360. *The Sommelet Reaction. Part VI.* Methyleneamines. A Proposed Mechanism for the Reaction.*

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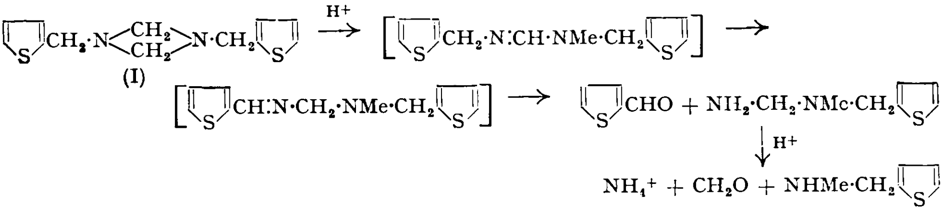
Molecular-weight determinations have shown that the methylene derivatives of benzylamine, *p*-nitrobenzylamine, and 2 : 4 : 6-trimethylbenzylamine are trimeric; they depolymerise during distillation. Since no evidence was found for the existence of a dimer, the mechanism postulated for the Sommelet reaction by Hartough and Dickert (*J. Amer. Chem. Soc.*, 1949, **71**, 3922) is without foundation. Methyleneamines are rapidly hydrolysed by acids even in the cold and therefore their salts, though they can be prepared in anhydrous solvents, have only transient existence in hot aqueous solution.

A probable mechanism for the Sommelet reaction is proposed and discussed.

Methyleneamines play an important part in the Sommelet reaction (Part I, *J.*, 1949, 2700). Since reports on their physical and chemical properties are in many respects conflicting, some of these properties have been studied further.

Our work was prompted particularly by recent papers of Hartough *et al.* (*J. Amer. Chem. Soc.*, 1948, **70**, 4013, 4018) on *N*-methylenethienylmethylamines. Methylene-2-thienylmethylamine showed a peculiar behaviour on distillation : although it appeared to boil at about 100°/0·5 mm. it had to be heated to 170—180° before distillation took place; the distillate was liquid and, although it had no constant boiling point or refractive index, the authors assumed it to be the dimer and ascribed to it the structure (I). After redistillation, for which the same superheating was necessary, the liquid solidified to the crystalline trimer.

Hartough and Dickert (*ibid.*, 1949, **71**, 3922) observed that " hydrolysis " of the alleged dimer with dilute acid at pH 3 to 6·8 gave 2-formylthiophen and *N*-methyl-2-thienylmethylamine. This is the Sommelet reaction, which occurs with other methyleneamines in the same circumstances (Part I, *loc. cit.*; Graymore, *J.*, 1947, 1116). Hartough and Dickert rejected the mechanism suggested in Part I in favour of the following :



No evidence was presented for any of the steps in the above series of reactions, which were based solely on the assumption of structure (I) for the starting material and this assumption, in turn, was justified mainly by the production of 2-formylthiophen and methyl-2-thienylmethylamine, supposedly by the above series of reactions.

We have investigated the molecular weight, the behaviour on distillation, and the hydrolysis of methyleneamines. Our results do not accord with Hartough and Dickert's assumptions.

Molecular Weights.—Ingold and Piggott (*J.*, 1922, **121**, 2795) advanced the theory that azomethines dimerise to compounds containing a four-membered ring, methylene-*p*-toluidine being given as a stable example of this type (Ingold and Piggott, *J.*, 1923, 2745). The validity of their conclusions hinged on the molecular weight of methylene-*p*-toluidine for which the single value of 254 was reported (dimer, 238). However, by careful cryoscopic measurements in four solvents, Miller and Wagner (*J. Amer. Chem. Soc.*, 1932, **54**, 3698) have shown that the compound is trimeric at low temperatures (5—80°). In molten

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* Part V, preceding paper.

camphor, however, the molecular weight was nearer to a dimer (213); and the vapour at 250°, as Ingold and Piggott (1923, *loc. cit.*) have shown, is monomeric.

This variation of the degree of polymerisation of methyleneamines with the temperature explains the conflicting reports: *e.g.*, Graymore (*J.*, 1947, 1116) stated that methylenebenzylamine and methylene-*p*-nitrobenzylamine were dimers (Rast method) but Mayer and English (*Annalen*, 1918, **417**, 76) found methylene-*o*-nitrobenzylamine to be trimeric (ebullioscopy in chloroform); Fuson and Denton (*J. Amer. Chem. Soc.*, 1941, **63**, 654) obtained a slightly higher than double molecular weight for a compound which was later shown (Part II, *J.*, 1949, 2704) to be methylene-2 : 4 : 6-trimethylbenzylamine (ebullioscopy in chloroform).

We determined the molecular weights at room temperature by the method of " isothermic microdistillation " (Barger, *J.*, 1904, **85**, 286; *Ber.*, 1904, **37**, 1754), using the improved procedure of Niederl, Kasanof, Kisch, and Subba Rao (*Microchemie*, 1949, **34**, 132). The crystalline methylene compounds of benzylamine, *p*-nitrobenzylamine, and 2 : 4 : 6-trimethylbenzylamine were found to be trimeric. Further, methylenebenzylamine does not dissociate in the concentration range 0·03—0·08M; the variations in molecular weight were within the experimental error. At room temperature therefore the crystalline stable methyleneamines are trimeric.

Distillation.—Irregular distillation is not peculiar to methylenethienylmethylamine. Methylenebenzylamine behaved in the same way: considerable overheating (oil-bath at 180—200°) was necessary, the vapours passing over at 100—130°/1 mm., showing no definite boiling temperature. Redistillation proceeded in the same way. The distillate was viscous and gradually solidified to a glass which crystallised during several days and was then found to be pure trimer. The crystalline trimer distilled over the same temperature range, overheating being necessary, and it did not solidify immediately in the receiver.

The boiling point is too high for a monomer (the isomeric benzylidenemethylamine boils at 90—91°/30 mm.; Ingold and Shoppee, *J.*, 1929, 1204), but too low for a dimer which would probably boil higher than dibenzylamine (186°/19 mm.). It is evident that the methyleneamine vaporises by depolymerisation for which a high temperature is required; hence the need for overheating. The observed vapour temperature is that of an overheated monomer. Condensation does not result in immediate trimerisation; the liquid may contain some monomer, but is probably a mixture of polymers which is gradually converted into the trimer, the most stable form. A similar process occurs in the preparation of methylenebenzylamine by mixing solutions of benzylamine and formaldehyde: an oil separates at once but does not crystallise immediately even on inoculation. The presence of hydroxyl ions appears to hasten the formation of crystalline trimer. On the other hand, when the pure trimer was dissolved in alcohol and precipitated by the addition of water, it immediately crystallised.

It was considered a possibility that Hartough's " dimer " contained some methylenebisamine, $R{\cdot}NH{\cdot}CH_2{\cdot}NH{\cdot}R$. An alleged compound of this type, methylenebisbenzylamine, was reported by Kampff (*Annalen*, 1890, **256**, 220) but it appears to have been the trimer of methylenebenzylamine (Hunt and Wagner, *J. Org. Chem.*, 1951, **16**, 1792). Methylenebisamines formed from aromatic amines, however, are well known (Eberhardt and Welter, *Ber.*, 1894, **27**, 1804; Bischoff and Reinfeld, *ibid.*, 1903, **36**, 41). The preparation of methylenebisbenzylamine was therefore attempted. When two mols. of benzylamine were treated with one mol. of aqueous formaldehyde a heavy oil separated after the addition of water. A few crystals of methylenebenzylamine gradually separated; when freed from benzylamine by water, the oil solidified and was identified as methylenebenzylamine. Distillation of this oil gave two fractions consisting of benzylamine and methylenebenzylamine, respectively. It appears therefore that the oil consists mainly of benzylamine and its methylene compound; whether methylenebisbenzylamine is present, probably in equilibrium with the other two compounds, is a matter for conjecture; but if it is, it certainly does not survive distillation.

Hartough, Meisel, Koft, and Schick (*J. Amer. Chem. Soc.*, 1948, **70**, 4013) claimed that methylenethienylmethylamine, as prepared from thienylmethylamine and formaldehyde, is dimeric and that the trimer is only obtained on distillation. We found, however, that the oil formed on mixing solutions of the amine and formaldehyde solidified to the trimer after some stirring and cooling, even more readily than methylenebenzylamine.

Methylene-*p*-nitrobenzylamine was also distilled: overheating was again necessary and the distillate, a brown oil, crystallised rapidly to the trimer.

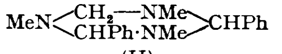
From these experiments it is concluded that there is no evidence for the existence of a dimer, and therefore Hartough and Dickert's reaction mechanism is without foundation. Even if such a dimer existed it is not likely that it would contain the four-membered ring of (I). The formation of methyleneamines being reversible, their structure will be determined by energy considerations. The trimer which is generally believed to contain a 1 : 3 : 5-triazine ring (cf. Morton, "The Chemistry of Heterocyclic Compounds," McGraw-Hill, New York, 1946, p. 513), is more stable than the monomer because the bond energy of six C–N bonds is apparently higher than that of three C:N bonds: Pauling ("The Nature of the Chemical Bond," Cornell Univ. Press, New York, 1940, pp. 53, 131) gives 48·6 kcals./mole for the C–N bond and 94 kcals./mole for C:N. A four-membered ring would have the same bond energies as a six-membered one; but it would have considerably more energy owing to strain and therefore would be less stable. Indeed, although Hale and Lange (*J. Amer. Chem. Soc.*, 1919, **41**, 380) appear to have established the existence of the $\mathrm{>C<\genfrac{}{}{0pt}{}{NH}{NH}>CO}$ system in derivatives of urea, it is doubtful if compounds containing the $\mathrm{>C<\genfrac{}{}{0pt}{}{\overset{|}{N}}{\underset{|}{N}}>C<}$ ring have ever been prepared. [The example given in "The Ring Index" (Patterson and Capell, Reinhold Publ. Corp., New York, 1940, p. 34) is a compound of doubtful structure.]

There is another objecton against Hartough and Dickert's proposed course of the Sommelet reaction. As a second step, it includes the prototropic rearrangement of an azomethine system, which has been shown to occur only in a very strongly basic medium (Ingold and Shoppee, *loc. cit.*) and is "in the highest degree unlikely" (Shoppee, *Nature*, 1948, **162**, 619) under the slightly acidic conditions of the reaction.

In further support of their mechanism Hartough and Dickert refer to the yield of aldehyde obtained. Their mechanism allows only a 50% yield and Hartough and Dickert never obtained more. By coincidence, the method given in *Org. Synth.*, 1949, **29**, 87, also results in approximately a 50% yield from 2-chloromethylthiophen. In the presence of hexamine, however, the course of the reaction suggested by Angyal and Rassack (Part I, *loc. cit.*) allows higher yields; and it has been found that by improving the procedure, particularly by using 50% acetic acid solution (Part III, *J.*, 1950, 2141), a 74% yield of 2-formylthiophen is obtained either from 2-chloromethylthiophen or from 2-thienylmethylamine.

Final proof that aldehyde formation is not dependent on the presence of a dimer was afforded by showing that 2-formylthiophen could be obtained from the crystalline trimer of methylenethienylmethylamine. Hartough and Dickert's method for "hydrolysing the dimer" gave a comparable yield.

Distillation of methylenebenzylamine was tried after addition of a small amount of sulphuric acid. This might facilitate depolymerisation, in analogy with the aldehyde trimers. Distillation occurred as before but the distillate was quite fluid and did not crystallise. Acid hydrolysis yielded some benzaldehyde. This behaviour was reminiscent of Graymore and Davies's distillation (*J.*, 1945, 293) of *N*-benzylhexaminium chloride which yielded an oil, b. p. 70—72°/30 mm., to which they assigned structure (II). It was claimed that hydrolysis of their product yielded benzaldehyde, methylamine, and formaldehyde, the latter having been identified by smell alone. The boiling point is much too low, however, for a compound of structure (II). On repeating Graymore's experiment we found that the main fraction consisted of a mixture of benzylidenemethylamine and a smaller amount of benzyldimethylamine; no formaldehyde was found amongst the hydrolysis products. Thus when a hexaminium compound, or a methyleneamine, is heated with



$\mathrm{MeN<\genfrac{}{}{0pt}{}{CH_2{-}NMe}{CHPh{\cdot}NMe}>CHPh}$

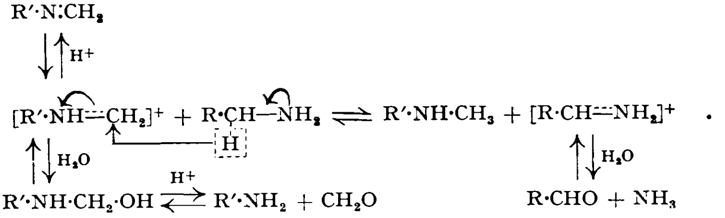
(II)

a strong acid in the absence of solvents, a Sommelet reaction occurs; the two cases are analogous, for in each a cyclic methyleneamine with one nitrogen atom in the quaternary state is involved.

Hydrolysis.—Hartough and Dickert (*loc. cit.*) claim that at pH 1—2 methylenethienylmethylamine exists as a salt of the monomer [evidence, stated to be in a paper by Hartough and Meisel (*J. Amer. Chem. Soc.*, 1948, **70**, 4019) is, however, not discernible]. Although methyleneamines, like most Schiff's bases, are rapidly hydrolysed by acids, they might form stable salts with strong aqueous acids. Under anhydrous conditions such salts were obtained, *e.g.*, methylenebenzylamine in anhydrous ether gave a monohydrochloride of the trimer, and a monopicrate of the trimer separated from anhydrous ethanol. After this work was completed, a hydriodide of the trimer was reported by Hunt and Wagner (*loc. cit.*). However, when the solvents contained small amounts of water, the salts, which were immediately precipitated, were the hydrochloride and picrate, respectively, of benzylamine. Methylenethienylmethylamine gave analogous results. In aqueous solutions, therefore, salts of the methyleneamines can have only transient existence [cf. the analogous results of Hunt and Wagner (*loc. cit.*) with alkylidenebisamines]. The water-insoluble methylenethienylmethylamine trimer dissolved immediately in an equivalent amount of N/10-hydrochloric acid, but the pH of the solution gradually increased from an initial value of *ca.* 2·2 to 3·7. This indicates that the compound dissolves first as the salt of a weak base (the Schiff's base) but then changes to the salt of a stronger base (thienylmethylamine); the half-life of the conjugate acid, in 0·04M-solution at 15°, is approximately 1 min.

Mechanism of the Sommelet Reaction.—In Part I (*loc. cit.*) it was shown that the Sommelet reaction is essentially a hydrogenation–dehydrogenation process in which a Schiff's base is hydrogenated at the expense of an amine. Several related reductions of Schiff's bases are known, such as the Plöchl–Eschweiler, the Leuckart, and the Wallach reaction, which have been extensively studied by Wagner and his school. (For leading references see McLaughlin and Wagner, *J. Amer. Chem. Soc.*, 1944, **66**, 251; Staple and Wagner, *J. Org. Chem.*, 1949, **14**, 559.) The reaction discussed by McLaughlin and Wagner (*loc. cit.*) is particularly similar to the Sommelet reaction. All these reactions appear to be acid-catalysed.

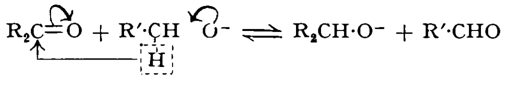
It is believed that the active intermediate is the conjugate acid of a Schiff's base, the mesomeric cation $R\cdot{}^{+}NH{:}CH_2 \longleftrightarrow R\cdot NH\cdot CH_2^{+}$ (III). This contains a strongly electrophilic carbon atom which can attack water (hydrolysis of the Schiff's base), aromatic rings (aminomethylation), activated methylene groups (Mannich reaction; Liebermann and Wagner, *J. Org. Chem.*, 1949, **14**, 1001), formaldehyde (Plöchl–Eschweiler reaction), or formic acid (Wallach and Leuckart reactions). In the last two cases a hydrogen atom with its two bonding electrons, *i.e.*, a hydride ion, is transferred to the cation, as in certain other organic redox reactions (Alexander, "Principles of Ionic Organic Reactions," Chapman and Hall, London, 1950, pp. 167—170). It is suggested that the mesomeric cation may similarly attack amines, abstracting a hydride ion according to the following proposed mechanism for the Sommelet reaction (horizontal sequence of the scheme):

(III)  . . . (1)

In the most favourable form of the reaction, *i.e.*, when hexamine is used, R′ = H.

In aqueous solution the main reaction of the mesomeric cation will be hydrolysis according to the vertical sequence of the scheme. This process is much faster than the Sommelet reaction, hence in strongly acid solution it goes to completion without discernible formation of aldehyde. Only in the pH range in which the amine and the methyleneamine are in equilibrium—and (III) is constantly re-formed—can the slower Sommelet reaction gain preponderance. The proposed mechanism therefore explains the pH limits (*ca.* 3—7) of the Sommelet reaction : amine and Schiff's base must coexist for the reaction to occur.

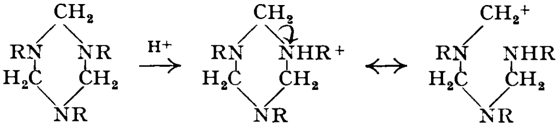
It may be noted that amines are ammono-alcohols, and Schiff's bases ammono-carbonyl compounds; therefore reaction (1) is the ammono-analogue of the reaction between carbonyl compounds and alcoholic alkali (Alexander, *op. cit.*) :



$$R_2C{=}O + R'{\cdot}\underset{H}{CH}\ O^- \rightleftharpoons R_2CH{\cdot}O^- + R'{\cdot}CHO \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

In the aquo-system (2), owing to the strong electron-affinity of the oxygen atom, the carbonyl carbon atom is sufficiently electrophilic to attract the hydride ion; but the alcohol will not release it until its electron density has been increased by its transformation into an alkoxide ion (Hammett, " Physical Organic Chemistry," McGraw-Hill, 1940, p. 361). On the other hand, in the ammono-system (1) the amine releases the hydride ion (amines, when un-ionised, are readily oxidised) but the Schiff's base is not sufficiently electron-attracting until converted into its conjugate acid. Hence the different pH requirements of these two reactions.

The cation (III) can be formed not only from Schiff's bases but also from hydroxymethylamines or from methylenebisamines (Staple and Wagner, *loc. cit.*). A similar cation can result as a first step in the acid hydrolysis of trimeric methyleneamines :



and in an analogous way also from hexamine.

While the proposed mechanism cannot be regarded as proved, it is compatible with all the known features of the Sommelet reaction. The electronic effects of groups attached to the carbon and nitrogen atoms account for the direction of the reaction and for some of its limitations. Two aspects of the present work seem to support this mechanism : (i) the demonstration that the conjugate acid of methyleneamines has a definite, though short, existence in aqueous solution : (ii) the fact that a Sommelet reaction occurs when the conjugate acids of Schiff's bases are heated in the absence of a solvent.

EXPERIMENTAL

M. p.s are corrected. Microanalyses by Mrs. E. Bielski.

Materials.—Methylenebenzylamine was prepared from a solution of benzylamine hydrochloride by the addition of excess of formaldehyde and excess of sodium hydroxide solutions. An oil separated which became semi-solid. Crystallisation from aqueous ethanol at −10° gave a 95% yield of colourless crystals, m. p. 50°. Methylenethienylmethylamine, m. p. 55°, was prepared in the same way in 90% yield, and crystallised from ethanol.

p-Nitrobenzylamine hydrochloride (7·56 g.) was dissolved in ethanol (40 c.c. of 80%), and hexamine (5·6 g.) and formaldehyde (0·4 c.c. of 40%) were added. A cream-coloured precipitate formed immediately; after 5 min.' boiling, the solution was cooled, and the precipitated methylene derivative recrystallised from ethyl acetate (nearly colourless needles, m. p. 161·5°; Graymore, *loc. cit.*, 1947, reported m. p. 158°). Prolonged heating, as described by Graymore, is not needed. Methylene-2 : 4 : 6-trimethylbenzylamine, m. p. 150°, was prepared by Fuson and Denton's method (*loc. cit.*).

Molecular-weight Determinations.—These were carried out according to the directions of Niederl *et al.* (*loc. cit.*), with azobenzene as a standard and acetone as solvent. It was necessary to keep the capillaries in a room of approx. constant temperature. Found : for methylene-*p*-nitrobenzylamine, 490 (trimer requires 492); for methylene-2 : 4 : 6-trimethylbenzylamine 440, 458 (trimer requires 483).

The usual procedure was reversed in the case of methylenebenzylamine. Instead of comparing a solution of the compound with several concentrations of azobenzene, the azobenzene concentration was kept constant and three dilutions (0·03, 0·05, 0·08M) of the Schiff's base were used. If dissociation of the trimer occurred in dilute solution, the movements of the menisci plotted against the concentrations would lie on a curve and not on a straight line. A straight line, however, was obtained from which the molecular weight was calculated as 350 (trimer requires 357).

Salts of Methylenebenzylamine.—Dry hydrogen chloride was passed into a solution of methylenebenzylamine (0·5 g.) in anhydrous ether (100 c.c.). The precipitate which separated immediately was washed repeatedly with anhydrous ether and dried over sulphuric acid. The *hydrochloride* melted at 125° (Found: Cl, 9·75. $C_{24}H_{27}N_3$,HCl requires Cl, 9·0%). Methylenebenzylamine showed evidence of its ability to combine with more than one mol. of acid : the precipitate, before washing, contains Cl approx. 15%, and slowly decomposes with the liberation of hydrogen chloride and some benzaldehyde. Thorough washing, however, removes the excess of acid and the salt is then stable in dry air. The same experiment, but with ether saturated with water, resulted in a somewhat slower separation of leaflets which melted, alone and in admixture with benzylamine hydrochloride, at 248°.

A solution of methylenebenzylamine (0·5 g.) in anhydrous ethanol (10 c.c.) was added to a saturated solution (10 c.c.) of picric acid in anhydrous ethanol. The mixture was heated to the b. p.; on cooling, the *picrate*, m. p. 110° (0·38 g.), of the trimer crystallised (Found : N, 14·2. $C_{24}H_{27}N_3,C_6H_3O_7N_3$ requires N, 14·3%). Recrystallisation from aqueous alcohol gave benzylamine picrate, m. p. 196°. The same experiment, but with 95% ethanol, gave benzylamine picrate (1·0 g.), m. p. alone and in admixture with an authentic sample, 198°.

Salts of Methylenethienylmethylamine.—Dry hydrogen chloride was passed through a solution of methylenethienylmethylamine (0·5 g.) in anhydrous ether (100 c.c.). After thorough washing with anhydrous ether and drying over sulphuric acid, the *hydrochloride* of the trimer was obtained as colourless crystals, m. p. 118°, stable in dry air (Found : Cl, 9·3. $C_{18}H_{21}N_3S_3$,HCl requires Cl, 8·65%).

Apparently the Schiff's base of thienylmethylamine is somewhat less readily hydrolysed than that of benzylamine, because use of ether saturated with water gave a mixture of the hydrochlorides of thienylmethylamine and methylenethienylmethylamine. Recrystallisation from ethanol–ether gave leaflets, which melted, alone and in admixture with thienylmethylamine hydrochloride, at 188°. Hartough and Meisel (*loc. cit.*) report 188—189°.

Methylenethienylmethylamine (0·5 g.) in anhydrous ethanol (10 c.c.) gave, as above, the *picrate* (0·32 g.) of the trimer, which, recrystallised from anhydrous ethanol, melted at 133° (Found : N, 13·75. $C_{18}H_{21}N_3S_3,C_6H_3O_7N_3$ requires N, 13·9%). Recrystallisation from aqueous ethanol gave thienylmethylamine picrate, m. p. 175° (Hartough and Meisel, *loc. cit.*, report 181—182°). Only the latter was obtained from 95% alcohol.

2-*Formylthiophen.*—A mixture of 2-chloromethylthiophen (41·5 g.), hexamine (88 g.), and 50% acetic acid (260 ml.) was heated under reflux for 4 hr. Concentrated hydrochloric acid (125 ml.) was added and heating continued for 5 min. After cooling, the mixture was extracted with ether (3 × 100 ml.), and the extract dried and evaporated. Distillation of the residue gave a fore-run of acetic acid and then the aldehyde (26 g., 74%), b. p. 63—66°/6 mm.

Distillation of N-*Benzylhexaminium Chloride.*—The salt (70 g.) was heated *in vacuo* to 200°, whereupon it decomposed and a colourless oil (14·2 g.) distilled at 68—86°/24 mm. On redistillation the main fraction boiled at 86—91°/30 mm. Three grams were hydrolysed by steam-distillation with excess of hydrochloric acid; benzaldehyde was determined in the distillate as its 2 : 4-dinitrophenylhydrazone, m. p. 237° : 2·08 g. of aldehyde were found. A test for formaldehyde with resorcinol and concentrated sulphuric acid was negative.

The residue from the steam-distillation was evaporated to dryness and the resulting solid extracted with chloroform. The insoluble material (0·89 g.) was methylamine hydrochloride, m. p. 223°. The chloroform-soluble hydrochloride (0·33 g.) gave a base, b. p. 165—172° (picrate. m. p. 94·5°, undepressed by benzyldimethylamine picrate).

Hydrolysis of Methylenethienylmethylamine.—A solution of methylenethienylmethylamine (125 mg.) in ethanol (5 ml.) was quickly added to 0·05N-hydrochloric acid (20 ml.). The pH of the solution was measured at frequent intervals with a Leeds and Northrup Universal pH Potentiometer Assembly. The following are minutes and pH's : ¼, 2·4; ½, 2·55; 1, 2·85; 1½, 3·0; 2, 3·15; 3, 3·3; 4, 3·45; 5, 3·52; 10, 3·65; 15, 3·7.

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