The author wishes to take this opportunity of acknowledging his indebtedness to Dr. H. P. Armes of the Chemistry Department of the University of Manitoba for the suggestion of the problems dealt with in this thesis; and for the helpful advice given him in solving it.

J. M. Calman, B. Sc.

A STUDY OF THE EFFECTS OF GROUPS AND THEIR POSITION ON THE RATE OF REDUCTION OF THE NITRO GROUP OF SOME BENZENE NITRO COMPOUNDS

SECTION A OF THE "THESIS PRESENTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE

by

J. M. Calman, B. Sc.

April 15, 1929

I N T R O D U C T I O N

This paper is intended to summarize the results of work done to determine the effect of different groups and their position in the benzene nucleus on the extent of reduction of the nitro group in benzene compounds.

Most of the previous work relating to this subject has been done in an effort to discover the orientating influence of groups already substituted in the benzene nucleus on entering groups.

The relation between groups and activity has been studied by Kolbe (1), Cohen and McCandlisch (2), Gough and Thorpe and others.

The first mentioned author (1) notes that if the second substituent in an aromatic nitro compound were also a nitro group, then reduction of the nitro group as a whole would either stop, or proceed very slowly after the first nitro group was completely reduced. He formulated this fact as follows:

$$(C_6H_4NO_2)NO_2$$

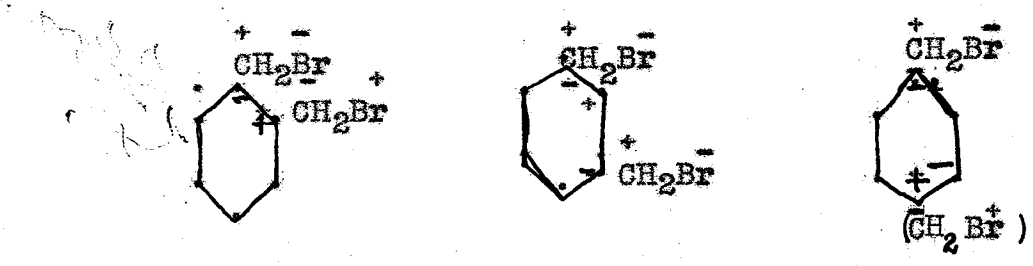
In addition to the above fact, Cohen and McCandlisch (2) found that complete reduction of dinitro benzene was obtained only after prolonged treatment with Ammonium sulphide at a

very high temperature. They believed that this behaviour of dinitrobenzene might be due to increased basicity of the nucleus due to formation of amino groups.

These authors also dealt with the reduction of many other polysubstituted aromatic nitro compounds by treatment with ammonium sulphide. From their results they finally concluded that if the groups secondary to the nitro group in the benzene compounds were acidic in character, reduction would be most complete. If the nitro group were in the ortho position to a methyl or ester group, reduction would be of a much lesser extent and might in fact be hindered.

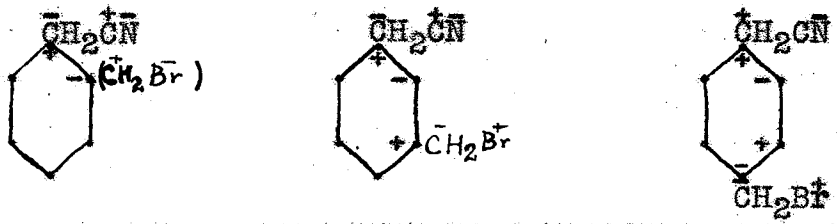
A review of the above reference indicates that interest centered rather on the final products of reduction than on the effects of groups on the activity of the nitro group.

Gough and Thorpe (3) found that ortho and para xylyene dibromides would react with potassium cyanide to form dicyanides; whereas meta xylylene dibromide would react with potassium cyanide to yield a monocyanide under precisely similar conditions. They explained this behaviour of the three isomers by use of the Lapworth (4) "Key atom" theory in the following fashion:



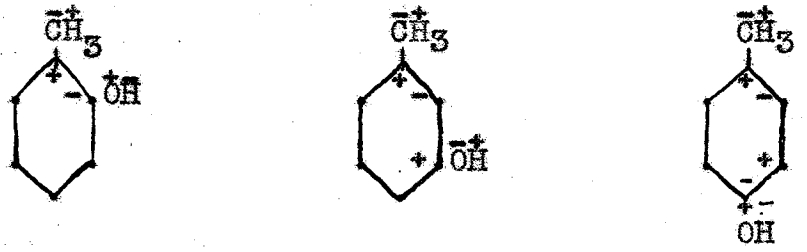
In the above structural formulae the heavily marked bromine atom is considered the key atom and the alternate polarities in the three dibromides are as shown above.

When the cyanogen group replaces the key bromine atoms the new key atom will be the nitrogen (in heavy letters), and as can readily be seen, this change in the key atom will enhance the negativity of the bromine in the ortho and para derivatives at the same time that it neutralizes the normal negativity of the bromine in the meta position.



This explanation seemingly accounts for the sluggishness of the remaining bromine atom of the meta xylylene dibromide as compared to the activities of it in the ortho and para positions.

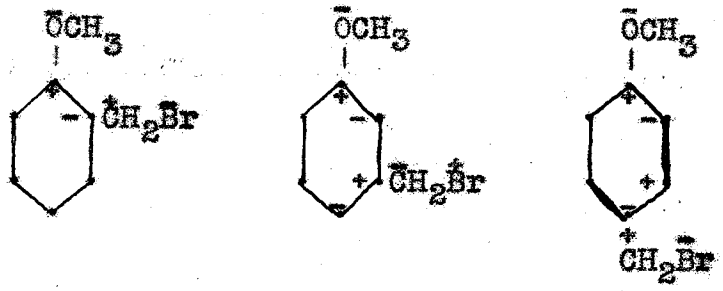
Another case investigated is that of the cresols, (Dawson and Mountford (5)). In this case the hydrogens of the alkyl radicle are assumed to be the key atoms and as a study of the following structures would indicate,



The hydroxyl H in the meta derivative has its positivity enhanced. In the ortho and para positions, however, the positivity of the hydroxyl hydrogen is at least partially neutralized. The authors (5) found that in practice the meta derivative actually possesses a higher ionization constant.

Lapworth and Shoesmith (6), who studied the alkali hydrolysis of the three isomeric methoxy benzyl bromides, found the ortho and para derivatives to be more readily acted on than the meta and explained the facts in the following manner:

Assuming the methoxy oxygens in the following structures to be the key atoms,



the normal negativity of the bromine atom will, in the case of the meta derivative be at least partially neutralized. While in the ortho and para derivatives the negativity of the bromine will be enhanced.

THEORY

A brief survey of the theories of substitution in the benzene nucleus must be made, in order to perceive the basic theory involved in this problem; even though assuming the theory and structure of benzene (2).

The leaders in the attempts to solve the problem of substitution in the benzene nucleus have been Hubner (8), Noelting (9), Crum Brown (10), Thiele (11), Holleman (12), Flurschiem (13), Vorlander (14), Lapworth (4), Kermack and Robinson (15), in chronological order.

Hubner (9) formulated the following explanation of substitution:

> "If the second substituting group in the case of disubstitution in the benzene nucleus be an acid or negative substituent it will enter the nucleus by replacing a hydrogen atom at the para and ortho positions to the least acid substituent already present."
>
> "Conversely, if an acid substituent were already present such an acid or negative entering group would be orientated to the meta position."

Noelting (9) formulated practically the same rule in the following manner:

> "A neutral, basic, or weakly acid group of the type:
>
> CH_3, Cl, Br, I, NH_2 or H,
>
> occupying the primary position would orientate such groups as;
>
> Cl, Br, I, HN_2, H_2SO_4

partly to the ortho, but mainly to the para positions.

"If, however, the primary substituted groups are acid in character as are:

$$NO_2,\ COOH,\ SO_3H$$

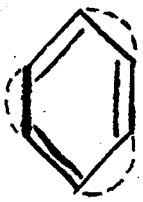
then such groups as:

$$Cl,\ Br,\ I,\ CH_3$$

will be orientated to the meta position mainly, and only in part to the ortho and para positions.

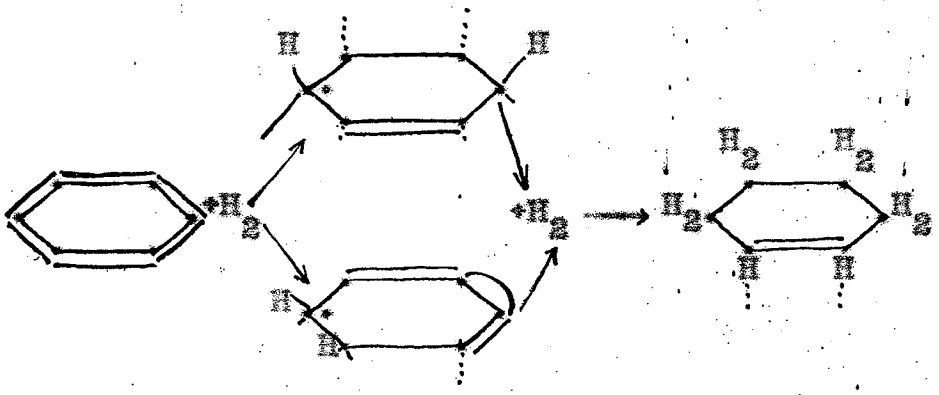
Thiele (11) explained substitution in the benzene nucleus in the following manner:

"Assuming the structure of benzene to be:



in which the residual valencies inherent in conjugate systems of double bonds are mutually saturated, the benzene nucleus is now represented by a(structure) formula which explains its saturated character."

"If benzene has such a structure then its reduction to the corresponding hydro derivatives will be as follows:



As is seen, ortho para addition takes place because

there is free residual affinity at those positions, but meta addition could only take place by the breaking up of the ring.

Further discussion of this theory and its development by Werner must be omitted owing to lack of space.

Various other theories have been suggested particularly by Crum Brown, Obermiller, Holleman, Vorlander, Flurschiem and others, but since those of both Crum Brown and Obermiller are virtually the same as Holleman's theory of substitution they will be omitted.

According to Holleman (12) the rules of substitution may be formulated as follows:

1. The rate of ortho para substitution is greater than the rate of meta substitution.
2. For ortho and para orientating groups the order of substitution ranges thus:

$$OH \quad NH_2 \quad Cl \quad I \quad Br \quad CH_3$$

3. For meta orientating groups the order of substitution varies as follows:

$$COOH \quad SO_3H \quad NO_2$$

According to Henrich "Theories of Organic" pages 205-206, the above hypothesis are merely rules which it is true hold in the majority of cases observed, but do not explain the fundamental principles underlying substitution and as a consequence are being disregarded more and more.

Shortly after Holleman, Vorlander (14), made and effort to explain substitution by the following set of rules:

1. Unsaturated groups such as:

NO_2, CN, CHO, COOH, SO_3H

will cause meta substitution.

2. Saturated groups of the type:

Cl, Br, I, CH_3, OH, CH_2Cl, CH_2COOH.

will cause ortho para orientation.

Vorlander himself finally stated that the above rules would not satisfactorily explain all the results obtained in substitution in practice.

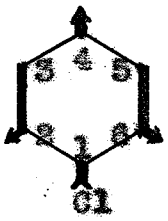
For example, if meta substitution occurs ortho-para substitution may also occur. If orthe substitution occurs the para and meta substitution also occur; whereas if para substitution predominates some ortho, and little or no meta substitution will occur. In addition to this it may be said that either the substituents will hinder disubstitution, in which case meta orientation will result, or they will promote disubstitution in which case ortho-para orientation will be the rule.

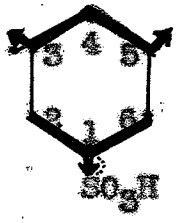
Flurschiem (13) explained substitution on the basis of a redistribution of chemical affinity. Assuming that:

1. There is no such thing as directive affinity and that all affinity is attractive force acting evening in all directions from the atomic center to the atomic surface.
2. The total valency is a constant for each element and if certain bonds employ large portions of the total affinity store there is less left over to furnish the remaining bonds by which the atom is attached to others.
3. There is then, a difference between firm and loose bonds between atoms.

In the case of benzene he symbolizes such a system by

the following diagrams:

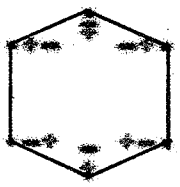
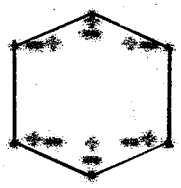




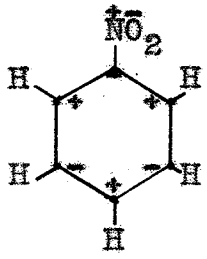
In which heavy lines represent large drafts of affinity, and light lines, slight affinity demands. The arrows indicate the directions of forces which he imagines to be emanating from the various substituents. This theory has been unable to stand under the test of a close examination by Holleman, Obermiller and others.

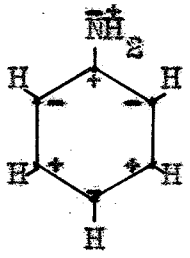
Vorlander (14) also attempted to explain substitution by means of affinity relationship and he did so in the following manner:

> "Assuming the bound and free charges on the carbon atoms in the benzene nucleus are alternately positive and negative, either the positive or negative charges will predominate at the alternate carbon atoms according to circumstances:"

e.g. I  II 

> Depending on the nature of the original substituent the nucleus after substitution will have a predominance of either positive (+) or negative (-) charges.

I 

II 

In the case of nitro benzene the nitrogen has a positive polarity, induced by oxygen, while in aniline the nitrogen has a negative polarity induced by its two adjoined positive hydrogen atoms.

A glance at the preceding formulae shows that the meta hydrogen atoms in nitro benzene are held by negative carbon atoms, while the ortho-para hydrogen atoms are held by positive carbon atoms indicating that in the meta position substitution would be more difficult than in the ortho or para positions, the opposite being the case with aniline.

On the basis of the above assumptions Verlander formulated the following rules;

I In the case of disubstitution by nitration or halogenation the entering group will be orientated to the meta position by such side chains as

SO_3H, NO_2, CHO, COOH

which consist of positive atoms or groups acting as such.

II The entering group in nitration or halogenation will be orientated to the ortho and para positions if the side chain consists of negative atoms or groups acting as such

e.g. Cl, I, Br, OH, OCH_3, NH_2

Lapworth (4) formulating his principles of induced alternate polarities in chains of atoms held that:

> "The laws of change in the carbon compounds are the mathematically necessary results of the operations of the laws of valency applied to the migration of the point or condition of free valency arising from a dissociation akin to ionization. These considerations indicate that the alternate atoms in such a chain of carbon atoms might be expected to exhibit similar powers of acting as seats of ionic activity".

In other words, the alternate atoms might be expected to show similar polarities.

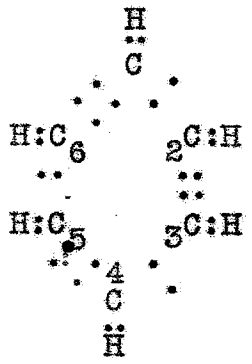
Lapworth further assumes that:

> "each atom in its organic chemical combinations can be associated with a given (maximal) number of bonds or valency lines; and whilst any atom may not have more than this maximal number associated with it, it may have less; and, lastly, the total number of these bonds or valency lines (whole and fractional) in any part of the molecule remains constant unless there is definite reason to postulate that some have passed to or from another part of the molecule, or to or from the surroundings."

A further extension of these axioms results in the "key-atom conception, for which Lapworth lays down the rule that the term "key-atom" shall be applied only to that atom which is considered responsible for a certain effect, and not to one producing the most striking effects or even to one which has an effect on every property. All these postulates lead to the same results in practice as do Vorlander's (14).

Kermack and Robinson (15) developed an hypothesis of 'Induced alternate polarities' along slightly different lines. Where Lapworth (14) developed his theories on a general basis and then showed the possibility of their agreement with the electronic conceptions of valency; Robinson (15) built up his system on Lewis' ideas of atomic structure.

According to Lewis' theory, the outer shells of the atoms of carbon, hydrogen and chlorine possess four, one and seven electrons respectively. In chemical combination among the carbon derivatives of these atoms Lewis assumes that an octet of electrons in the outer sphere of an atom is a stable grouping; and that this total of eight electrons can be obtained by the carbon atom sharing electrons with the other atoms in the compound. On this basis the ordinary single bond of organic chemistry is represented by a pair of electrons held in common by two atoms; and the ethylene bond is represented by two such pairs of shared electrons. Thus the formula of benzene becomes:



If now the hydrogen atom (1) be replaced by a chlorine atom, a rearrangement of electrons around the ring will take place. As a result the carbon atoms (1) (3) and (5) will become systems of unstable octets (positive groupings on the Kermack Robinson view), while the carbon atoms (2) (4) and (6) will turn into the stable octet systems. Thus the difference in chemical nature between ortho and para positions on the one hand and the meta position on the other is accounted for on the basis of these

assumptions.

In the case of nitro benzene, if the two oxygen atoms form complete octets the nitrogen becomes an unstable system, thus carbon atoms (1), to which the nitro group is attached, will be a stable system instead of unstable as is chlorobenzene. Obviously in this case, the atomic systems (1) (3) and(5) are stable on this basis, whilst the systems (2) (4) and (6) are unstable. Thus as has been shown this set of assumptions offers an explanation of the different orientating influence of such atoms or groups as chlorine and nitro.

METHOD

The method used is a variation of that described by Thorpe and Whiteley (16) for the estimation of nitro groups by reduction with stannous chloride.

In the present instance duplicate half gram samples of the nitro compound to be reduced were weighed into glass stoppered hundred centimeter graduated flasks. Twenty cubic centimeters of ninety-five percent alcohol were then added to each half gram sample in order to dissolve it. Then ten cubic centimeters of approximately 2.5 normal standard stannous chloride solution were pippetted into each flask and the flasks stoppered.

The two duplicates and a blank were then immersed in a

thermostatically controlled electric water bath, which was set at a temperature of thirty three degrees; for a period of thirty minutes. The duplicates and blank were then removed and cooled for ten minutes in order to check the reaction.

Both reaction mixtures and blank were diluted to one hundred cubic centimeters with distilled water after the ten minute interval had elapsed and the excess unoxidized stannous chloride remaining was titrated with half normal standard iodine solution, using starch paste solution on a spot plate to obtain the end point.

The difference between the amount of stannous chloride first used and the amount present after reaction is a direct measure of the rate of reduction of the nitro group for the time and at the temperature at which the reaction proceeded.

The reactions were carried out in the manner stated for the following reasons;

I TEMPERATURE

It was found that a higher temperature carried the reactions, in the case of some isomers; too close to completion without in any wise changing the comparative velocity with which the nitro group of each set of isomers was reduced. Conversely a lower temperature would not carry the reaction far enough, so that in the case of such isomers as para nitro toluene or para nitro phenol there would be no reduction when their isomers had already been reduced to a considerable degree.

II TIME

Here again the same factors had to be taken into consideration as have already been mentioned in dealing with the question of temperature; but in addition to these factors there arose another, that of efficiency. It was found that a period of thirty minutes would not only carry the reactions to a point where comparison of velocities was possible, but also allowed a sufficient interval in which to prepare duplicate solutions for reaction, and allowed time for the titration of a preceding reaction mixture.

III WEIGHT OF MATERIAL

The consistant use of half gram samples of material was desirable for the following reasons:

It was a useful standard of comparison.

It was simplified calculations and was easily weighed.

It was sufficiently large to lower the percentage of error in weighing, yet sufficiently slight to allow of ready solution. Finally it yielded a large enough percentage of reduction under the conditions of the reactions.

IV SOLUTIONS

Half normal iodine solutions were used because a sufficient quantity of this strength of solution could be prepared to allow for a much larger number of titrations than would have been possible with more dilute solutions, in view of the facilities available.

The use of alkaline tartarate was discontinued because it resulted in precipitation of the amino compounds formed by the

reduction of the nitro groups and the tendancy of these precipitates to mask the end point.

The purpose of the blanks with each set of experiments was to obtain a constant, check of the exact values of the stannous chloride and iodine solutions with reference to one another.

The solution mentioned were prepared in the following fashion:

(a) 2.5N STANNOUS CHLORIDE SOLUTION

One hundred and fifty grams tin were dissolved in barely sufficient concentrated hydrochloric acid. The liquor was then decanted and fifty cubic centimeters of concentrated hydrochloric acid added. The solution was then diluted to one litre.

(b) N/2 IODINE SOLUTION

Sixty three point five grams iodine were dissolved in potassium iodide solution and the solution diluted to one litre.

(c) ALKALINE TARTARATE SOLUTION

Ninety grams of sodium carbonate and one hundred and twenty grams of rochelle salts were dissolved in distilled water and the solution diluted to one litre.

The following compounds were purified by repeated crystallization and distillation till their boiling points and melting points became constant:

TABLE No I

Name of Compound	Isomers					
	Ortho		Meta		Para	
	B.P.	M.P.	B.P.	M.P.	B.P.	M.P.
Nitro Benzene	210	5.4				
Chlor. Nitro Benzene		32.5		44.5		83.0
Iodo " "		49.0		36.0		171.0
Br. " "		41.0		56.0		125.0
Nitro Toluene	220			150.0	237.0	(52)
" Anisol		9.0		(?)		54.0
" Benzaldehyde		44.0		58.0		106.0
" Phenol		42.0		96.0		114.0
Ethyl Nitro Benzoate		30.0		47.0		57.0
Nitro Benzoic Acid		147.0		140.0		238.0
Nitro Aniline		71.0		114.0		146.0
Dinitrobenzene		117.0		90.0		171.0

E X P E R I M E N T A L

A. DATA

The original experimental data consists of:

I The number of cubic centimeters of half normal iodine solution required to neutralize the excess stannous chloride in each.

II The number of cubic centimeters of half normal iodine solution required to neutralize the stannous chloride in the blank, which represents the amount of stannous chloride used for each individual experiment.

B. RESULTS

The results are calculated from the above data in the following manner:

I The percentage of available "NO_2" in each compound, which is required in order to derive the weight in grams of"NO_2" available in each of the compounds used, calculated thus:

Formula I $$\frac{U}{MW} \times 100 = x$$

where U = the theoratical equivalent weight of "NO_2"

MW = the theoretical equivalent weight of each compound.

and x = percent "NO_2" available.

II The grams "NO_2" available in each compound, required for the purpose of calculating the percent of available "NO_2" actually reduced, obtained by the use of the following formula:

Formula II $$X\ W = y$$

where = percent "NO_2" theoretically available.

W = the weight of each compound used in each experiment.

and y = the grams "NO_2" available in each case

III The grams of available "NO_2" actually reduced in each experiment, which are required in order to calculate the percent available "NO_2" actually reduced in each case are obtained as follows:

Formula III $((a-b)) \times (\cdot 0038275) = z$

Where a = number of ccs N/2 iodine solution required to titrate the stannous chloride in each blank (e.g.) number of ccs iodine required to neutralize the amount of stannous chloride used, before each experiment.

b = the number of ccs N/2 iodine solution required to neutralize the stannous chloride which remains unoxidized after each experiment.

$\cdot 0038275$ = the value of 1 cc N/2 iodine solution in grams "NO_2".

and z = grams "NO_2" actually reduced.

The percent of available "NO_2" actually reduced is obtained by use of the following formula:

Formula IV $y \times z$ = percent "NO_2" actually reduced.

Where y = grams"NO_2" available in each compound

z = grams available "NO_2" actually reduced

TABLE No. I

EXPERIMENTAL RESULTS META NITRO COMPOUNDS

Name of Compound	No. of cc's N/2 "I_2" Solution		% "NO_2" available	Grams "NO_2" available	Grams available "NO_2" actually reduced	% Available "NO_2" actually reduced
	After reaction	Before reaction				
$C_6H_5NO_2$	35.8	44.8	37.3	0.1865	0.0344	18.4
$ClC_6H_4NO_2$	23.8	44.8	30.06	0.1503	0.0803	53.4
I "	30.4	40.8	18.4	0.0920	0.0398	43.2
Br "	27.8	39.9	22.7	0.1135	0.0463	40.7
CH_3 "	40.4	44.7	33.5	0.1675	0.0164	9.7
OCH_3 "	34.6	39.9	30.06	0.1503	0.0202	13.4
CHO "	25.5	41.0	30.46	0.1523	0.0693	45.5
OH "	38.5	44.8	33.09	0.1654	0.0241	14.5
$COOH_2H_5$"	31.5	39.9	23.5	0.1175	0.0320	27.2
COOH "	29.4	44.2	27.5	0.1375	0.0566	41.1
NH_2	16.5	44.6	33.3	0.1665	0.1076	64.4
NO_2	16.3	43.01	54.7	0.2735	0.1021	37.3

TABLE No II

EXPERIMENTAL RESULTS OF ORTHO NITRO COMPOUNDS

Name of Compound	No. of cc's N/2 "I" solution required		% "NO_2" available	Grams "NO_2" available	Grs. Available "NO_2" actually reduced	% Available "NO_2" actually reduced
	After reaction	Before reaction				
$C_6H_5NO_2$	35.5	44.8	37.3	0.1865	0.0344	18.4
$ClC_6H_4NO_2$	17.7	44.8	30.06	0.1503	0.1037	68.9
I "	25.4	40.8	18.4	0.092	0.0584	64.0
Br "	25.5	39.9	22.7	0.1135	0.0551	48.5
CH_3 "	36.8	44.7	33.5	0.1675	0.0310	18.5
OCH_3"	30.5	39.9	30.06	0.1503	0.0359	23.8
CHO "	22.5	41.0	30.46	0.1523	0.0708	46.6
OH "	36.4	44.8	33.09	0.1654	0.0320	19.3
$COOC_2H_5$ "	28.5	39.9	23.5	0.1175	0.0436	37.1
COOH "	30.2	44.2	27.5	0.1375	0.0535	38.9
NH_2 "	30.5	44.6	33.3	0.1665	0.0539	32.3
NO_2 "	23.5	43.01	54.7	0.2735	0.0746	27.0

TABLE No III

EXPERIMENTAL RESULTS OF PARA NITRO COMPOUNDS

Name of Compound	No of cc's N/2 "I" solution required		% "NO_2" available	Grams "NO_2" available	Grs. available "NO_2" actually reduced	%available "NO_2" actually reduced
	After reaction	Before reaction				
$C_6H_5NO_2$	35.8	44.8	37.3	0.1865	0.0344	18.4
Cl $C_6H_4NO_2$	31.0	44.8	30.06	0.1503	0.0528	35.1
I "	32.5	40.8	18.4	0.0920	0.0317	34.4
Br "	33.2	39.9	22.7	0.1135	0.0256	22.5
CH_3 "	43.3	44.7	33.5	0.1675	0.0053	3.1
OCH_3 "	38.5	39.9	30.06	0.1503	0.0053	3.5
CHO "	29.9	41.0	30.46	0.1523	0.0424	27.8
OH "	44.5	44.8	33.09	0.1654	0.0011	0.66
$COOC_2H_5$ "	25.5	39.9	23.5	0.1175	0.0570	48.5
COOH "	24.6	44.2	27.5	0.1375	0.0750	54.5
NH_2 "	40.0	44.6	33.3	0.1665	0.0176	10.5
NO_2 "	28.3	43.01	54.7	0.2735	0.0562	20.5

TABLE NO IV

FOR THE PURPOSE OF COMPARISON THE PERCENTAGE OF AVAILABLE "NO_2" ACTUALLY REDUCED WERE SET IN THIS TABLE IN DESCENDING ORDER

Ortho	% Available "NO_2" reduced	Meta	% Available "NO_2" reduced	Para	% Available "NO_2" reduced
$C_6H_5NO_2$	18.4				
$C_6H_4ClNO_2$	68.9	$C_6H_4NH_2NO_2$	64.6	$C_6H_4COOHNO_2$	54.5
$C_6H_4INO_2$	64.0	$C_6H_4ClNO_2$	53.4	$C_6H_4COOC_2H_5NO_2$	48.5
$C_6H_4BrNO_2$	48.5	$C_6H_4CHONO_2$	45.5	$C_6H_4ClNO_2$	35.1
$C_6H_4CHONO_2$	46.6	$C_6H_4INO_2$	43.2	$C_6H_4INO_2$	34.5
$C_6H_4COOHNO_2$	38.9	$C_6H_4COOHNO_2$	41.1	$C_6H_4CHONO_2$	27.8
$C_6H_4COOC_2H_5NO_2$	37.1	$C_6H_4BrNO_2$	40.7	$C_6H_4BrNO_2$	22.5
$C_6H_4NH_2NO_2$	32.3	$C_6H_4NO_2NO_2$	37.3	$C_6H_4NO_2NO_2$	20.5
$C_6H_4NO_2NO_2$	27.0	$C_6H_4COOC_2H_5NO_2$	27.2	$C_6H_4NH_2NO_2$	10.5
$C_6H_4OCH_3NO_2$	23.8	$C_6H_4OHNO_2$	14.5	$C_6H_4OCH_3NO_2$	3.5
$C_6H_4OHNO_2$	19.3	$C_6H_4OCH_3NO_2$	13.4	$C_6H_4CH_3NO_2$	3.1
$C_6H_4CH_3NO_2$	18.5	$C_6H_4CH_3NO_2$	9.7	$C_6H_4OHNO_2$	0.66

TABLE No V

THE ISOMERS OF THE COMPOUNDS USED AND THE PERCENT REDUCTION OF THEIR NITRO GROUPS ARE SET SIDE BY SIDE HORIZONTALLY IN THIS TABLE

ORTHO	% Available "NO_2" reduced	META	% Available "NO_2" Reduced	PARA	% Available "NO_2" Reduced
$C_6H_4ClNO_2$	68.9	$C_6H_4ClNO_2$	52.4	$C_6H_4ClNO_2$	35.1
$C_6H_4INO_2$	64.0	$C_6H_4INO_2$	43.2	$C_6H_4INO_2$	34.5
$C_6H_4BrNO_2$	48.5	$C_6H_4BrNO_2$	40.7	$C_6H_4BrNO_2$	22.5
$C_6H_4CHONO_2$	46.6	$C_6H_4CHONO_2$	45.5	$C_6H_4CHONO_2$	27.8
$C_6H_4COOHNO_2$	38.9	$C_6H_4COOH.NO_2$	41.1	$C_6H_4COOH.NO_2$	54.5
$C_6H_4COOC_2H_5NO_2$	37.1	$C_6H_4COOC_2H_5NO_2$	27.2	$C_6H_4COOC_2H_5NO_2$	48.5
$C_6H_4NH_2NO_2$	32.3	$C_6H_4NH_2NO_2$	64.6	$C_6H_4NH_2NO_2$	10.5
$C_6H_4NO_2NO_2$	27.0	$C_6H_4NO_2NO_2$	37.3	$C_6H_4NO_2NO_2$	20.5
$C_6H_4OCH_3NO_2$	23.8	$C_6H_4OCH_3NO_2$	13.4	$C_6H_4OCH_3NO_2$	3.5
$C_6H_4OHNO_2$	19.3	$C_6H_4OHNO_2$	14.5	$C_6H_4OHNO_2$	0.66
$C_6H_4CH_3NO_2$	18.5	$C_6H_4CH_3NO_2$	9.7	$C_6H_4CH_3NO_2$	3.1
$C_6H_5NO_2$	18.4				

C O N C L U S I O N S

A. EFFECTS OF TYPES AND POSITION OF GROUPS

I (a) Positive groups ortho to the nitro group do not favor reduction of the nitro group to the same degree as do such negative groups or atoms as:

Cl, Br, I

but favor reduction to a greater degree than do such groups as:

OH, CH_3

Positive groups favor reduction in the following order:

CHO , COOH , COOR , NO_2

(b) Negative groups ortho to the nitro group favor reduction in the following order:

Cl I Br NH_2 OCH_3 OH CH_3

II (a) Positive groups meta to the nitro group favor reduction of it in the following order:

CH_2 COOH NO_2 COOR

(b) Negative groups meta to the nitro group favor its reduction in the following order:

NH_2 Cl I Br Oh OCH_3 CH_3

III (a) Positive groups para to the nitro group influence its reduction in the following order:

COOH , COOR , CHO , NO_2

(b) Negative groups para to the nitro group influence its reduction in the following order:

Cl I Br NH_2 OCH_3 CH_3 OH

B. EFFECTS OF POSITION WITHIN TYPES

It is seen that regardless of position the halogens always show the same relationship amongst themselves with regards to their effect or influence on the rate of reduction of the nitro group. The order of influence is always as follows:

Cl I Br

The negative "NH_2" group which, in the ortho position has far less influence on the rate of reduction of the nitro group than has the "Br"; in the meta position is the most influential of all the groups studied. In the para position it again is far less influential than the "Br".

The "OH" group which in the meta position follows "Br" amongst the negative group as regards influence on the rate of reduction of the nitro group, in the para position is the least influential of all the groups studied, while in the ortho position it has very little more influence on the rate of reduction of the nitro group than has the "CH_3" group which in this (the ortho position) is least influential of all the groups studied.

The "OCH_3" group which in the ortho position has more influence on the rate of reduction than has the "OH" group, in the meta position has less influence than it.

C. EFFECTS OF WEIGHT OF GROUPS

In the case of the negative halogens (Cl, I, Br) an increase in weight seems to be accompanied by a decreased influence on the rate of reduction of the nitro group. Iodine is anomalous in its behaviour, but both this anomaly and the statement already made hold true whether for the ortho, meta or para positions.

In the case of such groups as "OH" and "OCH_3", replacement of the "H" by "CH_3" is accompanied by an increased influence on the rate of reduction of the nitro group in the ortho and para position, and a decreased influence in the meta.

Replacement of the "H_2" of "NH_2" by "O_2" in the case of "NO_2" causes a decreased influence in the ortho and meta positions, and an increased influence in the para position.

Oxidation of the "CHO" group to COOH causes decreased influence in the ortho position and a progressive increase in influence in the meta and para positions.

Replacement of the "H" of COOH by an alkyl group:

e.g. COOH ——————→ COOR

is accompanied by a decreased influence on the rate of reduction of the nitro group in ortho, meta and para positions,

BIBLIOGRAPHY

SECTION A

(1) Kolbe	Annalin	1850	76	38
(2) Cohen & McCandlisch	J. C. S.	1905	87	1257
(3) Gough & Thorpe	"	1919	115	1155
(4) Lapworth	"	(1901	79	1265
	"	(1922	121	416
		(1925	127	1742
(5) Dawson & Mountford	"	1918	113	937
(6) Lapworth & Sholsmith	"	1922	121	1391
(7) Theory of Benzene (Kekule)	Annalen	1858	106	129
(8) Hubner	Berichte	1875	8	873
(9) Noelting	"	1876	9	1797
(10) Crum Brown	J. C. S.	1892	61	367
(11) Thiele	(Berichte	1898	31	978
	(Annalen	1899	306	87
(12) Holleman "Die Direkte Einfuhrung Von substituenten in den Benzolkern		1910		
(13) Flurschien (Journal prakt. chemie		1902	66	321
(" " "		1905	71	497
(Berichte		1906	39	2015
(14) Vorlander	Annalen	1902	320	122
(15) Kermack & Robinson	J. C. S.	1922	121	427
(16) Thorpe & Whiteley - Students Manual of Organic Chem. Analysis			211	212

S E C T I O N B

A STUDY OF THE CONDENSATION OF BENZYL CYANIDE WITH SOME AROMATIC NITRO COMPOUNDS

PRESENTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF "MASTER OF SCIENCE" OF THE UNIVERSITY OF MANITOBA

by

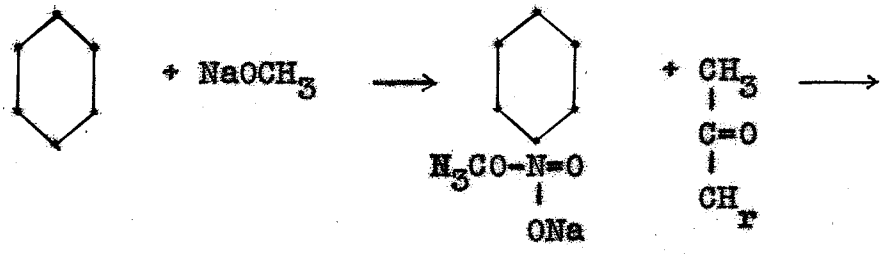
J. M. Calman, B. Sc.

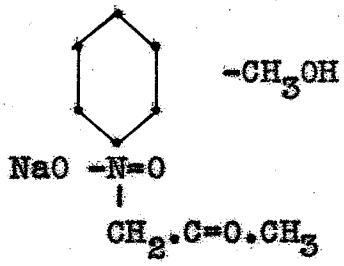
April 15th.1929

I N T R O D U C T O R Y

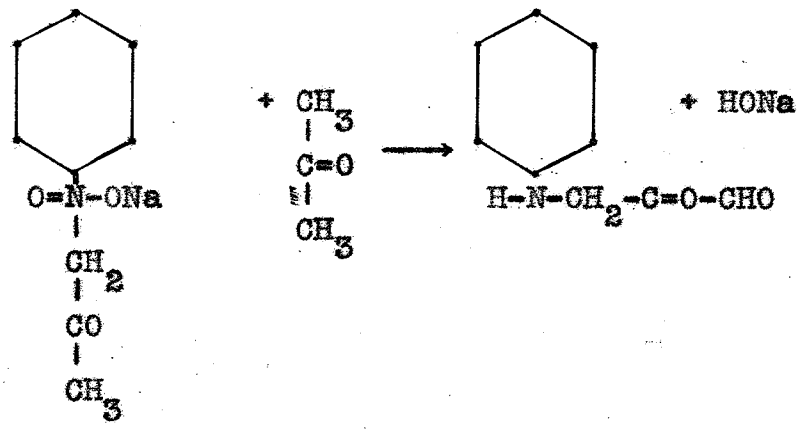
Very little work has been done with reference to the condensations of the aromatic nitro compounds with such compounds as benzyl cyanide, dimethylaniline and other allied compounds.

Reissert (1) studied the condensation of nitro benzene with sodium methylate and acetone. He formulated the reaction in the following manner:





Reissert also studied the behaviour of dinitro benzene with acetone and sodium methylate. He formulated the reaction as follows:

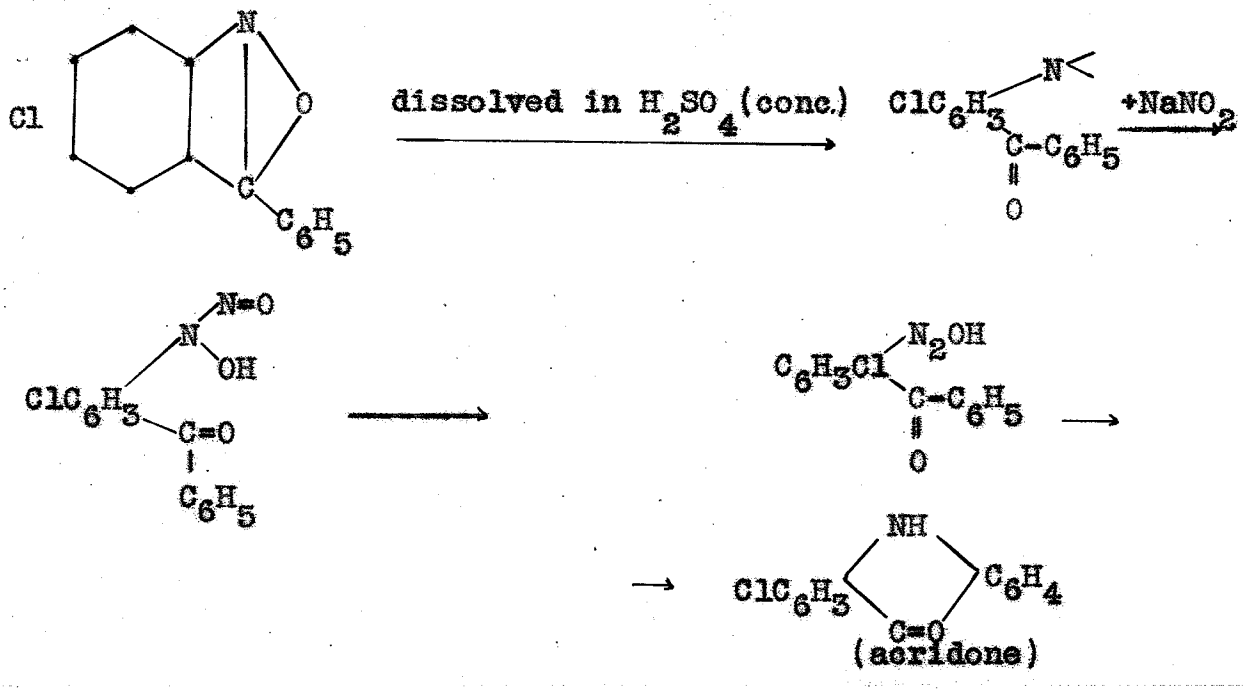


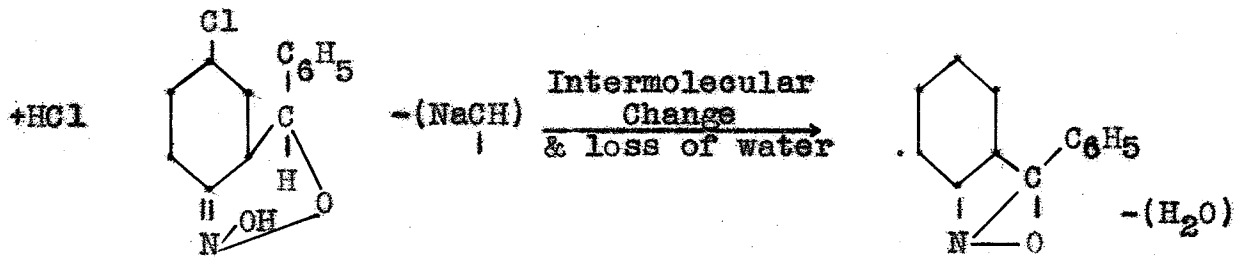
Reissert also studied the behaviour of nitro benzene with acetone and sodium methylate. He formulated the reaction as follows:

$$C_6H_4(NO_2)_2 + CH_3COCH_3 \downarrow$$

$$CH_6N_2O_3 + H_2O$$

Barnburger (2) studied the behaviour of chlor phenyl anthranil and its convertion into chlor acridone. He formulated the reaction in the following manner:





It (4) was found that the best results were obtained when equimolecular weightsof para chlor nitro benzene and benzyl cyanide were reacted with two molecular equivalents of sodium ethylate in alcoholic solution and refluxed for two minutes.

The reaction mixture was then cooled and acidified with hydrochloric acid because the condensation product did not dissolve in it as it did in organic acids.

Coke prepared no dirivatives of this compound because it was relatively inactive with acids, bases, oxidizing and reducing agents. He did, however, prove its constitution by means of the Bamberger umlagerung reaction. He proved the constitution to be that chlor phenyl enthranil and by combustions, determined the empirical formula to be $C_{13}H_8ONCl$.

A complete survey of the methods and theory involved in these condensations can be obtained in the reference (4) mentioned.

Coke (4) made a careful investigation of the properties, nature and constitution of the condensation products of the ortho and para isomers of chlor nitro benzene.

His (4) attempts to prepare deivatives of the meta chlor nitro benzene, were on the whole unsuccessful. The product obtained was generally a semi liquid with a slight yield of the ortho chlor nitro benzene derivative. He (4) did, however, prepare enough of the meta condensation products to enable him to establish the fact

that the main product of the reaction between meta chlor nitro benzene and sodium benzyl cyanide, was identical with the product of the condensation of ortho chlor nitro benzene with sodium benzyl cyanide.

The purpose of this paper is to set out the results of work done in verifying his results with reference to the condensation of meta chlor nitro benzene and to establish the conditions most favorable to the reaction. It is also intended to show that the other product of the meta condensation has been isolated in sufficient quantities to identify it.

THEORETICAL

The principal involved in this work is that on which all condensations are based; that is, if two or more organic molecules unite with or without elimination of component elements, in such fashion that the new union is effected between carbon atoms. This union may or may not be effected by use of intermediary matallic derivatives of the compounds to be united.

In the case of the condensation of the three chlor nitro benzene derivatives with benzyl cyanide the union was effected in the following manner:

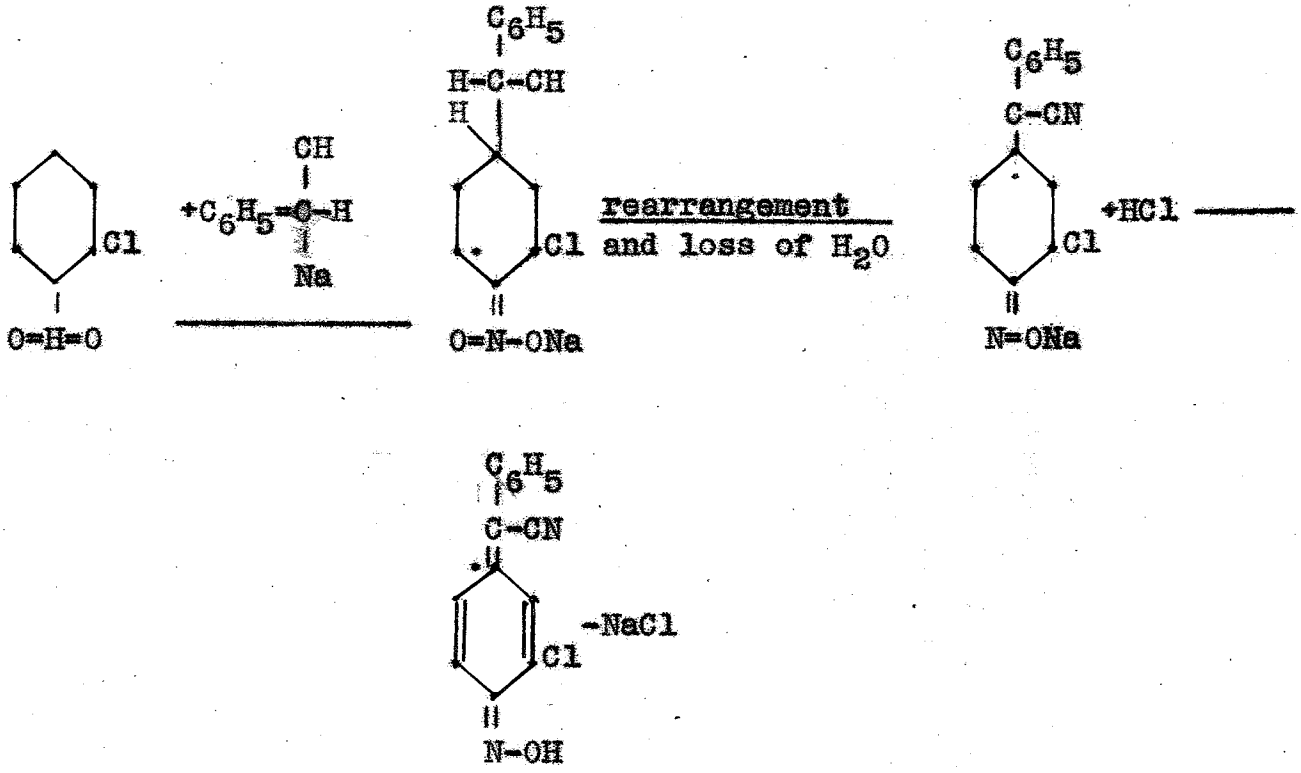
1. Condensation of ortho chlor nitro benzene with benzyl cyanide in the presence of sodium ethoxide:

Coke (4) that the product of the ortho condensation was produced by condensation of the meta chlor nitro benzene with benzyl cyanide in the presence of sodium ethoxide.

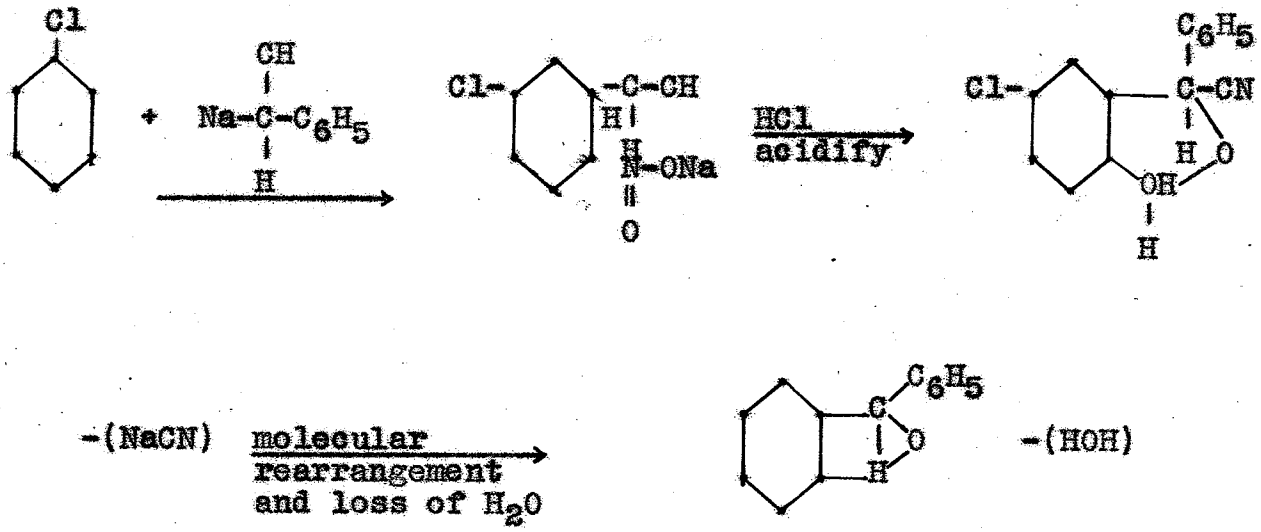
In the case of meta chlor nitro benzene yielding condensation products it is evident that it can yield only one compound corresponding to that obtained from the condensation of the ortho chlor nitro benzene.

It is, however, possible that it might yield two compounds related to that obtained from the para chlor nitro benzene condensation e.g.:

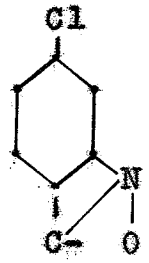
see page 37



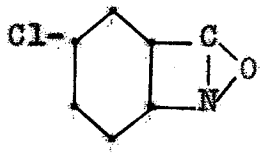
II Condensation of para chlor nitro benzene with Benzyl cyanide in presence of sodium ethoxide.



The question naturally arose as to whether the meta condensation yielded products corresponding to those obtained from both the ortho and para derivatives, and as already stated



I



II

formula I corresponding to the para chlor nitro benzene condensation derivative and, formula II not corresponding to it.

Since Coke (4) had already shown that a product corresponding to that obtained by the ortho chlor nitro condensation, it remained only to verify that result, and in addition to attempt the isolation of any other compounds resulting from the meta condensation, in the hope of proving that either one or both of the chlor phenylanthranils above had been produced.

EXPERIMENTAL PROCEDURE AND CONDENSATIONS ACTUALLY CARRIED OUT

In all the succeeding preparations the chemicals used were carefully purified both by recrystallization and redistillation till their boiling and melting points were constant within one degree centigrade.

In all cases the quantities used were molecular equivalents or some fraction or multiple of molecular equivalents of the compounds reacted in each condensation process.

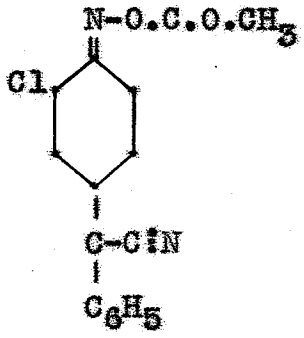
Condensations were attempted successfully not only with meta chlor nitro benzene and benzyl cyanide in the presence of sodium ethoxide but also with alpha nitro naphthaline and benzyl cyan-

ide in the presence of sodium ethoxide.

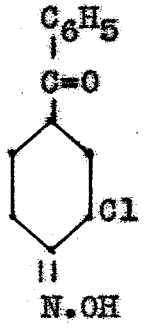
The condensation of meta chlor nitro benzene and benzyl cyanide in the presence of sodium ethoxide was shown to result in the formation of at least two compounds:

I A predominant yellow crystalline compound corresponding to that described by Coke (4), which after repested crystallization gave a melting point of 135°C and charred at 146°C.

This compound formed (a) yellow crystalline compound with acetic anhydride which, after repeated crystallization, gave a melting point of 156°C and frothed at 157°C.

I 

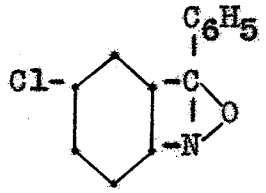
(b) a creamy white crystalline oxime with alkaline peroxide in alcoholic solution which gave a melting point of 97°C.

II 

(c) a creamy white crystalline oxime with concentrated nitric acid in acetic (glacial) acid solution which gave a melting point of 97°C.

II A minor quantity of brownish flaky crystalline material, which

after repeated crystallization gave a melting point which rose from 82°C after the first recrystallization to 115°C after the fifth, when the melting point remained constant.



By actual weight it was found that forty parts of the major yellow compound were formed, to each one part of the minor brownish material. Repeated changes in procedure finally raised the proportions of the secondary product to one in twenty.

In case of the condensation of alpha nitro naphthaline with benzyl cyanide in the presence of sodium ethoxide, it was found that the reaction resulted in the formation of at least two compounds:

(a) A powdery, dry-grass green compound with a melting point of .... 177°C.

(b) A brownish yellow compound with a melting point of ... 135°C.

The second product is produced in larger quantities and behaves in a manner analogous to that of the primary condensation product of meta chlor nitro benzene and benzyl cyanide. e.g:

(1) It forms an acetate (yellow) which is semi liquid at normal temperatures.

(2) It forms an oxime (brown) which is a viscid liquid at normal temperatures.

EXPERIMENT A

Condensation of meta Cl nitro benzene with benzyl cyanide in presence of sodium ethoxide

1 molar equi.,	Benzyl cyanide	1.48 grs.
1 " "	M_6Cl nitro benzene	2,000 "
1 " "	Sodium metal	.293 "
1 " "	95% alcohol	20.0 cc's

0.293 grams clean sodium metal was dissolved in 20.0 cc's 95% ethyl alcohol and 1.48 grams benzyl cyanide added. The solution turned dark brown red. 2.00 grams meta chlor nitro benzene were added and the mixture boiled on a water bath under a reflux condenser for twenty minutes.

At first the reaction mixture was a clear deep red solution, but after twenty minutes it turned a deep brown and a heavy precipitate began to settle.

The reaction mixture was then cooled in ice and neutralized with hydrochloric acid till it turned from alkaline to neutral to litmus. A golden yellow precipitate formed and a little was filtered off, washed and small portions recrystallized from the following solvents:
Benzol, Alcohol, Ether, Chloroform, Acetic acid and mixtures of all of them in various proportions. Crystallization from benzol was most satisfactory and yielded fine microscopic yellow crystals with a melting point of 135°C and charring at 146°C.

The experiment was repeated with the period of boiling under the reflux changed to two minutes. A thick gum resulted.

The experiment was repeated and the period of boiling under the reflux changed to five minutes. Again a thick gum was produced.

The experiment was again repeated and the period of boiling changed to ten minutes and again a gum formed.

The process was repeated at all the above temperatures and acetic acid used as an acidifying agent, but always with a gum resulting from the process.

It was, therefore, concluded that boiling for twenty minutes, acidifying with hydrochloric acid and recrystallizing out of benzol would yield the maximum yield of the yellow compound.

PROPERTIES OF THE PREDOMINANT YELLOW META CONDENSATION PRODUCT

When a small quantity of the yellow product was dissolved in dilute sodium hydroxide a deep red solution formed. Addition of acid changed the color to golden yellow and at the neutral point the original product precipitated.

FORMATION OF THE ACETYL DERIVATIVE OF THE PREDOMINANT YELLOW META CONDENSATION PRODUCT

1.0 grs. of substance were dissolved in 5.0 cc's of acetic anhydride and boiled for 2 minutes; a brown liquid formed which was poured into cold water, when a yellow crystalline material precipitated, which melted at 156°C and frothed at 157°C.

FORMATION OF THE OXIME OF THE PREDOMINANT YELLOW META CONDENSATION PRODUCT

0.5 grams of substance were dissolved in glacial acetic

acid and concentrated nitric acid added. The solution changed from yellow to green and on boiling the color changed to brown and then to yellow, while brown nitrous oxide fumes were evolved. The solution was then cooled and dilute alkali added till the solution was neutral to litmus when a slight amount of creamy white crystals precipitated melting at 68°C. When recrystallized the melting point changed permanently to 98°C but most of the material was lost.

The oxime could also be formed by boiling in alcoholic alkaline peroxide, but the yield was not improved.

NITROGEN COMBUSTIONS

I Original predominant yellow meta condensation product

Calculated	-	N=10.92%
Found	-	(1) N=10.98% 25.5°C 745.5 min. (2) N=10.66% 25.5°C 744.0 "

II Acetyl derivative

Calculated	-	N= 9.38%
Found	-	(1) N=9.38% 23.5°C 745.2 min. (2) N=9.3 % 21.0°C 745.0 "

Having verified the formation of the main yellow meta condensation product noted by Coke (4) it was next attempted to isolate the by-product (Cl phenyl anthranil.)

As before mentioned when the reaction mixture was acidified a little brown red gum precipitated, and it was suspected that this might consist of an intimate mixture of the predominant yellow product and the Cl phenylanthranil or its isomer, before mentioned (Theoretical discussion).

Accordingly the following set of experiments were

carried out to verify this assumption.

Condensation of meta chlor nitro benzene with benzyl cyanide in the presence of sodium ethoxide to prepare Cl Phenyl anthranil

1 molar equivalent	Benzyl cyanide	1.48 grams
1 " "	M Chlor nitro benzene	2.000 "
1 " "	Sodium metal	.243 "
	95% Alcohol	20.0 cc's

The 0.243 grams sodium were dissolved in the alcohol and added to the 1.48 grams benzyl cyanide. A red solution formed to which was added the 2.0 grams meta chlor nitro benzene. The mixture was boiled under a reflux condenser for two minutes when a purple coloration was observed, cooled in ice and dissolved in the minimum quantity of dry ether.

The ethereal solution was shaken up with consecutive portions of dilute sodium hydroxide till the alkaline layer was no longer discolored.

The ethereal layer was then dried with anhydrous sodium sulphate for twenty four hours, and the ether distilled off on a water bath.

The residue was then dissolved in a minimum quantity of anhydrous ether and allowed to crystallize out in a vaccum dessicator. - A gummy residue remained.

The experiment was repeated and absolute alcohol used as a crystallization medium. - A gummy residue again formed.

The experiment was repeated but the reaction mixture refluxed for twenty minutes, and equal portions of it treated with both ether and alcohol as crystallization media, but again a gummy residue remained.

The experiment was then repeatedly performed, but the conditions changed in various ways. For example the mixture was boiled for five, ten, fifteen and twenty minutes and the reaction mixture dissolved in alcohol and ether as crystallization media but a gummy residue was produced each time.

The experiment was again repeated, but the equivalent quantities of reagents were changed; but always a gum was produced.

The gummy residues were then treated with alcoholic potash and the alkaline solutions, which turned green, were then acidified. The green coloration disappeared and minute quantities of flaky creamy material precipitated.

The treatment was then continued till about 0.25 grams of the creamy flakes were accumulated. These flakes had a melting point 115°C after repeated recrystallizations.

The above compound was then treated according to Bamburgers (2) directions for the "umlagerung" of phenylanthranil to acridone as follows:

"INTRA MOLECULAR CHANGE" OF Cl PHENYL ANTHRANIL

A small quantity of finely powdered substance was dissolved in two cc's of cold concentrated sulphuric acid, by rubbing the mixture in an ice bath, till a clear syrup formed. Enough powdered cold sodium nitrite was added to change the color of the mixture and the whole stirred well in the ice bath. The whole reaction mixture was then allowed to stand for twenty-minutes after which it was poured into cold distilled water.

The resultant precipitate was then dissolved inalcohol and recrystallized. It was found that an intense violet fluores-

cence could be obtained, but only in aqueous alcoholic solution.

EXPERIMENT B

Condensation of alpha nitro naphthaline with benzyl cyanide in the presence of sodium ethoxide

2 molar equivalents	alpha nitro naphthaline	3.46 grams
2 " "	Benzyl cyanide	2.34 "
2 " "	Sodium metal	0.46 "
	95% ethyl alcohol	20.0 cc's

The 0.46 grams sodium metal was dissolved in the 20 cc's 95% alcohol and the 2.34 grams benzyl cyanide added. The 3.46 grs. alpha nitro naphthaline were then added and the mixture, which turned a violet red, was boiled on the water bath under a reflux condenser for twenty minutes, when it turned a dark brown.

The reaction mixture was then cooled and diluted - a grass green precipitate settled out. This was filtered off, dried, and recrystallized from benzene. The mother liquor was acidified and a brown yellow precipitate formed. This was filtered off, dried and recrystallized from benzene.

The melting point of the first precipitate was 177°C.

The melting point of the second precipitate was 135°C.

The experiment was repeated using varying equivalents of the reacting substances, and with variations in the times of heating, but the results were similar.

The second precipitate was produced in much larger quantities than the first, and yielded an acetate and oxime, both of which were viscid liquids at normal temperatures.

The experiment was repeated, but the method of separating the reaction products were changed: That is the reaction mixture after cooling was dissolved in a minimum quantity of ether and treated with consecutive portions of dilute or concentrated sodium hydroxide till the sodium hydroxide layer was no longer discolored. At that point a heavy precipitate of a dark red precipitate formed, which when dissolved in water, decomposed and yielded the brown compound.

The sodium hydroixde layer when acidified yielded a grass green precipitate similar to the green product before mentioned.

The melting point of the first (grass green) is 177°C

The melting point of the second (yellow brown) 135°C.

The ethereal solution was dired with anhydrous sodium sulphate for 24 hours, the ether distilled off on a water bath, and the residue dissolved in anhydrous ether and allowed to recrystallize a dark brown gum formed.

The experiment was repeated, using alcohol as a recrystallization medium, but again a gum formed.

C O N C L U S I O N S

It has been shown that meta chlor nitro benzene will condense with benzyl cyanide in the presence of sodium ethoxide to form:

(1) A predominant yellow crystalline compound similar to the condensation product of ortho chlor nitro benzene and benzyl cyanide.

(2) A secondary flaky creamy yellow compound, which can be changed to an acridone by means of the "Umlagerung" of Bamburger.

(3) That alpha nitro naphthane will react with benzyl cyanide in a manner analogous to that of meta chlor nitro benzene.

BIBLIOGRAPHY

SECTION B

		No.	No.	Pages
(1) Reissert	Berichte	1904	37	831-838
(2) Bamburger	"	1909	42	1710
(3) H.P. Armes	Unpublished private communication.			
(4) C. E. Coke	"Thesis" - a private communication.			