HOWARD

Rearrangement of Methyl & Dimethyl Aniline

A Quantitative Separation & Determination of Primary, Secondary, Tertiary, & Quaternerary Amines

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REARRANGEMENT OF METHYL AND DIMETHYL ANILINE

A QUANTITATIVE SEPARATION AND DETERMINATION OF PRIMARY, SECONDARY, TERTIARY, AND QUATERNERARY AMINES

BY

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THESIS

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June 3, 1913.

I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY

Joseph W. Howard

ENTITLED Rearrangement of Methyl and Dimethyl Aniline. A Quantitative Separation and Determination of Primary, Secondary, Tertiary, and Quaternerary amines.

BE ACCEPTED AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE DEGREE OF Master of Arts in Chemistry in the Graduate School.

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Recommendation concurred in:

Committee
on
Final Examination

TABLE OF CONTENTS.

TABLE OF CONTENTS.

INTRODUCTION.

Introduction.

Some of the chemical reference books state that when methyl anilin is heated to 330° it changes over into para toluidin. The investigation of this rearrangement and also the rearrangement of di methyl anilin was assigned to the author.

Obviously, if such reactions do occur, the product received will be a mixture of amines, which must be separated and estimated quantitatively in order to study the reaction thoroughly.

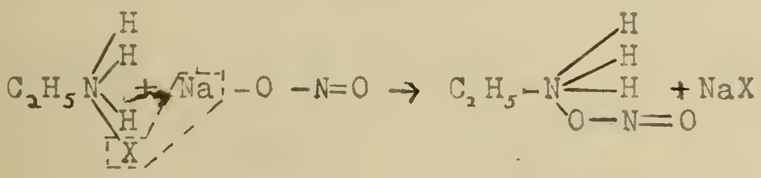
Accordingly, the investigation of methods of separation and determination of the four classes of amines was first taken up. The results are recorded in this thesis.

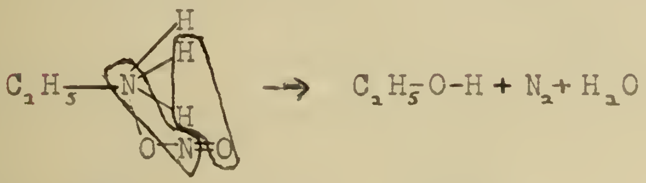
HISTORICAL.

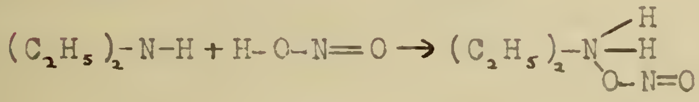
Chapter I.

Historical.

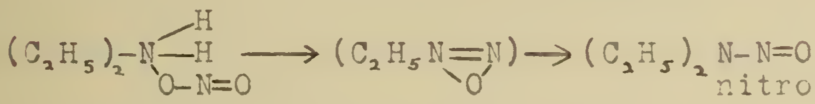
A method of separating the amines was first devised by Heintz (1). He found that if a mixture of amines in acid solution was treated with nitrous acid the following took place.





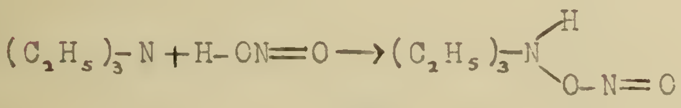


$$(C_2H_5)_2-N-H + H-O-N=O \rightarrow (C_2H_5)_2-N(-H)(-H)(-O-N=O)$$

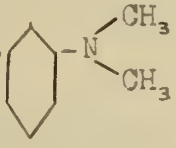


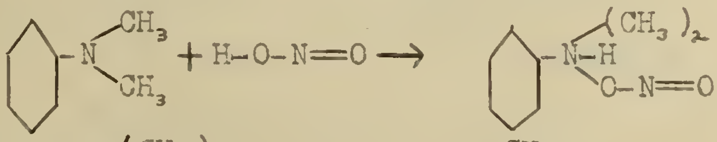
$$(C_2H_5)_2-N(-H)(-H)(-O-N=O) \longrightarrow (C_2H_5N=N-O) \longrightarrow (C_2H_5)_2N-N=O$$

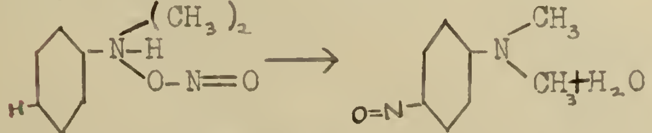
nitroso compound.



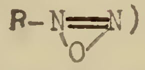
$$(C_2H_5)_3-N + H-ON=O \longrightarrow (C_2H_5)_3-N(-H)(-O-N=O)$$

The nitrite formed in the last reaction exists only in very small quantities in strongly acid solution, and in the actual separation the free tertiary base will be received. If the tertiary base is aromatic, as  , it will react with nitrous acid in this manner:-

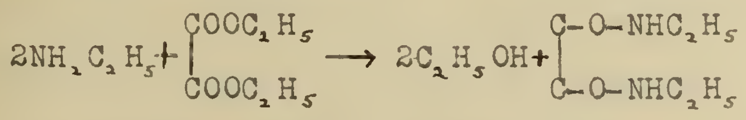




Heintz only reported the final products of these reactions, but that the reactions go thru the stages indicated has been

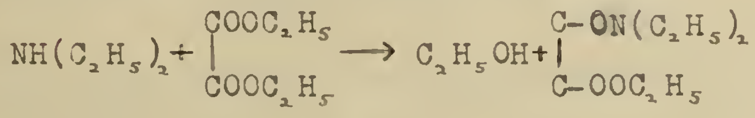
clearly shown by Wallach (2), who has isolated the intermediate compounds(excepting ). When determining amines, if nitrogen gas comes off,we know that a primary amine was present. If a light yellow oil is formed,the secondary amine is shown to be present. If the base was not visibly acted upon,we conclude that it is the tertiary. If all three amines were present,the primary is destroyed,and it is possible to separate the other two. This is done by extracting them with ether, evaporating the ether,and then adding strong hydrochloric acid. This forms the hydrochloride of the tertiary amine. Another ether extraction will take out the nitroso compound of the secondary amine. If the tertiary hydrochloride is now treated with sodium hydroxide,the tertiary base will set free,and may be removed by ether extraction. This method would probably give a very good quantitative separation of secondary and tertiary amines,but a correct determination of the primary from the products formed would be impossible in the aromatic series.

Four years after the work of Heintz,Hoffman(3)used the di ethyl ester of oxalic acid as a separating agent. With primary amines it gives:-



$$2NH_2C_2H_5+\begin{array}{l}COOC_2H_5\\|\\COOC_2H_5\end{array}\longrightarrow 2C_2H_5OH+\begin{array}{l}C-O-NHC_2H_5\\|\\C-O-NHC_2H_5\end{array}$$

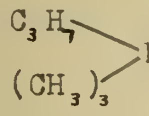
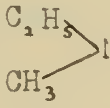
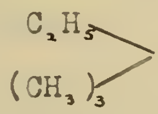
The secondary base reacts thus :-



$$NH(C_2H_5)_2+\begin{array}{l}COOC_2H_5\\|\\COOC_2H_5\end{array}\longrightarrow C_2H_5OH+\begin{array}{l}C-ON(C_2H_5)_2\\|\\C-OOC_2H_5\end{array}$$

There is no reaction with the tertiary base

The separation is gained by distilling off the free tertiary base, drawing off the primary product by suction, and thus leaving the secondary behind. This method is not applicable for all cases, because all tertiary bases are not volatile, and thus would not distill over. The facts, also, that the reaction must be absolutely water free, and no provision is made for an excess of oxalic ester if added, would render the manipulations difficult where a quantitative separation and determination is desired.

Another method of distinguishing between primary, secondary, and tertiary amines consists in the determination of the number of alkyl groups with which the amine can combine. For example if a compound C_3H_9N is propyl amine $C_3H_7NH_2$, it should yield when heated with excess of methyl iodide a compound  $\begin{matrix} C_3H_7 \\ (CH_3)_3 \end{matrix} > NI$ or $C_6H_{16}NI$. If C_3H_9N is  $\begin{matrix} C_2H_5 \\ CH_3 \end{matrix} > NH$, the same treatment should yield  $\begin{matrix} C_2H_5 \\ (CH_3)_3 \end{matrix} > NI$ or $C_5H_{14}NI$. Lastly if C_3H_9N is $(CH_3)_3N$, there should be obtained $(CH_3)_4NI$ or $C_4H_{14}NI$. A titration of the iodine ion of the quaternerary ammonium iodide formed is sufficient to determine whether C_3H_9N is primary, secondary, or tertiary. As this statement indicates, this method only tells which amine is present and in no way offers a separation. Accordingly, we can not use it in our determinations.

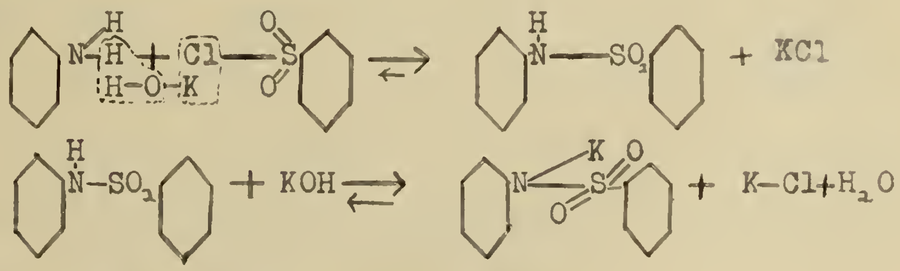
The quantitative text books offer as a method of estimating amines, the formation of a platinum salt and its determination.

The following reaction, $2RNH_2 + H_2PtCl_6 \rightarrow R(NH_2)_2PtCl_6$, illustrates the character of the compound formed. We have in this only a method of estimation of an amine known to be present.

O.Hinsberg (4),however,has devised a method combining both a separation and determination to the best advantage. He is the first to offer a separation of the first three from the quaternerary. A mixture of the four bases is treated with alkali. If the primary,secondary,and tertiary are volatile, they may be removed by steam distillation. This has the advantage of being a purifying process as well. But if the first three are non-volatile,they may be separated from the quaternerary by ether extraction.

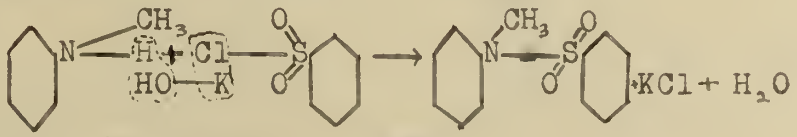
The mixture of the first three bases is then treated with benzene sulphonyl chloride in a solution of potassium hydroxide. The following reactions take place:-

(1) For primary amine.



This potassium salt is soluble in water.

(2)
For secondary amine.



This product is insoluble in water or alkali.

The tertiary amine does not react and may be removed by

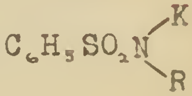
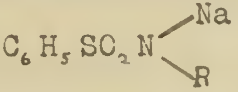
steam distillation or extration with ether. The ether extraction will also remove the secondary sulphonic amide. The ether extraction, therefore, is evaporated and the mixture treated with strong hydrochloric acid. This forms the hydrochloride of the tertiary base, which is insoluble in ether. Accordingly, if an ether extraction is now made, the secondary sulphonic amide will be received in a pure state. The tertiary hydrochloride solution is made alkaline with sodium hydroxide solution, and the base is set free, and may be extracted with ether. If now the original alkaline solution is acidified, the sulphonic amide of the primary base is set free and precipitates, and may be extracted with ether.

One of the great advantages of this process is that there is no danger from an excess of benzene sulphonyl chloride. In alkaline solution, it is changed into the sodium salt of sulphonic acid, which is not soluble in ether. Upon acidifying the solution this sodium salt is changed to the free sulphonic acid, which is also non-extractable with ether.

Hinsberg examined this reaction qualitatively with the amine bases of fatty compounds, also with anilin and its homologues, Ethyl anilin, Phenylendiamin, Napthylamins and alkyl naphthylamins.

Napthalene sulphonyl chloride has been found to work equally as well as benzene sulphonyl chloride (5).

Fisher(6) used this process for the determination of single amino acids, receiving in two cases 80% yield, and in one case 90% yield.

In 1905 O.Hinsberg and J.Kessler (7) carried out some quantitative separations and determinations of primary and secondary amines by this process. They found that both  $C_6H_5SO_2N\begin{matrix}K\\R\end{matrix}$ and $(C_6H_5SO_2)_2NR$ were formed during the reaction. The latter being insoluble in alkali comes out at the same time.as the secondary sulphonic amide. But by treating this mixture with sodium alcoholate under a reflux condensor for 15 minutes, the di-sulphonyl compound is changed into the sodium salt of the monosulphonic amide,  $C_6H_5SO_2N\begin{matrix}Na\\R\end{matrix}$. If this is now diluted with water, the alcohol evaporated, and the residue cooled, the free secondary sulphonic amide may be extracted. After extraction, the residue is acidified, and the free primary sulphonic amide extracted from it.

They also found that when the base had more than six carbon atoms, a further treatment was necessary in order to form the sodium salt of the primary sulphonic amide. The mixture of primary and secondary bases was treated as previously with sodium alcoholate. This would destroy any di-sulphonyl compound formed. The mixture of primary and secondary sulphonyl compounds was dissolved in ether, metallic sodium added in small pieces, and the whole warmed for 6 - 8 hours upon a water bath. The mixture was filtered, and the sodium salt washed with ether to remove all traces of the secondary. The secondary sulphonic amide is soluble in the ether, and will be regained upon evaporation. The sodium salt of the primary is treated with acid and the free primary product received. Among the

best results received are these:-

(1)	Pseudocumidin	95.5 %
	Diamylamin	98.8 %
(2)	Heptylamin	99. %
	Piperidin	92.8 %
(3)	Butylamin	91.7 %
	Diethylamin	95.1 %

This method seems to be superior to all others in ease of manipulation. For this reason it was decided to use it to gain not only further data upon the separation and determination of primary and secondary, but also tertiary and quaternerary amines.

EXPERIMENTAL.

Chapter 11.

Experimental.

1.Preparation of Materials.

Methyl Anilin. The methyl anilin used was from Kalbaum's stock,and was purified by fractional distillation. The constant boiling portion came over at 189°- 90° (uncorr.).

Dimethyl Anilin. This was also the Kalbaum product,and was purified in the same manner as the methyl anilin. The constant boiling portion came over at 187°- 8° (uncorr.).

Paratoluidin. The paratoluidin was purified by recrystallization from ligroin. The last traces of ligroin present were removed by drying in a vacuum dessicator over sulphuric acid and then over calcium chloride.

Trimethyl Phenyl Ammonium Iodide. This compound was prepared by heating molecular proportions of methyl iodide and dimethyl anilin in a pressure flask over a steam bath for two hours. It was purified by recrystallization from ninty-five per cent alcohol and dried on a porous plate and then in a vacuum dessicator over calcium chloride. A yield of fifty-one per cent was received.

Benzene Sulphonyl Chloride. This compound was made by mixing one hundred grams of phosphorous pentachloride and one hundred grams of sodium benzene sulphonate (previously dried at 120°). A violent reaction took place. When this was over the products were poured into large portions of water. This was shaken vigorously to destroy the phosphorous oxychloride formed in the reaction. The benzene sulphonyl chloride was ex-

tracted with ether and fractionally distilled. It was necessary to distill three times in order to get a perfectly clear product. The pure product came over under the conditions:-

Pressure.	Temperature (uncorr.).
20	133°
22	136°
25	140°

The yield was about fifty grams.

2. Determination of Methyl Anilin.

Eight mixtures were prepared, each containing one gram of methylanilin, four grams of benzene sulphonyl chloride, and one hundred cubic centimeters of a one to four solution of potassium hydroxide. The first five were heated over a steam bath the times indicated, and the last three were refluxed. The resulting solutions were cooled, extracted with ether, the ether extract dried over anhydrous sodium sulphate and evaporated to dryness. The crystals formed were further dried by passing over them a current of air. Results:-

Flask Number.	Time.	Weight of Product.	% Error.
1	½ hour.	2.6 grams.	13.
2	1 "	2.48 "	7.8
3	1½ "	2.80 "	21.5
4	2 "	3.10 "	34.8
5	2½ "	2.60 "	13.
6	½ "	2.99 "	30.
7	1 "	2.70 "	17.4
8	1½ "	3.00 "	30.4

The theoretical yield is 2.3 grams. Some of these check fairly well, but all are uniformly high.

Another series of determinations were made using ether as a medium in place of an aqueous solution of potassium hydroxide. Different weights of methyl anilin were treated with ten per cent excess of benzene sulphonyl chloride in varying volumes of ether. These mixtures were refluxed, the ether evaporated off, and the product after air drying was weighed. Results :-

Number.	c.c.Ether.	Weight of Methyl Anilin.	Time.	Prod.	Theory.	% Yield.
1	50	0.5 grams	30 min.	.55	1.15	47.9
2	75	0.75 "	45 "	.80	1.73	46.2
3	75	1.0 "	1 hour	1.27	2.3	55.2
4	100	1.5 "	1½ "	1.65	3.46	44.5
5	100	2.0 "	2 "	2.49	4.6	54.1
6	100	2.5 "	2½ "	3.00	5.7	52.6

These results give an average yield of 50.1 per cent yield.

A series of experiments was also carried on in the absence of a medium. The methyl anilin was treated with ten per cent excess of benzene sulphonyl chloride, and this mixture heated on a water bath. The products received were all subjected to steam distillation. The remainder was extracted with ether, dried, and weighed. In a few cases considerable substance seemed to come over with the steam, but when this was extracted and weighed it proved to be negligible. The following results were obtained.

Number.	Weight of Methyl Anilin.	Time.	Prod.	Theory.	% Yield.
1	0.75 grams	45 min.	.99	1.73	57.2

2	1.00 grams	1 hour.	1.35	2.30	58.6
3	1.50 "	1½ "	2.40	3.46	69.9
4	2.00 "	1¾ "	3.45	4.60	75.
5	2.50 "	2 "	3.70	5.70	66.6
6	1.5 "	2 "	2.75	3.46	79.4

Increasing the time of heating increased the percentage yield. The results are, however, too far below theory.

The next series of determinations were tried in sodium carbonate solution. Mixtures of methyl anilin, ten per cent excess of benzene sulphonyl chloride, and one hundred cubic centimeters of a one to four solution of sodium carbonate were refluxed. The product formed was extracted with ether weighed and dried. Results :-

Number.	Weight of Methyl Anilin.	Time.	Prod.	Theory.	% Error.
1	1.00 grams.	1 hour.	2.27	2.30	- 1.3
2	1.50 "	1.5 "	3.38	3.46	- 2.3
3	2.00 "	2.0 "	4.58	4.60	- .43
4	1.50 "	1.5 "	3.38	3.46	- 2.3
5	2.00 "	2.0 "	4.59	4.60	- .5

This gave results nearest to theoretical of any of the methods tried. As these determinations were made by weighing on horn pan balances, it was decided to carry out further determinations using more accurate manipulation. All weighings were made on analytical balances. The methyl anilin was weighed by means of a weight pipette. The final products were weighed in one hundred and twenty-five cubic centimeters Earlenmeyer flasks. Considerable difficulty was experienced because of "bumping"

while the mixtures were heating. Accordingly in each case the reflux condensor was boiled out with ether, and this ether was used to extract the final product. Two methods of drying the crystals were used. In the first, air, dried by passing thru sulphuric acid, was passed over the crystals for one and one-half hours. Results :-

Number.	Weight of Methyl Anilin.	Product.	Theory.	% Error.
1	1.4642	3.3587	3.3799	-.5
2	1.1823	2.7135	2.7291	-.6
3	1.2550	2.8800	2.8871	-.5

In the next series, however, air drying gave positive error. Accordingly, heating at different temperatures for different times was tried. Results :-

						% Error	
No.	Weight of Methyl Anilin.	Time.	Temp.	Prod.	Theory.	Heated.	Air Dryed.
1	1.4696	5 min.	96	3.3566	3.3924	- 1.	+ 1.8
2	1.7379	15 "	103	3.9623	4.0117	- 1.	+1.5
3	1.2568	15 "	103	2.8736	2.9012	- .9	+1.4
4	2.1289	5 "	92	4.8748	4.9143	- .8	+2.0
5	1.7665	5 "	95	4.0500	4.0591	- .2	+1.2
6	1.4291	5 "	88	3.2548	3.2989	- 1.	+3.

3. Determination of Para-Toluidin.

In the first determination the method was carried on as in the last determination of methyl anilin,namely,using potassium carbonate sodium as a medium. But the necessary potassium salt was not formed. Accordingly,twenty-five grams of potassium hydroxide was added to one of these carbonate solutions. Much heat was evolved,and upon ether extraction,a large portion of the free compound was received. In another trial,the carbonate solution was evaporated to dryness and then extracted with ether. But a large portion of the free compound was received here also.

Next,weighed amounts of para-toluidin were treated with an excess of benzene sulphonyl chloride in fifty cubic centimeters of a one to ten potassium carbonate solution,and this mixture was shaken vigorously for ten minutes. A solution of one hundred grams of solid potassium hydroxide in one hundred cubic centimeters of distilled water was added in small amounts to the carbonate solution,shaking after each addition. A solid flucculent mass was formed,which went into solution upon slight dilution. The formation of this solid may be regarded as an end action. The alkaline solution was extracted with ether to see if any free product was formed. Results :-

Number.	Product.
1	.0974
2	.1827
3	.3824
4	.2758

Theory	0.0000

If the salt had been completely formed, nothing would have been extracted with ether. But, in each case, the product obtained melted at 128° - 9° and analyzed for sulphur and nitrogen ; it was, therefore, the free primary compound.

Each of these products was treated with twenty cubic centimeters of the one to one potassium hydroxide solution, and extracted with ether again. These solutions were then acidified and extracted again. Results :-

Number.	Product.
1	.0156
2	.0236
3	.0372
4	.0426

The original alkaline solution which had been previously extracted with ether was acidified and again extracted with ether, with the results :-

Number.	Product.
1	.8500
2	1.2786
3	2.0892
4	1.3502

Combining the results of the two acid extractions gives the following :-

No.	Weight of Para-Toluidin.	Product.	Theory.	% Error.
1	.3919	.8656	.9046	- 4.2
2	.6149	1.3022	1.4193	- 8.

3	1.0346	2.1264	2.3882	- 9.2
4	.6774	1.3928	1.5639	- 10.

This increasing error is probably due to the difference in time of extractions. Number 1 was acified and extracted at once while the others were acidified and extracted at intervals of one day. Accordingly in the following experiments the alkaline solutions were extracted at once.

No.	Weight of Para-Toluidin.	Product.	Theory.	% Error.
1	.4886			
	Alkaline extract :-	.0456		
	Acid extract :-	1.0752	1.1278	- 4.6
2	.3142			
	Alkaline extract :-	.1037		
	Acid extract :-	.6940	.7253	- 4.3
3	.2807			
	Acid extract :-	.6107	.6479	- 5.
4	.3994			
	Alkaline extract :-	.0390		
	Acid extract :-	.8978	.9238	- 2.8
5	.3156			
	Acid extract :-	.7079	.7285	- 2.8

The sum of alkaline and acid extractions gives a value which is slightly above theory. It was necessary to use great care in drying the sulphonic compound received here. The last of the ether evaporation was allowed to take place in the open, that is, the separatory funnel used in introducing the extrac-

tion in the flask, was removed before all of the ether evaporated. The product was further dried by passing over it a current of dry air and then transfering it to a dessicator. Heating at 120° or allowing to stand on steam bath for some time caused charring and considerable loss of weight.

4. Separation and Determination of Methyl Anilin and Para-Toluidin.

A mixture of the two amines was shaken for ten minutes in fifty cubic centimeters of a one to ten sodium carbonate solution with an excess of benzene sulphonyl chloride. The one to one potassium hydroxide solution was added in small portions with thorough shaking. Upon extraction of the alkaline and then the acidified solution, the following results were obtained.

Amine.	Weight.	Product.	Theory.
Primary	.3808	.5747	.8977
Secondary	1.3430	3.8009	3.1001

These results are greater then the theoretical amount of the secondary product possible. Accordingly the product extracted from the alkaline solution was treated with fifty cubic centimeters of a one to four solution of potassium hydroxide in ninty-six per cent alcohol, and refluxed for thirty minutes on the steam bath. The result was diluted with water and the alcohol evaporated off. An ether extraction now removed the secondary product, and, upon acidification of aqueous solution, the remainder of the primary compound was received. The products were dried by a current of dry air.

Results :-

Amine.	Weight.	Product.	Theory.	% Error.
		.5747		
		.3721		
Primary	.3808	.9468	.8977	+ 5.
Secondary	1.3430	3.1252	3.1001	+ .8

Other determinations were run using four grams of sodium dissolved in absolute alcohol in place of the solution of potassium hydroxide in ninty-six per cent alcohol,and the amount of water used in dilution was one hundred cubic centimeters.

Results :-

Primary.				Secondary.			
Charge.	Product.	Theory.	% Error.	Charge.	Product.	Theory.	% Error.
.3224	.7457	.7442	+ .1	.5780	1.2840	1.3340	- 3.7
.2478	.6137	.5720	+8.	.6626	1.4831	1.5295	- 3.0
.3960	.9663	.9141	+ 4.5	.8247	1.9272	1.9031	+ 1.2

5. Separation and Determination of Methyl and Dimethyl Anilines and Para-Toluidin.

The mixture of these amines was treated in the same manner as the mixture of methyl anilin and para-toluidin. The extraction of the alkaline solution also removed the unchanged dimethyl anilin. After the treatment with sodium alcoholate and evaporation of the alcohol,the secondary and the free tertiary compounds were again extracted and twenty cubic centimeters of concentrated hydrochloric acid were added. This formed the hydrochloride of the tertiary base,and the secondary sulphone

compound was removed from it by extraction with ether. The hydrochloride was then treated with sodium hydroxide solution and the free tertiary base extracted with ether. Results :-

Primary.				Secondary.			
Weight	Product	Theory	% Error.	Weight	Prod.	Theory	% Error
.3540	.7935	.8171	- 2.7	.8786	1.8310	2.0281	- 9.6
.4400	1.0104	1.0157	- .5	.8021	1.7298	1.8516	- 6.7
.3044	.6872	.7026	- 2.2	.9391	2.0256	2.1676	- 6.5
.3695	.8060	.8529	- 5.5	1.0616	2.2516	2.4506	- 8.1

Tertiary.

Weight	Product	Theory	% Error.
1.1363	.4017	1.1363	
1.1288	.8694	1.1288	
1.3029	.9082	1.3029	
1.4494	1.0476	1.4494	

The great loss of the tertiary base is probanly due to the fact that it was not removed from the alcoholate solution before the evaporation of the alcohol. Being volatile in steam, some of it would be carried off. Another cause of error is the blue dye which dimethyl anilin forms with benzene sulphonyl chloride. Accordingly another separation was tried, in which the extraction was made before the alcohol was evaporated off. Results :-

Weight of Amine.	Class.	Product.	Theory.	% Error.
.3417	P	.8774	.7888	+ 11.0
.7886	S	1.8453	1.8204	+ 1.3
1.5450	T	1.5200	1.5450	- 1.6

6. Separation and Determination of Methyl and Dimethyl Anilins, Para Toluidin, and Trimethyl Phenyl Ammonium Iodide.

A mixture of the four amines was treated with twenty cubic centimeters of distilled water and thoroughly shaken. The quaternerary compound went into solution, and the other three bases were extracted with ether. The quaternerary was regained by evaporating the water to dryness. The other three bases, after the evaporation of the ether, were treated in the same manner as used in the last separation and determination of methyl and dimethyl anilins and para toluidin.

Three separations and determinations were made in this way, but the results received were not entirely satisfactory. Lack of time prevented carrying out any more determinations or making any further study to discover the sources of error.

CONCLUSION.

Conclusion.

The primary amine can be determined with ninty-seven percent accuracy, when present alone. This can be raised to ninty-nine percent by a second treatment with sodium alcoholate. The secondary base can be determined, when alone, with ninty-nine percent accuracy...When both the primary and the secondary bases are present, each can be determined with ninty-nine percent accuracy. If the mixture contains primary, secondary, and tertiary, the first two can be determined with ninty-nine, and the tertiary with ninty-eight percent accuracy. It is believed that as equally accurate separation and determination of the four classes of amines can be received, but sufficient time did not remain to offer experimental evidence.

BIBLIOGRAPHY.

BIBLIOGRAPHY.

(1) Ann. 138, 319 (1866).

(2) Chem. Cen. 07, (II) 54.

(3) Ber. 3, 776 (1870).

(4) Ber. 23, 2962.

(5) Ber. 35, 3779.

(6) E.Fisher. Untersuchengen uber Aminosauren, Polypeptide undProteine. (1899-1906). Pages 128, 130, & 139.

(7) Ber. 38, 906 (1905).