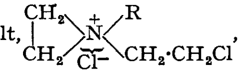
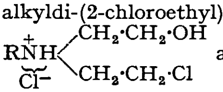
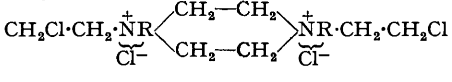
99. *The Chemistry of 2-Chloroalkylamines. Part II. Reactions of Tertiary 2-Chloroalkylamines in Water.*

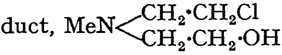
By W. E. Hanby, G. S. Hartley, E. O. Powell, and H. N. Rydon.

The reactions which take place when dilute aqueous solutions of methyl-, ethyl-, *n*-propyl-, and *iso*propyl-di-(2-chloroethyl)amines, $NR(CH_2{\cdot}CH_2Cl)_2$, are kept at room temperature have been studied. The first stage of the reaction has been shown to be a comparatively fast cyclisation to the quaternary ethyleneimonium salt, , which is in tautomeric equilibrium with the alkyldi-(2-chloroethyl)amine. The second stage, which is slower, comprises hydrolysis to  $R\overset{+}{N}H{<}\begin{smallmatrix}CH_2{\cdot}CH_2{\cdot}OH\\CH_2{\cdot}CH_2{\cdot}Cl\end{smallmatrix}\ \underset{}{Cl^-}$ and $R\overset{+}{N}H(CH_2{\cdot}CH_2{\cdot}OH)_2$ Cl^-, some reversion to the hydrochloride of the starting material, $R\overset{+}{N}H(CH_2{\cdot}CH_2Cl)_2$ Cl^-, under the influence of hydrochloric acid produced in the hydrolytic reaction, and some dimerisation to the piperazinium dimer,



This paper is concerned with the study of the reactions which take place at room temperature in dilute aqueous solutions of the tertiary 2-chloroalkylamines, $NR(CH_2{\cdot}CH_2Cl)_2$, the preparation of which has been described in Part I (preceding paper). Since these substances differ from 2 : 2′-dichlorodiethyl sulphide ("mustard gas") only in the replacement of the thio-ether grouping, –S–, by the alkylimino-grouping, –NR–, we expected them to react similarly with water. "Mustard gas" is very rapidly hydrolysed in aqueous solution, and Ogston (unpublished work) has shown that its reaction with water is a very clear example of the Hughes–Ingold S_N1 type of aliphatic substitution; we anticipated that the tertiary 2-chloroalkylamines would provide further examples of this type of reaction although it seemed probable that their greater basic strength would enormously reduce the rate of ionisation of the β-chlorine atoms in acid solution, under which conditions the central nitrogen atom would be positively charged.

Our first experiments, carried out with methyldi-(2-chloroethyl)amine, $NMe(CH_2{\cdot}CH_2Cl)_2$, appeared to bear out these expectations. In aqueous solution, measurements of chloride ion concentration showed that the free base disappeared at a rate which was, in the initial stages, independent of the concentration of alkali; reaction with thiosulphate also occurred at the same initial rate. In acid solution no reaction was detectable and, correspondingly, the reaction with water appeared to stop after one of the two chlorine atoms had become ionic. When, however, we attempted to measure the rate of hydrolysis, in the presence of excess alkali, by an electrical conductivity method we obtained results incompatible with this simple view of the reaction mechanism; we found that the conductivity increased with time over the first few minutes and, since the hydroxyl ion is much the most mobile of anions, were forced to conclude that the process was, not a mere replacement of hydroxyl by chloride ions as in simple hydrolysis, but an actual production of additional ions. It will be convenient to discuss our further experiments in two sections, the first devoted to this initial ionisation stage and the second to the subsequent slower reactions.

The Action of Water on Methyldi-(2-chloroethyl)amine.—(1) *The initial reaction.* We will first record a few fundamental physico-chemical properties of the base. By quickly pouring a slight excess of alkali into an aqueous solution of the hydrochloride and observing whether or not a transient turbidity is produced it is possible to estimate the solubility of methyldi-(2-chloroethyl)amine in water as about 1·2% at room temperature; by shaking for a sufficient time very much larger amounts of base can be brought into solution owing to the occurrence of the sequence of reactions described below. Rapid half-neutralisation of an aqueous solution (more dilute than 1%) of the hydrochloride in the presence of indicators gave an approximate pK_a value of 6·1 for the methyldi-(2-chloroethyl)ammonium ion, corresponding to a base dissociation constant of $1{\cdot}2 \times 10^{-8}$. The value of pK_a for methyldi-(2-hydroxyethyl)amine, $NMe(CH_2{\cdot}CH_2{\cdot}OH)_2$, is 8·3, while that for the half-hydrolysis product,  $MeN{<}\begin{smallmatrix}CH_2{\cdot}CH_2Cl\\CH_2{\cdot}CH_2{\cdot}OH\end{smallmatrix}$, is presumably intermediate although we were unable to determine it experimentally owing to rapid hydrolysis.

Velocity measurements on the reactions occurring in aqueous solutions of methyldi-(2-chloroethyl)amine were carried out using the following technique.

Reaction of the free base with water was initiated either by rapid addition, with shaking, of a neutralising quantity of barium hydroxide solution to a freshly prepared solution of the hydrochloride, or by rapid additions of water to the free base previously weighed into a dry graduated flask; by the latter method it was possible to effect solution, by shaking, within a few seconds, whereupon the solution was at once made up to volume and transferred to the thermostat. The reaction was arrested, in aliquot samples withdrawn at chosen times, by addition of a known excess of dilute nitric acid. Aliquot parts of the acidified solution were then titrated (*a*) electrometrically with silver nitrate and (*b*) with barium hydroxide, using both bromophenol-blue (mid-pH 3·8) and alizarin-yellow (mid-pH 11·0); the last-mentioned titration had to be carried out rapidly since further reaction occurs at high pH. The silver nitrate required then measures the total chloride ion; the titration to pH 3·8, less the added nitric acid, the acid produced in excess of that required to neutralise the weak bases present; and the titration from pH 3·8 to pH 11·0, the amount of weak base, both reactant and resultant, present; in all cases the acid production measured by titration to pH 3·8 is decreasingly negative during the primary reaction and remains then nearly zero until a very late stage of the reaction.

Typical results of measurements carried out by this procedure on 1% solutions at 10° and 25° are shown in Figs. 1—4; the method of initiating the reaction had no influence on its course. It is clear from the curves that the reaction consists of unimolecular disappearance of weak base, without neutralisation of the remainder, and concomitant unimolecular appearance of a quaternary ammonium salt; at 25° the half-change time is about 7 minutes ($k_1 = 0{\cdot}0016$ sec.$^{-1}$).

That this initial reaction does indeed result in the disappearance of all the methyldi-(2-chloroethyl)amine was demonstrated by the following experiment, which also shows that the reaction is reversed in the presence of hydrochloric acid.

Methyldi-(2-chloroethyl)amine (5·0 g.) was dissolved in water (500 c.c.) by shaking and the resulting solution kept at 25° for 45 minutes, during which time the pH fell from 8·5 to 7·0. The solution was then rapidly extracted five times with benzene; the extract was dried (Na_2SO_4) and the benzene removed under reduced pressure, leaving a very small residue (less than 300 mg.) which was not further examined. N-Hydrochloric acid (32 c.c.) was then added to the benzene-extracted aqueous solution, bringing the pH from 7·0 to 3·0, and the solution was then kept at room temperature for 65 hours. At the end of this time, 5N-sodium hydroxide (6·4 c.c.) was added, bringing the pH to 7·5; the solution, which now smelt strongly of methyldi-(2-chloroethyl)amine, was again extracted five time with benzene immediately after the alkali addition. Evaporation of the dried extract gave a residue (2·5 g.) which was treated with picric acid (3·7 g.) in benzene (50 c.c.). The precipitated picrate (4·9 g.; 40% on the original base) was identified as methyldi-(2-chloroethyl)ammonium picrate by m. p. and mixed m. p. 132—133°.

FIG. 1.

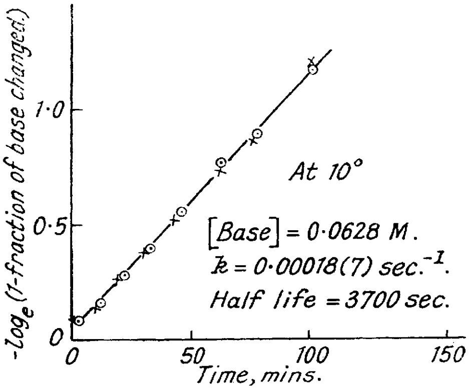
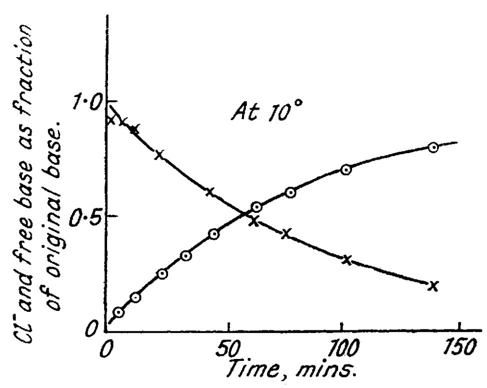


FIG. 2.



x, *Free base measurements.*
⊙, *Cl⁻ measurements.*

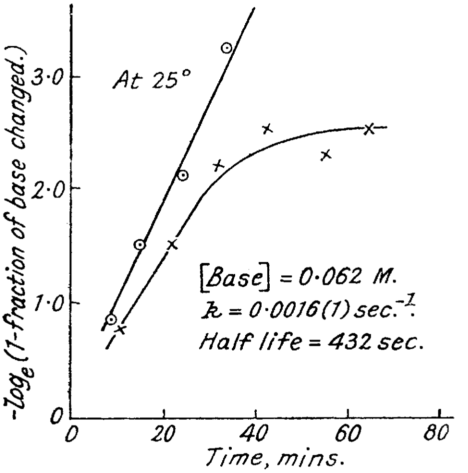


FIG. 3.

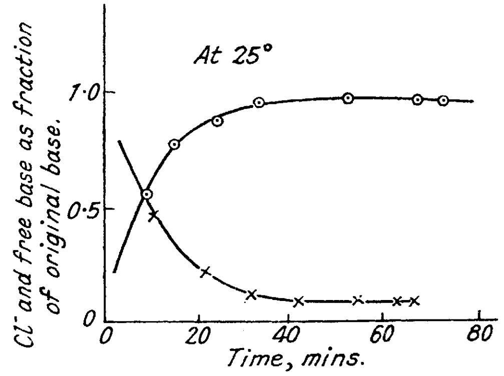


FIG. 4.

It has been shown in Part I (*loc. cit.*) that methyldi-(2-chloroethyl)amine readily undergoes dimerisation to the piperazinium dimer (VI); this compound does not revert to the original amine in the presence of hydrochloric acid, and the experiment just described thus indicates that the intermediate quaternary ammonium salt is not the dimer. Further evidence in support of this conclusion was obtained by investigation of the reaction of methyldi-(2-chloroethyl)amine with sodium thiosulphate. This reaction, followed by titration of excess of sodium thiosulphate with iodine at intervals, was found to proceed initially at the same rate as the formation of the quaternary ammonium salt, but, unlike the latter reaction, continued at a comparable rate until all the chlorine had become ionic. If the free base was allowed to react with water for a short time and a thiosulphate titration was then rapidly carried out, it was found that there was an instantaneous consumption of thiosulphate equivalent to the amount of chloride ion formed by the reaction of the base with water. Presumably the reaction with thiosulphate is of the S_N1 type:

(i) $NMe(CH_2{\cdot}CH_2Cl)_2 \longrightarrow CH_2Cl{\cdot}CH_2{\cdot}NMe{\cdot}CH_2{\cdot}\overset{+}{C}H_2$ (slow; rate-determining).

(ii) $CH_2Cl{\cdot}CH_2{\cdot}NMe{\cdot}CH_2{\cdot}\overset{+}{C}H_2 + S_2O_3^{--} \longrightarrow CH_2Cl{\cdot}CH_2{\cdot}NMe{\cdot}CH_2CH_2{\cdot}S_2O_3^-$ (fast).

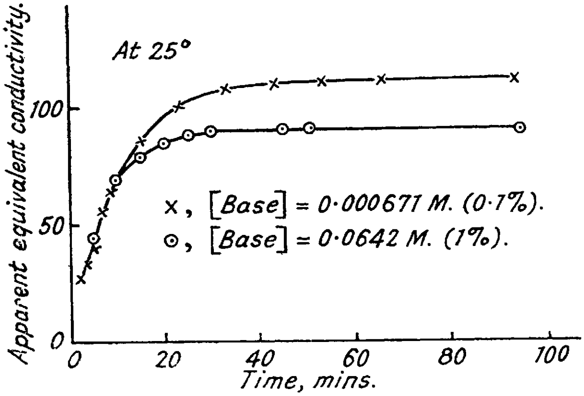
The instantaneous reaction of thiosulphate with the intermediate quaternary ammonium salt formed in the reaction of the base with water shows that the latter can replace the carbonium ion in the rapid stage (ii) of the above reaction. This instantaneous reaction provides a useful analytical method for determining the rate of disappearance of the reactive quaternary ammonium salt in the later stages of the reaction and also serves to distinguish it from the much more stable dimer, which does not react with thiosulphate.

Direct evidence for the univalent nature of the intermediate quaternary ammonium cation was obtained as the result of electrical conductivity measurements carried out by Mr. F. J. Kettel. Solutions of methyldi-(2-chloroethyl)amine were made up by direct weighing into dry flasks and addition of water; the change of conductivity with time was followed at two concentrations, 0·00067 and 0·064 molar.

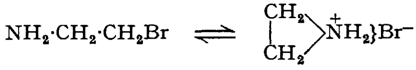
Owing to the non-availability at the time of suitable non-inductive resistance boxes, conductivities were measured with direct current. To eliminate the production of hydrogen and hydroxyl ion at the electrodes, these were made of platinum gauze plated with silver which was then partly converted electrolytically into chloride. The electrodes were situated in wide tubes connected by a length of narrow-bore tubing suitably bent so as to enable the whole apparatus to be accommodated in the thermostat. By this means the resistance was almost completely confined to the narrow tube which concentration changes propagated from the electrodes would not enter in the short time required for measurement, and a high voltage (120 v. dry cell) could be applied at low current density, thus reducing both the magnitude and the effect of polarisation. Resistance was measured by the orthodox bridge with galvanometer detection, and calibration measurements on standard potassium chloride solutions gave results in good agreement with accepted values.

The results are shown graphically in Fig. 5. The conductivity values reached after 60 minutes correspond to equivalent conductivities of 113 and 92 respectively; owing to the considerable contribution of dissociated base at the lower concentration the former figure is rather too high. Nevertheless, solutions of recrystallised dimer show a higher equivalent conductivity (124) at 0·00067 molar and a lower conductivity (82) at 0·064 molar. The cation of the intermediate quaternary salt is thus clearly of lower valence type than the bivalent cation of the piperazinium dimer; it must, therefore, be univalent.

FIG. 5.

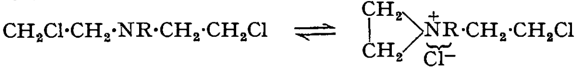


It has been shown (Howard and Marckwald, *Ber.*, 1899, **32**, 2036; Freundlich and Neumann, *Z. physikal. Chem.*, 1914, **87**, 69; Freundlich and Saloman, *ibid.*, 1933, **166**, *A*, 161) that there is a tautomeric equilibrium in solution between 2-bromoethylamine and ethyleneimonium bromide :



$$NH_2{\cdot}CH_2{\cdot}CH_2Br \rightleftharpoons \{(CH_2)_2\overset{+}{N}H_2\}Br^-$$

There seems to be no reason why a similar equilibrium should not be set up in aqueous solutions of alkyldi-(2-chloroethyl)amines, thus :



$$CH_2Cl{\cdot}CH_2{\cdot}NR{\cdot}CH_2{\cdot}CH_2Cl \rightleftharpoons (CH_2)_2\overset{+}{N}R{\cdot}CH_2{\cdot}CH_2Cl\ \ Cl^-$$

(I.) (II.)

We accordingly identify * the reactive intermediate quaternary ammonium salt formed rapidly in aqueous solutions of methyldi-(2-chloroethyl)amine, (I; R = Me), with the quaternary salt, *methyl-2-chloroethylethyleneimonium chloride*, (II; R = Me). It will be seen that the

---

* Since this work was carried out, in the summer of 1942, Goldberg (*J.*, 1945, 826) has postulated a similar quaternary ethyleneimonium salt as an intermediate in some reactions of diethyl·2-chloroethylamine.

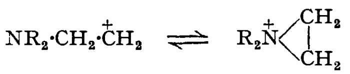
ethyleneimonium salt (II) fulfils all the requirements of the experimental findings; it is clear, also, that it must be the main organic component of a 1% solution of the amine (I; R = Me) which has been kept at 25° for 45 minutes, and we have been able to isolate a *mercurichloride*, probably that of (II; R = Me), from such a solution, as follows.

A solution of methyldi-(2-chloroethyl)amine (2·5 g.) in water (250 c.c.) was kept at 25° for 45 minutes; mercuric chloride (9 g.), dissolved in hot water (45 c.c.), was then added and the solution rapidly cooled. Crystallisation of the precipitate from hot water yielded N-*methyl*-N-2-*chloroethylethyleneimonium chloride bismercurichloride* in flattened needles, m. p. 197° (decomp.) (Found: Hg, 57·5. $C_5H_{11}NCl_2,2HgCl_2$ requires Hg, 57·4%); the m. p. was depressed to 163—170° on admixture with the mercurichloride of methyldi-(2-chloroethyl)amine, m. p. 187—188° (Part I, *loc. cit.*).

Work, described below, with other alkyldi-(2-chloroethyl)amines shows that this type of ring–chain tautomerism is of general occurrence and is responsible for the peculiarities of the reactions of these tertiary 2-chloroalkylamines in aqueous solution. It is of interest to note that the ethyleneimonium cation may be regarded as a stabilised form of the carbonium cation postulated by Hughes and Ingold as an intermediate in S_N1 aliphatic substitution reactions. With the tertiary 2-chloroalkylamine the rate-determining ionisation stage:

$$NR_2{\cdot}CH_2{\cdot}CH_2Cl \rightleftharpoons NR_2{\cdot}CH_2{\cdot}\overset{+}{C}H_2 + Cl^-$$

is followed at once, in the absence of substances reacting more rapidly than water, by cyclisation to the still very reactive, but more stable, ethyleneimonium ion, thus:

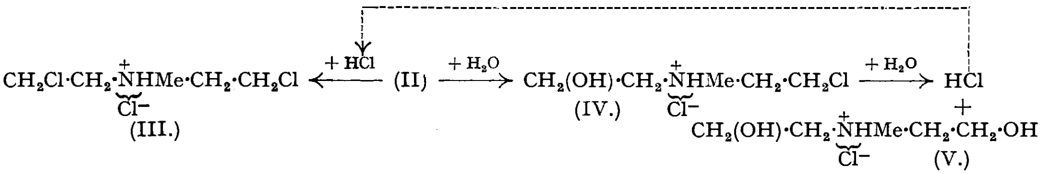


Clearly this type of tautomerism is to be expected whenever there is, in the carbonium ion, a suitably placed hetero-atom capable of carrying a positive charge; the position of the equilibrium between the carbonium and ethyleneimonium (or other heteronium) ions will depend on both steric factors and the relative tolerance, as compared with the carbon atom, of the hetero-atom for a positive charge.

(2) *The later reactions.* The ethyleneimonium chloride (II; R = Me) formed in the primary reaction of methyldi-(2-chloroethyl)amine with water is not very stable, and the solution undergoes further, comparatively slow, changes on keeping; these subsequent reactions have, in fact, already begun somewhat to confuse the simplicity of the picture in the later stages of the primary reaction. On keeping, the solution slowly becomes more acid, but this is not due to any detectable extent to reaction of the second β-chlorine atom since the chloride ion concentration does not increase even after several days. The dual-indicator titration method described above indicates that the main reaction is formation of weak base hydrochloride at the expense of quaternary ammonium chloride; concurrently the rapid thiosulphate titration figure diminishes and finally falls almost to zero, indicating the disappearance of ethyleneimonium salts.

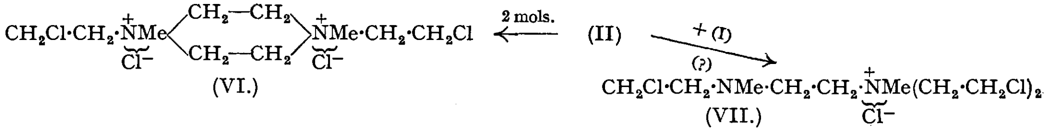
After 48 hours at 25° the chloride ion content of a 1% solution of methyldi-(2-chloroethyl)-amine corresponds very closely to that calculated for the ionisation of one chlorine atom; the pH of the solution has changed from about 7·0 (45 minutes after initiation of the reaction) to about 5·5, and titration shows that 55—65% of the salts present are weak-base hydrochlorides. The amount of such hydrochlorides present when a steady state is reached decreases with rise of temperature, being about 40 equivs. % at 0° and 80 equivs. % at 60°, both in 1% solution. The proportion of weak-base hydrochlorides also decreases with increasing initial concentration of methyldi-(2-chloroethyl)amine; an 11% solution, made up by shaking until all the free base had dissolved, contained less than 10 equivs. % of weak base hydrochloride after 72 hours at 25°. The isolation experiments described in Part I (*loc. cit.*) show that, after 48 hours at 25°, a 1% solution of methyldi-(2-chloroethyl)amine contained about 35 equivs. % of the hydrochloride of the half-hydrolysis product (IV), and 25 equivs. % of the hydrochloride of the original amine (III).

These results all indicate that, on keeping, the ethyleneimonium salt (II) undergoes hydrolysis to the half-hydrolysis product (IV); the hydrochloric acid liberated in this process brings about some reversal of the ring–chain tautomerism, and methyldi-(2-chloroethyl)ammonium chloride (III) also appears in the solution. The constancy of the chloride-ion concentration requires stoicheiometrically that methyldi-(2-hydroxyethyl)amine hydrochloride (V) must also be present, in amount equivalent to (III). We may thus depict the hydrolytic reactions as follows :



$$\underset{\text{(III.)}}{CH_2Cl{\cdot}CH_2{\cdot}\overset{+}{N}HMe{\cdot}CH_2{\cdot}CH_2Cl\ Cl^-} \xleftarrow{+HCl} (II) \xrightarrow{+H_2O} \underset{\text{(IV.)}}{CH_2(OH){\cdot}CH_2{\cdot}\overset{+}{N}HMe{\cdot}CH_2{\cdot}CH_2Cl\ Cl^-} \xrightarrow{+H_2O} HCl + \underset{\text{(V.)}}{CH_2(OH){\cdot}CH_2{\cdot}\overset{+}{N}HMe{\cdot}CH_2{\cdot}CH_2{\cdot}OH\ Cl^-}$$

The later reactions in water are not, however, restricted to these hydrolyses. The instantaneous thiosulphate titre reaches effectively zero, and acidimetric titrations reach their final value, in about 70 hours at 25° when weak base hydrochlorides do not account for the whole of the chloride ion present in the solution. Part of the ethyleneimonium chloride (II) must, therefore, have been converted into a stable quaternary ammonium salt. In Part I (*loc. cit.*) we describe the isolation, as picrate, from 1% solutions kept at 25° for 48 hours, of some 25 equivs. % of the piperazinium dimer (VI), in both *cis-* and *trans*-forms; clearly this dimer is the main stable quaternary ammonium salt present in the final equilibrium solution. The amount of this dimer increases with increasing initial concentration of the solution, and an 11% solution was shown to contain 79 equivs. % after 10 days at room temperature. An unexpected finding with this 11% solution was that the chloride-ion concentration became stabilised at about 6% less than half the total chlorine present; this may be due to some formation of the open-chain dimer (VII). The formation of the piperazinium dimer (VI) probably takes place by interaction of two molecules of the ethyleneimonium salt (II), although other mechanisms are not excluded, and we may thus write the dimerisation reactions occurring in the later stages of the reaction with water as follows :

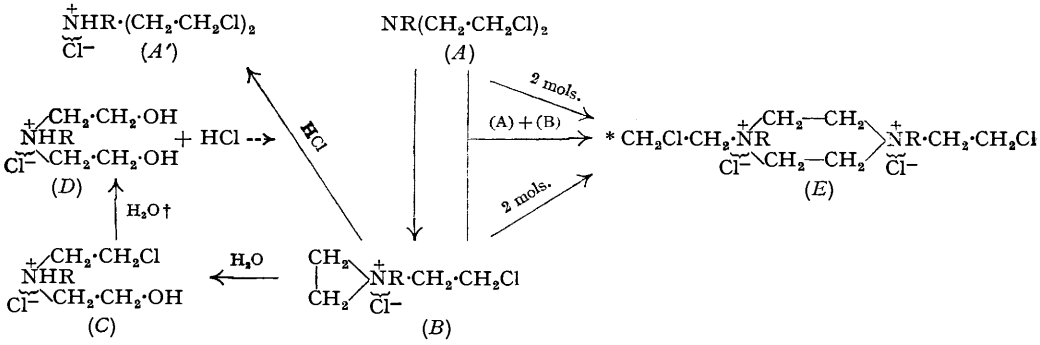


$$(II) \xrightarrow[(?)]{+(I)} \underset{\text{(VII.)}}{CH_2Cl{\cdot}CH_2{\cdot}NMe{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{+}{N}Me(CH_2{\cdot}CH_2Cl)_2\ Cl^-}$$

It is emphasised that, in a 1% solution, the analytical results indicated the presence of not more than about 1 equiv. % of (VII); furthermore, we were quite unable to isolate (VII), or any derivative of (VII), from aged solutions of methyldi-(2-chloroethyl)amine. In the generalised scheme given below, which combines all the processes known to take place in dilute (*ca.* 1%) solutions of alkyldi-(2-chloroethyl)amines, we have accordingly omitted the open-chain dimer (VII); in the generalised scheme we indicate also the possibilities that the piperazinium dimer (VI) may arise, wholly or in part, from (I) without the intervention of (II).

The mechanism of dimer formation might be decided by measurements in aqueous alcohol when dimerisation, at least in the case of the methyl compound, is the almost exclusive reaction. [One of us (E. O. P.) in collaboration with Dr. C. L. Hewett, examined the dimerisation in the radically different solvent benzene; the reaction was then found to follow more closely the second-order equation than the first.]

The Action of Water on Some Other Alkyldi-(2-*chloroethyl*)*amines.*—The following reaction scheme based on the work just described shows diagrammatically the various processes which occur when a dilute (*ca.* 1%) solution of an alkyldi-(2-chloroethyl)amine is kept at room temperature :



$$\underset{(A')}{\overset{+}{N}HR{\cdot}(CH_2{\cdot}CH_2Cl)_2\ Cl^-}$$

* Alternative routes. † A further ethyleneimonium salt may intervene in this reaction.

The following analytical procedure, which is unfortunately not applicable to methyldi-(2-chloroethyl)amine (A; R = Me) owing to unfavourable values of the dissociation constants of the hydrolysis products (C and D; R = Me), has enabled us to follow approximately the course of events in solutions of ethyl-, *n*-propyl- and *iso*propyl-di-(2-chloroethyl)amines, (A; R = Et, Pr^{α}, Pr^{β}):

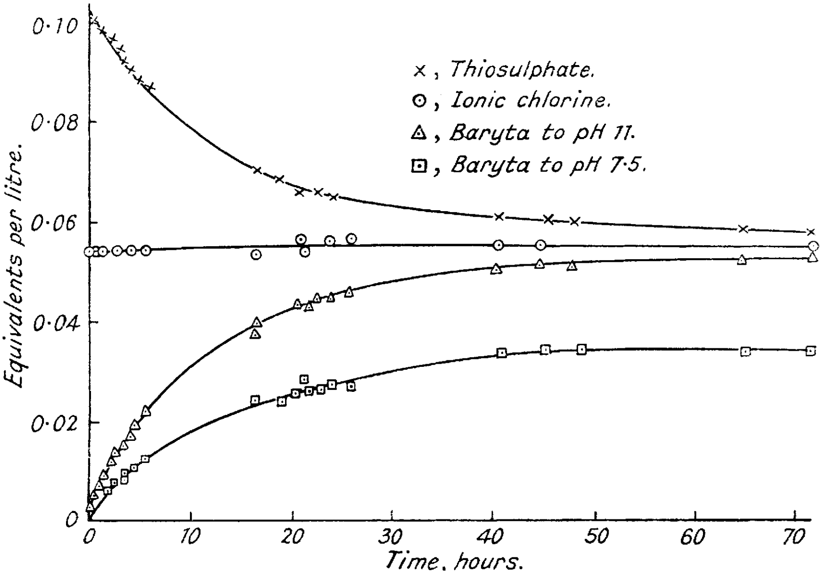
The base under investigation (5·0 g.) was weighed out and made up to 500 c.c. with water at 25°; the mixture was shaken or stirred vigourously until solution was complete. The time of complete solution was taken as zero time for the experiment. The resulting solution was kept at 25° and aliquots removed from time to time for the following titrations:

(i) *Sodium thiosulphate.* 10 C.c. of the reaction solution were added to 15 c.c. of 0·1N-sodium thiosulphate containing suspended chalk. After 30 minutes at room temperature, the excess of thiosulphate was titrated with 0·1N-iodine.

(ii) *Silver nitrate.* 10 C.c. samples were removed, treated with 10 c.c. of 0·1N-nitric acid, and titrated electrometrically with 0·1N-silver nitrate.

(iii) *Barium hydroxide.* Two 10 c.c. samples were removed and run into 10 c.c. lots of 0·1N-nitric acid. One sample was then titrated to pH 7·5 using bromothymol-blue, and the other to pH 11·0 using alizarin yellow.

FIG. 6.



$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}N(CH_2{\cdot}CH_2Cl)_2$, 0·0546M *in water at* 25°.

The experimental results were plotted graphically, making allowance in the barium hydroxide titrations for the added nitric acid, and the composition of the solution at various times was calculated, using the smoothed curves, as follows. Let a = original concentration of (A), b = sodium thiosulphate titre, c = barium hydroxide titre to pH 7·5 and d = barium hydroxide titre to pH 11·0, all in equivs./l. Then

$a = [A] + [A'] + [B] + [C] + [D] + [E]$

$b = 2([A] + [A']) + 2[B] + [C]$ (since, under the experimental conditions used, A, A', and B react with two equivalents, and C with one equivalent, of thiosulphate).

$c = [A] + [A'] + [B]$ (the alternative possibility that $c = [A] + [A']$ is ruled out by the fact that c was alway larger than $d - c$; the whole of B, and not only a part, must have titrated before pH 7·5 since the bromothymol-blue end-point was always sharp).

$d - c = [D] = [A] + [A']$ (this equality follows from the constancy of Cl^-).

Solving for $[A]$ . . . . $[E]$ we find

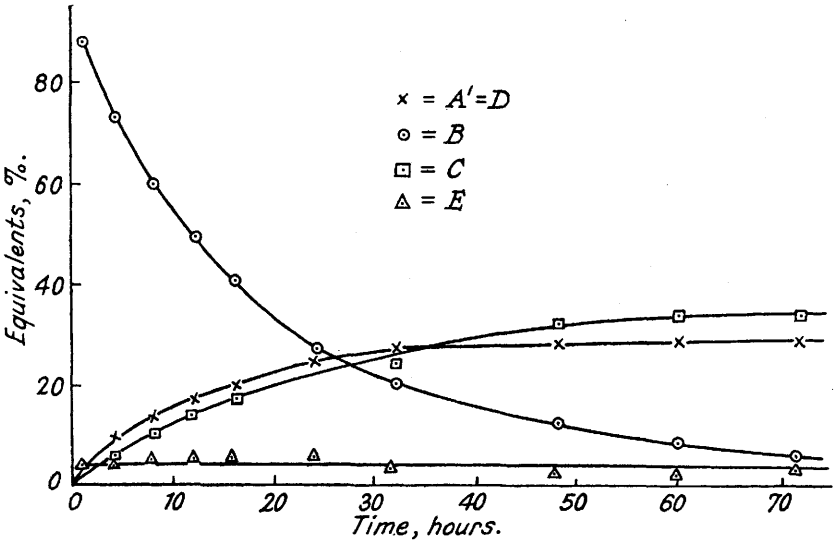
$$[A] + [A'] = [D] = d - c \qquad [C] = 2c - d$$

$$[B] = \frac{b - d}{2} \qquad [E] = \frac{2a - b - d}{2}$$

We wish to emphasise that the values obtained in this way are subject to rather large experimental errors, depending as they do on differences between titres each of which may themselves be in error; the values obtained do, however, at least give a good general picture of the trend of events in the solutions studied.

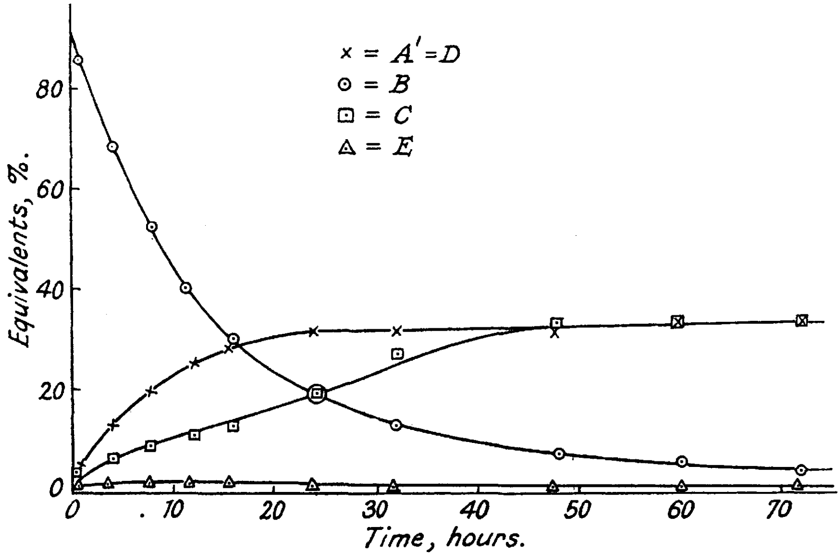
The experimental values obtained for (A, R = Pr$^{\alpha}$) are shown in Fig. 6, and the calculated equivalent percentages of the various components for 1% solutions of the three bases (A; R = Et, Pr$^{\alpha}$ and Pr$^{\beta}$) in Figs. 7, 8, and 9. In every case rapid cyclisation to the ethyleneimonium chloride (B) occurs during solution of the base; some dimer (E) is formed concurrently but the absolute amount is too small to enable any conclusion to be drawn as to whether or not further dimer is formed from B. Unfortunately time did not permit the extension of the rapid thiosulphate titration to the later stages of the reaction with the methyl compound when dimer is formed in much larger amount. This rapid cyclisation reaction is followed by the hydrolytic disappearance of B; the process is formally unimolecular, with the following first-order velocity constants:

FIG. 7.



$CH_3{\cdot}CH_2{\cdot}N(CH_2{\cdot}CH_2Cl)_2$, 0·059M in water at 25°.

FIG. 8.

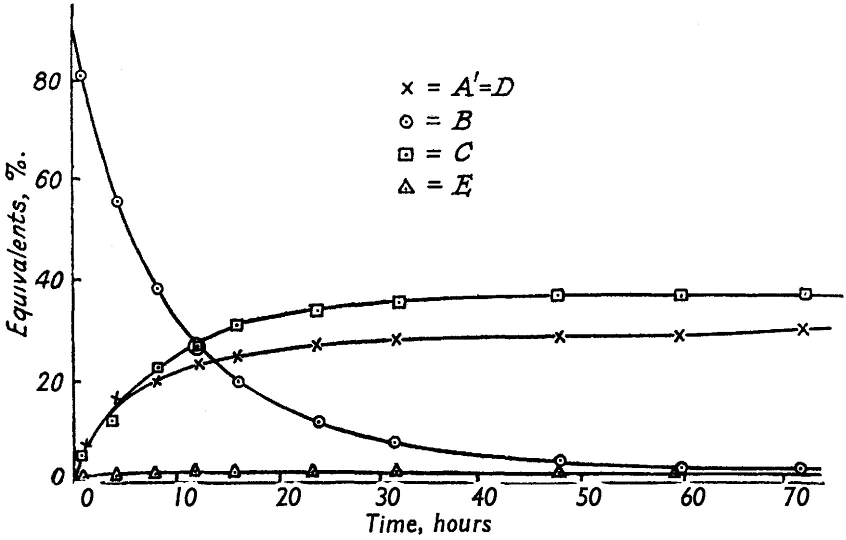


$CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}N(CH_2{\cdot}CH_2Cl)_2$, 0·0546M in water at 25°.

A; R =	Et.	Pr$^{\alpha}$.	Pr$^{\beta}$.
$k_1 \times 10^5$ (secs.$^{-1}$)	1·37	1·81	2·61

The formation of the reaction products proceeds, as shown in Figs. 7, 8, and 9, until a steady state is reached in about 70 hours at 25°; the compositions of the resulting equilibrium solutions are summarised in the following table, to which have been added the probable values for methyldi-(2-chloroethyl)amine (*A*; R = Me) estimated from the isolation experiments described in Part I:

FIG. 9.



$CHMe_2 \cdot N(CH_2 \cdot CH_2Cl)_2$, 0·0545M in water at 25°.

Composition (equivs. %) of 1% solutions of alkyldi-(2-chloroethyl)amines (A) after 70 hours at 25°.

R.	(*A*) + (*A*′).	(*B*).	(*C*).	(*D*).	(*E*).
Me	*ca.* 20	—	*ca.* 35	*ca.* 20	*ca.* 25
Et	28	5	35	28	4
Pr^{α}	32	3	32	32	1
Pr^{β}	30	2	37	30	1

It will be seen that changes in R have only a small effect on the degree of hydrolysis but have a large effect on the amount of piperazinium dimer (*E*) produced, which decreases rapidly with increase in the size of R; in Part I (*loc. cit.*) a similar effect was demonstrated for the rate of heat dimerisation of the bases. Clearly the effect depends on the size of R rather than on its electron-releasing power and is therefore probably steric in nature.

We are indebted to the Director General of Scientific Research (Defence), Ministry of Supply, for permission to publish this work, and to Messrs. J. E. Cave-Browne-Cave and J. W. G. McLauchlan for technical assistance.

CHEMICAL DEFENCE EXPERIMENTAL STATION,
PORTON. NEAR SALISBURY.

[*Received, July 17th*, 1946.]