatile products. Steam distillation of the tarry residue yielded 0.5 gms. of the anti-diazocyanide, m.p. 105° after recrystallisation from petrol, and no nitrile. No crystalline product could be obtained from the tarry residue by extraction with petrol, benzene or ether.

(b) Qualitative experiments carried out with MERCURY and ZINC showed that these metals had no catalytic effect on the decomposition of 4-chlorobenzene-syn-diazocyanide in acetone.

DECOMPOSITION OF THE SYN-DIAZOCYANIDES IN AQUEOUS SOLUTION.

(1) WATER.

5 gm. of 4-chlorobenzene-syn-diazocyanide were suspended in 50 cc. of water in a flask connected to a nitrometer. In 3 days at room temperature only 25 cc. of nitrogen were given off.

The flask was detached from the nitrometer and heated on the water bath for 2 hours when a good deal of tar-formation took place. The contents were then steam-distilled and an orange red solid came over, the distillate smelling strongly of isocyanide.

The red solid, crystallised from petroleum ether (40-60) melted at 104° and mixed melting point showed it to be trans- 4- chloro benzene diazocyanide. A non-volatile tarry residue remained.

(II) QUEOUS ALCOHOL.

15 gm. of 4-chlorobenzene-syn-diazocyanide were dissolved in 50cc. of alcohol and poured into 300 cc. of water. The suspension was allowed to decompose at room temperature protected from light. After standing overnight the flask contained a turbid brown tarry mixture which was steam-distilled, yielding an orange solid. The steam distillate was dissolved in ether and extracted with dilute caustic soda, but the alkaline extract on neutralisation gave no colour with neutral ferric chloride thus indicating the absence of a phenol.

The ether extract on drying and evaporation yielded 1.5 gms. only of trans-4-chlorobenzene- diazocyanide m.p. and mixed m.p. 105° .

(III) ALCOHOLIC HYDROCHLORIC ACID -

20 gms. of 4-chlorobenzene-syn-diazo-cyanide were suspended in 100 cc. of 2N.HCl. + 50 cc. water and left standing overnight. The mixture frothed a good deal and nitrogen and hydrogen cyanide

were given off. The mixture was then heated under reflux for two hours and darkened rapidly with tar-formation. Steam distillation yielded only a trace of trans-diazocyanide m.p. and mixed m.p. 104°, no phenol, and no other volatile product.

DECOMPOSITIONS IN D I E T H Y L E T H E R.

(a) WITHOUT METALLIC CATALYST.

In the absence of metallic catalyst, very little decomposition of the syn-diazocyanides occurred in ether solution, and, after standing for a few days, the corresponding trans-diazocyanide could be obtained in almost quantitative yield from the solution. The slight amount of tarring that usually took place was probably due to the presence of a little moisture.

(b) WITH METALLIC COPPER AS CATALYST.

Decompositions of syn-diazocyanides in ether with copper powder were not easy to control, for, although there was some evolution of nitrogen, solutions, even after standing for more than a week, tended to decompose violently upon evaporation to dryness.

(1) 17 gms. of 2-chlorobenzene syn-diazocyanide were dissolved in 250 cc. of ether and 5 gms. of copper powder added. A slow evolution of nitrogen began and the mixture was then refluxed for 1 hour, and allowed to stand for 3 days. Nitrogen was still being slowly evolved. The ether was distilled off and found to contain an excess of hydrogen cyanide and acetaldehyde (character-

ised by formation of its 2,4-dinitrophenylhydrazone m.p. and mixed m.p. 162°).

When nearly all the ether had been removed the reaction became violent. Dense yellow fumes were given off and a brown tarry solid passed over into the condenser; a good deal of heat was evolved and a bulky porous tar was left behind in the reaction flask. The tarry residue was steam-distilled, yielding a viscous oil, which was hydrolysed to remove nitrile in the usual manner, the final products being -

- (i) 0.2 gm. 2-chlorobenzoic acid (3%) m.p. and mixed m.p. 138°
(by hydrolysis of 2-chlorobenzonitrile.)
- (ii) 0.65 gms. (6%) of chlorobenzene, identified by nitration followed by condensation with aniline, giving 2,4-dinitro-
di phenylamine m.p. and mixed m.p. 155°.
- (2) 31 gms. of the syn-diazocyanide from 5-chloro-
-o-toluidine were dissolved in 220 cc. of dry ether and 5 gms. of copper powder added. The slow nitrogen evolution which began immediately, was accelerated by warming at intervals for 5 days.

The solvent was distilled off and a violent reaction again took place near the end of the distillation, even though the latter part of the distillation was carried out very slowly.

The solvent was again found to contain an excess of hydrogen cyanide and acetaldehyde by the usual tests.

Steam-distillation of the residue yielded a pale-brown oil

which was treated in the usual manner yielding -

- (i) 0.35 gm. (2%) of 5-chloro-o-toluic acid, m.p. and mixed m.p. 171° by hydrolysis of the 2-methyl- 4-chlorobenzonitrile.
- (ii) 2.0 gms. (14%) of 3-chlorotoluene, identified as its trinitro derivative m.p. and m.m.p. 149° (3 chloro- 2,4,6- trinitro toluene) The nitration of the 3-chlorotoluene was carried out as on p. 98.
- (3) 28 gm. of the syn- diazocyanide from 4-chloro-o-toluidine was dissolved in 250 cc. of dry ether and 5 gms. of copper powder added. Nitrogen evolution in this case was much more vigorous than in the previous cases, and continued slowly all the following day. The reaction mixture was allowed to stand for a week with warming at intervals, but even in this case the same violent reaction occurred as the last traces of solvent were being removed, leaving a bulky porous tar in the reaction flask. The solvent was again found to contain an excess of hydrogen cyanide and acetaldehyde.

Steam-distillation of the tarry residue followed by the usual procedure, yielded -

- (i) 1.1 gms. (4%) of 4-chloro-o-toluic acid, m.p. and mixed m.p. 169° , by hydrolysis of the 4-chloro-o-toluonitrile.
- (ii) 1.7 gms. (9%) of p. chlorotoluene, b.p. $158^{\circ}-162^{\circ}$, identified by oxidation with alkaline permanganate to p. chlorobenzoic acid, m.p. and mixed m.p. 237° .
- (4) 22 gms. of 4-bromobenzene-syn- diazocyanide were dissolved in 200 cc. of ether and 5 gms. of copper powder added. A slow evolution of nitrogen began immediately, and the mixture was refluxed for 2 hours before standing for 3 days.

The solvent was distilled off as usual, but in this case no violent reaction occurred. The solvent was again found to contain an excess of hydrogen cyanide and acetaldehyde.

The tarry residue, worked up in the usual way, yielded -

(i) 1.0 gm. (6%) of bromobenzene, identified as follows -

0.5 gm. warmed to 50° for 2 hours with 2.5 cc. conc. nitric acid and 2.5 cc. conc. sulphuric acid. The mixed was cooled and poured on to crushed ice and the yellow solid filtered and crystallised from dilute methyl alcohol m.p. 126° unchanged on admixture with a pure specimen of 4-nitrobromobenzene.

(ii) 0.5 gm. (3%) of p. bromobenzoic acid m.p. and mixed m.p. 251° obtained by hydrolysis of p. bromobenzonitrile with caustic soda.

(5)

30 gms. of MOIST 4-chlorobenzene syn-diazocyanide was dissolved in 350 cc. of ether and 5 gms. of copper powder added. The reaction was accelerated by warming, but a slow nitrogen evolution was still taking place after 4 days.

The solvent was distilled off and found to contain an excess of hydrogen cyanide and acetaldehyde. Near the end of the distillation a very violent reaction took place and a good deal of the product was lost.

About 0.5 gm. of p. chlorobenzonitrile was isolated, m.p. and mixed m.p. 92°.

Only a trace of chlorobenzene was isolated as the bulk of it had evidently been lost during the violent decomposition.

DECOMPOSITIONS OF THE SYN- DIAZOCYANIDES IN CARBON TETRACHLORIDE.

Dry solutions of syn- diazocyanides in carbon tetrachloride isomerised quantitatively to the corresponding anti- diazocyanides, and this method was adopted for the preparation of the anti- diazo-cyanides.

(1) WITH METALLIC COPPER AS CATALYST.

(a) 23 gm. of 4-chlorobenzene syn- diazocyanide (probably moist) were dissolved in 200 cc. of carbon tetrachloride and 5 gms. of copper powder added. Practically no reaction took place in the cold, but slow nitrogen evolution began on warming. The mixture was refluxed for 1 hour when some tar formation took place and a good deal of hydrogen cyanide was given off.

The solvent was distilled off and the remaining tarry residue was steam-distilled, yielding a pale-yellow solid which was extracted with ether. The ether extract was dried over calcium chloride and the ether evaporated off leaving a yellow discoloured solid m.p.c. 55°. This was purified by vacuum distillation yielding a white solid m.p. 54-55° (2 gms.), melting point unchanged on admixture with a pure specimen of p. dichlorobenzene.

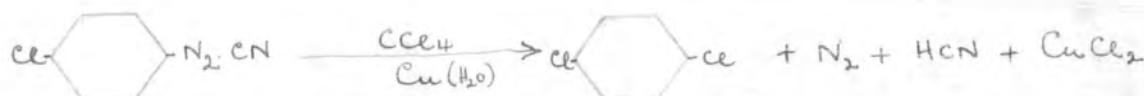
The aqueous residue in the flask after steam-distillation was tested for copper salts as follows -

- (i) The solution, acidified with dilute hydrochloric acid gave a copious brown-black precipitate of copper sulphide with hydrogen sulphide.
- (ii) Addition of ammonia gave a deep blue colouration.

- (iii) Addition of ferrous sulphate solution followed by acid ferric chloride gave no colouration and thus showed the absence of cyanide ions.
- (iv) Addition of silver nitrate gave a copious precipitate of silver chloride (insoluble in boiling dilute nitric acid).

This proved clearly the presence of copper and chloride ions in the steam-distillate.

Yield - 2.0 gm. (9%) of p. dichlorobenzene



(b) 16 gm. of 2-chlorobenzene syn-diazocyanide was dissolved in 200 c.c. of dry carbon tetrachloride and 5 gms. of copper powder added. Reaction started only on warming, then continued steadily for about $2\frac{1}{2}$ hours and was completed by refluxing for $\frac{1}{2}$ hour. The solvent was distilled off using a fractionating column and found to contain no hydrogen cyanide. The tarry residue was steam-distilled, and the oily solid which came over was extracted with ether, the ether removed, and the residue hydrolysed by boiling with aqueous caustic soda until all ammonia was evolved.

The alkaline solution was worked up as usual yielding -

- (i) 1.0 gm. (7%) of oil, b.p. $175-181^\circ$, identified as o. dichlorobenzene by nitration to the dinitro derivative 1.2. dichloro.3.5. dinitrobenzene m.p. and mixed m.p. 110° .
- (ii) 1.7 gm. (12%) of O. chlorobenzoic acid m.p. and mixed m.p. 137° .
- (c) A repeat of experiment (b) was carried out, more care being

taken to keep out moisture from the reaction. 19 gms. of syn-compound decomposed in 200 cc. carbon tetrachloride with copper powder yielded -

- (1) 2.0 gm. (14%) of o. dichlorobenzene
- (2) 0.6 gm. (4%) of o. chlorobenzonitrile.

Both compounds were identified as previously and aqueous extracts after steam-distillation of the tar, were found to contain excess of copper and chloride ions, and no cyanide ions.

(d) 30 gms. of the syn- diazocyanide from 4- chloro-o-toluidine were dissolved in 250 cc. of dry carbon tetrachloride and 5 gms. of copper powder added. No reaction took place at room temperature, but on warming a steady evolution of nitrogen began and continued for 3 hours; a good deal of hydrogen cyanide was given off too. After standing overnight the solvent was distilled yielding a pale red oil, which was extracted from the steam-distillate with ether. Removal of the ether and distillation yielded 4.5 gms. of oil b.p. 200°.

The oil was identified as 2.4- dichloro toluene as follows -

(a) 1 gm. of the oil was suspended in 50 cc. of water, 10 gms. of permanganate added and the mixture refluxed for 20 hours. The resulting mixture was decolourised by passing sulphur dioxide in excess. Some oil was unchanged but a little white crystalline solid separated. This was filtered, washed with cold water and recrystallised from hot water, m.p. 163°, unchanged on admixture with an authentic specimen of 2.4- dichlorobenzoic acid.

(b) 1 gm. of the oil was nitrated with 3 cc. fuming nitric

acid and 3 cc. of conc. sulphuric acid, by warming at 60° for 1 hour. The mixture was cooled and poured on to ice, the yellow solid which separated was crystallised from dilute methyl alcohol and had m.p. and mixed m.p. 104-105°, corresponding to 2·4· dichloro- 3·5· dinitrotoluene.

Yield = 4·5 gms. (17%) of 2·4· dichlorotoluene.

The aqueous residue in the flask after steam-distillation was found to contain excess of copper and chloride ions, by the usual tests.

(e) 22 gm. of 4-bromobenzene syn- diazocyanide were dissolved in 200cc. of dry carbon tetrachloride and 5 gms. of copper powder added. No reaction took place in the cold, but a steady evolution of nitrogen began on warming. The mixture was refluxed for 4 hours and went almost black.

The solvent was distilled off and found to contain no hydrogen cyanide. The remaining tarry residue was steam-distilled, yielding a pale yellow solid which was extracted with ether and finally crystallised from dilute methyl alcohol. 2 gms. m.p. 66°.

The aqueous residue in the flask after steam-distillation, contained an excess of copper and chloride ions, but no cyanide ions.

An authentic specimen of 4-bromo chlorobenzene was prepared as follows, for checking with the compound m.p. 66°.

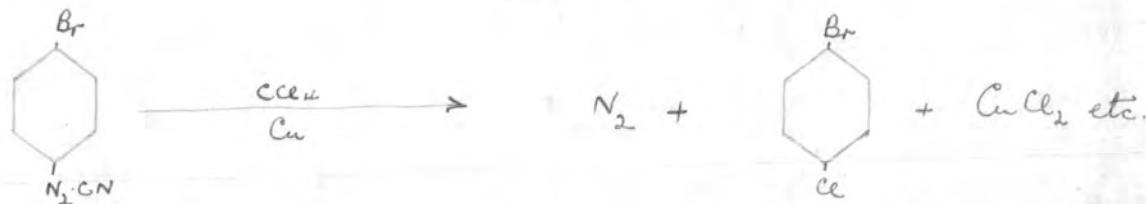
PREPARATION OF p. BROMOCHLOROBENZENE -

12.5 gm. of p. chloraniline was dissolved in 20cc. of conc. sulphuric acid + 12 cc. of water, cooled, and diazotised at 0-5° by addition of a concentrated solution of 7 gm. of sodium nitrite in water. Cuprous bromide was prepared by adding 18 gms. of copper sulphate in 60 cc. of water to 9 gms. of potassium bromide in 20 cc. of water and passing sulphur dioxide into the solution until precipitation was complete.

The cuprous bromide was filtered, washed well with water, and added to 30 cc. of hydrobromic acid in a 50 cc. flask cooled well in ice.

The diazonium solution was then added slowly to the copper solution with shaking, the mixture being heated under reflux on the water bath as soon as the reaction slackened. The mixture was finally steam-distilled when a yellow solid plus a little red oil came over. This was extracted with ether, washed well with dilute caustic soda, then with water, the ether distilled off and the solid residue crystallised from dilute methyl alcohol gave 8.8 gms. m.p. 66°, unchanged on admixture with the compound obtained above.

Yield = 2 gms. (10%) of p. bromochlorobenzene



(f) 25 gms. of the syn- diazocyanide obtained from 5-chloro-o-toluidine

were dissolved in 180 cc. of carbon tetrachloride and 5 gms. of copper powder added. The mixture was warmed gently for a few seconds and a very vigorous reaction took place so that the reaction had to be controlled by cooling. The mixture darkened rapidly and nitrogen evolution continued for about an hour.

The mixture was then refluxed for 1 hour and some hydrogen cyanide was given off. The solvent was distilled off and found to contain hydrogen cyanide.

Steam-distillation of the tarry residue gave a pale-brown oil and later, a small amount of pale yellow solid. The whole was extracted with ether, dried over calcium chloride and distilled directly giving 5.3 gms. b.p. 190-203°, which solidified easily on cooling in ice.

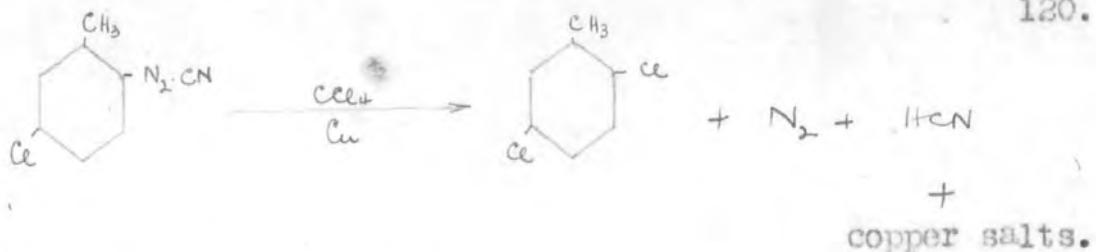
This was identified as 2.5. dichlorotoluene as follows -

1 gm. of the oil was mixed with 7 gms. of fuming nitric acid and 3½ gms. of concentrated sulphuric acid, and, after standing for $\frac{1}{2}$ hour at room temperature, was poured on to crushed ice.

An almost white solid separated immediately and was filtered and crystallised twice from dilute methyl alcohol in white needles m.p. 100-101°, unchanged on admixture with an authentic specimen of 2.5. dichloro 4.6. dinitrotoluene.

The aqueous residue after steam-distillation was again found to contain an excess of copper and chloride ions and a trace of cyanide ions (detected by ferrous sulphate solution followed by ferric chloride which gave a very slight Prussian Blue precipitate).

∴ YIELD = 5.3 gms (25%) of 2.5. dichlorotoluene.



(g) 38 gms. of the syn- diazocyanide from 4-chloro-o-toluidine were dissolved in 280 cc. carbon tetrachloride, 5 gm. of powdered chalk were added to keep the solution neutral, followed by 5 gms. of copper powder. The mixture was warmed gently and a fairly vigorous nitrogen evolution began. The mixture stood overnight and the solvent, distilled off, was found to contain hydrogen cyanide.

The tarry residue, steam-distilled, and extracted with ether yielded 4.8 gms. of oil, b.p. 190-200°. A trace of nitrile remained, and was detected by boiling with caustic soda.

The oil was identified as 2,4-dichlorotoluene as follows -

1 gm. of the oil, 7 gms. of fuming nitric acid and 4 gms. of conc. sulphuric acid were warmed at 70-80° on the water bath, with shaking, for $\frac{1}{2}$ hour. The mixture was cooled and poured on to crushed ice, yielding a pale-yellow solid which crystallised from meths in white needles m.p. 105°, unchanged on admixture with an authentic specimen of 2,4-dichloro-3,5-dinitrotoluene.

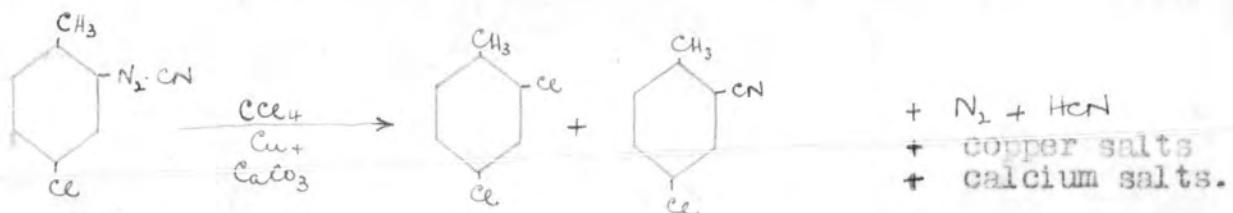
The aqueous residue left in the flask after steam distillation was filtered hot and the filtrate tested as follows -

- (i) Part was boiled with dilute nitric acid and gave a copious precipitate of silver chloride on addition of silver nitrate
- (ii) Addition of ammonium hydroxide and ammonium oxalate gave a copious precipitate of calcium oxalate.
- (iii) Part was acidified with dilute hydrochloric acid and gave a copious precipitate of copper sulphide when treated with hydrogen sulphide.

(iv) The solution gave no colouration with ferrous sulphate solution followed by ferric chloride solution

∴ The solution contained an excess of calcium, copper, and chloride ions, and no cyanide ions.

YIELD = (a) 4.8 gms. (19 $\frac{1}{2}$) of 2,4-dichlorotoluene
 (b) a trace of nitrile.



(h) Experiment (g) was repeated without addition of calcium carbonate, 30 gm. of syn- compound being dissolved in 250 cc. carbon tetrachloride and 5 gms. copper powder added.

Yields were - (a) 4.2 gm. (16%) of 2,4-dichlorotoluene (identified as in (g)), and also by oxidation with alkaline permanganate to 2,4-dichlorobenzoic acid, m.p. and mixed m.p. 163°.

(b) a trace of nitrile.

(2) DECOMPOSITIONS IN CARBON TETRACHLORIDE WITH OTHER METALS AS CATALYSTS.

The metals SILVER, MERCURY, IRON, LEAD and ZINC were tried and found to have no catalytic activity whatever on solutions of syn- diazocyanides in carbon tetrachloride.

e.g. (a) 25 gms. of 4-chlorobenzene-syn- diazocyanide were dissolved in 250 cc. of carbon tetrachloride, 15 gms. of mercury were added

and the mixture shaken well to disperse the metal. No sign of reaction took place even on gentle warming.

The mixture was refluxed for 1 hour after standing overnight, and was then decanted off from the metal. The metallic residue contained no mercuric chloride as it did not blacken on addition of ammonia. A little of the solvent was distilled off and found to contain no cyanide. The rest of the solution was boiled with charcoal and filtered, and on concentration yielded 30 gms. of TRANS- diazocyanide m.p. and mixed m.p. 105° . Concentration of the mother liquor yielded a further 2.5 gms. of trans- diazocyanide and a trace of tarry material.

(b) 15 gms. of 4- chlorobenzene syn- diazocyanide were dissolved in 150 cc. of carbon tetrachloride and 5 gms. of iron powder added. A very slight nitrogen evolution began on warming but soon stopped completely. The flask was warmed on the water-bath for an hour but there were no further signs of reaction. The solution was decanted from the metallic residue, and the latter, extracted with water, was found to contain no ferrous or ferric salts. The rest of the solution was filtered hot after addition of a little charcoal and yielded 12.3 gms. of trans- diazocyanide m.p. and mixed m.p. 105° , and further concentration of the mother liquor yielded a slight tarry residue which probably contained a little more trans- diazocyanide.

(c). 5 gms. of 4- chlorobenzene syn- diazocyanide were dissolved in 50 cc. of carbon tetrachloride and 5 gms. of lead powder added. No

reaction took place even on warming. The mixture was refluxed for 1 hour and then decanted from the metallic residue. The lead residue was filtered off, washed with a little carbon tetrachloride, boiled with a little water and filtered. The filtrate contained no lead salts since it gave negative reactions with potassium iodide solution, dilute sulphuric acid and hydrogen sulphide.

The carbon tetrachloride solution on concentration yielded 4 gms. of trans- diazocyanide m.p. and mixed m.p. 105°.

(d) 18 gms. of 4-chlorobenzene syn- diazocyanide were dissolved in 180cc. of carbon tetrachloride and 4 gms. of zinc dust added. No reaction took place even on warming, no zinc salts were formed and the solution after filtration and concentration yielded 14 gms. of trans- diazocyanide, m.p. and mixed m.p. 105°.

DECOMPOSITIONS OF THE SYN- DIAZOCYANIDES IN BENZENE.

As in carbon tetrachloride, dry solutions of the syn- diazocyanides in benzene isomerised quantitatively to the corresponding anti- diazo-cyanides.

Addition of copper powder, however, brought about evolution of nitrogen and hydrogen cyanide. The copper was not attacked, as aqueous residues from steam-distillates contained no copper salts, and the tars did not appear to contain any cuprous cyanide.

(1) WITH METALLIC COPPER AS CATALYST.

(a) 28 gms. of syn- 4-chlorobenzene diazocyanide were dissolved in 250 cc. of benzene in a R.B. flask under reflux, and 5 gms. of copper powder were added. A slow evolution of nitrogen began at room temperature and was accelerated by warming. After standing overnight the mixture was refluxed for 1 hour, and the solvent distilled off was found to contain an excess of hydrogen cyanide.

The remaining tarry residue was steam-distilled, yielding a small amount of a pale-brown solid which collected in the condenser. This was extracted with methyl alcohol and filtered boiling after addition of charcoal. White glistening plates separated on cooling m.p. 77° , unchanged on admixture with an authentic specimen of 4-chloro-diphenyl. Yield 0.5 gm. (1.5%).

This experiment was repeated under identical conditions using 20 gm. of syn- compound in 200 cc. of dry benzene, and yielded 0.35 gms. (1.5%) of 4- chlorodiphenyl, m.p. and mixed m.p. 77° . In each case the aqueous residue in the steam-distillate was found to contain no copper ions.

(b) 24 gms. of the syn- diazocyanide from 4-chloro-o-toluidine were dissolved in 200 cc. of dry benzene and 5 gms. of copper powder added. A slow evolution of nitrogen began at room-temperature. On warming, the decomposition became vigorous and had to be controlled by cooling - a good deal of hydrogen cyanide was evolved.

The mixture was allowed to stand overnight and was then refluxed for 1 hour. The solvent was then distilled off and found to

contain an excess of hydrogen cyanide.

The tarry residue was steam-distilled and yielded a trace of solid which separated in the condenser. This was extracted with ether, the ether evaporated off and the semi-solid residue boiled with aqueous caustic soda until all ammonia was evolved.

The alkaline liquor was extracted with ether, but evaporation of the ether yielded no product. Acidification of the alkaline portion yielded a white solid which was filtered and washed with water giving

0.3 gms. (2%) of 4-chloro-o-toluic acid, m.p. and mixed m.p. 169°.

Extractions of the tarry residue with

- (a) petroleum ether (60-80), (b) methyl alcohol and
- (c) benzene, in that order, yielded no identifiable products.

Several further decompositions were carried out in benzene with the syn-diazocyanides from 4- and 5-chloro-o-toluidine in presence of copper powder. They yielded traces of nitriles only and no diphenyls could be obtained either by steam-distillation of the tarry residues or by extraction of the latter with various solvents.

It is possible that distillation of the tarry residues in a high vacuum would have been more successful, but unfortunately this method was not tried.

(c) 26 gms. of 4-bromobenzene syn-diazocyanide were dissolved in 200 cc. of dry benzene and about 5 gms. of copper powder were

added. A slow evolution of nitrogen only began on warming. The mixture was warmed gently for an hour, and a good deal of nitrogen and hydrogen cyanide were evolved. The reaction was completed by refluxing for four hours, and the solvent distilled off, was found to contain a good deal of hydrogen cyanide. The tarry residue was steam-distilled and a pale-yellow solid separated in the condenser. This was extracted with ether, the residue after removal of the ether, being boiled with aqueous caustic soda until all ammonia was evolved. On cooling the diluted alkaline solution shining plates separated. These were crystallised from dilute methyl alcohol and gave 0.3 gm. m.p. 89° (corresponding to 4-bromo-di phenyl).

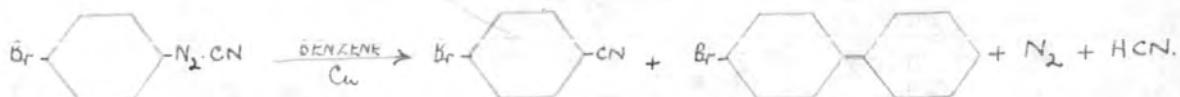
Acidification of the alkaline liquor yielded 0.5 gms. of p. bromobenzoic acid, m.p. and mixed m.p. 251° after recrystallisation from dilute alcohol.

The copper was not attacked as the aqueous residue left after steam-distillation was found to contain no copper salts.

Yields are -

(i) 0.3 gms. 4-bromodiphenyl (1.1%)

(ii) 0.5 gms. 4-bromobenzonitrile (2.2%)



(d) Experiment (c) was repeated under the same conditions using 15 gms. of 4-bromo benzene-syn-diazocyanide in 150 cc. dry benzene and yielded finally —

(i) 0.65 gms. p. bromobenzoic acid, m.p. 253°, 5.0%

(ii) 0.15 gms. p. bromodiphenyl, m.p. 88.5° (1.0%)

(e) 16 gms. of 2-chlorobenzene-syn-diazocyanide were dissolved in 150 cc. of dry benzene and 5 gms. of copper powder added. The mixture was warmed slightly to start the reaction and a fairly vigorous evolution of nitrogen began. When this had almost stopped, the mixture was refluxed for hour to complete the reaction. The solvent was distilled off and found to contain an excess of hydrogen cyanide. The remaining tarry residue was steam-distilled yielding a brown oily solid which was extracted with ether and hydrolysed in the usual manner. This yielded 0.8 gms. of 2-chlorobenzoic acid m.p. and mixed m.p. 137° and a non-hydrolysable brown oil (0.5 gms.) b.p. 269-274°. The oil was boiled for 3 hours with 0.5 gms. of chromic trioxide in 20 cc. acetic acid + a few drops of concentrated sulphuric acid.

No oxidation product could be isolated and no unchanged oil was recovered.

Yields -

(i) 0.8 gms, 2-chlorobenzoic acid, m.p. 137° (5%)

(ii) 0.5 gms. oil, b.p. 269-274° - not identified.

The experiment was therefore repeated as follows -

18 gms. of 2-chlorobenzene syn-diazocyanide were dissolved in 250 cc. of dry benzene and 5 gms. of copper powder added. The mixture was treated as previously and yielded finally, 1.1 gms of 2-chlorobenzoic acid, m.p. and mixed m.p. 137°, and 0.6 gms. of a pale-brown oil, b.p. 270°-275°.

This time, 0.3 gms. of the oil were nitrated by mixing with 1.0 cc. of fuming nitric acid and 1.0 cc. of concentrated sulphuric acid and warming to 60-65° for $\frac{1}{2}$ hour. The nitration mixture was cooled and poured on to crushed ice. A pale-brown solid product separated, and after filtration, it was crystallised from meths with addition of charcoal; it was only sparingly soluble in hot meths. A pale-yellow solid was obtained m.p. 153-4°.

3 further re-crystallisations from meths gave m.p. 157° - small, pale-yellow prisms.

For purposes of comparison, a specimen of 2-chloro-diphenyl was prepared as follows -

80 cc. of concentrated hydrochloric acid and 80 cc. of water were added with vigorous stirring to 28 gms. of o. chloraniline, so that the base hydrochloride separated as a finely divided solid. This was cooled to 0° and diazotised by adding 16 gms. of solid sodium nitrite in portions. The diazonium solution so obtained was filtered and 30 gms. of zinc chloride dissolved in the smallest possible amount of dilute hydrochloric acid was added.

The white zinc chloride - double salt separated rapidly and was quickly filtered and washed well with acetone. It was then transferred to a 1 litre flask containing 170 cc. of benzene, 80 cc. of acetone, and 15 gm. of powdered chalk. The mixture was shaken well and 10 gms. of zinc dust added. No reaction took place for about 5 minutes, then a vigorous nitrogen evolution took place and the reaction had to be controlled by cooling. The col-

ourless mixture had gone dark-brown. After the vigorous reaction had subsided the mixture was refluxed for $1\frac{1}{2}$ hours and went much clearer again. It was then cooled, filtered, the solvents distilled off, and the liquid residue steam-distilled.

The steam-distillate was extracted with ether, the extract washed with dilute alkali then with dilute acid and finally with water. The ether extract was dried over calcium chloride, and the ether distilled off.

The red-brown oil left was distilled directly and 6.0 gms. b.p. $273-4^{\circ}$ obtained.

1 gm. of this oil was nitrated as previously by warming with 3 cc. of fuming nitric acid and 3 cc. of concentrated sulphuric acid, and yielded finally, after twice recrystallising the crude nitration product from meths, pale yellow prisms m.p. 157° , melting point unchanged with the nitration product previously obtained.

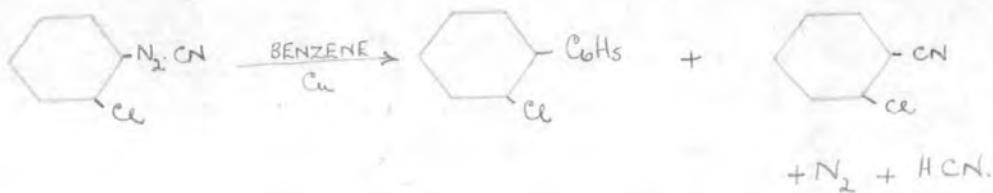
Mascarelli and Gatti⁶³ say that nitration of 2-chloro-diphenyl yields 2-chloro- 3¹. 4¹. dinitro diphenyl,



m.p. 158°

∴ the yields in the decomposition of 2-chlorobenzene-syn-diazo-cyanide in benzene with copper powder are -

- (i) 1.1 gms. 2 chlorobenzonitrile (7%), identified by hydrolysis to 2-chlorobenzoic acid, m.p. and mixed m.p. 137° .
- (ii) 0.6 gms. 2-chlorodiphenyl, (3%), identified by nitration to 2-chloro- 3¹. 4¹. dinitro-diphenyl, m.p. and mixed m.p. 157° .



DECOMPOSITIONS IN BENZENE WITH OTHER METALS AS CATALYSTS.

(a) ZINC -

10 gms. of 4-chlorobenzene syn- diazocyanide were dissolved in 100 cc. of dry benzene and 5 gms. of zinc shavings added. No reaction took place in the cold or on warming. The mixture was refluxed 2 hours, and the solvent, distilled off, contained no cyanide. The residue in the flask was steam-distilled and yielded 7.8 gms. of the trans- diazocyanide m.p. and mixed m.p. 105°. A slight tarry residue remained, probably due to the fact that the original syn- diazocyanide was not perfectly dry.

The aqueous residue after steam-distillation gave a negative test with dilute sodium hydroxide and with ammonium sulphide, and hence contained no zinc ions.

(b) SILVER -

Experiment (a) was repeated using 3 gms. of silver powder in place of the zinc. Only a very slight evolution of nitrogen occurred on warming.

The silver was not attacked, and the residue after removal of the solvent yielded 8.4 gms. of the trans- diazocyanide m.p. and mixed m.p. 104-5°.

A slight non-volatile tar remained.

(c) IRON -

20 gms. of 4- chlorobenzene syn - diazocyanide were dissolved in 200 cc. of dry benzene and 5 gms. of iron filings added. No reaction took place in the cold, but on warming a fairly steady evolution of nitrogen began, and continued steadily for about $1\frac{1}{2}$ hours, and the solvent, distilled off, gave a copious precipitate of silver cyanide with alcoholic silver nitrate solution. The tarry residue left was steam distilled. An orange solid (trans-) came over first and was followed later by a little white solid. The whole was extracted with ether. The ether, evaporated off left a slight tarry residue which was refluxed with zinc and concentrated hydrochloric acid, (to convert trans- diazo-cyanide to the amine which would remain in solution). The mixture was filtered and small discoloured shining leaflets separated out overnight and were filtered off. These were crystallised from dilute methyl alcohol, with addition of charcoal, and yielded 30 mg. of 4- chlorodiphenyl, m.p. 76° , unchanged on admixture with an authentic specimen.

TABLE XXII.

SUMMARY OF THE DECOMPOSITIONS OF THE SYN- DIAZOCYANIDES IN BENZENE AND CARBON TETRACHLORIDE, USING COPPER POWDER AS CATALYST.

		EVOLVED.	FORMED.	CYANIDE FORMED.	PRODUCTS.	TAR	IN TAR.
3-CHLORO-(MOIST)	CARBON-TETRA-CHLORIDE	57	12	EXCESS	7% o.DICHLOROBENZENE	72	10·2
3-CHLORO-	"	55	4	NONE	14% o.DICHLOROBENZENE	71	10·4
4-CHLORO-o-TOLYL-	"	45	TRACE	TRACE	17% 2·4·DICHLOROTOLUENE	80	7·5
5-CHLORO-o-TOLYL-	"	—	TRACE	TRACE	25% 2·5·DICHLOROTOLUENE	45	10·2
4-CHLORO-(MOIST)	"	—	6	EXCESS	9% p.DICHLOROBENZENE	—	—
4-BROMO-	"	—	—	NONE	10% p.BROMO-CHLOROBENZENE	—	—
4-CHLORO-o-TOLYL (Excess chalk present)	"	—	TRACE	TRACE	19·5% 2·4·DI-CHLOROTOLUENE	—	—
4-CHLORO-o-TOLYL	"	—	TRACE	TRACE	16% 2·4·DI-CHLOROTOLUENE	—	—
3-CHLORO-	BENZENE	33	5	EXCESS	3% 2-CHLORODIPHENYL	63	13·8
3-CHLORO-	"	36	7	EXCESS	3% 2-CHLORODIPHENYL	64	13·0
4-BROMO-	"	—	5	EXCESS	1% 4-BROMODIPHENYL	—	—
4-BROMO-	"	33	3	EXCESS	1·1% 4-BROMODIPHENYL	63	10·5
4-CHLORO-	"	—	3	EXCESS	1·5% 4-CHLORODIPHENYL	—	—
4-CHLORO-o-TOLYL	"	—	2	EXCESS	None identifiable.	—	—

INVESTIGATION OF THE TARS FORMED IN THE DECOMPOSITIONS OF THE SYN-DIAZOCYANIDES IN VARIOUS SOLVENTS.

The properties of these tars have already been discussed on pages 68-71.

The following example will serve to show how the nitrogen content of the copper-containing tars was found. The tar used was obtained from the decomposition of the syn-diazocyanide from 5-chloro-o-toluidine in carbon tetrachloride with copper powder.

About 0.5 gm. of the dry, powdered tar was analysed for nitrogen by the Kjeldahl method. After distilling off the ammonia into a measured volume of standard sulphuric acid, the residue in the flask contained copper, chiefly as hydroxide.

This was dissolved by acidification with acetic acid, an excess of potassium iodide solution was added, and the liberated iodine was titrated with sodium thiosulphate, using starch as indicator.

Standard solutions -

Caustic soda = 0.1062 N.
 Sulphuric acid = 0.1036 N.
 Sodium thiosulphate = 0.1190 N.

(A) Weight of tar = 0.7025 gms.

The ammonia formed was distilled into 100 cc. of sulphuric acid, and the excess of sulphuric acid was equivalent to 57.10 of caustic soda.

∴ Ammonia formed = $(100 \times 0.1036) - (57.1 \times 0.1062)$ cc N. solution
 = 4.30 cc N. solution.
 = 6.12 cc. N. solution per gm. of tar

The copper in the solution was equivalent to

15.1 cc. of .1190 N sodium thiosulphate

$$\equiv 15.1 \text{ cc. of } .1190 \times \frac{1.000}{.7025} \text{ cc. N. solution gm. tar.}$$

$$\equiv 2.558 \text{ cc. N. thiosulphate per gm. tar.}$$

$$(B) \text{ Weight of tar } = .5077 \text{ gms.}$$

The ammonia formed was distilled into 50 cc. of sulphuric acid, and the excess of acid was equivalent to 19.4 cc. of caustic soda.

$$\begin{aligned} \therefore \text{Ammonia formed} &\equiv (50 \times .1036) - (19.4 \cdot 1062) \text{ cc N. solution} \\ &= 3.12 \text{ cc. N. solution.} \\ &= \underline{\underline{6.15 \text{ cc. N. solution per gm. of tar.}}}\end{aligned}$$

The copper in the solution was equivalent to 10.85 cc. of .1190 N. sodium thiosulphate

$$\equiv 10.85 \times .1190 \times \frac{1.000}{.5077} \text{ cc. N. per gm. tar}$$

$$\equiv \underline{\underline{2.544 \text{ cc. N. thiosulphate per gm. tar.}}}$$

Taking the average of the results obtained in (A) and (B)

$$\begin{aligned} \% \text{ COPPER} &= 6.3 \times 2.551 \\ &= \underline{\underline{16.08 \%}}\end{aligned}$$

$\therefore \% \text{ NITROGEN}$ for copper-free material

$$\begin{aligned} &= 6.14 \times 0.14 \times \frac{100}{(100 - 16.08)} \\ &= \underline{\underline{10.24 \%}}\end{aligned}$$

The summary of the results obtained are shown in tables IX (page 59) and XXII (page 132).

The figures given in these two tables do not cover every decomposition carried out, because, for many of the earlier decompositions, a reasonably accurate method of measuring the nitrogen evolved, had not been obtained.

Tars were only analysed for nitrogen when copper had been used in the decomposition, for, as already indicated, tars other than these were unsuitable for the purpose.

A tar containing one nitrogen atom per aryl group, e.g. $\text{C}_6\text{H}_4\text{N}-\text{C}_6\text{H}_3-\text{N}-$ etc., should contain from 9-11% of nitrogen, whereas one containing two nitrogen atoms per aryl group, e.g. $\text{C}_6\text{H}_4\text{N}_2-\text{C}_6\text{H}_3\text{N}_2-$ etc., should contain from 16-20% of nitrogen.

All the tars evolved ammonia on boiling with caustic soda solution, due probably to hydrolysis of traces of nitrile or anti-diazocyanide in the tar.

REDUCTION OF THE TARS.

Reduction of several tars was carried out using either,

- (a) Stannous chloride and hydrochloric acid in alcohol, OR -
- (b) Zinc and hydrochloric acid in glacial acetic acid.

The latter method seemed to be the more satisfactory.

The following examples show the method used -

(1) REDUCTION OF THE TAR FORMED IN THE DECOMPOSITION OF 2-CHLOROBENZENE SYN- DIAZO CYANIDE IN CARBON TETRACHLORIDE WITH COPPER POWDER.

5 gms. of the finely powdered tar were dissolved (almost completely), in 200 cc. of boiling alcohol. 10 gms. of stannous chloride and 50 cc. of concentrated hydrochloric acid were added, the whole mixture being refluxed for 20 hours.

Excess of alcohol was then distilled off, and the residue was made alkaline and steam-distilled. Some ammonia was evolved, and the turbid distillate was tested as follows -

- (a) A portion was diazotised and added to alkaline β -naphthol, yielding a light orange dye -
- (b) A further portion was made alkaline and shaken with a few drops of benzoyl chloride, yielding a benzoyl derivative which was crystallised from dilute alcohol, m.p. 99° , unchanged on admixture with the authentic benzoyl derivative obtained from o.chloraniline.

The distillate was further tested for DIAMINES as follows -

- (a) No precipitation or colouration was given with acidic ferric chloride solution, showing absence of ortho-diamines.
- (b) The distillate gave no precipitate with sodium nitroso in acid solution and no colouration when the acidified solution was warmed with a 1% solution of acetaldehyde in 50% alcoholic solution, thus showing absence of meta- diamines.
- (c) The distillate gave no colouration when just acidified with dilute hydrochloric acid and treated with excess of silver

nitrate solution, neither did it give a methylene blue type of dye with hydrogen sulphide and ferric chloride, thus showing absence of para - diamines.

(2) Experiment (1) was repeated using the tar obtained in the decomposition of 4-bromo benzene syn- diazocyanide in ether with copper powder.

After working up as usual, steam-distillation yielded a trace of p. bromaniline, identified by formation of its benzoyl derivative, m.p. and m.m.p. 304°. Diamines were tested for as in (1) and found to be absent.

(3) Reduction of the tar obtained from the decomposition of 4-chlorobenzene syn- diazocyanide in ether with copper powder, by the previous method, yielded a trace of p. chloroaniline, identified by formation of its benzoyl derivative, m.p. and m.m.p. 142°.

(4) The tar obtained in the decomposition of 2- chlorobenzene syn- diazocyanide in benzene with copper powder, was reduced in a different manner.

5 gms. of the finely powdered tar was dissolved in 30 cc. of hot, glacial acetic acid, 10 gms. of granulated zinc and 20 cc. of concentrated hydrochloric acid were then added and the mixture refluxed for 3 hours. The previous procedure was then carried out. Steam-distillation yielded a trace of o.chloroaniline, identified by formation of its benzoyl derivative m.p. and mixed m.p. 99°, and its azo- β - napthol derivative, m.p. and mixed m.p. 166° after recrystallisation from dilute methyl alcohol.

Diamines were tested for as previously, but could not be detected.

i.e. ALL Tar- reductions yielded small quantities of the mono- amines (corresponding to the syn- diazocyanide used in the original reaction), and no signs of diamines.

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D.

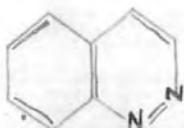
P A R T II.

THE PREPARATION OF
CINNOLINE DERIVATIVES.

PAGE	SECTION	
1	1	HISTORICAL INTRODUCTION
39	2	THE PREPARATION OF NEW CINNOLINE DERIVATIVES FROM SUBSTITUTED 2-AMINO-BENZOPHENONES
38	3	ORIENTATION OF THE THREE NEW CINNOLINES
44	4 (a)	CONDENSATION OF 2-CHLORO-3:5-DINITROBENZOIC ACID WITH SODIUM ACETOACETATE.
53	(b)	CONDENSATION OF 2:4- DINITRO-CHLOROBENZENE WITH SODIUM ACETOACETATE
54	5	UNSUCCESSFUL ATTEMPTS TO SYNTHESISE CINNOLINE DERIVATIVES
57	6	EXPERIMENTAL SECTION
90		INDEX

SECTION I.HISTORICAL INTRODUCTION.

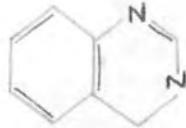
CINNOLINE, or 3:4- benzpyridazine, is one of the four isomeric benzodiazines of the general formula, $C_8H_6N_2$, viz:-



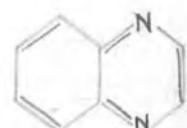
CINNOLINE



PHTHALAZINE



QUINAZOLINE



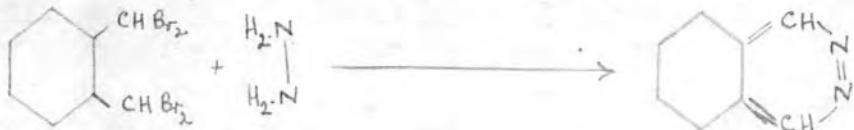
QUINOXALINE

As will be seen later, the preparation of cinnoline presents many difficulties, whereas phthalazine, quinazoline and quinoxaline are all prepared very easily.

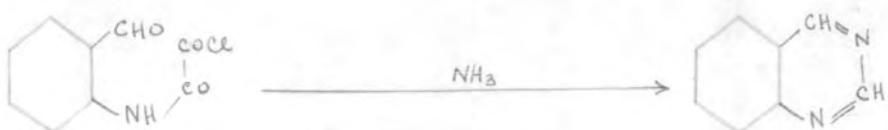
To illustrate this, a brief account of the preparation of the three isomers of cinnoline is given here -

PREPARATION OF PHTHALAZINES, QUINAZOLINES AND QUINOXALINES.PHTHALAZINE - 4:5- BENZPYRIDAZINE.

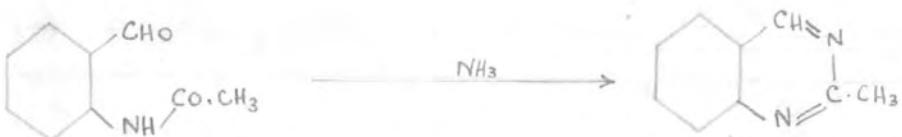
Phthalazines are prepared by heating $\omega\omega\omega\omega'$ - tetrachloro- or tetrabromo-o- xylenes with hydrazines in dilute alkaline solution^{1,2.}

QUINAZOLINE - BENZPYRIMIDINE.

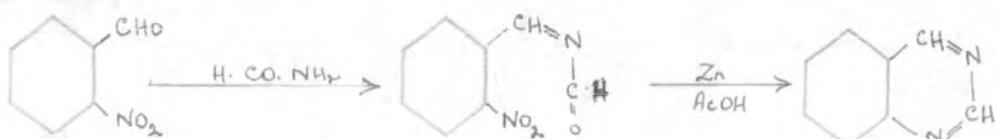
1. 2- oxaryl-amino benzaldehyde is heated with alcoholic ammonia in a sealed tube at 150° , and the product distilled from calcium carbonate.³



Other 2-acidyl-amino benzaldehydes can be used. Thus 2- acetamido-benzaldehyde yields 3-methyl-quinazoline.



2. Ortho nitro-benzaldehyde is condensed with formamide, and the product reduced with zinc and dilute acetic acid at about 30° .⁴



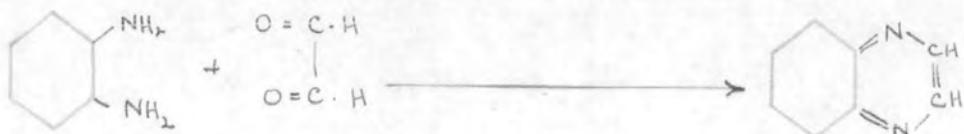
3. Ortho amino-benzylamine is heated with acyl chlorides -



The resulting 3:4- dihydro quinazoline may be oxidised to the quinazoline with alkaline potassium ferricyanide.⁵

QUINOXALINE - BENZPYRAZINE.

1. Ortho-phenylene diamine is heated with the bisulphite derivative of glyoxal in aqueous solution with the bisulphite derivative of glyoxal in aqueous solution at $50-60^\circ$.⁶

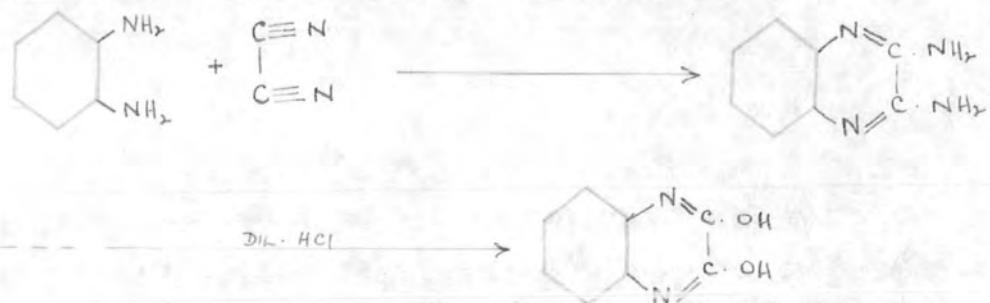


2. Dihydrlic phenols are condensed with alkylene diamines



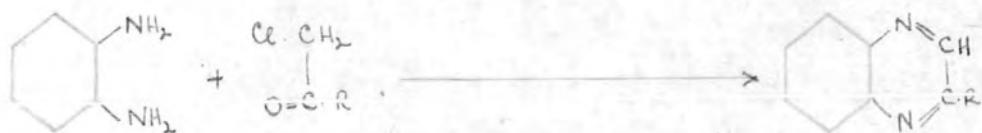
The resulting tetrahydroquinoxalines are oxidised to the quinoxalines with potassium ferricyanide in alkaline solution.⁷

3. Dihydroxy quinoxalines are prepared by treating o. phenylene diamines with cyanogen and hydrolysing the resulting diamino quinoxalines with dilute hydrochloric acid.



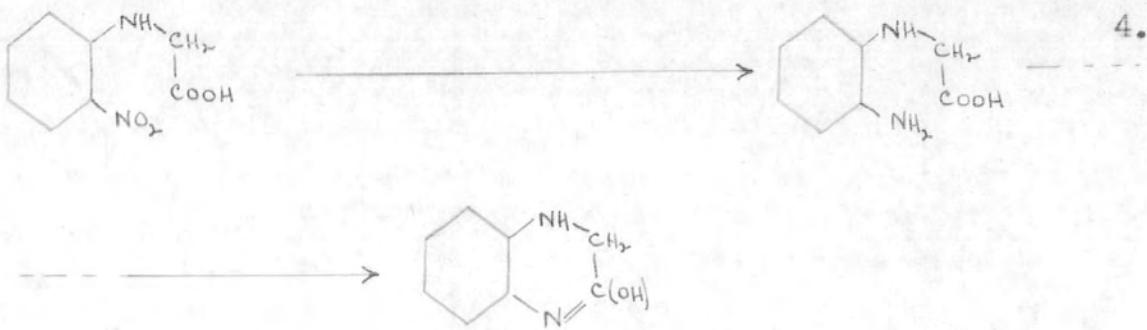
4. Substituted quinoxalines can be prepared by condensing α - chloro-ketones, α - aldehydo-alcohols, or α - keto-alcohols with o. phenylene diamine

e.g.



5. α - Hydroxy - dihydro quinoxalines can be prepared by the reduction of 2-nitrophenyl- α - amino fatty acids.

e.g.



The general properties of the isomeric benzodiazines are summarised in the following table -

PROPERTIES OF THE ISOMERIC BENZODIAZINES.

	CINNOLINE	PHTHALAZINE	QUINAZOLINE	QUINOXALINE
m.p.	39°	91°	48°	31°
b.p.		315-17° (some decomp.)	243°	229°
<u>LOUR and CRYSTALLINE FORM.</u>	BRIGHT YELLOW NEEDLES FROM	BRIGHT YELLOW NEEDLES FROM ETHER.	PLATES FROM LIGROIN	WHITE NEEDLES FROM ETHER.
<u>ODOUR</u>	GERANIUM LIKE	SIMILAR TO QUINOLINE	SIMILAR TO PHTHALAZINE	LIKE QUINOLINE WHEN COLD AND PIPERIDINE WHEN HOT
<u>LUBILITY</u>	VERY SOLUBLE	VERY SOLUBLE	VERY SOLUBLE WITH NEUTRAL REACTION	SOLUBLE IN ALL PROPORTIONS IN COLD. LESS SOLUBLE IN HOT.
a) <u>WATER.</u>				
b) <u>ORGANIC SOLVENTS</u>	Easily soluble in ligroin. Forms an addition compound with ether.	Easily soluble in most. Sparingly soluble in ether. Insoluble in ligroin.	Easily soluble in all except ligroin.	Readily soluble in all solvents.
<u>SICITY</u>	STRONG	STRONG	FEEBLE	FEEBLE
<u>IDATION</u>	Hot alkaline permanganate → pyridazine - 2:3-dicarboxylic acid.	Hot alkaline permanganate → pyridazine-4:5-dicarboxylic acid.	Hot alkaline permanganate - (a) pyrimidine dicarboxylic acid. (b) 4-oxy-8 quinazoline	Stable to dichromic in boiling dilute sulphuric acid. Hot alkaline permanganate gives pyridazine - 2:3-dicarboxylic acid.
<u>DUCTION</u>	Easily reduced to DIHYDRO-CINNOLINE but no further.	Sodium amalgam gives 1.2.3.4-tetra-hydro-phthalazine. Zinc and cold hydro-chloric acid gives oxyethylene-diamine.	Sodium in alcohol gives DIHYDRO-QUINAZOLINE.	Sodium in alcohol 1.2.3.4-tetra-hydro-quinoxaline.

SIMPLE AND COMPLEX SALTS OF THE BENZODIAZINES.

All of the isomeric benzodiazines form a well-defined series of simple and complex salts, by which each may easily be characterised. A summary of the more important derivatives is given here -



CINNOLINE

Hydrochloride - B.HCl.

Glistening compact crystals, m.p. 160° , easily soluble in water and alcohol.

Platinichloride - $\text{B}_2 \cdot \text{H}_2\text{Pt. Cl}_6$

Yellow needles, m.p. 280° (d), sparingly soluble in alcohol.

Aurichloride - $\text{B}_2 \cdot \text{H}_2\text{Au Cl}_5$

Dark-yellow needles, m.p. 146° , soluble in alcohol.

Methiodide - $\text{B. CH}_3\text{I.}$

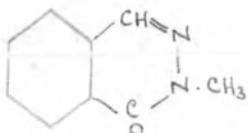
Dark red-brown shining needles, m.p. 168° , soluble in alcohol.

Picrate - $\text{B. C}_6\text{H}_3\text{N}_3\text{O}_7$

Small amber prisms, m.p. 190° , sparingly soluble in alcohol.

PHTHALAZINE.Hydrochloride - B. HCl.White needles m.p. 231° , soluble in alcohol.Hydriodide¹⁰ - B. HIYellow crystals, m.p. 203° , easily soluble in water.Aurichloride - B. HAuCl₄.Yellow needles, m.p. 200° Chloroplatinate - B₂.H₂PtCl₆Yellow-brown sparingly soluble needles which blacken at 260° without melting.Ferrocyanide¹⁰ - B₂. H₄Fe(CN)₆

Yellow prisms from water.

Methiodide - B. CH₃IYellow needles m.p. $235-40^{\circ}$ from methyl alcohol. Treatment of this with fresh silver oxide yielded N-methyl phthalazone.Picrate - B. C₆H₃N₃O₇Sparingly soluble crystals, m.p. $208-10^{\circ}$.QUINAZOLINE.Aurichloride - B. HCl.AuCl₃.H₂O.Orange-red, sparingly soluble rhombs, m.p. 185° .Chloroplatinate - B₂.H₂Pt Cl₆Orange-yellow prisms, m.p. $> 250^{\circ}$.

Picrate - B. C₆H₃N₃O₇

Yellow needles from alcohol, m.p. 188-190°.

Methiodide - B. CH₃I.

Sparingly soluble prisms from water m.p. 163-5°.

QUINOXALINE.

Hydrochloride - B.H Cl.

White needles from alcohol, m.p. 184°(d.)

Sulphate - B.H₂SO₄.

White plates from alcohol, m.p. 186-7°.

Chloroplatinate - B₂. H₂Pt Cl₆.

Yellow needles, high m.p.

Oxalate -

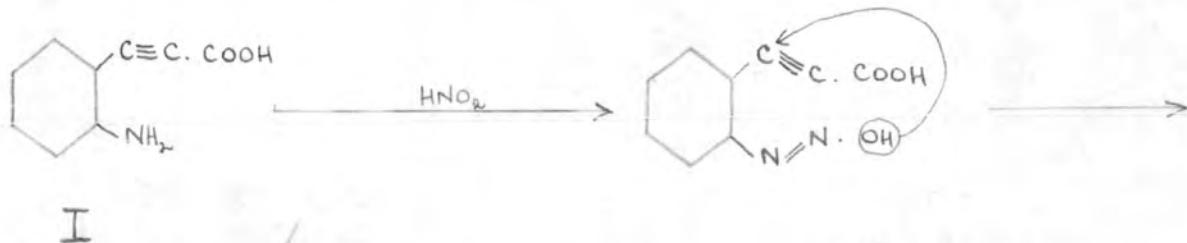
Sparingly soluble white needles from water, m.p. 169°.

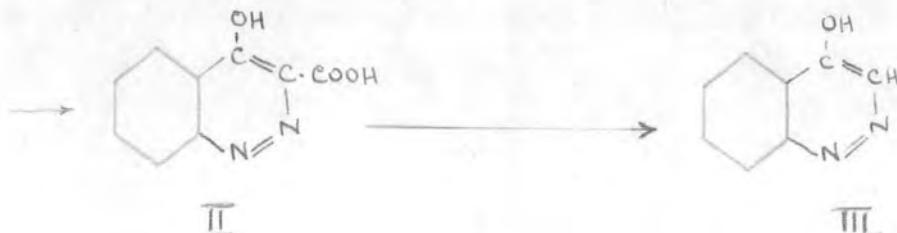
Methiodide - B.CH₃I.

Orange-coloured plates from alcohol, m.p. 176°.

THE PREPARATION OF CINNOLINE.

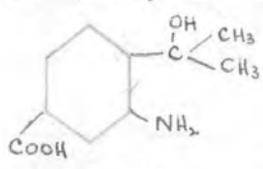
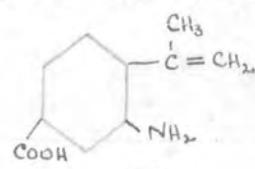
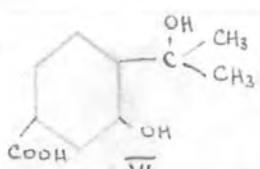
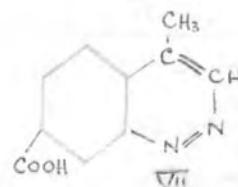
In 1883, V. von Richter¹¹ prepared the first cinnoline derivative, 4-hydroxycinnoline - 3-carboxylic acid, by heating the aqueous diazonium chloride of ortho-amino phenyl propionic acid (I). The conversion involved the transfer of the hydroxy-group from the diazo-group to the α - carbon atom as shown -





The hydroxy-cinnoline carboxylic acid (II), lost carbon-dioxide on heating, and was converted to hydroxy-cinnoline (III). Richter distilled this latter compound with zinc dust in an attempt to reduce it to cinnoline, but the product was only a viscous yellow oil which could not be crystallised.

In the following year, Widman¹² discovered a reaction similar to Richter's in his investigations on the action of nitrous acid on 3-amino- 4- (α - hydroxyisopropyl)- benzoic acid (IV), and 3-amino-4- isopropyl benzoic acid (V).

IVVVIVII

The former compound reacted normally on treatment with nitrous acid, yielding the corresponding hydroxy-compound with loss of nitrogen.

The latter compound (V), did not lose nitrogen on treatment with nitrous acid, but underwent ring-closure with formation of 4- methyl cinnoline-7-carboxylic acid (VII).

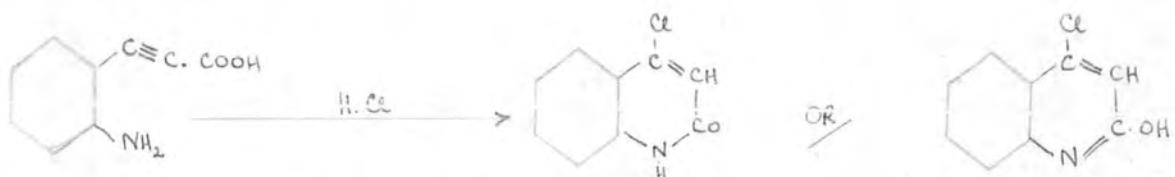
This reaction is not of the same type as that noted by Richter (loc.cit.), because in this case the side-chain contains a double-bond, and anhydride formation must take place as shown -



Formation of a cinnoline derivative is rather striking here because Fischer¹³ had already shown that the analogous ortho-diazo cinnamic acid was converted to ortho-cumaric acid on heating the aqueous solution, thus -



In 1892, Busch and Kleitt¹⁴ repeated Richter's original work. They used Richter's method for the preparation of hydroxy-cinnoline from ortho-nitrophenyl propionic acid, and confirmed the main points of his data. They did find however, that amino-phenylpropionic acid, contrary to Richter's statement, did not dissolve on warming with dilute hydrochloric acid, but was instead converted chiefly to p. chloro-carbostyryl as shown -



They therefore achieved complete diazotisation of amino phenyl propionic acid by making it into a fine paste with five parts of concentrated hydrochloric acid and an equal weight of water, and adding to this solution the calculated amount of sodium

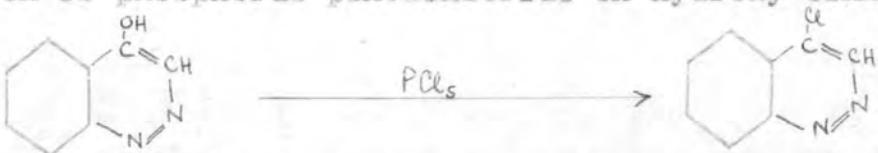
nitrite. They thereby obtained crude hydroxy-cinnoline carboxylic acid in 60% yield.

In attempting the reduction of hydroxy-cinnoline to cinnoline, Busch and Klett modified Richter's method and carried out the distillation with zinc in a stream of hydrogen - without any success however. The product again was a bright yellow oil which smelt strongly of nitrile and rapidly turned brown in the air.

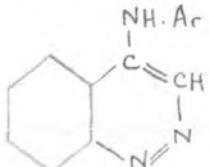
The following reducing agents were next tried,

- (a) zinc and acetic acid,
 - (b) zinc and hydrochloric acid,
 - (c) sodium in alcohol, and
 - (d) hydriodic acid and red phosphorus in a sealed tube,
- but none of these reagents gave the required product.

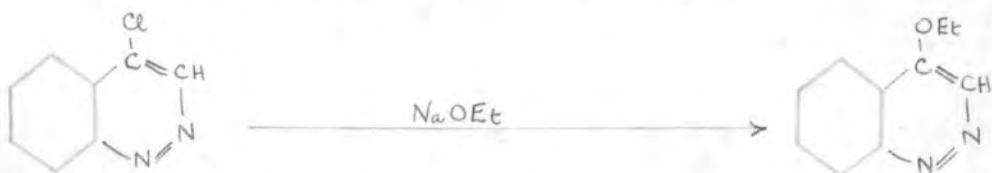
The next stage in the attempted preparation of cinnoline by Busch and Klett, was the preparation of chloro-cinnoline by the action of phosphorus pentachloride on hydroxy-cinnoline -



Chloro-cinnoline was very reactive, being reconverted to hydroxy-cinnoline merely by boiling its aqueous solution. It reacted vigorously with aniline and other amines to give compounds of the type -



and with sodium ethoxide to give hydroxy-cinnoline ethyl ether -

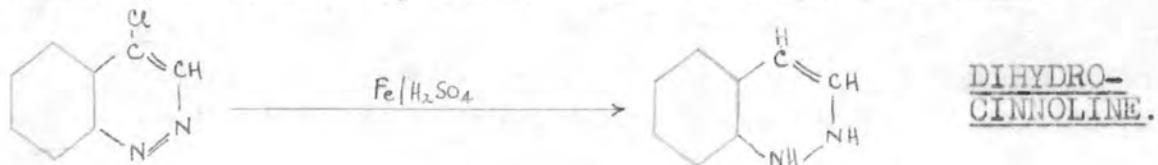


Its hydrochloride, hydriodide and chloroplatinate were also prepared.

No success was met with when attempts were made to reduce chloro-cinnoline by the methods tried with hydroxycinnoline; the product in all cases was again a brown, nitrile-like oil.

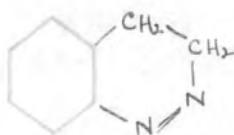
Further investigation on kindred heterocyclic compounds was carried out by Busch and Rast¹⁵ before a successful method for the reduction of chloro-cinnoline was found.

The method finally adopted was one which was commonly used in the cinchona alkaloid series - reduction with iron-filings and dilute sulphuric acid. When chloro-cinnoline was reduced by this method, the product was dihydro-cinnoline -

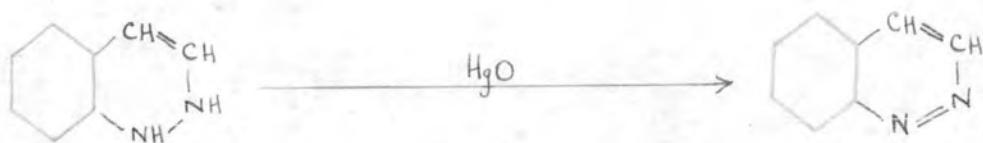


Dihydro-cinnoline was found to be a feeble base whose salts were decomposed in aqueous solution. It was recovered unchanged after boiling its alcoholic solution with an excess of sodium, this remarkable stability to reduction indicating that it could not have the structure shown below, with a double-bond between the nitrogen atoms, since the azine ring is not normally easily

reducible -



The oxidation of dihydrocinnoline to cinnoline presented some difficulties, but was finally accomplished by Busch and Rast by boiling it in benzene solution for three hours with an excess, (12 equivalents), of fresh mercuric oxide -



The free cinnoline was obtained in the form of bright-yellow crystalline aggregates, m.p. 39° , on crystallisation from ligroin.

Crystallisation from ether yielded an addition compound, $C_8H_6N_2 \cdot (C_2H_5)_2O$, in white needles, m.p. $24-5^{\circ}$.

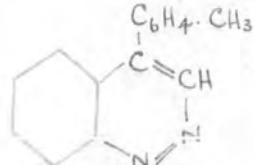
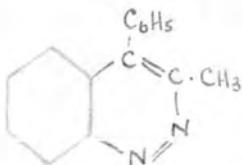
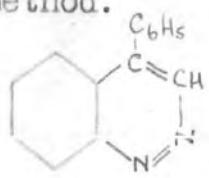
Cinnoline was found to be a strong base which formed stable salts with mineral acids and was easily soluble in water and in the common organic solvents. It possessed a characteristic smell, rather reminiscent of geraniums, and had a bitter, quinine-like taste. Its properties have been summarised in the table on p. 5 and on page 6 of this thesis.

A somewhat easier route to the cinnoline ring system than the method of Richter was explored by Stoermer and Fincke.¹⁶ Employing the reaction originally discovered by Widman (loc.cit.), namely the cyclisation of diazotised 2-amino-diarylethylenes, these workers showed that α -(2-aminophenyl)- α -aryl ethylenes (I), passed smoothly and spontaneously to the corresponding 4-aryl cinnolines (II), on diazotisation -

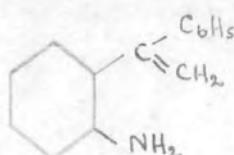


The requisite diarylethylenes were obtained by treating the appropriate diaryl betones with a Grignard reagent, followed by dehydration of the resulting carbinols by boiling with dilute sulphuric acid.

4- phenyl cinnoline (III), 4- phenyl- 3- methyl-cinnoline (IV), and 4- p. tolyl-cinnoline (V) were synthesised by this method.

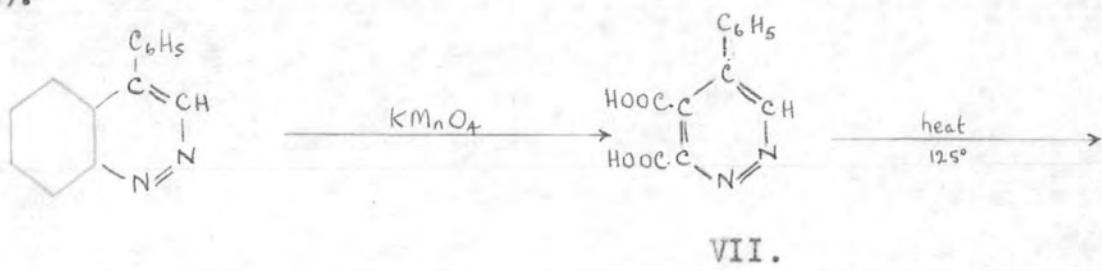


Thus, 4- phenyl cinnoline was obtained as its hydrochloride by diazotising 2-amino-diphenyl-ethylene (VI), in hydrochloric acid at room-temperature.

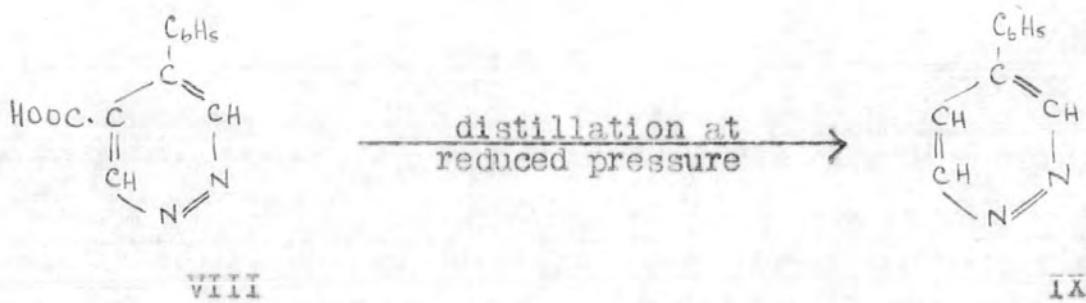


VI.

The free base, liberated by the action of ammonia on its hydrochloride, was crystallised from light petrol in sulphur-yellow, glistening prisms, m.p. 67°. Oxidation of 4-phenyl cinnoline with hot potassium permanganate solution, yielded 4-phenyl-pyridazine-5:6-dicarboxylic acid, (4-phenyl-cinnolinic acid), (VII). This acid was heated at 125° for four hours, yielding 4-phenyl-pyridazine-5-carboxylic acid (VIII), which on distillation at reduced pressure yielded 4-phenyl-pyridazine (IX).



VII.



VIII

IX

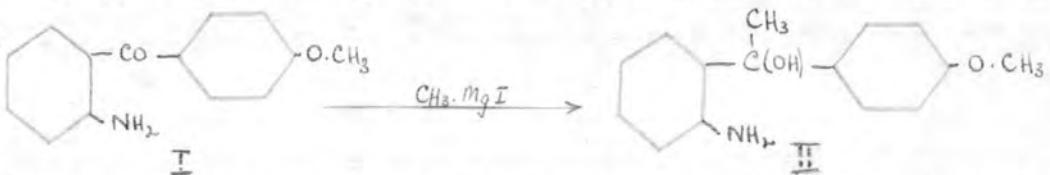
Stoermer and Fincke also observed that substitution of a bromine atom for a hydrogen atom on the β - ethylenic carbon atom of the diaryl-2-amino ethylenes, tended to inhibit the cyclisation of the diazonium salt.

Thus, α -bromo- β - (2-amino-as-diphenyl)-ethylene, $\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \overset{\text{C}_6\text{H}_5}{\text{C}} = \text{CH} \cdot \text{Br}$, did not yield a bromo-derivative on treatment with nitrous acid, but gave only a poor yield of 4-phenyl-cinnoline.

This is in accordance with Fischer's¹³ discovery that 2-amino- cinnamic acid did not cyclise on treatment with nitrous acid, but was merely converted to the hydroxy-compound.

In 1912, Stoermer and Gaus¹⁷, carried out a comprehensive study of 4-anisyl- cinnoline, proving its structure by degradation to pyridiazine.

Their starting material was 2-amino-4¹- methoxy-benzophenone (I), prepared by the method of Ullmann and Bleier¹⁸ (see p. 24). This was converted smoothly to (2-aminophenyl)-4-anisyl methyl carbinol (II), by treatment with methyl magnesium iodide -



This carbinol was converted to the ethylene (III), by heating for one hour with 10% sulphuric acid, this in turn being converted to 4-anisyl-cinnoline (IV), by treatment with the calculated amount of sodium nitrite in cold 10% sulphuric acid -

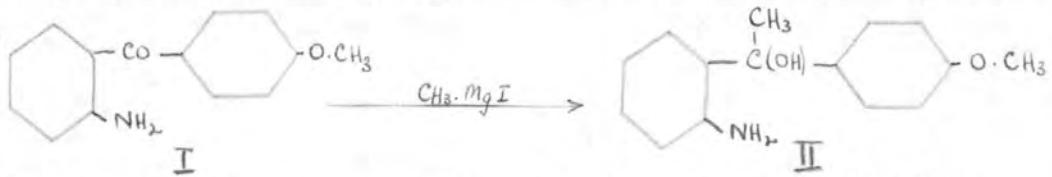
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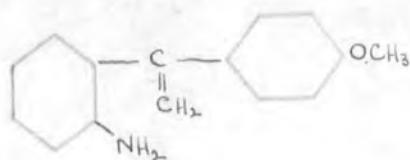
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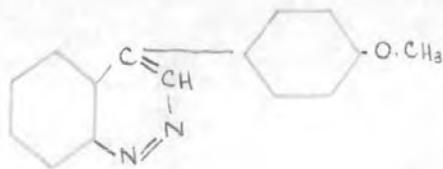
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四



IV

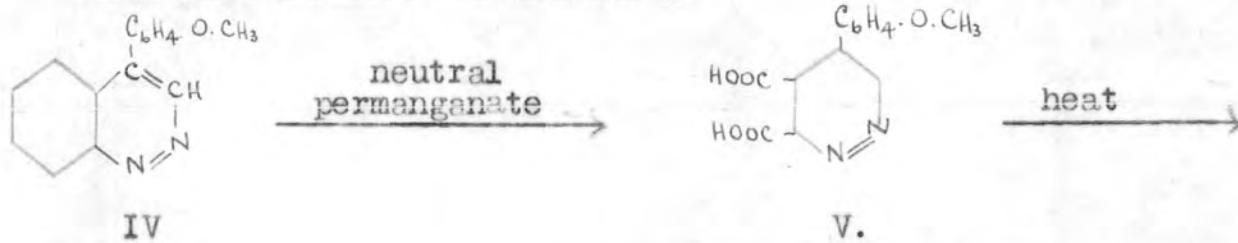
The structure of anisyl-cinnoline was proved by degradation as follows -

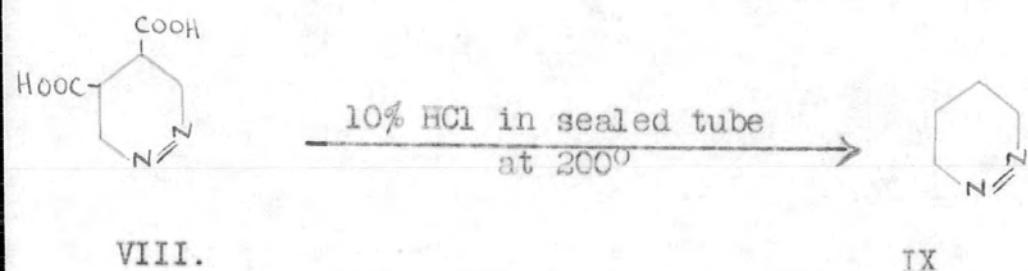
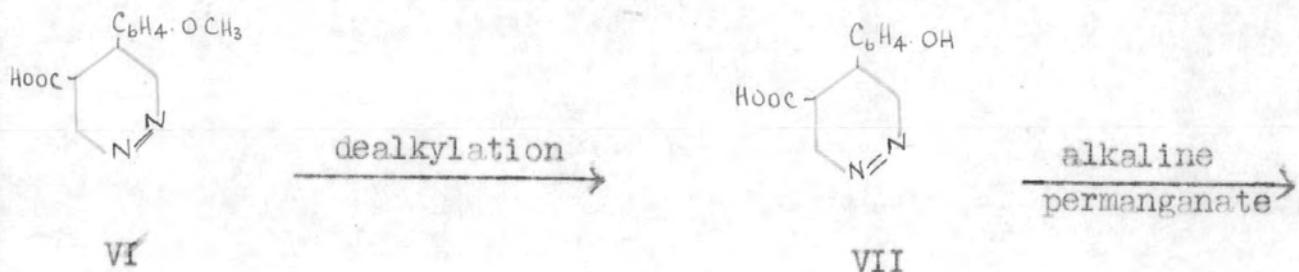
Oxidation of anisyl cinnoline by aqueous potassium permanganate yielded 4-anisyl-cinnolinic acid (V), which readily lost carbon-dioxide on heating to give 4- anisyl-pyridazine- 5- carboxylic acid (VI). De-alkylation of this acid yielded pyridazine-4- (4-hydroxy phenyl) - 5 - carboxylic acid (VII), which was oxidised readily with warm alkaline potassium permanganate solution to pyridazine - 4:5- dicarboxylic acid (VIII).

This product was de-carboxylated to pyridazine (IX), in one stage involving the loss of two carboxyl groups, by heating it with 10% hydrochloric acid in a sealed tube, for two hours at 200°.

The pyridazine was identified by the preparation of its picrate. The reactions involved are depicted below -

DEGRADATION OF ANISYL-CINNOLINE.





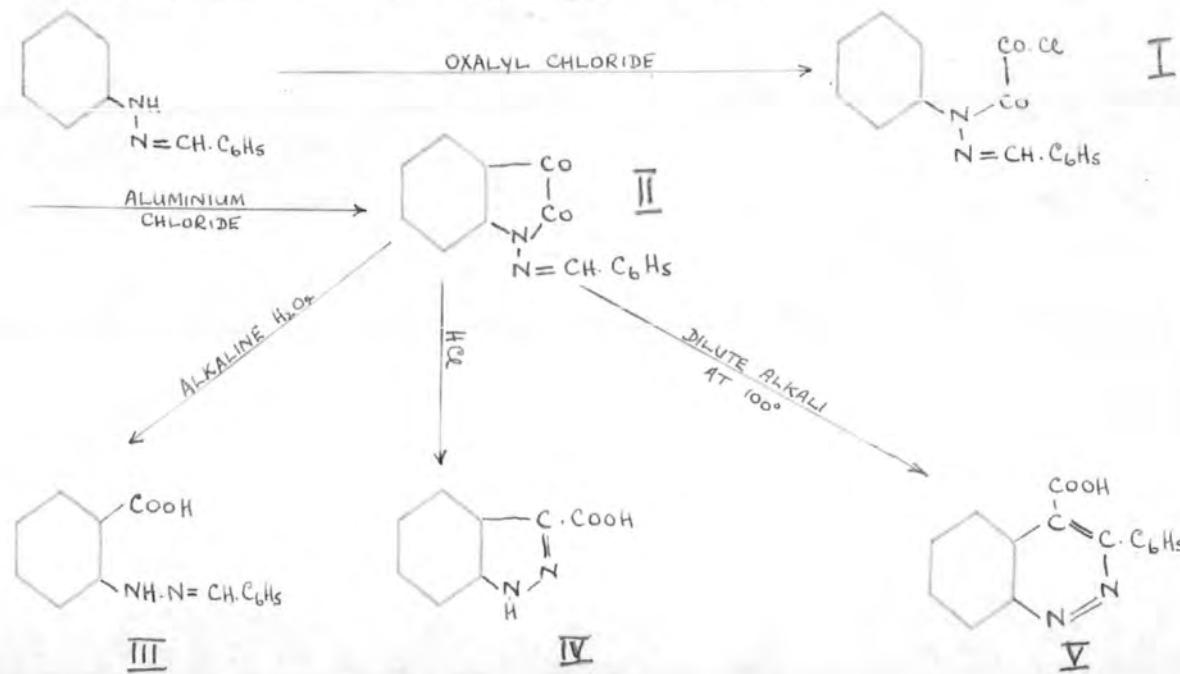
In 1924, in the course of an investigation of derivatives of N - amino-isatin, Stollé and Becker¹⁹ discovered a new method for the synthesis of cinnoline derivatives.

They prepared N- benzylidene-amino-isatin (II), by condensing oxalyl chloride with benzal phenylhydrazine in ethereal solution, and heating the resulting α - chloroxalyl - β - benzal-phenylhydrazine (I) either alone, or in carbon disulphide in the presence of aluminium chloride.

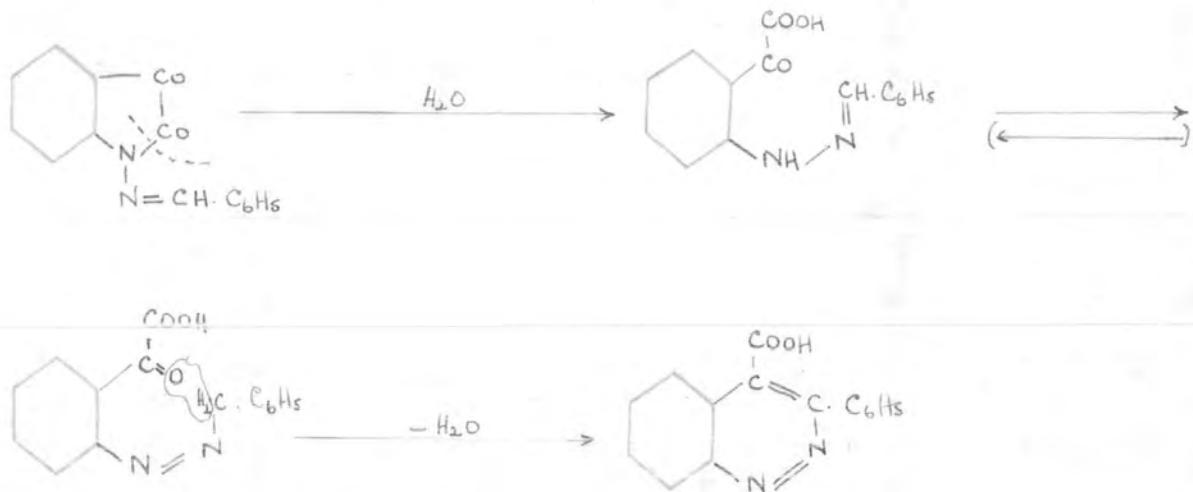
The hydrolysis of N- benzylidene-amino-isatin was carried out by three methods -

- (a) Hydrolysis with alkaline hydrogen peroxide converted it normally to N- benzylidene- 2- hydrazino-benzoic acid (III).
- (b) By boiling with hydrochloric acid it underwent a molecular rearrangement, and was converted to indazole-3-carboxylic acid (IV), with loss of benzaldehyde.
- (c) By heating with dilute alkali at 100° for 1 hour it again underwent a molecular rearrangement, and was converted to 3-phenyl-cinnoline-4-carboxylic acid. (V).

The reactions involved are depicted below -

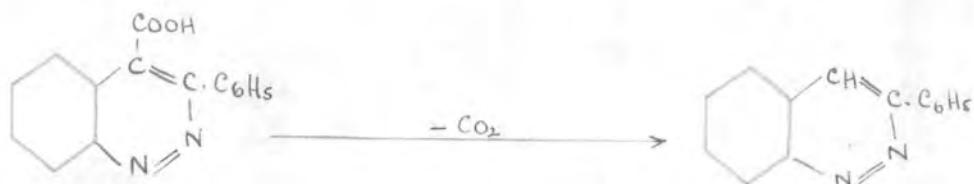


The formation of a cinnoline derivative by the alkaline hydrolysis of N-benzylidene-amino-isatin, may be explained by the following series of reactions which involve fission of the isatin ring, followed by cyclisation of the resulting ketonic acids:-



The same mechanism can be also applied to explain the formation of indazole-3-carboxylic acid in the acid hydrolysis of N-benzylidene-amino-isatin.

3-phenyl-cinnoline-4-carboxylic acid was obtained in yellow plates on crystallisation from alcohol. It melted at 344° with gas evolution, probably being converted to α -phenyl-evolution, probably being converted to 3-phenyl-cinnoline (VI), with loss of carbon dioxide - (cf. Richter's 4-hydroxy-cinnoline-3-carboxylic acid - p. 9)



VI.

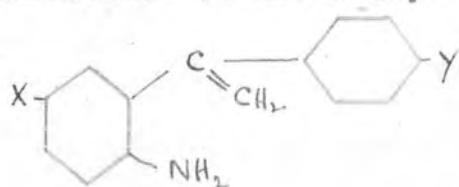
This method of preparation of cinnoline derivatives has not been investigated further, but may be capable of wider application.

As will be seen from the preceding introduction, the chemistry of cinnoline and its derivatives has received scant attention in recent years.

A discouraging factor in this field of research has doubtless been the lack of a convenient method of preparation, in contrast to the isomeric phthalazines which are readily accessible and have, in consequence been widely studied.

Our work on cinnolines was carried out with a twofold object -

- (a) To investigate new methods of synthesis of the cinnoline ring system, and
- (b) To study the effect of nuclear substituents on the ease of cyclisation of diazotised o.-amino aryl ethylenes of the type -

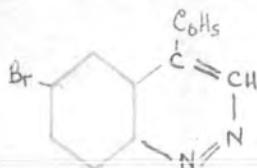


Owing to the advent of the war the investigation had to be left incomplete, and no new methods of synthesis of cinnoline derivatives were found. Even so, it appears to us that Stoermer's method (see p. 14), is by far the most convenient for the prepara-

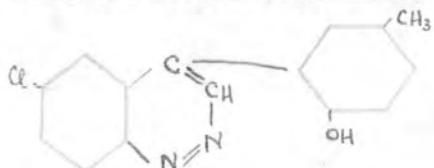
tion of cinnolines.

Using the Stoermer reaction, we prepared three new cinnoline derivatives -

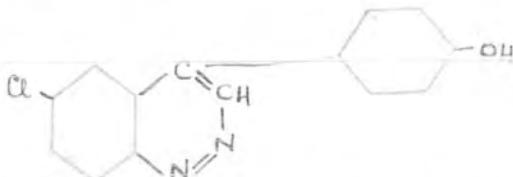
(a) 6-bromo-4-phenyl cinnoline.



(b) 6-chloro-4-(2¹-hydroxy-5¹-methyl phenyl) - cinnoline



(c) 6-chloro-4-(4¹-hydroxy phenyl)- cinnoline



The yields, based on the diarylethylenes were in all cases reasonably high, so the scope of this method for the synthesis of cinnolines containing substituted aryl nuclei, is in all probability fairly high.

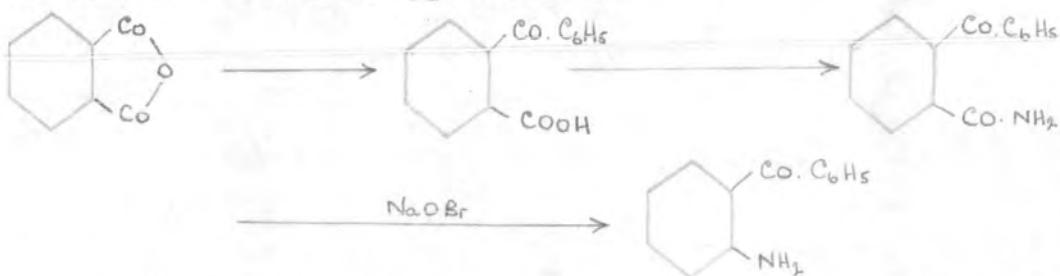
The main difficulty in applying Stoermer's method lies in the preparation of convenient substituted 2-amino-benzophenones. Various methods are available for the preparation of these compounds, but most of them are tedious and rather restricted in their application, and the overall yields are seldom good.

A summary of the chief methods of preparation of 2-amino benzophenones is given here.

PREPARATION OF 2-AMINO-BENZOPHENONES.

1. The Graebe and Ullman method.²⁰

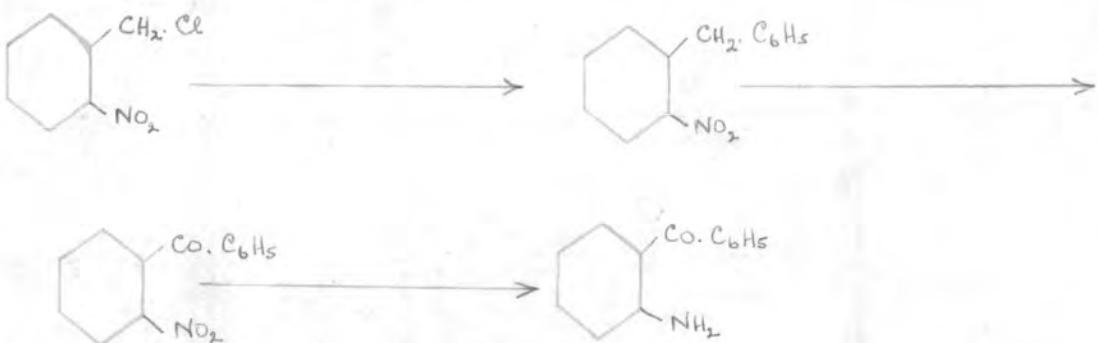
Phthalic anhydride and benzene were condensed in the presence of aluminium chloride to give o. benzoyl benzoic acid. This acid was converted to the amide and thence to the amine by the action of sodium hypobromite.



Although this method is a roundabout one it has a wide scope since various substituted phthalic anhydrides are available, and can be used in the initial condensation.

2. THE GEIGY and KOENIGS METHOD.²¹

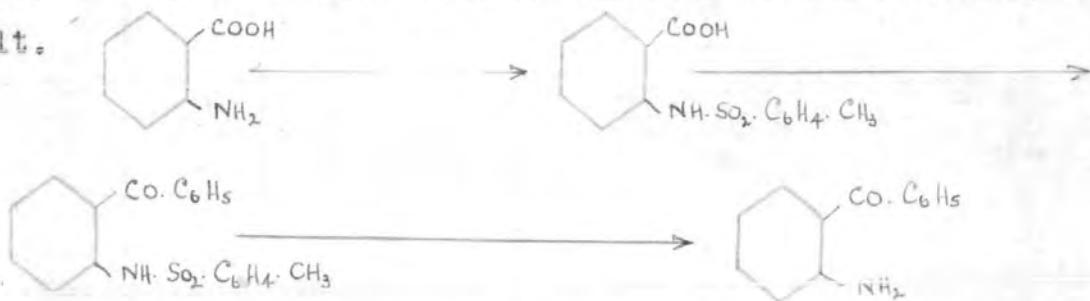
Ortho-nitrobenzyl chloride and benzene were condensed by the Friedel-Crafts method to ortho-nitro-diphenylmethane. This was oxidised to o. nitrobenzophenone by chromic and acetic acid, and subsequently reduced to the amine by the action of tin in alcoholic hydrochloric acid.



This method has very little scope as o.nitro benzyl chloride is not readily available, and the reaction does not work using toluene or naphthalene in place of benzene.

3. THE ULLMANN AND BLEIER METHOD.

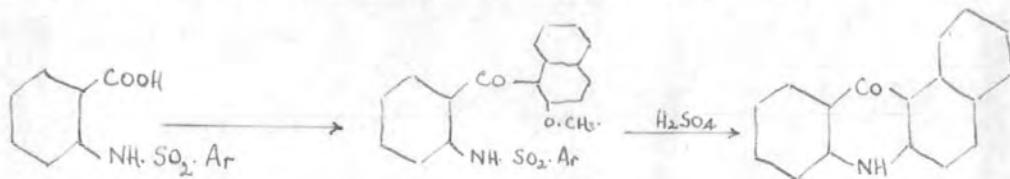
These workers found that the para-toluene-sulphonyl derivative of anthranilic acid condensed readily with hydrocarbons, phenol-ethers etc., in the presence of aluminium chloride, yielding the p.toluene-sulphonyl derivative of the corresponding amino-benzophenone. Hydrolysis of this latter compound was said to go very readily by warming with concentrated sulphuric acid, but we have found that the hydrolysis was extremely difficult.



We also found that the yields in the initial Friedel-Crafts condensation were poor, the sulphone, $\text{CH}_3\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\text{C}_6\text{H}_5$, always being formed as a by-product.

As a continuation of this method, Ullman and Denzler²² condensed p.toluene sulphonyl anthranilic acid with the methyl ethers of the three di-hydroxyphenols, pyrogallol, and α - and β -naphthol. Hydrolysis of the products with concentrated sulphuric acid yielded the ortho-amino benzophenones, except

in the case of the β -naphthol methyl ether derivative. This was converted to naphthyl acridone as shown -



4. THE CHATTAWAY AND ANGEL METHOD.

Chattaway²³ showed that at a high temperature and under the influence of a catalyst, diacyl anilides readily underwent re-arrangement into acyl-amino ketones, the migrating acyl group invariably replacing a hydrogen atom in the para- or ortho- position with respect to the amino-group.

It was later shown that when the ortho or para-position was already occupied by an alkyl group, as in dibenzoyl-o-toluidine or dibenzoyl-p-toluidine, the migrating group always entered the para- or ortho- position respectively, with respect to the amino-group.

e.g.

(a).



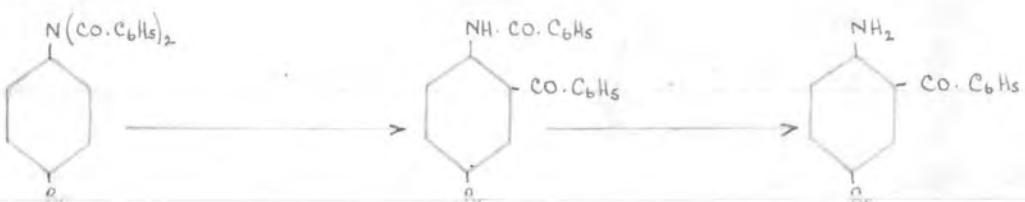
(b).



The resulting benzamido-benzophenones were hydrolysed to the amino-benzophenones by prolonged boiling with alcoholic hydrochloric acid.

Continuing this work, Angel²⁴ investigated the effect of negative groups in the para- position to the amino group. The migration did not go so readily in this case, but he found that the dibenzoyl-derivative of 4-chloro- or 4-bromo-aniline underwent this change after heating at 230° for 24 hours, using zinc chloride as a catalyst.

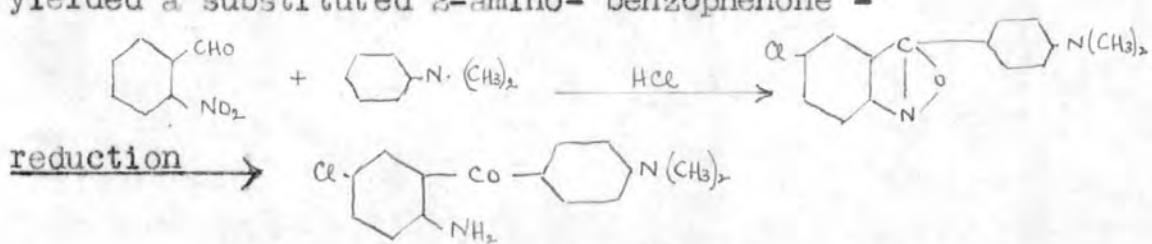
Prolonged hydrolysis of the resulting benzamido-derivative with alcoholic hydrochloric acid, yielded the free amino-benzophenone.



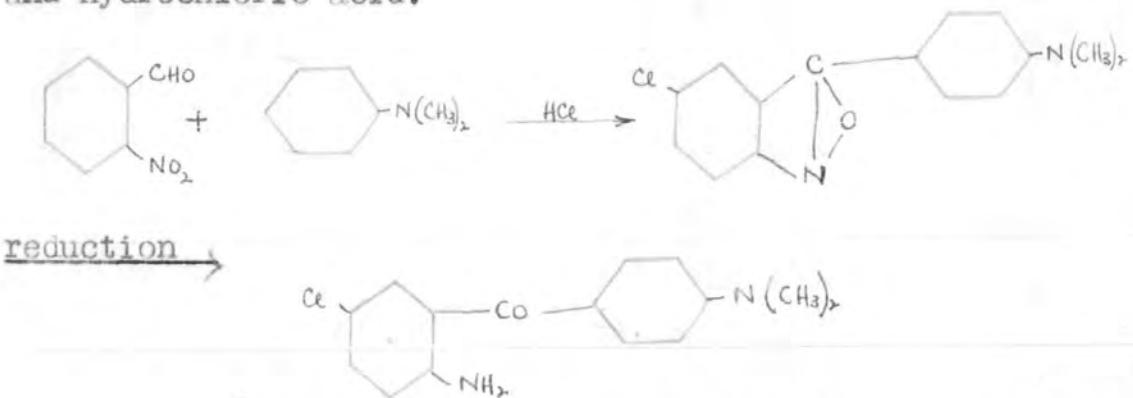
The overall yields in this reaction were not good, as the initial stage, (migration of the benzoyl group), only occurred to the extent of about 50%. The method is described fully in the Experimental Section (p. 57).

5. THE ZINCKE METHOD.

(a) Zincke and Prenntzell²⁵ found that o.nitro-benzaldehyde and dimethylaniline reacted to form an anthrostan on heating together in glacial acetic acid saturated with hydrochloric acid gas. Reduction of the anthrostan with zinc and acetic acid yielded a substituted 2-amino- benzophenone -



(b) As a continuation of method (a) Zincke and Siebert²⁶ found that o.nitrobenzaldehyde condensed readily with phenol or p. cresol at room temperature, in glacial acetic acid saturated with hydrochloric acid gas. The anthroxans so formed were converted to the amino-benzophenones by reduction with tin and hydrochloric acid.



Although this method is restricted in scope, it is very easy to carry out and affords an excellent overall yield of the amino-benzophenone. The reactions involved in this condensation are discussed more fully on pages 38-40 of this thesis, and improved experimental details are given in the Experimental Section (p. 61).

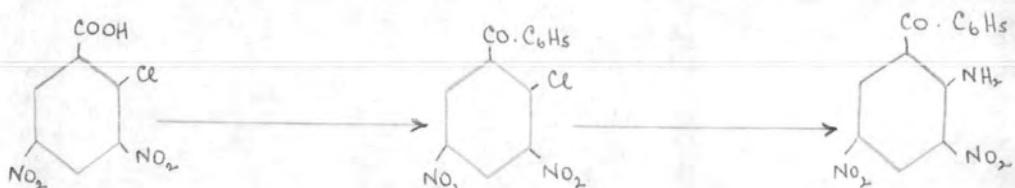
6. ULLMANN AND BROIDO'S METHOD.²⁷

Ullmann and Broido's method can only be applied to the preparation of 2-amino-3:5- dinitro-benzophenone and 2-amino 5-nitro- benzophenone.

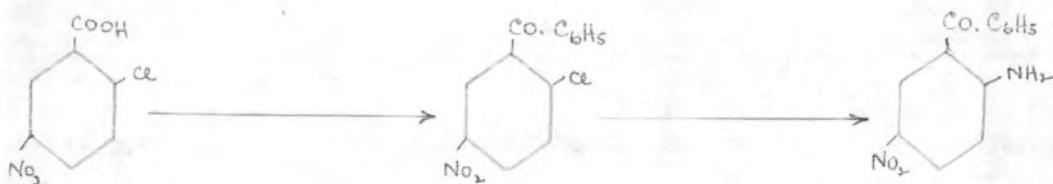
2-chloro-benzoic acid was di-nitrated, converted to the acid chloride by the actions of phosphorus pentachloride, and,

without further purification, condensed with benzene in the presence of aluminium chloride.

The resulting 2-chloro- 3:5 dinitro- benzophenone reacted easily with ammonia gas in boiling amyl alcohol to give 2-amino- 3:5- dinitro benzophenone -



(b) 2-chloro-5-nitrobenzoic acid was converted similarly to 2-amino-5-nitro-benzophenone, but in this case, the product reacted with ammonia only on heating to 180° in a sealed tube for 3 hours.



This method gave excellent overall yields of product.

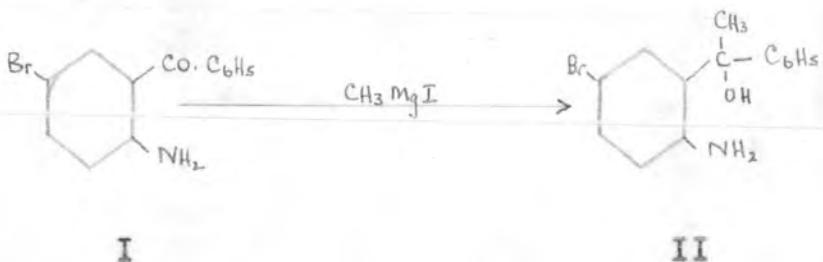
SECTION 2.

THE PREPARATION OF NEW CINNOLINE DERIVATIVES FROM SUBSTITUTED 2-AMINO-BENZOPHENONES.

I. 6-BROMO-4-PHENYL CINNOLINE.

(a) Phenyl-(5-bromo-2-aminophenyl)-methyl carbinol:

5-bromo-2-amino benzophenone (**I**), was prepared by the method of Angel²⁴ (loc.cit.), and condensed with methyl magnesium iodide to give phenyl- (5- bromo-2-aminophenyl)- methyl carbinol (**II**), in good yield.



The carbinol crystallised from a mixture of ether and ligroin in pale-yellow thick prisms, m.p. 100°. It gave high values for carbon on analysis, possibly due to the facility with which the carbinol undergoes dehydration - this explanation being supported by the fact that its N- acetyl and N-benzoyl derivatives gave similar high values, whereas the N-benzoyl ethylene (q.v.) gave satisfactory analytical data.

The N-acetyl derivative formed cream-coloured, long prismatic needles, m.p. $181-2^{\circ}$, after recrystallisation from aqueous methanol, and the N-benzoyl derivative colourless prisms, m.p. 196° , from aqueous ethanol.

(b) α - Phenyl- α - (5-bromo- 2 amino phenyl)- ethylene.

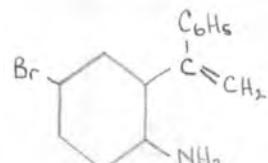
Dehydration of the carbinol was carried out smoothly by refluxing it for about 3 hours with dilute sulphuric acid. The sulphate of the amino-ethylene separated from this solution on cooling - two sulphates being isolated according to the strength of acid used.

When 4 N, (20%), sulphuric acid was used in the dehydration, a sulphate m.p. 107° was obtained in white feathery crystals. This sulphate was extremely hygroscopic and somewhat unstable, being decomposed slowly in cold water and rapidly in hot, to the free amino-ethylene. Analysis showed that it probably had the formula - $C_{14}H_{12}NBr \cdot H_2SO_4 \cdot 2H_2O$.

Treatment of the carbinol with 2N (10%) sulphuric acid under identical conditions yielded a second sulphate of the amino-ethylene in fine white needles, m.p. 154° . Although this compound appeared to be rather more stable than the compound m.p. 107° , it likewise decomposed slowly in aqueous solution.

Each of the above sulphates on basification and benzoylation yielded the same benzamido compound, α - phenyl - α - (5-bromo-2-benzamido phenyl)- ethylene, as colourless prismatic needles from aqueous alcohol, m.p. and m.m.p. 113.5° - 114° .

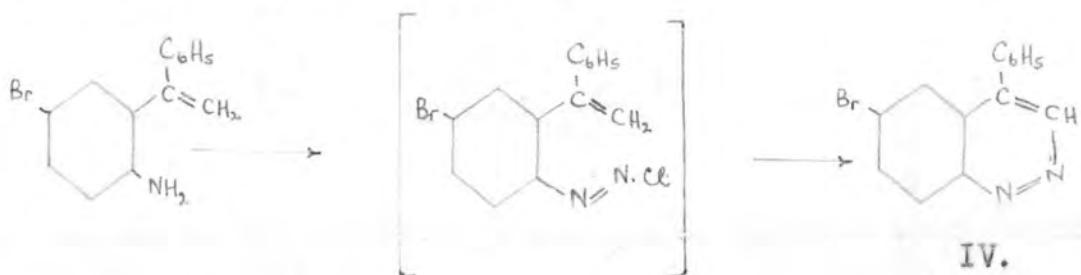
The free amino-ethylene itself (III), was a non-crystallisable oil.



6-bromo-4-phenyl cinnoline.

The cinnoline (IV), was obtained by treating a solution of the amino-ethylene in dilute sulphuric acid, with an equivalent amount of sodium nitrite. Initial diazotisations were carried out at 10°*C*, but it was later found that the reaction went equally well at 40°*C*, the free cinnoline base separating immediately from the solution in small, pale-yellow needles.

It crystallised from aqueous methanol in pale-yellow, light, silky needles, m.p. 143.5- 144.5°, which had a very faint geranium-like odour. This very faint colour was rather surprising since the corresponding unbrominated compound, phenyl cinnoline, has been described by Stoermer and Fincke (*loc.cit.*), as a sulphur-yellow compound.



6-bromo-4-phenyl cinnoline was obviously only weakly basic, since it separated as the free-base from acid solution. As expected therefore, the presence of bromine in the nucleus lowered the basic power of the cinnoline, since Stoermer and Fincke found that 4-phenyl cinnoline separated as its hydrochloride from dilute hydrochloric acid solution. The presence

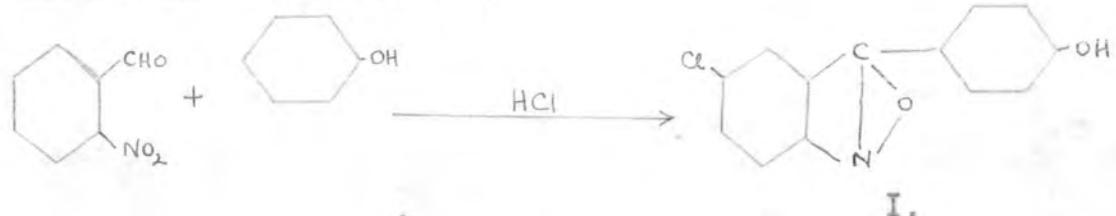
of bromine in the nucleus obviously had no adverse effect on the cyclisation of diazotised α - phenyl- α - (5-bromo-2-amino phenyl)-ethylene, since this was practically instantaneous.

6-bromo-4-phenyl cinnoline gave an immediate precipitate on treatment with chloroplatinic acid, and a picrate m.p. 270-5° on treatment with picric acid in benzene solution.

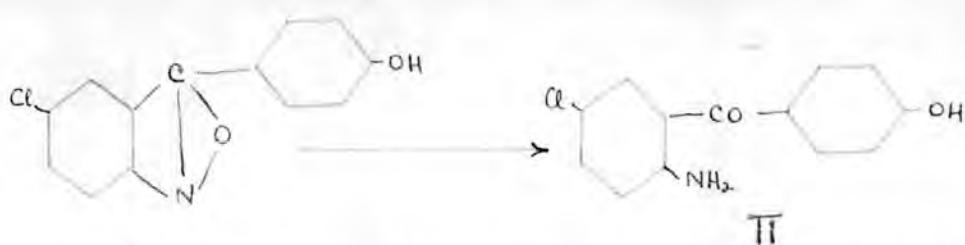
6 - CHLORO-4- (4'- HYDROXY PHENYL) - CINNOLINE.

(a) 5-chloro-3-amino-4'- hydroxy-benzophenone.

Following the method of Zincke and Siebert²⁶ (loc.cit.), o. nitrobenzaldehyde and phenol were condensed together at room-temperature, in acetic acid saturated with hydrochloric acid gas, yielding the anthroxan (I).



Zincke and Siebert reduced this anthroxan to the amino-benzophenone using tin and hydrochloric acid in alcoholic solution, followed by removal of tin salts with hydrogen sulphide, and precipitation of the base with ammonia. We tried this method of reduction several times and found that, besides being tedious, it gave only poor yields of the amino-benzophenone (II).



Further investigation of the reduction of the anthrostanone showed us that it could be carried out rapidly and easily using iron-filings in acetic acid, the base being obtained in good yield merely by filtration and dilution. After several recrystallisations from aqueous methanol, the amino ketone was obtained as yellow flattened needles, m.p. 177-178°. (Zincke and Siebert gave m.p. 174°). It was characterised by the preparation of its dibenzoyl derivative which crystallised from ethanol in colourless needles, m.p. 143°.

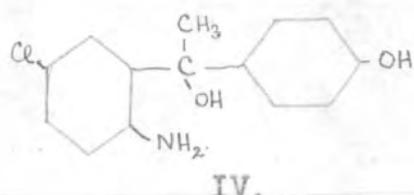
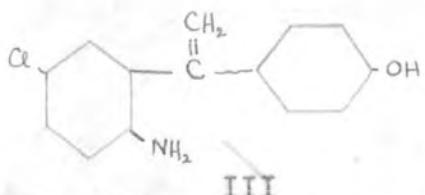
(b) α - (5-chloro-3-amino phenyl) - α - (4'- hydroxyphenyl) -ethylene.

We found that 5-chloro- 2-amino- 4'- hydroxybenzophenone (II), was recovered unchanged after heating for several hours with one to four equivalents of methyl magnesium iodide in ethereal solution.

Further investigation showed that the amino-ketone condensed with the Grignard reagent only when six to seven equivalents of the latter were used, and the solution was heated for five hours.

The product so formed was obtained in faint yellow cubes, m.p. 159°, after several recrystallisations from aqueous methanol. It was recovered unchanged after refluxing for several hours with sulphuric acid, varying in strength from 2N - 8N, and a small test showed that it gave an immediate precipitate with sodium nitrite in acid solution.

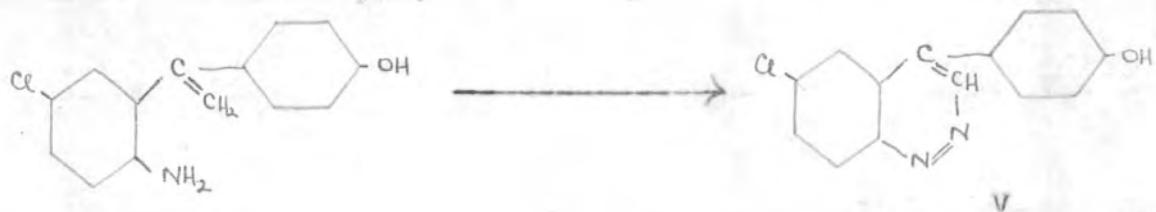
Analysis confirmed the fact that this compound was the ethylene (III), and not the carbinol (IV), hence the latter must have undergone spontaneous dehydration.



The ethylene was characterised by the preparation of its dibenzoyl derivative, m.p. $130\cdot 5 - 132^{\circ}$, obtained in clusters of colourless prisms on recrystallisation from methanol, or in slender prismatic needles from aqueous acetone.

(c) 6-chloro-4-(4'-hydroxyphenyl)-cinnoline.

The cinnoline (V), separated immediately in 70% yield on addition of aqueous sodium nitrite to a solution of the amino-ethylene in hydrochloric acid, but in dilute sulphuric acid the yield was lower, (50%), and accompanied by partial resinification.



It was only sparingly soluble in boiling alcohol, and crystallised from this solvent in small, shining plates. It was much more soluble in acetic acid, and crystallised from

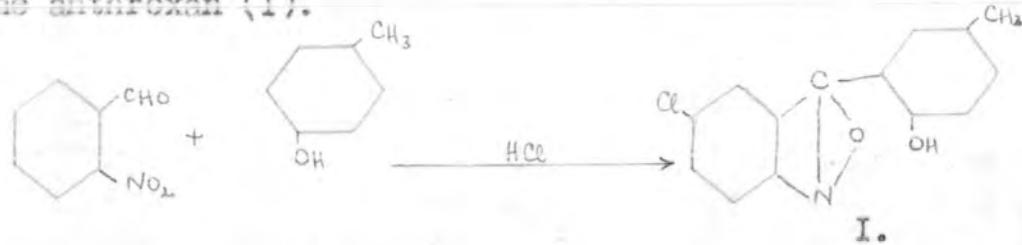
slightly aqueous acetic acid in lustrous yellow plates with a red reflex, m.p. 257-259° (d.).

The cinnoline was characterised by the preparation of its O-benzoate, which formed small, pale-yellow needles, m.p. 156°, from aqueous alcohol.

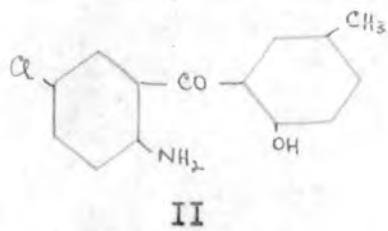
6-CHLORO-4-(2'-HYDROXY-5'-METHYL PHENYL) - CINNOLINE.

(a) 5-chloro-2-amino-2'-hydroxy-5'-methyl-benzophenone.

Ortho-nitro benzaldehyde and p.cresol were condensed together in acetic acid saturated with hydrochloric acid gas, according to the method of Zincke and Siebert (loc.cit.), yielding the anthrostan (I).



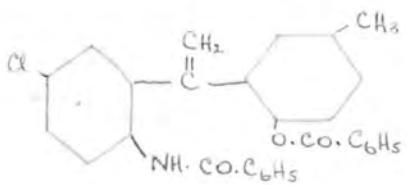
This was reduced to the amino benzophenone (II), using iron and acetic acid as previously, since we again found this method to be much superior to the reduction with tin and hydrochloric acid, used by Zincke and Siebert.



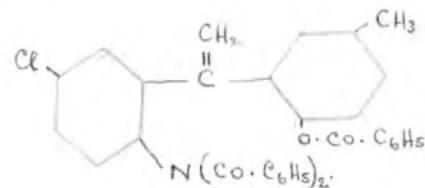
The amino benzophenone was characterised by the preparation of its sparingly soluble dibenzoate, obtained as small stout needles, m.p. 156-157° on crystallisation from a mixture of alcohol and benzene.

(b) α -(5-chloro-2-aminophenyl) - α -(2'-hydroxy-5'-methylphenyl) - ethylene.

Treatment of the aminobenzophenone with seven equivalents of methyl magnesium iodide as previously, yielded a red-brown resinous residue which defied all attempts at crystallisation. In our early efforts to isolate the pure product, we found that benzylation of the resin furnished a crystalline derivative of the amino-ethylene (III), m.p. 119° . This substance was accordingly hydrolysed with alcoholic potash, since it had been found that the parent amino-ketone was recoverable by a similar hydrolysis of its dibenzoyl compound. We found however that the product of hydrolysis of the dibenzoyl m.p. 119° was a resin which on re-benzylation gave a new benzoyl derivative m.p. 235° , which appeared from analysis to have the formula $C_{26}H_{26}O_4NCl$, and we therefore regard it as a tri-benzoyl derivative (IV).

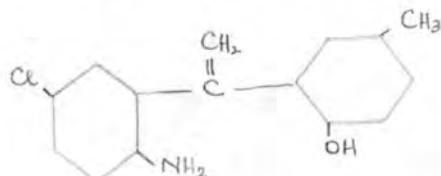


III



IV.

This latter compound was not investigated further, for the amino-ethylene (V) was isolated in the meantime by converting the original resin to its hydrochloride, purifying this, and re-converting it to the base.



V.

6-chloro-4-(2'-hydroxy-5'-methyl phenyl)-cinnoline.

The hydrochloride of the amino ketone was treated with sodium nitrite in dilute hydrochloric acid at 0°, yielding the cinnoline immediately. It was purified exactly as described for 6-chloro-4-(4'-hydroxyphenyl)-cinnoline, being obtained in the form of small, golden, prismatic needles, m.p. 260-261°(d).

We were also able to obtain the cinnoline by the action of hydrochloric acid and sodium nitrite on the crude resinous diaryl ethylene. The cinnoline was characterised by the preparation of its benzoate, obtained as yellow prisms m.p. 140°, on recrystallisation from a mixture of ether and ligroin.

Reaction between 2-amino-3:5 dinitro benzophenone and methyl magnesium iodide.

2-amino-3:5-dinitro-benzophenone was prepared by the method of Ullmann and Broido²⁷ (loc.cit.), and an attempt made to condense it with methyl magnesium iodide. When two equivalents of the Grignard reagent were used, the amino-benzophenone was recovered unchanged, and with an excess of Grignard reagent, a good deal of oxidation took place, with liberation of iodine.

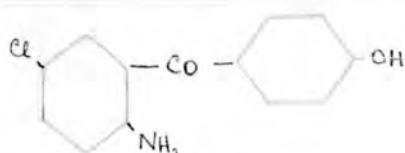
In the latter case the product was merely a viscous acid - insoluble oil.

The reaction also failed when 2-benzamido-3:5 dinitrobenzophenone was used in place of the amino-compound.

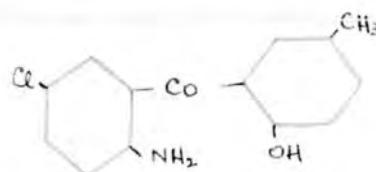
In the benzoylation of 2-amino-3:5-dinitrobenzophenone, only a poor yield of the benzamido-derivative was obtained - probably due to steric-hindrance in the molecule.

SECTION 3.ORIENTATION OF THE THREE NEW CINNOLINES.

The orientations of the three new cinnolines are obviously dependent on those of the related 2-amino-benzophenones, and in the case of the two phenolic ketones, (I) m.p. 178° and (II) m.p. 114° , no rigid proof of structure appears to exist.

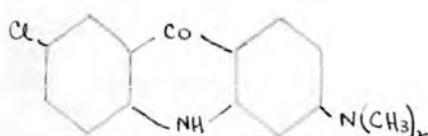


I

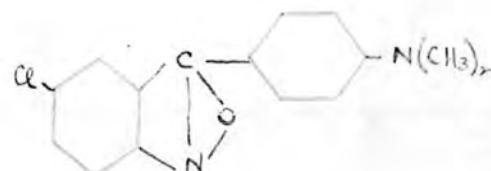


II

In 1905, Zincke and Prenntzell²⁵ condensed ortho-nitro-benzaldehyde with dimethylaniline in the presence of hydrochloric acid, obtaining a compound of empirical formula, $C_{15}H_{13}N_2OCl$. The chlorine was not present as an anion and was therefore presumably attached to the nucleus. This compound, which possessed feebly basic properties and was strongly fluorescent in dilute alcohol or ether, was possibly an acridone (III), or an anthranil (IV).



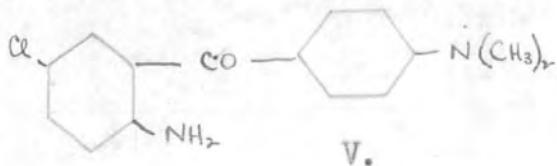
III



IV

On reduction with zinc and hydrochloric acid, it took up two hydrogen atoms, yielding a product which possessed strongly

basic properties and which gave an acetyl and diazonium derivative, showing that it must have the formula (V).



On heating this reduction product with hydriodic acid, Zincke and Prenntzell found that it was converted to 1-4'-diamino diphenylmethane (VI), which on deamination yielded diphenylmethane. (VII)



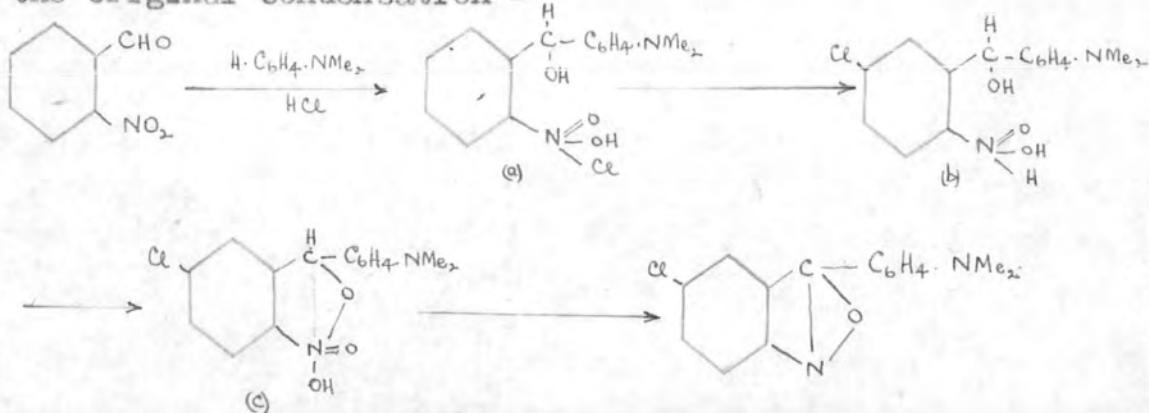
VI



VII

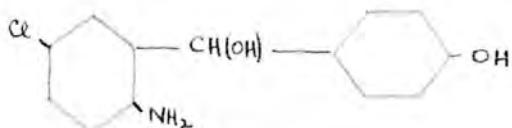
Hence, on this evidence, formula IV is much more likely than formula III for the original product, since an acridone derivative would not split so easily to a benzophenone on reduction.

Zincke and Prenntzell suggest the following mechanism for the original condensation -



In the stage (a) → (b) where the chlorine enters the nucleus and is replaced by hydrogen, the reaction is comparable with the conversion of phenyl nitrosamines to nitrosobenzene derivatives.

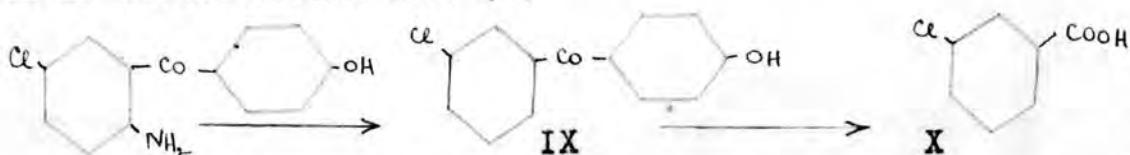
As already indicated, Zincke and Siebert showed that phenol and p. cresol reacted with o. nitrobenzaldehyde in the same way as dimethyl aniline, yielding anthroxans which were reduced to the corresponding benzhydrol derivatives (e.g. VIII) by heating with hydriodic acid and phosphorus - the chlorine being unattacked.



VIII.

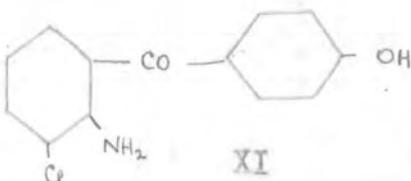
The position of the chlorine atoms in these compounds had not been proved, but by means of the procedure described below we were able to establish the correctness of the constitutions assigned to the ketones, as far as the positions of the chlorine atoms are concerned.

Zincke and Siebert described the conversion of the ketone m.p. 178° to 3-chloro-4'-hydroxybenzophenone (IX), a result which we have in part confirmed by oxidising this compound to m. chlorobenzoic acid (X)

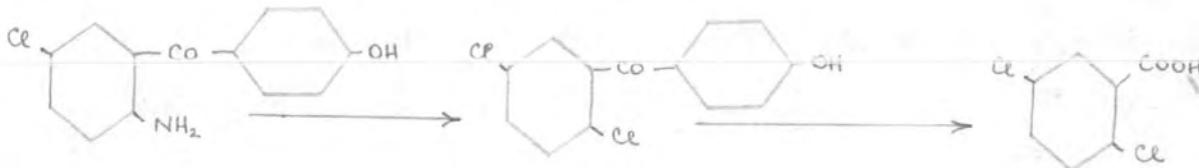


3-chloro-4'-hydroxybenzophenone however, could also arise from the ketone m.p. 178° if the latter were represented by an

alternative structure (XI) with the chlorine atom on C₃ instead of C₅.



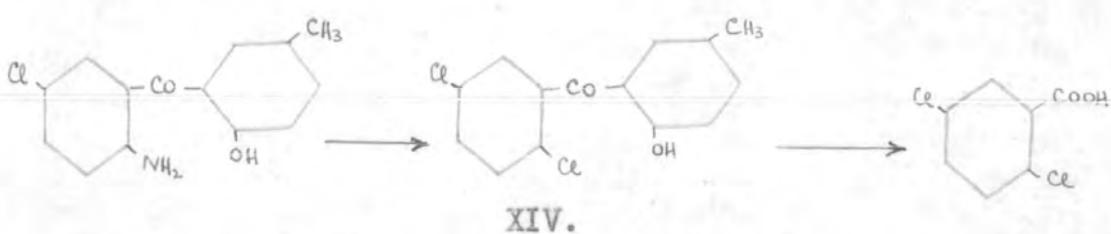
We have eliminated this possibility by converting the amino-ketone m.p. 178° into 2:5- dichloro-4'- hydroxybenzophenone (XII) by the Sandmeyer reaction*, proving the structure of this latter compound by oxidising it to 2:5- dichlorobenzoic acid (XIII) with permanganate at 40°.



*

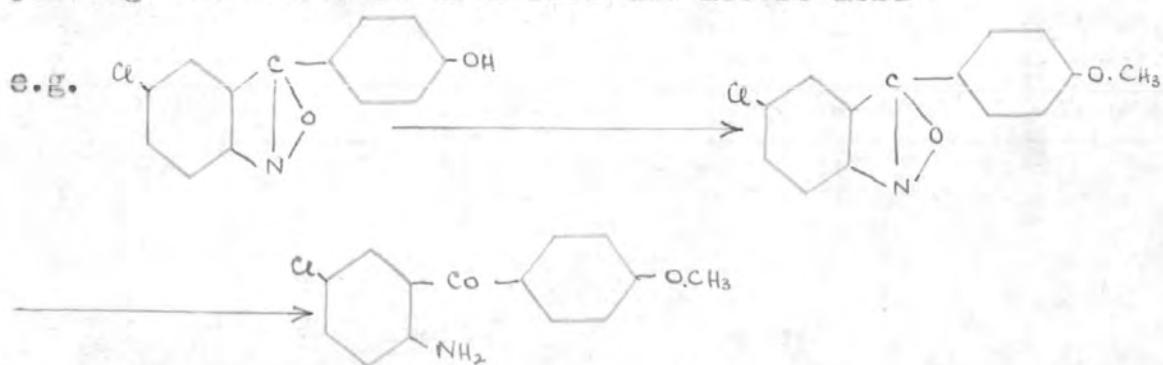
FOOTNOTE. In one of a number of preliminary attempts to prepare 2:5- dichloro-4'-hydroxybenzophenone from the amino-benzophenone, the amount of sodium nitrite was not rigidly controlled, but the other conditions were as described above. The major crystalline product in this case was a poor yield of a substance which crystallised from aqueous methanol in canary-yellow hair-like needles, m.p. 234-6° (Found, N = 5.7; Cl = 15.8%).

The position of the chlorine atom in the second amino-ketone (m.p. 114°) was similarly established by converting it to 2:5-dichloro-2¹-hydroxy - 5¹-methyl benzophenone (XIV), followed by oxidation of the latter to 2:5- dichlorobenzoic acid.



The preparation of these dichlorobenzophenones from the amino benzophenones, contradicts the experience of Zincke and Siebert who were unable to prepare any derivative of the diazotised amino ketones except 3-chloro-4¹-hydroxy-benzophenone, (the recorded m.p. of which is considerably lower than that found by us.).

In an attempt to establish the position of the phenolic groups in each of the amino-ketones, we prepared the methyl ethers of the two anthroxans, and reduced these to the corresponding amino-ketones with iron and acetic acid -



On the assumption that the positions assigned to the phenolic groups in the ahtnroxans are correct, it was anticipated that oxidation of the methoxy-amino-ketones would furnish anisic acid and 4-methoxy-isophthalic acid respectively -

e.g.

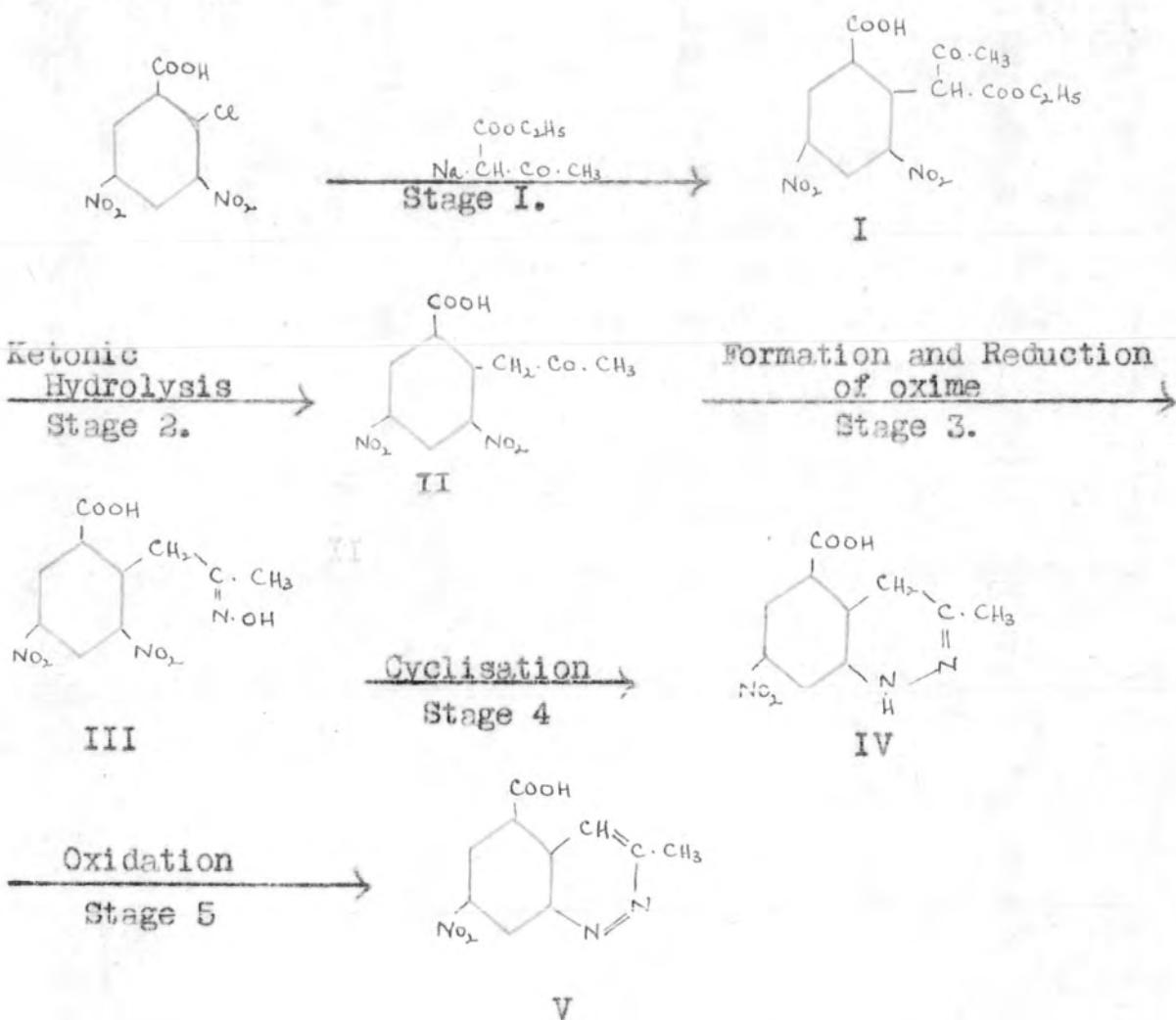


However, the ketone in equation (b) was incompletely oxidised by alkaline permanganate, and no crystalline product could be obtained when the oxidation was continued in acid solution.

In view of this result the ketone in (a) was diazotised with a view to obtaining a phenol more amenable to oxidation, but, in spite of several trials, almost the whole of the product was an alkali-insoluble resin, and only a trace of crystalline phenol could be obtained.

SECTION 4.CONDENSATION OF 2-CHLORO- 3,5- DINITRO BENZOIC ACID WITH ACETO ACETIC ESTER.

An investigation of the condensation between 2-chloro-3,5-dinitro benzoic acid and acetoacetic ester was undertaken with the object of carrying out the following series of reactions.



Stage 1.

Condensation of 2-chloro-3:5- dinitro benzoic acid with sodium acetoacetate to yield ethyl - α - (2:4. dinitro - 6 - carboxy phenyl)-aceto acetate. (I).

Stage 2.

Ketonic hydrolysis of this compound to α - (2:4. dinitro- 6- carboxy phenyl)- acetone. (II).

Stage 3.

Preparation of the oxime of (II) and reduction of the 2-nitro group (probably in two stages involving the reduction of both nitro-groups).

Stage 4.

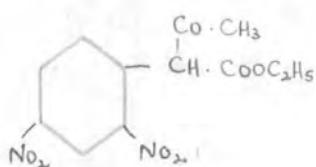
Cyclisation of the α -amino oxime to a dihydro cinnoline derivative (IV).

Stage 5.

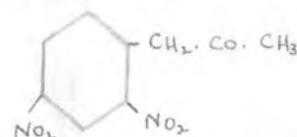
Oxidation of the dihydro cinnoline to a cinnoline derivative (V).

The initial condensation between sodium aceto acetate and 2-chloro-3-5- dinitro benzoic acid was accomplished successfully when carried out in alcoholic solution, but went much more readily in ethereal solution following the method used by Borsche²⁸ who used 2:4 dinitrochlorbenzene in place of the acid.

Borsche found that his product (VI) was readily hydrolysed by sulphuric acid to 2:4. dinitro- phenyl acetone (VII).



(VI)

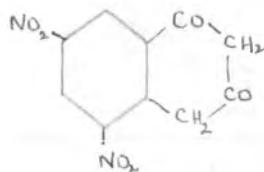


(VII)

We isolated our condensation product (I) in the crude state in good yield, but found that it needed repeated recrystallisation from methanol before the pure compound could be obtained. It was almost always contaminated with traces of unchanged 2-chloro-3:5- dinitro-benzoic acid, even when an excess of sodium acetoacetate was used in the initial condensation.

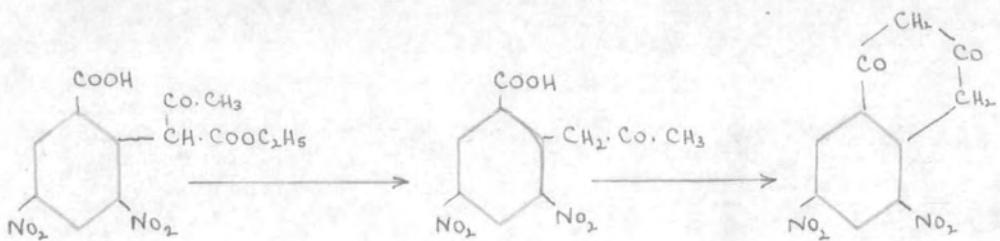
This compound (I) was not readily hydrolysed by sulphuric acid like Borsche's compound (VI).

Attempted hydrolysis by boiling with dilute sulphuric acid yielded a very small amount of a compound analysis of which showed that it was probably (VIII).



VIII.

It was probable therefore that some ketonic hydrolysis did take place, followed by cyclisation
e.g. —

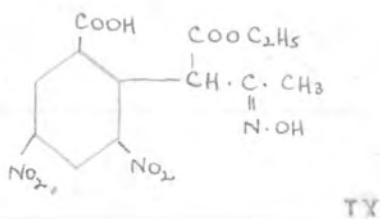


Several further attempts were made to hydrolyse this compound in both acid and alkaline solution, but no definite product could be isolated.

DERIVATIVES ofEthyl - α - [2.4. dinitro-6-carboxyphenyl] - 7 - aceto acetate.(a) OXIME.

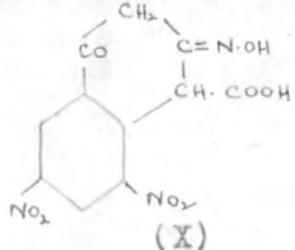
The compound (I) was condensed with hydroxylamine hydrochloride in alcoholic solution in the presence of excess of sodium acetate, yielding two distinct derivatives which were separated by fractional crystallisation from methanol.

The normal oxime (IX) was not obtained.

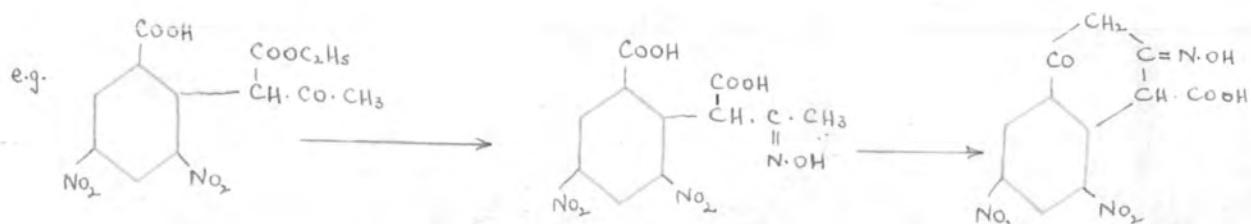


The less soluble oxime was isolated in small pale-yellow needles which melted at 230° with decomposition and frothing.

Analysis showed that its formula was probably - (X)

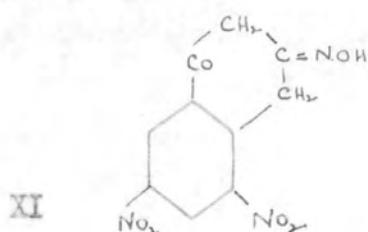


Showing that hydrolysis and cyclisation had taken place as shown.

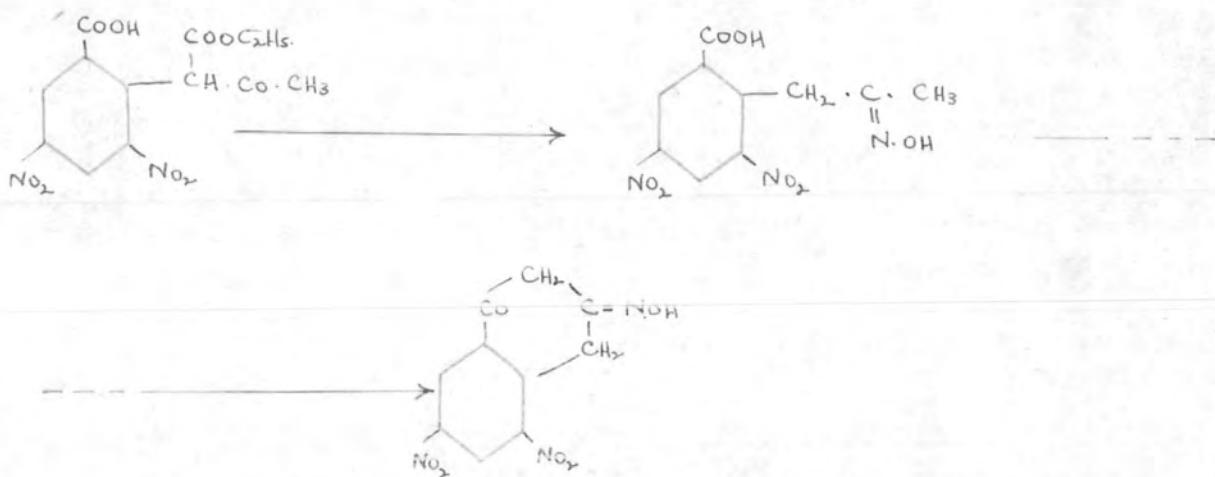


The more soluble oxime was isolated as bright yellow needles which melted at 239° without decomposition, analysis

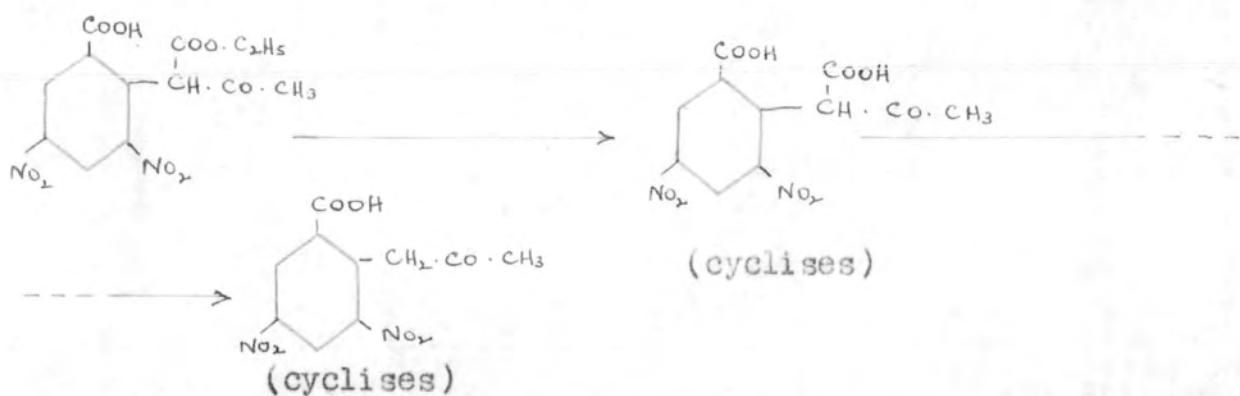
showed that it was probably (XI),



which could be formed by hydrolysis and cyclisation as shown

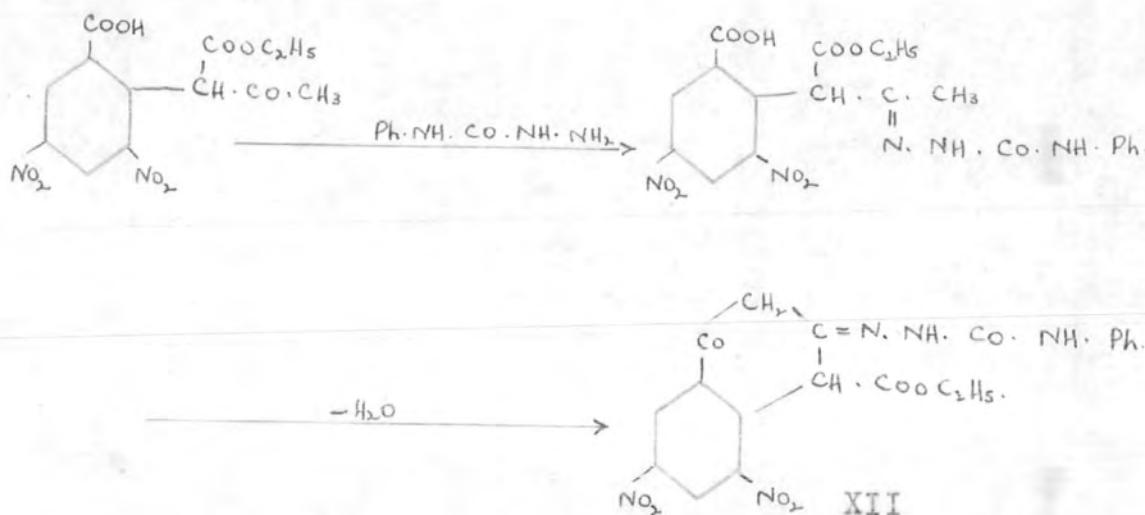


It is therefore likely that under the original conditions of oxime formation (heating the alcoholic solution in the presence of an excess of sodium acetate), hydrolysis takes place in two stages, followed by cyclisation -



(b) PHENYL SEMI-CARBAZONE.

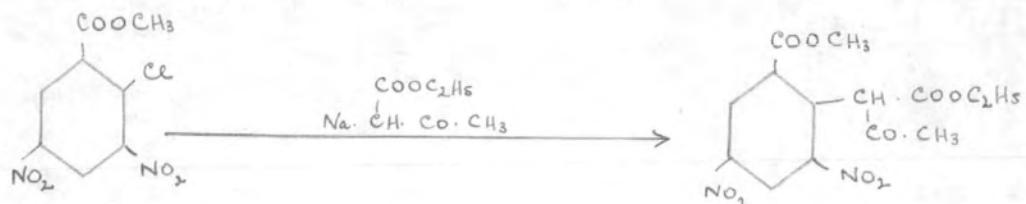
Condensation of ethyl α - β : γ -dinitro- δ -carboxy-phenyl- γ -acetoacetate with phenyl semicarbazide hydrochloride in the presence of sodium acetate yielded a compound analysis of which seemed to indicate that it had the formula (XII). The probable course of the condensation is shown -



Unfortunately it was not possible to investigate these derivatives any further, hence, although it is fairly certain that ring closure does take place, we cannot be certain how this happens.

Condensation between the methyl ester of 2-chloro-3:5. - dinitrobenzoic acid and sodium acetoacetate.

The methyl ester of 2-chloro-3:5. dinitro benzoic acid was prepared and condensed with sodium acetoacetate in ethereal solution as indicated previously, in the hope that the product (XIII), would show less tendency to cyclise.



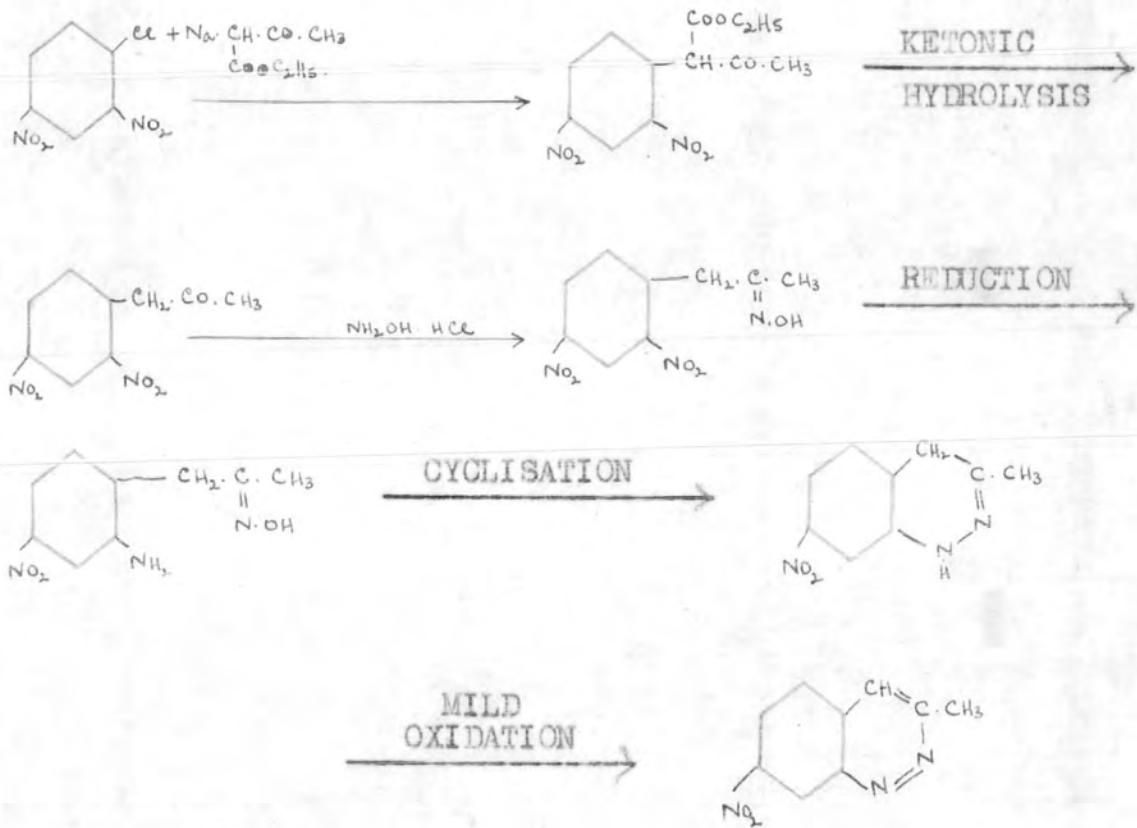
XIII.

The initial product however was a deep red oil which could not be crystallised and apparently withstood all attempts at hydrolysis by acid and alkaline reagents.

SECTION 4 (b).

CONDENSATION of 2:4 - dinitro chlorbenzene with sodium aceto-acetate.

The condensation between 2:4. dinitro-chlorbenzene and sodium acetoacetate was next carried out with the object of attempting the following series of reactions -



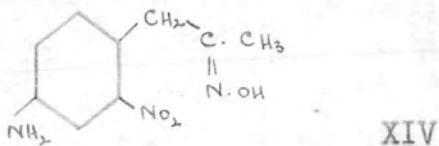
For the preparation of 2:4- dinitrophenyl-acetone we used the method of Borsche (loc.cit.), which was quite satisfactory.

Reduction of dinitrophenyl acetone in acid solution failed completely, yielding only a non-crystalline tar, we therefore attempted reduction of its oxime.

The oxime was not reduced by sodium hydrosulphite in aqueous alcoholic solution, and ammonium sulphide yielded an indefinite product.

Careful reduction of the oxime with sodium hydrosulphide in alcoholic solution yielded a monoamine which was easily soluble in dilute mineral acids and whose diazo-solution gave a deep-red dye with alkaline β -naphthol.

It probably had the formula XIV, since reduction of the 3-nitro-group would probably have led to ring-closure.



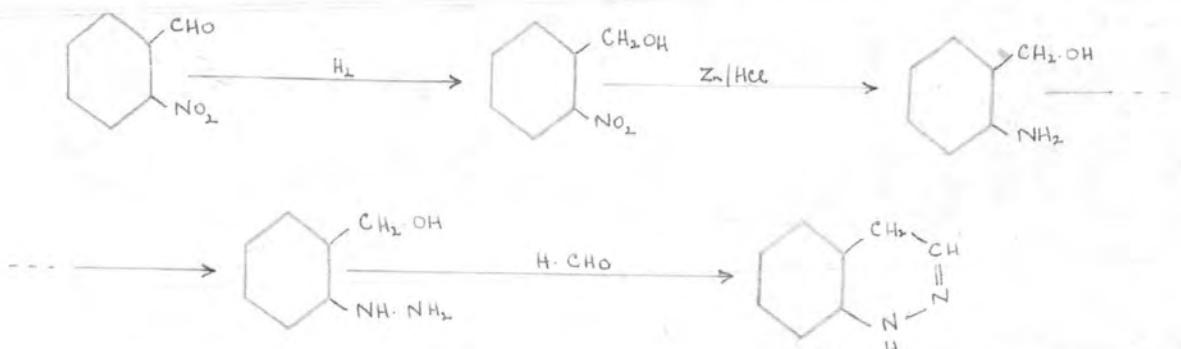
However, owing to lack of time, we were unable to confirm the position of the amino-group.

SECTION 5.UNSUCCESSFUL ATTEMPTS TO SYNTHESISE CINNOLINE DERIVATIVES.

Other methods of synthesis of cinnoline derivatives which were investigated, are mentioned briefly below -

1. From ortho-nitrobenzaldehyde.

The following series of reactions were contemplated -



Ortho-nitrobenzaldehyde was reduced to ortho-nitrobenzyl alcohol with aluminium isopropoxide in isopropyl alcohol²⁹, and thence to the amino-compound with zinc in alcoholic hydrochloric acid.³⁰ This was diazotised and reduced in an attempt to prepare the phenyl hydrazine. The product was an amorphous orange-coloured solid which could not be crystallised. It formed a high-melting chloroplatinate but would not condense with acetophenone or other ketones. We therefore concluded that it was a reduced indazole, formed by cyclisation, as follows -



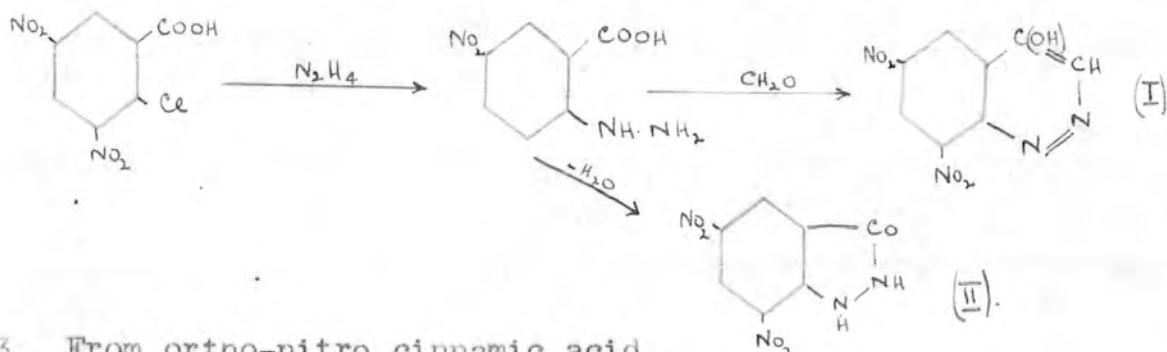


The experiment was repeated starting from o.nitro benzyl benzoate in an attempt to prevent this cyclisation. Ortho-nitro benzyl benzoate was reduced to o.amino benzyl benzoate by the method of Paal and Bodewig.³¹ Diazotisation and reduction of the diazo-solution however, resulted in hydrolysis of the benzoate with deposition of benzoic acid.

2. From 2-chloro- 3:5- dinitrobenzoic acid.

2-chloro-3:5- dinitro benzoic acid was condensed with hydrazine hydrate in alkaline solution in presence of formaldehyde, in an attempt to prepare 4-hydroxy-6:8- dinitro-cinnoline.(I)

However, the formaldehyde took no part in the reaction, and the product was merely 5:7-dinitro-3-oxy-indazole.(II). This compound was insoluble in all the common organic solvents, but crystallised from water in yellow prisms which decomposed at about 200° without melting. (cf. Purgotti and Contardi.³²)

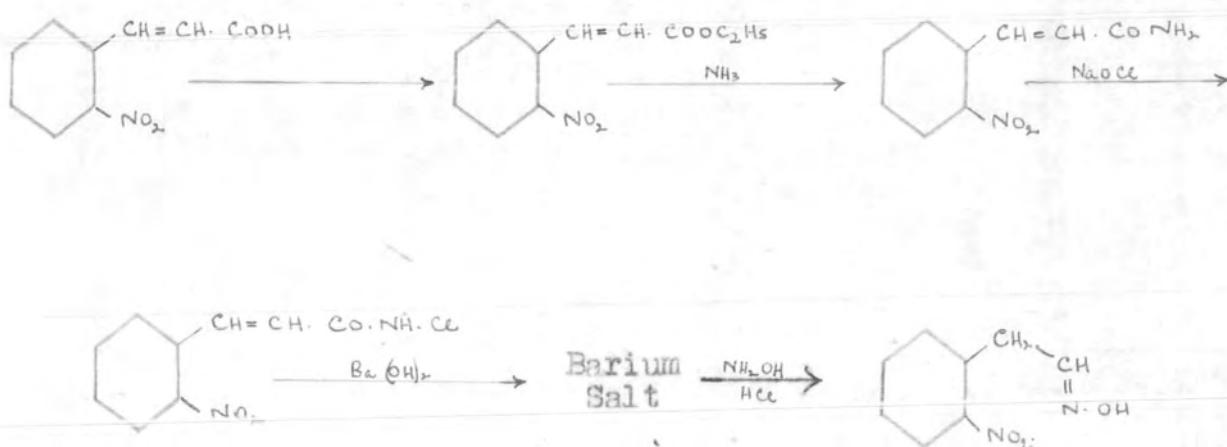


3. From ortho-nitro cinnamic acid.

Ortho-nitro phenyl acetaldoxime was prepared by Weermann's method as follows ³³

Ortho-nitro ethyl cinnamate was converted to the amide by

the action of alcoholic ammonia, and thence to the chloramide by shaking with sodium hypochlorite solution in amyl alcohol. The chloramide was converted to o. nitrostyryl barium carbamide by warming with $N/3$ baryta solution, and treatment of this latter compound with hydroxylamine hydrochloride in aqueous solution yielded o.nitro phenyl acetaldoxime.



Attempted reduction of the o.nitro phenyl acetaldoxime with alcoholic sodium hydrosulphide yielded only a black tarry product.

EXPERIMENTAL SECTION.

Preparation of 2-amino-5-bromo-benzophenone (cf. Angel,²⁴, loc.cit.)

52.5 gms. of p.bromaniline (1 equivalent), 100 gms. of benzoyl chloride (2.1 equivalents) and 12 gms. of anhydrous zinc chloride were mixed in a round-bottom flask fitted with air condenser and calcium chloride tube.

After the vigorous reaction had subsided, the mixture was heated at 180° for 2 hours and then at 210-230° for 23 hours. The dark-brown semi-crystalline product was hydrolysed by refluxing for 41 hours with 900 cc. of alcohol and 600 cc. of conc. hydrochloric acid. The solution was steam-distilled to remove alcohol and ethyl benzoate, distillation being stopped when the distillate was no longer turbid. The tarry residue was made alkaline and steam-distilled, and 25 gms. of p. bromaniline recovered.

The remaining tarry residue was extracted thrice with fairly conc. hydrochloric acid, the extracts were diluted well with water, and the crude benzophenone which separated filtered.

The residue was again extracted with hot conc. hydrochloric acid containing a little alcohol, and precipitated with water as above.

The acid mother liquor was extracted with 50cc. of chloroform and the solvent evaporated off, leaving about 0.5 gm. of the crude benzophenone.

The crude bromo amino benzophenone was purified by crystallisation from a mixture of chloroform and petrol (after

boiling with charcoal).

Yield 18.5 gms. m.p. 111° (43.5 % on the basis of the p. bromaniline used up).

Reaction between 2-amino-5-bromo-benzophenone and methyl magnesium iodide.

5 gms. of the bromo amino ketone in 125 cc. of dry ether were added slowly to a cold solution of methyl magnesium iodide prepared from 2 gms. of magnesium (4 equivalents) and 12 gms. of methyl iodide in 50 cc. of dry ether.

The dark red mixture so obtained was refluxed for 10 minutes, when solid began to separate and the mixture went much lighter in colour. It was cooled and decomposed by the addition of ice and a little dilute hydrochloric acid. The ether layer was dried over sodium sulphate and evaporated to dryness leaving a reddish oily residue which soon solidified on scratching. It was recrystallised from a mixture of ether and ligroin and separated in colourless cubic crystals m.p. 100° , 4.3 gms. (86%).

Analysis gave C = 58.48, H = 5.14, N = 5.054

C₁₄H₁₄NO Br requires C = 57.53 H = 4.84, N = 4.79.

Dehydration of the carbinol.

(a) 2 gm. of the crude carbinol were refluxed for $2\frac{1}{2}$ hours with 60 cc. of 10% sulphuric acid. Fine white needles separated in cooling. These were redissolved in a little hot dilute sulphuric acid with addition of a little alcohol and filtered boiling after addition of charcoal. Long white needles

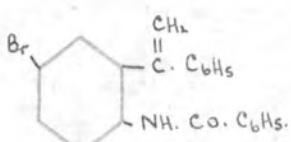
separated 1.3 gm. m.p. 154° (A).

(b) 0.5 gm. of pure carbinol were refluxed for $3\frac{1}{2}$ hours with 60 cc. of 4N(20%) sulphuric acid - white feathery needle clusters separated rapidly on cooling, 0.54 gm. m.p. 107° (B).

These experiments were repeated several times and in each case it was found that 3N (10%) sulphuric acid yielded a sulphate m.p. 154° and 4N, (20%), sulphuric acid, a sulphate m.p. 107° . Both sulphates were partially hydrolysed to an oil in cold water, the lower melting sulphate (B) being hydrolysed more easily.

Each sulphate on neutralisation with dilute ammonia and extraction with ether yielded an oily non-crystallisable residue which was benzoylated in pyridine in each case. Identical compounds m.p. and mixed m.p. 113.5° , were obtained in each case. These were analysed and found to correspond to the benzoyl derivative of the amino-styrene.

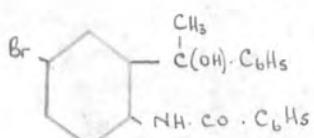
Found C = 67.0, H = 4.29



$C_{21}H_{16}NOBr$,
requires C = 66.70, H = 4.27.

Benzoylation of the bromocarbinol itself with benzoyl chloride and pyridine, yielded a monobenzoyl derivative m.p. 196° .

This was analysed -



Found C = 64.43
H = 4.56

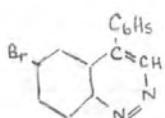
$C_{21}H_{18}NO_2Br$ requires C = 63.61
H = 4.56

Preparation of the cinnoline.

(a) 0.25 gm. of the sulphate m.p. 154° was dissolved in warm dilute sulphuric acid (20cc), cooled to room temperature, a slight excess of solid sodium nitrite added, and the mixture shaken well. Pale, yellow flakes separated rapidly - these were dissolved in hot dilute alcohol, boiled with charcoal and filtered. Faint yellow needles separated on cooling - 0.15 gms. m.p. 145°.

The cinnoline was analysed -

Found C = 59.72, H = 3.07, N = 9.57.



C₁₄H₉N₂Br, requires C = 58.96, H = 3.18, N = 9.83

Preparation of the antitoxin from o. nitrobenzaldehyde and phenol.

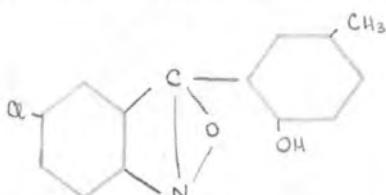
The following method is a slight modification of that of Zincke and Siebert²⁶.

10 gms. of o.nitrobenzaldehyde and 6.5 gms. of phenol were dissolved in 80 cc. of glacial acetic acid, cooled in ice, and saturated with dry hydrochloric acid gas. The mixture turned deep red and was warmed on the water-bath for 10 minutes and then left in a warm place for 2 hours.

Fine yellow crystals soon began to separate from the warm solution. These were filtered off, more product being obtained by dilution of the filtrate with a little water.

The product was crystallised from dilute alcohol, 10.6 gms. (64%) m.p. 241°.

Preparation of the anthroxan from o.nitrobenzaldehyde and p.cresol.



The previous method was repeated using 7.5 gms of p.cresol in place of the phenol. 9.9 gms. of the pure anthroxan, m.p. 310° (58%), were obtained after recrystallisation from dilute alcohol.

Preparation of 2-amino-5-chloro- 4'-hydroxy-benzophenone.

10 gms of the anthroxan, m.p. 241° , were suspended in 200cc. of hot glacial acetic acid on the water-bath and 5 gms. of iron filings added. The solid went rapidly into solution. 50 cc. of water were then added followed by a further 10 gms. of iron filings, added in 2 gm. portions over a period of 2 hours. The solution was cooled, diluted with 50cc. of water and filtered twice to remove sludge. The filtrate was then heated to about 100° and water added until solid just began to separate. Yield 9.6 gms. (crude). The product was recrystallised thrice from dilute methanol, yielding 7.2 gm. (70%) of the amino benzophenone in very pale yellow needles, m.p. 178° .

Preparation of 2-amino-5-chloro-2'-hydroxy- 5'-methyl-benzophenone.

The other anthroxan, m.p. 210° , was reduced exactly as previously, and gave a 70% yield of the pure amino benzophenone as bright yellow needles m.p. 115° after recrystallisation.

Reaction of 2-amino-5-chloro-4'-hydroxy-benzophenone with methyl magnesium iodide.

(a) 0.9 gm of the amino-ketone dissolved in 50cc. of dry ether was added to a cold solution of 4 equivalents of methyl magnesium iodide, prepared from 0.35 gms. of magnesium and 2.1 gms. of methyl iodide in 25 cc. of ether. The solution turned orange yellow and a yellow solid separated out rapidly. The mixture was refluxed for 1 hour, cooled, and decomposed with ice and dilute acid. The product after recrystallisation from alcohol had m.p. 176° (0.8 g.) and proved to be the unchanged amino-ketone.

(b). 1.0 gm of the amino-ketone, dissolved in 70cc. of dry ether was added to a cold solution of 6 equivalents of methyl magnesium iodide in 25cc of ether. An orange-yellow solid separated and some gas was evolved. The mixture was allowed to stand for 10 minutes and was then refluxed for 5 hours. It was then decomposed as usual, the ether layer separated, dried, and evaporated. The oily residue left was dissolved in a little methanol, boiled with charcoal and filtered.

0.54 gms of yellow crystals m.p. $155-7^{\circ}$ were obtained. Repeated recrystallisation from dilute methanol gave a product m.p. 159° in almost colourless prisms.

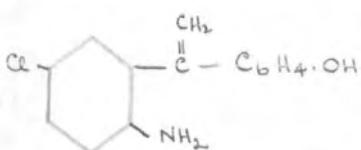
In a repeat of this experiment, 4.8 gms. of amino ketone in 250cc ether added to a solution of methyl magnesium iodide prepared from 3 gms. of magnesium and 18 gms. of methyl iodide in 120cc. of ether, yielded finally 3.29 gms. (69%) of product, m.p. 158° .

Analysis showed that this compound was the styrene and not the carbinol -

Found, C = 68.23, H = 4.76

Required for

$C_{14}H_{12}NOCl$, C = 68.40
H = 4.93



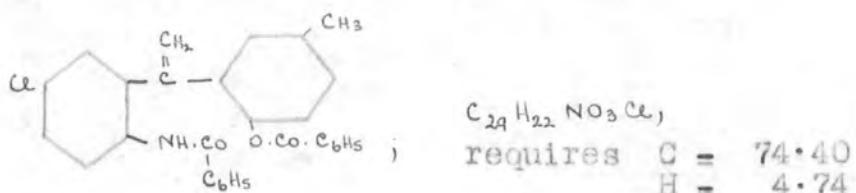
Condensation of 2-amino-5-chloro-2'-hydroxy-5'-methyl benzophenone with methyl magnesium iodide.

12 gms. of the anthrostan m.p. 115°, dissolved in 400cc. of ether, were added to a cold solution of 5 equivalents of methyl magnesium iodide, prepared from 7.2 gms. of magnesium and 45 gms. of methyl iodide in 250cc. of ether. The solution went deep-red, an orange-coloured solid separated, and some gas was evolved. The reaction mixture was worked up as usual, yielding 13.0 gms. of a viscous non-crystallisable residue.

This residue was di-benzoylated as follows -

1.75 gm of viscous oil, 1.75 gm benzoyl chloride (2 equivs) and 1.3 gms of pyridine (2.2 equivalents) were heated at 100° in a stoppered flask for 3 hours. The mixture was cooled and the red viscous residue decomposed with ice and dilute sulphuric acid, extracted with ether and the ether extract washed first with 2% caustic soda and then with water. Evaporation of the ether left a red, semi-crystalline residue. This was crystallised from dilute methyl alcohol yielding 0.52 gms of white needles m.p. 110-111°. Repeated recrystallisation from methanol gave white needles, m.p. 119°, which were analysed.

Found C = 74.37, H = 4.85



In a repeat of this benzylation, 13.0 gms of viscous residue with 13 gms of benzoyl chloride and 11.0 gms. of pyridine yielded 7.55 gms. of dibenzoyl derivative m.p. 119°.

Hydrolysis of the dibenzoyl derivative m.p. 119° in an attempt to obtain the pure carbinol.

(A) Trial hydrolysis on the dibenzoyl derivative of 2-amino-5-chloro-2'-hydroxy-5'-methyl-benzophenone.

0.38 gms of the dibenzoate (m.p. 157°) were suspended in 4.5 cc of boiling alcohol and 0.27 gms of potassium hydroxide (3 equivalents), in 1 cc of water added. The solid went into solution at once and the deep orange-coloured mixture was refluxed for 2 hours. The excess of alcohol was distilled off and the resinous residue recrystallised from acetic acid - m.p. 114°. Mixed m.p. (114°) showed that it was the free base, 2-amino-5-chloro-2'-hydroxy-5'-methyl benzophenone.

(B) Hydrolysis of the dibenzoate (m.p. 119°)

9.5 gms of the dibenzoate m.p. 119° was dissolved in 40cc of alcohol and hydrolysed with 5.5 gm of potassium hydroxide dissolved in 20cc of water as in (A). The mixture darkened appreciably on hydrolysis. A copious amorphous precipitate

separated on dilution. This was dissolved by addition of a little alcohol. The solution was then just acidified, neutralised with ammonia, the excess of ammonia boiled off and the solution extracted with ether. The ether extract was dried and evaporated leaving a brown, non-crystallisable viscous residue which was insoluble in acid or alkali.

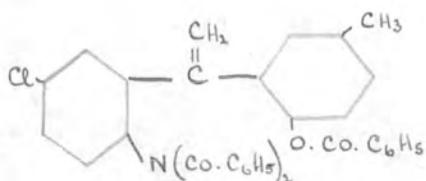
This was rebenzoylated as follows in an attempt to recover the dibenzoyl derivative -

1.28 gms of the viscous residue was dissolved in 3 cc of pyridine and treated with 1.3 gms of benzoyl chloride. The mixture was then heated in a stoppered flask on the water-bath for 3 hours. The product was cooled and decomposed with ice and dilute sulphuric acid, extracted with ether and the extract dried and evaporated. The solid was very sparingly soluble in ether and alcohol and easily soluble in benzene m.p. (225) 228° (0.85g). It was repeatedly recrystallised from ethanol and finally obtained in fine white needles m.p. 235°.

Analysis showed that it was probably the tribenzoate of α - (5-chloro-3-aminophenyl) α - (2'-hydroxy- 5' - methylphenyl) ethylene.

Found C = 75.45, H = 4.67, N = 2.38 (2.60)
Cl = 6.55%

$C_{36}H_{26}NO_4Cl$, requires - C = 75.60
H = 4.59
N = 2.45
Cl = 6.21



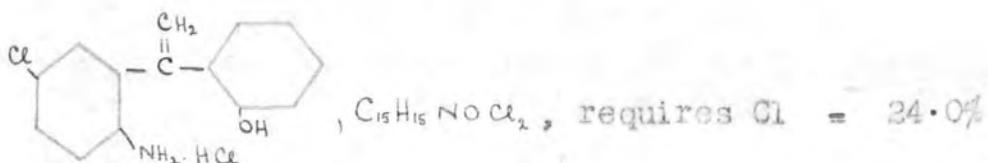
Isolation of the pured - (-3-amino-5-chloro-phenyl) - α - (2'-hydroxy- 5'- methyl-phenyl) ethylene.

(a) Preparation of the hydrochloride.

The viscous product obtained in the Grignard reaction (see p. 63) was dissolved in hot methyl alcohol, a few drops of concentrated hydrochloric acid added, and allowed to cool. Fine pale yellow needles, m.p. 215-220° (d) separated. These were purified by dissolving in hot methyl alcohol, (charcoal) and precipitating by addition of a few drops of concentrated hydrochloric acid.

The product was finally obtained in the form of pale yellow prisms m.p. 223° (d.) Analysis showed that it was the hydrochloride of the required α - (-3-amino-5-chloro-phenyl) - α' - (2-hydroxy-5-methyl phenyl) ethylene.

Found Cl = 23.5%

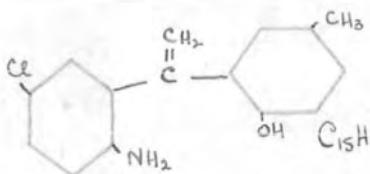


(b) Preparation of the free base.

3.5 gm of the hydrochloride (m.p. 223°) was dissolved in 20 cc. of aqueous methanol and a slight excess of ammonia added. After being warmed on the water-bath for 10 minutes, the solution was cooled and extracted with ether. Concentration of the dried extract and addition of a little ligroin (bp. 40-60°), precipitated some resin followed by crystalline material. The latter was repeatedly crystallised from ether-ligroin, from which

the diaryl ethylene separated in clusters of cream-coloured prismatic needles m.p. 108° (yield ca. 50%)

Found C = 69.05; H = 5.4



$C_{15}H_{14}NOCl$, requires C = 69.3, H = 5.4%

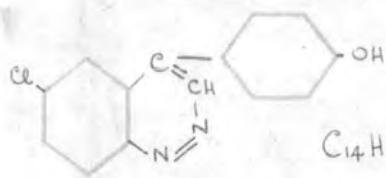
6-chloro-4-(4'-hydroxyphenyl)-cinnoline.

(a) 1.0 gm. of α - (5-chloro-2 amino phenyl)- α - (4'hydroxyphenyl)-ethylene (m.p. 158-9°) was dissolved in 50cc of 2N sulphuric acid, cooled to 5° and treated at once, with stirring, with 0.25 gm of sodium nitrite in 10cc of water. An orange-yellow solid separated along with some darker coloured resinous material. After 1 hour the precipitate was collected and dissolved in alcohol with addition of a little ammonia, and the hot solution acidified with glacial acetic acid. The cinnoline which separated on cooling, crystallised from slightly aqueous acetic acid in lustrous yellow plates with a red reflex, m.p. 257-259° (decomp.) - 0.5 gms.

It was only sparingly soluble in boiling alcohol, separating from this solvent in small yellow shining plates with a red reflex.

(b) 1.0 gm of the α - (5-chloro-2-aminophenyl) - α - (4'-hydroxyphenyl)-ethylene was dissolved in 60cc of 2N hydrochloric acid and diazotised at 5° as in (a). The yield was better in this case (0.67 gms) and there was no formation of resinous material.

Found C = 65.3; H = 3.5



$C_{14}H_9ON_2Cl$, requires C = 65.5, H = 3.5%

The cinnoline was characterised by benzylation as follows -

0.5 gm of the cinnoline, 0.3 gms of benzoyl chloride and 2cc of pyridine were heated on the water bath for 2 hours in a stoppered flask. The residue was cooled and decomposed with ice and dilute sulphuric acid. It was purified by crystallisation from aqueous alcohol (charcoal), being obtained in small pale yellow needles m.p. 156° (0.45 gms).

Found C = 69.8, H = 3.8; N = 7.8; Cl = 9.6%

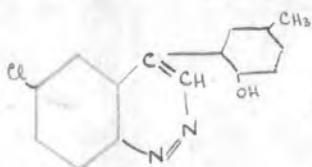
$C_{21}H_{13}O_2N_2Cl$ requires C = 69.9; H = 3.6; N = 7.8; Cl = 9.85%

6-chloro-4-(2'-hydroxy-5'-methyl phenyl)- cinnoline.

A suspension of the hydrochloride of α - (5-chloro-2-aminophenyl)- α - (2'-hydroxy-5'-methyl phenyl)- ethylene, (2.5 gms, m.p. 222° (d)) in 150cc of dilute hydrochloric acid, was cooled to 0° , and a solution of sodium nitrite (0.63 gm) in 10 cc of water added slowly with mechanical stirring. The precipitate was collected after 1 hour and purified exactly as described for 6-chloro-4-(2'-hydroxy-5'-methyl phenyl)-cinnoline.

The pure cinnoline formed small, golden, prismatic needles (0.9 gm) m.p. $260-261^{\circ}$ (decomp.)

Found C = 66.7; H = 4.2; N = 10.2%



$C_{15}H_{11}ON_2Cl$, requires, C = 66.5; H = 4.1 N = 10.35%

The compound was also obtained by the action of hydrochloric acid and sodium nitrite on the crude resinous diaryl-ethylene. Like the analogue already described, this hydroxy-cinnoline was very sparingly soluble in both cold and hot alcohol, benzene and ethyl acetate.

The cinnoline was characterised by the preparation of its benzoate as follows -

0.4 gm of the cinnoline was heated at 100° for 2 hours for 2 hours with 0.25 gm of benzoyl chloride and 1cc of pyridine. Some decomposition occurred and only a poor yield of the benzoate, (30%), was obtained. This was very soluble in methyl alcohol and was obtained in yellow prisms m.p. 140° after repeated recrystallisation from ether-ligroin.

Found C = 69.9; H = 4.0

$C_{22}H_{15}O_2N_2Cl$ requires C = 70.5; H = 4.0

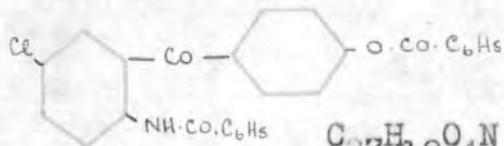
The following benzoyl derivatives were prepared.

(a) Dibenzoyl of 5-chloro-3-amino-4'-hydroxy benzophenone.

1.0 gm of the amino ketone (m.p. 176°) was heated with 1.1 gm of benzoyl chloride (2 equivalents) and 1.2 gm of pyridine at 100° for 3 hours. The product after cooling was decomposed by ice and dilute sulphuric acid. The solid obtained was recrystallised from ethanol in which it was sparingly soluble,

being obtained in fine white needles m.p. 140° (1.0 gm). Repeated recrystallisation raised the m.p. to 143° .

Found C = 70.6, H = 3.84%



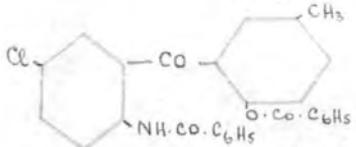
$C_{27}H_{18}O_4N$ Cl requires C = 71.1
H = 3.98%

(b) Dibenzoyl of 5-chloro-2-amino-2'-hydroxy-5'-methylbenzophenone.

1.0 gm of the amino ketone (M.P. 115°), 1.1 gm of benzoyl chloride and 1.2 gm of pyridine were heated as in (a) above.

The sparingly soluble dibenzoyl derivative separated from benzene-alcohol in small stout needles m.p. $156-157^{\circ}$.

Found C = 71.5, H = 4.4



$C_{28}H_{20}O_4NCl$, requires C = 71.5, H = 4.3%

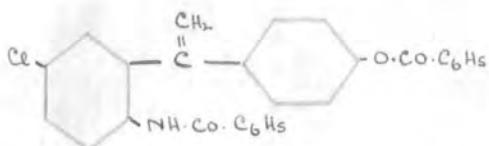
(c) Dibenzoyl derivative of α -(5-chloro-2-aminophenyl)- α -(4'-hydroxyphenyl)ethylene.

1.0 gm of the diaryl ethylene (m.p. $158-159^{\circ}$) was benzoylated with 1.1 gm of benzoyl chloride and 1.1 gm of pyridine as previously.

The dibenzoyl derivative was somewhat sparingly soluble in methanol; it separated from this solvent in clusters of colourless prisms, and from aqueous acetone in very slender,

prismatic needles, m.p. $130\cdot5 - 132^{\circ}$ in each case.

Found C = 73·9, H = 4·3



$C_{28}H_{20}O_3NCl$, requires C = 74·0, H = 4·45%

3-chloro-4'-hydroxybenzophenone.

1 gm of 5-chloro-2-amino- 4'- hydroxy benzophenone was dissolved in 15 cc of absolute alcohol and treated successively with 1 cc of concentrated sulphuric acid and 5 cc of amyl nitrite added at 10° with shaking. After 5 minutes the solution was warmed somewhat, and when the reaction had subsided the solution was refluxed for 5 minutes, diluted with water, and extracted with ether. The extract was washed with water and with 4% sodium hydroxide solution; the latter was then acidified with hydrochloric acid, and the free phenol extracted with ether. The crude product was crystallised several times from aqueous methanol (charcoal), from which the phenol separated in fluffy, somewhat discoloured needles m.p. $169\cdot5-171^{\circ}$. (Zincke and Siebert, loc.cit., describe the compound as colourless needles m.p. 161°); yield, approximately 50%

Found C = 67·2; H = 4·1

Calculated for $C_{13}H_9O_2Cl$, C = 67·1; H = 3·9%

The phenol dissolved easily in warm aqueous sodium carbonate.

Oxidation of the phenol in alkaline potassium permanganate solution gave m. chlorobenzoic acid, m.p. 153-155° after recrystallisation from hot water.

2:5- Dichloro-4'-hydroxybenzophenone.

1.0 gm of 5-chloro-2-amino-4'-hydroxybenzophenone was warmed with 20 cc of concentrated hydrochloric acid, 5 cc. of water being added to obtain complete solution. The solution was diazotised at 5° by the addition of 0.4 gm of sodium nitrite in 20cc. of water, starch iodide being used as an indicator.

The clear solution was added during 10 minutes to a solution of 2 gms of cuprous chloride in 20cc of concentrated hydrochloric acid plus 20cc of water. The resultant suspension was boiled for 5 minutes, filtered cold, and the crude product crystallised from aqueous methanol (charcoal), from which the dichloro-phenol separated in dense, brittle, yellow prisms, m.p. 171-172.5°; yield 80%.

The compound gave a deep brown colouration with ferric chloride in alcohol, and dissolved in aqueous sodium carbonate.

Found: C = 58.6; H = 2.9, Cl = 27.1

$C_{13}H_8O_2Cl_2$ requires C = 58.4; H = 3.0; Cl = 26.6%

Oxidation of 2:5- dichloro-4'-hydroxybenzophenone.

0.4 gm of the phenol was dissolved in 20cc of 0.2N - sodium carbonate, mixed with 75 cc of 2% potassium permanganate, and left overnight at 40-45°. The solution was filtered, concentrated, and acidified, and the precipitate collected.

Some unchanged phenol (ca. 50mg.) was removed by dissolving the crude product in ether and extracting the acid fraction with aqueous sodium bicarbonate. The purified acid, after crystallisation from hot water, formed needles (0.15 gm), m.p. 153-154°, both alone and when mixed with an authentic specimen of 2:5.dichlorobenzoic acid prepared by the method of Grauw.³⁴

The identity of the acid was confirmed by the preparation of the m. nitroanilide (via the acid chloride in pyridine solution); this derivative separated from aqueous methanol in colourless needles m.p. 151-152° both alone and when mixed with an authentic specimen.

Found N = 9.0; Cl = 22.4%

$C_{13}H_8O_3N_2Cl_2$ requires, N = 9.0; Cl = 22.8%

5-chloro-2-amino-4'-methoxybenzophenone.

5.0 gm of the anthroxan, m.p. 239-240°, were added to a solution of 0.6 gm of sodium in 50cc of methanol. The clear orange solution which soon formed was treated with a large excess of methyl iodide (10cc) and heated under reflux. After half an hour, crystalline material separated; this was redissolved by the addition of 25 cc of benzene, and refluxing continued for a further 3 hours. The solution was concentrated, water added, and the whole extracted with ether. The extract was washed with dilute sodium hydroxide solution and with water, dried and evaporated. Crystallisation of the residue from

acetone gave long, brittle, yellow needles (4.5g.) of the chloro-methoxanthrostan, m.p. 143-145°.

Found C = 65.35; H = 4.25

$C_{14}H_{10}O_2NCl$ requires C = 64.7, H = 4.0%

(b) 4.0 gm of the above anthrostan was dissolved in 40cc of glacial acetic acid and reduced with 6 gm of iron filings as described for the methoxyanthrostan, m.p. 98° (q.v.) for $2\frac{1}{2}$ hours.

The product was isolated and crystallised first from aqueous methanol, and then from a small volume of absolute methanol, from which the amino-ketone (3.5g.) separated in dense yellow rhombs or prisms, m.p. 100-101°.

Found: C = 64.1, 64.4; H = 4.9, 4.6.

$C_{14}H_{12}O_2NCl$ requires C = 64.3; H = 4.6%

2:5- Dichloro-2'-hydroxy-5'-methylbenzophenone.

3.0 gms of 5-chloro-2-amino-2'-hydroxy-5'-methylbenzophenone was dissolved in 40cc. of warm glacial acetic acid to which was added 5cc. of concentrated hydrochloric acid.

This was cooled to 5-10°; and the suspension diazotised with a solution of 1 gm of sodium nitrite in 50cc. of water.

This solution, which contained an appreciable flocculent precipitate, was added during 10 minutes to a hot solution of 6 gms of cuprous chloride in 60cc of concentrated hydrochloric acid and 50cc of water; the suspension was then boiled for a few minutes and cooled. The product, crystallised twice from alcohol (charcoal), yielded the dichloro-compound in long yellow

needles (2g.), m.p. 149-150°.

The product was insoluble in aqueous sodium carbonate, and only moderately soluble in hot alcohol.

Found: C = 60.1; H = 3.6; Cl = 24.8.

$C_{14}H_{10}O_2Cl_2$ requires, C = 59.75; H = 3.6; Cl = 25.25%.

A suspension of the dichlorophenol in aqueous sodium carbonate was oxidised by essentially the same procedure as that described for the oxidation of 2:5-dichloro-4'-hydroxybenzophenone.

The resultant 2:5.-dichlorobenzoic acid (0.25 gm from 1.0 g. of the phenol) had m.p. and mixed m.p. 153-154°, and the identification was confirmed by its conversion into the m-nitroanilide, m.p. and mixed m.p. 151-152°.

(When freshly prepared, the m-nitroanilide frequently shows a double melting point, melting at 138-139° to a vitreous mass which on further heating becomes opaque and then melts sharply at 151-152°.)

5-Chloro-2-amino-2'-methoxy-5'-methylbenzophenone.

(a) 2.0 g. of the anthroxan, m.p. 208-209°, was added to a solution of 0.2 g of sodium in 35cc of methanol, and refluxed with 3cc of methyl iodide for 1½ hours.

After dilution with water, the crystalline product obtained on scratching was twice recrystallised from aqueous methanol, the methoxy-anthroxan forming elongated yellow laminae, m.p. 96-98°; more was obtained from the mother-

liquors after removal of unmethylated anthroxan with dilute sodium hydroxide solution; total yield 75%.

Found: C = 65.6; H = 4.1; Cl, = 12.7..
 $C_{15}H_{12}O_2NCl$ requires C = 65.8; H = 13.0%

(b). 1.25 gm of the methoxy anthroxan, m.p. 96-98°, was dissolved in 13.5 cc. of glacial acetic acid and heated on the water-bath with 2g. of iron filings added during 1½ hours; water being added after the reduction had been in progress for ten minutes. After 1½ hours the solution was largely diluted with water and extracted with ether. The filtered extract was washed with sodium carbonate solution then with water, dried, and evaporated.

The residue was crystallised from aqueous methanol, the amino-ketone being obtained in small, dull yellow prisms, m.p. 100-101°, strongly depressed on admixture with the parent anthroxan.

Found: C = 65.5; H = 5.1
 $C_{15}H_{14}O_2NCl$ requires C = 65.3; H = 5.1%

This ketone did not form a semi-carbazone under the ordinary conditions, but yielded an N-acetyl derivative, which separated from aqueous methyl alcohol in cream-coloured, brittle prismatic needles, m.p. 136-137°.

Found, C = 64.7; H = 5.2
 $C_{17}H_{16}O_3NCl$ requires C = 64.2; H = 5.1%

ACTION OF METHYL MAGNESIUM IODIDE ON 3-amino-3:5- DINITRO BENZOPHENONE.

(a) Using 2 equivalents of Grignard reagent.

1.43 gms of the amino-ketone dissolved in 250cc of benzene were added to a Grignard solution made from 0.25 gms of magnesium and 1.5 gms of methyl iodide in 20cc of ether plus 50cc of benzene. The solution turned dark red and was refluxed for 3 hours. It was cooled and decomposed with ice and dilute hydrochloric acid. The benzene layer (which contained a good deal of free iodine), was washed with sodium thiosulphate solution and then with water. On concentration and precipitation with petrol, yellow needles, m.p. 165° were obtained (1.1 gms). These were found to be unchanged 3-amino-3:5- dinitrobenzophenone.

(b) Using 4 equivalents of Grignard reagent.

5.7 gms of the amino-ketone dissolved in 500cc of benzene were added to a solution of methyl magnesium iodide made from 2.1 gms of magnesium and 12.6 gms of methyl iodide in 150cc of ether.

The mixture was worked up as in (a) but the product was a dark-red tar which was insoluble in boiling 30% sulphuric acid. A good deal of free iodine was also liberated.

Benzoylation of 3-amino-3:5- dinitro benzophenone.

5.0 gms. of the amino-ketone were dissolved in 9 cc. of pyridine, and 5 gms of benzoyl chloride added, the mixture being heated at 100° in a stoppered flask for 3 hours. It was then

cooled and decomposed by addition of ice and dilute sulphuric acid. A black oily tar separated and solidified on standing. This was crystallised from methyl alcohol (charcoal). 2.60 gms of unchanged amino-ketone were recovered (m.p. and mixed m.p. 166°) along with 1.5 gms of benzoate m.p. (186) 190°.

Repeated recrystallisation gave the benzoyl derivative in white silky needles, m.p. 198°.

Found, C = 61.14 ; H = 3.14

$C_{20}H_{13}N_3O_6$ requires, C = 61.40; H = 3.35%.

Action of methyl magnesium iodide on 2-benzamido-3:5-dinitrobenzophenone.

1.0 gms of the ketone m.p. 198° in 100cc of benzene, were added to 5 equivalents of methyl magnesium iodide prepared from 0.3 gm of magnesium and 2.0 gm of methyl iodide in 50cc. of ether.

A brown solid separated immediately and the solution was refluxed for three hours. It was then cooled and decomposed with ice and dilute sulphuric acid. It was worked up as usual and yielded only a black tarry solid which could not be crystallised.

Condensation of 2-chloro-3:5- dinitrobenzoic acid with sodium acetoacetate.

The 2-chloro-3:5- dinitrobenzoic acid used in these reactions was prepared by the nitration of o.chlorobenzoic acid according to the method of Ullmann.³⁵

cooled and decomposed by addition of ice and dilute sulphuric acid. A black oily tar separated and solidified on standing. This was crystallised from methyl alcohol (charcoal). 2.60 gms of unchanged amino-ketone were recovered (m.p. and mixed m.p. 166°) along with 1.5 gms of benzoate m.p. (186) 190°.

Repeated recrystallisation gave the benzoyl derivative in white silky needles, m.p. 198°.

Found, C = 61.14 ; H = 3.14

$C_{20}H_{13}N_3O_6$ requires, C = 61.40; H = 3.35%.

Action of methyl magnesium iodide on 2-benzamido-3:5-dinitrobenzophenone.

1.0 gms of the ketone m.p. 198° in 100cc of benzene, were added to 5 equivalents of methyl magnesium iodide prepared from 0.3 gm of magnesium and 2.0 gm of methyl iodide in 50cc. of ether.

A brown solid separated immediately and the solution was refluxed for three hours. It was then cooled and decomposed with ice and dilute sulphuric acid. It was worked up as usual and yielded only a black tarry solid which could not be crystallised.

Condensation of 2-chloro-3:5- dinitrobenzoic acid with sodium acetoacetate.

The 2-chloro-3:5- dinitrobenzoic acid used in these reactions was prepared by the nitration of o.chlorobenzoic acid according to the method of Ullmann.³⁵

It was characterised by the preparation of its anilide which crystallised from methyl alcohol in yellow needles m.p. 214° .

A typical condensation is described -

(a) 1.48 gms of sodium (2 equivalents) were dissolved in 20cc of absolute alcohol and added to a solution of 5gm of ethyl acetoacetate (1.2 equivalents) in 50cc of ether. To this solution was added 7.9 gm of the dinitrochlorobenzoic acid (1 equivalent) dissolved in 150cc of ether. The resulting orange-red solution was refluxed for half an hour, and on cooling a dark red oil separated. The mixture was extracted thrice with water and once with dilute alkali and the combined extracts were just acidified with dilute nitric acid. The yellow oil which separated solidified rapidly and was filtered and dried - 8.2 gms m.p. $134-5^{\circ}$ (75%)

Repeated recrystallisation of this solid from slightly aqueous methanol gave the product in white crystalline nodules. m.p. 144°

Found, C = 46.43; H = 3.64; N = 8.61
 $C_{13}H_{12}N_2O_9$ requires, C = 45.9; H = 3.56; N = 8.23.

Extraction of the acidified mother-liquor with ether yielded 1.8 gms of unchanged dinitrochlorobenzoic acid, identified by the preparation of its anilide, m.p. and m.m.p. 214° .

(b) Several further preparations were carried out using up to four equivalents of sodium acetoacetate, and heating the

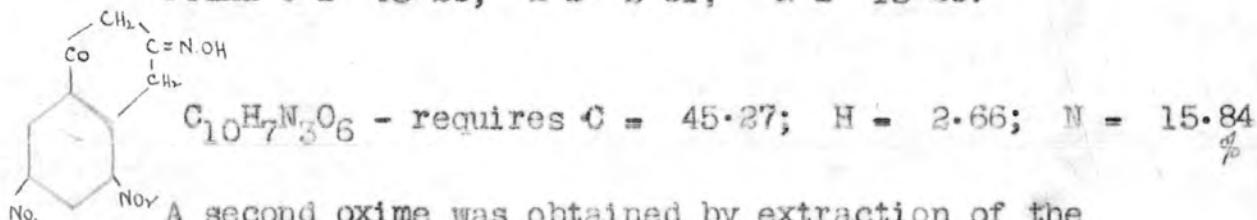
reaction mixture for a longer time, but the yield could not be improved and the product was less pure than that obtained in (a).

Oximes of α - [$\bar{\beta}$ -4 dinitro-6-carboxy phenyl] -ethyl acetoacetate.

To a mixture of 3.0 gms of hydroxylamine hydrochloride and 6.0 gms of crystalline sodium acetate in 100cc. of water was added a solution of 3.0 gms of the ester (m.p. 142°) in 35cc of alcohol. The mixture was then heated at 100° for four hours. The resulting dark-red solution was cooled, diluted with water, and just acidified with dilute hydrochloric acid. The orange-coloured solid which separated was filtered and dried - 0.73 gm., m.p. (190) 204°. This compound was easily soluble in alcohol and sparingly soluble in benzene. Recrystallisation from dilute methyl alcohol yielded bright-yellow needles, m.p. (200) 215°.

The compound was finally obtained pure after five recrystallisations from a benzene-alcohol mixture, in bright yellow needles m.p. 239°.

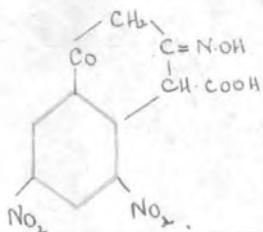
Found C = 45.26; H = 2.81; N = 15.68.



A second oxime was obtained by extraction of the original mother-liquor with ether. Concentration of the ether extract yielded red prismatic crystals - finally obtained as pale-yellow needles, m.p. 230° (d.), after four recrystal-

lisations from a benzene-alcohol mixture.

Found, C = 42.64; H = 2.39.



$C_{11}H_7N_3O_8$ requires C = 42.71; H = 2.28%.

The mixed melting point of the two oximes was c. 220°.

This second oxime was sparingly soluble in benzene yielding a pale-yellow solution but dissolved easily in acetone or alcohol to give a deep red solution.

Condensation of the methyl ester of 2-chloro-3:5-dinitrobenzoic acid with sodium acetoacetate.

(a) Preparation of the methyl ester.

19 gms. of 2-chloro-3:5-dinitrobenzoic acid were dissolved in the minimum amount of absolute methyl alcohol. The solution was cooled in ice and saturated with hydrochloric acid gas. Solid began to separate after about 1 hour, and the solution was then refluxed for a short while. Thick, white prisms of the ester separated on standing overnight m.p. 89-90° (19.3 gms.).

(b) 10 gms of the above ester were dissolved in a mixture of ether (200cc) and methyl alcohol (80cc), and added to a cold solution of sodium ethyl acetoacetate, prepared by refluxing 12 gms of acetoacetic ester (2 equivalents), and 1.9 gm of sodium (2 equivalents) in ether (120cc) + methyl alcohol (30cc).

The dark-red solution was left at room-temperature for a fortnight. It was then extracted with three 100cc-portions of water, and the combined aqueous extracts acidified with dilute nitric acid. The orange-coloured viscous oil which separated was extracted with ether, removal of the ether leaving 16.8 gms of a deep-red viscous oil which could not be crystallised.

Attempted hydrolysis of this oil with alcoholic sulphuric acid was unsuccessful. The product was a thick, viscous, dark-brown oil which smelt strongly of acetic acid.

Preparation of 2:4- dinitrophenyl- acetoacetic ester.

The methods used for the preparation and hydrolysis of 2:4- dinitrophenyl-acetoacetic ester were essentially those of Borsche.²⁸

(a) Preparation.

4.6 gms of sodium (2 equivalents) were added to a solution of 26 gms of acetoacetic ester (2 equivalents) in 200cc of ether and refluxed until all the sodium had dissolved.

A solution of 20 gms of 3:4-dinitro chlorobenzene (1 equivalent) in 100cc of ether was added to the above solution and the resulting deep-red mixture refluxed for 1 hour. The solution was then cooled and extracted thrice with water then once with dilute caustic soda. The extracts were acidified with excess of dilute nitric acid; the yellow-brown solid which separated was crystallised from alcohol (charcoal), yielding 15 gms. of 3:4-dinitrophenyl acetoacetic ester as bright-yellow needles m.p. 94-95°.

Extraction of the acid solution with ether only yielded a non-crystallisable oil.

Hydrolysis of 2:4-dinitrophenylacetooacetic ester.

6 gms of the ester, (m.p. 94-95°), were dissolved in 36 cc. of concentrated sulphuric and 12 cc. of water added at once with stirring and without cooling. The clear solution darkened, the temperature rose to about 100° and a vigorous evolution of carbon dioxide took place. The temperature was kept at 100° and the solution stirred well until all carbon-dioxide was evolved - the solution was then cooled and poured into 200cc of cold water. The pale-brown oil which separated soon solidified and was filtered and dried - 4.3 gms m.p. 74° (95%).

Recrystallisation from dilute alcohol, (charcoal), yielded pure 2:4-dinitro-phenyl acetone in very pale-yellow

needles m.p. 75°.

Preparation of 2:4- dinitrophenyl acetone- oxime.

2.0 gm of the ketone were dissolved in 60cc of alcohol and treated with a solution of 2.0 gm of hydroxylamine hydrochloride and 6 gm of crystalline sodium acetate in 50cc of water.

The solution was refluxed for 2½ hours, cooled, diluted and extracted with ether.

After removal of the ether the residue was crystallised from alcohol (charcoal) - 2.1 gms m.p. 136-7°. Recrystallisation from dilute alcohol gave the oxime as long white needles, m.p. 138°.

Borsche³⁶ gives m.p. 138°.

Attempted reduction of 2:4- dinitrophenyl acetone.

0.5 gm of the ketone was dissolved in 10cc of alcohol and 10cc of concentrated hydrochloric acid were added. The solution was diluted with water and extracted with ether, but evaporation of the ether only left a dark-red non-crystallisable tar.

Reduction of the oxime of 2:4- dinitrophenyl acetone.

The oxime was recovered unchanged after leaving with an excess of sodium bisulphite in aqueous-alcoholic solution at room-temperature for 24 hours.

Reduction with ammonium sulphide yielded only a viscous

non-crystalline product.

The reduction was finally carried out with sodium hydrosulphide as follows -

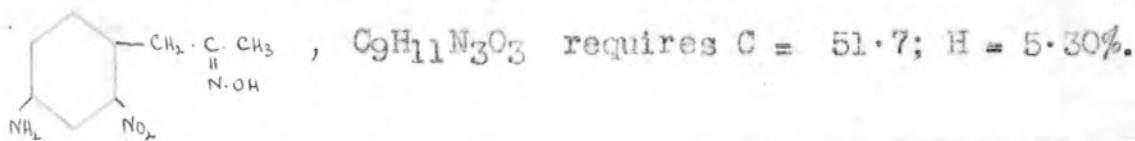
2.0 gms of the oxime, m.p. 138° , were dissolved in 100cc of warm alcohol and precipitated in a finely divided condition by cooling rapidly and added 150cc of water. To this was added a solution of sodium hydrosulphide in 40cc of water, freshly prepared from 0.7 gm of caustic soda (2 equivalents).

The mixture was shaken well for one hour at room-temperature, but very little solid went into solution. Solution was effected by heating on the water-bath for a short while, the resulting deep-red solution being left for 2 days.

After this time, large red-brown prismatic needles had separated from the solution and were filtered off - 0.57 gm, m.p. (185) 198° .

Five recrystallisations from methanol gave the pure compound in yellow needles, m.p. 205° .

Found C = 52.00; H = 5.13.



The mono-amine was easily soluble in dilute mineral acids and its diazo-solution gave a deep-red dye with alkaline β -naphthol solution.

Attempted preparation of the phenyl hydrazine from ortho-amino benzyl alcohol.

7.5 gms of o.amino benzyl alcohol were dissolved in 16 cc of concentrated hydrochloric acid, cooled to 0° and 20 gms. of ice added. The amine was diazotised by addition of 0.42 gms of sodium nitrite in 10 cc. of water.

The cold diazo-solution was then poured into 90cc. of a cold solution of sodium sulphite, freshly prepared from 13.5 gms of caustic soda. A bright orange-coloured solid separated rapidly. The mixture was warmed to 60° for three hours and then acidified with 40cc of concentrated hydrochloric acid - it was then cooled in ice and filtered.

9.5 gms of dry solid were obtained, along with a little resinous material. The solid was sparingly soluble in hot water, being reprecipitated in amorphous flakes by the addition of concentrated hydrochloric acid. It was easily soluble in dilute alkali, reduced Fehling's solution on warming, and gave a bulky yellow precipitate with chloroplatinic acid in hydrochloric acid solution. It was practically completely insoluble in all the common organic solvents, and could not be crystallised.

An attempt to condense it with acetophenone in aqueous-alcoholic sodium acetate solution failed - the product was a dark brown viscous oil.

Preparation of the benzoate of ortho-nitro-benzyl alcohol.

Ortho-nitro benzyl benzoate was prepared by two methods -

- (a) Direct benzylation in pyridine solution.
- (b) By refluxing 20 gms of o.nitrobenzyl chloride with 35 gms. of sodium benzoate in concentrated aqueous solution.

The product crystallised from dilute methyl alcohol in white plates, m.p. 101° .

Reduction of ortho-nitro benzyl benzoate²³.

13.2 gms of ortho-nitrobenzyl benzoate were dissolved in 250 cc of warm alcohol, 50cc of concentrated hydrochloric acid added and the mixture cooled to 0° . Excess of zinc dust was then added slowly in small portions with shaking, the reaction being complete when a drop of the reaction mixture dissolved in dilute hydrochloric acid to give a clear solution.

The mixture was filtered, diluted, excess of sodium acetate added, and the whole extracted twice with ether. Evaporation of the ether left a pale-brown oil which was dissolved in dilute hydrochloric acid, the amine hydrochloride being precipitated by the addition of concentrated hydrochloric acid. (m.p. 143°).

Attempted preparation of the phenyl hydrazine from ortho-amino benzyl benzoate.

8.5 gms of the hydrochloride m.p. 143° were dissolved in 100 cc of water, 8cc. of concentrated hydrochloric acid added, and the solution cooled rapidly to 0° . 4 gms of ice were then added and the solution diazotised by the addition of

3.4 gms of sodium nitrite dissolved in a little water. Reduction of this solution as previously with sodium sulphite yielded a buff-coloured precipitate which proved to be benzoic acid (m.p. and m.m.p. 120° after recrystallisation from hot water.)

Reaction between hydrazine, formaldehyde and 2-chloro-3:5-dinitro benzoic acid.

13.0 gms of hydrazine sulphate (1/10 mol.) and 21.2 gms of anhydrous sodium carbonate (1/5 mol.) were dissolved together in 100cc of water and added to a solution of 24.65 gms of 2-chloro-3:5- dinitrobenzoic acid (1/5 mol.) and 10cc of 40% formaldehyde in 200 cc of alcohol.

The resulting deep-red solution was refluxed for three hours and deposited deep-red needles of a sodium salt on cooling.

The suspension was decomposed by the addition of dilute hydrochloric acid and the resulting yellow solid filtered off. (18.7 gms.)

It was insoluble in all the common organic solvents but crystallised from hot water in long yellow needles which decomposed without melting at about 200° .

Analysis showed that the product was 5:7- dinitro indazolone.

Found, C = 37.13; H = 1.7

$C_7H_4N_4O_5$ requires, C = 37.50; H = 1.8%.

Attempted reduction of ortho-nitrophenyl- acetaldoxime.

The oxime was prepared by the method of Weermann²⁵ (loc.cit.)

0.17 gms of caustic soda (2 equivalents), were dissolved in 10cc of water, the solution saturated with hydrogen sulphide, and the excess of gas aspirated off.

0.44 gms of ortho-nitrophenyl acetaldoxime were dissolved in 10cc of alcohol and added to this solution. The mixture was warmed to 50° for a short while and the solid rapidly went into solution. On cooling the precipitated sulphur was filtered off and the filtrate diluted with water and extracted with ether.

Evaporation of the ether yielded a black semi-solid residue. Attempts were made to purify this by crystallisation from a mixture of benzene and ligroin, but no crystalline product could be obtained.

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369. *Decomposition Reactions of the Aromatic Diazo-compounds.*
 Part VIII. *The Diazocyanides.*

By OLIVER STEPHENSON and WILLIAM A. WATERS.

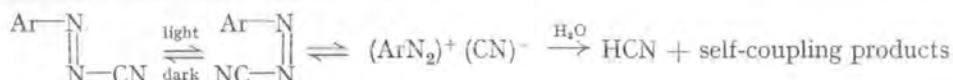
A study of diazocyanides derived from halogenated aromatic amines has revealed the following facts.

1. *anti*-Diazocyanides, though thermally stable, may be converted photochemically into the isomeric, reactive, *syn*-diazocyanides.

2. *syn*-Diazocyanides exist, in alcoholic solution, in tautomeric equilibrium with diazonium cyanides, for, on treatment with silver nitrate, they rapidly precipitate silver cyanide.

3. Neutral solutions of *syn*-diazocyanides easily give self-coupling products, consequent upon a hydrolysis in which free hydrogen cyanide is liberated.

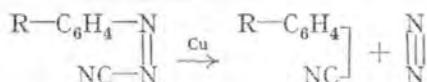
4. Solutions of *syn*-diazocyanides in non-ionising solvents isomerise to *anti*-diazocyanides even in the absence of light :



5. Copper appears to be the only metal which catalyses the decomposition of the *syn*-diazocyanides.

6. In non-ionising solvents, such as carbon tetrachloride, benzene, and ether, *syn*-diazocyanides yield free radicals upon warming with copper powder, the respective final products being $\text{C}_6\text{H}_4\text{RCl}$, $\text{C}_6\text{H}_4\text{R}\cdot\text{Ph}$, and $\text{C}_6\text{H}_5\text{R}$ plus acetaldehyde, together with, in each case, free hydrogen cyanide. Only in carbon tetrachloride solution does the copper appear to be attacked. The main reaction product is always a black tar, which is not a polyazo-compound.

7. It is concluded that Hantzsch's theory that the *syn*-diazo-compounds decompose to give vicinal radicals which promptly unite,

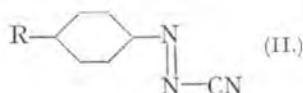
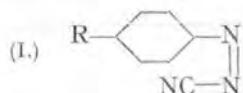


does not accord with experimental fact.

It appears that the radicals formed by the decomposition of the *syn*-diazo-compounds react with neighbouring solvent molecules, and therefore must have an independent free existence.

DIAZOCYANIDES can easily be prepared in a state of purity from halogenated aromatic amines, and their reactions in non-aqueous solvents have been examined in order to discover to what extent the theories postulated for the mechanisms of decompositions of diazoacetates, diazohydroxides, and diazonium chlorides can be generalised.

Hantzsch and Schultze (*Ber.*, 1895, 28, 666), who first studied the diazocyanides, showed that they existed in two isomeric forms of greatly different stability, and pointed out that both isomers were azo-compounds, $\text{Ar}\cdot\text{N}:\text{N}\cdot\text{CN}$, and not diazonium salts, since (a) they were coloured, and (b) they dissolved readily in non-ionising solvents such as benzene. The labile, reactive, form was given the *syn*-diazo-structure (I), and the stable form the *anti*-diazo-structure (II) in accordance with the generally observed fact that of two geometrical isomers the more stable has the *trans*-structure.

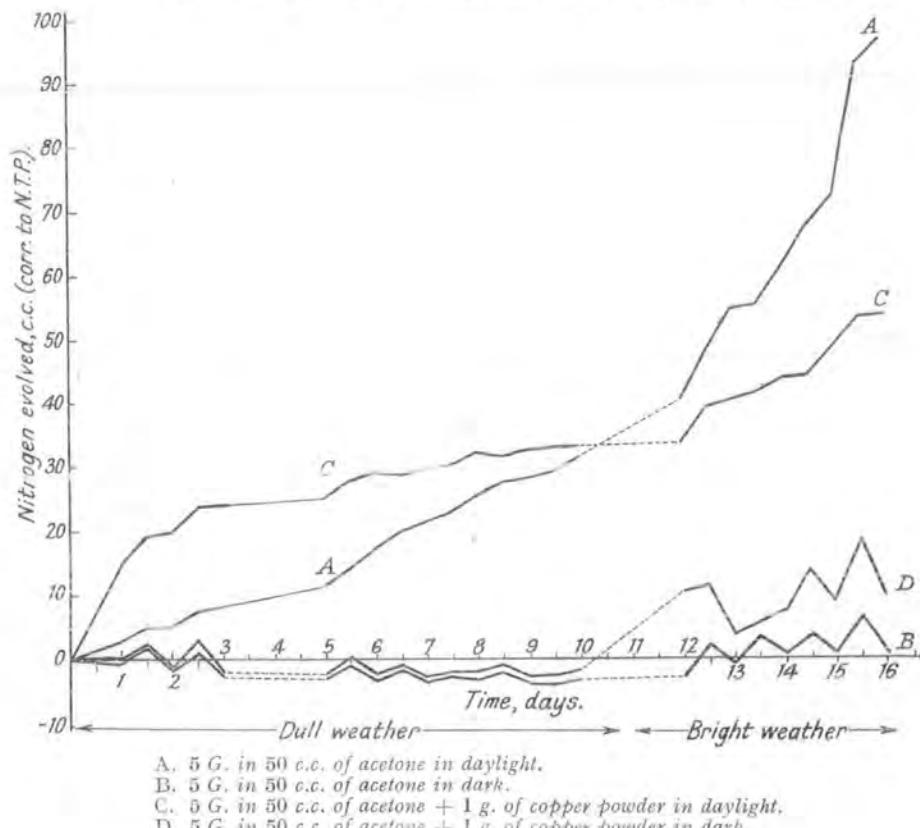


Moreover, these authors discovered that alcoholic solutions of the labile forms of the diazocyanides could be decomposed catalytically by adding copper powder, nitrogen

photochemical decomposition of the *anti*-diazocyanides in both ethyl alcohol and acetone are identical with those obtained by the thermal decompositions of the corresponding *syn*-diazocyanides.

The figure also indicates the effect of adding copper powder as a catalyst. Metallic copper undoubtedly influences the course of the decomposition of the *syn*-diazocyanides, for the final decomposition products are not the same in each case, but, as will be seen, copper has no obvious direct action upon the *anti*-diazocyanides. Curves *B* and *D* were given by solutions immersed in a bath of black dye, through which a little light evidently penetrated on bright days. They seem to indicate that in the dark a small loss of gas occurs, possibly on account of oxidation of the solution.

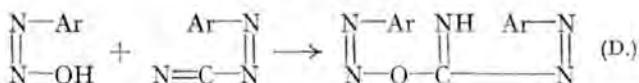
Photochemical Decomposition of p-Chlorobenzene-anti-diazocyanide in Acetone.



Under non-ionising solvents, such as benzene or carbon tetrachloride, evolution of nitrogen does not occur, for the *anti*-diazocyanides can be recovered quantitatively from their solutions, even after exposure to light, merely by evaporation of the solvent.

The syn-Diazocyanides and Diazonium Cyanides.—The reverse change, from the labile *syn*- to the stable *anti*-diazocyanide, does not seem to be a photochemical reaction. With a number of new diazocyanides we have found, in exact accordance with the observations of Le Fèvre and Vine, that the *dry* solids do not isomerise in the dark, but that all solutions rapidly undergo changes. However, the isomerisation of a *syn*- to an *anti*-diazocyanide is quantitative only in non-ionising solvents such as benzene and carbon tetrachloride. Even in ether there is some side reaction, and in alcohol and acetone *syn*-diazocyanides rapidly darken and gradually evolve nitrogen to the extent of 20–40% of the total quantity of the diazo-group present. The residual product from these solvents is a tar, together with free hydrogen cyanide and very little, if any, *anti*-diazocyanide.

Now, Heller and Meyer (*Ber.*, 1919, **52**, 2287) reported that attempts to prepare a $\text{NPh}:\text{N}\cdot\text{C:NH}$ *syn*-diazocyanide in a slightly alkaline solution afforded instead a red alkali-metal salt of a compound of type (VIII), solutions of which, on keeping, give off nitrogen and leave tarry products smelling of *iso*-cyanide. They considered (VIII) to be derived from the diazonium cyanide, for it could easily be obtained by a partial hydrolysis (C), followed by a coupling reaction :



or, in brief, $2\text{Ar}\cdot\text{N}_2\cdot\text{CN} + \text{H}_2\text{O} = \text{Ar}\cdot\text{N}_2\cdot\text{O}\cdot\text{C}(\text{NH})\cdot\text{N}_2\cdot\text{Ar} + \text{HCN}$; whence, 2 mols. of *syn*-diazocyanide should yield 1 mol. of free hydrogen cyanide.

The great facility with which the cyano-group of the *syn*-diazocyanides will condense with compounds of the types ROH and R'NH has also been demonstrated by Hantzsch and Schultze (*Ber.*, 1895, **28**, 2078), who found that, in the presence of a trace of alkali, alcoholic solutions of *syn*-diazocyanides reacted as follows :



One may conclude, therefore, that the moderately rapid decomposition which occurs in neutral solutions of *syn*-diazocyanides in alcohol is due to hydrolysis and self-coupling, and one can therefore understand why Hantzsch and his colleagues found that the *syn*-diazocyanides had to be prepared by adding potassium cyanide solution to a cold acid solution of a diazonium salt, and not by adding a diazonium salt solution to an excess of an alkaline solution of potassium cyanide.

Since the neutral solutions of the *syn*-diazocyanides in ionising solvents can soon change in this way, their ultimate thermal decomposition reactions, in which nitrogen is evolved, are not necessarily decomposition reactions of the *syn*-diazocyanides themselves.

In water dilute acid, alcohol, or acetone, the ultimate decomposition of a *syn*-diazo-cyanide produced some nitrogen, hydrogen cyanide, a little *isocyanide*, and much tar, and is a complex decomposition in which the solvent can play an integral part. From solutions of *syn*-diazocyanides in ethyl alcohol about 40% of the diazo-groups present may be evolved as nitrogen, acetaldehyde is an invariable reaction product, and, in part, the diazocyanide group is replaced by hydrogen. If copper powder is added, the initial rate of evolution of nitrogen is accelerated and the total percentage of nitrogen evolved is somewhat greater, though only a little of the aromatic nitrile is formed.

Solutions of *syn*-diazocyanides in acetone evolve about 20% of their diazo-groups in the form of nitrogen, but give scarcely any simple products, other than hydrogen cyanide. Again, the decomposition in acetone is catalysed by copper powder. In this case over 50% of the diazo-groups may be eliminated as nitrogen, free hydrogen cyanide is not formed, but some aromatic nitrile is formed instead. The decomposition of the *syn*-diazocyanides in alcohol or acetone is not catalysed by metals other than copper (compare the diazonium chlorides; *J.*, 1937, 2007; this vol., p. 864).

Non-polar Decompositions of syn-Diazocyanides.—Solutions of *syn*-diazocyanides in the non-ionising solvents carbon tetrachloride, benzene, cyclohexane, and ether do not lose nitrogen on warming, but give the stable *anti*-diazocyanides. However, a decomposition can be initiated in these solvents also by adding copper powder, and 30—50% of the diazo-groups present may be eliminated as nitrogen, leaving complex tarry residues from which simple reaction products, other than some *anti*-diazocyanide, can be isolated only in small yields. This copper-catalysed reaction has been studied by using the purified *syn*-diazocyanides obtained from *o*- and *p*-chloroanilines, *p*-bromoaniline, 4- and 5-chloro-*o*-toluidine, and the simpler reaction products have been isolated by steam-distillation and characterised.

When carbon tetrachloride was used, the aryl chloride $\text{C}_6\text{H}_4\text{R}\cdot\text{Cl}$ was formed from the cyanide $\text{C}_6\text{H}_4\text{R}\cdot\text{N}_2\cdot\text{CN}$ in 10—20% yield. Hydrogen cyanide was also formed, and aqueous extracts of the reaction products regularly contained both cupric and chloride ions. No appreciable quantities of the nitrile could be isolated, so one must conclude that the

fission of the aromatic diazo-compounds, and makes it quite evident that this decomposition is characteristic of the covalent diazo-compounds and not of the diazonium kation.

Moreover, it is also evident that the two radicals which result from the scission of the azo-group as nitrogen gas do not unite at once, even with the *syn*-diazo-compounds, but react in a complex manner with vicinal solvent molecules. Hantzsch's mechanism for the decomposition of the aromatic diazo-compounds (A; p. 1797) has therefore no foundation in experimental fact. In contrast, one can point out that the Gattermann reaction, $C_6H_4R\cdot N_2 \xrightarrow{Cu} C_6H_4R\cdot CN + N_2$, is favoured only when ionisation is possible, and the view that this reaction may be a reaction of a diazonium salt (this vol., p. 864) thus receives some further slight support.

EXPERIMENTAL.

syn-Diazocyanides were prepared from (a) *p*-chloroaniline, (b) *o*-chloroaniline, (c) *p*-bromoaniline, (d) 4-chloro-*o*-toluidine, and (e) 5-chloro-*o*-toluidine by the procedure of Le Fèvre and Vine (*loc. cit.*). Damp reaction products were rapidly purified by dissolving them in ice-cold ether-light petroleum, shaking the solution for 10 mins. with sodium sulphate, filtering, and then blowing off the ether with a current of dry air.

The following diazocyanides have not been described previously: *o*-Chlorobenzene-*syn*-diazocyanide, m. p. 49°, orange (Found : Cl, 21.1. $C_7H_4N_2Cl$ requires Cl, 21.45%); *o*-chlorobenzene-anti-diazocyanide, m. p. 78°, bright red (Found : Cl, 21.4%); 4-chloro-*o*-toluene-*syn*-diazocyanide, m. p. 49°, orange-yellow (Found : Cl, 19.6. $C_8H_6N_2Cl$ requires Cl, 19.7%); 4-chloro-*o*-toluene-anti-diazocyanide, m. p. 68°, red (Found : Cl, 19.6%); 5-chloro-*o*-toluene-*syn*-diazocyanide, m. p. 60°, orange (Found : Cl, 19.7%); 5-chloro-*o*-toluene-anti-diazocyanide, m. p. 75°, red (Found : Cl, 19.7%).

Dry specimens of the *syn*-diazocyanides could be kept for some days in the dark, but damp specimens gave off hydrogen cyanide on keeping, and formed tarry products, smelling of *iso*-cyanide and containing only a little *anti*-diazocyanide.

Freshly prepared alcoholic solutions of the *syn*-diazocyanides of the above five bases reacted immediately with alcoholic silver nitrate, precipitating silver cyanide and leaving practically colourless diazonium nitrate solutions which would couple with alkaline β -naphthol. After a short time the alcoholic solutions turned reddish-brown and then would not couple. Acidified solutions, however, did not change colour on keeping. The data in Table I were obtained by treating solutions of 5-chloro-*o*-toluene-*syn*-diazocyanide with silver nitrate after various times, and collecting and weighing the silver cyanide formed.

TABLE I.

Sample 1.		Sample 2.	
Dissolved in neutral EtOH (0.0189M).	Dissolved in neutral EtOH (0.0147M).	Dissolved in EtOH made n/2 with HNO_3 (0.0148M).	
Time, mins.	% of CN reacting.	Time, mins.	% of CN reacting.
1.25	68.2	3.7	78.3
4.5	64.3	10	70.0
8.0	58.1	24	65.3
11.5	55.4	41	63.5
22.0	50.1	60	65.2
40	47.3	145	64.6
82	48.4	285	59.9 γ
187	47.3 γ	3 days	58.7 γ
			3 days
			75.5 β

In the above calculations the diazocyanide was assumed to be 100% pure, but evidently the purity of Sample 2 was 93.5% and that of Sample 1 still less. The reactions with Sample 2 were carried out in a darkened room, except for α which had been exposed to sunlight for $\frac{1}{2}$ hour, and for β which had been exposed to light for 2 days. The estimations γ were carried out by adding acidified silver nitrate. With other *syn*-diazocyanides figures ranging from 98% to 77% of the theoretical CN content were obtained by dissolving dry specimens in alcohol and adding silver nitrate as soon as all the solid had dissolved.

Alcoholic solutions of all the *anti*-diazocyanides gave no immediate precipitates when treated with alcoholic silver nitrate, but on exposure to light silver cyanide was gradually formed and the solution became paler. Eventually, reduction of the white silver cyanide precipitate occurred.

The effect of prolonged exposure to light of solutions of the *anti*-diazocyanides has already

filings were used there was a slight evolution of nitrogen, and a trace of 4-chlorodiphenyl was isolated from (a).

Decompositions in Dry Ether.—These were not easy to control for, although there was some evolution of nitrogen when copper was added, even after standing for some days the solutions tended to decompose violently upon evaporation to dryness. They gave residues smelling strongly of isocyanide. The ethereal distillates invariably contained acetaldehyde (identified as its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 164°) and also free hydrogen cyanide. From (b) (17 g. in 250 c.c.) 6% of chlorobenzene and 3% of *o*-chlorobenzonitrile were obtained; (c) (22 g. in 200 c.c.) gave 6% of bromobenzene, identified by nitration, and also 3% of nitrile; (d) (28 g. in 250 c.c.) gave 8% of *p*-chlorotoluene, identified by oxidation to *p*-chlorobenzoic acid, and 4% of nitrile; (e) (21 g. in 220 c.c.) gave 10% of *m*-chlorotoluene (identified as its trinitro-derivative, m. p. 149°) and 2% of nitrile.

From a decomposition of (a) in cyclohexane a little nitrile was obtained.

The tars obtained from decompositions carried out in alcohol or acetone in the absence of copper were dark brown, pitch-like materials which easily softened on warming. Those obtained from all decompositions carried out with the use of copper were hard, black, porous, coke-like materials, which could easily be dried and powdered. They did not tend to soften on warming, and dissolved only with difficulty in warm concentrated sulphuric acid. It was not possible to separate the organic matter from the finely divided copper particles. Table II gives, for the actual experiments detailed above, the percentage of the diazo-group evolved as nitrogen, the yield of non-volatile tar, and also its nitrogen content, the last two figures being calculated for organic copper-free material.

TABLE II.

<i>syn</i> -Diazo-compound.	Solvent and catalyst.	% of diazo-group evolved as N ₂ .	% of tar formed.	% of N in tar.
b	EtOH, no Cu	36	60	—
e	EtOH, no Cu	39	41	—
b	EtOH + Cu	51	55	14.3
e	EtOH + Cu	56	53	13.9
c	Acetone, no Cu	25	73	—
e	Acetone, no Cu	21	ca. 95	—
b	Acetone + Cu	46	46	12.7
d	Acetone + Cu	67	58	10.9
a	C ₆ H ₁₂ + Cu	—	71	17.5
a	Ether + Cu	—	51	12.7
c	Ether + Cu	—	60	12.4
b	Ether + Cu	40	—	16.9
d	Ether + Cu	67	66	15.3
e	Ether + Cu	—	46	14.0
b	Benzene + Cu	33	63	13.8
b	Benzene + Cu	36	64	13.0
c	Benzene + Cu	33	63	10.5
e	Benzene + Cu	—	76	10.1
b	CCl ₄ + Cu	57	72	10.2
b	CCl ₄ + Cu	55	71	10.4
d	CCl ₄ + Cu	45	80	7.5
e	CCl ₄ + Cu	—	45	10.2

A tar containing one nitrogen atom per aryl group should give 9—11% of nitrogen and one containing two such atoms per aryl group should afford 16—20%.

The tars all evolved some ammonia on boiling with sodium hydroxide solution. Reduction of several was carried out by means of both stannous chloride and hydrochloric acid in alcoholic solution and also of zinc and hydrochloric acid in glacial acetic acid solution. The reduction products contained small quantities of the monoamines (a)—(e) originally used, but no sign of diamines.

The authors thank Mr. K. H. Saunders for his helpful suggestions, and the Dyestuffs Research Committee of Imperial Chemical Industries, Ltd., for gifts of chemicals.

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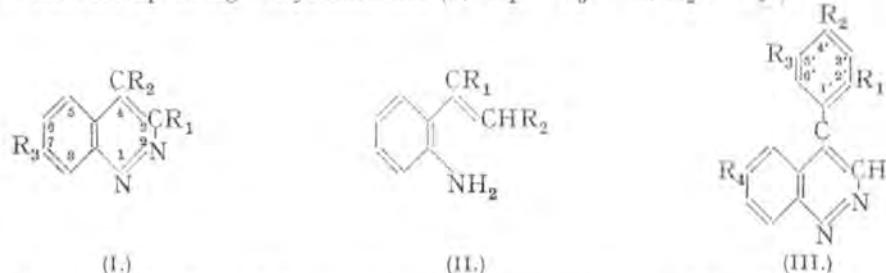
[Received, August 9th, 1939.]

58. Cinnolines. Part I. Some New Examples.

By JAMES C. E. SIMPSON and OLIVER STEPHENSON.

The syntheses are described of 6-bromo-4-phenyl-, 6-chloro-4-(4'-hydroxyphenyl)-, and 6-chloro-4-(2'-hydroxy-5'-methylphenyl)-cinnoline by the Stoecker reaction [cyclisation of diazotised α -(2-amino-phenyl)- α -arylethylenes]. During the course of the work a number of new benzophenone derivatives have been prepared.

THE chemistry of cinnoline compounds has received scant attention since the discovery, nearly sixty years ago, of the first derivatives, 4-hydroxycinnoline-3-carboxylic acid (I; $R_1 = CO_2H$, $R_2 = OH$, $R_3 = H$) (von Richter, *Ber.*, 1883, **16**, 677) and 4-methylcinnoline-7-carboxylic acid (I; $R_1 = H$, $R_2 = Me$, $R_3 = CO_2H$) (Widman, *Ber.*, 1884, **17**, 722). Cinnoline itself (I; $R_1 = R_2 = R_3 = H$) was prepared from the former acid some years later by Busch and Rast (*Ber.*, 1897, **30**, 521). A discouraging factor in this field has doubtless been the lack of a convenient method of preparation, in contrast to the isomeric phthalazines, which are readily accessible and have in consequence been widely studied. A somewhat easier route to the cinnoline ring system than the method of von Richter, which involved cyclisation of diazotised *o*-aminophenylpropionic acid, was explored by Stoermer and Fincke (*Ber.*, 1909, **42**, 3115). Employing the reaction originally discovered by Widman (*loc. cit.*), namely, the cyclisation of diazotised *o*-aminoarylethylenes, these authors showed that α -(*o*-aminophenyl)- α -arylethylenes (II; $R_1 = aryl$, $R_2 = H$), on treatment with nitrous acid in presence of hydrochloric acid, passed smoothly and spontaneously into the corresponding 4-arylcinnolines (I; $R_1 = R_3 = H$, $R_2 = aryl$).



4-Phenyl-, 4-phenyl-3-methyl-, and 4-*p*-tolyl-cinnoline were synthesised by this means, the requisite diarylethylenes being obtained from the appropriate diaryl ketones and a Grignard reagent, followed by dehydration of the resulting carbinols. Later, Stoermer and Gaus (*Ber.*, 1912, **45**, 3104) prepared 4-*p*-anisyl- and 4-*p*-hydroxyphenyl-cinnoline, the latter by demethylation of the former. Stoermer and Fincke observed also that the substitution of bromine for hydrogen on the β -ethylenic carbon atom of (II) tended to inhibit the cyclisation of the diazonium salt, (II; $R_1 = \text{Ph}$, $R_2 = \text{Br}$) giving only 4-phenyl-cinnoline in poor yield; but (apart from Widman's acid) the influence on ring closure of strongly polar substituents in either of the two aryl nuclei has not been studied.

In this paper we describe the syntheses of *6-bromo-4-phenyl-4-cinnoline* (III; $R_1 = R_2 = R_3 = H$, $R_4 = Br$), *6-chloro-4-(4'-hydroxyphenyl)cinnoline* (III; $R_1 = R_3 = H$, $R_2 = OH$, $R_4 = Cl$), and *6-chloro-4-(2'-hydroxy-5'-methylphenyl)cinnoline* (III; $R_1 = OH$, $R_2 = H$, $R_3 = Me$, $R_4 = Cl$) by the Stoermer reaction. The yields, based on the diarylethylenes, were in all cases reasonably high, so the

transformation of the ketone into 2 : 5-dichloro-2'-hydroxy-5'-methylbenzophenone, followed by oxidation of the latter to 2 : 5-dichlorobenzoic acid. Incidentally, the preparation of these dichloro-ketones contradicts the experience of Zincke and Siebert, who were unable to prepare any derivatives of the diazotised amino-ketones except 3-chloro-4'-hydroxybenzophenone (the recorded m. p. of which is considerably lower than that found by us).

In an attempt to establish the position of the phenolic group in each of the amino-ketones, we prepared the methyl ethers of the two anthroxans [(VI; $R_1 = R_3 = H$, $R_2 = OMe$) and (VI; $R_1 = OMe$, $R_2 = H$, $R_3 = Me$)], and reduced these to the corresponding *amino-ketones*. On the assumption that the positions assigned to the phenolic groups in the anthroxans are correct it was anticipated that oxidation of the methoxy-amino-ketones would furnish anisic acid and 4-methoxyisophthalic acid respectively. However, the ketone from (VI; $R_1 = OMe$, $R_2 = H$, $R_3 = Me$) was incompletely oxidised by alkaline permanganate, and no crystalline product could be obtained when the oxidation was continued in acid solution. In view of this result, the ketone from (VI; $R_1 = R_3 = H$, $R_2 = OMe$) was diazotised with a view to obtaining a phenol more amenable to oxidation, but, in spite of several trials, almost the whole of the product was an alkali-insoluble resin, and only a trace of crystalline phenol could be obtained.

It is our intention to develop this preliminary work when an opportunity occurs.

EXPERIMENTAL.

(Melting points are uncorrected.)

Phenyl-(5-bromo-2-aminophenyl)methylcarbinol (IV).—An ethereal solution of methylmagnesium iodide prepared from 2 g. of magnesium and 12 g. of methyl iodide was treated with a similar solution of 5-bromo-2-aminobenzophenone (5 g., m. p. 110°, prepared by the method of Angel, *loc. cit.*, who gives m. p. 111°), added slowly with cooling. The resultant deep red solution was refluxed for 1 hour, solid material separating. The product was decomposed with ice and dilute hydrochloric acid, and the ethereal solution dried over sodium sulphate and evaporated. The residue, which rapidly solidified, was recrystallised from ether-ligroin (b. p. 40–60°), yielding pale yellow, thick prisms of the *carbinol*, m. p. 100° (Found: C, 58.3, 58.5; H, 5.05, 5.1; N, 5.05. $C_{14}H_{14}ONBr$ requires C, 57.5; H, 4.8; N, 4.8%). The high values for carbon are possibly attributable to the facility with which the carbinol undergoes dehydration, this explanation being supported by the facts that the *N*-acetyl and the *N*-benzoyl derivative give similar high values, whereas the *N*-benzoyl ethylene (*q.v.*) gives satisfactory analytical data.

The *N*-acetyl derivative of the carbinol was prepared by treatment of the latter in excess of pyridine with acetic anhydride at room temperature. After 4 days the solution was diluted with water, and the acetamido-compound recrystallised from aqueous methanol, forming cream-coloured, long, prismatic needles, m. p. 181–182° (Found: C, 58.4; H, 4.5. $C_{16}H_{16}O_2NBr$ requires C, 57.5; H, 4.8%). The *N*-benzoyl derivative (from pyridine and benzoyl chloride) separated from aqueous alcohol in colourless prisms, m. p. 196° (Found: C, 64.4; H, 4.6. $C_{21}H_{16}O_2NBr$ requires C, 63.8; H, 4.6%).

Derivatives of α -Phenyl- α -(5-bromo-2-aminophenyl)ethylene.—(i) After the foregoing carbinol (0.5 g.) had been refluxed for 2½ hours with 4N-sulphuric acid (60 c.c.), white feathery crystals, m. p. 107°, separated on cooling (Found: C, 40.6; H, 5.2. $C_{14}H_{12}NBr_2H_2SO_4 \cdot 2H_2O$ requires C, 41.2; H, 4.4%). This *sulphate* was extremely hygroscopic and somewhat unstable, being slowly decomposed in cold water, and rapidly in hot, to the free amino-ethylene.

(ii) Treatment of the carbinol with 2N-sulphuric acid under identical conditions yielded a second sulphate of the amino-ethylene; this salt crystallised from the acid solution in fine white needles, m. p. 154°. Although this compound appeared to be rather more stable than the sulphate, m. p. 107°, it likewise decomposed slowly in aqueous solution.

(iii) Each of the above sulphates was shaken with aqueous-alcoholic ammonia, and the base was isolated by extraction with ether. In each case the uncrySTALLISABLE oil obtained was identified as the same diaryl-ethylene by benzoylation (benzoyl chloride and pyridine), α -phenyl- α -(5-bromo-2-benzamidophenyl)ethylene separating in each instance from aqueous methanol in colourless prismatic needles, m. p. and mixed m. p. 113.5–114° (Found: C, 67.0; H, 4.3. $C_{21}H_{16}ONBr$ requires C, 66.65; H, 4.2%).

6-Bromo-4-phenylcinnoline.—A solution of the sulphate (0.4 g.), m. p. 150°, in warm dilute sulphuric acid was cooled to 10° and treated with solid sodium nitrite (0.1 g.). The crystalline *cinnoline*, which separated almost immediately in nearly quantitative yield, was recrystallised from aqueous alcohol containing ammonia and subsequently from ether-ligroin or slightly aqueous methanol. It formed yellow, light, silky needles, m. p. 143.5–144.5°. The same result was obtained when the addition of sodium nitrite was carried out at 40° (Found: C, 59.7, 59.9, 59.9; H, 3.1, 3.0, 3.5; N, 9.6; Br, 26.9. $C_{14}H_9N_2Br$ requires C, 58.95; H, 3.2; N, 9.8; Br, 28.0%). No explanation can be advanced in respect of the high carbon values, which were obtained with three different samples. A solution of the cinnoline in concentrated hydrochloric acid gave an amorphous insoluble chloroplatinate, and benzene solutions of the base and picric acid gave a crystalline picrate, m. p. 270–275° (decomp.). The base showed no tendency to form a sulphate in aqueous solution.

5-Chloro-2-amino-4'-hydroxybenzophenone (VII; $R_1 = R_3 = H$, $R_2 = OH$, $R_4 = NH_2$).—The anthroxan prepared from *o*-nitrobenzaldehyde and phenol had m. p. 240–241° after crystallisation from alcohol (Zincke

dried, and evaporated. A solution of the residue in aqueous methanol deposited the diaryl-ethylene in faintly yellow cubes, which after several recrystallisations had m. p. 159°; yield, 6·7 g. (Found : C, 68·2; H, 4·8. $C_{11}H_{12}ONCl$ requires C, 68·4; H, 4·9%). It was recovered unchanged after being refluxed with sulphuric acid of various concentrations up to 8N.

The dibenzoyl derivative, prepared with benzoyl chloride and pyridine, was somewhat sparingly soluble in methanol; it separated from this solvent in clusters of colourless prisms, and from aqueous acetone in very slender, prismatic needles, m. p. 130·5—132° in each case (Found : C, 73·9; H, 4·3. $C_{28}H_{20}O_3NCl$ requires C, 74·0; H, 4·45%).

6-Chloro-4-(4'-hydroxyphenyl)cinnoline.—The suspension obtained by cooling a solution of the above aminoethylene (1 g.) in warm 2N-hydrochloric acid (60 c.c.) was treated at 5° with sodium nitrite (0·25 g. in 10 c.c. of water). After 1 hour, the precipitate was collected and dissolved in alcohol by the addition of ammonia, and the hot solution acidified with glacial acetic acid. The cinnoline, which separated on cooling, crystallised from slightly aqueous acetic acid in lustrous yellow plates with a red reflex, m. p. 257—259° (decomp.) (Found : C, 65·3; H, 3·5. $C_{14}H_9ON_2Cl$ requires C, 65·5; H, 3·5%).

The benzoate, prepared by the usual method, crystallised from aqueous alcohol in small, pale yellow needles, m. p. 156° (Found : C, 69·8; H, 3·8; N, 7·8; Cl, 9·6. $C_{21}H_{13}O_2N_2Cl$ requires C, 69·9; H, 3·6; N, 7·8; Cl, 9·85%).

5-Chloro-2-amino-2'-hydroxy-5'-methylbenzophenone (VII; $R_1 = OH$, $R_2 = H$, $R_3 = Me$, $R_4 = NH_2$).—The anthroxan prepared from *p*-cresol and *o*-nitrobenzaldehyde melted at 208—209° (Zincke and Siebert, loc. cit., give m. p. 210°). On reduction with iron and acetic acid under the conditions already described for the anthroxan, m. p. 240°, a 65% yield of the pure amino-ketone was obtained; this formed small dull yellow needles, m. p. 114—115°, from acetic acid (Zincke and Siebert give m. p. 115°). The sparingly soluble dibenzoyl derivative separated from benzene-alcohol in small stout needles, m. p. 156—157° (Found : C, 71·5; H, 4·4. $C_{28}H_{20}O_4NCl$ requires C, 71·5; H, 4·3%). This derivative (380 mg.) was refluxed for 2 hours with 6 c.c. of 5% alcoholic potassium hydroxide, and the solution then concentrated, diluted with water, and made slightly acid with acetic acid; two crystallisations of the product from aqueous acetic acid gave the ketone, m. p. and mixed m. p. 114°.

2 : 5-Dichloro-2'-hydroxy-5'-methylbenzophenone (VII; $R_1 = OH$, $R_2 = H$, $R_3 = Me$, $R_4 = Cl$).—The foregoing amino-ketone (3 g.) was dissolved in warm glacial acetic acid (40 c.c.) and concentrated hydrochloric acid (5 c.c.) and cooled to 5—10°, and the suspension diazotised with sodium nitrite (1 g. in 50 c.c. of water). The solution, containing an appreciable flocculent precipitate, was added during 10 minutes to a hot solution of cuprous chloride (6 g.) in concentrated hydrochloric acid (60 c.c.) and water (50 c.c.); the suspension was then boiled for a few minutes and cooled. The product, crystallised twice from alcohol (charcoal), yielded the dichloro-compound in long yellow needles (2 g.), m. p. 149—150°, insoluble in aqueous sodium carbonate and only moderately soluble in hot alcohol (Found : C, 60·1; H, 3·6; Cl, 24·8. $C_{14}H_{10}O_2Cl_2$ requires C, 59·75; H, 3·6; Cl, 25·25%).

A suspension of the dichloro-phenol in aqueous sodium carbonate was oxidised by essentially the same procedure as that described for the oxidation of 2 : 5-dichloro-4'-hydroxybenzophenone. The resultant 2 : 5-dichlorobenzoic acid (250 mg. from 1 g. of the phenol) had m. p. and mixed m. p. 153—154°, and the identification was confirmed by its conversion into the *m*-nitroanilide, m. p. and mixed m. p. 151—152°. (When freshly prepared, the *m*-nitroanilide frequently shows a double melting point, melting at 138—139° to a vitreous mass which on further heating becomes opaque and then melts sharply at 151—152°.)

5-Chloro-2-amino-2'-methoxy-5'-methylbenzophenone (VII; $R_1 = OMe$, $R_2 = H$, $R_3 = Me$, $R_4 = NH_2$).—The anthroxan (2 g.), m. p. 208—209°, was added to a solution of sodium (0·2 g.) in methanol (35 c.c.) and refluxed with methyl iodide (3 c.c.) for 1½ hours. After dilution with water the crystalline precipitate obtained on scratching was twice recrystallised from aqueous methanol, the methoxy-anthroxan forming elongated yellow laminae, m. p. 96—98°; more was obtained from the mother-liquors after removal of unmethylated anthroxan with dilute sodium hydroxide solution; total yield, 75% (Found : C, 65·6; H, 4·1; Cl, 12·7. $C_{15}H_{12}O_2NCl$ requires C, 65·8; H, 4·4; Cl, 13·0%).

A solution of the methoxy-anthroxan (1·25 g.) in glacial acetic acid (12·5 c.c.) was heated on the water-bath with iron filings (2 g.), added during 1½ hours; water (4 c.c.) was added after the reduction had been in progress for 10 minutes. After 1½ hours the solution was largely diluted with water and extracted with ether. The filtered extract was washed with sodium carbonate solution and water, dried, and evaporated. A solution of the residue in aqueous methanol yielded the amino-ketone in small, dull yellow prisms, m. p. 100—101°, strongly depressed by the parent anthroxan (Found : C, 65·5; H, 5·1. $C_{14}H_{14}O_2NCl$ requires C, 65·3; H, 5·1%).

The ketone did not form a semicarbazone under the ordinary conditions, but yielded an N-acetyl derivative, which separated from aqueous methyl alcohol in cream-coloured, brittle, prismatic needles, m. p. 136—137° (Found : C, 64·7; H, 5·2. $C_{17}H_{16}O_3NCl$ requires C, 64·2; H, 5·1%).

α -(5-Chloro-2-aminophenyl)- α -(2'-hydroxy-5'-methylphenyl)ethylene and Derivatives.—A solution of 5-chloro-2-amino-2'-hydroxy-5'-methylbenzophenone (12 g.) in ether (400 c.c.) was refluxed with an ethereal solution of methylmagnesium iodide (from 7·2 g. of magnesium and 45 g. of methyl iodide) for 5 hours. The product was worked up in the usual way, yielding a brown viscous residue (13 g.). Portions of this material were treated as follows :