Chandler

The Molecular Rearrangement of Carbon Compounds

THE MOLECULAR REARRANGEMENT OF CARBON COMPOUNDS

BY

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THESIS

Submitted in Partial Fulfillment of the Requirements for the

Degree of

DOCTOR OF PHILOSOPHY

IN CHEMISTRY

IN

THE GRADUATE SCHOOL

OF THE

UNIVERSITY OF ILLINOIS

1917

UNIVERSITY OF ILLINOIS

THE GRADUATE SCHOOL

MAY 12 1917

I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY EDWARD MARION AUGUSTUS CHANDLER

ENTITLED THE MOLECULAR REARRANGEMENT OF CARBON COMPOUNDS

BE ACCEPTED AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

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ACKNOWLEDGEMENT.

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This investigation was begun in the Department of Chemistry of the University of Illinois during the fall of 1915 at the suggestion of Dr. C. G. Derick. The author wishes to express his most sincere appreciation and gratitude to Dr. Derick for the hearty encouragement, invaluable help, and wise counsel given him during the entire progress of the work. He also desires to thank and express his gratefulness to Dr. Roger Adams, Professor W. A. Noyes, and Dr. Oliver Kamm for many valuable suggestions and criticisms given during Dr. Derick's absence from the University. Without the kind and efficient service of Miss Marion E. Sparks (Librarian of the Department of Chemistry), the compilation of the larger part of the Bibliography would have been impossible.

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I - INTRODUCTION.

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The work embodied in this thesis is a continuation of a study begun in this laboratory several years ago by Dr. C. G. Derick and J. W. Howard relative to the mechanism of the Hofmann rearrangement.

The modern movement in organic chemistry offers an interesting contrast with the spirit of the older organic chemistry. The early organic chemists in their enthusiastic desire to synthesize certain definite compounds encountered many side reactions with which they did not concern themselves. The success achieved in obtaining the particular compound sought, regardless of whether the yield was one per cent or ninety per cent, simply threw a veil of indifference and darkness over these "deep seated" reactions and thus the sink was made the recipient of what modern organic chemistry is proving to be of profound theoretical and practical importance.

The modern trend of organic chemistry then is towards the quantitative. This implies a consideration of all the factors involved in producing the maximum yield in the most feasible manner and at the minimum cost. This then means a study of the energy changes, mass relations, relative cost of materials, and the kinetics of all the possible reactions or "collisions" which would occur under the conditions of the experiment. The knowledge obtained from such a study enables one to regulate the conditions so as to decrease to a minimum the yield of undesired products,

predict all of the reactions that will take place, and obtain a maximum yield of the product sought.

Then too, as a result of this modern movement, many physical properties such as melting and boiling points have been found inadequate as criteria of purity of organic compounds. Certain sugars, for example, have identical physical properties but their difference in optical activity shows them to be distinct compounds. Conductance measurements in this laboratory by Derick and his students have also detected impurities in acids which the ordinary physical properties, such as melting points and boiling points, do not reveal.

The study of the mechanism of the Hofmann rearrangement is in accord with this quantitative modern movement and has been made by the author as described in this thesis.

A Carius electric furnace constructed and calibrated by Derick and Howard in this laboratory has made possible a quantitative study of the effect of temperature and time on the rearrangement. The effect of pressure has been studied by varying the charges in the bombs at definite temperatures.

The mixtures of the different classes of amines resulting from the rearrangements have been separated by a method for the quantitative separation and determination of primary, secondary, tertiary amines, and quarternary ammonium compounds, which has been perfected and whose accuracy has been determined.

The physical properties of the individual amines in each class have been determined and their identification made in so far as materials and time would allow.

II - HISTORICAL.

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I. General Historical.

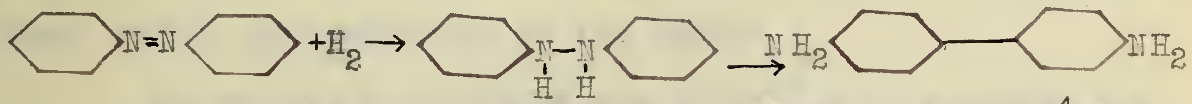
As the Hofmann rearrangement involves the migration of alkyl groups from the nitrogen atom of aromatic amines to carbon atoms in the benzene nucleus, it is interesting, historically, to note the behavior and results of similar migrations of other elements and groups. Such a study then involves the following rearrangements and transformations: (a) The Benzidine Conversion; (b) The Semidine Rearrangement; (c) Rearrangement of Imid Bases; (d) Rearrangement of Hydrazines; (e) Rearrangement of Nitrosamines; (f) Nitroamine Transformation; (g) Rearrangement of Aryl Hydroxyl Amines; (h) Rearrangement of Phenylsulphamic Acid; (i) The Migration of Halogens from the Side-Chain Nitrogen Atom to the Benzene Nucleus; and (j) The Migration of Acyl Groups from the Side-Chain Nitrogen Atom to the Benzene Nucleus.

Wohler's artificial production of urea[I] by heating an aqueous solution of ammonium cyanate to the temperature of boiling water, involved an intramolecular change which stimulated and aroused a keen and lively interest in organic chemistry. Thus began the study of intramolecular rearrangements.

(a) The Benzidine Conversion.

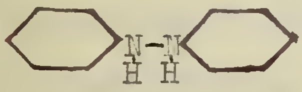
Seventeen years after Wohler's classic discovery Zinin[2] found that when an alcoholic solution of azobenzene is treated with ammonia and hydrogen sulphide, benzidine is formed. He

naturally thought that benzidine was the direct reduction product of azobenzene. Eighteen years later, Hofmann[3] showed that benzidine is not a primary but a secondary product in the reduction, and that this compound is the result of the transformation of the intermediate substance hydrazobenzene which first forms. He showed that hydrazobenzene and benzidine were isomeric but that their properties are entirely different. His explanation of the mechanism of this rearrangement is that there are two distinct phases which characterize the formation of benzidine. "In the first place," says he, "the molecule of azobenzene assimilates a molecule of hydrogen, but this hydrogen remains in a very feeble state of combination, being eliminated by a great variety of agents. It is only under the influence of acids that the hydrogen molecule becomes incorporated in the system, if I may use this expression, and fixed benzidine, a substance of stability is formed."



The investigation was taken up later by Schultz[4] who discovered that a small amount of a second isomer, diphenylene, was simultaneously formed with benzidine.

Benzidine



Diphenylene

In 1884 Schultz[5] continued his research on hydrazo compounds and found that rearrangement took place by treating these

substances with stannous chloride, thus forming derivatives of benzidine and diphenylene together with a small amount of aniline.

Both Erdmann[6] and Teichmann[7] obtained hydrazobenzene by the reduction of nitrobenzene. This hydrazobenzene was found to undergo the usual rearrangement into benzidine.

The same results were found by Löb[8] when nitrobenzene was reduced electrolytically in an alcoholic hydrochloric acid solution.

The benzidine rearrangement was investigated later by Chattaway[9] who confirmed the results obtained by previous investigators in this field. In regard to the mechanism of the change, he says: "Much that is known of similar isomeric changes points to the conclusion that transference from nitrogen to the ring can only take place when the nitrogen is exerting its higher valency. This may explain the advantage, in these transformations, of the hydrochloride of the base."

It was found by Rassow and Rülke[IO] also by Sachs and Whittaker[II] that the transformation of hydrazobenzene into benzidine may also be brought about by organic acids. In order to make this conversion feasible, these workers noted that some substance must be present to combine with the benzidine as fast as it is formed; the best substance for this purpose was found to be benzaldehyde.

The velocity of the benzidine transformation was investigated during the next two years by Van Loon[I2].

He found that benzidine could be determined quantita-

tively when precipitated from a slightly acid solution with potassium sulphate. Hydrazobenzene was shaken until dissolved in a known amount of acid, then treated with potassium sulphate; the benzidine sulphate thus formed was weighed. He found that at room temperature eighty four per cent of the hydrazobenzene was converted into benzidine, while ninety per cent was transformed at the same temperature when normal hydrochloric or hydrobromic acid was used. Only sixty-six and four tenths per cent of the hydrazobenzene was rearranged when the reaction was carried out at 100° in the presence of tenth normal hydrochloric acid; the hydrazobenzene was partially decomposed into azobenzene and aniline. At room temperature the velocity of the transformation seemed to have increased with, but more rapidly than, the concentration of the acid. The velocity was also found to be independent of the nature of the acid, but to decrease when methyl or ethyl alcohol was used as the solvent instead of water.

Tichwinsky[13] considered that in aqueous or alcoholic solution, the presence of a strong mineral acid favors the transformation of a trivalent into a pentavalent nitrogen; that is, the acid favors the formation of a stronger base.

He noted that hydrogen chloride does not ionize in benzene solution and hence no transformation took place. His results relative to the rearrangement of hydrazobenzene into benzidine in the presence of organic acids, acetic acid for example, confirmed those of Rassow and Rülke.

Duval[14] in his investigation of compounds of the diphenyl, diphenylmethane, and diphenylethane series, finds that the

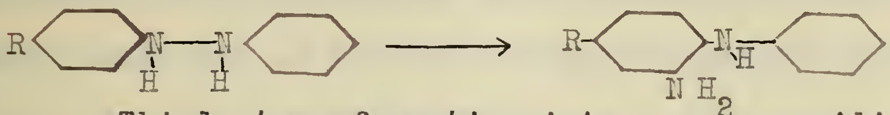
reactions are entirely different from those in the benzene series, and that the benzidine rearrangement does not take place.

(b). The Semidine Rearrangement.

Several years later, investigations were carried out on rearrangement of substituted hydrazobenzenes. Jacobson and his students[15] reduced azo derivatives with an alcoholic solution of stannous chloride and hydrochloric acid. They found that the hydrazo compound thus formed would simultaneously rearrange into several products which could easily be separated and identified. Bohn[16] also Nölting and Werner[17], and even Jacobson himself at first regarded the change as analogous to the benzidine rearrangement. Subsequent investigation showed, however, that this was not the case because the hydrogen in the para position was substituted by other groups which remained intact during the transformation, and hence, the mechanism of the change must be different. The work of Täuber[18] on the " Formation of an Ortho-amidoditolylamine from Para-hydrazotoluene", and of Witt and Schmidt[19] on the " Products of the reduction of Alkyated Azo-Colors of the Naphthalene Series" together with the later work of Jacobson[20] show conclusively that the change is a half benzidine rearrangement, and that the nature of the substituent, exerts a marked influence on the course of the reaction. The change is called the semidine rearrangement. It has been shown that when the hydrazo derivative of one constituent is treated with stannous chloride in acid solution, several changes may take place. First, a change into benzidine

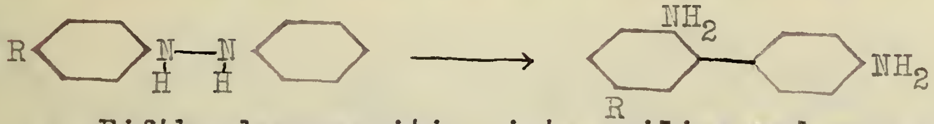
with the elimination of the substituent,

Second, the formation of an ortho semidine,

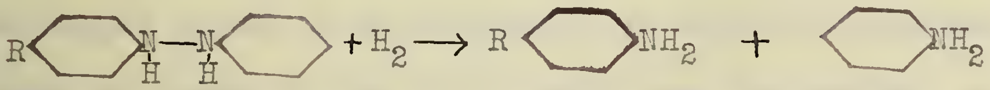


Third, transformation into a para semidine,

Fourth, the formation of a diphenyl base,



Fifth, decomposition into aniline and a para substituted aniline,

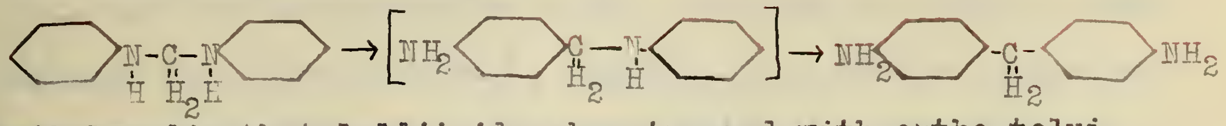


These investigators have also found that when substituents are in both of the para positions, decomposition into two molecules of base takes place. It was also noted that the ortho semidine rearrangement is diminished if there are present methyl groups ortho to the hydrazo group.

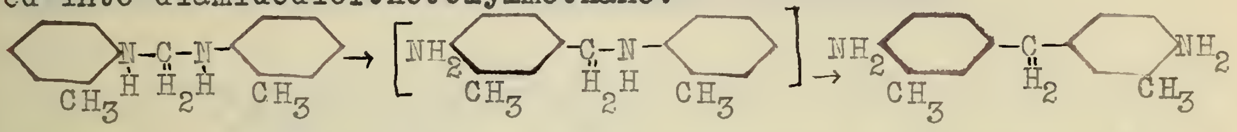
(c). Rearrangement of Imid Bases.

During the same period that Jacobson was working on semidine rearrangement, Eberhardt and Welter[21] were investigating the rearrangement of imid bases into diamidodiphenylmethane derivatives. They found that these imid compounds rearranged in the presence of hydrochloric acid or amine hydrochlorides when heated on the water-bath for about twelve hours. Methylenediphenyldiimid, for example, was found to rearrange

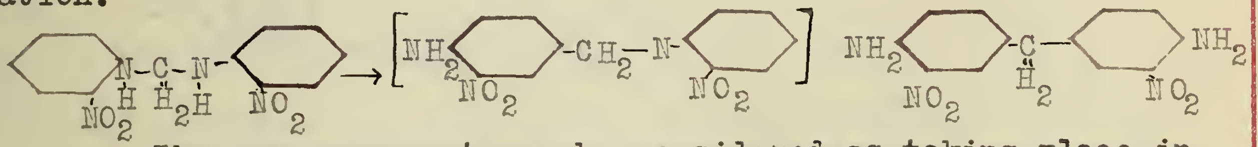
into diamidodiphenylmethane;



Methylenediorthotolyldiimid, when treated with ortho-toluidinehydrochloride on the water-bath for several hours was changed into diamidodiorthotolylmethane:



The Nitro derivatives were found to undergo the same transformation.

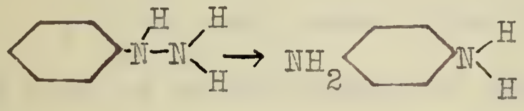


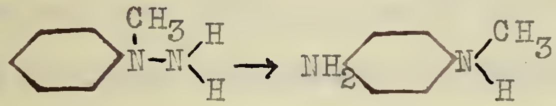
The rearrangement may be considered as taking place in two steps: first, a rearrangement to form an intermediate substance as shown in the above reactions, and second, a rearrangement of this intermediate substance into the diphenylmethane derivative.

(d). Rearrangement of Hydrazines.

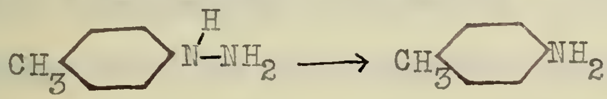
The rearrangement of hydrazines to diamines was investigated up to 1895 only with hydrazo compounds. Thiele and Wheeler[22] have investigated the rearrangement of simple hydrazines and have found that if there are no substituents in the para position the compounds are converted into paradiamines. The hydrazine compounds were found to rearrange completely only when heated with fuming hydrochloric acid at 200°, while the hydrazo compounds rearranged in the presence of a much weaker acid and at a lower temperature. These workers found that dilute sulphuric acid would bring about rearrangement but the yield was

small and part of the hydrazine was oxidized. Even in water solution the hydrochloride of the hydrazine was found to rearrange when heated at 200°, but the yield of the rearranged product was very small. Phenylhydrazine and unsymmetrical methylphenyl hydrazine were transformed respectively into paraphenylenediamine and methylparaphenylenediamine.





When the para position was occupied with some substituent other than hydrogen,an amine group would not rearrange to the ortho position but would split off in the form of ammonium chloride, and the corresponding substituted amine would remain. Paratolylhydrazine, therefore, would give para toluidine.

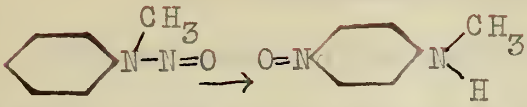


Unsymmetrical diphenylhydrazine was found to give only resinous products.

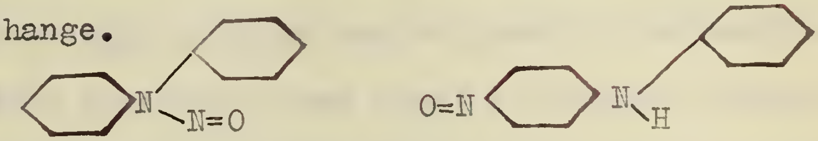
(e). Rearrangement of Nitrosamines.

In 1886 Fischer and Hepp[23] found that the nitrosamines derived from aromatic amines underwent intramolecular rearrangement when treated with alcoholic hydrogen chloride.

Methylphenylnitrosamine, for example, undergoes transformation into p-nitrosomethylaniline.



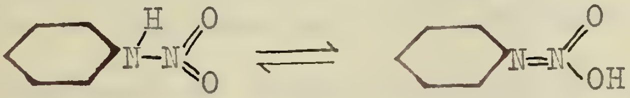
Other nitroso derivatives of this type were found to undergo the same change.



A good many years later Fischer[24] found that when hydrobromic acid is used instead of hydrochloric acid, nitric oxide is eliminated; the latter is oxidized by the air, and the reaction of the nitrogen peroxide with hydrobromic acid liberates bromine and forms brominated by-products. When phenylmethylnitrosamine is treated in ether solution with an alcoholic solution of hydrobromic acid, there was precipitated a mixture of the hydrobromides of methylaniline, p-nitrosomethylaniline, p-bromomethylaniline, and o-p-dibromomethylaniline, while the mother liquor was found to contain phenylmethylnitrosamine, p-bromphenylmethylnitrosamine together with the hydrobromides of methylaniline, p-bromomethylaniline, and p-nitrosomethylaniline. These disturbing factors were found not so pronounced when hydrochloric acid was used. Even in the experiments where hydrochloric acid was used, he found that the disturbing factors were very much decreased if that solvent was chosen in which the hydrochloride of the nitroso base is the least soluble. Fischer further noted that if the para position in the nitrosamine holds some substituent other than hydrogen, hydrobromic acid may bring about a quantitative conversion into the second base; thus p-bromomethylaniline is formed from p-bromophenylmethylnitrosamine.

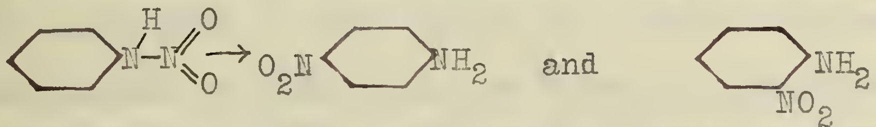
(f). Nitro-amine Transformation.

The molecular rearrangement of nitramine (benzenediazotic acid) into ortho and para nitraniline was thoroughly studied by Bamberger and his students[25] four years beginning with the year 1893. His primary purpose was to prove the structure of phenylnitramine. Many reactions were carried out which favored the two following tautomeric formulae:



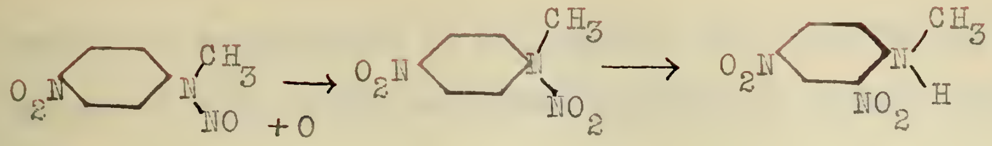
Most of the evidence, however, was in favor of the first formula, although Bamberger claimed that "neither can be regarded as established".

It was found that when phenylnitramine is heated on the water-bath, decomposition took place with the formation of several products: namely, nitrogen, carbon dioxide, nitrous oxide, nitrosobenzene, ortho-and paranitraniline, also ortho and paranitrophenol. Rearrangement was also found to take place when the salt is treated with dilute mineral acids even in the cold;



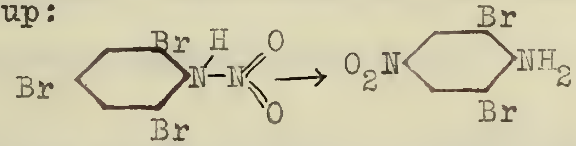
also when boiled in water; by passing hydrogen chloride into a cold etherial solution of the acid; or, when acted upon by a mixture of glacial acetic and sulphuric acids at 0 - 10°.

Later, Stoermer[26] found that when certain nitroso derivatives of secondary amines were oxidized to nitro derivatives, they could undergo rearrangement when treated in the same manner as described by Bamberger.

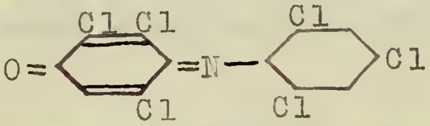


Whenever the para position was occupied by some other group, the wandering group from the nitrogen goes to the ortho position.

In 1902 Orton[27] found that s-trisubstituted anilines were capable of rearrangeing with ease into nitroamino derivatives by treatment of thier solutions in acetic acid with nitric acid and acetic anhydride. Later[28] it was found that the products of transformation varied according to the nature of the groups ortho and para to the amino group in the original substance. Thus, bromine in the para position to the amino group is replaced by the nitro group:



Chlorine may also be replaced but not under the same conditions. With the proper precautions no chlorine is eliminated if the temperature is kept below 15°, and the nitroamino-s-trichlorbenzene is converted into hexachlorphenyliminoquinone,



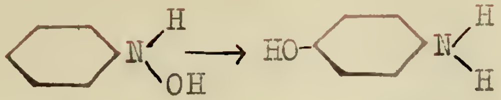
It was also noted that the color changes characteristic of unsubstituted nitroamines during rearrangement were the same as those of the trisubstituted nitroamines. No case was observed where the nitro group went into the meta position. The mono-and disubstituted nitroamines were also studied. In all of these investigations several important facts were noted: The transfor-

mation is accelerated by all acids; the activity of the acids is in accord with their relative activity in other reactions; chloric and perchloric acids bring about the transformation twice as rapidly as does hydrochloric acid; the reagent should be able to combine with the nitroamine, probably in such a way as to make the nitrogen pentavalent; water, acetic acid, or mixtures of the two were the best solvents; the rate of change is proportioned to the square of the concentration of the acid; the change is about thirty times as fast at 25° as it is at 0°; the transformation is accompanied by the formation of nitrous acid and the conversion of nitroamine into a diazonium salt. In aqueous solution the transforming agent or catalyser must not be present below a certain concentration, not below two hundredth normal in the case of hydrochloric acid.

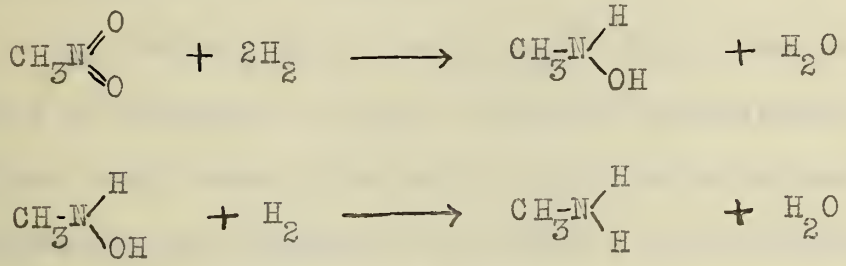
(g). Rearrangement of Arylhydroxylamines.

During the same period while working on the electrolytic reduction of aromatic nitro compounds, Gatterman[29] found that not only was the nitro group reduced to the amino group, but that in most cases a hydroxyl group was substituted in the para position.

From nitro benzene, for example, he obtained p - aminophenol. During the same year in an attempt to prepare phenylhydroxylamine Friedlander[30] obtained, instead of this substance, p-amidophenol. He came to the conclusion that phenylhydroxylamine is an unstable substance which rearranges instantly, as represented by the following equation:

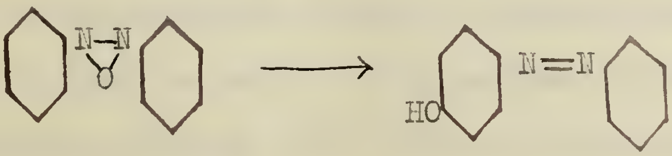


Two years previous to Gatterman's and Friedlander's researches, Hoffmann and Meyer[31] investigated the reduction of aliphatic nitro compounds and found that the reduction takes place in two phases; the reduction of nitromethane, for example, may be represented by the two equations:



Methylhydroxylamine as formed in the first equation reduces Fehling's solution and may be isolated. These investigators found, however, that nitrobenzene and nitrophenol did not yield any substance which would reduce Fehling's solution, due to the instantaneous rearrangement of such substances as soon as formed.

In the electrolytic reduction of nitrobenzene there is also formed some azoxybenzene. This rearranges under the influence of sulphuric acid into oxyazobenzene which, when reduced should give p-amidophenol and an equivalent amount of aniline.

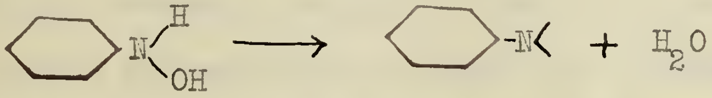


As this has not been shown to be the case, Gatterman holds that precedence must be given to the first explanation as the mechanism of the reaction.

By further study Bamberger[32] found that B-phenylhydroxylamine is obtained in long colorless needles when nitrobenzene is boiled for a short time with water and zinc dust. The phenylhydroxylamine so obtained rearranges to paraamidophenol when treated with mineral acids. Cold dilute mineral acids, however, sometimes favored the formation of azoxybenzene. Under the proper conditions a good yield of the rearranged product could be obtained. During the same year Wohl[33] made a study of the reduction of nitro compounds and obtained results which confirmed those of Bamberger.

A few years later Bamberger[34] found that arylhydroxylamines would sometimes rearrange into both ortho and para aminophenols even though the para position did not contain any substituent other than hydrogen. These substances were formed by the action of sulphuric acid, alum solution, or by the action of water. Ethyl or methyl alcoholic sulphuric acid induces the formation of derivatives of para or ortho phenetidine or anisidine; p-amino sulphonic acids are sometimes formed. Other products occasionaly produced are p-aminodiphenylamine bases, p-hydro-

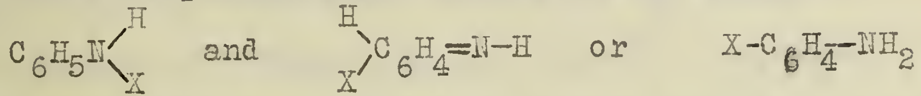
xydiphenyl amines, quinols, resorcinol ether, and polymeric benzylenimines. The mechanism of these changes Bamberger explains by the assumption that an unsaturated substance is first formed by the splitting off of water:



If this product is methylated in the para position a benzylenimin is formed:

The product usually recombines with water to form an iminoquinol which immediately rearranges into a p-aminophenol:

A number of reactions are given later[35] in support of his view that an unsaturated substance, $C_6H_5N\lt$, is the product first formed in the rearrangement of arylhydroxylamines. He cites that additive products are formed of the types



$C_6H_5N\lt{}^{H}_{X}$ and ${}^{H}_{X}\gt C_6H_4{=}N{-}H$ or $X{-}C_6H_4{-}NH_2$

As an example of the first type may be mentioned the formation of ortho and para-aminodiphenylamine by the action of aniline on phenylhydroxylamine. As an example of the second type is the formation of p-aminophenolsulphonic acid by the action of sulphuric acid on phenylhydroxylamines.

(h). Rearrangement of Phenylsulphamic Acid.

The rearrangement of phenylsulphamic acid was investigated during the same period by Bamberger and Hinderman[36]. They found that sulphur dioxide converts phenylhydroxylamine into a

mixture of phenylsulphamic acid and orthoamidobenzenesulphonic acids:

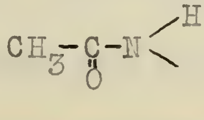
It was naturally supposed that the phenylsulphamic acid might be capable of transforming into the orthoamidobenzenesulphamic acid. Bariumphenylsulphamate was therefore prepared and heated at 180° for four and one half hours, but paraamidobenzenesulphamic acid was formed. A few months later Bamberger and Kunz[37] found that the potassium salt of phenylsulphamic acid is easily transformed into the corresponding ortho-acid when treated with acetic acid containing a few drops of concentrated sulphuric acid and kept at 0° for about eighty hours. It was further observed that the ortho-acid is transformed into the para-acid when heated with sulphuric acid for several hours. These changes indicate that the course of the reaction is conditioned by the temperature at which the substance is heated, and also by the strength of the mineral acid used. The mechanism of the preparation of sulphanilic acid may be explained in the light of the above changes and observations.

(i). The Migration of Halogens from Side chain Nitrogen to Nuclear Carbon.

The migration of halogens from side chain nitrogen to the benzene nucleus was first observed in 1886 by Bender[38]. He prepared acetchloranilide by treating a concentrated aqueous solution of acetanilide with a concentrated solution of bleaching powder in the presence of acetic acid. The compound when

recrystallized from dilute acetic acid melted at 91°, and when heated at 172° became yellow and effervesced violently (exploding if too large amount was used), and was changed into parachloracetanilide, melting at 172°. He also noted that the same change took place when the substance was warmed with absolute alcohol or treated with cold concentrated hydrochloric acid. The acetchloranilide was found to be stable towards rearrangement when treated with hot water, but rearrangement did take place if the substance was boiled in water for a long time.

In his study of the laws which govern substitution in benzene compounds, Armstrong[39] refers to Bender's preparation of acetchloranilide and its conversion into the isomeric parachloracetanilide. His experimental work led him to believe that the phenomenon of substitution in such compounds is not as simple as supposed, and that the isomeric change into derivatives of amines is a very common occurence. He believed that the reagents united directly with the nitrogen or oxygen, and that there came into play the residual valence of these atoms. He also suggested that during the change, " the centric benzene nucleus assumed momentarily the highly unstable ethenoid form".

In an earlier paper during the same year Armstrong[40] discusses the relative positions in the benzene ring taken by substituents when the nucleus is previously mono-substituted. He holds to the view of Kekule, that additive compounds are first formed in all cases of substitution by the union of the interacting substances. In his table illustrating the para-ortho-law, he includes the radical  $CH_3-\underset{\overset{\|}{O}}{C}-N{<}^{H}$ as one which

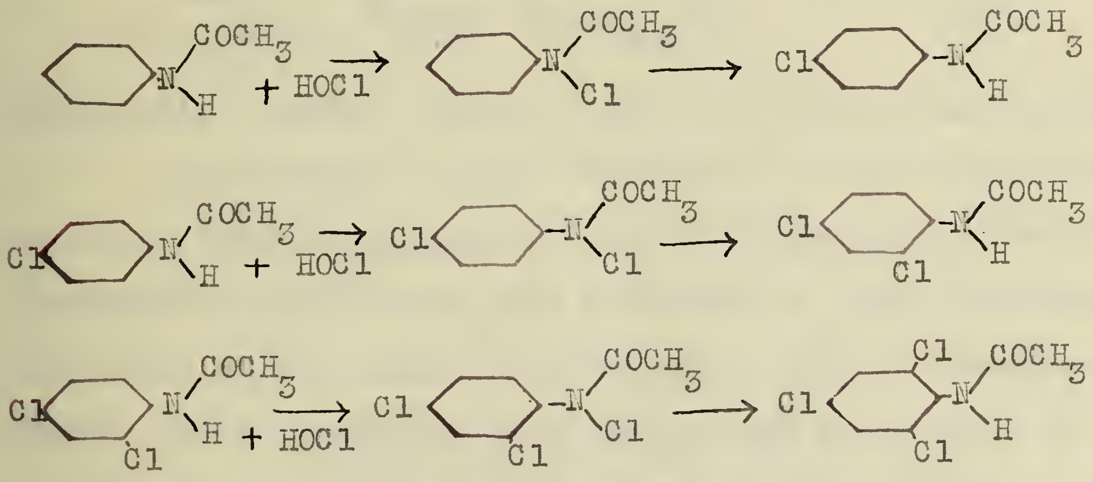
favors para and ortho substitution of halogens. " It will be noted that R", says he (referring to the radical originally in the ring)," in all compounds which obey the para-ortho-law is either a monad simple radical or a compound radical in which the grouping element of the radical is combined with one or more monad radicals; whereas in compounds subservient to the meta law the grouping element of the radical R is associated with one or more polyad atoms".

Morely[41] in a criticism of Armstrong's work held that basicity and negativity are the controlling factors in orientation. He advocated that the more "basylous" (basic) a radical is the more it will induce para and ortho substitution, and the more " chlorous " (negative) a radical is the more likely it will induce meta substitution.

In 1895 Slossen[42] also carried out a number of experiments involving the action of hydrobromous and hypochlorous acids on acid anilides. Phenylacetylchloramine and other similar types of compounds were prepared by treatment of acid anilides with hypochlorous acid. This acid was made by saturating a ten per cent solution of sodium carbonate with chlorine, the excess of chlorine being displaced by a current of air. In this way he was successful in obtaining the entire product as the nitrogen chloride. It was also noted that the slightest amount of acetic acid, as used by Bender, would cause rearrangement of the nitrogen bromide, while no change took place if carbonic acid was used.

Several years later Chattaway and Orton[43] in their

study of substituted nitrogen chlorides, considered more thoroughly the rearrangement of this class of compounds. They found that the carbonic acid method used by Slossen was very general. It was observed that the chlorine atom migrated to the para position in the ring. They further noted that the halogen shifted to the ortho position if there was present originally a substituent in the para position; also, if the para position and one ortho position were occupied, the halogen went to the other ortho position. These workers never observed the simultaneous formation of both ortho and para compounds. The mechanism of this reaction they explained by the halogen first replacing a hydrogen of the imine ($>N-H$) or amine ($-N{<}^{H}_{H}$) group, then the subsequent migration of the halogen to the nucleus. This is practically the same view as held by Armstrong and his students. These changes may be represented as follows:



It was therefore held that the relative position of the nitrogen atom to the carbon atoms of the ring is the important factor which conditions the position taken up by the halogen. The presence of other groups did not exert any specific orientating influence. In all the cases investigated by these workers

[illegible]

$$[illegible]$$

$$[illegible]$$

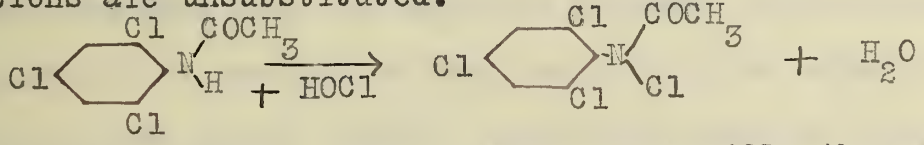
$$[illegible]$$

[illegible]

[illegible]

the rearrangement took place with ease. In some cases the reaction is so violent (as noted by Bender and also by Slossen), that it must be carried out under water. According to them, " The slightest amount of acetic acid causes the complete conversion of the substance into p-chloracetanilide". It is interesting to note, however, that Bender was able to recrystallize the substance from acetic acid solution.

During the same year Chattaway and Orton[44] worked with brom - substituted anilides and found the reactions similar to those of the corresponding chlor-compounds. In a later paper[45] the ease with which the hydrogen atom linked to the nitrogen atom is replaced with halogen is emphasized. It was observed that this hydrogen atom is replaced with just as much ease when the para and both ortho positions are substituted as when these positions are unsubstituted.



Bromination, however, takes place more rapidly than chlorination.

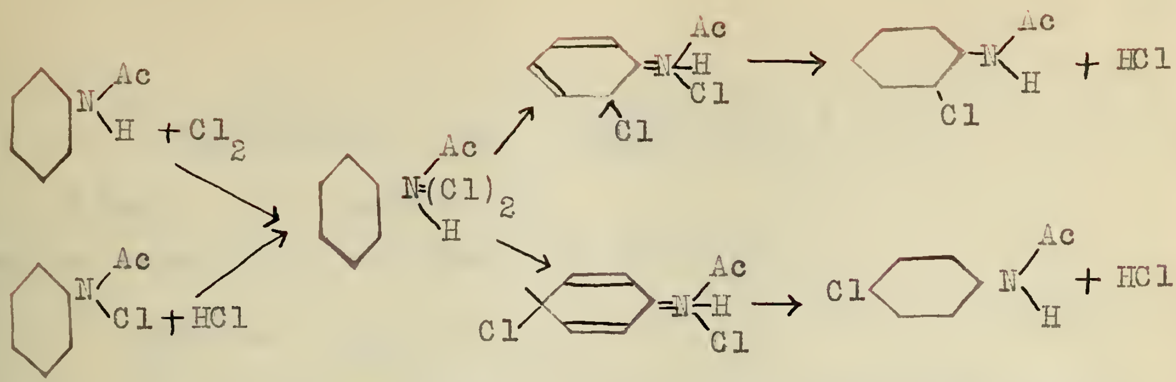
In reference to the complexity of the change which produces parachloracetanilide from phenylacetylchloramine, Armstrong[46] says: "It is very difficult to form any precise conception of the manner in which such 'isomeric changes' are brought about. Something more than a mere interchange of position of the radicals is involved in them; some agent intervenes; but the operation of the agent is easily overlooked, as only a minute quantity suffices in many cases, the action being "fermentative in character". He suggested that hydrogen chloride was

very probably the catalyst, because the nitrogen chloride was stable toward rearrangement so long as the acid was not present. This was found to be the case when Slossen's method was used;under such conditions the notrogen chloride was produced in alkaline solution. When purified from hot alcohol to which a little sodium acid carbonate or finely divided calcium carbonate had been added, the compound was unchanged after having been kept for several months in the dark. A drop of hydrochloric acid, however, caused rearrangement. Says he: "In attempting to explain the manner in which the isomeric change is effected, it appears legitimate to assume that it is dependent on the combination of the chloramine with hydrogen chloride. A condition of extreme instability is thus engendered, and probably the first consequent change is one in which an atom of chlorine attached to the nitrogen atom escapes from the molecule together with an atom of hydrogen from the nucleus; a chlorine atom then slips into the nucleus in place of the latter, whilst the atom of hydrogen introduced in the molecule of hydrogen chloride takes the place of the chlorine atom of the chloramine, the ortho- and para- derivatives being formed according to the conditions prevailing at the moment of change." Again he says "An increasing body of evidence tends to show that in the case in contemplation, the process of change is of a complex character and largely extramolecular - in that it involves the co-operation of several distinct molecules and their units in a conducting system."

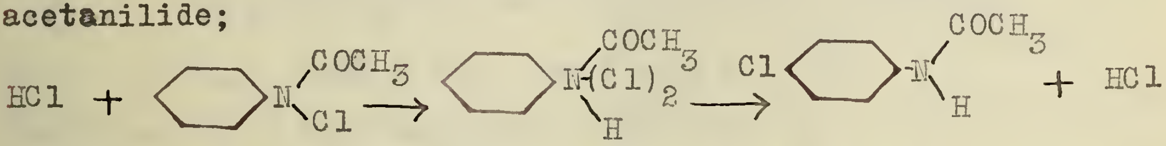
Thinking it very improbable that the rearrangement involved more than one molecule, Blanksma[47] was led to study the

velocity of the transformation. Acetchloranilide is transformed into p-chloracetanilide in the presence of hydrochloric acid. Since iodine is liberated from potassium iodide only by the former of the two compounds, the reaction was able to be followed quantitatively. He carried out the reaction at 25° in twenty per cent acetic acid and found the velocity constant to be that for a monomolecular reaction. Hence he concluded that the transformation was simply an intramolecular rearrangement of the atoms within the one molecule. In other words, only one compound underwent a change in concentration during the transformation. He also found that the speed was proportional to the square of the concentration of the hydrochloric acid, and that the speed is increased with the concentration of the acetic acid. He further noted that light increased the velocity of the reaction.

Chattaway and Orton[48] carried out similar experiments using acetchlor-p-chloranilide. Their observations confirmed the results of Blanksma in that hydrochloric acid has a specific action on the rearrangement of phenyl chloramines; that the velocity of transformation is monomolecular; also that light accelerates the reaction. The idea suggested itself to Orton[49] that the chlorine atom first forms an unstable additive product with the catalyst thus making the nitrogen atom pentavalent (a view suggested by Armstrong in 1887), whereupon the additive product immediately rearranges, and the benzene nucleus assumes the ortho or para quinoid form. During this rearrangement the halogen migrates to the ortho or para position:



Acree and Johnson[50] have elaborated Blanksma's work and have found that the transformation is not brought about by the mere presence of hydrogen ions, but that an unstable additive intermediate product is formed which rearranges into the halogen acetanilide;



In support of this view they show that acetchloraminobenzene rearranges one thousand times as fast in hydrobromic acid as in hydrochloric acid of the same concentration; that the velocity of rearrangement is much less in dilute acetic acid than when hydrochloric acid is present even though the acetic acid furnishes more (I.5 times as much) hydrogen ions than the hydrochloric acid; that the rearrangement takes place almost instantly in ligroin by chlorine and bromine; that pure acetchloraminobenzene may stand unchanged under dilute sulphuric acid for several days; that the positive ion CH CONHClC H is not the substance which rearranges into p-chloracetanilide, because if this were true the velocity of rearrangement would be proportional to the concentration of the hydrogen ions and would satisfy the following, from Walker's equation:

$$CH_3CO\overset{+}{N}HClC_6H_5 \rightleftharpoons CH_3CONClC_6H_5 + H^+$$

or $$K\,C_{salt} = C_{base} \times C_H$$

Then the velocity of rearrangement would be

$$\frac{dx}{dt} = C_{base} \times C_H ,$$

but this has not been found to be the case; that which does rearrange is an intermediate undissociated salt which is greatly hydrolysed, the amount present being so small that it is almost completely dissociated. From the mass law we have then,

$$CH_3CONHCl_2C_6H_5 \rightleftharpoons CH_3CONClC_6H_5 + H^+ + Cl^-$$

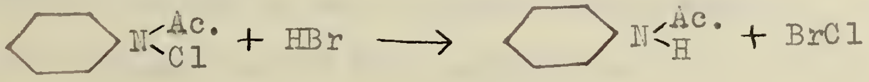
or $$K\,C_{salt} \times C_H + C_{Cl} = C_{base} \times C_H^2 .$$

The velocity of rearrangement then would be

$$\frac{dx}{dt} = K_{trans.} \times C_{salt} = \frac{K_{trans.} \times C_{base} \times C_H^2}{K}$$

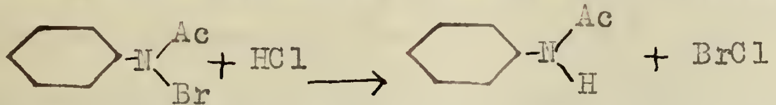
Acree and Johnson claim that this is what they found to be the case.

Subsequent investigation by Orton and Jones[51] with acetchloramino-p-chlorbenzene showed that the only catalyst is hydrochloric acid. The catalytic action of other acids also of bromine and chlorine, as mentioned by Acree, could not be confirmed. Chlorine and bromine did not react until hydrochloric acid was formed. They also found that the chloramines could not be directly brominated or chlorinated, for in glacial acetic acid hydrobromic acid reacts quantitatively with chloramines according to the following equation:

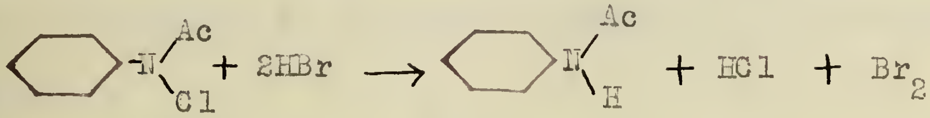


Now BrCl is a powerful brominating agent and hence a rapid

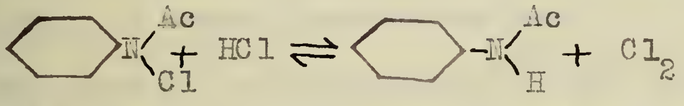
bromination (a dimolecular reaction) follows. A similar reaction was noted with an aromatic bromamine and hydrochloric acid, thus:



and direct bromination immediately followed. When the reaction is carried out in dilute acetic acid, it may be represented as follows:



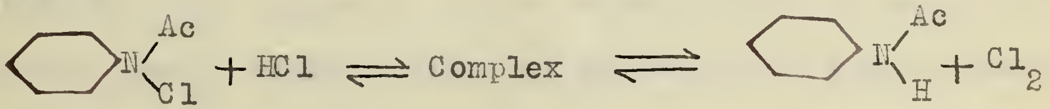
Direct bromination, in this case, follows slowly.



$$K = \frac{[\text{Chloramine}]\,[\text{HCl}]}{[\text{Anilide}]\,[\text{Cl}_2]}$$

While direct chlorination follows here. In the presence of glacial acetic acid the reaction is dimolecular and is driven completely to the right. If the acetic acid present is less than 65%, or if the concentration of the hydrochloric acid is small as compared with the amount of chloramine, the reaction is found to be monomolecular and proportional to the square of the concentration of the hydrochloric acid. No simple relation was found between the velocity of the change and the concentration of the catalyst in 70% to 90% acetic acid solutions.

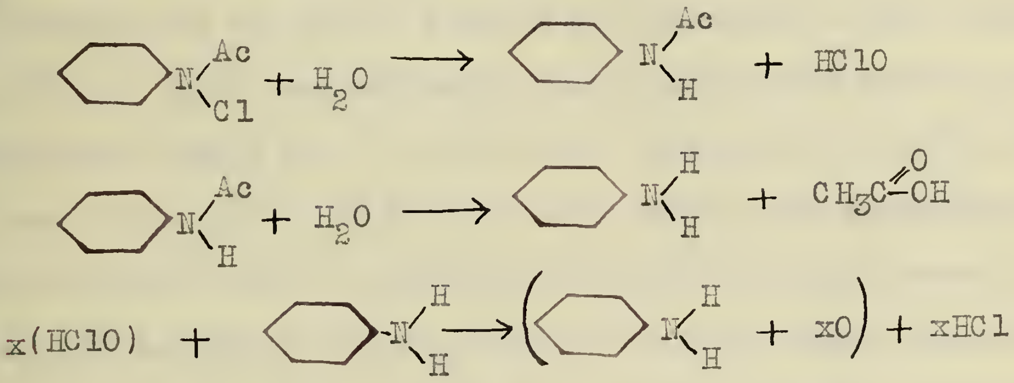
The equilibrium



suggested as a possibility by Acree involves the formation of an intermediate compound which Orton and Jones think unnecessary although their results do not exclude its existence. It was found also that the properties of the complex must vary in the case of

different anilides; that the concentration of the complex varies with the composition of the medium; and that not only the constitution of the anilide but also the composition of the medium conditions the speed of transformation of the intermediate complex into chloranilides. They conclude that " To avoid such a number of arbitrary assumptions it seems at least simpler to regard chlorination as occuring directly and not by way of such a complex ".

Chattaway and Gray[52] subsequently investigated the behavior of acetchloraminobenzene in aqueous solution and found that when the concentration of the catalyst is very small, the main reactions are hydrolysis and reduction of hypochlorous acid:



There is, however, a slight transformation of chloramine into chloranilide but the change is "quite subsidiary". It was further noted that larger concentration of hydrochloric acid furnished more chlorine due to the reaction

and hence when chlorine and anilide are present in high concentrations the main reaction is the transformation into chloranilide. It was also found that high concentration of other acids did not cause a similar change in the reaction as did

hydrochloric acid.

The velocity of the rearrangement of acetochloranilide into p-chloracetanilide was investigated a few years later by Rivett[53]. The reaction was carried out at first in aqueous solution using various concentrations of hydrochloric acid as the catalyst. He found the reaction to be monomolecular, and that the velocity increased with the increase of the hydrochloric acid concentration. It was held that only the non-ionized acid exerted the catalytic action. The relation between the velocity constant and concentration of the acid is expressed by the equation $K=(I-\alpha)\ C\ (A+B\alpha C)$ where K is the velocity constant, α the degree of dissociation of the acid, and C the concentration of the acid. A and B are constants whose values are 0.050 and 0.22 respectively. The reaction was carried out at a temperature range of 0 - 30° and the temperature coefficient was found to be 3.27 for I0° over said range. The transformation was also carried out in solutions of acetic, trichloracetic, oxalic, and sulphuric acids. In none of these cases could constant values be obtained for K. The effect of adding chlorides of lithium, sodium, potassium, rubudium, caesium, ammonium, magnesium, calcium, barium, strontium, and zinc to the solution was also studied. The effect of sulphuric acid was also investigated. It was found, in these cases, that the velocity constant could be calculated from the equation

$$K = (HCl)\left[0.050 + a(H^+) + b(Cl^-) + d(M^+)\right]$$

where the specific constants a , b , and d , depend upon the

nature of the ions.

(j). Migration of Acyl Group from Side chain Nitrogen to Nuclear Carbon.

It has been observed by Chattaway[54] that an acyl group may also migrate to the benzene nucleus. This happens, however, only in the case of the diacetanilides. Chattaway found that the rearrangements take place only at somewhat high temperatures and under the influence of catalysts, zinc chloride, and hydrochloric acid being most effective. The yield of the ketones formed from the transformation were found to be very poor, due perhaps to the simultaneous formation of resinous and tarry products. There were indications of the corresponding ortho derivative being formed in the transformation but it could not be isolated. Klingel[55] prepared p-aminoacetophenone by using a mixture of acetanilide and acetic anhydride. He regarded the reaction as a direct substitution of the acetyl group into the ring without the formation of an intermediate product. Chattaways observations, however, support the view that a diacetanilide is first formed which in turn rearranges to the corresponding ketone. Chattaway and Lewis[56] showed that the benzoyl group could also rearrange from the amine nitrogen. In thier experiments with dibenzoyltoluidines, they found analogous transformations into isomeric benzoylaminomethyl benzophenones. The temperature at which transformation best takes place is higher, (being about 230°) than the temperature necessary to effect rearrangements in the case of the diacetanilides.

2. The Hofmann Rearrangement.

In an attempt to prepare a blue or violet dye which would rival the one of Hofmann, Bardy[57] (the chemical director of Poirrier and Chappat's Aniline factory in Paris) made use of methyl and dimethyl aniline.These substances were prepared by heating mixtures of aniline hydrochloride and methyl alcohol in an autoclave at 250-300° for three to four hours. No particular attention was given to the by-product which was formed during the reaction.

The results of Bardy were confirmed a few years later by Hofmann[58] whose careful investigations led to observations of great theoretical and industrial importance. Ten kilos of aniline hydrochloride were treated with six kilos of methyl alcohol and the mixture heated in a large autoclave from eight to ten hours at 280-300°. The reaction product was then treated with sodium hydroxide and subjected to steam distillation. There was obtained an oil distilling at 200° which consisted of a mixture of methyl and dimethyl aniline. There was observed another substance a higher boiling oil to which the French investigators gave little attention as they were interested especially in the industrial importance of the oil distilling at 200°. As regards this by-product these French investigators satisfied themselves by saying that in this process there are formed high boiling polymeric compounds. Hofmann was led to believe that after the amine group had been completely methylated the benzene nucleus was next attacked. In order to prove this he heated the hydrochlor-

ides of the methyl and dimethyl aniline obtained in the first operation with an excess of methyl alcohol in an autoclave at 300° for twelve hours. The reaction product was treated with sodium hydroxide and subjected to steam distillation as before, but there was obtained in this case an oil which distilled at 2I0-300°. The separation of the constituents of this oily mixture by fractional distillation alone proved futile. Treatment with platinum chloride produced an oily salt which crystallized very slowly. However, when this oil was treated with methyl iodide, crystalline iodides were formed, which upon treatment with silver oxide gave alkaline hydroxy compounds showing the presence of tertiary bases. Undoubtedly primary and secondary bases were also formed, but perhaps were overlooked. These iodides were recrystallized from alcohol and changed into the corresponding chlorides by treatment with silver chloride. The chlorides thus formed were converted into platinum salts which, upon analysis, gave results which proved that hydrogens of benzene nucleus had been replaced by methyl groups. There was thus obtained the following series of bases: dimethyl aniline from the fraction distilling at I96 - 200°; dimethyltoluidine from the fraction distilling at 209 - 2II°; dimethylxylidine from the fraction distilling at 2I8 - 222°; dimethyl cumidine from the fraction distilling at 225 - 230° and 240 - 245°; and dimethyl cymidine from the fraction distilling at 255 - 260° and 270 - 275°. The corresponding pentamethylated derivative was sought for in vain, probably due to its very slow power of crystallization. It was supposed that during the course of the

reaction methyl iodide and water were formed and that methyl iodide was the agent of substitution, the reaction going through the respective stages; aniline → methyl aniline → dimethylaniline → toluidines → xylidines → cumidines → cymidines. His experiments led him to believe that a quarternary compound (formed by the action of methyl iodide on the dimethyl derivative in question) was produced during the reaction.

During the next year Hofmann[59] investigated the quarternary compound and expected to obtain evidence relative to its formation under the conditions of his previous experiments. He also interested himself in the changes which this quaternary compound would undergo when heated at high temperatures under pressure. He expected the change to take place according to the following scheme: quaternary → tertiary → secondary → primary.

Trimethyl phenyl ammonium iodide was heated in a bomb tube at 200° but no change took place. The compound was then heated for a day at 220 - 230° and also at higher temperatures which resulted in the formation of the hydriodes of tertiary, secondary, and primary bases respectively - the methyl groups having migrated to the benzene nucleus. The product thus formed at 220 - 230° when treated with alkali gave an oil which distilled at 200-280°. A fraction distilling at 186° was finally obtained which, upon analysis, was found to be dimethyl toluidine. The quarternary compound formed from it was found upon analysis to be trimethyltoluyl ammonium iodide. Fractional distillation did not completely separate the higher boiling portions. Fractions,

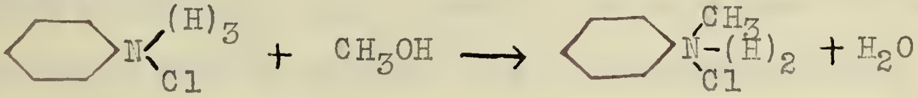
however, were collected at 200 - 203°, 203-208°, 208-212°, 212-220°, which, upon treatment with methyliodide, gave crystalline substances having the composition of trimethyl toluylammonium iodide. The corresponding quaternary hydroxide was formed by treatment with silver hydroxide and subjected to distillation whereby there was obtained an oil distilling at 205° and having the same composition of the dimethyl toluidine distilling at 186°. Hofmann concluded, therefore, that two isomeric toluidines are formed by the action of heat upon trimethylphenylammonium iodide.

The fractions distilling at 203 - 220° were treated with methyl iodide; there was thus formed the crystalline trimethyl toluylammonium iodide, also a substance which reacted with methyl iodide with difficulty. This substance distilled at 196° and upon analysis was found to be dimethylxylidine.

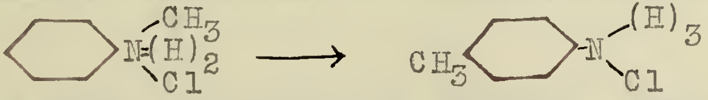
Trimethyl phenyl ammonium iodide was then heated at 335°. When the resulting product was treated with water and the acid solution subjected to steam distillation there was obtained a mixture of liquid and solid hydrocarbons. The residue, when treated with caustic soda and then distilled, yielded a mixture of substances of an oily nature, the principal portion of which distilled at 217 - 230°. This portion was again distilled, fractions being made at 217 - 223°, 223 - 225°, 225 -228°, and 226 - 228°, all of these fractions furnished crystalline hydrochlorides. Analysis of all the platinum salts led to the same formula $C_6H_2(CH_3)_3NH_2$, thus indicating the possibility of isomeric cumidines. These salts were decomposed and an oil was

obtained distilling at 225-227° which was found to be a cumidine. Methylation of this substance showed it to be a primary base. The dimethyl cumidine so obtained distilled at 213-214°, and under no condition could it be made to react with methyl iodide to form the corresponding quarternary compound. Hofmann suggested that the inability of the dimethyl cumidine to react with methyl iodide must be connected in some way with the arrangement of the atoms in the molecule.

During the same year Hofmann[60] investigated the influence of heat on methyl aniline hydrochloride. Aniline hydrochloride was heated with methyl alcohol for several hours at 230-250° and there was formed a honey-like mass consisting mainly of methyl aniline hydrochloride:



The tube was then heated at 350° for a day whereby a crystalline hydrochloride was formed by rearrangement as follows:



In other words, methyl aniline was transformed into toluidine. The purified toluidine melted at 45°. A similar experiment with methyl aniline hydrochloride was carried out but only liquid substances were formed; no evidence of a crystalline toluidine was observed. Higher alkylated anilines[61] were also studied in a similar manner. Ethyl aniline hydrochloride was heated at 300-330° under pressure for a period of twelve to eighteen hours: there was formed a mixture of the hydrochlorides of the two bases which upon analysis of their platinum salts were shown to

have the formulae:

$$C_6H_5(C_2H_5)NH_2HCl \quad \text{and} \quad C_6H_3(C_2H_5)NH_2Cl$$

The same mono-substituted compound was earlier prepared by Beilstein and Kuhlberg[62] by the nitration and subsequent reduction of ethyl benzene. Amyl aniline hydrochloride, when heated at 300-340° under pressure for twelve hours, rearranged in an analogous manner, and analysis showed the resulting hydrochloride to have the formula:

$$C_6H_4(C_5H_{II})NH_2HCl$$

Diphenyl amine hydrochloride was prepared and heated for a day at 360° but no rearrangement took place. Tetramethyl ammonium iodide was likewise heated at the same temperature for a day but it too remained unchanged. This, however, is very doubtful as several experiments carried out in this laboratory indicate that the quarternary iodide rearranges more readily and at a lower temperature than does the corresponding quarternary chloride.

In a later investigation Hofmann[63] showed that the cumidine which he obtained three years previous is identical with the one which is obtained by nitration and subsequent reduction of mesitylene, and it was proved to be mesidine. Both substances had the same boiling point, 225 - 226°, and smell. Both substances also yield a red compound when heated with mercuric chloride in the presence of aniline.

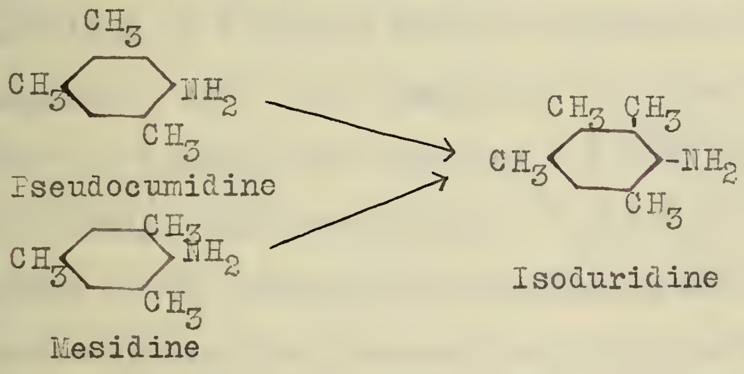
A few years later while investigating the derivatives of mesidine, Eisenberg[64] also confirmed the fact that Hofmann's cumidine was mesidine.

In 1882 Hofmann[65] prepared a cumidine by the action of methyl alcohol on xylidine hydrochloride. This cumidine had the same chemical and physical properties(m.p. 62°, b.p. 234°) as the one obtained by Schaper[66] by the nitration and subsequent reduction of pseudocumene. Cumidine was methylated whereby there was formed mono and dimethyl cumidine together with a small amount of the iodide of the ammonium base. By treatment with alkali the cumidine was set free, and the mono and dimethyl cumidine were separated by treatment with hydrochloric acid. The primary amine comes down as a crystalline salt while the secondary and tertiary remain in the mother liquor as soluble hydrochlorides. The solution was treated with alkali setting free the secondary and tertiary compounds, and on cooling, the mono methylated (secondary) base is obtained as a crystalline compound.

Sometime later Hofmann[67] investigated an oil which was simultaneously formed during the preparation of large amounts of solid cumidine. This crude oil boiled at 240 - 300°. Hofmann thought that since cumidine was formed by the methylation of xylidine hydrochloide, this oil would probably contain methylated homologues of cumidine. Among the several products obtained was a pale yellow oil which distilled at 252 - 253° and which upon analysis was found to be tetramethyl aniline melting at 14°.

During the next year Nölting and Baumann[68] undertook the study of the same reaction. Pseudo cumidine hydrochloride was heated in a sealed tube with methyl alcohol for ten hours

at 200 , and also for ten to twelve hours at 300°. From the resulting product there was obtained a liquid primary base which when purified by fractionation distilled at 250° and solidified to a crystalline mass when cold. Analysis of the hydrochloride and platinum salt showed it to be tetramethylamidobenzene. A similar experiment with mesidine hydrochloride and methyl alcohol gave the same tetramethylamidobenzene. These tetramethyl amino benzenes were found to be identical with the one which Hofmann obtained from the higher boiling products in the preparation of the crystalline cumidine. Diazotization of these tetramethyl amino benzenes gave phenols which melted at 80 - 81° and which were identical with the tetramethyl phenol obtained by Hofmann. Nölting and Baumann concluded that since the same bases are formed from pseudocumidine and mesidine, they must be derivatives of isodurol and may be called isoduridine,



A few months later Hofmann[69] gave further study to cumidine. Dimethyl cumidine was prepared by refluxing a mixture of cumidine and methyl iodide on the water bath until the reaction was complete. At the end of the reaction the mixture which distilled at 220 - 230° consisted of methyl and dimethyl cumidine together with some unchanged cumidine. This was treated

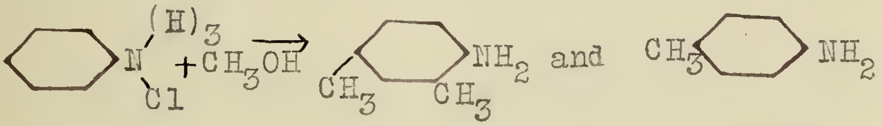
with methyl iodide and heated in a bomb at 240 - 250° for eight hours. From the reaction product, Hofmann obtained pentamethyl aniline melting at I5I - I52°, and distilling undecomposed at 277 - 278°, together with the hydrocarbon hexamethyl benzene. Attempts to prepare pentamethyl amino benzene from tetramethyl amino benzene in a similar way were unsuccessful.

During the latter part of the same year Nölting and Forel continued their investigation of the Hofmann rearrangement. Having prepared the six theoretical isomeric xylidines, they heated the hydrochlorides of the same with methyl alcohol in sealed tubes at 300-320°, whereby a rearrangement occured during which amino trimethyl benzenes were formed. α-orthoxylidine, $C_6H_3(\overset{1}{N}H_2)(\overset{3\cdot4}{C}H_3)_2$, gave a solid pseudocumidine, $C_6H_2(\overset{1}{N}H_2)(\overset{3\cdot4\cdot6}{C}H_3)_3$ together with a small amount of liquid isomers; vic-orthoxylidine $C_6H_3(\overset{1}{N}H_2)(\overset{2\cdot3}{C}H_3)_2$, gave a liquid amino trimethyl benzene which distilled at 240° (the acetyl derivative melted at I80° but further study of it was abandoned); α-metaxylidine, $C_6H_3(\overset{1}{N}H_2)(\overset{2\cdot4}{C}H_3)_2$, gave the crystalline mesidine $C_6H_2(\overset{1}{N}H_2)(\overset{2\cdot4\cdot6}{C}H_3)_3$ as already shown by Hofmann; vic-metaxylidine, $C_6H_3(\overset{1}{N}H_2)(\overset{2\cdot6}{C}H_3)_2$, gave the same glossy white crystalline mesidine; s-metaxylidine, $C_6H_3(\overset{1}{N}H_2)(\overset{3\cdot5}{C}H_3)_2$ gave a crystalline isocumidine which melted at 67-68° and distilled at 245°; paraxylidine, $C_6H_3(\overset{1}{N}H_2)(\overset{2\cdot5}{C}H_3)_2$, gave the crystalline cumidine $C_6H_2(\overset{1}{N}H_2)(\overset{2\cdot4\cdot5}{C}H_3)_3$.

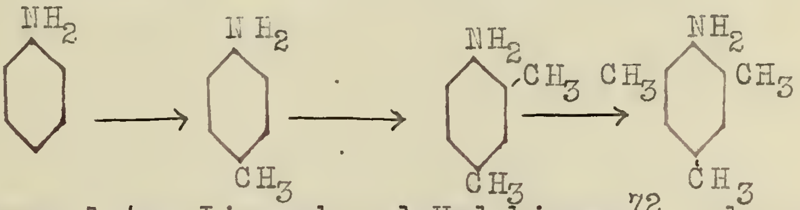
Three years later Limpach[7I] obtained isocumidine from symmetrical metaxylidine by the same method as used by Nolting and Forel, thus confirming the results obtained by the latter workers. The methylation, however, was carried further and there

was obtained Hofmann's amino pentamethyl benzene together with a new amino tetramethyl benzene $C_6H\overset{1}{(NH_2)}\overset{2\cdot3\cdot4\cdot5}{(CH_3)_4}$.

During the same year Limpach[71] also investigated the laws which govern the substitution of methyl groups into the benzene ring. The reaction was carried out in the usual way namely, by heating the amine hydrochloride with methyl alcohol under pressure at 250-300° for about twelve hours. Aniline hydrochloride and methyl alcohol gave I:2:4-metaxylidine and para-toluidine:

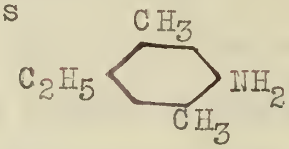


No traces of ortho- or meta-toluidine were observed. Both ortho- and para-toluidine hydrochlorides gave in a similar way I:2:4-meta-xylidine and mesidine. Attempts to further methylate mesidine were unsuccessful, and hence, contrary to the results obtained by Nölting and Baumann. Limpach concludes then, that the methyl group migrates first to the para position to form para-toluidine, then to one of the ortho positions giving rise to I:2:4-meta-xylidine, and finally to the other ortho position to give mesidine. The results of the rearrangement may be indicated as follows:



A few years later Limpach and Hodgkinson[72] made use of the Hofmann rearrangement in the preparation of ethyldimethylaminobenzene (ethylxylidine). Para-xylidine hydrochloride was heated with ethyl alcohol in an autoclave at 250-300° for six

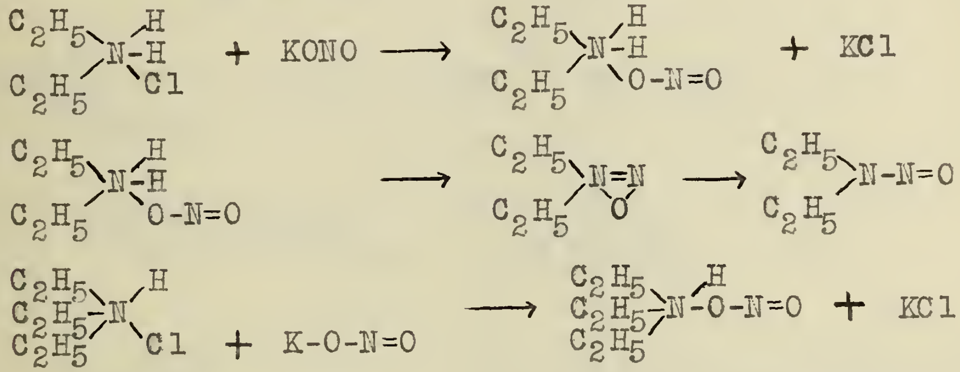
hours. The pure base thus formed distilled at 245-248°, and the formula proposed for the same is



The ethyl group migrated to the position para to the amino group.

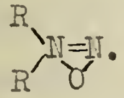
3. Separation and Determination of Amines.

The first method discovered for the separation of amines was the one of Heintz[73]. He treated a mixture of the hydrochlorides of diethyl- and triethylamine with a concentrated neutral solution of potassium nitrite, and upon distillation obtained nitrosodiethylamine.



He was also able to obtain pure nitrosodiethyl aniline according to the method of Geuther[74] by dissolving the distilled product in concentrated hydrochloric acid, with subsequent distillation in the presence of sodium hydroxide. In this way he obtained diethyl aniline entirely free from triethyl aniline. The mechanism of this reaction was not investigated by Heintz as he was interested mainly in the efficiency of the separation.

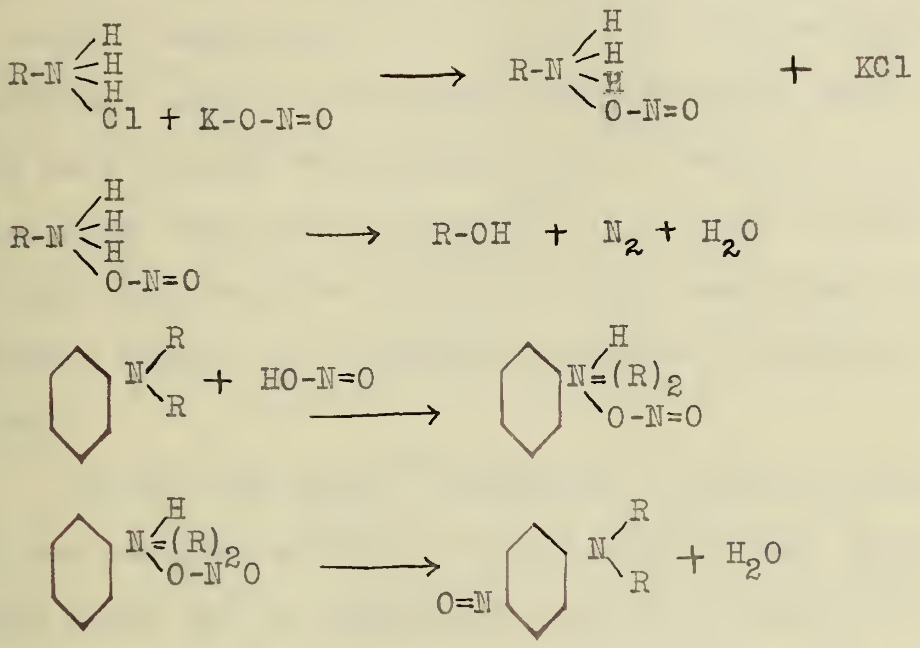
A good many years later Wallach[75] had occasion to investigate the nitrites of amines and was able to isolate all of the intermediate compounds as indicated above with the exception of



It was noted, however, that the isolation of these nitrites is conditioned by their formation in neutral solution. They are

readily decomposed by the slightest amount of acid.

As regards the action of nitrous acid on primary aliphatic amines and tertiary aromatic amines, the reactions may be indicated respectively as follows:



When a primary amine is present a nitrite is formed which, upon decomposition, evolves nitrogen. The secondary amines give nitrosamines when treated with nitrous acid; an intermediate nitrite is also formed in this case. Tertiary amines do not give any evidence of an appreciable reaction with nitrous acid. When all three amines are present in a mixture, the problem of separation by means of nitrous acid really concerns itself with the secondary and tertiary amines, as the primary is decomposed during the reaction. The separation is based upon the fact that treatment with hydrochloric acid forms the hydrochloride of the tertiary amine, while the nitroso derivative of the secondary amine is not attacked; the latter may then be extracted with

ether. The free tertiary amine may be obtained by treatment with alkali and extracting with ether.

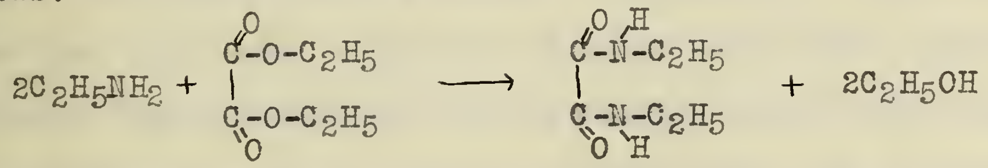
In their determination of the amines in plant extracts, Sachsse and Kormann[76] were the first investigators to determine primary amines by the amount of nitrogen evolved. Some years later König[77] makes use of this method in the determination of aminoacid- and acid amid-nitrogen. The apparatus which these workers used was not very simple and the results were not satisfactory. Some years later Fischer[78] in a study of amino acids found that they could be determined with ease upon treatment with either benzene or naphthalene sulphonyl chloride in alkaline solution.

In 1910 Van Slyke[79] developed a method which was simple, rapid, and accurate enough for very general use. The nitrogen in amino acids can be determined in a few minutes with an error within 0.05 mg. of nitrogen. The principle of the method is based upon the fact that in solution, nitrous acid decomposes spontaneously with the formation of nitric oxide according to the following equation:

$$2HNO_2 \rightleftharpoons HNO_3 + NO$$

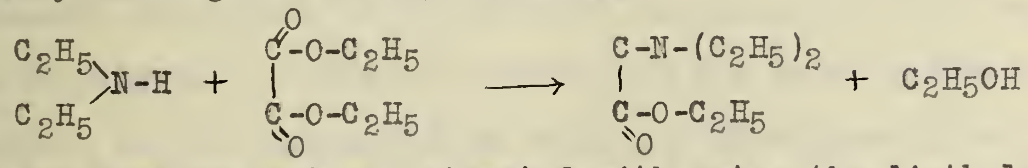
The air in the apparatus is displaced with nitric oxide. The solution to be examined is then introduced; nitrogen is evolved and mixes with nitric oxide. The bulb containing a solution of alkaline permanganate absorbs the nitric oxide, and the nitrogen is measured in a special gas burette. The method cannot be used, however, for the determination of nitrogen in aromatic amines.

It is of interest to note that Hofmann's[80] attempt to separate the three classes of ethyl amines by fractional distillation proved futile. Although the boiling points of the amines are far apart (I9°, 56°, and 90° respectively for ethyl-, diethyl- , and triethyl amine) the separation could not be made even though more than a kilo. of the mixed amines was used. It was suggested ("Organic Chemistry of Nitrogen" page I9) that this was perhaps due to the gradual falling off of their vapor pressures with the temperature. Very recently, however, Garner and Tyrer[8I] showed that a mixture of the three amines could be separated without difficulty by using a ten bulb fractionating column. They were able to obtain eighty per cent of pure diethyl amine by two fractional distillations. Hofmann found, however, that these amines when perfectly dry could be separated by treatment with dry ethyl oxalate. The triethyl amine does not react and may be distilled off. Ethyl amine gives diethyloxamide as follows:



$$2C_2H_5NH_2 + \begin{array}{l} \overset{O}{\overset{\|}{C}}\text{-}O\text{-}C_2H_5 \\ | \\ \underset{\|}{\underset{O}{C}}\text{-}O\text{-}C_2H_5 \end{array} \longrightarrow \begin{array}{l} \overset{O}{\overset{\|}{C}}\text{-}\overset{H}{N}\text{-}C_2H_5 \\ | \\ \underset{\|}{\underset{O}{C}}\text{-}\underset{H}{N}\text{-}C_2H_5 \end{array} + 2C_2H_5OH$$

Diethylamine gives diethyloxamethane:



$$\begin{array}{l} C_2H_5 \\ C_2H_5 \end{array}\!\!>N\text{-}H + \begin{array}{l} \overset{O}{\overset{\|}{C}}\text{-}O\text{-}C_2H_5 \\ | \\ \underset{\|}{\underset{O}{C}}\text{-}O\text{-}C_2H_5 \end{array} \longrightarrow \begin{array}{l} C\text{-}N\text{-}(C_2H_5)_2 \\ | \\ \underset{\|}{\underset{O}{C}}\text{-}O\text{-}C_2H_5 \end{array} + C_2H_5OH$$

If the mixture is then extracted with water the diethyloxamide dissolves but the ester does not. Saponification of the aqueous solution also of the water insoluble product thus liberates the primary and secondary amines.

Hofmann's[82] mustard oil reaction and isonitrile reaction for detecting primary amines are good for qualitative work but cannot be used when a quantitative separation is desired. Primary and secondary aliphatic amines react with carbon disulphide to give sulpho-carbamic acids as follows:

$$2RNH_2 + CS_2 \longrightarrow RNH-C-S-S-NH_3R$$

$$2R_2NH + CS_2 \longrightarrow R_2N-C-S-S-NH_2R_2$$

These salts when heated with mercuric chloride give an amine and mustard oil (isothiocyanate) which may be detected by its peculiar smell:

$$R-NHC=S=S-NH_3R \qquad R-N=C=S + R-NH_2 + H_2S$$

Aromatic amines react differently. The isonitrile reaction may be used both with alkyl and aryl primary amines. The amine is heated with chloroform and alcoholic potash and isonitrile with its peculiar smell is formed:

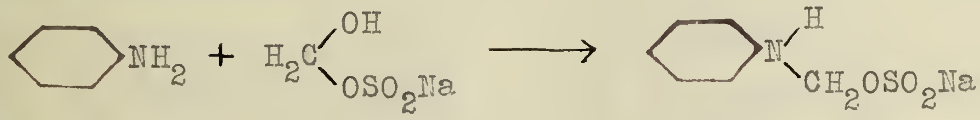
$$R-NH_2 + CHCl_3 \longrightarrow R-N-C + 3HCl.$$

Two years later Fischer[83] ,Eisenberg[84], and Chretein[85], found that when acid solutions of amine salts were treated with potassium ferrocyanide,difficulty soluble salts were formed which differed in their degree of solubility, the primary aromatic amine salt being the most soluble. This difference in solubility gave a means of separating the three classes of amines, as the corresponding salts are decomposed upon treatment with alkali with the formation of an alkaline ferrocyanide and the liberation of the free base which may be obtained by distillation. This method of separation is applicable to both aliphatic and aromatic amines. In the aliphatic series, however, the

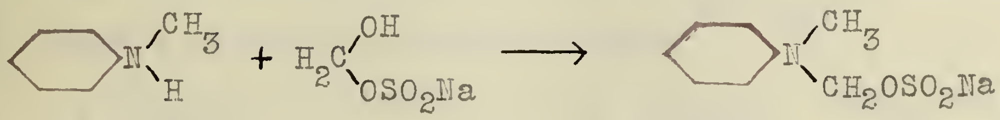
tertiary amine is the first to form a difficultly soluble ferrocyanide. If ammonium bases are present they may be isolated as carbonates by precipitation with carbon dioxide.

In I895 Delpine[86] developed a method for separating aliphatic amines which is based on the observations of Henry[87] namely; that methylamine reacts with formaldehyde to give the compound $(CH_2=N-Me)_3$ distilling at I66°; dimethylamine and formaldehyde form the compounds $HO-CH_2-N-Me_2$ and $CH_2-(N-Me_2)_2$ distilling at 80 - 85°; while trimethylamine is not attacked and distills at 9°. Fractional distillation then separates these amines efficiently. The free primary and secondary amines may be regenerated by boiling with an alcoholic solution of hydrochloric acid. He claimed this method to be more simple than Hofmann's ethoxalate method.

Some years later a modification of this method was applied to the aromatic amines when Bucherer[88] treated a mixture of aniline, methyline, and dimethylaniline with formaldehydesulphite. The dimethylaniline was not attacked and could be extracted with ether. Aniline and methylaniline reacted respectively as follows:



and

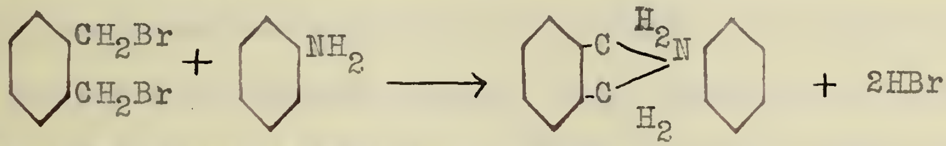


These salts were treated with sulphuric acid freeing the amines. Subsequent treatment with benzaldehyde bisulphite produced a

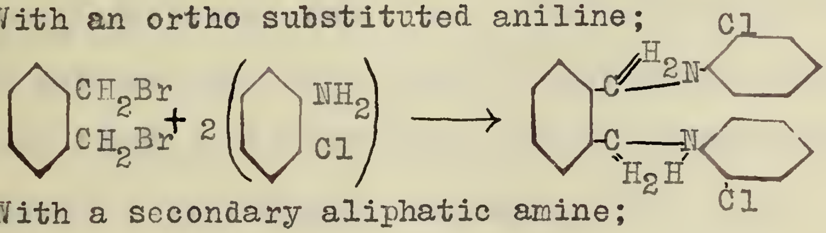
reaction with aniline but left the methylaniline unattacked, the latter being removed by ether extraction.

Several methods have been devised which are limited in the separation and determination of only one or two amines. Among these methods may be mentioned the determination of amines by the formation of the corresponding platinum salts as described in text books on analytical chemistry; the separation of a primary aromatic amine from the corresponding secondary and tertiary amines by precipitation of the former with citraconic acid as found by Michael[89] the separation of primary amines and diamines from other amines by precipitating the metaphosphates of the former in ether solution as discovered by Schlomann[90] the method of Scholtz and his students by which primary and secondary amines may be detected by the use of ortho xylidine dibromide. Several reactions involving the use of the last method may be given as follows:

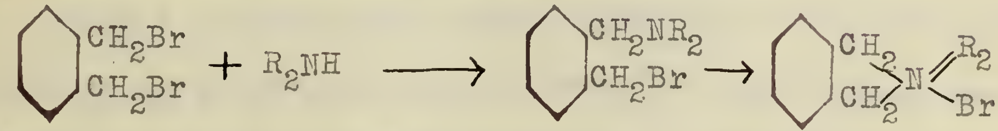
(a) With aniline;



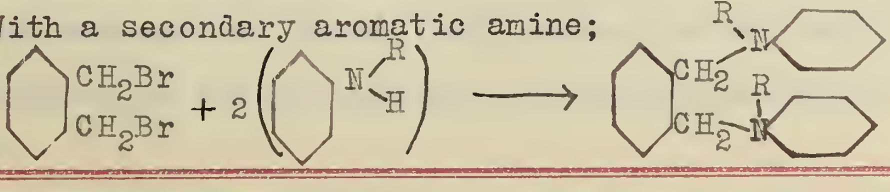
(b) With an ortho substituted aniline;



(c) With a secondary aliphatic amine;



(d) With a secondary aromatic amine;



(e) With tertiary amines substituted diammonium bromides are formed.

In 1903 Meunier[91] found that primary and secondary amines react with an etherial solution of magnesium ethyl iodide, evolving ethane according to the following equations:

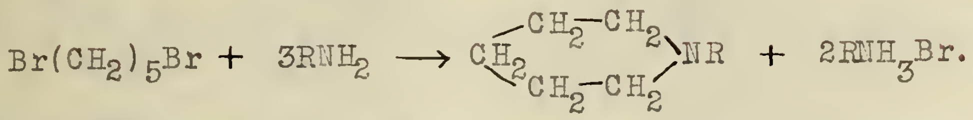
$$RNH_2 + C_2H_5Mgl \longrightarrow RNHMgl + C_2H_4$$
$$R_2NH + C_2H_5Mgl \longrightarrow R_2NMgl + C_2H_4$$

Tertiary amines were found not to react with organo-magnesium compounds.

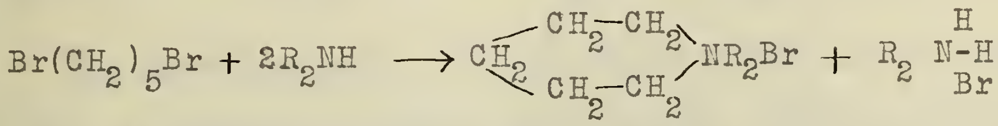
During the next year Sudborough and Hibbert[92] showed that the reaction proceeds quantitatively when carried out in amyl ether, but that two moles of gas are evolved if the mixture containing a primary amine is heated, while only one mole of gas is evolved in case a secondary amine is similarly treated. These observations[93] later furnished a method for the quantitative estimation of a mixture of primary and secondary amines even in the presence of a tertiary base, as the latter is not attacked by the organomagnesium compound even though it be heated at 125°. In 1914 Moureu and Mignonac applied this reaction to a number of amines of different types and obtained results which confirmed those of Meunier, and also those of Sudborough and Hibbert. The method was found to be a general one for distinguishing primary and secondary from tertiary amines.

Another method (with limitations) for determining the three classes of amines is that of Braun[94]. The reagent used is dibromo-n-pentane. He showed that primary amines having the nitrogen attached to an open chain, a heterocyclic carbon ring, or

a benzene ring in which there is no ortho substituent, react with reagents to give tertiary piperidines:



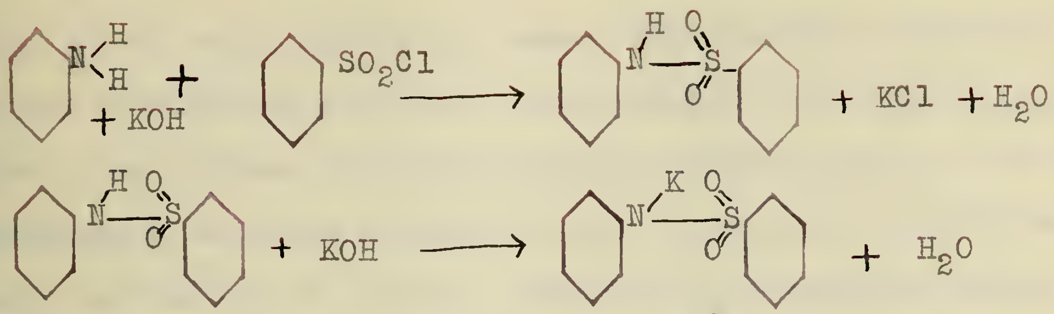
Pentamethylenediamine derivatives are formed if the benzene ring has one or both ortho positions substituted as shown by Scholtz and Wasserman[95]. Secondary amines of the aliphatic or piperidine series react to give quarternary piperidinium compounds:



Tertiary pentamethylenediamine bases are also formed in small amounts if secondary aromatic amines are present. Ortho substituted secondary amines, on the other hand, yield large amounts of these bases. Both aliphatic and aromatic tertiary amines form diammonium bromides:

$$Br(CH_2)_5Br + 2R_3N \longrightarrow NR_3Br(CH_2)_5NR_3Br.$$

In 1890 Hinsberg[96] devised a method, based upon the observations of Schotten[97] and also of Baumann and his students[98] which may be used for both the separation and determination of amines. If a quarternary amine is also present the primary, secondary, and tertiary amines may be separated from it by ether extraction or by steam distillation if volatile. The mixture of the three amines is then treated with benzenesulphonyl chloride in alkaline solution, whereby there is formed the sulphonyl derivative of the primary amine, the potassium salt of this primary derivative, and the sulphonyl derivative of the secondary amine according to the following equations:



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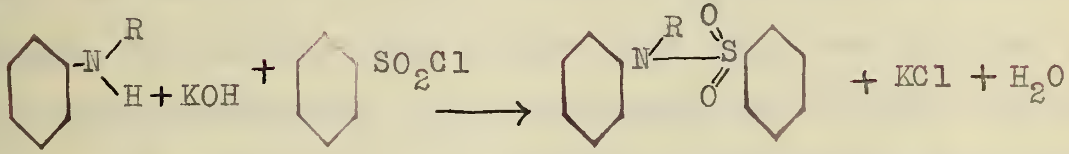


The tertiary amine is not attacked and may be extracted with ether or removed by steam distillation. Ether extraction also removes the sulphonyl derivative of the secondary amine. The ether solution is now treated with hydrochloric acid which forms the ether insoluble hydrochloride of the tertiary amine which may be easily separated from the unattacked secondary derivative. The sulphonyl derivative of the primary amine may be obtained by treating the original aqueous solution with hydrochloric acid and extracting with ether. Some years later Solonina[99] investigated the action of benzenesulphonyl chloride on a number of aliphatic and aromatic primary amines, and found that disulphonyl derivatives of the type $R\text{-}N\text{-}(SO_2C_6H_5)_2$ are formed when an excess of reagent is used. The derivatives of this type are insoluble in alkali, and Solonina concludes that Hinsberg's method, which depends upon the different solubilities of these reaction products in alkali, is inapplicable to the separation of amines.

In accord with these observations Hinsberg and Kessler[100] reinvestigated the method and made a few modifications which

avoided the difficulty pointed out by Salonina. The mixture of amines, after being throughly shaken with benzene sulphonyl chloride in alkaline solution, was refluxed with alcoholic sodium ethylate for fifteen minutes. By this procedure one of the benzenesulphonyl chloride groups was split from the disubstituted primary derivative and changed into the corresponding sodium salt $C_6H_5SO_3Na$. The solution was diluted with water and filtered from the secondary derivative. Upon acidifying the filtrate and extracting with ether the mono substituted derivative of the primary amine was recovered. The sulphonyl derivative of the secondary amine is not decomposed by this process. They also found that benzenesulphonyl derivatives of primary aliphatic or hydrocyclic amines which contain more than six carbon atoms, are insoluble in alkaline solution, and that they form sodium derivatives in ether solution which are insoluble in the latter. The separation of primary amines of this type from secondary amines was carried out successfully according to the modified method. The mixture of amines is shaken with the reagent in alkaline solution, then refluxed with sodium ethylate to destroy the disulphonyl derivative of the primary amine. The solution is diluted with water, hydrochloric acid added, and the mixture filtered. The dry sulphonyl derivatives are dissolved in anhydrous ether, metallic sodium added and the solution warmed on the water-bath for about eight hours. The sodium derivative of the primary amine is filtered and the sulphonyl derivative freed by treatment with hydrochloric acid. The sulphonyl derivative of the secondary amine is

obtained by evaporating the filtrate. A number of amines determined by the above method are the following:

Butylamine -------------------91.7%
Diethylamine-------------------95.1%

Amylamine---------------------85.4%
Piperidine--------------------90%

Pseudocumidine----------------95.5%
Diamylamine-------------------98.9%

Camphylamine------------------98%
Diethylamine------------------83.3%

Heptylamine-------------------99%
Piperidine--------------------92.8%

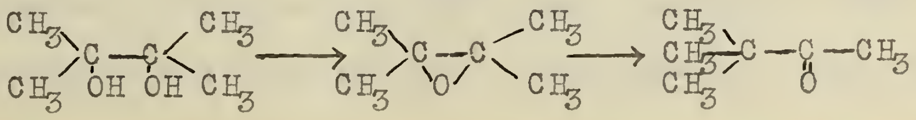
Camphylamine------------------87%
Methylaniline-----------------93.9%

The formation of crystalline benzenesulphonyl derivatives of primary and secondary amines, and the ease of their characterization, led us to decide that this method, with further modifications to increase its accuracy, was the most suitable for the separation and determination of the products that were expected from the rearrangement. A detailed description of our modification of the method is found in the experimental part of this thesis.

III - THEORETICAL.

III - THEORETICAL.

All intramolecular rearrangements may be considered as belonging to the reversible or non-reversible types of chemical reactions. In his study of the isomerism of formyl phenylacetic ester, Wislicenus[IOI] showed that ordinary temperature each isomer changes slowly into the other until equilibrium between the two is established, but that low temperatures the solid form was more readily produced while at high temperatures the liquid modification was more easily formed. He also found that equilibrium was dependent upon the nature and concentration of the solvent. These tautomeric changes illustrate intramolecular rearrangements of the reversible type. As an example of a rearrangement of the non-reversible type may be mentioned the change of the Δ^2 unsaturated acids into their Δ^1 isomers, the transformation being easily accomplished by boiling with alkalis. In the above cases of rearrangements it is noted that the transformation involves only a change of position of the atoms or groups already within the molecule. On the other hand certain rearrangements take place by the addition to or the splitting from the molecule of atoms or groups such as H, halogens, H_2O, N etc., whereby an intermediate substance is formed which is isomeric with the final product of the rearrangement. The well known change of pinacone into pinacolin by the splitting out of water is an example of this type of rearrangement:



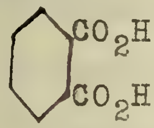
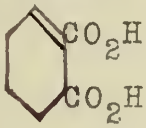
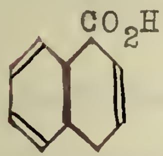
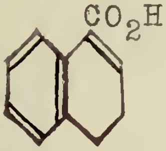
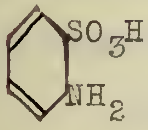
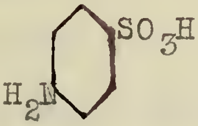
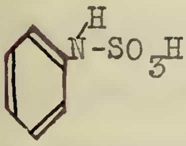
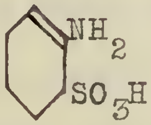
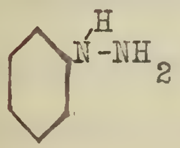
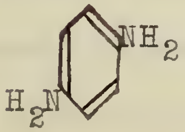
Rearrangements of the former class Derick[102] calls "rearrangements without reaction," while the latter class of rearrangements are termed "rearrangements with reaction."

A review of the many specific cases of intramolecular rearrangement shows that these transformations do not all take place with the same velocity. If left to themselves some compounds would require many years to affect a complete isomeric transformation, hence in many cases catalysts are used to accelerate the reaction. The catalysts sometimes used are hydroxyl ions, acids, heat, zinc chloride etc., as pointed out by Derick in one of his tables illustrating true rearrangements of the non-reversible type. Nernst[103] states that reaction velocity is an important factor to be considered in chemical transformations. Also that many organic compounds would not have seen the light of day had the reactions proceeded with greater velocity. In many cases this velocity may be determined by estimating the amount of substance changed in unit time.

It is perhaps generally accepted that true rearrangements of the non-reversible type take place in such a way as to produce substances more stable towards rearrangement. Phenyl hydrazine, for example, when heated in the presence of hydrochloric acid is unstable towards rearrangement and hence is readily transformed into p-phenylene diamine - an isomeric substance which is stable towards rearrangement. It is evident then that the initial unstable substance, under the conditions of the experiment, gradually changes into the final substance stable toward rearrangement, and that there is a decrease of free energy

in the transformation. Up to the present time it has been impossible to measure this decrease in free energy. In an attempt to discover a criterion of stability in such rearrangements Derick[I04] found that if the substance involved is an electrolyte, non-reversible intramolecular rearrangements took place in the direction to decrease the ionization constant. The logarithm of the ionization constant of acids and bases was chosen[I05] as a criterion of the possibility of rearrangement, that is, of the stability of compounds of this type. The following examples illustrate how well Derick's criterion holds for the substances before and after rearrangement:

Table I

Non-reversible Rearrangements		Ionization Constants at 25°			
		K		$\text{Log } K \times IO^{5}$	
Before	After	Before	After	Before	After
		$5.9 \times IO^{-4}$	$7.6 \times IO^{-5}$	I.772	0.882
		$I.I4 \times IO^{-4}$	$8.I4 \times IO^{-5}$	I.058	0.909
		$3.3 \times IO^{-3}$	$5.8I \times IO^{-4}$	2.5I9	I.764
		$I.0 \times IO^{-1}$	$3.3 \times IO^{-3}$	4.000	2.5I8
		$I.6 \times IO^{-9}$	$3.I \times IO^{-10}$	I.204	0.492

In order then to accertain the relative stability of two isomeric substances one has only to compare the logarithm of their ionization constants.

Fitcher and Pfister's[106] very general principle, that the Δ^{2} unsaturated acids of the aliphatic series have greater ionization constants than any of their isomers, increases the validity of Derick's principle that true rearrangements of the non-reversible type take place in the direction to decrease the free energy of ionization. A few examples will serve to illustrate this fact:

Table II

Name	Ionization constant K	 Log K × 10^{6}
Δ^{1}-Hexanoic acid	1.89×10^{-5}	1.277
Δ^{2}-Hexanoic acid	2.64×10^{-5}	1.428
Δ^{3}-Hexanoic acid	1.74×10^{-5}	1.241
Δ^{4}-Hexanoic acid	1.91×10^{-5}	1.282
Δ^{1}-Pentanoic acid	1.48×10^{-5}	1.172
Δ^{2}-Pentanoic acid	3.35×10^{-5}	1.526
Δ^{3}-Pentanoic acid	2.09×10^{-5}	1.322

Derick finds that this principle holds for unsaturated acids in both open chain and ring series. The Δ^{2} ring unsaturated acids, for example, formed by the reduction of the corresponding $\Delta^{1,3}$ unsaturated acids, are capable of rearranging into their Δ^{1} isomers. The numerous examples of such rearrangements in the literature led to the advancement of Thiele's partial valence

theory as an explanation of the fact that Δ^2 unsaturated acids are the direct reduction products of the corresponding $\Delta^{1,3}$ unsaturated acids. In the case of terephthalic acid it has been shown that when weak reducing agents are used and the reaction velocity kept slow the $\Delta^{2,5}$ unsaturated acid is formed. This acid has both double unions Δ^2 with respect to the carboxyl groups, and according to the principle of Fichter and Pfister would be most unstable toward rearrangement. This has been found to be the case. Derick summarizes by saying "Hence it is evident that the compounds from which Thiele deduced his theory of partial valence, as well as other acids which obey the same rule, must be compounds which are formed with weak reducing agents involving small energy changes and where the speed of reaction is small so that compounds result which are very unstable toward ionization, and therefore toward rearrangement".

In their investigation of aromatic (N) diacylamines Chattaway and his students[107] found that if the acyl radicals are formyl (HCO-), acetyl (CH_3CO-), propionyl (C_2H_5CO-), benzoyl (C_6H_5CO-), or any one of these acyl radicals with halogen, one acyl radical will rearrange to the benzene nucleus if the compound is treated with zinc chloride or hydrochloric acid gas. The latter substances merely catalyzed the reaction. This was proved by Blanksma[108] in his study of the rate of change of (N) chloracetanilide into p-chloracetanilide when he found the reaction to be monomolecular. In the course of their investigation Chattaway and Lewis state that "the transference of more than

one acyl group into the nucleus has, however, not yet been affected" and yet "this process of intramolecular rearrangements, which follows a precisely similar course to the other well known migrations of groups from the amine nitrogen atom into the ortho and para positions of the ring, could in all probability, be carried to the further stage in which two groups would be introduced into the nucleus". It is not clear from the above statements whether these investigators meant that one acyl group could be made to migrate to the nucleus as in the case of acetanilide, or whether both of the acetyl groups of diacetanilide are capable of rearranging into the ring. This led Derick and Bornmann[109] to further investigate the problem. The initial compounds and their rearranged products were prepared and their ionization constants determined. Their results are given in the following table:

Table III

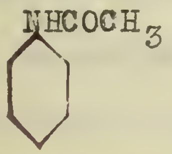
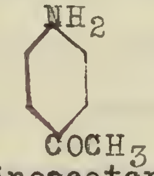
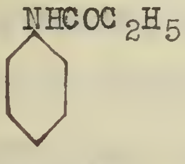
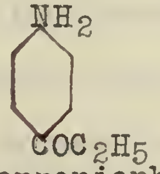
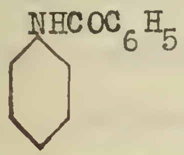
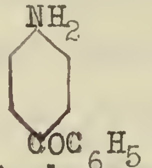
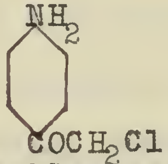
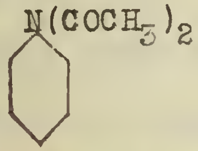
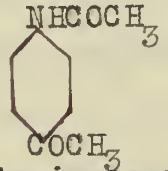
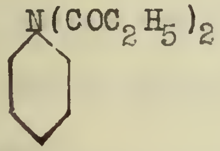
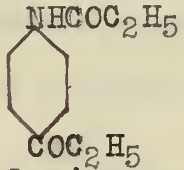
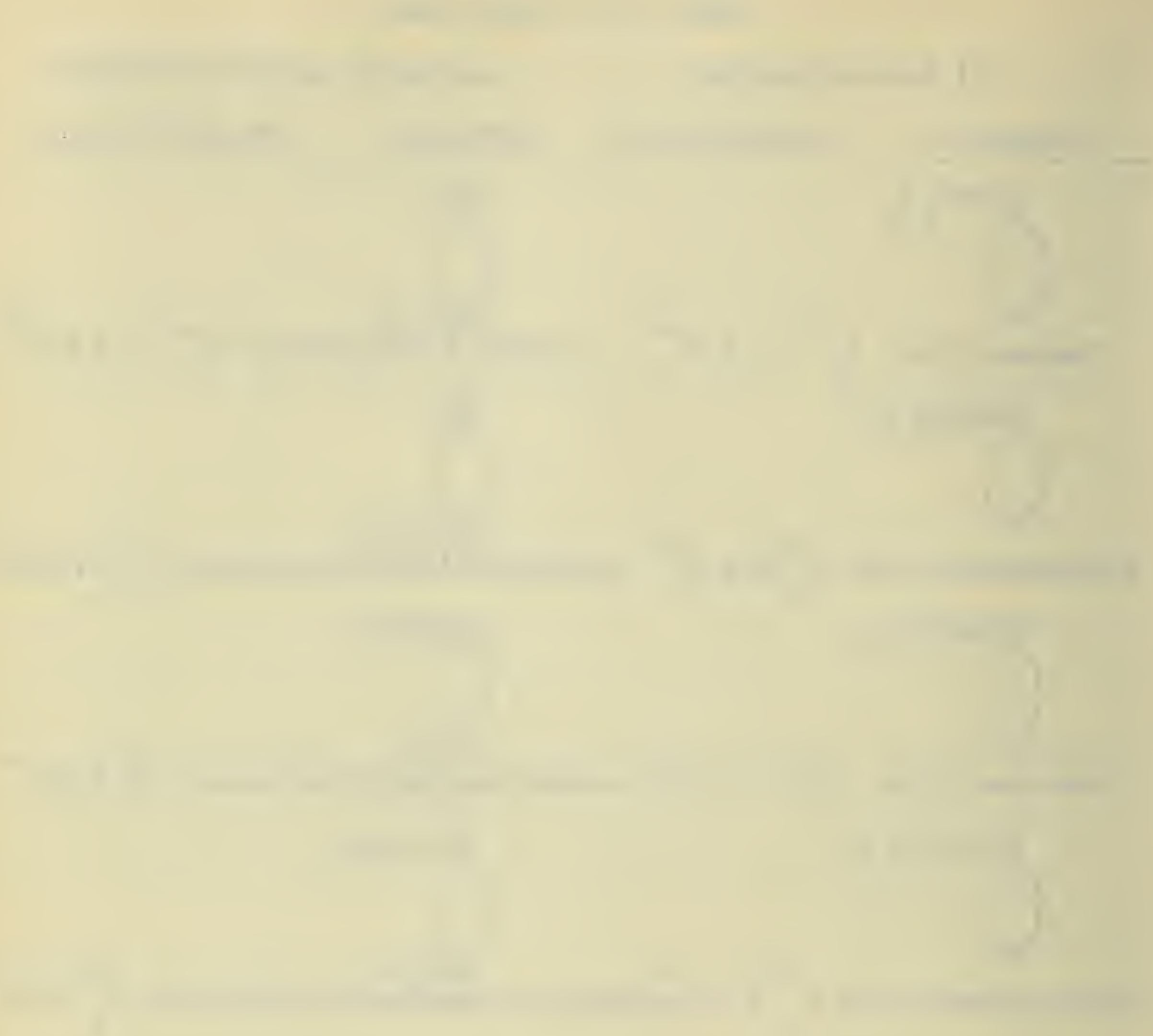
(N) Monoacylamine		Isomeric Acylaminoketone	
Compound	Ionization K.	Compound	Ionization K.
 Acetanilide	$k_b^{28°} = 1 \times 10^{-13}$	 p-Aminoacetophenone	$k_b^{29°} = 4.5 \times 10^{-10}$
 Propionanilide	$k_b^{30°} = 3 \times 10^{-13}$	 p-Aminopropiophenone	$k_b^{30°} = 2.4 \times 10^{-10}$

Table III (Continued)

(N) Monoacylamine		Isomeric Acylaminoketone	
Compound	Ionization K.	Compound	Ionization K.
 Benzanilide	$k_b^{26^\circ}\ 2 \times 10^{-13}$	 p-Aminobenzophenone	$k_b^{26^\circ} = 5.7 \times 10^{-10}$
 Chloracetanilide	$k_b^{26^\circ} = 2 \times 10^{-13}$	 p-Aminochloracetophenone	$k_b^{26^\circ} = 2.3 \times 10^{-10}$
 Diacetanilide	$k_b^{25^\circ} = 7 \times 10^{-13}$	 p-Acetylaminoacetophenone	$k_b^{25^\circ} = 2 \times 10^{-13}$
 Dipropionanilide	$k_b^{26.5^\circ} = 5\ 10^{-9}$	 p-Propionylaminopropiophenone	$k_b^{24^\circ} = 4 \times 10^{-12}$

From the it is seen that (N) diacylamines have greater ionization constants than the corresponding acylaminoketones, hence, according to Derick's criterion, rearrangements of the former into the latter are possible. Chattaway's experiments have found this to be the case. The table also shows that the monoacylamines have smaller ionization constants than their corresponding aminoketones. Rearrangement then of the former into the latter may be predicted to be impossible. This also has been found by Chattaway to be the case. Derick and Bornmann likewise found this to be the case for chloracetanilide. It may be stated



[illegible]

with certainty then that "the criterion for the possibility of non-reversible intramolecular rearrangements, namely that these rearrangements take place in the direction to decrease the ionization constant, holds for mono- and diacyl aromatic amines."

Referring to the migration of atoms or groups from N-substitution products of aniline to the benzene nucleus Sidgwick states[IIO] "It is remarkable that in nearly all of them a body of feebly basic or neutral or acidic character is converted into one of more pronounced basicity". This, however, is not necessarily the case, for example, the quarternary ammonium compounds are more basic than the corresponding rearranged products. Numerous other examples may also be given to show that Sidgwick's statement has no general application. Derick's criterion is a much better one for these rearrangements namely, that rearrangement takes place in the direction to decrease the ionization constant.

It is well known that the nitro and sulphonyl groups only require monosubstitution on the aminic nitrogen of aromatic amines for rearrangement to take place. It is evident then that some groups require disubstitution while others only require monosubstitution before rearrangement can occur. Since the ionization constant is influenced by the negative nature of the radical, Derick's study[III] of the polarity of over a hundred groups has given much light on this question. From a few examples in his negativity tables it may be seen how different groups affect the ionization. θ represents the negativity of each group in question :

Table IV

Radical	Formula	K	log K	θ
Formyl	$HCO-$	$k_a = 2.I4 \times IO^{-5}$	-3.670	272.4
Acetyl	CH_3CO-	$k_a = I.86 \times IO^{-5}$	-4.73I	2II.0
Propionyl	C_2H_5CO-	$k_a = I.45 \times IO^{-5}$	-4.839	206.0
Benzoyl	C_6H_5CO-	$k_a = 6.9 \times IO^{-5}$	-4.I6I	240.0
Phenyl	C_6H_5	$k_a = I.3 \times IO^{-10}$	-9.886	IOI.5
Ammonium	NH_4-	$k_b = I.87 \times IO^{-5}$	-4.738	2II.4
Methylammonium	CH_3NH_3-	$k_b = 5.00 \times IO^{-4}$	-3.300	302.8
Urea	NH_2CONH_3-	$k_b = I.5 \times IO^{-14}$	-I3.824	72.2
Phenylammonium	$C_6H_5NH_3-$	$k_b = 4.6 \times IO^{-10}$	-9.337	IO7.0

In light of the above results Derick and Bornmann conclude from their experimental study that those acyl radicals which have a negativity between 206 (the value for the propionyl group) and 355 (the value for the chloracetyl radical) require disubstitution upon the aminic nitrogen in aromatic amines in order that rearrangement into the corresponding acylaminoketones may take place. In other words, the acid radical of all acids having ionization constants between $I.45 \times IO^{-5}$ and $I.55 \times IO^{3}$ require disubstitution upon the aminic nitrogen atom of aromatic amines in order that rearrangement might occur. The ionization constant of phenylsuphamic acid is in the order of IO^{-1}, while those of the corresponding rearranged ortho and para acids at 25 are $3.3 \times IO^{-3}$ and $5.8I \times IO^{-4}$, respectively. One predicts then from Derick's criterion that phenylsulphamic acid may rearrange into aniline-ortho or aniline-para-sulphonic acid. The nitro

and sulphonyl radicals have each a negativity of about 750 and 740, respectively. It is obvious then that acyl radicals having negativities approaching 740 require only monosubstitution, while those whose negativities are between 206 and 355 require disubstitution upon the aminic nitrogen atom of aromatic amines before rearrangement into the corresponding acylaminoketones is possible. This limit, however, has not yet been definitely determined.

In their investigation with aromatic stereoisomeric acids Roth and Stoermer[II2] find Derick's criterion to hold. They find that the stable acids have lower heats of combustion, smaller dissociation constants, and are less soluble in water than the corresponding labile isomers as indicated in the following table:

Table V.

Acid	Heat of Combustion in kg. cal.	Disso. K $\times 10^{-5}$	No. of l. of H_2O at 25° req. to dissolve one mole of acid.
allo-Cinnamic ↓	I048	I4.I	I7.5
Cinnamic	I04I	3.8	270
Methylcumarinic ↓	II69	5.4	250
Methylcumaric	II62	2.I	2I20
Ethylcumarinic ↓	I324	4.5	333
Ethylcumaric	I3I8	2.I	2II0
Isoamylcumarinic ↓	I793	4.2	2070
Isoamylcumaric	I79I	I.4	II900
Acetylcumarinic ↓	I2I3	II	I80
Acetylcumaric	I209	5	I430

Table V (Continued)

Acid	Heat of Combustion in kg.cal.	Disso. K $\times 10^{-5}$	No. of l. of H_2O at 25° req. to dissolve one mole of acid.
allo-Piperonylacrylic	1078	10.91	400
↓			
Piperonylacrylic	1069	2.5	7000
allo-p-Hydroxycinnamic	998	8.44	41.6
↓			
p-Hydrocinnamic	992	2.34	126
allo-p-Methoxycinnamic	1174	9.29	90.6
↓			
p-Methoxycinnamic	1164	2.1	2500

The arrow indicates the direction of the non-reversible intramolecular rearrangement.

The results obtained in his study of aromatic acyl amines has led Derick to investigate other aromatic amines with the purpose of seeking further evidence which would confirm his criterion of stability and rearrangement. The present investigation deals with the mechanism of the rearrangement of alkyl anilines.

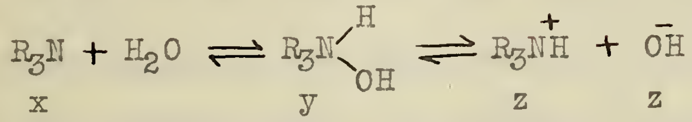
The rearrangement of alkyl anilines was first investigated by Hofmann after whom it was named. It belongs to the class of true intramolecular non-reversible rearrangements and consists of the transformation of methylaniline hydrochloride into p-toluidine hydrochloride under the influence of heat. The mechanism suggested by Hofmann was that the process consisted of two phases. First, methyl chloride split off from one molecule of methylaniline hydrochloride and then added again to a second molecule forming dimethylaniline hydrochloride. Methyl

chloride is therefore, the agent of substitution into the benzene ring to form the toluidines, xylidines, cumidines, and cymidines. If trimethylphenylammoniumiodide is used as the "ausgangs" material he says that the methyl groups "wander" from the nitrogen atom into the ring to form tertiary, secondary, and primary amines.

An hypothesis has been advanced below, in light of the results obtained from investigations with aromatic acyl amines, and has received partial substantiation by the work of Derick and Howard and in the experimental part of this thesis. Since disubstitution of acyl groups upon the aminic nitrogen of aromatic amines is necessary in order to produce compounds that can rearrange, and since such disubstituted compounds are electrolytes whose ionization constants are several thousand times as strong as the ionization constants of the rearranged products, similar changes would be expected with aromatic alkyl amines before rearrangement would occur. A table which follows gives the ionization constants of methylated anilines and their possible rearranged products - the toluidines. It may be pointed out, however, that the ionization constants given (with the exception of the value for phenyltrimethylammonium hydroxide) are not the true but the apparent ionization constants. The values that should be used are the ones at the temperature of rearrangement, but as they are unknown we simply offer in a qualitative way their values at ordinary temperature where they have been measured.

When a primary, secondary, or tertiary amine is dis-

solved in water two changes take place. Water adds to the amine to form the quarternary hydroxide, and the latter undergoes an electrolytic dissociation according to the following scheme:



$$\underset{x}{R_3N} + H_2O \rightleftharpoons \underset{y}{R_3N\begin{smallmatrix}H\\OH\end{smallmatrix}} \rightleftharpoons \underset{z}{R_3\overset{+}{N}H} + \underset{z}{\overset{-}{O}H}$$

where x is the concentration of the amine, y the concentration of the hydrated amine, and z the concentration of the ions.

Then $\frac{x}{y}$ = constant, $= b$; $x = by$;

and from Ostwald's law $\frac{z^2}{y} = K$.

This K represents the real strength of the base. Ordinarily, the concentration of the ions is measured in a solution in which the total concentration of all three forms of the base is known, the first and non-hydrated form being neglected. It is evident that such a calculation does not give the true ionization constant K, but the apparent ionization constant K_1. Accordingly

$$K_1 = \frac{z^2}{x + y}.$$

Substituting the value for x, we have

$$K_1 = \frac{z^2}{by + y} = \frac{z^2}{y(b + I)} = \frac{z^2}{y} \times \frac{I}{b + I}.$$

Therefore $K_1 = K \times \frac{I}{b + I}$.

The apparent ionization constant then is smaller than the true ionization constant, and the more so the greater the proportion of anhydrous amine present. There are very little hydrochlorides of these amines present at the high temperature at

which the rearrangements are carried out, so we will be dealing mainly with the free amines. The relative values for the true ionization constants then will be little affected.

It may be pointed out that Moore[113] has solved the problem of determining the value of the true ionization constant separate and distinct from the hydration constant. By measuring the partition coefficients and the degree of dissociation at different temperatures, and by making the assumption that the temperature coefficients of these two quantities are constant (which is justifiable for small differences of temperature), he obtained a sufficient number of equations to solve the problem and to determine for any amine the true dissociation constant and the amount of non-hydrated form present. His results show that in aqueous solution at 20°, two thirds of the ammonia is present in the non-hydrated form NH_3, the remainder consisting mainly of NH_4OH and a small amount of ions; in the case of triethylamine only about one third is present in the non-hydrated form $(C_2H_5)_3N$. The true dissociation constants calculated at 20° for these two bases are:

Ammonia ---------- True K $= 5.23 \times 10^{-5}$.

Triethylamine----- True K $= 64 \times 10^{-5}$.

The introduction of three ethyl groups into ammonia has increased the ionization constant only twelve times. The introduction of a fourth ethyl group, however, greatly increases the basicity of the base and the resulting quarternary hydroxide has an ionization constant whose value is greater than I. An analogous behavior would therefore be expected when the hy-

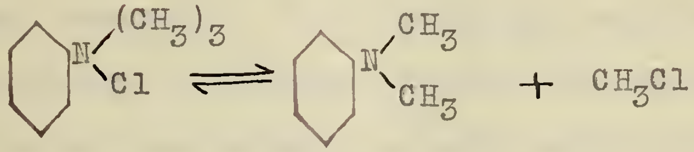
drogen atoms linked to the nitrogen atom of aniline hydroxide are replaced with alkyl radicals.

Table VI.

Compound	Ionization K
Methyl aniline	$k_b^{18°} = 2.55 \times 10^{-10}$
Dimethyl aniline	$k_b^{18°} = 2.42 \times 10^{-10}$
Phenyltrimethylammonium hydroxide	$k_b^{18°} = > 1$
Ortho-toluidine	$k_b^{18°} = 3.0 \times 10^{-10}$
Meta-toluidine	$k_b^{15°} = 3.9 \times 10^{-10}$
Para-toluidine	$k_b^{18°} = 1.6 \times 10^{-9}$
Dimethyl-o-toluidine	$k_b^{15°} = 3.08 \times 10^{-9}$
Dimethyl-m-toluidine	$k_b^{25°} = 2.4 \times 10^{-9}$
Dimethyl-p-toluidine	$k_b^{15°} = 6.36 \times 10^{-9}$

It is noticed that no great change takes place in the ionization constants of the methylated anilines and their corresponding rearranged products until the quarternary stage is reached. Hence the hypothesis is advanced that *rearrangement only occurs in the quarternary stage and all classes of alkyl anilines must change into this stage before rearrangement is possible.* Accordingly, several experiments were carried out in which methyl aniline hydrochloride and phenyltrimethylammonium chloride were heated at different temperatures and for different periods of time. Upon analysis of the bomb products various classes of amines were obtained as a result of the rearrangement. The quarternary compound has been isolated as a result of heating methyl aniline hydrochloride at 290-300° for one week and furnishes suffi-

cient evidence to support the hypothesis advanced. When phenyltrimethylammonium chloride is heated below 300° the main reaction which takes place is dissociation according to the following equilibrium:

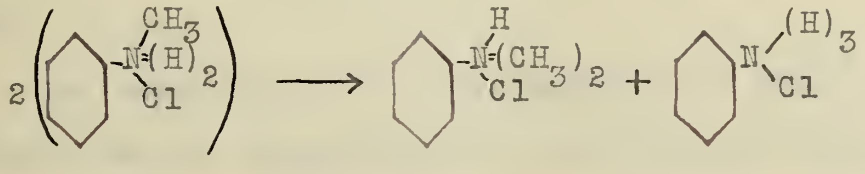


This experiment and all other experiments in which the bombs opened with pressure prove conclusively that methyl chloride may be dissociated from an aminic nitrogen atom to which are linked a methyl group and a chlorine atom, and that methyl chloride is the methylating agent in these rearrangements. This fact confirms Hofmann's explanation relative to the methylating agent in such rearrangements.

The physical properties of the rearranged products have been determined and furnish more evidence in support of the hypothesis advanced above. A more detailed discussion of these points is given in the experimental part if this thesis.

Time did not permit the study of dimethyl aniline hydrochloride as the "ausgangs" material in a separate series of experiments.

In light of this hypothesis methylaniline hydrochloride goes through the following stages to form the necessary quarternary compound before rearrangement can occur:



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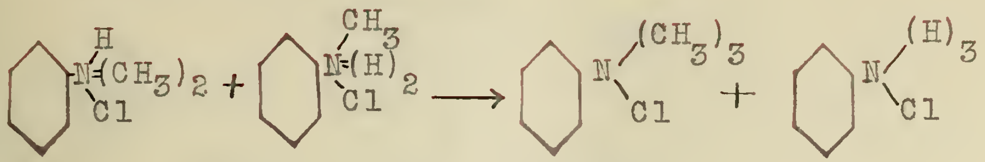
$$[illegible]$$

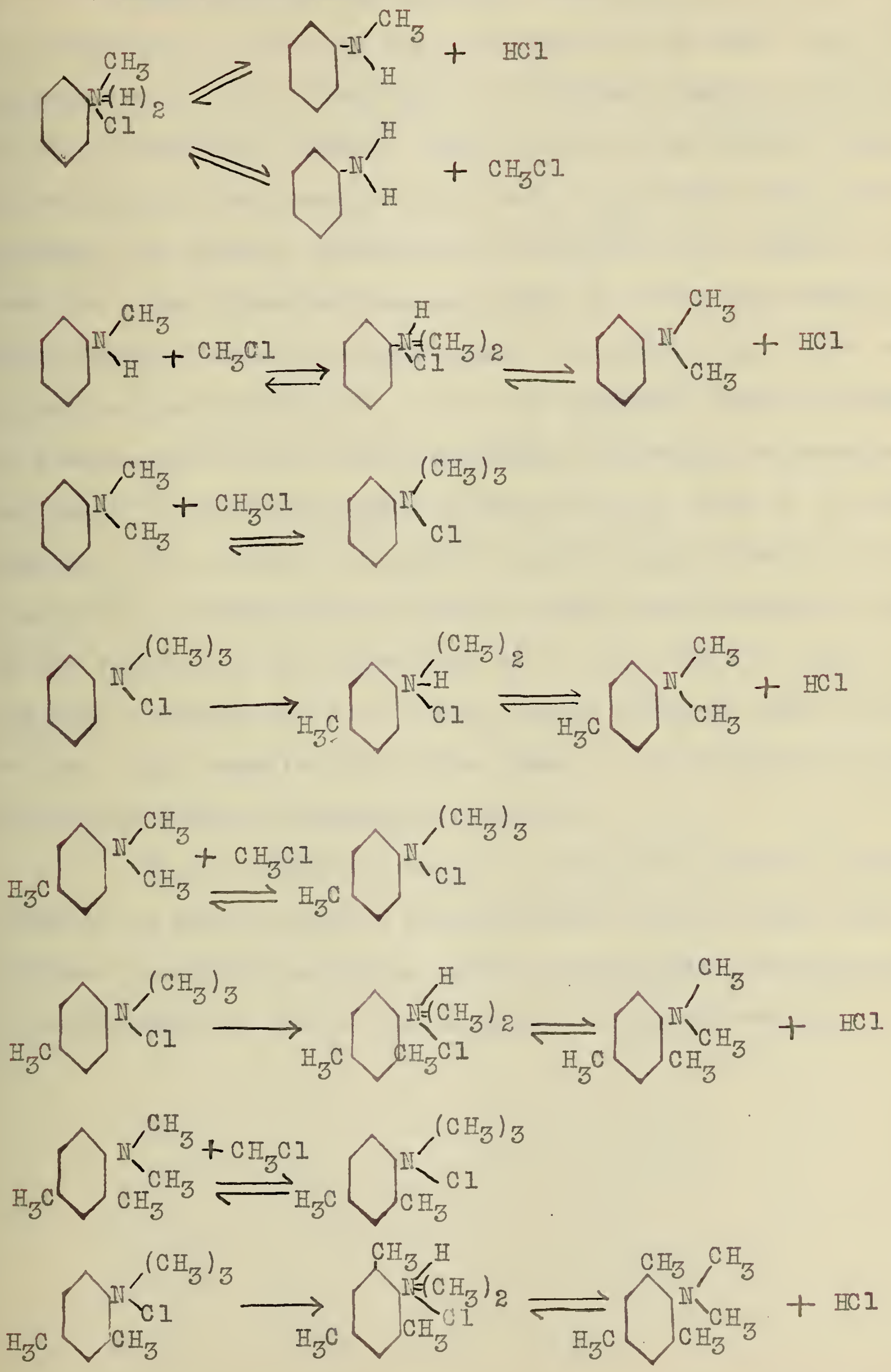


The quarternary compound  $N(CH_3)_3Cl$ may then rearrange to give the toluidines. As Hofmann pointed out, it may be considered that these changes are actually brought about by the methylaniline hydrochloride dissociating into aniline and methyl chloride, and that the latter then attacks methyl aniline or the undissociated hydrochloride to form dimethylaniline hydrochloride, and then begins the methylation of the benzene ring. In accordance with the hypothesis advanced in this thesis, however, the experimental results show that rearrangement takes place only when the quarternary stage is reached.

In the light of our hypothesis neither methyl aniline nor dimethyl aniline can rearrange into corresponding toluidines. This is true because they cannot form quarternary compounds due to the absence of an acid or negative group. The amine nitrogen atom must be pentavalent before rearrangement can take place. Derick and Howard (unpublished work) heated methyl aniline and dimethyl aniline at 340-50° for four hours but found that no rearrangement took place under the conditions of the experiment, thus refuting the careless statement found in many text books that methyl aniline will rearrange into toluidine under the influence of heat.

The mechanism of the rearrangement of methyl aniline hydrochloride may be represented by the following reactions as point

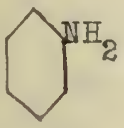
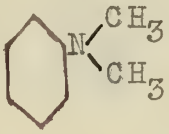
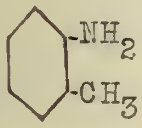
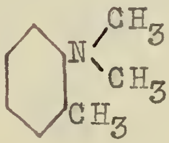
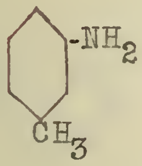
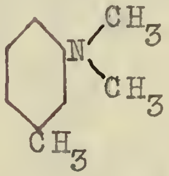
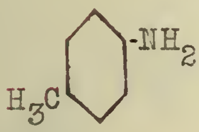
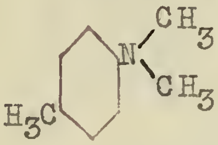
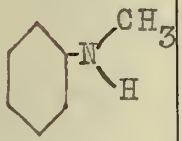
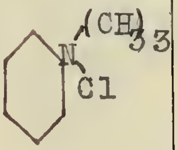
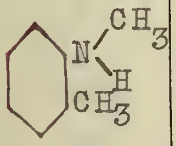
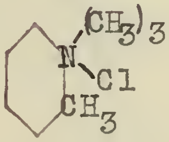
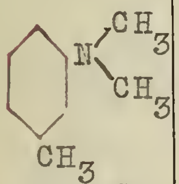
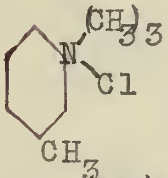
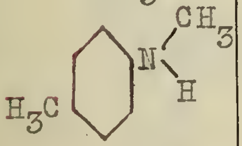
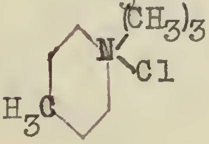
ed out by Derick and Howard:



From the volume standpoint, according to the principle of LeChatelier, if all of the substances in the bomb are in the gaseous state, and if the sum of the volume changes on one side of the equation are greater than the sum of the volume changes on the other, that reaction will take place which will tend to decrease the volume. LeChatelier's principle then seems to oppose the above dissociations and tends to drive the reaction in the direction of the products least dissociable under the conditions of the experiment. It is very probable that the degree of dissociation of all the quarternary compounds represented in the above table is the same. If this be true, then it is noted that for each molecule of methyl chloride that attacks the ring a molecule of hydrochloric acid is formed thus causing no change in the volume. On the other hand it is very certain that all of the bomb products are not in the gaseous state at 300 . If this is true, that reaction will take place in the direction to form the higher boiling rearranged products.

In the following table is given the possible rearranged products of methyl aniline hydrochloride together with their physical constants and those of the corresponding benzenesulphonyl derivatives as far as can be found in the literature:

Table VII.

Amine	m.p.	b.p.	Sulphonyl Derivative m.p.	Sulphonyl Derivative b.p.	Amine	m.p.	b.p.	Sulphonyl Derivative m.p.	Sulphonyl Derivative b.p.
		184°	109°				190°		
		197	124						
		199	95				215		
							208		
		189	79						
		208							
		207							
		208							

[illegible]

Table VII (Continued).

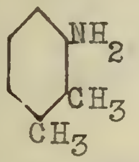
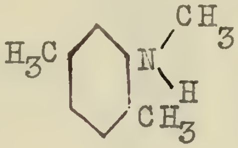
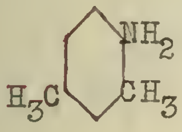
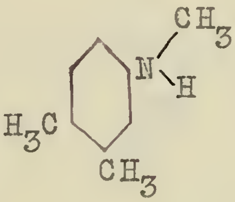
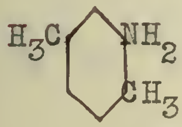
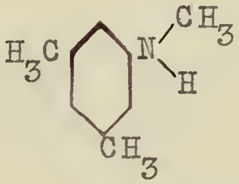
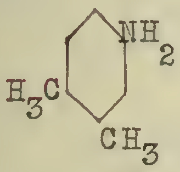
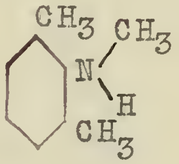
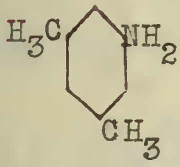
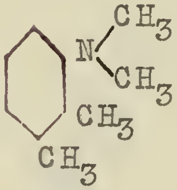
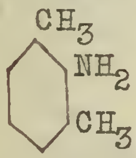
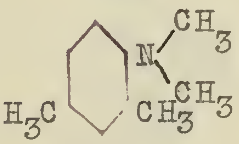
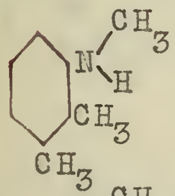
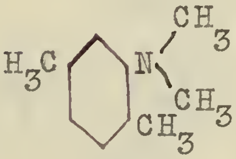
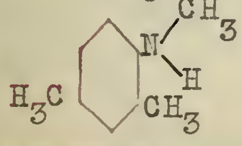
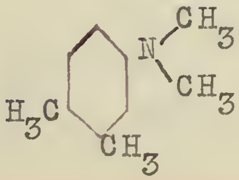
Amine			Sulphonyl Derivative		Amine			Sulphonyl Derivative	
	m.p.	b.p.	m.p.	b.p.		m.p.	b.p.	m.p.	b.p.
		223°					227°		
		212	129°						
	15.5	213	139						
	49	226	118				227		
		221					200		
		216					203		
		223					205		
		221					232		

Table VII (Continued).

Amine			Sulphonyl Derivative		Amine			Sulphonyl Derivative	
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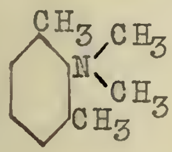
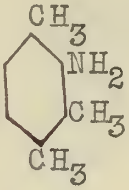
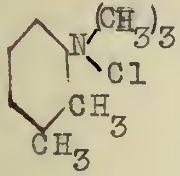
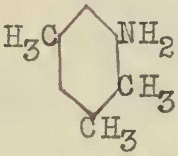
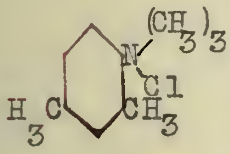
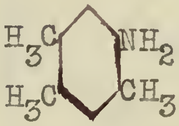
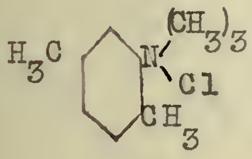
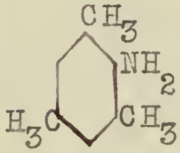
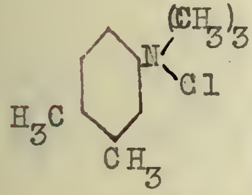
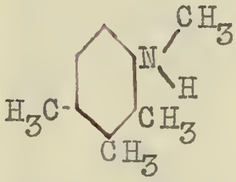
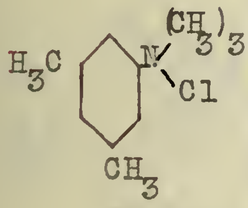
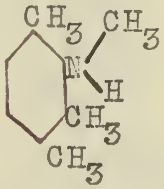
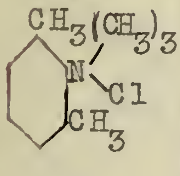
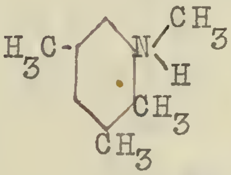
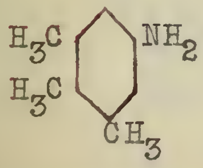
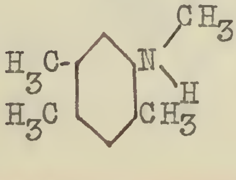
		185°					245°		
						37			
						68	235	137°	
							227		
									
									
									
	78°	245				44	237	137	

Table VII (Continued).

Amine			Sulphonyl Derivative		Amine			Sulphonyl Derivativ	
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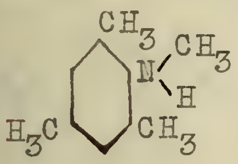
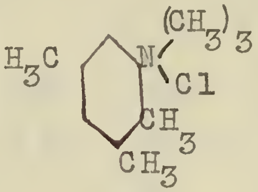
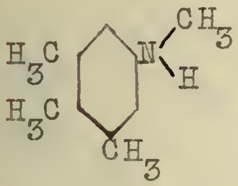
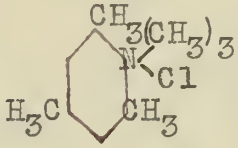
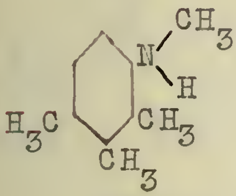
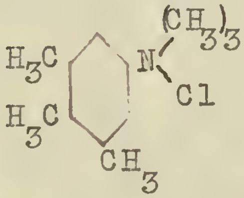
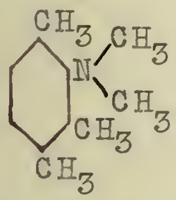
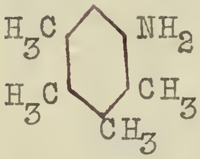
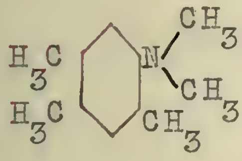
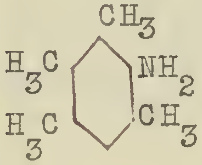
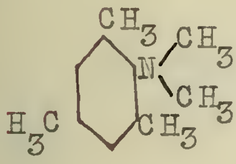
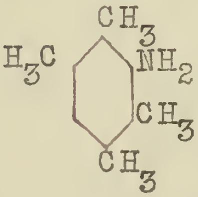
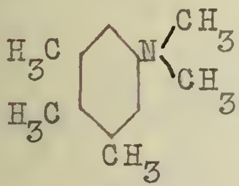
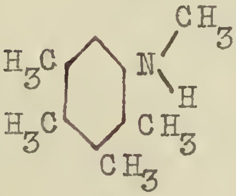
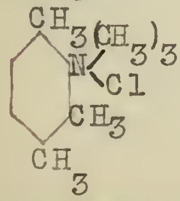
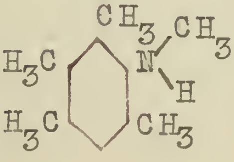
		228°							
									
									
						66°	260°		
						24	255		
						75	26I		
									
									

Table VII (Continued).

Amine			Sulphonyl Derivative		Amine			Sulphonyl Derivative	
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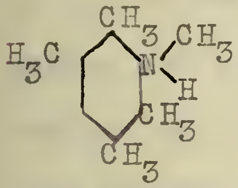
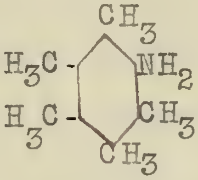
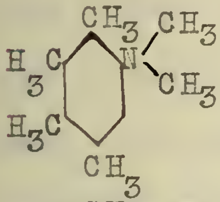
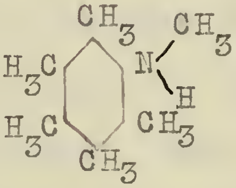
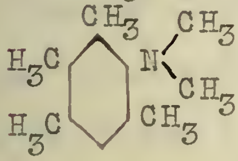
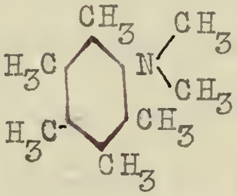
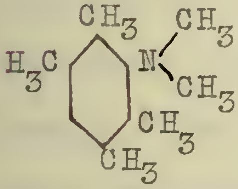
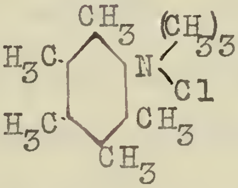
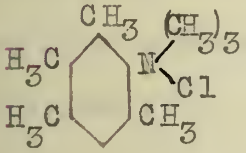
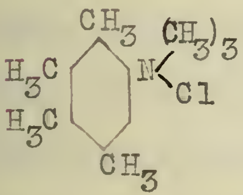
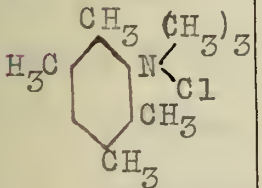
						151°	277°		
									
									
									
									
									
									

In his review of the entire field of molecular rearrangements Derick[114] has summarized and classified much of the mass of material that one finds scattered throughout the literature. It is evident that such summaries and classifications of this nature are invaluable to the chemist whether he be teacher or whether he is engaged in research. An attempt has been made in this thesis to complete the table, as far as possible within the time alloted, giving references etc. to each class of rearrangement thus rendering it a great time saver to those carrying on investigations in this field. In general, Table VII shows that the element or radical is rearranged from C→C, C→O, O→C, C→N, N→C, O→O, O→N, N→O, and N→N, also whether the change is from the open chain to the ring or vice versa. The first vertical column contains a list of the radicals or elements that rearrange. The first horrizontal row contains the elements between which rearrangement may occur, the arrow showing the direction of such rearrangement, while the second horrizontal row gives the position of the element in the first row, that is, whether the elements between which rearrangement occurs are in the open chain (Op), in the ring (R), or whether from open chain to the ring (Op→R), or vice versa (R→Op). The numbers in the third horrizontal row indicate the class to which each rearrangement of a given group is assigned. In the vertical columns below the classes Derick's system of marking is also used:

o designates occasional occurence,

c designates common occurence,

r designates rare occurence,

Table VIII.

	Element or Radical.	C ⟶ C				C ⟶ O				O ⟶ C				C ⟶ N				N ⟶ C				O ⟶ O				O ⟶ N				N ⟶ O				N ⟶ N			
		Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op	Op	R	Op ↓ R	R ↓ Op
	Class	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
1	Alkyl	115 c	116 c	r	o	r	x	x	r	117 o	x	r	x	118 c	119 o	r	r	120 c	121 c	122 c	123 o		x	x	x	124 c	125 r	126 r	x		x	x	127 o	128 o			
2	Aryl	129 c	130 r	131 r			x	x			x		x	132 c	133 r			134 o					x	x	x		x		x		x	x		135 r			136 o
3	Acyl		137 r				x	x		138 o	r		x	139 r				140 o		141 c			x	x	x	142 o	x		x	143 o	x	x					
4	Aracyl						x	x		144 o	x		x										x	x	x	145 c	x		x		x	x					
5	Hydroxyl	146 c	147 o	148 r			x	x			x		x	149 r				150 c	151 r	152 c			x	x	x		x		x		x	x		153 o			
6	Oxyalkyl	154 o					x	x			x		x										x	x	x		x		x		x	x					
7	Axyaryl						x	x			x		x										x	x	x		x		x		x	x					
8	Aldehyde						x	x			x		x										x	x	x		x		x		x	x					
9	Carbonyl						x	x			x		x										x	x	x		x		x		x	x					
10	Carboxyl		155 o				x	x			x	156 o	x										x	x	x		x		x		x	x					
11	Carboxyalkyl						x	x			x		x	157 r									x	x	x	158 o	x		x		x	x					
12	Carboxyaryl						x	x			x		x	159 o									x	x	x	r	x		x		x	x					
13	Amine	160 r					x	x			x		x							161 c			x	x	x		x		x		x	x					
14	Alkylamine						x	x			x		x										x	x	x		x		x		x	x					
15	Arlyamine		162 r				x	x			x		x							163 c			x	x	x		x		x		x	x		164 o			
16	Nitro		165 r		166 r		x	x			x		x							167 o			x	x	x		x		x		x	x					
17	Nitroso						x	x			x		x							168 o			x	x	x		x		x		x	x					
18	Isonitroso					x	x	x	x	x	x	x	x		v	v			v		v	x	x	x	x	x	x	x	x	x	x	x	x		v	v	v
19	Hydrogen	169 c	170 c		c	171 c	172 c	x	173 c	174 c	x	175 o	x	176 c	c		177 c	178 c		c		179 c	x	x	x	180 c	x	181 o	x	182 c	x	x	183 o	184 o	185 r		186 r
20	Halogen	187 c	188 o				x	x		189 r	x		x	190 r			191 r	192 o	193 r	194 c			x	x	x		x		x		x	x					
21	Sulphonic		195 r	196 r			x	x			x		x							197 c				x	x		x		x		x	x					
22	Double union	198 c	199 c	200 c	c	201 c	x	x	c	202 c	x	203 c	x	c	c		c	204 c		205 c			x	x	x	206 c	x	207 o	x	208 c	x	x	209 r	210 r			211 r

x designates impossible, because of constant valence law, and

y designates impossible for trivalent but possible for pentavalent nitrogen.

It is seen from the table that the alkyl group for class I may rearrange from C→C in the open chain, or, that the alkyl group for class 19 will rearrange from a nitrogen atom in the open chain to a carbon atom in the ring, and so on. No cases of rearrangement were observed (within the short time of working up the table) for most of the blank spaces found in the table.

IV - EXPERIMENTAL.

IV - EXPERIMENTAL.

I. Preparation and Purification of Materials.

Aniline. A Kahlbaum product was used which was purified by steam distillation and subsequent fractional distillation. The fraction was used which distilled at I8I.5° to I82.5° (uncorr.).

Methyl Aniline. This was a Hofmann and Kropff product and was purified in the same way as was Aniline. The fraction which distilled at I93.5 - 94.5° (uncorr.) was used.

Dimethyl Aniline. This was a Kahlbaum product and was subjected to the same purification as the above compounds. The fraction used distilled constant at I89 - 90° (uncorr.).

Dimethyl-p-toluidine. This product was purified in the same way as the above aromatic amines. The compound distilled constant at 208 - 9° (uncorr.).

Benzenesulphonyl chloride. One kilo. of phosphorus pentachloride was mixed with an equal weight of previously dried sodium benzene sulphonate in a large evaporating dish and placed under the hood until the reaction was complete. The resulting liquid product was carefully poured in small portions into a large amount of water and shaken thoroughly for some time in order to decompose the phosphorus oxychloride formed during the reaction. When cool the benzenesulphonyl chloride was extracted with ether and dried over calcium chloride. After distilling off the ether the product was distilled under diminished pressure

(using woods metal as a bath) under the following conditions:

Pressure	Temperature (uncorr.)
I2 mm	I23°
I0 "	I20
8 "	II7

A perfectly clear and colorless product was obtained by one distillation.

Methyl iodide. As large amounts of this compound were to be used during the course of this work the method of Walker was found very efficient and convenient. A sketch of the apparatus used together with a detailed description of the procedure and precautions are found in his article. The condensed vapors of boiling methyl alcohol are saturated with iodine by dropping on the latter, and allowed to flow in a fine stream into a mixture of yellow and red phosphorus in methyl alcohol where the reaction begins immediately. When the reaction is completed, noticed by the absence of any iodine color in the solution, a little water is poured down the condenser to destroy any phosphonium compounds that might be formed. The methyl iodide is distilled, washed with dilute sodium carbonate solution, then with water and dried by several pieces of calcium chloride. The product was now very pure and distilled constant at 42.5° to 43° (uncorr.).

Methylaniline hydrochloride. Twenty five grams of the pure methylaniline were dissolved in four hundred cubic centimeters of dry ether and dry hydrochloric acid gas passed into the solution until a white solid separated out. When the react-

[illegible]

[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]

[illegible]

[illegible]

[illegible]

ion was completed the ether was decanted, the white product washed with dry ether, dried on a porous plate placed on the radiator, and kept in a dessicator over calcium chloride. After standing for some time one sample assumed a gree color while another turned yellow, but these changes in color did not affect the composition of the compound. A sample of each colored product was titrated with standard potassium hydroxide solution to confirm the presence of one molecule of HCl in the products with the following results:

Product	Wt. used	Theoretical KOH Equivalent	Found
White	0.2082	0.0815	0.0813
Yellow	0.2314	0.0904	0.0903
Green	0.3074	0.1203	0.1195

Dimethyl aniline hydrochloride. Twenty grams of pure dimethyl aniline were dissolved in four hundred cubic centimeters of dry ether and dry hydrochloric acid gas passed in until a white solid separated out. The ether was decanted and the product washed by decantation with dry ether. The product was then quickly transfered to a filer paper in a funnel and the paper pressed firmly between the fingers in order to rid the substance from as much ether as possible. The product was then quickly transferred to a porcelain plate, broken up by a porcelain spatula and gently agitated over the radiator until the ether had escaped. It was then transferred to a weighing bottle and dried for a day in a vacuum dessicator containing sulphuric acid, potassium hydroxide

and phosphorus pentachloride;m.p. 80-85° with decomposition. Dimethylaniline hydrochloride is very hydroscopic and hence must be handled very quickly and carefully.

Trimethylphenylammonium iodide. Molecular proportions of methyl iodide and dimethyl aniline were placed in a pressure flask and set aside at room temperature. The reaction began in a few minutes with a great evolution of heat and was complete within an hour. The white product was recrystallized from ninety five per cent alcohol, filtered by suction, dried on a porous plate and kept in a dessicator over calcium chloride.

Trimethylphenylammonium chloride. Trimethylphenylammonium iodide was dissolved in water and moist silver oxide (prepared by treating a solution of sodium hydroxide with a solution of silver nitrate and washing the black precipitate several times by decantation with water) added in excess to precipitate the iodine as silver iodide. The supernatent layer was decanted and filtered and the silver iodide washed by decantation. This filtered solution was saturated with hydrochloric acid gas and evaporated to a very viscous liquid on the water-bath. After allowing to cool the yellow crystalline but sticky product was filtered by centrifudging for ten minutes. The crystalline cream colored substance was then dried in a vacuum dessicator over calcium chloride. On standing for several days the product became yellow. The filtrate from the centrifudged product was evaporated further and more of the compound obtained.

2. Test of Analytical Method.

The perfection of an analytical method was found very necessary in order to intelligently separate and determine the products resulting from the rearrangements in this investigation. In light of this fact an attempt was made to perfect the method used by Derick and Howard (Howard's Doctors Thesis 1915) which always resulted in fairly large errors in the determination of the secondary and tertiary amines. The amines used by Howard were para-toluidine, methylaniline, and dimethylaniline. The large error in the determination of dimethylaniline seemed, according to Howard, to be due in part to volatility, but mainly to the formation of a blue dye during the course of the reactions involved in the separation. In order to obviate this difficulty of dye formation dimethyl-p-toluidine was used instead of dimethylaniline. The amines used in this work then to test out the analytical method were aniline, methylaniline, and dimethyl-p-toluidine.

(a) Modification I.

A mixture of the amines mentioned above was shaken vigorously fot ten minutes in fifty cubic centimeters of (1:10) sodium carbonate solution with twenty percent excess of benzenesulphonyl chloride. A solution of (1:1) potassium hydroxide was added in small amounts shaking and cooling after each addition until a white solid separated out which indicated the end of the reaction. The mixture was now diluted with water until the solid went back into solution and then extracted with ether.

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

This ether extract contained the disulphonyl derivative of aniline, the sulphonyl derivative of methylaniline, and the free tertiary amine, dimethyl-p-toluidine. The alkaline solution contained the potassium salt of the mono sulphonyl derivative of aniline.

The ether extract was evaporated and the residue refluxed for thirty minutes with fifty cubic centimeters of sodium alcoholate (four grams of sodium in fifty cubic centimeters of absolute alcohol) in order to convert the disulphonyl derivative of the primary amine into the sodium salt of the corresponding monosulphonyl derivative. The refluxed product was diluted with water to one hundred and fifty cubic centimeters and extracted with ether. This ether extract contained the sulphonyl derivative of methyl aniline and the free tertiary amine. The alkaline layer contained the sodium salt of benzenesulphonaniline which was added to the original alkaline solution containing the same product. The ether extract was evaporated and the residue treated with twenty-five cubic centimeters of hydrochloric acid. The solution assumed a light blue color when the first portion of the acid was added but disappeared when the total amount was added and subsequently shaken. Upon extracting this acid solution with ether a fine white granular precipitate slowly settled out in the separatory funnel. This precipitate was very probably some of the hydrochloride of the tertiary amine thrown out of solution due to its insolubility in concentrated hydrochloric acid. This ether extract was evaporated, the benzenesulphonmethylaniline dried in

a current of air and weighed until constant within about two tenths of one per cent. The acid layer was diluted and the white precipitate went into solution. Also, there separated an ether layer which, perhaps, is accounted for by the previous formation of an ether-acid complex at the stage where concentrated hydrochloric acid solution is extracted with ether. This solution was made alkaline with solid potassium hydroxide (to keep down the volume) and extracted with ether. The ether was evaporated and the free tertiary amine dried in a current of air and weighed until constant within about one per cent. The original alkaline solution which contained the sodium salt of benzenesulphonaniline was acidified with hydrochloric acid, extracted with ether, the ether evaporated and the sulphonyl derivative of the primary amine dried and weighed until constant within about two tenths of one per cent. The following results were obtained:

Substance	Charge	Weight of Deriv.	Theoret. wt. of Deriv.	% Error
Aniline	0.490	I.245	I.227	I.45%
Methyl aniline	0.497	I.295	I.I46	I2.94
Dimethyl-p-toluidine	0.536	0.5II	0.536	-4.62

The products dried very slowly by the dry air method. In case of the free tertiary amine constant weight (within about one per cent) was not obtained until after twenty-four hours after drying and weighing at intervals of five minutes. It was assumed that some volatile product was formed. During the drying of the tertiary amine it assumed a greenish dark brown granular and sticky appearance. The primary derivative crystallized readily into a cream colored mass while the secondary derivative crys-

tallized more slowly into a brown solid.

(b) Modification II.

Another separation was made with a few modifications in the procedure as described below. The ether extracts were not dried over anhydrous sodium sulphate in order to get an idea of the approximate amount of moisture held by the products after evaporating the ether, drying in a stream of dry air, with subsequent drying in a vacuum dessicator over calcium chloride. The mixture of amines was shaken vigorously for ten minutes in fifty cubic centimeters of a (I:IO) sodium carbonate solution with twenty per cent excess benzenesulphonyl chloride. A solution of (I:I) potassium hydroxide was added in small amounts, shaken and cooled after each addition, until a white solid precipitated out. The mixture was diluted until the solid went into solution and then extracted with ether. The ether extract was evaporated and the residue refluxed with sodium alcoholate for thirty minutes. This mixture was then diluted to one hundred and fifty cubic centimeters and extracted with ether. The alkaline layer was added to the original alkaline layer, made acid with hydrochloric acid, the primary monosulphonyl derivative extracted with ether, dried in a current of dry air and finally in a vacuum dessicator over calcium chloride and weighed. The previous ether extract containing the secondary sulphonyl derivative and free tertiary amine was evaporated and the residue treated with twenty five cubic centimeters of concentrated hydrochloric acid. This acid solution was diluted with water before extracting with ether in order to keep at a mininum the formation of the ether acid com-

plex which, perhaps, makes ether extraction incomplete. This diluted acid solution was then extracted with ether, the ether evaporated and the secondary sulphonyl derivative dried in a current of air, allowed to stand in a vacuum dessicator over calcium chloride, and weighed.

The aqueous (acid) layer was made alkaline with solid potassium hydroxide and extracted with ether. The ether was evaporated, the free tertiary amine dried in a current of air, placed in a vacuum dessicator over calcium chloride and weighed. The primary and secondary derivatives crystallized in the same manner as described in the previous separation.

The tertiary amine was obtained as a dark reddish brown liquid, but accompanied by a small amount of a lighter colored liquid which readily volatilized when dried in an electric vacuum dessicator at 38°C. The following results were obtained from the separation:

Aniline

Charge	Wt. of deriv.	Theoret. wt.	%error
(I) 0.504	I.254	I.262	-0.68
(2) 0.486	I.210	I.217	-0.55
	Methyl Aniline		
(I) 0.493	I.276	I.I37	I0.90
(2) 0.482	I.230	I.II3	I0.5I
	Dimethyl-p-toluidine		
(I) 0.533	0.478	0.533	-I.02
(2) 0.525	0.466	0.525	-I.I2

(c) Modification III.

The large error observed in case of the secondary derivatives necessitated another separation in an effort to trace its cause and to eliminate it if possible. Accordingly a mixture of the same amines was shaken for ten minutes in fifty cubic centimeters of (I:IO) sodium carbonate solution with twenty per cent excess of benzenesulphonyl chloride. The mixture was treated(as previously described) with potassium hydroxide and extracted with ether. When the ether was evaporated the product in flask #2 had a bluish violet color similar to the dye observed by Howard, while the product in flask #I was ginger colored similar to that observed in previous separations. The aqueous layer containing the potassium salt of the primary sulphonyl derivative was set aside. The colored products mentioned above were refluxed as usual with sodium alcoholate, diluted to one hundred and fifty cubic centimeters and extracted with ether. The alkaline layer was added to the original alkaline layer, made acid, extracted with ether, and the primary sulphonyl derivative dried and weighed. The ether extracts were evaporated and about thirty-five cubic centimeters of a reddish brown liquid remained. This liquid was treated with twenty five cubic centimeters of hydrochloric acid, diluted with water, and extracted with ether. The ether extract was dried over anhydrous sodium sulphate, evaporated, dried in a current of dry air and the secondary sulphonyl derivative weighed. The aqueous (acid) layer was treated with solid

potassium hydroxide, and a small ether layer was formed but soon disappeared due to the heat of the reaction. A white precipitate (some potassium chloride) separated occasionaly at this stage but went into solution upon further dilution. This solution was then extracted with ether, the ether dried over anhydrous sodium sulphate, evaporated and the free tertiary amines dried and weighed in the usual manner. The results of this separation are as follows:

Aniline

	Charge	Wt. of Deriv.	Theoret. wt.	%error
(I)	0.508	I.087	I.27I	-I4.47
(2)	0.509	I.I32	I.274	-II.I4
		Methylaniline		
(I)	0.468	I.I75	I.I22	4.72
(2)	0.484	I.2I6	I.II6	8.96
		Dimethyl-p-toluidine		
(I)	0.5I8	0.393	0.5I8	-24.I3
(2)	0.5I8	0.44I	0.5I8	-I4.86

In this separation the results show a drop in the yield of the primary sulphonyl derivative, a very low yield of the free tertiary amine, and an excess of the secondary sulphonyl derivative. The primary sulphonyl derivative can be obtained in amounts close to the theoretical yield. The trouble seemed to center around the secondary sulphonyl derivative and free tertiary amine. As dimethyl-p-toluidine and methyl-p-toluidine have the same boiling point, namely 208°, it was thought very probable

that the former compound contained some of the latter as an impurity. This would account for the positive error of the secondary sulphonyl derivative and the large negative error of the free tertiary amine. Also it was thought possible that the small yield of tertiary amine was perhaps due to the volatility of the same on evaporating the ether and subsequent drying in a current of air. Whenever the ether extract containing the tertiary amine was evaporated, there remained with the amine a volatile liquid which disappeared after passing dry air over it for about two hours. It is very probable that some of the free tertiary amine was carried off with it.

An attempt was made to determine the tertiary amine by evaporating the aqueous (acid) solution containing the hydrochloride of the tertiary amine and weighing it as such. Check experiments were carried out using dimethyl-p-toluidine and concentrated hydrochloric acid. Mixtures of the amine and acid were shaken, cooled, and extracted with ether. The aqueous layer was evaporated, but instead of a crystalline addition product, a dark red oily substance was obtained. This method was then abandoned.

In order to detect the presence of primary and secondary amines as impurities in dimethyl-p-toluidine, check portions of the latter were vigorously shaken in one hundred cubic centimeters of (I:4) sodium carbonate solution with ten per cent excess of benzenesulphonyl chloride and refluxed for one hour. The mixture was cooled and extracted with ether. The aqueous layer was acidified with hydrochloric acid and extracted with ether.

This ether extract was dried over anhydrous sodium sulphate, evaporated, and the resulting product weighed. The formation of a crystalline derivative confirmed the presence of a primary amine in the dimethyl-p-toluidine used. The original ether extract was evaporated, treated with twenty-five cubic centimeters of concentrated hydrochloric acid and extracted with ether. The ether extract was dried over anhydrous sodium sulphate, evaporated, and the product dried in a current of dry air and weighed This crystalline derivative showed that a secondary amine (probably methyl-p-toluidine) was also present in the original tertiary amine. The aqueous layer was made alkaline with solid potassium hydroxide and extracted with ether. This ether extract was dried in the usual manner, evaporated, and the free tertiary amine dried in a current of air and weighed. The results of this experiment are as follows:

No.	Charge	Wt. of Deriv.	Theoret. Wt.
		Primary Amine	
I	0.000	0.I89	0.000
2	0.000	0.I7I	0.000
		Secondary Amine	
I	0.000	0.476	0.000
2	0.000	0.502	0.000
		Tertiary Amine	
I	I.304	0.669	I.304
2	I.309	0.575	I.309

Violent bumping occurred during the refluxing and some of the reaction mixture was lost, but the results nevertheless are

sufficient evidence to confirm the presence of impurities in dimethyl-p-toluidine. It is apparent from the above results that about fifty per cent of the tertiary amine is made up of other substances. This undoubtedly accounts for a part, at least, of the per cent error obtained for methyl aniline and dimethyl-p-toluidine in previous separations.

3. Purification of Dimethyl-p-toluidine.

In light of the above results an attempt was made to purify dimethyl-p-toluidine by making the sulphonyl derivatives of any primary and secondary amines contained therein. The method used was that carried out for the regular separation of primary, secondary, and tertiary amines in previous experiments. The following results were obtained:

Charge	Primary Derivative	Secondary Derivative	Free Tertiary Amine
I0.005	I.493	0.840	8.864

It is evident that the original charge was contaminated with primary and secondary amines.

In order to get rid of further traces of these impurities, the free tertiary amine obtained above was subjected to a second separation with the following results:

Charge	Primary Derivative	Secondary Derivative	Free Tertiary Amine
2.I53	0.I34	0.267	I.739

Larger amounts of this purified tertiary amine were subjected to the regular amine separation with the following results:

Primary

	Charge	Wt. of Derivative	Theoret. Wt. of Derivative	% Error
(I)	0	0.08I	0.000	0.35
(2)	0	0.076	0.000	0.32
		Secondary		
(I)	0	0.299	0.000	I.37
(2)	0	0.259	0.000	I.I7
		Tertiary		
(I)	I0.I42	9.286	I0.I42	-8.44
(2)	I0.258		I0.258	

The above results show that the sodium alcoholate used to split off one of the benzene sulphonyl groups from the corresponding disubstituted primary amine, might also have some effect on the tertiary amine in the way of splitting off a methyl group. Accordingly the method was modified by separating the tertiary amine from the mixture before refluxing with the alcoholate. After shaking the original amine (dimethyl-p-toluidine) with benzene sulphonyl chloride in alkaline solution with subsequent addition of potassium hydroxide, the mixture was diluted and extracted with ether. The remainder of the procedure was the same as described in previous separations. The results obtained are as follows:

No.	Charge	Wt. of Derivative	Theoret.Wt.of Derivative	% Error
		Primary		
I	0.000	0.023	0.000	0.I5
2	0.000	0.0I9	0.000	0.I4
		Secondary		
I	0.000	0.437	0.000	3.I5
2	0.000	0.367	0.000	2.78
		Tertiary		
I	6.4I9	5.490	6.4I9	-I4.47
2	6.I5I	5.347	6.I5I	-I4.70

It is evident that the results do not throw any light on the difficulty.

4. Determination of Methyl Aniline.

Methyl aniline was determined by subjecting it to the regular process of amine separation. Such a procedure would detect the presence of impurities such as primary and tertiary amines. The following results were obtained:

	Charge	Wt. of Deriv.	Theoret. Wt.	% Error
I	0.860	I.859	I.86I	-0.I3
2	0.866	I.989	I.999	-0.5I

It is evident that the methyl aniline used is very pure and can be determined with an accuracy of five tenths of one per cent.

5. Volatility of Dimethyl-p-toluidine on Evaporation.

It was observed in all previous experiments that dimethyl-p-toluidine was volatile to an appreciable extent, and

that constant weight could not be obtained by drying with air which was previously bubbled through concentrated sulphuric acid. In order to determine more precisely the extent of this volatility, experiments were carried out using check portions (0.646 grams and 0.631 grams respectively) of the pure tertiary amine. Dry air was passed over the products as in previous experiments and weighings were made from time to time until constant weight was obtained. The results are tabulated as follows:

Evaporation Data.

Time		Wt. of Product. (Checks)	
Hours	Minutes	(1)	(2)
0	0	0.6463	0.6310
0	25	0.6348	0.6200
0	45	0.6284	0.6160
1	05	0.6228	0.6125
1	25	0.6176	0.6084
1	40	0.6138	0.6057
2	00	0.6074	0.6010
3	50	0.5616	0.5678
4	15	0.5544	0.5630
4	35	0.5464	0.5577
5	00	0.5374	0.5524
5	15	0.5316	0.5504
5	30	0.5285	0.5464
5	45	0.5223	0.5446
6	00	0.5190	0.5407
6	30	0.5065	0.5345

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Hours	Minutes	(I)	(2)
6	45	0.5035	0.5308
7	I5	0.49I2	0.5249
7	30	0.4884	0.52I2
7	45	0.4826	0.5I82
8	I5	0.4740	0.5II6
8	35	0.4664	0.5058
9	45	0.4378	0.4866
I3	55	0.3I26	0.3970
I5	55	0.2596	0.3662
I6	40	0.2330	0.3456
I8	I5	0.I873	0.3II0
20	I0	0.I244	0.2683
23	00	0.0272	0.2022
24	05	0.0084	0.I756
27	05	0.0064	0.0782
28	30	0.0059	0.0307
30	45	0.0059	0.0065
33	I0	0.0059	0.0040
35	55	0.0059	0.0040

It is noticed that constant weight was not obtained until after thirty-five hours in case of check # 2 and thirty hours in case of check # I, at which time the amount of product left in the flasks was 0.004 grams and 0.006 grams respectively. Practically all of the amine was carried off by the air under the conditions of the experiment. It is interesting to note the appreciable volatility of this tertiary amine in spite of its

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high boiling point. This experiment was repeated but in this case the charge was dissolved in ether, the ether evaporated as far as possible on the steam-bath and the flask connected with the drying apparatus. The weight of the initial charge was 0.7482 grams. Weighings were made every ten minutes for two hours with the following results:

Evaporation Data.

Time Hours	Minutes	Wt. of Product
0	0	I.I344
0	I0	0.7383
0	20	0.7272
0	30	0.7I84
0	40	0.7095
0	50	0.7022
I	00	0.695I
I	I0	0.6874
I	20	0.6804
I	30	0.6730
I	40	0.6649
I	50	0.6570
2	00	0.6498

These results are more uniform than those in the previous experiment but the loss in weight between each interval was greater than desired.

Another experiment was carried out with the charge dissolved in ether, but in this case the Drechsel tower containing

the sulphuric acid was allowed to stand in a freezing mixture of salt and ice. When all signs of ether disappeared by heating on the water-bath the flask was connected with the drying apparatus and the weighings carried out at ten minute intervals. The weight of the initial charge was 0.76I2 grams. The results obtained are as follows:

Evaporation Data.

Time		
Hours	Minutes	Wt. of Product.
0	0	I.2590
0	I0	0.7742
0	20	0.7578
0	30	0.7530
0	40	0.7500
0	50	0.7498
I	00	0.7483
I	I0	0.7472
I	20	0.7462

The results show that if most of the ether is driven off on the steam-bath, constant weight may be obtained in thirty minutes within seven tenths per cent. The weight is practically constant after forty minutes treatment with cool dry air. This method, consequently, was used to dry all of the tertiary amines obtained from the separations which are mentioned later.

6. Determination of Dimethyl Aniline.

In order to determine the source of error obtained by Derick and Howard in the yield of secondary amines, dimethyl ani-

line was subjected to the modified method of amine separation with the following results:

No.	Charge	Wt. of Deriv.	Theoret. Wt.	% Error
		Primary.		
1	0.000	0.008	0.000	Negligible
2	0.000	0.009	0.000	"
		Secondary.		
1	0.000	0.113	0.000	4.58
2	0.000	0.083	0.000	3.37
		Tertiary.		
1	1.066	0.725	1.066	-32.00
2	1.061	0.730	1.061	-45.34

The four per cent error is practically that obtained by Derick and Howard and seemed to be due to the presence of some secondary amine in the original tertiary amine charge. The volatility of dimethyl aniline was found to be very great. Even drying by a cold stream of dry air did not keep down the volatility of the amine. No blue dye was formed in this separation due to the fact that dimethyl aniline was extracted before refluxing with sodium alcoholate.

7. Test for Contamination by Reagents.

In order to determine whether or not the reagents used in the previous separations contaminated the derivatives by increasing their weight, especially as found with the secondary amine, a blank separation was carried out using the modified method of separation. One cubic centimeter of benzenesulphonyl

chloride was used, and the amounts of the other reagents were the same as used in previous separations. The following results were obtained:

No.	Charge	Wt. of Deriv.	Theoret. Wt.
		Primary.	
I	0.000	0.008	0.000
2	0.000	0.005	0.000
		Secondary.	
I	0.000	0.042	0.000
2	0.000	0.04I	0.000
		Tertiary.	
I	0.000	0.000	0.000
2	0.000	0.000	0.000

The original ether extract when separated from the aqueous (alkaline) layer and evaporated left no residue. The ether extract from the refluxed solution, however, did give a residue upon evaporation of the ether. This yellowish-brown solid was, perhaps, a contributing factor toward the positive error obtained in previous separations in case of secondary amine derivatives. A particle of this substance was placed upon a piece of moistened red litmus paper and the latter immediately turned blue. This indicated that some of the sodium alcoholate was extracted by ether. A bit of the substance when heated on a platinum foil left a white residue. When this brown substance was treated with ether none of it seemed to go into solution.

It was supposed, therefore, that the secondary amine derivative could be extracted while this salt would remain behind.

In light of this fact another separation was made using a mixture of primary, secondary, and tertiary amines as used in previous experiments. In order to keep down the loss of tertiary amine it was decided not to evaporate the original ether extract, but to add the concentrated hydrochloric acid directly to it, thus forming the hydrochloride of the tertiary amine which could easily be separated from the ether layer. The evaporated ether extract from the refluxed mixture containing sodium alcoholate (which in previous separations was considered as pure secondary amine derivative, but in the previous blank separation found to be, in part, sodium alcoholate) was again extracted with ether, the ether evaporated and the product dried and weighed. This separation with these two additional modifications gave the following results:

No.	Charge	Wt. of Deriv.	Theoret. Wt.	% Error
		Primary.		
I	0.7I2	I.786	I.783	0.II
2	0.725	I.8I5	I.8I5	0.00
		Secondary.		
I	0.62I	I.I88	I.39I	-I4.53
2	0.635	I.262	I.465	-I3.84
		Tertiary.		
I	0.554	0.553	0.554	-C0.02
2	0.554	0.554	0.554	00.00

The yield of the secondary amine derivative in the above separation is below the theoretical yield. In all previous

separations a positive error was obtained. It was thought that the negative error in this separation was perhaps due to the method of extracting the alkaline residue containing the secondary amine derivative.

It was thought that the addition of hydrochloric acid to the sodium alcoholate might break up the latter and thus render the extraction of the secondary derivative more quantitative. Accordingly another separation was made using the same amines as employed in previous experiments. Twenty five cubic centimeters of hydrochloric acid were added to the sodium alcoholate solution after refluxing in order to decompose the alcoholate before extracting with ether. The following results were obtained:

No.	Charge	Wt. of Deriv.	Theoret. Wt.	% Error
		Primary		
I	0.6I3	I.5I9	I.534	-0.98
2	0.627	I.554	I.570	-I.03
		Secondary		
I	0.549	I.359	I.268	7.I6
2	0.544	I.338	I.255	6.63
		Tertiary.		
I	0.660	0.640	0.660	-3.0I
2	0.680	0.667	0.680	-I.95

The above results show that the hydrochloric acid did not completely break up the alcoholate. It was thought that dilution of this acid solution before extracting with ether would

assist in decomposing the alcoholate. Accordingly a separation of the three classes of amines was carried out as described in the above experiment with the modification that after adding twenty five cubic centimeters of hydrochloric acid to the refluxed alkaline solution, the latter was diluted with water to four times its volume and then extracted with ether. The results are as follows:

No.	Charge	Wt. of Deriv.	Theoret. Wt.	% Error
		Primary		
I	0.623	I.537	I.560	-I.53
2	0.639	I.585	I.60I	-0.97
		Secondary		
I	0.584	I.355	I.347	0.57
2	0.586	I.352	I.35I	0.06
		Tertiary		
I	0.656	0.632	0.656	-3.7I
2	0.642	0.6I0	0.642	-5.00

The results show that dilution, in addition to the treatment with hydrochloric acid, is necessary in order to obtain a quantitative yield of the secondary amine derivative.

8. Perfected Method of Separation.

As the previous separation proved very efficient it was decided to adopt it, with the exception of changing the stage of the acid treament of the sodium alcoholate solution, as the procedure for the separation of the various amines obtained from the rearranged bomb products. In order to further prove the

efficiency of the method, eight more separations were carried out. The description of the perfected method in detail is as follows: The mixture of amines (aniline, methylaniline, and dimethyl-p-toluidine) was vigorously shaken for ten minutes in fifty cubic centimeters of (1:10) sodium carbonate solution and twenty per cent excess of benzene sulphonyl chloride. Erlenmeyer flasks of two hundred and fifty cubic centimeters capacity with rubber stoppers were used for this shaking. The liquid adhering to the rubber stopper was carefully removed by means of a steel spatula and added to the contents of the flask. A solution of (1:1) potassium hydroxide was added in small amounts to the mixture, shaking and cooling after each addition until a grayish white solid began to separate. This indicates the end of the reaction. The mixture was then diluted with water until the solid went into solution and extracted three times with ether. The aqueous (alkaline) layer contained the potassium salt of the mono-substituted benzene sulphonyl derivative of the primary amine, and was set aside. The ether extract contained the di-substituted benzene sulphonyl derivative of the primary amine, the benzene sulphonyl derivative of the secondary amine, and the free tertiary amine. Twenty five cubic centimeters of concentrated hydrochloric acid were added to this ether extract and the mixture carefully shaken and cooled. On addition of the hydrochloric acid the solution assumed a greenish-blue color which gradually faded, on shaking, to one having a white cloudy appearance. After standing a few minutes the heavier acid layer was colored a dark red due to the presence of the tertiary

amine in the form of its hydrochloride; the ether layer was slightly cloudy. The ether layer was separated and the acid layer extracted three times with ether. The free tertiary amine in this acid solution was liberated by treatment with solid potassium hydroxide (in order to keep down the volume) cooled and diluted a little and extracted three times with ether, This ether extract was dried over anhydrous sodium sulphate for a few minutes, decanted into a weighed one hundred and fifty cubic centimeter Erlenmeyer flask, and the ether evaporated on the steam bath. During this evaporation the sodium sulphate was washed three sucessive times with ether and the latter poured into the flask on the steam bath. After all of the ether seemed to have been removed by this process, the product was further dried by passing a current of cold dry air over it until a constant weight was obtained within about five tenths per cent. The dry air was obtained by bubbling air through concentrated sulphuric acid in a tower which stood in a freezing mixture of salt, ice, and water. The weighings were made at three minute intervals, and the dry air was not allowed to pass too rapidly over the free amine on account of the appreciable volatility of the latter.

The ether solution containing the disubstituted benzenesulphonyl derivative of the primary amine and the benzene sulphonyl derivative of the secondary amine was evaporated on the water bath until a small amount of a yellow liquid remained. This liquid was refluxed for thirty minutes with sodium alcoholate (four grams of sodium in fifty cubic centimeters of absolute alcohol) in order to break down the disulphonyl derivative of the

primary amine into the corresponding mono-sulphonyl derivative. Only one benzene sulphonyl group is removed by this process. When cool, the solution is diluted with one hundred cubic centimeters of water and extracted three times with ether. This alkaline layer was added to the original alkaline solution which contained the potassium salt of the benzenesulphonyl derivative of the primary amine. The ether extract which contained the secondary amine sulphonyl derivative and some undecomposed sodium alcoholate was evaporated until all of the ether was driven off. There remained in the flask about fifty cubic centimeters of a light yellow solution. In order to break up the alcoholate, the solution was treated with twenty five cubic centimeters of hydrochloric acid and one hundred cubic centimeters of water. The mixture was carefully shaken, cooled, and extracted three times with ether. The aqueous layer was discarded. The ether extract was evaporated until a clear yellow oil remained containing but a small amount of solvent. In order to insure the decomposition of final traces of alcoholate, about seventy-five cubic centimeters of water were added to this yellow oil and the whole carefully shaken until the rich cream colored solid (the secondary amine derivative) separated out. This was then extracted three times with ether, the ether extract dried over anhydrous sodium sulphate, evaporated, dried, and weighed in the same manner as was the tertiary amine. The secondary amine derivative crystallized slowly in light-yellow colored needles having a peculiar odor. The combined alkaline solutions which contained the primary amine derivative were carefully acidified with concen-

trated hydrochloric acid, cooled, and extracted three times with ether, the ether dried over anhydrous sodium sulphate, evaporated and the product dried and weighed in the same manner as was the free tertiary amine and the secondary amine derivative. The product crystallized out in diamond shaped plates and had a pleasant characteristic odor.

The original charges of amines were weighed in weight pipettes by difference, thirty-five drops being used each time, as far as possible, for uniformity. The results obtained by this pdocedure are as follows:

Primary.

No.	Charge	Wt. of Deriv.	Theoret. Wt.	% Error
I	0.6266	I.5930	I.5696	I.49
2	0.6378	I.6I86	I.5976	I.03
3	0.63I6	I.6038	I.5822	I.36
4	0.64I6	I.6268	I.6072	I.22
5	0.6356	I.6072	I.5922	0.94
6	0.64I8	I.6I95	I.6077	0.73
7	0.6433	I.634I	I.6II5	I.40
8	0.6400	I.6I66	I.6032	0.83

Secondary.

No.	Charge	Wt. of Deriv.	Theoret. Wt.	% Error
I	0.5530	I.2620	I.2763	-I.I2
2	0.5534	I.2508	I.2772	-2.I4
3	0.5468	I.24I0	I.2620	-I.66
4	0.5452	I.2309	I.2583	-2.I7
5	0.57I8	I.3I00	I.3I97	-0.75
6	0.5498	I.2504	I.2689	-I.45

No.	Charge	Wt. of Deriv.	Theoret. Wt.	% Error
7	0.5518	1.2498	1.2735	-1.86
8	0.5494	1.2496	1.2680	-1.88
		Tertiary.		
1	0.6480	0.6366	0.6480	-1.76
2	0.6576	0.6444	0.6576	-2.01
3	0.6616	0.6404	0.6616	-3.21
4	0.6514	0.6373	0.6514	-2.16
5	0.6536	0.6354	0.6536	-2.78
6	0.6608	0.6475	0.6608	-2.01
7	0.6558	0.6332	0.6558	-3.45
8	0.6555	0.6360	0.6555	-2.97

The total per cent of amines recovered in each check is given as follows:

1	98.61%
2	96.88
3	96.49
4	96.89
5	97.41
6	97.27
7	96.09
8	95.98
Average	96.95%

The method then involves an error of only about three per cent. in these separations. Only by the most careful work can the error be brought within this amount. The separation is very tedious and long. Each experiment (check separations) in-

volves over forty extractions and about sixty weighings. When one is thoroughly familiar with the method a quantitative separation may be accomplished in two days.

9. Carius Electric Furnace.

A few years ago Derick and his students calibrated the ordinary Carius gas furnace and found that a uniform and constant temperature could not be maintained. They found the two ends of the furnace to vary from twenty-five to fifty degrees in temperature, and variations of the same magnitude at different levels within the furnace. Vapor baths were also found to be inefficient They found that the bomb contents did not gradually reach the desired temperatures as the bath was heated, but, that there was a sudden rise of temperature only when the vapor bath began to boil. This sudden jump in temperature within the bombs caused explosions and fires in many cases.

For this investigation the electrically controlled Carius furnace constructed, calibrated and used by Derick and Howard (Unpublished work) was employed and found to be very efficient. The construction of the furnace as described by them is as follows: "The core of the furnace consists of an ordinary iron gas pipe three inches in diameter and thirty inches long. This pipe was threaded on both ends and fitted with heavy iron screw caps, making the total length of pipe plus caps thirty-two inches. A 5/8 inch hole was placed in the end and near the edge of one of the caps, through which the pyrometer couple might be introduced into the furnace, and also to act as an outlet for

gas in case of explosion.

"A strip of asbestos paper twenty-eight inches wide, and of sufficient length to make a wrapping of three thicknesses was moistened and wrapped tightly around the pipe, in such a way as to leave the threaded ends of the pipe uncovered.

"A loop of no. 18 copper wire was fastened tightly around each end of the pipe over the asbestos, allowing a sufficient lead from the loop to make external connections. Thirteen feet of no. 30 nicrome wire (diam. 0.252mm.) were wound around the asbestos-covered pipe uniformly and fastened firmly to the copper loops at each end.

"This coil was then covered with three layers of moistened asbestos paper, and a second coil of nicrome wire with copper terminals wound over it. The process was repeated a second time making a total of three coils on the furnace. The last coil was covered with wet asbestos paper until the diameter of the pipe plus the asbestos covering was five inches, and the whole allowed to dry.

"A portion of 'magnesia mixture' steam pipe covering five inches in diameter and thirty inches long was fastened firmly around this core in such a way as to allow the threaded ends (plus caps) of the pipe to project and be of easy access.

"In order to prevent loss due to heat of radiation at the ends, caps of magnesia mixture were made. Each cap consisted of a section of magnesia mixture four inches long, lined with sheet aluminium three inches in width, and a round sheet of

aluminium placed across one end and resting on the strips of aluminium lining. This left a space of one inch between the round sheet of aluminium and the end of the magnesia which was packed with asbestos and covered with a piece of cloth bound over the end. In one of the caps a one and one-half inch outlet hole was made corresponding to the hole on the iron cap for the introduction of the pyrometer couple.

"The copper terminal wires from the coils were insulated by means of glass tubing and led out through the opening in the magnesia covering. They were connected to a series of three knife switches and two binding posts (fastened to a board on top of the furnace) in such a way that one, two, or three coils could be used at a time. The whole furnace was placed in an iron cradle for support".

The temperature was found to be constant within ten degrees for the two ends of the furnace. A Hoskins thermo-electric pyrometer was used to register the temperature. The desired temperature was reached more quickly by using all three coils, and then maintained constant within five to ten degrees by switching off one or two coils, depending upon the temperature desired, and with the aid of carbon resistance.

IO. Calibration of Thermocouples.

Two furnaces were used in this work in order to save time as a number of runs were made. Several hours were required during each experiment in the heating and cooling of the furnaces. In light of this fact two thermocouples were calibrated

using the substances water, naphthalene, m-dinitrobenzene, and sulphur. The thermocouples were clamped so as to be in a vertical position. The lower ends of the same were allowed to come in contact with the vapors of the boiling substances mentioned above and the temperatures recorded as registered by the pyrometers. The substances were heated in heavy Jena test tubes (one inch in diameter and six inches long) which were inclosed in magnesia mixture steam pipe covering in order to keep the radiation of heat down to a minimum. Both thermocouples checked each other within two degrees and registered temperatures which were close to those as recorded for the compounds in Van Nostrand's Chemical Annual for the year I9I4. The results are tabulated as follows:

Substance	Temp. of Pyrometer (I)	(2)	Temp. by Van Nostrand
Water	I00°	I00°	I00°
Naphthalene	2I8	2I9	2I8.2
m-Dinitrobenzene	300	302	297
Sulphur	450	45I	448

II. General Method of Bomb Procedure. Separation and Analysis of Bomb Products.

An attempt was made to check Derick and Howard's work by repeating experiment #4 as described by them (unpublished work). This involved the heating of methylaniline hydrochloride at 240-50° for two hours in a bomb having a volume of one hundred and twenty cubic centimeters. Their work was confirmed and the results obtained are found on later pages of this thesis.

The effect of time and pressure were studied at 300-10°. The effect of temperature was studied at 220-30°, 240-50°, 300-10°, and 340-50°.

Weighed charges of the substances to be investigated were sealed in heavy Jena glass bomb tubes and heated in the furnaces for definite periods and at definite temperatures as recorded later in this work. After the products were heated and allowed to cool, the bombs were first opened by placing their tips in the sharp flame of the blast lamp. An ether extraction was first made in order to remove any free amines, hydrocarbons, alkyl halides, or other ether soluble substances that might have been formed in the reaction. The remainder of the bomb product, which consisted of the hydrochlorides of the amines, was extracted with hot water. This solution was cooled and then extracted with ether in order to remove the last traces of ether soluble material which the original ether extract did not take up. The solid jelly and crystalline mass found in the bomb after heating made this second ether extraction necessary. Practically no hydrolysis took place upon the addition of water to the bomb products. The water extract was then evaporated to dryness or to a solid jelly-like mass on the steam-bath and weighed until constant within five tenths of one per cent.

Two accurately weighed charges (usually eleven to twelve grams) were taken from this dried water soluble product and treated with about fifty cubic centimeters of (1:10) sodium carbonate solution in order to liberate the free amines. The amines were then extracted three times with ether, dried over anhydrous so-

dium sulphate, the ether evaporated on the steam-bath and the product dried as described in the method of separation on page I05 of this thesis. Each check of amines was then subjected to a quantitative separation into their classes by means of benzenesulphonyl chloride as described in our perfected method of separation on page I05 of this thesis.

The results of the separation are recorded under the following heads: Heating Conditions; Original Charges; Bomb Volume; Ether Extract; Water Extract Combined; Check Portions; Free Amines; Per Cent of Check Portion; Primary Derivatives; Secondary Derivatives; and Free Tertiary Amines.

I2. Bomb Analyses.

Experiment I.- Methylaniline hydrochloride at 240-50° for two hours.

Heating Conditions.

Time		
Hours	Minutes	Temperature
0	0	24°
0	30	75
0	50	I40
I	40	240
2	40	250
3	40	250

The bombs opened without pressure and the products were greenish yellow and transparent in appearance.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
I	22.I79	I20cc.	"Nil"	43.325
2	2I.506	I20"	"	

	Check Portion	Free Amines	Per Cent of Check Portion
I	II.I74	8.085	72.35
2	II.559	8.426	72.89

	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
I	3.503	II.457	I.938
2	3.459	I2.060	I.946

The blue dye found by Derick and Howard in similar experiments was not present with the free tertiary amines, due to the separation of the latter before refluxing with sodium alcoholate.

Experiment 2.- Methylaniline hydrochloride at 240-50° for four hours.

Heating Conditions.

Time		
Hours	Minutes	Temperature
0	0	24°
0	30	80
I	00	I75
2	00	250
2	45	250
3	I5	250
4	00	250
4	30	245
5	30	250
6	00	250

The bombs opened without pressure and the products were greenish yellow and transparent in appearance.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
I	20.I30	I20cc.	"Nil"	40. 206
2	20.2I3	I20"	"	

	Check Portions	Free Amines	Per Cent of Check Portion
I	II.097	7.965	7I.77
2	II.473	8.473	73.85

	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
I	2.835	II.6I4	I.9I9
2	3.0I5	I2.I20	2.483

Experiment 3.- Methylaniline hydrochloride at 290-300°

for one week.

Heating Conditions.

Time Hours	Minutes	Temperature
0	0	25°
I	0	I75
3	I5	290
4	00	300
6	30	300
I2	00	295
I6	I5	300
I8	I0	300
24	30	300
30	I0	300
40	30	295
46	00	290
52	I0	300
60	05	300
70	I5	300
75	20	300
85	25	300
90	I5	300
I00	30	295
II0	00	300
I20	I0	300
I25	45	300
I36	50	300
I42	I0	300

Hours	Minutes	Temperature
I48	30	300
I53	I0	300
I58	20	300
I63	I5	300
I68	00	295
I7I	I5	300

The bombs opened with tremendous pressure and the products had a solid black charry appearance. The gas evolved on opening the bomb burned with a greenish yellow flame. There was present among the bomb products a small amount (about 3cc.) of a faint yellow transparent oil.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
I	I5.075	I20 cc.	0.208	II.470
2	I7.444	I20 "	0.347	

	Check Portions	Free Amines	Per Cent of Check Portion
I	4.230	I.452	34.32
2	4.205	I.388	33.0I

	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
I	0.548	0.428	0.889
2	0.527	0.4I3	0.905

The "Check Portions", when treated with sodium carbonate solution to free the amines, left an appreciable amount of insoluble tarry product behind. The derivatives obtained were viscous and sticky and too small in amount to identify. The main reaction seemed to be one of decomposition.

Experiment 4.- Phenyltrimethylammonium chloride at 220-230° for twelve hours.

Heating Conditions.

Time		
Hours	Minutes	Temperature
0	0	25°
2	0	220
3	I0	230
6	I5	230
7	30	225
9	I5	230
I0	30	230
I2	I5	230
I3	I5	230
I4	00	230

The bombs opened with pressure and the products were light yellow and transparent in appearance with a syrup-like consistency. There was also present in the bombs a small amount of a fine white crystalline substance. The gas evolved burned with a greenish yellow flame.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
I	I6.268	I20 cc.	0.0I0	30.872
2	I7.000	I20 "	0.0I6	

	Check Portions	Free Amines	Per Cent of Check Portion
I	I2.I54	5.827	47.9
2	I2.003	5.692	47.4

No.	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
I	0.053	0.727	5.242
2	0.050	0.703	5.079

Experiment 5.- Phenyltrimethylammonium chloride at 240-250° for four hours.

Heating Conditions.

Time Hours	Minutes	Temperature
0	0	24°
I	I5	I50
2	00	240
3	I5	250
4	05	250
5	30	250
6	00	250

The bombs opened with pressure and the products were yellow and transparent in appearance with a syrup-like consistency. A small amount of a fine white granular substance was also present. The gas evolved burned with a greenish yellow flame.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
I	I6.480	I20 cc.	0.026	30.569
2	I6.398	I20 "	0.02I	

	Check Portions	Free Amines	Per Cent of Check Portion
I	I2.28I	5.926	48.8
2	I2.038	5.735	47.6

No.	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
I	0.I92	0.738	5.I96
2	0.I85	0.695	4.9I2

Experiment 6.- Phenyltrimethylammonium chloride at 300-3I0° for three hours.

Heating Conditions.

Time		
Hours	Minutes	Temperature
0	0	25°
0	50	I35
2	30	300
3	I5	3I0
4	30	3I0
5	30	3I0

The bombs opened with pressure and the products had a dark red and somewhat crystalline and viscous appearance. The gas evolved burned with a greenish yellow flame. A yellow oil separated out upon the addition of water and was extracted with ether. This product was combined with the direct ether extract.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
I	I6.349	I20 cc.	2.53I	27.I53
2	I6.404	I20 "	2.687	

No.	Check Portions	Free Amines	Per Cent of Check Portion
1	12.387	7.596	61.32
2	12.906	7.745	60.01

	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
1	2.920	5.844	3.200
2	3.101	5.993	3.174

The ether soluble product crystallized slowly into a dark red sticky mass having a peculiar odor.

Experiment 7.- Phenyltrimethylammonium chloride at 220-230° for twelve hours.

Heating Conditions.

Time		
Hours	Minutes	Temperature
0	0	20°
1	10	220
3	15	230
6	30	230
7	15	230
9	20	225
10	15	230
11	30	230
12	10	230
13	10	230

This experiment was made in order to show that dimethyl aniline exists together with methyl chloride under the conditions

of the experiment.

The bombs were cooled in a mixture of solid carbon dioxide and ether, opened and quickly connected to a gas burette and an absorption apparatus. The bomb was then taken out of the Dewar tube and rubbed with a cloth. In a few minutes the liquid product began to boil and the gas evolved was caught in the burette over a ten per cent solution of potassium hydroxide. Final traces of the gas were swept out with a stream of carbon dioxide from the tank. From the burette the gas was run over into the absorption apparatus which contained sodium alcoholate. Only a small amount of the gas was absorbed. The gas had an ether-like odor somewhat similar to that of methyl iodide, and burned with a greenish yellow flame. Four hundred and thirty cubic centimeters of gas were collected from bomb #I, and three hundred and ninety cubic centimeters from bomb # 2. In round numbers, the theoretical yield of gas corresponding to the weight of the free dimethyl aniline obtained is four hundred and fifty-five cubic centimeters and four hundred and six cubic centimeters respectively.

The products remaining in the bombs were treated with water. A small amount of oil separated out which was extracted with ether.

No.	Original Charge	Bomb Volume	Ether Extract	Boiling Point of Ether Soluble Product
I	I6.329	I20cc.	2.462	I89 - 9I° (uncorr.)
2	I6.279	I20 "	2.I98	

The water soluble product was lost by accident. These results show that the reaction carried out under the above conditions is mainly one of dissociation into methyl chloride and di-

methyl aniline.

The potassium hydroxide solution in the gas burette and the sodium alcoholate in the absorption apparatus gave positive tests for chlorine, thus indicating some absorption in both solutions.

Experiment 8.- Phenyltrimethylammonium chloride at 300-3I0° for twelve hours.

Heating Conditions.

Time Hours	Minutes	Temperature
0	0	24°
2	0	300
4	I5	3I0
6	30	3I0
8	45	3I0
9	30	305
I0	I0	3I0
I2	30	3I0
I3	30	3I0
I4	05	3I0

The bombs opened with pressure and the products had a black-red and somewhat crystalline and viscous appearance. A small amount of oil separated upon the addition of water and was extracted with ether. This product was added to that obtained by direct ether extraction. The gas evolved burned with a greenish yellow flame.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
I	I6.463	I20cc.	2.568	27.092
2	I6.4I7	I20 "	2.794	

	Check Portions	Free Amines	Per Cent of Check Portion
I	II.853	6.403	54.02
2	II.947	6.650	55.66

	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
I	2.448	5.905	2.435
2	2.6I5	5.8I8	2.527

The ether soluble product was recovered as an oily sticky mass.

Experiment 9.- Phenyltrimethylammonium chloride at 300-310° for three hours. Effect of pressure.

Heating Conditions.

Time Hours	Minutes	Temperature
0	0	20°
2	0	300
3	05	310
3	45	310
4	15	310
5	00	310

The bombs opened with pressure and the products had a dark red and somewhat crystalline and viscous appearance. A small amount of oil separated on adding water to the bomb charges and was extracted with ether. This oil was added to the product obtained by direct ether extraction. The gas evolved burned with a greenish yellow flame.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
1	8.218	120cc.	1.375	12.931
2	8.233	120 "	1.480	

	Check Portions	Free Amines	Per Cent of Check Portion
1	5.968	3.485	58.39
2	5.917	3.423	57.85

	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
1	1.105	3.496	1.274
2	1.079	3.481	1.062

The ether soluble product was obtained as an oily sticky mass.

Experiment 10.- Phenyltrimethylammonium chloride at 340-350° for three hours.

Heating Conditions.

Time Hours	Minutes	Temperature
0	0	20°
2	30	340
3	15	350
4	30	350
5	00	350
6	30	350

The bombs opened with considerable pressure and the products had a blackish-brown solid appearance. The gas evolved burned with a greenish-yellow flame.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
1	16.283	120cc.	3.761	24.725
2	16.348	120 "	3.844	

	Check Portions	Free Amines	Per Cent of Check Portion
1	11.911	6.610	55.49
2	11.987	6.583	54.91

	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
1	2.417	1.904	3.517
2	2.582	1.863	3.465

The ether soluble product crystallized readily in brown needles. This product was more dry in appearance than corresponding products in previous experiments.

Experiment II.- Phenyltrimethylammonium chloride at 300-3I0° for twelve hours. Effect of pressure.

Heating Conditions.

Time Hours	Minutes	Temperature
0	0	20°
2	0	300
3	30	3I0
4	I5	3I0
6	I0	305
8	05	3I0
9	I5	3I0
I0	30	305
II	I5	3I0
I2	20	3I0
I4	00	3I0

The bombs opened with pressure and the products had a dark red and somewhat crystalline and viscous appearance. The ether soluble product crystallized in a dark needle-like sticky mass. The gas evolved burned with a greenish-yellow flame.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
I	8.253	I20cc.	I.I77	I4.277
2	8.223	I20 "	I.643	

	Check Portions	Free Amines	Per Cent of Check Portion
I	6.023	3.534	58.67
2	5.996	3.339	55.68

	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
I	I.I35	3.960	I.II7
2	I.088	3.854	0.998

Experiment 12.- Methylaniline hydrochloride at 300-310° for three hours.

Heating Conditions.

Time Hours	Minutes	Temperature
0	0	30°
2	0	300
2	30	310
3	00	310
3	45	310
4	00	310
5	00	310

The bombs opened with very slight pressure and the products were dark red with a green fluoresence, but transparent and jelly-like in appearance.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
1	16.253	120cc.	"Nil"	32.232
2	16.298	120 "	"	

	Check Portions	Free Amines	Per Cent of Check Portions
1	11.954	8.783	73.47
2	11.990	8.867	73.95

	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
1	6.109	9.987	1.564
2	6.087	10.159	1.575

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Experiment I3.- Methylaniline hydrochloride at 340-50° for three hours.

Heating Conditions.

Time Hours	Minutes	Temperature
0	0	25°
2	20	340
3	00	350
3	45	350
4	30	350
5	20	350

The bomb opened with slight pressure and the product had a jelly consistency together with some crystalline substance. The whole mass had a greenish-red fluoresence.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
I	I6.268	I20cc.	0.060	I6.I24

	Check Portions	Free Amines	Per Cent of Check Portion
I	8.098	6.498	80.24
2	7.826	6.323	80.79

	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
I	8.265	3.I90	0.858
2	7.920	3.097	0.805

Experiment I4.- Phenyltrimethylammonium chloride at 300-3I0° for ninety-six hours.

Heating Conditions.

Time		
Hours	Minutes	Temperature
0	0	30°
2	0	300
3	30	3I0
5	45	3I0
I2	I5	3I0
I6	I0	3I0
25	30	3I0
30	30	3I0
36	00	3I0
4I	I5	3I0
50	05	305
54	30	3I0
60	45	3I0
66	I0	3I0
76	30	3I0
80	I0	3I0
84	20	3I0
87	I5	3I0
90	00	305
94	25	3I0
96	20	3I0
98	00	3I0

The bombs opened with great pressure. The gas evolved burned with a greenish-yellow flame. A small portion of the bomb product was a yellow transparent oil (about three cubic centimeters); another portion was reddish-brown and crystalline in appearance, while the larger portion seemed to consist of a tarry and charred substance.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
	I6.283	I20cc.	I.362	II.06I

No.	Check Portions	Free Amines	Per Cent of Check Portion
I	5.077	2.027	39.92
2	5.0I3	I.985	39.59

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No.	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
I	I.232	0.672	I.I85
2	I.I89	0.658	I.090

The "Check Portions", when treated with sodium carbonate solution to free the amines, left an appreciable amount of tarry substance behind.

Experiment 15.- Methylaniline hydrochloride at 300-10° for twelve hours.

Heating Conditions.

Time Hours	Minutes	Temperature
0	0	25°
2	05	300
3	00	310
4	30	310
5	00	310
5	45	310
6	15	310
7	00	310
8	05	305
9	20	310
10	00	310
11	30	310
12	05	310
13	15	310
14	05	310

The bombs opened with very slight pressure and the product consisted of a reddish-brown crystalline substance together with some charred material.

No.	Original Charge	Bomb Volume	Ether Extract	Water Extract Combined
	16.303	120cc.	0.350	15.822

	Check Portions	Free Amines	Per Cent of Check Portions
1	7.855	5.841	74.36
2	7.893	5.906	74.82

	Primary Derivatives	Secondary Derivatives	Free Tertiary Amines
1	6.914	1.887	1.653
2	7.032	1.851	1.695

The "Check Portions", when treated with sodium carbonate solution to free the amines, left a small amount of tarry residue.

I3. Check of Analytical Data.

The simplest method found to check the analytical work was that used by Derick and Howard in their study of the "Rearrangement of Alkyl Anilines" (unpublished work). The standard used was the weight of the free amine charge for each analysis; the following set of ratios was calculated for each analysis:

The ratio $\frac{\text{Wt.of Primary Derivative}}{\text{Wt.of Free Amine Charge}}$ was used for primary amines;

the ratio $\frac{\text{Wt.of Secondary Derivative}}{\text{Wt.of Free Amine Charge}}$ for secondary amines; and

the ratio $\frac{\text{Wt.of Free Tertiary Amine}}{\text{Wt.of Free Amine Charge}}$ for the tertiary amines.

The results obtained are found in Summary I as follows:

Summary I.

				Ratios								
				Primary			Secondary			Tertiary		
Exp.	Temp.	Time	Vol.	(I)	(2)	Av.	(I)	(2)	Av.	(I)	(2)	Av.
I	240-50°	2hrs.	I20cc.	.43	.4I	.42	I.4I	I.43	I.42	.23	.23	.23
2	240-50	4 "	I20 "	.35	.35	.35	I.45	I.43	I.44	.24	.29	.27
3	290-300	Iwk.	I20 "	.37	.38	.37	.29	.29	.29	.6I	.65	.63
4	220-30	I2hrs.	I20 "	.0I	.0I	.0I	.I2	.I2	.I2	.89	.89	.89
5	240-50	4 "	I20 "	.03	.03	.03	.I2	.I2	.I2	.87	.85	.86
6	300-I0	3 "	I20 "	.38	.40	.39	.76	.77	.76	.42	.40	.4I
8	300-I0	I2 "	I20 "	.38	.39	.38	.92	.87	.89	.38	.38	.39
9	300-I0	3 "	I20 "	.3I	.3I	.3I	I.00	I.00	I.00	.36	.3I	.34
I0	340-50	3 "	I20 "	.36	.39	.37	.28	.28	.28	.53	.53	.53
II	300-I0	I2 "	I20 "	.32	.32	.32	I.I2	I.I5	I.I3	.3I	.29	.30
I2	300-I0	3 "	I20 "	.69	.68	.68	I.I3	I.I4	I.I3	.I7	.I7	.I7
I3	340-50	3 "	I20 "	I.27	I.25	I.26	.49	.49	.49	.I3	.I3	.I3
I4	300-I0	96 "	I20 "	.6I	.59	.60	.33	.33	.33	.58	.54	.56
I5	300-I0	I2 "	I20 "	I.I9	I.I9	I.I9	.32	.3I	.3I	.28	.28	.28

On examining the results it is found that the greatest difference between check results, as regards the primary amines, is three parts in thirty-nine or seven per cent, as indicated in

experiment 10 for the three hour run at 340-50° in a bomb having a volume of one hundred and twenty cubic centimeters. If the average values are considered, one finds a difference of three and one half per cent to be the greatest difference between the two check results of a given experiment. Similarly for the secondary amines, the greatest difference between check results is five parts in ninety-two or five per cent, as is shown by experiment 8 for the twelve hour run at 300-10° in a bomb having a volume of one hundred and twenty cubic centimeters. The average value amounts to three per cent. For the tertiary amines, the greatest difference between check results is five parts in twenty-nine or seventeen per cent, as shown by experiment 2 for the four hour run at 240-50° in a bomb having a volume of one hundred and twenty cubic centimeters. This gives the greatest difference as eight and one half per cent from the average results. The per cent differences between the check results for all runs are 6%, 18%, 8%, 2%, 11%, 7%, 14%, 7%, 8%, 2%, 1%, 9%, and 3%, giving an average difference between the check results of 6.9%, or a difference of 3.45% between the average results. These results are in accord with those of Derick and Howard (unpublished work). It is evident then that the analytical work upon which the conclusions in this thesis are based possess a total error not greater than six and nine tenths per cent.

14. Interpretation of the Analytical Data Obtained from the Rearrangements.

In the theoretical part of this thesis the hypothesis

advanced postulates that methaniline hydrochloride rearranges only in the quarternary stage. In accordance with this view methylaniline hydrochloride must change into dimethylaniline hydrochloride and aniline, followed by the change of dimethylaniline hydrochloride into phenyltrimethylammonium chloride with the additional formation of free aniline. Two molecules of aniline must be produced for each molecule of the quarternary compound formed during the course of the reaction in order to furnish enough methyl groups. If the rearrangement occurs in the quarternary stage the first product of rearrangement should be dimethyl amino methyl benzene. When the secondary amine has been completely changed into this substance in accordance with the hypothesis advanced and the above reactions, two thirds of the bomb product should consist of aniline.

On the other hand, if the change of methyl aniline hydrochloride into the quarternary compound involves the dissociation of the former into aniline and methyl chloride with the subsequent methylation of the secondary amine by methyl chloride until the quarternary stage is reached, the first product of rearrangement (the tertiary amine or its corresponding hydrochloride), may also dissociate changing to a secondary and finally to a primary amine. Two mols of methyl chloride are dissociated in changing to the primary amine, and hence it is evident that primary amine methyl benzenes should be the final products of the rearrangement. In other words, no aniline would be found at the end of the experiment under such conditions.

For all the rearrangements which are carried out at the lower temperatures and for intervals of from two to twelve hours the primary amine derivatives will be chiefly if not entirely, aniline, The secondary amines will be chiefly, if not entirely, methyl aniline. This is shown in the experiments by a steady increase in the per cent of primary amines. When a maximum is reached two molecules of aniline (as mentioned above) have been produced. On the other hand there should be a decrease of secondary amines as the rearrangement proceeds, with a possible but not very probable increase when the primary amine has reached its maxinum since, when aniline is methylated by methyl chloride under the conditions of these experiments, it is no doubt transformed very readily into the quarternary stage. The quarternary compound thus formed rearranges very rapidly, since its rearrangement takes place best at the moment of its formation.

The fact that the primary and secondary amines are weighed as the corresponding sulphonyl derivatives, while the tertiary amines are weighed in the free state, makes it impossible to calculate the per cent of primary and secondary amines formed in the rearrangement until thier nature has been determined, unless they consist of aniline and methyl aniline respectively. This suggested a preliminary method to Derick and Howard of attacking the problem of the interpretation of thier analytical results. If thier interpretation is correct the sum of the ratios of primary, secondary, and tertiary amines to the total free amines in each experiment should equal I.00 within the experimental error as determined under Summary I.

Their interpretation has been found to be correct, and hence used in the following summary. SummaryII, accordingly, has been prepared from Summary I, by multiplying the weight ratios of the primary amines by the fraction

$$\frac{\text{Molecular Wt. of Aniline}}{\text{Mol. Wt. of Sulphonyl Deriv.}} = \frac{93}{233} = 0.399;$$

and the weight ratios of the secondary amines have been multiplied by the fraction

$$\frac{\text{Mol. Wt. of Methyl Aniline}}{\text{Mol. Wt. of Sulphonyl Deriv.}} = \frac{107}{247} = 0.433.$$

For the tertiary amines the weight ratio of the free amine as found is used. The results of these calculations are recorded in the following summary:

Summary II.

Exp.	(I) Temp.	(2) Time	(3) Vol.	(4) Primary as Free Aniline			(5) Secondary as Free Methyl Aniline			(6) Ter. as found		
I	240-50°	2hrs.	I20cc.	.I7	.I6	.I6	.6I	.6I	.6I	.23	.23	.23
2	240-50	4 "	I20 "	.I3	.I3	.I3	.63	.6I	.62	.24	.29	.26
3	290-300	Iwk.	I20 "	.I5	.I5	.I5	.I3	.I3	.I3	.6I	.65	.63
4	220-30	I2hrs	I20 "	.003	.003	.003	.05	.05	.05	.89	.89	.89
5	240-50	4 "	I20 "	.0I	.0I	.0I	.05	.05	.05	.87	.85	.86
6	300-I0	3 "	I20 "	.I5	.I5	.I5	.33	.33	.33	.42	.40	.4I
8	300-I0	I2 "	I20 "	.I5	.I5	.I5	.40	.38	.39	.38	.38	.38
9	300-I0	3 "	I20 "	.I2	.I2	.I2	.43	.4I	.42	.36	.3I	.33
I0	340-50	3 "	I20 "	.I4	.I5	.I5	.I2	.I2	.I2	.53	.53	.53
II	300-I0	I2 "	I20 "	.I2	.I2	.I2	.48	.50	.49	.3I	.29	.30
I2	300-I0	3 "	I20 "	.28	.27	.27	.49	.49	.49	.I7	.I7	.I7
I3	340-50	3 "	I20 "	.5I	.50	.50	.2I	.2I	.2I	.I3	.I3	.I3
I4	300-I0	96 "	I20 "	.24	.24	.24	.I4	.I4	.I4	.58	.54	.56
I5	300-I0	I2 "	I20 "	.47	.47	.47	.I4	.I3	.I3	.28	.28	.28

Summary II (Continued).

Sum of Primary, Secondary, and Tertiary Averages.

Exp.	Primary	(7) Secondary	Tertiary	Total	(8) % Deviation from I.00
I	.I6	.6I	.23	I.00	
2	.I3	.62	.27	I.02	2%
3	.I5	.I3	.63	.9I	-9
4	.003	.05	.89	.94	-6
5	.0I	.05	.86	.92	-8
6	.I5	.33	.4I	.89	-II
8	.I5	.39	.38	.92	-8
9	.I2	.42	.34	.88	-I2
I0	.I5	.I2	.53	.80	-20
II	.I2	.49	.30	.9I	-9
I2	.27	.49	.I7	.93	-7
I3	.50	.2I	.I3	.84	-I6
I4	.24	.I4	.56	.94	-6
I5	.47	.I3	.28	.88	-I2

Conclusions from Summary II.

It is noted that the fractional ratios of the free amines to the initial charges have been used rather than the percentage form of expression. If, then, the primary amine is aniline, and the secondary amine is methyl aniline, the sum of the fractions for each class of amines should equal unity within experimental error. Column 8 shows this to be the case with experiments I and 2 when methyl aniline hydrochloride was heated, hence no rearrangement has occurred as is supported by the melting point data of Summaries IV and V. These results confirm the work of Derick and Howard with the same compound. Thus in these two experiments the primary amine is aniline, and the secondary amine is methyl aniline under the conditions of the experiment.

On the other hand, experiments 3, 6, 9, I0, II, I3, and I5 clearly show that rearrangement has occurred since the sum of the fractions for each class of amines does not equal I.00 within the experimental error. The amount of deviation from I.00 gives a measure of the rearrangement, that is, of the shift of the CH_3 groups into the ring. This fact is further supported by the melting point data in Summaries IV and V. If accurate interpretation could be found relative to the nature of the rearranged products, then their corresponding sums of the fractions for the several classes of amines would also equal I.00 within experimental error, due to the use of proper ratio of free amine to derivative.

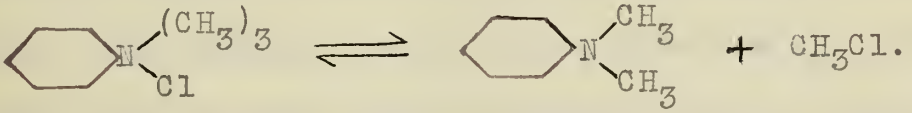
In experiments 4, 5, 8, I2, and I4, only slight rearrangement has occurred, as is also supported by the melting point data. Experiments I0 and I3, on the other hand, show decided rearrangement as one would expect under the conditions of the experiments. The melting point data further substantiates this fact. The quarternary compound is rearranging as fast as it is formed and only a very small amount of aniline, if any, would remain at the completion of the rearrangement.

Experiments 6, 8, 9, II, and I5 give similar results within the experimental error. If one compares the per cent deviation from I.00 for the sum of the fractions for each class of amines of Summary II, one gets -II%, -8%, -I2%, -9%, and -I2%, all agreeing with each other within experimental error.

I5. Influence of Time upon the Rearrangement.

Derick and Howard have shown in the case of methyl ani-

line hydrochloride at or below the temperature of 230°, that a variation in the time of heating from two to forty-eight hours has a negligible effect on the course of the reaction since no shift of CH_3 groups occurred, and only equilibria were established between primary, secondary, and tertiary amine and their hydrochlorides. One would expect the same result in the case of the quarternary compound only if no shift of CH_3 groups into the ring occurs. On examining experiments 4 and 5 one finds the same general results within experimental error due to the establishment of the following equilibrium:



The reaction then is one of dissociation into dimethyl aniline and methyl chloride with no rearrangement. That this is the case is shown by the very small per cent of primary and secondary derivatives obtained in these experiments and the fact that the yield of tertiary amine is 90% or more; hence no appreciable rearrangement of CH_3 groups to the ring could have taken place at or below 250°. It is difficult to see how primary and secondary amines can be formed unless water is present to give hydrochloric acid from methyl chloride or a methyl group shifts to the ring. In fact water is not present and the small per cent of primary and secondary derivatives is definite evidence of no rearrangement but just an establishment of the above equilibrium. All of these experiments in which the bombs opened with pressure

prove conclusively that methyl chloride may be dissociated from the aminic nitrogen atom to which are linked a methyl group and a chlorine atom, and that methyl chloride is the methylating agent in these rearrangements. It is only when the quarternary compound is formed that the bombs open with pressure. This is observed too when methylaniline hydrochloride is heated above 300°. It does not follow, however, that the tertiary amine in this latter case will be dimethyl aniline, because rearrangement of the quarternary compound occurs best at the moment of its formation. We may expect as tertiary amines then dimethyl aminomethyl benzenes, together, perhaps with a little unchanged dimethyl aniline. The gas evolved upon opening the bombs was shown in all cases to be methyl chloride. The equilibrium mentioned above, therefore, must have been established. This is in accord with the findings of Derick and Howard with methyl aniline hydrochloride when the time does not exceed forty-eight hours and the temperature is 250° or below.

On the other hand, at 300° the time does become an important factor in the rearrangement. On comparing experiment I4 with experiment 6 one notices that the primary amines have increased from I5% to 24%, or an increase of nine parts in twenty-four or 37%, while the secondary amines show a decrease from 33% to I4% on nineteen parts in thirty-three or 54%. The tertiary amines have increased from 4I% to 56% or fifteen parts in fifty-six or about 27%. Similar results are obtained when experiment 8 is compared with experiment I4. Experiment I4 is the only one in comparison with experiment 6 at 300-I0° that shows a decrease in secondary

amines and an increase in tertiary amines. An increase from three hours to twelve hours heating as shown in experiment 8 gives an increase in the secondary amines and a decrease in the tertiary amines. Time has no influence on the rearrangement from three to twelve hours heating at 300-10°; the influence is marked, however, from twelve to ninety-six hours heating. This may be clearly seen by comparing experiments 6, 8, and 14 in column seven of Summary II. The percentages of primary amines for three, twelve, and ninety-six hours heating are 15%, 15%, and 24% respectively. The percentages of secondary amines are 33%, 39%, and 14% respectively while the tertiary amines are 41%, 38%, and 56% respectively. A run made at 300-10° for forty-eight hours resulted in an explosion.

16. Influence of Pressure upon the Rearrangement at the Temperatures 300 - 10°

The first experiments which were attempted in the study of the effect of pressure on the rearrangement were tried in bombs having a volume of sixty cubic centimeters, or just one half the capacity of the bombs ordinarily used namely, one hundred and twenty cubic centimeters. All such experiments resulted in explosions. Better results were obtained when one half of the charge ordinarily employed was used in bombs having a volume of one hundred and twenty cubic centimeters.

For the three hour runs Experiments 6 and 9 give the percentages of primary amines as 15% and 12%, which check each other within the experimental error. The secondary amines, on the other hand, have the percentages 33% and 42%, and the tertiary

amines give the percentages 41% and 34%. This gives a difference of 9% between secondary amines, and a difference of 7% between the tertiary amines, thus indicating that there is probably a slight effect caused by pressure on the course of the rearrangement at 300-10° for three hours.

For the twelve hour runs Experiments 8 and 11 give the percentage of primary amines as 15% and 12% which agree with each other within the experimental error. The percentages of the secondary amines are 39% and 49%, while those of the tertiary amines are 38% and 3%.

These results show also that pressure does have a slight effect on the course of the rearrangement at 300-10° when the heating lasts for twelve hours. On the other hand if experiments 9 and 11 are compared one finds the percentages of primary, secondary, and tertiary amines to check each other within the experimental error, showing that the time of heating from three to twelve hours does not influence the course of the rearrangement. It may be concluded then that pressure has only a slight influence on the rearrangement during three and twelve hours heating at 300-10°.

17. Influence of Different Temperatures upon the Rearrangement.

It is noted in experiments 4 and 5 that a variation in temperature from 220° to 250° has no apparent influence upon the reactions, as the relative percentages of primary, secondary, and tertiary amines check each other within the experimental error. This increase in temperature shifts the equilibrium which analy-

ses will not show, due to the fact that the analyses show the state in the bombs when the dissociation of the hydrochlorides is negligible. Each bomb tube in these experiments undergoes the same change on cooling and the point where the dissociation of the hydrochlorides is negligible is the same for each, hence the same analyses. Derick and Howard also find this to be the case with methylaniline hydrochloride for the same reason just pointed out for experiments 4 and 5 where the quarternary compound was heated.

On the other hand, when the temperature is increased from 250° to 300° rearrangement occurs. Since this is a non-reversible reaction the analytical results must be different from those of experiments 4 and 5 where we had the establishment of an equilibrium with little or no rearrangement, for upon cooling the bombs, the amines with one or more methyl groups in the ring cannot change back to the quarternary compound and then establish an equilibrium between it and the primary, secondary, and tertiary amines. The same general results are obtained when the temperature is increased to 350°. In experiments 6, and 10 the percentages of primary amines are 15%, 15% respectively; those of the secondary amines are 33%, and 12%; while those of the tertiary amines are 41%, and 53%.

It is noted then that increases from 250° to 350° clearly show that temperature is the main variable in these rearrangements.

18. Formation of Phenyl Trimethyl Ammonium-Chloride in the Bombs.

Experiments 1, 2, 3, 12, 13, and 15 discussed in this section involve the heating of methyl aniline hydrochloride.

Since our hypothesis postulates that methyl aniline hydrochloride rearranges only in the quarternary stage, it is evident that this compound must be formed during the course of the rearrangement. The weight of the water extracts of the bomb products together with the data in Summaries I and II make it possible to determine the percent of the quarternary compound formed in each experiment where methyl aniline hydrochloride was used as the "ausgangs" material. As pointed out by Derick and Howard: "It also offers a means of justifying the interpretation-------------------------that the primary amine is aniline, the secondary amine is methyl aniline, and the tertiary amine is dimethyl aniline".

The water extract of the bomb products is composed of phenyl trimethyl ammonium chloride together with the hydrochlorides of primary, secondary, and tertiary amines. If any other organic substances are formed during the rearrangement, with the exception of salts of organic bases, they will be previously extracted with ether. Since experiments 1, 2, 3, 12, 13, and 15 in Summary II indicate that the primary amine is (at least for the most part) aniline, the secondary amine methyl aniline, and the tertiary amine dimethyl aniline, their weights as hydrochlorides may be calculated from the corresponding sulphonyl derivatives, as suggested by Derick and Howard, as follows:

(a) For primary amines

$$\frac{\text{Mol. Wt. of Aniline Hydrochloride}}{\text{Mol. Wt. of Aniline Sulphonyl Deriv.}} = \frac{129}{233} = 0.55;$$

(b) for secondary amines

$$\frac{\text{Mol.Wt.of Methyl Aniline Hydrochloride}}{\text{Mol.Wt.of Methyl Aniline Sulphonyl Deriv.}} = \frac{143}{247} = 0.58;$$

(c) for tertiary amines

$$\frac{\text{Mol.Wt.of Dimethyl Aniline Hydrochloride}}{\text{Mol. Wt. of Dimethyl Aniline}} = \frac{151}{121} = 1.30$$

or

$$\frac{\text{Mol.Wt.of(N)Dimethylaminotrimethyl Benzene HCl}}{\text{Mol.Wt.of(N)Dimethylaminotrimethyl Benzene}} = \frac{199}{163} = 1.22.$$

The weights of the hydrochlorides of the primary, secondary, and tertiary amines are calculated by means of these ratios and the proper data from the experiments as follows:

(a) Primary amines

Wt. of sulphonyl deriv. × 0.55 = Wt. of hydrochloride.

(b) Secondary amines

Wt. of sulphonyl deriv. × 0.58 = Wt. of hydrochloride.

(c) Tertiary amines

Wt. of tertiary amine × I.30 = Wt. of hydrochloride.

or

Wt. of tertiary amine × I.22 = Wt. of hydrochloride.

The results thus obtained are given in Summary III.

Summary III.

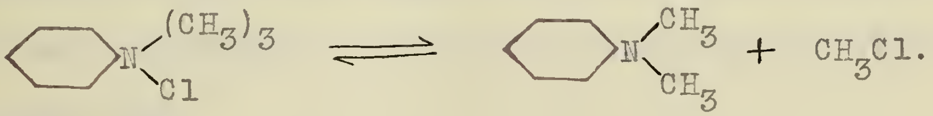
Exp.	Check	(I) Primary as Aniline Hydrochloride	(2) Secondary as Methyl Aniline Hydrochloride	(3) Tertiary as Dimethyl Aniline Hydrochloride
I	I	I.93	6.65	2.52
	2	I.90	6.99	2.53
2	I	I.56	6.74	2.49
	2	I.66	7.03	3.23
3	I	0.30	0.25	I.I6
	2	0.29	0.24	I.I8
I2	I	3.36	5.79	2.03
	2	3.35	5.89	2.05
I3	I	4.55	I.85	I.I2
	2	4.36	I.80	I.05
I5	I	3.80	I.I0	2.I5
	2	3.87	I.07	2.20

		(4) Sum of Primary, Second., and Tertiary	(5) Weight of Hydrochloride Found	(6) Theoretical Per Cent Found
I	I	II.I0	II.I7	98.94
	2	II.42	II.55	98.87
2	I	I0.79	II.09	97.29
	2	II.92	II.47	I03.92
3	I	I.7I?	4.23?	40.42?
	2	I.7I?	4.2I?	40.6I?
I2	I	II.I8	II.95	93.55
	2	II.39	II.99	94.99
I3	I	7.52	8.I0	92.83
	2	7.2I	7.83	92.08
I5	I	7.05	7.86	89.69
	2	7.I4	7.89	90.49

Conclusions from Summary III.

It is evident that if any phenyl trimethyl ammonium chloride is formed in experiments I and 2 it is well within the experimental error of 6.9% and hence is negligible. It may be concluded then that no quarternary compound is formed in the bombs at or below 250°. This is further supported by the fact that in

experiments 1 and 2 where methylaniline hydrochloride was heated at 240-50°, the bombs opened without pressure, hence no methyl chloride remains and its rate of recombination with the amines under the conditions of the experiments is very rapid. The fact that the bombs opened without pressure proves that the quarternary compound had not formed, and hence no shift of methyl groups into the ring had occurred. On the other hand, when the quarternary compounds were heated the bombs opened with pressure and the gas is methyl chloride as proved in experiment 7. It does not follow, however, that a shift of methyl groups has occurred in these cases. The bombs in experiments 4 and 5, in which the quarternary compound was heated at 220 - 30° and 240 - 50° respectively, opened with pressure but analyses showed that no rearrangement had taken place. At the temperatures in question the reaction was simply one of dissociation into dimethyl aniline and methyl chloride with no rearrangement. We have then the establishment of the following equilibrium:



The small percent of primary and secondary derivatives obtained in these two experiments, together with the fact that the yield of tertiary amine is at least ninety per cent, is conclusive proof of the establishment of the above equilibrium. This means that the rate of combination of methyl chloride with dimethyl aniline and other tertiary amines to form the quarternary compound is too slow for completion of the equilibrium that exists at or-

dinary temperatures during the time of the cooling of the bomb as was the case with methyl chloride and aniline giving methyl aniline, and methyl chloride and methyl aniline giving dimethyl aniline.

In experiments 3, I3, and I5, the hypothesis advanced demands that the quarternary compound shall be formed since the tertiary amine is not dimethyl aniline. In experiment I2 about sixty per cent of the tertiary amine is dimethyl aniline as noted from the boiling point data in Summary V. However, in the experiments where methyl aniline hydrochloride was heated at 300° to 350°, the bombs opened with pressure like all experiments on heating the quarternary compound - suggesting the possibility that methyl chloride was escaping and that the quarternary compound had formed, as analyses and melting point data show that methyl groups have shifted into the ring. The pressure in the bombs from experiments I2, I3, and I5 was slight however in comparison with that in bombs from experiment 3. The gas evolved on opening the bomb had a characteristic odor and burned with a greenish yellow flame as pointed out in experiment 7 and as described in the literature for methyl chloride.

The isolation of the quarternary compound from experiment 3 gives more evidence in favor of the hypothesis advanced in this thesis. It was accomplished as follows: The check portions of the water soluble bomb product which contained the quarternary compound together with the hydrochlorides of primary, secondary, and tertiary amines, were treated with a (I:I0) solution of sodium carbonate in order to free the amines and extracted with ether.

A small portion of the aqueous extract containing the quarternary compound was treated with a solution of platinum chloride, evaporated almost to dryness on the water bath, the sodium chlorplatinate removed by extraction with methyl alcohol and the platinum salt of the quarternary compound obtained as a yellowish red crystalline substance. The isolation of this quarternary compound also of methyl chloride proves that the quarternary compound had formed in the light of this work and that its formation is necessary for the rearrangement. The quarternary compound was not isolated, however, in other experiments where methyl aniline hydrochloride was heated.

The fact that the quarternary compound may rearrange at the moment of its formation indicates that it may not be found at the end of the experiment. On the other hand, if rearrangement has taken place, it is possible that when the bomb is cooled, a temperature may be passed through at which the quarternary compound may form but not rearrange.

It may be pointed out that the "Wt. of the Hydrochloride Found" in experiment 3 under column 5 was not pure hydrochloride but consisted in part of some tarry product which was soluble in water but insoluble in ether. This accounts for the corresponding low percentages found in column 6 namely 40.42% and 40.61%. These percentages would indicate that the quarternary compound was present in amount of about 60%, but it is doubtful whether more than about 40% or 50% was present. We are not certain, however, of the exact amount formed.

Summary 3 shows then that the quarternary compound must

be present in amounts which vary from 5% to 50%.

19. Identification of the Amines Found in Each Experiment.

The quantitative separation of the three classes of amines as developed in this thesis has greatly simplified the identification of the individual amines resulting from the rearrangement. The process of fractional crystallization or distillation which Hofmann used was very crude and laborious, and he was compelled to abandon it.

Physical methods, however, must be used for the identification of the individual amines in a given class as no other methods so far have been developed. Fractional crystallization is to be preferred of the available physical methods now in use, hence the formation of crystalline derivatives as a means of separating the three classes of amines produced during the course of the rearrangement.

From the data given in SummaryII it is evident that in experiments I and 2 the primary amine is aniline, the secondary amine is methyl aniline, and the tertiary amine is dimethyl aniline. This is true for all experiments below 250°. If these conclusions are correct the melting points of the original crystalline benzene sulphonyl derivatives of the primary and secondary amines before crystallization should be close to those of the monosulphonyl derivative of aniline and the sulphonyl derivative of methyl aniline. These melting points are recorded in Summary IV. It may be pointed out here that the procedure used in the

separation of the three classes of amines causes all of the ether soluble tarry products to be thrown in the fraction containing the secondary amines.

The tertiary amines in these experiments have been determined by fractional distillation. These fractions with their boiling points are also given in Summary IV.

(a) Summary IV.

Melting Points of Original Products Before Crystallization.

(I) Primary Sulphonyl Derivatives.

Exp.	Sinters	Softens	Melts	Remarks
I	98°	I00°	I07°	
2	97	I00	I05	
3				Sticky and not dry on porous plate
4				
5				
6	I00	I05	I09	
8	80	88	I03	
9	89	93	I06	
I0	I30	I35	I38	
II	88	93	I04	
I2	86	92	I02	
I3				Sticky on porous plate.
I4	85	89	95	
I5	65	73	83	

(2) Secondary Sulphonyl Derivatives.

Exp.	Sinters	Softens	Melts	Remarks
I	6I°	66°	74°	
2	60	64	72	
3				Sticky on porous plate.
4				" " " "
5	65	70	78	
6				Sticky on porous plate.
8				" " " "
9				" " " "
I0	I25	I30	I35	
II				Sticky on porous plate.
I2	60	65	72	
I3				Sticky on porous plate.
I4	I05	II6	I34	
I5				" " " "

(3) Tertiary Amines.

Exp.	B.P.	(First Frac.) Per Cent of Tertiary	B.P.	(Sec. Frac.) Per Cent of Tertiary	B.P.	(Third Frac.) Per Cent of Tertiary	B.P.
1	189-92°	100%					
2	189-92	100					
3	220	100					
4	189-92	90	280°	10%			
5	189-92	90	280	10			
6	215-22	60	228-35	10	235-80°	20%	
8	220-30	30	230-80	10	280	60	
9	205-10	60	210-15	20	280	20	
10	225-35	10	235-45	10	280	80	
11	205-8	30	208-20	10	280	60	
12	189-93	60	193-210	10	280	30	
13	280	100					
14	280	100					
15	280	100					

Conclusions from Summary IV.

The characteristic behavior of the sulphonyl derivatives of the primary and secondary amines is noteworthy. There is first a marked sintering to a small core several degrees below their true melting points, then a softening to a viscous opaque mass. This mass then suddenly clears to a liquid at a definate temperature and collects in the bottom of the tube. This last temperature is the melting point of the substance. The different melting points recorded in the literature are no doubt due to this characteristic behavior on the part of the derivatives in question. It has been shown in this laboratory (see Mr. Keener's thesis for A.B. degree) that the purified monosulphonyl derivative of aniline melts sharply at 109.3° (corr.), and that the sulphonyl derivative of methyl aniline when purified melts sharply at 79° (corr.).

The following conclusions may be drawn from Summary IV:

(I) The primary amine in experiments I and 2 is undoubtedly aniline as its melting point agrees very well with the true melting point of the corresponding sulphonyl derivative. Experiments 6, 8, 9, and II also show melting points which indicate that the primary amine is mainly aniline. When one considers the temperature at which the experiments were carried out, one would expect in these experiments mixtures of primary amines but in small amounts due to slight rearrangement. That this is the case will be shown later. The melting point of the sulphonyl derivative in experiment I0 is undoubtedly a derivative of some primary amine other than aniline. The low melting points observed in experiments I4 and I5 indicate that some aniline is present other than aniline. The low melting points observed for the sulphonyl derivatives of aniline show that one is dealing with mixtures of primary amines due to the well known fact that mixtures of these substances melt lower than the pure compounds. The derivatives in experiments 3, 4, 5, and I3, did not crystallize and hence were mixtures of primary amines.

(2) The derivatives in experiments I,2,5, and I2, indicate that the secondary amine involved is methyl aniline. The tarry material present no doubt causes the difference in the melting point from 79° as observed in Summary IV. The tarry product observed in experiments 3,4,6,8,9,II,I3, and I5, may be due to mixtures of secondary amines.

(3) Experiments I and 2 show that the tertiary amine is dimethylaniline. Ninety per cent of the amine in experiments 4 and

5 is dimethyl aniline while I0% consists of some higher methylated amine. Experiment I2 shows only 60% of the tertiary amine to be dimethyl aniline.

These results are expected under the conditions of the experiments. As the temperature is increased from 250° to 300° and above, one notices a decrease in the per cent of dimethyl aniline and an increase in the per cent of other higher boiling tertiary amines. It may be pointed out that in those experiments having high boiling fractions the thermometer took a sudden and rapid rise usually from about 230° up to 280°. At this latter temperature the thermometer remained constant but no product distilled over. It may be concluded then that when methyl aniline hydrochloride and also the quarternary compound are heated at 220° to 250°, the tertiary amine is practically all dimethyl aniline, as pointed out in experiments I,2,4, and 5, Experiment I2 shows that when methyl aniline hydrochloride is heated at 300 - I0° the yield of dimethyl aniline has decreased to 60%.

In experiments I3, and I5, all of the tertiary amine is higher boiling, that is, one or more methyl groups have shifted into the ring. All experiments in which the quarternary chloride were heated 300° to 350° give the same results. These boiling points agree very well with those of the expected rearranged products as recorded in literature and given in a table in the theoretical portion of this thesis. A few of them are given as follows:

Dimethyl Aniline	B.P.	I93°
Dimethyl-o-toluidine	"	I83
Dimethyl-m-toluidine	"	2I5 (208)

Dimethyl-p-toluidine	B.P.	208°
Dimethyl mesidine	"	2I3 - I4
3- Dimethylamido-I,2-Dimethyl benzene	B.P.	I99 - 200°
4- Dimethylamido-I,3-Dimethyl benzene	"	203 - 05
4- Dimethylamido-I,2-Dimethyl benzene	"	226 - 227 (232)
2- Dimethylamido-I,3-Dimethyl benzene	"	I95 - 6
5- Dimethylamido-I,3-Dimethyl benzene	"	226 - 227
2- Dimethylamido-I,3,5-Trimethyl benzene	"	2I3 - 2I4

In order to further confirm the nature of the primary and secondary amines obtained as the results of these rearrangements, and to determine the presence of other primary amines than aniline and other secondary amines than methyl aniline, the sulphonyl derivatives were subjected to fractional crystallization.

Alcohol was found to be the most satisfactory solvent for the crystallization of these compounds. About two grams of the sulphonyl derivative in a test tube were dissolved in five cubic centimeters of ordinary alcohol by warming. The solution was cooled and allowed to stand a short while. If crystals separated they were filtered by suction, washed with fifty per cent alcohol and dried. If no crystals formed after standing, water was gradually added until a precipitate formed. This precipitate was redissolved by warming and the solution cooled spontaneously when crystallization resulted within a few moments in most cases. Sometimes crystals formed only after the solution stood several hours in other cases seeding or scratching with a glass rod was necessary to induce crystallization. In a few cases the products could not be made to crystallize under any circumstances.

After filtering the crystals by suction and washing with fifty per cent alcohol the melting points were taken by the ordinary capillary method using a small open beaker of sulphuric acid as a bath, and a glass rod as a stirrer. A second fraction was obtained by diluting the filtrate from the first crystallization with water. The precipitate obtained was dissolved by warming and allowed to crystallize. When this second dilution was made, especially with the derivatives of the secondary amines, a small amount of viscous material remained which would not dissolve even when warmed. In a few cases this viscous product crystallized and a melting point was able to be taken. This viscous or tarry product, as noted by Derick and Howard, seemed to have been the main cause of the low melting points of the derivatives before crystallization. The melting points of the derivatives in each fraction from all of the experiments carried out, together with the percentage of each fraction of the initial charge are given in Summary V.

(b) Summary V.

Melting Points after One Crystallization.

(I) Primary Sulphonyl Derivatives.

Exp.	Fraction	% of Primary	Sinters	Softens	Melts	Nature of Primary
I	I	90	I03°	I05°	I07°	Sulph.Deriv.of An.
	2	5	I04	I06	I07	" " "
2	I	90	I03	I06	I08	" " "
	2	5	I03	I05	I07	" " "
3	I					Sticky Product.
	2					" "
4	I					" "
	2					" "
5	I					" "
	2					" "

Summary V (Continued).

Exp.	Frac.	% of Primary	Sinters	Softens	Melts	Nature of Primary.
6	I	50	I05°	I07°	I08°	Sulph. Deriv. of An.
	2	35	88	92	98	(?)
8	I	55	I05	I07	I08	Sulph. Deriv. of An.
	2	I0	82	85	88	(?)
	3	20	73	78	82	(?)
9	I	55	II0	II5	II8	Sulph. Deriv. of p-Tol. etc.
	2	35	9I	93	98	(?)
I0	I	40	I40	I44	I47	(?)
	2	50	I20	I23	I25	Sulph. Deriv. of p-Tol. etc.
II	I	I0	I05	I08	II2	(?)
	2	60	85	90	I00	(?)
I2	I	60	95	98	I0I	(?)
	2	25	85	88	92	(?)
I3	I	75				Sticky Product.
	2	I5	70	74	80	(?)
I4	I	70	90	95	I07	Sulph. Deriv. of An.
	2					No Product.
I5	I	50	70	72	78	(?)
	2	20	62	75	98	(?)

(2) Secondary Sulphonyl Derivatives.

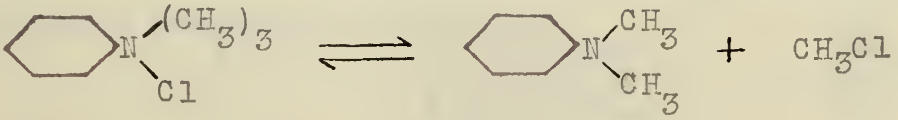
Exp.	Frac.	% of Secondary	Sinters	Soft.	Melts	Nature of Secondary.
I	I	85	72°	74°	77°	Sulph.Deriv.of Me. Aniline
	2	I0	73	75	77	" " "
2	I	80	74	75	78	" " "
	2	I5	74	75	77	" " "
3	I					Sticky Product.
	2					" "
4	I					" "
	2					" "
5	I	75	60	65	72	(?)
	2					No Product.
6	I	60	II5	I25	I27	(?)
	2	I0	II8	I25	I26	(?)
8	I	75	I25	I35	I44	(?)
	2	I0				Sticky Product.
9	I	90				Not Crystallized.
	2					No Product.
I0	I	50	I36	I40	I45	(?)
	2	40	I00	II0	I28	(?)
II	I	90				Not Crystallized.
	2					No Product.
I2	I	85	60	63	72	(?)
	2	I0	63	65	72	(?)
I3	I	80				Not Crystallized.
	2					No Product.

Summary V (Continued).

Exp.	Frac.	% of Secondary	Sinters	Soft.	Melts	Nature of Secondary.
I4	I	70	I00°	II0°	I23°	(?)
	2					No Product.
I5	I	90				Not Crystallized.
	2	5	75	82	90	(?)

Conclusions from Summary V.

The melting points of the sulphonyl derivatives of the primary amines of both fractions in experiments I and 2 show conclusively that at least ninety per cent of the derivatives is the sulphonyl derivative of aniline. In experiments 6, 8, and I4 we find the pure sulphonyl derivative of aniline (according to the melting point data obtained) is 50%, 55%, and 70% respectively of the original charge used. The melting points of the other fractions of the same experiments show that the derivatives are those of other primary amines than aniline - very probably ortho- and para-toluidine. A glance at the other experiments shows that the fractions are made up of sulphonyl derivatives of mixtures of primary amines, thus proving that a shift of methyl groups into the ring has occurred. The product obtained from experiment 3 was sticky and very small in amount. The primary and secondary derivatives in experiments 4 and 5 were negligible due to the establishment of the equilibrium



in which there is formed no appreciable amounts of primary and

secondary amines.

Experiments I and 2 of the secondary sulphonyl derivatives show that ninety-five per cent of the original charges is the sulphonyl derivative of methyl aniline. Experiments 5 and I2 show that the derivatives are contaminated with some other substance hence the low melting points observed. The viscous and tarry product spoken of earlier seemed to have prevented several of the fractions from crystallizing. Experiments 6, 8, IO, I4, and I5 clearly show that the derivatives are mainly those of other secondary amines than methyl aniline, and that one or more methyl groups have shifted into the ring under the conditions of the experiments as expected in the light of the hypothesis advanced and the result of the analyses.

In order to further characterize the derivatives of the primary and secondary amines obtained from the rearrangements they were first purified by treatment with a few cubic centimeters of alcohol, warmed to dissolve, and allowed to crystallize. In some cases water had to be added before crystallization resulted. Benzene sulphonyl derivatives of known amines were made and purified. Only a few of the desired amines were available hence the characterization is not complete. The derivatives made, together with their melting points are given as follows:

Derivative.	Melting Point.
Benzene sulphonyl derivative of aniline	II0°
" " " " o-toluidine	I23
" " " " p-toluidine	I2I.5
" " " " 3,4-xylidine	II9
" " " " methyl aniline	79

These derivatives were mixed with the purified rearranged derivatives having similar melting points and the melting points of the mixtures determined. The results obtained are given in Summary VI as follows:

(c) Summary VI.

Melting Points of Mixed Derivatives After Purification.

(I) Primary Sulphonyl Derivatives.

Exp.	Fraction	M.P. of Derivative	M.P.of Mixture	Nature of Derivative
I	I	I07°	I08°	Sulph. Deriv. of Aniline.
	2	I07	I08	" " "
2	I	I08	I08	" " "
	2	I07	I08	" " "
3	I			Sticky Product.
	2			" "
4	I			" "
	2			" "
5	I			" "
	2			" "
6	I	III	82	(?)
	2	I09	82	(?)
8	I	II2	83	(?)
	2	88		(?)
9	I	I2I	99	(?)
	2	I08	95	(?)
I0	I	I49		(?)
	2	I38		(?)
II	I	II2	82.5	(?)
	2	I08	9I	(?)
I2	I	I05		(?)
	2	97		(?)
I3	I			Sticky Product.
	2	78		(?)
I4	I	I39		(?)
	2			No Product.
I5	I	II5		(?)
	2	75		(?)

(2) Secondary Sulphonyl Derivatives.

Exp.	Fraction	M.P. of Derivative	M.P. of Mixture	Nature of Derivative.
I	I	79°	79°	Sulph. Deriv. of Me. An.
	2	78.5	79	" " "
2	I	79	79	" " "
	2	78.5	79	" " "
3	I			Sticky Product.
	2			" "
4	I			" "
	2			" "
5	I	78	79	Sulph. Deriv. of Me. An.
	2			No Product.
6	I	I32		(?)
	2	I26		(?)
8	I	I49		
	2			Sticky Product.
9	I			Not Crystallized.
	2			No Product.
I0	I	I49		(?)
	2	I4I		(?)
II	I			Not Crystallized.
	2			No Product.
I2	I	79	79	Sulph. Deriv. of Me. An.
	2	79	79	" " "
I3	I			Not Crystallized.
	2			No Product.
I4	I	I4I		(?)
	2			No Product.
I5	I			Not Crystallized.
	2	I05		(?)

Conclusions from Summary VI.

It is noted that the melting points of some of the derivatives after purification are very different from the corresponding melting points before purification. Experiments I and 2 of the primary sulphonyl derivatives show conclusively that the primary amine is aniline since the melting points of the derivatives and mixtures are the same within one degree. Experiments 6, 8, 9, and II, on the other hand, with the particular fractions having melting points close to those in experiments I and 2 do not contain

aniline as the primary amine since the melting points of the mixtures are not those for the benzene sulphonyl derivative of aniline. Fraction I of experiment 9 is not a derivative of para toluidine since the melting point of the mixture is not that for benzenesulphon-p-toluidine. Unfortunately no other suitable higher methylated primary amines were available so that further characterization had to be abandoned. The melting points of the other derivatives, however, undoubtedly show a shift of one or more methyl groups to the ring.

The melting points of the mixtures in experiments I and 2 of the secondary sulphonyl derivatives show conclusively that the secondary amine is methyl aniline. The same is true for experiment I2 and for fraction I of experiment 5. As other higher methylated secondary amines were not available the identification had to be abandoned. The melting points of the derivatives in other experiments, as was the case with some of the primary sulphonyl derivatives, undoubtedly show a shift of methyl groups to the ring. Time prevented further characterization of these derivatives.

20. Nature of the Substances Obtained by Direct Ether Extraction of the Bomb Products.

In order to determine the nature of the free amines obtained by direct ether extraction of the bomb products they were subjected to fractional distillation with the following results:

Exp.	% Boiling above 280°	Remarks
3	I00%	
6	I00	
8	I00	
9	I00	
I0	95	5% distilled at I89°.
II	I00	
I3	I00	
I4	I00	
I5	I00	

The thermometer made a rapid jump from 230° to 280° in all of these experiments and only a few drops of the products distilled over. The products should be subjected to vacuum distillation in order to determine more specifically their nature. The boiling point data show that the amines are not dimethyl aniline. It is to be noted that only from those bombs that open with pressure are appreciable amounts of ether soluble products obtained. In these experiments the hypothesis demands the formation of the quarternary compound, and hence the production of rearranged products as the analyses, melting point and boiling point data show.

In order to further substantiate the fact that these direct ether soluble products are none other than tertiary amines they were treated with benzene sulphonyl chloride in alkaline solution as described in the perfected method of separation on page I05 of this thesis. The results obtained are as follows:

Exp.	Wt.of Original Product.	Wt.of Recovered Product.	% Recovered as Tertiary Amine.
3	0.283	0.279	98.58%
6	2.523	2.5I5	99.68
8	2.095	2.082	99.37
9	I.476	I.465	99.25
I0	3.729	3.496	93.75
II	I.0I4	0.966	95.26
I3	I.288	I.264	98.I3
I4	I.360	I.352	99.4I
I5	0.340	0.335	98.52

These results show conclusively that the compounds are only tertiary amines. Primary and secondary amines could not be obtained here because under the conditions of the experiments they exist in the bombs as their corresponding hydrochlorides which are not extracted with ether.

V - THE MECHANISM OF THE HOFMANN REARRANGEMENT FOR METHYL ANILINE HYDROCHLORIDE.

V - The Mechanism of the Hofmann Rearrangement for Methyl Aniline Hydrochloride.

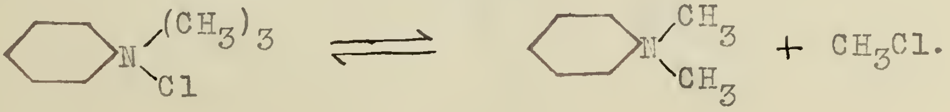
The first step in the rearrangement demanded by the hypothesis advanced in this thesis is the change of methyl aniline hydrochloride into dimethyl aniline hydrochloride and aniline hydrochloride. This is shown to be the case by experiments discussed in Summaries II, III, and IV, where methyl aniline hydrochloride was heated.

The percentages of primary, secondary, and tertiary amines in experiments I and 2 show that the temperature 250° or below has practically no influence on the rearrangement. Derick and Howard have shown also that at these temperatures the time of heating between two and forty-eight hours has no effect. Pressure has also been shown not to have any effect. These experiments show that at or below the temperature 250° , there are equilibria between primary, secondary, and tertiary amines. These equilibria are not independent of the temperature as one would at first be led to believe. This may be explained by the fact that when the bombs are allowed to cool they pass through the same temperature changes, and a temperature is finally reached at which the hydrochlorides of the three classes of amines are not appreciably dissociated. This temperature, where the equilibria proportions of primary, secondary, and tertiary amines, and perhaps quarternary compound become fixed by the formation of the corresponding hydrochlorides and perhaps the quarternary chloride, is undoubtedly the

same for all experiments in which the primary, secondary, tertiary and quarternary compounds are aniline, methyl aniline, dimethyl aniline, and phenyltrimethylammonium chloride.

Experiment 7 shows conclusively that when phenyltrimethylammonium chloride is heated at 220-30° for twelve hours it is dissociated into dimethyl aniline and methyl chloride since the bomb opened with pressure, due to the escape of methyl chloride. The latter substance was isolated in a gas burette and it burned with a greenish yellow flame thus proving it to be methyl chloride. An oil was obtained by ether extraction which distilled constant at 189-91° proving it to be dimethyl aniline. The percentage of the latter product thus obtained was 15%, showing that the quarternary compound had dissociated to the extent of 21.36% under the conditions of the experiment. The free amine bases could only be formed as a result of such a dissociation. One might think that the quarternary chloride had shifted a methyl group into the ring. But if this were true, hydrochlorides of tertiary amino alkyl benzenes would have been formed which would not have been extracted with ether. The fact that the oil obtained distilled at 189-91° proves that no higher methylated tertiary amines had been produced. In light of these facts no rearrangement has occurred under 250°.

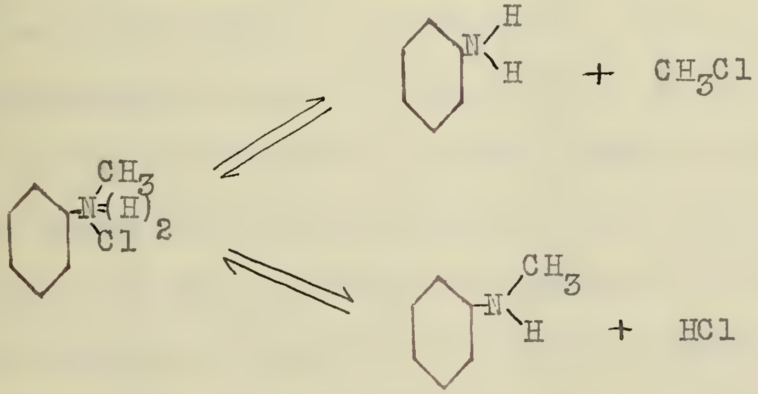
The following equilibrium then represents the condition of the bomb products under the condition of these experiments:

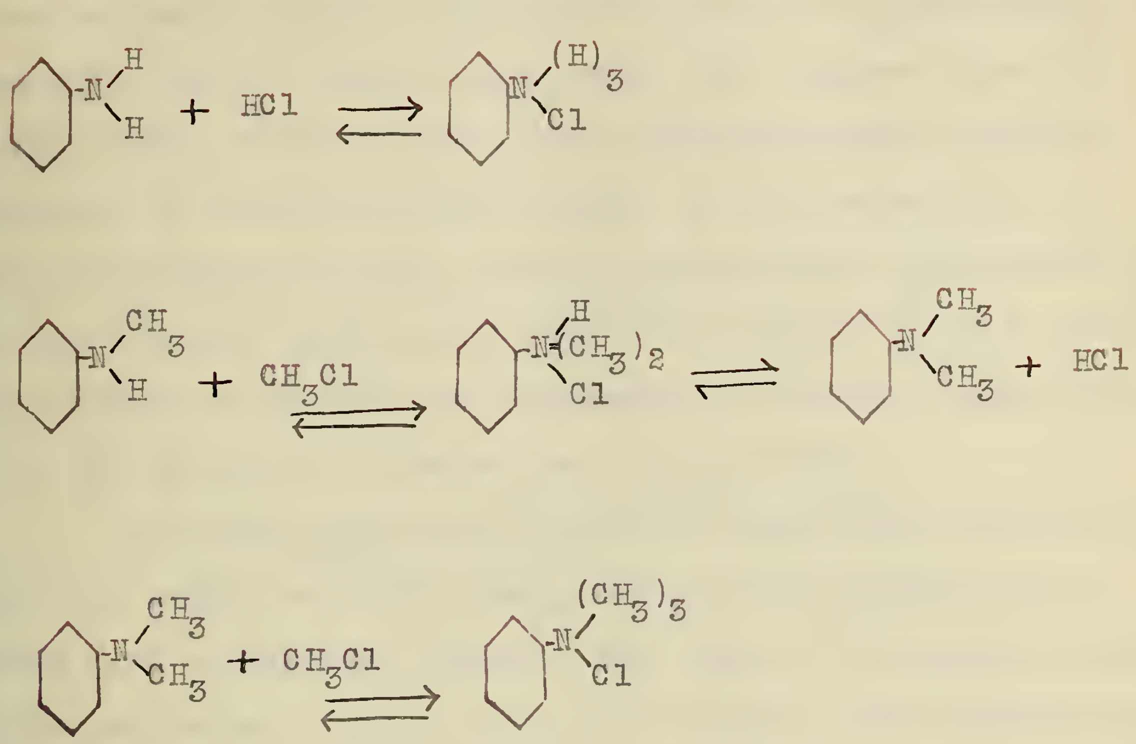


This experiment and all experiments in which the bombs opened with pressure prove conclusively that methyl chloride may be dissociated from an aminic nitrogen atom to which are linked a methyl group and a chlorine atom, and that methyl chloride is the methylating agent in these rearrangements. Hofmann's explanation that methyl chloride is the methylating agent in the Hofmann Rearrangement is substantiated by this fact.

Experimants 4 and 5, involving the heating of phenyltrimethylammonium chloride at the same temperatures namely, 220-30° and 240-50°, were bombs which opened with pressure and gave very small amounts of primary and secondary amines. Practically all of the product obtained was the free tertiary amine and methyl chloride.

The results of these experiments together with the fact that amine hydrochlorides split off hydrochloric acid when heated at high temperatures give sufficient and necessary data for interpreting the reactions that take place in experiments I, 2, 4, and5. The following equilibria indicate the condition of the bomb products when carried out under the conditions of these experiments:



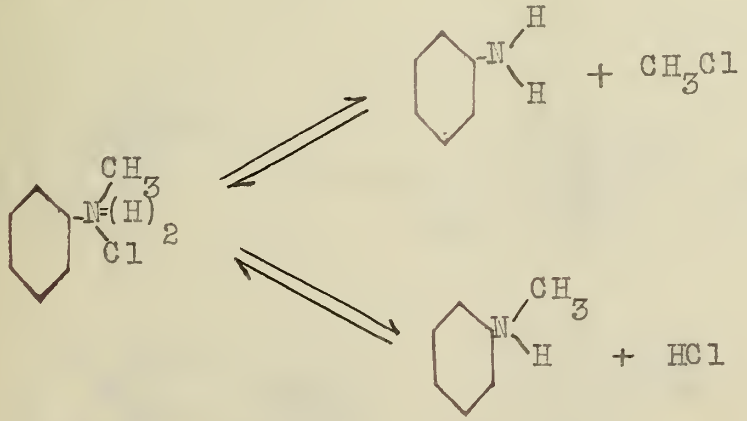


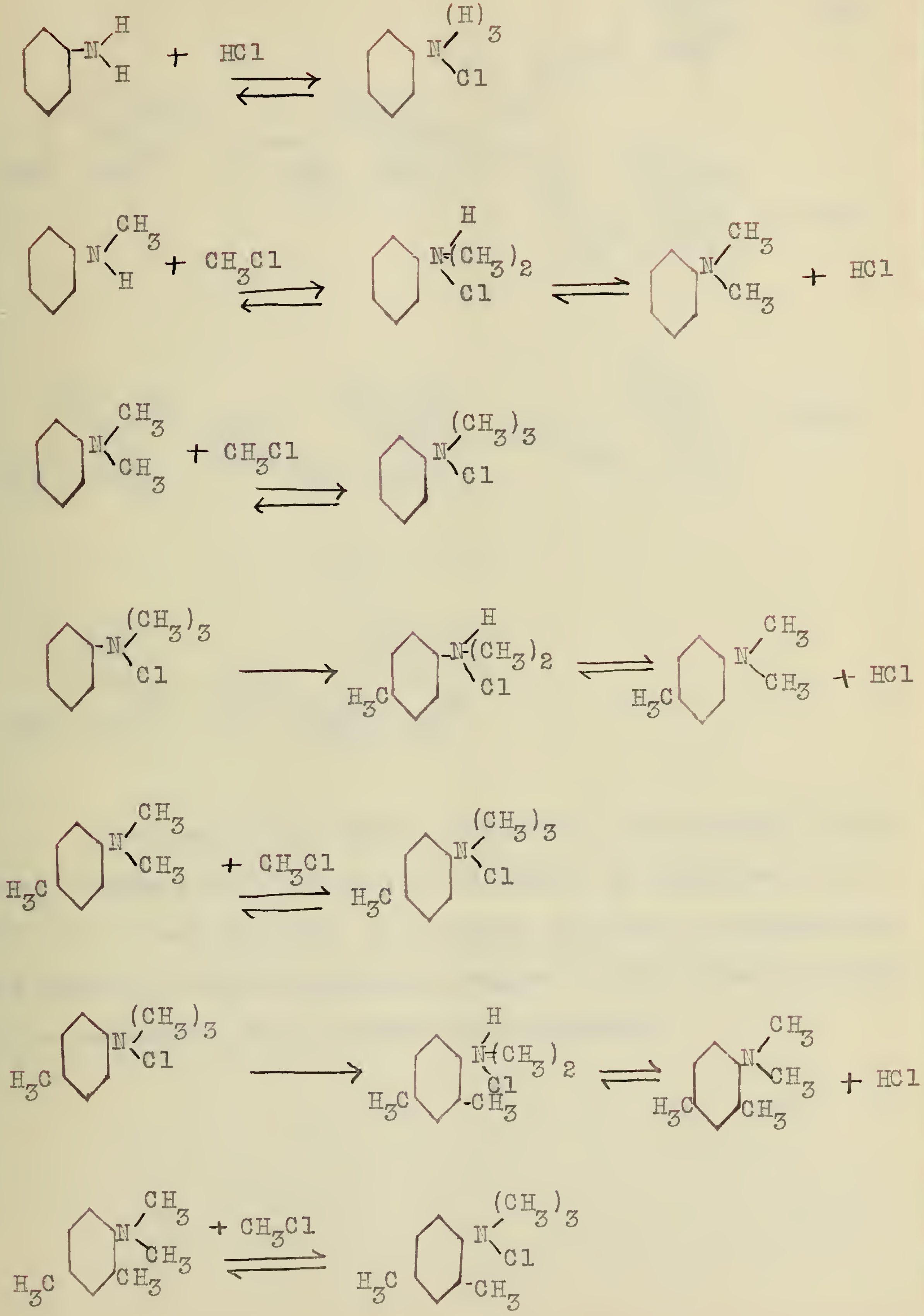
When the bomb is allowed to cool, a temperature is reached at which the equilibria are driven to completion in the direction of the four solid chlorides which no longer appreciably dissociate as pointed out in the above scheme.

In Summary III one finds that the percentage of quarternary compound formed in experiments 1 and 2 is within the limits of experimental error. In experiments 12, 13, and 15 a small per cent of the compound is no doubt formed. But in experiment 3 where methyl aniline hydrochloride was heated at 290-300° for one week, we have conclusive evidence that the quarternary compound has been formed to the extent of about 40% to 50%. The experimental data would seem to indicate, however, that about 60%

had formed. This is due to the fact that the "Wt. of the Hydrochloride Found" was not pure hydrochloride but contaminated by some water soluble tarry product which was observed when the "Check Portions" were treated with sodium carbonate solution. The isolation of the quarternary compound in this experiment by means of platinum chloride further substantiates the formation of this compound in the bomb beyond the possibility of a doubt. All attempts to isolate the quarternary compound in experiments I, 2, I2, I3, and I5, however, were unsuccessful.

In those experiments where the quarternary compound was formed as evidenced by the bombs opening with pressure, one should find rearranged products. That this is the case is shown by the analytical, melting point, and boiling point data as given in Summaries I, II, III, IV, V, and VI as discussed in this thesis. These data clearly show the existance of many non-reversible reactions as those giving the toluidines, methyl toluidines dimethyl toluidines, and other higher methylated aromatic amines which exist in the bombs under the conditions of the experiments as outlined in the following scheme:




H
N
H
+
HCl
(H)3
N
Cl
CH3
N
H
+ CH3Cl
H
N(CH3)2
Cl
CH3
N
CH3
+ HCl
CH3
N
CH3
+ CH3Cl
(CH3)3
N
Cl
(CH3)3
N
Cl
H
N(CH3)2
Cl
H3C
CH3
N
CH3
H3C
+ HCl
CH3
N
CH3
H3C
+ CH3Cl
(CH3)3
N
Cl
H3C
(CH3)3
N
Cl
H3C
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N(CH3)2
Cl
H3C
CH3
CH3
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CH3
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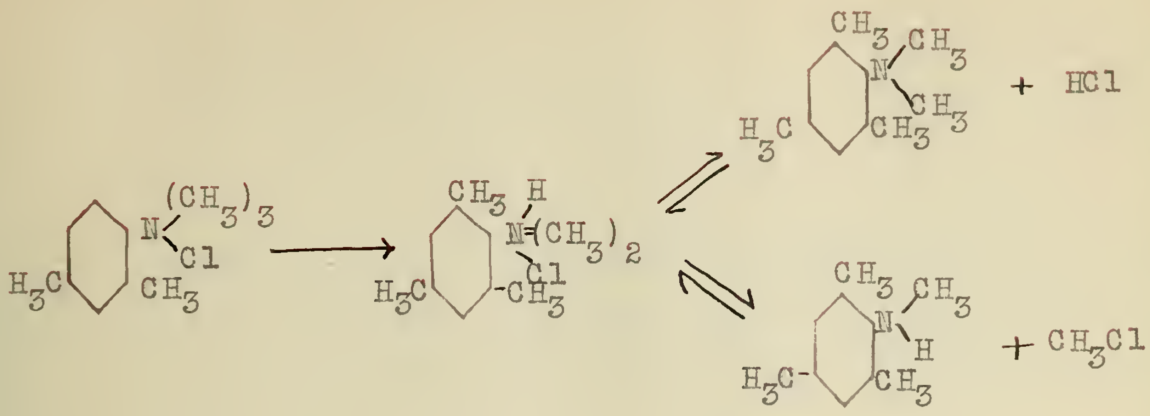

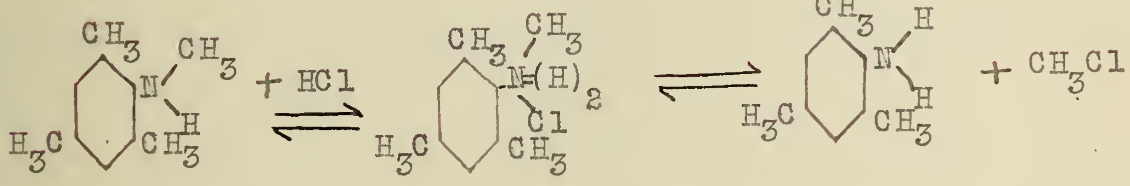

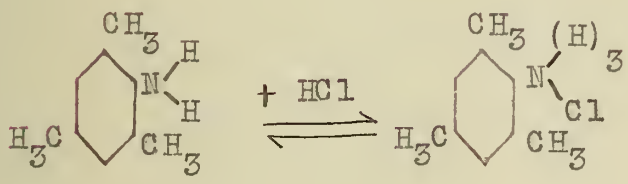

The analytical results obtained in this thesis, therefore, together with the data as discussed in Summaries I, II, III, IV, V, and VI, offer very strong evidence to substantiate the validity of the hypothesis advanced in this thesis relative to the mechanism of the Hofmann rearrangement.

VI - GENERAL SUMMARY.

VI - GENERAL SUMMARY.

1. A method for the quantitative separation and determination of primary, secondary, tertiary, and quarternary amines by means of benzene sulphonyl chloride has been perfected and its accuracy determined.

2. Methyl aniline hydrochloride when heated in bomb tubes at 250° to 350° rearranges giving a mixture of primary, secondary and tertiary amines.

3. The quarternary compound and methyl chloride are formed when rearrangement of the secondary and tertiary hydrochlorides occur, and may be isolated from the bomb product when the heating is carried out at 290-300° for several days.

4. Phenyltrimethylammonium chloride undergoes a decided change at 220-30° and at 350° as claimed by Hofmann.

5. When heated below 250°, the quarternary compound undergoes a dissociation into methyl chloride and dimethyl aniline without rearrangement.

6. In the rearrangement of the quarternary compound evidence is given that the shift of methyl groups into the ring begins appreciably at 300°.

7. At 300-10° a variation in the time of heating phenyltrimethylammonium chloride from three to forty-eight hours has practically no influence on the course of the rearrangement.

8. Pressure has little influence upon the rearrangement at 300-10°.

9. Temperature has little influence upon the rearrangement between the limits 200-50°; but it is the most important factor at 300-50°.

10. The heating of methyl aniline hydrochloride at 220-30° checks the results obtained by Derick and Howard namely, that an equilibrium is established between aniline, dimethyl aniline, and other hydrochlorides.

11. The Hofmann rearrangement occurs only when the quarternary compound is formed and a methyl group shifts from the quarternary nitrogen atom to the benzene ring.

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BIOGRAPHY.

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The author was born in Ocala, Florida, and received his elementary training in the public schools of that town. His high school training was received in the academy of the Florida Agricultural and Mechanical College at Tallahassee, Florida. He received the degree of Bachelor of Arts, and Bachelor's Diploma in Education from the Teachers' College of Howard University, Washington, D. C., in June 1913. In 1913-1914 he was a Scholar in Chemistry at Clark University, Worcester, Massachusetts, receiving the degree of Master of Arts in June 1914. In 1914-1915 he was a Student Assistant in Chemistry in the University of Illinois. During the summer of 1915 he made organic chemicals on a commercial scale for the University of Illinois. During 1915-1917 he was a Fellow in Chemistry in the University of Illinois.

The author is a member of the American Chemical Society and Phi Lambda Upsilon.