

LXXII.—*Methylation by Means of Formaldehyde. Part I. The Mechanism of the Interaction of Formaldehyde and Ammonium Chloride; The Preparation of Methylamine and of Dimethylamine.*

By EMIL ALPHONSE WERNER.

THE preparation of methylamine from formaldehyde and ammonium chloride is perhaps not so well known as it certainly deserves to be. Having occasion to make use of this reaction from time to time during the last few years, the author has studied this interesting and important change, the mechanism of which, it must be admitted, has up to the present remained decidedly obscure.

Several new facts have been brought to light which have greatly helped to disclose what is now believed to be the true mechanism of the progressive changes involved in this rather complex reaction.

The interaction of formaldehyde and ammonium chloride was first examined by Plöchl (*Ber.*, 1888, **21**, 2117), who, from a rather superficial study of the change, observed the formation of trimethylamine and the evolution of carbon dioxide. No attempt was made to give an explanation of the reaction whereby the amine was produced.

Some years later Brochet and Cambier (*Compt. rend.*, 1895, **120**, 449, 557; *Bull. Soc. chim.*, 1895, [iii], **13**, 392) reinvestigated this reaction, and showed what were the best conditions for the economic preparation of methylamine hydrochloride by its means.

The explanation which they have given, of what they considered to be the main reaction, is far from satisfactory, and they have been decidedly at fault in their observations concerning certain experimental facts connected with the reaction.

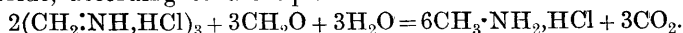
As a result of their investigations, they have drawn the conclusion that whilst methylamine is almost the sole product when ammonium chloride is used in excess, trimethylamine is the main product when formaldehyde is in excess.

The latter conclusion has not been confirmed.

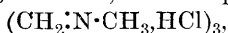
These investigators have evidently mistaken impure dimethylamine hydrochloride for the salt of the tertiary base, only a small quantity of which has been detected when formaldehyde was used in excess, and even then only when a relatively high temperature was attained.

As regards their explanation of the reaction, Brochet and Cambier have drawn the conclusion that "formaldehyde condenses

with ammonium chloride in a very complex manner"; it has been assumed that trimethylenetriamine hydrochloride, $(\text{CH}_2\cdot\text{NH},\text{HCl})_3$, is at once formed, as a result, probably, of the polymerisation of methyleneimine, $\text{CH}_2\cdot\text{NH}$, produced in the first instance; the polymeride then condenses further with formaldehyde, whether the latter is present in excess or not, to give methylamine hydrochloride, according to the equation



When the aldehyde is present in large excess, they state, "on arrive finalement au chlorhydrate du triméthylamine par une série de réactions identiques," that is, the compound,



is formed, which in its turn condenses with formaldehyde to form carbon dioxide, methylamine, and trimethylamine.

It must be admitted that the above equation still leaves the question of the origin of methylamine rather obscure, let alone the case of trimethylamine.

More recently, Knudsen (*Ber.*, 1914, **47**, 2694) has re-examined this reaction, and whilst he has forestalled the author in showing that dimethylamine was produced, he has not added any useful information towards the elucidation of the mechanism by which the amines take origin. Thus it has been assumed that dimethylamine and trimethylamine are produced from the decomposition of a complex, not to say doubtful, dimethylpentamethylenetetramine formed in the first instance as a result of the union of methylamine with excess of formaldehyde.

In both cases, then, obscure condensation reactions have been regarded as explaining the formation of all three amines. This, it will be shown, is quite unnecessary in order to explain the different changes, and, moreover, such a view is in contradiction to the observed facts.

Mechanism of the Formation of Methylamine and of Dimethylamine.

When a solution of ammonium chloride and formaldehyde (commercial formalin), in the proportions recommended by Brochet and Cambier, was gradually heated, a volatile liquid began to distil at 50° ; after heating at 104° until distillation had practically ceased, the amount of distillate obtained was equal to 22 per cent. of the weight of the formaldehyde solution taken. This distillate has been considered by Brochet and Cambier to consist of methylal and water only; thus they state that the product may contain from 60—79 per cent. of the former.

Whilst methylal formed a considerable portion of the distillate,

the chief constituent was methyl formate, an important fact which Brochet and Cambier have completely overlooked. The composition of the distillate was fairly constant, whether ammonium chloride or formaldehyde was present in an excess at the outset.

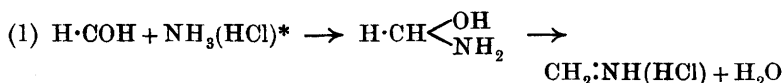
When methylamine hydrochloride and formaldehyde were heated in solution, 90° was reached before distillation was observed; the distillate contained methylal and methyl formate in nearly equal proportions; on the other hand, from dimethylammonium chloride and formaldehyde, after heating under similar conditions, a distillate was obtained which contained practically no methyl formate.

The following results represent the average composition of the distillates in the three respective cases:

	(I.)	(II.)	(III.)
Percentage composition of distillate.	NH ₄ Cl + CH ₂ O. <i>t</i> = 104°.	NH ₂ MeCl + CH ₂ O. <i>t</i> = 104°.	NH ₂ Me ₂ Cl + CH ₂ O. <i>t</i> = 110°.
Methyl formate.....	= 39.0	13.10	0.13
Methylal.....	= 34.6	13.32	8.70
Free formic acid.....	= 1.6	3.64	2.80
Water.....	= 24.8	69.94	88.37
	CO ₂ freely evolved.	CO ₂ freely evolved.	a trace of CO ₂ evolved.

Whilst the formation of methylal is a normal result of a reaction between formaldehyde and methyl alcohol (present in commercial formalin) promoted by hydrochloric acid set free during the process, the production of methyl formate (and carbon dioxide) in considerable quantity furnishes an important clue to the mechanism of the reaction. The oxidation of formaldehyde to formic acid, and of the latter to carbon dioxide, must, in the present circumstances, be provoked by the presence of another substance having an equal tendency to undergo reduction. Through the decomposition of water the desired result is attained, a simultaneous oxidation and reduction is brought about, and as a result of the latter, methylamine and dimethylamine are produced in accordance with the following scheme.

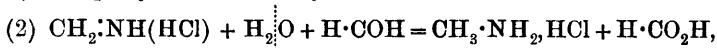
The first phase of the change gives rise to methyleneimine, thus:



It is the great tendency of formaldehyde to react with ammonia that no doubt determines a rapid dissociation of the haloid salt;

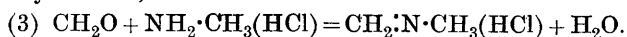
* When ammonium chloride and formaldehyde are mixed in solution, the liquid quickly becomes strongly acid from liberation of hydrogen chloride; the brackets are used here to indicate the dissociated salt.

the feeble base $\text{CH}_2\cdot\text{NH}$ remains largely dissociated, since titration, using phenolphthalein as indicator, shows all the hydrochloric acid to be in the free state. Its presence, however, prevents polymerisation of the base, and equilibrium (that is, neutralisation) is rapidly established by reduction and oxidation, thus:

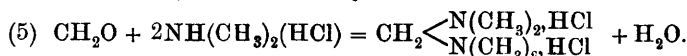


and whilst part of the formic acid is neutralised by esterification, the larger portion is oxidised to carbon dioxide and water.

As the temperature rises, the main reaction (2) is soon accompanied by a change similar to (1), in which methylammonium chloride takes part, whereby dimethylammonium chloride is ultimately formed, thus:



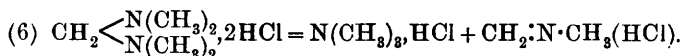
The next and final phase in the change is the result of a reaction between formaldehyde and dimethylammonium chloride, thus:



and since a stable saturated base is produced it will show no tendency to suffer reduction, and consequently there will be no oxidation of formaldehyde during this phase, as shown by the results obtained under III.

In accordance with this scheme, therefore, trimethylamine cannot be directly formed during the progress of the changes which give rise to the primary and secondary bases, and this explains why it has not been detected in the reaction product when the temperature was not allowed to rise above, say, 110° .

If, on the other hand, the temperature be carried too high, as was the case in Knudsen's experiments (*loc. cit.*) or the heating be unduly prolonged, a condition which can scarcely be avoided in dealing with the final mother liquors, after the separation of the bulk of the chlorides of methylammonium and of dimethylammonium, then some trimethylamine is undoubtedly produced. The evidence goes to show that the tertiary base, very probably, arises from the decomposition of the above methylene base, thus:



The unsaturated base, in the absence of excess of formaldehyde, is polymerised to the compound $(\text{CH}_2\cdot\text{N}\cdot\text{CH}_3)_3$,* the presence of which

* This base has been prepared by Henry (*Bull. Acad. roy. Belg.*, 1893, [iii], 26, 200), and later by Brochet and Cambier (*loc. cit.*), who determined its molecular weight.

can be shown by the formation of a copious precipitate on addition of picric acid. The picrate (m. p. 127° , Duden and Scharff, *Ber.*, 1895, **28**, 936) cannot be crystallised from water on account of the ease with which it dissociates.

Since the changes represented by equations (2) and (4) overlap during the progress of the reaction, the production of dimethylammonium chloride in moderate quantity cannot be avoided. Its separation from a considerable amount of methylammonium chloride is, however, a very simple matter, as described later on.

By adopting such conditions as were indicated by the above scheme, a very large yield of dimethylammonium chloride has been obtained with the use of much less formaldehyde than was found necessary by Knudsen (*loc. cit.*). The absence of condensation products in the early stages of the reaction, that is, both before and after large quantities of methylammonium and dimethylammonium chlorides have been produced, has been proved by the fact that no precipitation was produced on the addition of picric acid. This reagent forms sparingly soluble compounds with all the condensation products, or polymerides which have hitherto been supposed to play a part in the formation of the primary and secondary bases produced in this interesting and important reaction.

Preliminary experiments have proved the wide scope of the use of formaldehyde for methylating amino-compounds of various types, on the lines of the scheme just recorded. These, it is to be hoped, will be described in the near future.

EXPERIMENTAL.

The Preparation of Methylammonium Chloride.

The proportions of ammonium chloride and formaldehyde (40 per cent. formalin) * recommended by Brochet and Cambier (*loc. cit.*), namely, one part by weight of the former, and two parts by weight of the latter, were found after several trials to give the best results. Since about 35 per cent. of ammonium chloride has always been recovered unchanged, the molecular ratios $\text{NH}_4\text{Cl} : 2\text{CH}_2\text{O}$ required by theory are very closely represented by the above proportions.

Expt. I.—Two hundred and fifty grams of ammonium chloride and 500 grams of formaldehyde solution were gradually heated in a distillation flask, which carried a thermometer with the bulb well below the surface of the liquid. The temperature was slowly raised to 104° , and was not allowed to rise above this point, at which it

* Analyses of seven different samples of commercial formalin gave as a mean result 35 per cent. of formaldehyde, and in no case was a sample found to contain 40 per cent. The highest value was 37.4 per cent., the lowest 33.2 per cent.

was maintained until no more volatile liquid distilled; this required about four and a-half hours. The distillate weighed 110 grams. The product was allowed to cool, and after filtration from 62 grams of ammonium chloride which had separated, was concentrated by evaporation at 100° to about one-half of the original volume. After removal of 19 grams of ammonium chloride,* the liquid was again concentrated by evaporation until a crystalline scum had formed on the surface of the hot solution.

After cooling, 96 grams of methylammonium chloride (Found, Cl=52.46. Calc., Cl=52.59 per cent.) were separated; after further concentration a second crop (18 grams, Cl=52.39 per cent.) was obtained. The filtrate was now concentrated as far as possible at 100° and was left for twenty-four hours in a vacuum over sodium hydroxide, after which the semi-solid residue was digested with chloroform, when 20 grams of methylammonium chloride (Cl=52.63 per cent.) which had been washed with chloroform to remove dimethylammonium chloride, were obtained. The total yield was 128 grams.

From the chloroform solution, after removal of much of the solvent by distillation, 27.5 grams of dimethylammonium chloride were obtained (Found, Cl=44.38. Calc., Cl=43.5 per cent.).

A viscous residue (76 grams) which did not crystallise after remaining for a week in a vacuum over sulphuric acid, was finally obtained; it contained Cl=40.37 per cent. It was distilled, after the addition of an excess of a 40 per cent. solution of sodium hydroxide, and the alkaline vapours evolved were absorbed in an alcoholic solution of hydrochloric acid, when a small quantity of methylammonium chloride and a relatively large quantity of dimethylammonium chloride were obtained, but no trimethylammonium chloride could be detected. Formaldehyde was also regenerated by the action of sodium hydroxide on the viscous material, which no doubt contained much tetramethylmethylenediamine hydrochloride, $\text{CH}_2(\text{NMe}_2)_2 \cdot 2\text{HCl}$, which requires Cl=40.57 per cent.

Examination of Volatile Liquid Distillate.—This had D_{15}^{20} 0.927. Five c.c. after digestion with 50 c.c. of *N*-sodium hydroxide required 18.15 c.c. of *N*-sulphuric acid for neutralisation.

Five c.c., after removal of methyl formate and methylal by heat at 70° , left an acid liquid which required 1.65 c.c. of *N*-sodium hydroxide for neutralisation. Hence $\text{H} \cdot \text{CO}_2\text{Me} = 39.09$; $\text{CH}_2\text{O}_2 = 1.62$ per cent. The proportion of methylal was determined by difference after removal of water by anhydrous calcium chloride. The

* Ammonium chloride is very sparingly soluble in a concentrated solution of methylammonium chloride, and consequently its separation from the latter salt is very sharp.

separation of methyl formate from methylal by fractional distillation was found to be an extremely tedious process, and was abandoned as useless from an economic point of view. The value of the distillate is of importance, since all the formic acid can be easily recovered as sodium formate, after shaking with a solution of sodium hydroxide in the cold, and thus separated from methylal.

The following results illustrate the value of the whole process from an economic point of view. From an experiment with 4000 grams of formalin and 2000 grams of ammonium chloride, and without working up the final viscous residue, there were obtained 1037 grams of pure methylammonium chloride, 218 grams of nearly pure dimethylammonium chloride, 408 grams of anhydrous sodium formate, and 264 grams of pure methylal (b. p. 42—43°), whilst 698 grams of ammonium chloride were recovered. The yield of methylammonium chloride was equal to 79.6 per cent. of the weight of ammonium chloride which had entered into reaction. When the value of the by-products is taken into consideration, it will be seen that the methylammonium salt is obtained for a very small outlay.

Preparation of Dimethylammonium Chloride.

The formation of the above salt in this reaction has been recently pointed out by Knudsen (*loc. cit.*), but the method adopted for its preparation distinctly shows the absence of a reasonable appreciation of the probable mechanism of the changes. Thus, in an experiment designed with the object of obtaining the best yield of the secondary amine, a useless, not to say a wasteful, excess of formaldehyde was employed without any particular advantage. The following experiment, carried out on the lines of the present theory, gave a very good result.

Expt. II.—Two hundred grams of ammonium chloride and 400 grams of formalin were heated to 104°, as in Expt. I, and 65 grams of ammonium chloride were recovered. To the filtrate 300 grams of formalin were now added, and the solution was again heated at this stage to 115°, and maintained as nearly as possible at this temperature until no more liquid distilled. This required about three and a-half hours. Since methylammonium chloride, produced during the first stage, is less easily dissociated than ammonium chloride, a higher temperature was required to bring about reaction (3). It was noticed that whilst a volatile liquid commenced to distil at about 52° in the first stage, 92° was reached in the second stage before any liquid distilled, which is quite in agreement with theory.

The product was concentrated by evaporation at 100° until a scum appeared on the surface of the hot liquid; 7 grams of ammon-

ium chloride, and 27 grams of pure methylammonium chloride were recovered from the material which had separated after cooling. The product was now heated to 120°, until a portion when cooled became a semi-solid, crystalline mass, after which it was allowed to remain for two days in a partial vacuum over sodium hydroxide. It was then treated with chloroform as described under Expt. I, and 122 grams of nearly pure dimethylammonium chloride (Found, Cl=43·14. Calc., Cl=43·5 per cent.) were ultimately obtained. The final residue contained some trimethylammonium chloride, but was not further dealt with.

The yield of dimethylammonium chloride calculated on the weight of ammonium chloride which had entered into reaction (that is, 200 - 72 = 128 grams) was therefore 95·3 per cent. with the use of 700 grams of formaldehyde solution. Knudsen obtained a yield of 70 per cent. from 100 grams of ammonium chloride and 1000 grams of formalin.

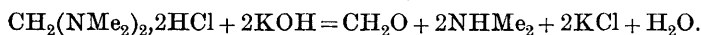
Production of Trimethylammonium Chloride from the Interaction of Formaldehyde and Dimethylammonium Chloride.

In order to prove the origin of trimethylamine, in accordance with the present theory, the following experiment was made.

Expt. III.—Dimethylammonium chloride (20·5 grams) and 45 grams of a solution of formaldehyde (molecular ratio 1:2) were heated in a distillation flask to 110° for four hours. The composition of the distillate, which weighed 18 grams, is given under III (p. 846). The product, after concentration as far as possible by evaporation at 100°, was heated to 120°, after which it was allowed to remain over sodium hydroxide, as in Expt. II. The residue was dissolved in chloroform, and on addition of ether (well dried) 4·5 grams of crystals were precipitated, which contained Cl=36·93 (C₃H₉N, HCl requires Cl=37·17 per cent.).

A platinichloride was prepared, which contained Pt=37·03 (C₃H₉N, H₂PtCl₆ requires Pt=36·95 per cent.).

The residue, after removal of the solvent, was distilled with a 40 per cent. potassium hydroxide solution; the alkaline distillate, which possessed a strong odour of formaldehyde, was easily proved to consist chiefly of dimethylamine with only a small proportion of the tertiary base. The original reaction product, tetramethylmethylenediamine hydrochloride, was readily hydrolysed when heated with a solution of potassium hydroxide, thus,



The small yield of trimethylamine was due to the relatively low temperature attained during the process.

Expt. IV.—The above was repeated, but the temperature was raised to 160°, after evaporation at 100°; a yield of 14 grams of trimethylammonium chloride was obtained, thus proving the origin of the tertiary base, as shown in the scheme, equation (6).

Behaviour of Methylammonium Chloride and Formaldehyde in the Presence of Ethyl Alcohol.

According to theory, no methylammonium chloride should result from the interaction of ammonium chloride and formaldehyde in the absence of water, a point which is not suggested by such an equation, as $2\text{CH}_2\text{O} + \text{NH}_3 = \text{CH}_3 \cdot \text{NH}_2 + \text{H} \cdot \text{CO}_2\text{H}$, which is given by Knudsen to show the formation of methylamine. The insolubility of ammonium chloride in pure alcohol presents a difficulty in the use of this salt; however, the test has been made with the methyl derivative.

Expt. V.—Seventeen grams of methylammonium chloride and 15 grams of paraformaldehyde (2 mols.) were heated with 50 c.c. of alcohol under reflux. The aldehyde was rapidly depolymerised and a clear, homogeneous solution was obtained as soon as the boiling point of alcohol was reached. After a short time the liquid gradually separated into two layers, and the change was completed after one hour. The lower layer when cold was a semi-solid, crystalline mass, from which 10.5 grams of methylammonium chloride were recovered.

The supernatant liquid was shaken with a saturated aqueous solution of calcium chloride, dried, and distilled; 46 grams of ethylal (b. p. 88—89°) were obtained, which was equal to 88.4 per cent. of the theoretical from 15 grams of formaldehyde. When molecular proportions of methylammonium chloride (17 grams) and paraformaldehyde (7.5 grams) were used, 13.5 grams of the amine salt were recovered, and 20 grams of ethylal were obtained.

No dimethylammonium chloride was formed, which bears out the part played by water in the general reaction.

Interaction of Formaldehyde and Ammonium Chloride in the Presence of Water alone.

It was pointed out, in the results given under Expt. I, that the yield of methylammonium chloride was equal to 79.6 per cent. of the weight of ammonium chloride which had entered into reaction. Theoretically, from equations (1) and (2) one molecular proportion of ammonium chloride should yield one of methylammonium chloride, that is, 126.1 parts of the latter salt from 100 parts of the former. With the use of commercial formalin there is inevitable

loss of formaldehyde as methylal, which, for obvious reasons, cannot be profitably counteracted by using an excess of the aldehyde solution. This loss of aldehyde is undoubtedly one of the factors that affects the ultimate yield of methylamine; when it was eliminated by the use of paraformaldehyde, a larger yield of the amine was obtained.

Expt. VI.—Twenty-seven grams of ammonium chloride, 30 grams of paraformaldehyde (molecular ratio 1:2), and 80 c.c. of water were gradually heated. At 80° a clear solution was obtained, and the temperature was maintained for four hours at 104°. Slightly more than one-third (9.06 grams) of the ammonium chloride was recovered, whilst 18.96 grams of pure methylammonium chloride were obtained. This equals 105.6 parts from 100 parts of ammonium chloride. The amount of dimethylammonium chloride produced was not estimated. It is not suggested from the results of this experiment that paraformaldehyde could be economically used on a large scale with advantage, since, quite apart from its relatively high cost, neither formic acid nor part of the unchanged aldehyde can be recovered as by-products. The experiment has served to support the views put forward, and perhaps on a small scale may have some advantage.

Many other points, dealing chiefly with the identification of the intermediate products, which have not been touched upon in the present paper, will be elaborated in a future communication.

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