Keith Raymond Millar

AN INVESTIGATION OF SOME REACTIONS
OF N-CHLOROCOMPOUNDS.

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The study of Chemistry is profitable, not only inasmuch as it promotes the material interests of mankind, but also because it furnishes us with insight into those wonders of creation which immediately surround us, and with which our existence, life and development, are most closely connected.

Justus von Liebig (1851).

A C K N O W L E D G M E N T

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C O N T E N T S

CHAPTER		Page
	ACKNOWLEDGMENTS	11
1	<u>HALOGEN DISPLACEMENT REACTIONS</u>	
	Introduction	1
	Experimental	22
	- Investigation of the displacement reactions of N-chloro compounds with lithium chloride in acetone.	23
	- In other solvent systems.	39
	- Displacement in aqueous solutions	40
	Summary	53
	References	54
2	<u>THE BASE STRENGTH OF N-CHLOROMORPHOLINE AND N-CHLOROPIPERIDINE.</u>	
	Introduction	57
	Experimental	65
	- Measured by spectroscopy	66
	- Measured by aspiration	69
	- Measured by distribution	73
	Summary	77
	References	78

3 THE ACTION OF HYDROCHLORIC ACID ON
N-CHLOROMORPHOLINE AND N-CHLOROPIPERIDINE

Introduction	79
Experimental	83
- Measurement of $[Cl_2]_E$ by spectroscopy	83
- Measurement of the equilibrium constant by removing chlorine	92
- E.M.F. measurements of the chlorine concentration	98
- <u>N</u> -chloromorpholine in hydrochloric acid	105
- <u>N</u> -chloropiperidine in hydrochloric acid	126
Summary	129
References	132

4 THE REACTION OF N-CHLORO-AMIDES AND
N-CHLORO-IMIDES WITH HYDROCHLORIC ACID

Part 1. <u>N</u> -chloroacetanilide	
Introduction	134
Experimental	144
Part 2. <u>N</u> -chloroacetamide and <u>N</u> -chlorosuccinimide	
Introduction	151
Experimental	157
- <u>N</u> -chloroacetamide	158
- <u>N</u> -chlorosuccinimide	160
Summary	171
References	173

CHAPTER

Page

5

N-CHLOROGUANIDINE

Introduction	175
Experimental	183
- Preparation and analysis of <u>N</u> -chloroguanidine	184
- Acid catalysed chlorinations of phenol by <u>N</u> -chloroguanidine	196
- Thermal decomposition	205
- The equilibrium existing between hydrochloric acid and <u>N</u> -chloroguanidine	214
Summary	226
References	230

6

CYANIDE DISPLACEMENT REACTION ON HALIDES

Introduction	233
Experimental	239
- Analytical procedures	240
- Preparation and properties of <u>N</u> -cyanomorpholine	243
- Possible effect of hydrogen cyanide	253
- Effect of added morpholine	257
- Effect of added piperidine	264
- Reaction in non-aqueous solvents	267
- Presence of cyanogen chloride	270
- Product analysis	274
Conclusions	280

CHAPTER

Page

Suggestions for future work

An investigation of the reaction
between N-chloromorpholine and
hydroxide ion in aqueous solution 282

References 287

7 PREPARATION AND PURIFICATION OF MATERIALS

Experimental 289

References 310

SYMBOLS AND FORMULAE APPEARING IN THE TEXT 313

FIGURES

Figure		Page
1.1	Energy diagram for the ionisation of a covalent molecule (from Ingold)	4
1.2	Asymmetric centre in an inversion reaction	7
1.3	Configuration of ammonia	18
1.4	Special filtering apparatus	31a
1.5	Sodium thiosulphate technique for AgCl^{36} counting	31a
1.6	Gas chromatograms of <u>N</u> -chloroacetamide / acetone mixtures	38a
1.7	Specific rate of $\text{HOCl} - \text{Cl}^-$ exchange as a function of pH	42
2.1	U.V. spectrum of acidified solutions of N-chloro compounds (Weil and Morris)	60
2.2	U.V. spectrum of <u>N</u> -chloromorpholine in perchloric acid	66a
2.3	U.V. spectrum of <u>N</u> -chloropiperidine in perchloric acid.	68a
2.4	Calibration of nitrogen aspiration apparatus	70a
2.5	Aspiration of <u>N</u> -chloromorpholine	70a
2.6	Distribution constant of <u>N</u> -chloropiperidine as a function of salt concentration	74a
2.7	Equilibrium constant for <u>N</u> -chloropiperidine as a function of acid strength.	74a
3.1	U.V. spectrum of chlorine in H_2O , H_2SO_4 , HCl and HClO_4	83a
3.2	Hydrolysis of chlorine	83a
3.3	Ratio of Cl_2^- to Cl_2 in hydrochloric acid solutions	86a

Figure		Page
3.4	U.V. spectrum of <u>N</u> -chloromorpholine in strong hydrochloric acid solution	86a
3.5	U.V. spectrum of <u>N</u> -chloromorpholine in different solvents	99a
3.6	Spectra of iodine monochloride; and iodine and potassium iodide both in acetic acid.	99a
3.7	E.M.F apparatus for chlorine measurement	104a
3.8	E.M.F. calibration graphs	104a
3.9	Rate of loss of chlorine from 0.6M hydrochloric acid	105a
3.10	Rate of disappearance of chlorine for the reaction, morpholine & chlorine in 0.491M hydrochloric acid.	112a
3.11	Morpholine and chlorine in 0.602M hydrochloric acid.	114a
3.12	Rate of production of chlorine for the reaction between <u>N</u> -chloromorpholine and hydrochloric acid ⁻ (0.316M)	112a
3.13	Rate of production of chlorine in 0.491M hydrochloric acid	119a
3.14	Rate of production of chlorine in 0.602M hydrochloric acid	119a
3.15	Rate of production of chlorine for the reaction between <u>N</u> -chloropiperidine and hydrochloric acid ⁻ (0.618M)	127a
3.16	Rate of production of chlorine in 0.876M hydrochloric acid.	127a
4.1	Acid catalysed rearrangement of <u>N</u> -chloroacetanilide	148a
4.2	Rate of production of chlorine in the reaction between <u>N</u> -chloroacetanilide and hydrochloric acid.	148a
4.3	Log ₁₀ chlorine concentration for the reaction between <u>N</u> -chloroacetanilide and hydrochloric acid.	156a

Figure		Page
4.4	U.V.spectrum of <u>N</u> -chloroacetamide in water and hydrochloric acid.	156a
4.5	Rate of chlorine production in the reaction between <u>N</u> -chloroacetamide and 0.315M hydrochloric acid.	160a
4.6	Rate of chlorine production 0.618M hydrochloric acid	161a
4.7	Rate of chlorine production in the reaction between <u>N</u> -chlorosuccinimide and hydrochloric acid.	162a
4.8	Rate of disappearance of chlorine in the reaction between succinimide and chlorine in 0.618M hydrochloric acid.	162a
5.1	U.V.spectrum of the yellow compound isolated by England from guanidine salts and hypochlorite	185a
5.2	U.V.spectra of mixtures of guanidine hydrochloride and chlorine	185a
5.3	U.V.spectra of mixtures of t-butyl hypochlorite and morpholine and piperidine.	189a
5.4	U.V.spectra of mixtures of guanidine salts and t-butyl hypochlorite.	189a
5.5	U.V.spectrum of pure <u>N</u> -chloroguanidine	195a
5.6	Paper chromatography of <u>N</u> -chloroguanidine degradation products	195a
5.7	Reaction between <u>N</u> -chloroguanidine and phenol in hydrochloric acid.	205a
5.8	Reaction between <u>N</u> -chloroguanidine and phenol in perchloric acid.	205a
5.9	Thermal decomposition apparatus.	207a
5.10	Rate of chlorine production in the reaction between <u>N</u> -chloroguanidine and 0.618M hydrochloric acid	207a
5.11	<u>N</u> -chloroguanidine in 0.316M hydrochloric acid.	217a

Figure		Page
6.1	Potentiometric titration of cyanides	244a
6.2	U.V.spectrum of <u>N</u> -cyanomorpholine	244a
6.3)	Rate of reaction of cyanide with <u>N</u> -chloromorpholine	261a
6.4)		
6.5	$\log k_2$ as a function of $\frac{1}{T}$	263a
6.6	Second order constants for the reaction between <u>N</u> -chloromorpholine and cyanide ion.	263a
6.7	Gas chromatogram of <u>N</u> -hydroxymorpholine	283
6.8	U.V.spectrum of <u>N</u> -hydroxymorpholine	286a
7.1	Boiling point of <u>N</u> -chloromorpholine	305a

CHAPTER 1

HALOGEN DISPLACEMENT REACTIONS

INTRODUCTION

A vast volume of literature exists on this subject, the major portion being concerned with nucleophilic aliphatic substitution reactions covered by the general equation:-

where the new bond is formed by co-ordination, and the old one broken by heterolysis, as indicated by the dotted line. There is necessarily an electron transfer from the substituting species Y to the centre of substitution in Alk, and from this centre to the expelled group X; hence Y becomes formally one electronic unit more positive and X one unit more negative.

A large number of well known reactions obey the above classification. Among them are the Finkelstein reactions, for example,

the Menshutkin reaction,

and various forms of Hofmann degradation. Another series of examples is provided by the acid or alkaline hydrolysis or

alcoholysis of alkyl halides,

Also included are the cyanisation reactions of alkyl halides which will be discussed later in Chapter 6.

Thus the reactions form a large and important class, though they were not generally considered to belong to a single class until their mechanism came to be carefully studied and the common mechanistic pattern recognised. The fundamental postulate is that a nucleophilic substitution has available two reaction mechanisms and both these reactions have been investigated in great detail, largely by Ingold and co-workers.¹

The first of these contains only one stage in which two molecules simultaneously undergo covalency change, and this mechanism is called bimolecular and is denoted by $\text{S}_{\text{N}}2$. It closely resembles the mechanism proposed by London² in that bonds are formed and broken synchronously and the mechanism can best be expressed by the equation,

in which ionic charge labels have been omitted since there are several possibilities. The transition state contains two partial and partially ionic bonds, which differ in length and polarity from fully formed bonds. For a "symmetrical substitution" reaction, such as that between an isotopically labelled bromide ion and an alkyl bromide molecule, the bonds

undergoing change could be described as half-ionic half-bonds and are best illustrated by

The second mechanism involves two stages; a slow heterolysis followed by a rapid co-ordination between the formed carbonium ion and the substituting agent. Since in the rate determining stage only one molecule is undergoing covalency change, the mechanism is labelled S_N1 :-

Hughes and Ingold³ considered that the effect of the group R on the reactivity of the halide R-X depended on whether the halide was reacting by the unimolecular mechanism S_N1 , or by the bimolecular mechanism S_N2 . If a change in R involved an increase in electron accession to the centre of substitution, then an increase in the unimolecular reaction rate of R-X will result. The result of such an increase in electron accession on the bimolecular reaction rate of R-X is, however, ambiguous since it is considered that an increase in electron accession to the reaction centre will tend both to repel the reagent and to expel the replaceable group. Because of these tendencies the accession of an electron by the reaction centre is expected to have a smaller effect on the rate of the

bimolecular mechanism than on the unimolecular reaction rate.

Ogg and Polanyi⁴ discussed the unimolecular ionisation reactions and the bimolecular negative ion reactions in terms of potential energy surfaces, and calculated the activation energies of several negative ion reactions. According to these workers, changes in R which weaken the R-X bond normally increase the rates of both unimolecular and bimolecular reactions, unless an increase in the steric hindrance of the molecule is produced, thus affecting the bimolecular reaction rate as noted by Meer and Polanyi⁵.

The energy of the initial heterolysis has to be set off against the energy of solvation of the ions and this energy difference approximates to the heat of ionisation in solution (Fig. 1.1)

Thus, in order that the mechanism shall be S_N1 a solvent of suitable polarity is essential (this fact is not always appreciated). The ionisation is assumed to proceed through

a transition state, that is, a state of maximum energy involving a partial charge transfer and also a stretched partial bond =

There are two main factors which will determine the molecularity of the reaction:- $Y^- + R-X \longrightarrow R-Y + X^-$

- (a) the activation energies of the two mechanisms, and
- (b) the concentration of the reactant Y .

Provided that both reacting species are in small and controllable concentrations the bimolecular mechanism of substitution should lead to second-order kinetics, as expressed by the equation

$$\text{Rate} = k_2 [Y] [Alk X]$$

which represents the typical kinetic form of reactions proceeding by the S_N2 mechanism. It does not express the universal form however, since there are a number of circumstances in which this same mechanism will lead to first-order kinetics; for instance, if one of the reactants is in constant excess, or if one reactant is a buffered component of a chemical equilibrium.

The unimolecular mechanism of substitution can also lead to first-order kinetics, with an overall rate equal to the heterolysis rate.

Evans⁶ has described the unimolecular reactions of the organic halide R-X in terms of more data on the

- (a) bond strength of R-X
- (b) ionisation potential of radical R, and
- (c) heat of solution of ion R^+ .

Evans also outlined the conditions which determine the mechanism of reactions, and the change of mechanism from bimolecular S_N2 to unimolecular S_N1 , established by Ingold and co-workers, has been interpreted in terms of a theory of activation energy.

A study of the stereochemical cause of substitutions at asymmetric carbon atoms has provided a clear picture of the mechanisms of the reactions. Below are illustrated various stereochemical possibilities with an optically active sec-butyl group.

- (i) Substitution with inversion of configuration:—

- (ii) Substitution with retention of configuration:—

- (iii) Substitution with racemization:—

In an inversion reaction, the three groups CH_3 , C_2H_5 , and H attached to the asymmetric centre are "pushed through" a plane including the central carbon atom and perpendicular to the C-X bond axis as illustrated on the following page.

(Fig. 1.2)

FIG 1.2.

The bimolecular nucleophilic substitution (S_N2) reaction occurs with very clear-cut inversion of configuration and this fact was firmly established by studying the stereo-chemistry and kinetics of substitution reactions of sulphonates. The simplest demonstration of the transition state (Fig. 1.2) was that secured by Hughes⁷ and his colleagues by the isotopic tracer method for the halogen exchange reaction between halide ions and alkyl halide molecules. Attack of nucleophiles on the planar carbonium ions occurs with equal probability from either side of the plane. The hydrolysis of α -phenylethyl chloride, for example, is one of many solvolysis reactions that give virtually complete racemization,

Steric hindrance in the substrate has been mentioned as a major factor in determining S_N2 reactivity. In addition, electronic factors are of equal importance. In reactions of negative ions with neutral substrates, strong dipoles in the

substrate have a predictable effect. If the dipole tends to draw electrons away from the seat of substitution, the reaction will be made relatively easy. An example is found in the high reactivity of α -haloketones and α -haloesters in S_N2 reactions :-

Allyl and benzyl compounds are quite reactive in S_N2 reactions unless they are greatly sterically hindered. The effect shows that the central carbon atom must have some of the character of a carbonium ion in the transition state of an S_N2 reaction. The carbon bond is flattened out to the sp^2 configuration, and electrons can be fed in from attached unsaturated groups, as is shown below :-

While all nucleophiles are bases, their reactivity does not always parallel their basic strength. However, if one stays within one family of the periodic table, reactivity of nucleophiles in series of analogous ions or molecules increases sharply with increasing atomic number. Thus the following

series of decreasing reactivity are observed, $I^- > Br^- > Cl^- \gg F^-$. This effect is due to the ability of the larger, more polarizable nucleophiles to give bonding interaction at large internuclear distances. The reactivity of leaving groups is somewhat unexpected. As would be expected an increase in the basicity of the groups decreases its reactivity, however, increasing the polarizability of the atoms by which leaving groups are attached to the substrate increases their reactivity and hence the same orders of reactivity are observed when the ions are compared, either as leaving groups or as entering nucleophiles.

The effect of solvent on the above reactions can best be understood by considering whether ions are being formed or destroyed, or neither, in the slow step of the reaction. Good ionizing solvents, such as water, are those in which the ions are stabilized by solvation. Hydroxylic solvents such as methanol, ethanol and acetic acid are intermediate in their ability to stabilize ions while solvents such as acetone and ether, which will dissolve some ionic materials (as ion pairs), are not very good ionizing media. Reactions of neutral substrates, which go by the S_N1 mechanism, are accelerated enormously by increasing the ionising power of the solvent. S_N2 reactions, which proceed between a negative ion and a neutral substrate are relatively little influenced by medium effects.

Precise information has long been available on the effect of solvents on reactions of the type,

and new data continues to appear. From the second order velocity constants obtained, together with a study of the derivatives, the several theories of chemical reactivity have been built up where R is variable and X and Y are constant. When these reactions take place in water, RX reacts usually to give an alcohol, whilst in alcoholic solution the product is inevitably an ether. Conant, Kirner & Hussey⁸ realised that such side reactions could be evaded by using acetone as the solvent. If however, R is an alkyl radical other than methyl, RX in any medium breaks down into HX and an olefin as Brusoff⁹ observed, and to avoid both solvolysis and olefin formation these reactions must necessarily be studied in non-hydroxylic solvents such as acetone using the methyl derivatives.

The merit of acetone is that it dissolves many ionic halides, and yet it is not so highly ionising that it fails to retain the Finkelstein substitutions in their bimolecular form. Acetone preserves the bimolecular mechanism over a wide variety of alkyl structures, permitting most of the kinetic comparisons which it was desired to make. With four halogens, sixteen types of Finkelstein reaction are theoretically possible; but, for homogeneous reactions in acetone, the seven which depend on fluorine have to be excluded as involving inconveniently low solubilities. Finkelstein substitutions in acetone are subject to a negative salt effect, which requires the standardisation of salt concentrations in any

comparison of rate.

A case which called for special treatment was that of tert-butyl bromide, the reaction with chloride ion as measured by the development of bromide ion was found to be only roughly of second order. De la Mare, Hughes, Ingold and Pocker¹⁰ showed that, in solvent nitromethane, the reaction was entirely unimolecular, consisting almost wholly of elimination. Hughes, Ingold and Mackie¹¹ concluded that, even in dry acetone, tert-butyl bromide undergoes some ionisation, with the result that a predominating bimolecular substitution is accompanied by a side reaction consisting mainly of elimination.

Maclwyn-Hughes¹² attempted to study the kinetics of the reaction between methyl bromide and iodide ion in acetone and he found that the reaction proceeded bimolecularly and at a rate about 1000 times faster than in water. Difficulty was experienced when it was found that the velocity decreased as the initial salt concentration was increased, and this was correctly attributed to the fact that the potassium salt of the product was only slightly soluble in acetone. This experiment was repeated by Farhat-Aziz and Maclwyn-Hughes¹³ using lithium salts instead of potassium. The rate of the reaction between the undissociated on un-ionized salt and the alkyl halide has been demonstrated to

be so small as to be insignificant. The same conclusion was drawn for these reactions in acetone by Evans and Sugden¹⁴ who found that, although the salt concentration was altered by a factor of 400 in the reaction

the second order constant for the reaction did not vary if allowance was made for the incomplete dissociation of the salt. For this reason Farhat-Aziz and Moelwyn-Hughes assumed the reactions taking place were the ionic replacements.

the instantaneous velocity of reaction is thus consequently

$$\frac{-d [\text{CH}_3\text{Cl}]}{dt} = k_2 [\text{CH}_3\text{Cl}] [\text{I}^-] - k_4 [\text{CH}_3\text{I}] [\text{Cl}^-]$$

If a and b are respectively the concentrations of the alkyl halide and the lithium salt, and if c and (c-x) are respectively the specific radioactivities of the initial solution of lithium halide and of a solution of the salt recovered from a reaction stopped after a time t, the second-order rate constant is given by the equation,

$$k_2 = \frac{2.303}{(a + b)t} \log_{10} \left[1 - \frac{x}{c} \left(1 + \frac{b}{a} \right) \right]^{-1}$$

Because lithium chloride is much less ionised than lithium iodide in acetone, corrections for this had to be made. Runs were repeated with various initial concentrations

of methyl and lithium halides and although they gave slightly different values there was no discernable trend. No general answer was given to the question of whether un-ionised molecules of lithium halide reacted with the methyl halide in acetone solution but such a supposition is not necessary, although without further study it cannot be ruled out.

Hughes, Ingold and Mackie¹⁵ investigated the reaction

in acetone under strictly controlled conditions.

The kinetics of six reactions of the type,

have recently been investigated by Bathgate and Moelwyn-Hughes¹⁶ in aqueous solution and the apparent energies of activation compared with the energies estimated for partial de-solvation of the ion and the polar molecule.

Dutka and Gal¹⁷ carried out a detailed investigation on the isotopic exchange reaction between organic iodides and iodide ion, although a large amount of literature¹⁸ had been compiled on this type of reaction, especially on the influence of

various cations such as sodium, potassium and lithium on the rate.

Hence it is apparent that nucleophilic substitution reactions involving the exchange of halide atoms have been thoroughly investigated for carbon compounds. Other halogen exchange reactions have been studied but the mechanisms of these cannot be dealt with under a single classification.

The exchange of chlorine between molecular chlorine and carbon tetrachloride which had been reported by Schulte¹⁹ as occurring under the influence of sunlight, ultraviolet light and X-radiation was shown by Pearson and Garner²⁰ to be of negligible significance. The mechanism of such an exchange would have been difficult to interpret, other than by utilisation of carbon tetrachloride breakdown products.

Many halogen exchange reactions have been demonstrated to occur through ionic intermediates. For example the exchange of chlorine-36 between chloride ion and phosphorus oxychloride, arsenic trichloride and selenium oxychloride, reported by Lewis and Sowerby²¹ has been shown to proceed by the formation of the ions POCl_4^- and AsCl_4^- . Similarly, the exchange demonstrated by Frazer²² as occurring between pyridinium chloride and acid chlorides in chloroform solution was shown to occur either through the intermediate formation of an addition complex between the chloride ion and acid chloride, or by ionisation of the acid chloride itself.

The conclusion which can readily be drawn from the text

so far is that the modes of halogen exchange reactions occurring on halogen atoms bound to carbon have been extensively studied and are limited to a few types. The main reported method is of course by nucleophilic substitution, although examples in which exchange occurs via ionic intermediates, breakdown products or by radical mechanisms²³ are not unknown.

Substitution mechanisms are beginning to be regarded more extensively than the conventional boundaries of organic chemistry would allow, the mechanism of substitution at carbon being regarded as a pattern on which the study of the mechanism of substitution at other elements might be based. For example, outside carbon substitutions, a large class of nucleophilic substitutions can be envisaged in the ligand replacements at transition metals which offer co-ordination numbers higher than four and consequently space figures higher than the tetrahedron. The first compound investigated was the optically active cis-form of dichlorobis-ethylenediamine cobalt - III.²⁴ S_N2 substitutions at octahedral cobalt do not involve quantitative stereochemical changes, as do S_N2 substitutions at tetrahedral carbon. The S_N2 cobalt substitutions do, however, involve considerable and often preponderating amounts of edge displacement, how much being dependent on the orienting effects of groups already present. Just as with S_N2 substitutions at tetrahedral carbon, so with these S_N2 substitutions by anions

at octahedral cobalt, bond fission and bond formation are truly synchronous.

In the study of mechanism in nucleophilic substitution outside the well-explored field of carbon, more attention has so far been paid to cobalt than any other element. Investigations on mechanisms in substitutions at several other elements, silicon, phosphorus and platinum, for example, have been begun.

25
G. Aksnes has carried out a detailed investigation of this type of reaction with phosphorus, utilizing the reaction of hydroxylion and isonitroso acetone with organofluorophosphorus compounds. Aksnes was interested in correlating the alkaline hydrolysis of some organofluorophosphorus compounds with the nucleophilic reaction between a reactivator and the same phosphorus compound.

The reactions between organic chloro- or fluorophosphorus compounds and nucleophilic reagents are generally believed to belong to A-2 mechanisms.^{26, 27} From theoretical reasoning it must be assumed that during the formation of the transition state, the collision complex adopts a bipyramidal (sp^3d hybridised) transition state with the reacting groups and the phosphorus atom collinear:-

Displacement reactions of optically active phosphorus compounds give strong evidence for this interpretation.²⁸ The activation energy necessary to form the transition complex should be expected to decrease with increasing residual positive charge on the phosphorus atom and this increase will render the P-atom more susceptible to attack from the nucleophile. The observed results were in accordance with earlier experiments carried out by Aksnes and Gramstad.²⁹

The strong influence of substituents in phosphorus compounds upon delocalization of the charge in nucleophilic substitution may be attributed to the fact that the available d-orbitals of phosphorus are involved in π bonding and these orbitals can enter into the σ bond structure of the activated complex. The character of the partial valence bonds of the activated complex thus approaches the character of true chemical bonds rather than special orientations of reacting molecules with correspondingly greater charge separation. Studies of the nucleophiles with very high reactivity with phosphorus compounds reveals that it is the oxygen atom in the reagents which participates in the displacement reaction³⁰ and this is most likely, due to its high negativity and small size.

Nucleophilic reactions with phosphorus compounds are dependent on two main factors of the nucleophilic reagent itself, namely (1) its basicity, and
(11) its polarisability^{31, 32}

However nucleophilic reactions on phosphorus depend also to a large extent on the polarity and polarisability of the phosphorus compounds.³⁰ The basicity effect of the nucleophilic reagent was shown by Aksnes to be most pronounced with phosphorus compounds of the highest polarity, and the polarisability effect of the reagent was most effective in reactions with the strongest polarisable substrate.

The nitrogen atom, like phosphorus, contains five electrons in the outer shell. The octet can be completed in two simple ways - by the formation of the N^{3-} ion or by the formation of three electron pair bonds. The ammonia molecule, NH_3 , is the simplest example of the latter, and the same electronic configuration is reached in amines, containing the $-NH_2$ group, in imides ($=NH$ or $>NH$), and in the numerous organic heterocyclic compounds in which there is resonance between the states $-N=$ and $=N-$. Three single bonds from a nitrogen atom are directed towards the apices of a trigonal pyramid; as has been demonstrated by electron diffraction for $N(CH_3)_3$.³³ A pyramidal configuration is to be expected, whether the orbitals are regarded as three p orbitals or three of four sp^3 orbitals, the unshared pair occupying one of the tetrahedral positions in the latter case.

Fig. 1.3. The two possible configurations of NH_3 ; N^1abc , (or N^2abc).

Proof of the non-linear arrangement of one double and one single bond formed by a nitrogen atom comes directly from

- (a) x-ray and electron diffraction studies
- (b) the existence of stereoisomers of compounds containing the systems $\text{>C}=\text{N-}$ or -N=N- , and thirdly
- (c) the optical activity of some oximes.

When the fourth available p orbital is used, four tetrahedral bonds may be formed, or the following structures can be considered $=\text{N}^+=$ $\text{>N}^+=$ or $-\text{N}^+\equiv$

In all cases, however, the stereochemistry is similar to that of carbon. The nitrogen atom in NH_3 and substituted ammonias possesses a pair of unshared electrons which may be used to form a fourth bond and these molecules are able to attach themselves to a great variety of metal compounds, forming the co-ordination compounds of Werner. Similarly the nitrogen atom may form four covalent bonds, giving rise to the ammonium ion NH_4^+ and the numerous substituted ammonium ions containing organic radicals in place of hydrogen. The tetrahedral nature of the ammonium ion has been proved in very few compounds both because of the difficulty of locating hydrogen atoms and because of the rotation of the ion in many crystals at ordinary temperatures.

Nucleophilic substitution reactions at a nitrogen atom are virtually unknown in the chemical literature. The author, in an earlier work involving the photolysis of N-chloroacetamide, prepared the N-chloro compound in an isotopically labelled form by an apparent exchange reaction

with lithium chloride (Cl-36) in solvent acetone.³⁴

Several possibilities exist for the reaction of N-halo compounds with nucleophilic reagents

- (1) Simple displacement: Reactions of this type are those included for study in the present paper. No previous work having been carried out.

- (2) Nucleophilic displacement at the halogen atom: (especially in acids)

A discussion of reactions of this type will be included in Chapter 3, together with rate constants for the rate of Cl_2 production of the reactions of many N-chloro compounds with hydrochloric acid. Brown³⁵ investigated the reaction of N-chloromorpholine with hydrobromic acid, finding the rate considerably faster than that observed with hydrochloric acid as would be expected since Br^- is the better nucleophile. No quantitative measurements on the rate of bromine production were made.

- (3) Elimination:

e.g. in the alchloroamines.³⁶

The reaction is a second order one between the imine and base; the rate paralleling the base

strength of the amine. Hauser, Le Maistre and Rainsford³⁷

give the most acceptable mechanism as

The present chapter is thus concerned with a detailed investigation of the displacement on N-chlorocompounds of radioactive chloride ion in varying solvents

EXPERIMENTAL

EXPERIMENTAL

(A) Investigation of the displacement reactions of
N - chlore compounds with lithium chloride in
acetone

In order that an exchange reaction may be studied it is obviously necessary to isolate one of the reacting species or products in an uncontaminated state. If the exchange reaction takes the form:-

then a measure of the concentration of any of the four species present will give information on the kinetics of the exchange.

If the reaction is of the type:-

which includes the reactions under investigation, then a measure of either the decrease in activity of X^* , or the increase in activity of MX^* is necessary, so that the kinetics may be adequately understood.

De la Mare³⁸ studied the kinetics of the interaction of chloride ions with simple alkyl chlorides in acetone by evaporating the samples at low temperature, dissolving the residual salt in water, and measuring the radioactivity with the type of counter used for liquid samples. Hughes, Ingold and Mackie³⁹ followed the progress of the reaction

by electrometric titration of the inorganic salts with silver nitrate, after removal of the organic material. Evans and Hamann⁴⁰ have recorded some rate constants for the reactions of potassium iodide with methyl and isopropyl bromide: their results being some 50% higher than those obtained by Fowden, Hughes and Ingold⁴¹ due to the method of following the reaction. They attempted to measure the disappearance of dissolved potassium iodide by the fall of electrical conductance, but under conditions in which a precipitate of potassium bromide was being formed between and round the electrodes, causing an ambiguous fall in conductance.

Owing to the unstable nature of N - chloro compounds in general, and the great solubility of these compounds in most organic solvents, then the possibility of isolating the N - chloro compound from solutions in acetone is small, and investigations were undertaken to find the most suitable method of extracting the lithium chloride from solution in order that its activity might be measured. It must be remembered at all times that the reactions taking place follow kinetically controlled paths and any experimental method which is to be used to separate the components of such a reacting solution must not alter the conditions under which the reaction is taking place. For instance, a high increase in temperature, which may be necessary to coagulate a required precipitate of a reaction component, will usually

speed up the reaction before the precipitate is completely formed, inconsistent results thus being obtained. Care must also be exercised when adding solutions to a reaction mixture to ensure that the added solutions are not going to catalyse the exchange before the required precipitation reaction is complete. Also, if the solvent of the added reagent differs from that of the exchanging system, then, before precipitation is completed, the change in solvent might promote exchange, which, if it is very rapid, could lead to ambiguous results.

For the reaction between N - chloro compounds and lithium chloride in acetone, two methods were used for measuring the activity of the lithium chloride:-

Precipitation of lithium chloride by the addition of organic solvents

When acetone solutions of lithium chloride were added to benzene, the solid lithium chloride precipitated and could be readily filtered off, dissolved in water, and analysed both for purity and activity. Other solvents were investigated but were found to be unsuitable for the following reasons:-

- (a) Ether - unsatisfactory because the lithium chloride separated out as extremely fine particles which could not be retained by normal filtering techniques.
- (b) Petroleum ether - both lithium chloride and N - chloro acetanilide could be precipitated by this solvent.
- (c) Carbon tetrachloride - precipitated both lithium chloride and N - chlorosuccinimide from acetone.

In order to ascertain the efficiency of benzene in precipitating lithium chloride from acetone solution several

recovery experiments were carried out. It should be realised that a complete recovery of product is not necessarily required, as long as the exact amount recovered, and the total amount present is known. For the reaction between N - chloro compounds and lithium chloride, the amount of lithium chloride recovered was determined either by the normal Mohr's chloride titration⁴², or by potentiometric titrations as described in Chapter 6 using silver nitrate and a silver chloride electrode.

The efficiency of benzene for the recovery of lithium chloride from acetone solution is well illustrated in Table 1.1. The temperature of the benzene in this set of experiments was kept at 20°C. As will be seen later, temperature plays an important part in the percentage recovery since lithium chloride possesses a negative solubility curve in acetone.⁴³

Table 1.1

Volume of Lithium chloride (0.166M)	Volume of Benzene added	Percentage recovery of LiCl
20	5	61.0
20	10	81.0
20	10	81.3
20	10	79.8
20	20	95.6
20	30	98.4

From the above set of results it can be seen that

- (i) the percentage of lithium chloride recovered depends on the volume of benzene used and
- (ii) the reproducibility of the percentage recovery is very good for a fixed volume of benzene.

The disadvantages of the benzene method were only demonstrated when experiments were attempted at 5.0°C . When ice cold solutions of lithium chloride (0.116M) in acetone were added to benzene kept at 5.0°C the normal precipitate of the chloride failed to appear, although on warming the mixture to approximately 10°C it slowly started to appear, being complete at room temperature. Since many of the N - chloro compounds studied were only stable in acetone at low temperatures an alternative method of measuring the activity of the lithium chloride had to be devised. One further disadvantage of the benzene method was that for dilute solutions of lithium chloride in acetone, which were necessary in many experiments, the percentage recovery of the solid dropped as can be seen by reference to Table 1.2.

Table 1.2

Molarity of Lithium chloride (20ml)	Volume of Benzene	Percentage recovery of LiCl
0.012	20	0-5
0.054	20	28-35
0.083	20	50-63
0.116	20	95.6

From these results it might be argued that for solutions of lithium chloride in acetone greater than 0.05M, the percentage recovery would be satisfactory since complete recovery is not required. The difficulty was that precipitation was not immediate in many solutions of lower concentration, leading to errors in sampling times.

An alternative method of analysing solutions of lithium chloride and N - chloro compounds was therefore developed and will now be described:-

Precipitation of chloride by silver nitrate

When aqueous silver nitrate was added to a solution of lithium chloride and N - chloroacetanilide in acetone an immediate white precipitate of silver chloride was formed. The precipitate was usually very coarse and when filtered through the special filtering adaptor (Fig.1.4) did not give a 'fixed source geometry' sample suitable for counting using the end window counter. This difficulty could be overcome by either

- (1) dissolving the precipitate in concentrated ammonium hydroxide and reprecipitating.
- (2) grinding the precipitate of silver chloride with ethanol in a mortar and refiltering, giving a very fine layer of silver chloride suitable for counting.

Both the above methods suffer from the disadvantage that they require considerable time per sample and this is tedious if a kinetic run is to be carried out.

The method developed to isolate the chloride ion in a form suitable for counting relied on the solubility of

silver chloride in solutions of sodium thiosulphate, according to the following equation:-

Such a solution of silver chloride was found to be suitable for counting in a liquid counting tube, enabling large numbers of samples to be handled. The sodium thiosulphate solutions were found to keep for several hours before visible precipitation of silver salts appeared. The method of preparing the samples will now be outlined.

A sample of the reaction mixture containing the N-chloro compound, lithium chloride and acetone was added to a slight excess of silver nitrate (0.1N) contained in a 50ml conical flask. The precipitated silver chloride was then filtered through a layer of Whatman No. 1 paper covered with a thin layer of asbestos in a Gooch crucible. The precipitate was washed well with distilled water to remove silver nitrate, and the Gooch crucible was transferred to the adaptor (A) of the special filtering apparatus which is illustrated in Fig. 1.4. The Gooch crucible was then filled with sodium thiosulphate solution (3M) and the contents were stirred until almost completely dissolved (about 2 minutes). The filtering apparatus was then connected to a water pump at (D) and a gentle suction applied. The above process was repeated until the last washing with sodium thiosulphate brought the total volume up to the previously accurately calibrated mark (B). The volume of the filtering apparatus

used was 13.90mls. The solution of radioactive silver chloride in sodium thiosulphate was then run directly into the counting tube (volume 11 ml.) via the tap (C). If the activity of the N - chloro compound was also required then the filtrate and washings from the first stage were counted and the N - chloro titre determined by the normal iodometric titration.

When aqueous solutions of silver nitrate were added to acetone solutions of N - chloroacetanilide, N - chlorosuccinimide, N - chloroacetamide and N - chloromorpholine, only a very faint white precipitate was evident after 60 minutes. When silver nitrate was added to a solution of the N - chloro compound which had been left for 60 minutes however, no such reaction was apparent, indicating a slow reaction between silver nitrate and the N - chloro group itself. This test indicated that the method outlined for the separation of the inorganic chloride from the N - chloro compound in acetone was complete and specific.

Because of the difficulty in analysing sodium thiosulphate solutions to determine the amount of chloride dissolved, the following method was developed to check the reproducibility of the thiosulphate technique.

5 ml. aliquots of a mixture of 0.05M lithium chloride (50 ml.) and 0.05M N - chloroacetanilide (50 ml.) in acetone were added to 5 mls. of silver nitrate contained in conical flasks. The precipitates of silver chloride were filtered through weighed, dried Gooch crucibles and the weight of

precipitate determined. The crucibles were then washed with thiosulphate as described above and were then dried and reweighed. The results are given in Table 1.3.

Table 1.3

Weight of precipitate*	0.0179	0.0173	0.0183	0.0178
Change in weight of Gooch crucible after washing	0.0002	0.0005	-0.0001	0.0002
* theoretical weight of precipitate 0.01788				

A further check on the accuracy of the method was obtained by utilising a standard solution of radioactive lithium chloride and measuring the activity of the resulting sodium thiosulphate solutions for varying volumes of the initial inorganic chloride. The results are given in Table 1.4 (see Fig. 1.5)

Having arrived at a satisfactory method of isolating the components of the reaction mixture, the next step was to investigate the stability of the N - chloro compounds in acetone under the conditions of the proposed experiments.

N - chloroacetanilide, lithium chloride and acetone

When 0.175M N - chloroacetanilide (50ml.) in acetone was added to 0.09M lithium chloride (50ml.) at 40° C, considerable decomposition was found to take place, only

FIG. 1.5.

Table 1.4

Volume of Lithium Chloride ³⁶ (ml.)	1.0	1.0	2.0	2.0	5.0	10.0
Activity (c/m)	571±6.0	563±6.1	1117±9.4	1122±9.4	2762±11.3	5535±13.8

67% of the N - chloro compound remaining unchanged after 40 minutes.

0.18M N - chloroacetanilide (5 ml.) was placed in a sealed, blackened tube with 0.09M lithium chloride (5 ml.) and the solution left for 20 hours at 40°C. At the end of this period no N - chloroacetanilide remained. When a similar experiment was performed with N - chloroacetanilide alone in acetone the percentage remaining was 71.2%, indicating that the presence of the lithium chloride had influenced the stability of the N - chloro compound. When a similar reaction was carried out at 35 °C it was found that at the end of 20 hours the percentage of N - chloroacetanilide present was 92.6 when the lithium chloride was absent and when the inorganic halide was included the N - chloro titre was zero.

The possibility that the decomposition in the presence of lithium chloride was due to the chloride being slightly acidic was discounted by adding a trace of lithium hydroxide such that the final pH was approximately 10. Decomposition was still found to take place - although definitely retarded.

Identical reactions were carried out in acetone solution between N - chloroacetanilide and lithium chloride in ordinary clear reaction vessels and in special darkened vessels to investigate the effect of light on the decomposition. In both vessels the N - chloro titre was greatly reduced but blackening the flask had a very definite effect, considerably reducing the rate of decomposition.

From a solution of 0.12M N - chloroacetanilide (5 ml.) and 0.1M lithium chloride (5 ml.) which had reacted until the N - chloro titre was zero, the lithium chloride was precipitated by pouring quickly into benzene (50 ml.). The lithium chloride was filtered at the pump and the remaining benzene/acetone mixture was reduced in volume to approximately 3 ml. utilizing a high vacuum at room temperature. Water was then added and the vigorously shaken mixture was allowed to cool to 0 °C, when white crystals appeared. These crystals were washed well with water and dried in a vacuum desiccator over silica gel. Analysed as follows = M.P 178.5 - 179 °C; mixed melting point with authentic p - chloroacetanilide 179 °C⁴⁴. A sample of the white crystals, when treated with 10% sodium hydroxide, yielded a compound which gave a strong primary amine test. Thus the product of the reaction between N - chloroacetanilide and lithium chloride in acetone was presumably a mixture of o- and p- chloroacetanilides.

When reaction mixtures of N - chloroacetanilide and lithium chloride in acetone were examined at 25 °C and 0 °C it was found that the N - chloro compound was more stable at the lower temperature, and even though decomposition

eventually took place slowly, a kinetic investigation of the exchange was undertaken in an endeavour to find some evidence for a reaction of the type: -

The details of two typical runs are given below:-

I [N - chloroacetanilide] = 0.045M
 [lithium chloride] = 0.028M Temperature 0 ° C

Activity of lithium chloride measured.

Time (minutes)	0	30	60	90	225	480
Activity (c/m)	496 (calculated)	493	497	488	492	494*

*No decomposition of N - chloroacetanilide apparent.

II [N - chloroacetanilide] = 0.045M
 [lithium chloride] = 0.028M Temperature 25 ° C

Activity of lithium chloride measured.

Time (minutes)	0	30	60	180	240
Activity (c/m)	497	493	483	496	501*

*No decomposition of N - chloroacetanilide apparent.

From these results it can be seen that no significant change in the activity of the lithium chloride occurs during the course of the experiment. A kinetic reaction was carried out at 45 ° C with the following results:-

III [N - chloroacetanilide] = 0.045M
 [lithium chloride] = 0.028M Temperature 45 °C

Activity of lithium chloride measured.

Time (minutes)	0	20	33	45	60	105	135	180
Activity (c/m)	330	323	322	327	325	215	203	-
Percentage <u>N</u> - chloroacetanilide Remaining	100	100	100	100	100	94.5	89.1	0

It is obvious that exchange takes place only when decomposition of the N - chloroacetanilide has begun. This result was substantiated when other exchange reactions gave identical results. As soon as the N - chloro titre starts to decrease the activity of the lithium chloride falls. From the above solution was isolated radioactive p- chloroacetanilide.

Reactions between lithium chloride and other N - chloro compounds were also investigated in acetone solution and these experiments will now be outlined.

N - chlorosuccinimide, lithium chloride in acetone

From stability studies on N - chlorosuccinimide solutions in acetone it was found that this compound was even more unstable than N - chloroacetanilide at high temperatures, solutions at room temperature however, were sufficiently stable over limited periods to enable kinetic investigations to be carried out.

I [N - chlorosuccinimide] = 0.025M
 [lithium chloride] = 0.025M Temperature 0 °C

This reaction was studied in blackened sealed tubes, the activity of the chloride being measured by the thiosulphate technique.

Time (minutes)	0	60	180	480	1440
Activity (c/m)	390 (calculated)	377	389	375	381

II $[N - \text{chlorosuccinimide}] = 0.025M$
 $[\text{lithium chloride}] = 0.010M$ Temperature $25^{\circ}C$

Time (minutes)	0	60	90	120	180
Activity (c/m)	390	386	375	388	377

N - chloroacetamide, lithium chloride and acetone

Solutions of N - chloroacetamide in acetone were shown to be relatively stable at room temperature over a period of several days, higher temperatures, as was found with other N - chloro compounds, causing decomposition.

I $[N - \text{chloroacetamide}] = 0.0337M$
 $[\text{lithium chloride}] = 0.0711M$ Temperature $35^{\circ}C$

Time (Minutes)	Volume of .0102N thio for 5 ml.	Activity of LiCl (c/m)
0	16.55	444
60	16.30	415
135	16.43	437
495	16.55	441
1440	17.01	434
2880	16.55	437

II [N - chloroacetamide] = 0.0337M
 [lithium chloride] = 0.0711M Temperature 25 ° C

Time (Minutes)	Volume of 0.0102N thio for 5 ml.	Activity of LiCl (c/m)
0	16.53	454
500	-	443
1230	-	454
1590	16.55	447
2490	-	436
6810	16.62	454

At the end of 6810 minutes one drop of 1.038 N hydrochloric acid was added to the solution. After a further 200 minutes the N - chloro titre was determined and found to have fallen to zero. The activity of the lithium chloride was found to be reduced to 315 c/m, indicating that exchange with decomposition had occurred in the presence of hydrochloric acid.

In order to identify the decomposition products of N - chloroacetamide in the presence of acetone the reaction mixtures were put through a gas liquid chromatography column. The results are illustrated in Fig. 1.6 The graphs are as follows:-

- (1) peak due to pure acetone. The same result was obtained for solutions of pure N - chloroacetamide lithium chloride in acetone.
- (2) this graph was obtained from solutions of lithium chloride and N - chloroacetamide in acetone to which perchloric acid has been added.

FIG 1.6

- (4), (5) and (6) these graphs were obtained by heating the reaction mixture of *N* - chloroacetamide, lithium chloride, perchloric acid and acetone, progressively reducing the volume.
- (3) graph of 'pure' α - chloroacetone which had been redistilled.

Further proof of the presence of α - chloroacetone was obtained by chemically testing for this compound in the reaction mixtures by the method outlined by H. Middleton⁴⁵.

When one drop of the reaction mixture was added to a small test tube containing three crystals of β - naphthol and 2 ml. of sodium hydroxide a violet red colouration was produced, a positive reaction for α - chloroacetone.

Investigation of other organic solvent systems

To ensure that a displacement reaction would not take place between *N* - chloro compounds and lithium chloride in other solvent systems the following organic materials were used.

(a) Dioxan and dioxan water mixtures

Solutions of *N* - chloroacetanilide and lithium chloride were prepared in dioxan and kept under nitrogen in blackened sealed tubes at 40 °C. Such solutions remained stable for more than four hours and no exchange of the halogen atoms took place. When the reaction temperature was increased to 54 °C the solution started decomposing after 3 hours and apparent exchange took place. *p*-chloroacetanilide was isolated.

In mixtures of dioxan and water (50:50), *N* - chloroacetanilide was found to be completely stable over a period

of six hours at 25 °C and no exchange took place for any of the concentration values used, ranging from 0.02M to 0.15M reagents.

(b) Ethyl acetate

The solvent systems which can be tried are limited by the solubility of lithium chloride. However, lithium chloride is moderately soluble in ethyl acetate⁴⁶ (1.78gm/100gm at 25 °C) and this solvent was tried without success. N - chloroacetanilide and N - chlorosuccinimide were found to be stable in this solvent for several hours but no exchange was observed to occur.

(c) The other solvent tried was n - propyl alcohol but the N - chloro compounds were found to decompose in this material after approximately 2 hours at 40 °C, and this system was abandoned. No exchange was observed.

Displacement Reactions in Aqueous solutions

(1) N - chloromorpholine and sodium chloride.

Aqueous solutions of N - chloromorpholine were found to be extremely stable when kept in the dark, the change in titre over a period of days being negligible. In order to investigate the exchange of halide ion between the inorganic sodium chloride and the N - chloro compound, solutions of both these compounds were mixed at 25 °C, and aliquots were withdrawn, the silver halide precipitated, and treated by the thiosulphate technique. The following results were obtained, indicating no exchange.

I $[N - \text{chloromorphaline}] = 0.0600M$
 $[\text{sodium chloride}] = 0.00724M$ Temperature $25^{\circ}C$

Time (minutes)	0	5	10	35	40	5 days
Sodium chloride activity (c/m)	469 (calculated)	470	469	452	468.5	464
N - chloromorphaline activity (c/m)	3.7	2.6	3.5	2.0	2.7	2.9

II $[N - \text{chloromorphaline}] = 0.085M$
 $[\text{sodium chloride}] = 0.084M$ Temperature $25^{\circ}C$

Time (days)	0	1	2	3	4	5
Sodium chloride activity (c/m)	483	464	475	481	443	478

An aqueous solution of N - chloromorphaline in a blackened flask gave no immediate precipitate with silver nitrate but after several hours a faint purple colouration was perceived in this solution. The results indicate the efficiency of the method for separating the inorganic halide from the organic compound. One conclusion which can readily be drawn from these results is that the amount of hypochlorous acid which exists in equilibrium with N - chloromorphaline must be extremely small, if present at all, since Anbar, Guttman and Rein⁴⁷ demonstrated the rapidity with which hypochlorous acid exchanged with chloride ion in solution under conditions of varying hydrogen ion concentration (see Fig. 1.7)

According to these workers,

the interaction between hypochlorous acid and chloride ion in aqueous solution may lead to three different results.

- (1) chlorine may be formed
- (2) the chlorine atoms may exchange
- (3) there may be an induced oxygen exchange between hypochlorous acid and water. In fact the first interaction

will lead to a simultaneous chlorine exchange and a chloride induced oxygen exchange⁴⁸. By using the equilibrium constant

for chlorine hydrolysis⁴⁹, together with the kinetic studies made by Shilar and Solodushenkov⁵⁰ on the hydrolysis of chlorine; the rate of chlorine formation from hydrochloric acid and hypochlorous acid could be implied. An activated complex ($H_3O^+ \cdot HOCl \cdot Cl^-$) which leads to chlorine exchange was suggested by Anbar et. al; the difference between the two possible modes of decomposition of the two available, similar, activation complexes is thought to be due to a different position and role of the water molecule. For chlorine exchange the water molecule is thought to be attached to the terminal chlorine which subsequently becomes hypochlorite chlorine

whereas in the case of chlorine formation the water molecule may be attached to the hypochlorous acid end of the complex ($H_2O \cdot H_2OCl \cdot Cl^-$) $\rightleftharpoons 2H_2O + Cl_2$.

The precursor of the ($H_2O \cdot ClCl \cdot H_2O$) complex is probably the ($HOClCl$)⁻ ion, the role of which in hypohalite chemistry has been discussed⁵¹. The rate determining step will therefore be a proton transfer to this trihalide-like ion, and the value obtained agreed well with comparable fast proton transfer reactions outlined by Eigen⁵². The precursor for the second type of activated complex is thought to be the hydrated H_2OCl^+ which only exists in much more acid solutions⁵³.

Hence if the equilibrium:-

exists, it must lie almost completely to the left since any activity which appeared in hypochlorous acid via the reactions outlined above, would rapidly appear in the N-chloromorpholine molecule since the reaction (2) is known to be extremely fast, and to lie very much to the left.

In an endeavour to understand the species present in aqueous solutions of N-chloro compounds, the following tracer experiments were carried out on compounds other than N-chloromorpholine using sodium chloride to provide the isotopically labelled halide ion.

N - chloroacetamide, sodium chloride (Cl-36) in water

When dilute (0.1N) silver nitrate was added to a solution of N-chloroacetamide in water no immediate precipitate appeared but the solution became distinctly cloudy. When the aqueous solution of N-chloroacetamide was allowed to stand for several hours and then added to silver nitrate no precipitate was obtained, indicating that the reaction proceeding is not a slow hydrolysis of the N-chloro group to produce chloride ion but takes place only by constant removal of one of the reaction species as the insoluble silver salt. Solutions of radioactive sodium

chloride and N - chloroacetamide were mixed at 25 °C and the activity of the halide ion was measured as a function of time, utilizing the thiosulphate technique. The following are results of typical runs:-

Run I

[N - chloroacetamide] = 0.0570M
[sodium chloride] = 0.0352M Temperature 25 °C

Time (minutes)	0	2	10	45	240
Sodium chloride activity (c/m)	906	905	882	884	-
Apparent % N - chloro compound remaining	100.0	100.0	100.0	100.0	100.0

Run II

[N - chloroacetamide] = 0.0415M
[sodium chloride] = 0.0352M Temperature 25 °C
[perchloric acid] = 0.0105M

Time (minutes)	0	3	38	111
Chloride activity (c/m)	909	906	862	-
Apparent % N - chloro compound remaining	100.0	100.0	100.0	100.0

Run III

[N - chloroacetamide] = 0.1830M
[sodium chloride] = 0.0352M Temperature 25 °C
[perchloric acid] = 0.1050M

Time (minutes)	0	100	125	720
Chloride activity (c/m)	903	623	566	326
Apparent % N - chloro compound remaining	100.0	97.3	-	94.4

From the results of these experiments the following points can be noted -

(a) no exchange takes place between neutral solutions of N - chloroacetamide and sodium chloride (neutral refers here to the absence of acid, since the pH of 0.102M N - chloroacetamide is 3.4).

(b) when acid was added, the activity of the halide decreased. The significance of this result will be discussed in a later section (see Chapter 3). It is generally accepted that N - chloroacetamide in aqueous solution exists in equilibrium with hypochlorous acid⁵⁴ but from these results it can be concluded that either the amount of the oxyacid is extremely small or that the equilibrium

does not readily proceed from right to left (see page¹⁵⁵). Robb⁵⁴ attempted to evaluate the equilibrium constant for the above reaction by an absorption spectrographic technique.

He concluded that the solutions studied contained quantities of nitrogen trichloride and consequently he abandoned the method. A value of the equilibrium constant has been obtained in the present work by an E.M.F method

(page 98) and the quantity obtained would indicate that both the above reasons are probably partially correct in explaining the non exchange of the halide ion in aqueous solution.

N - chlorosuccinimide, sodium chloride (Cl-36) in water

Run I

[N - chlorosuccinimide] = 0.0378M
[sodium chloride] = 0.0352M Temperature 25 ° C

Time (minutes)	0	29	80	240
Chloride activity (c/m)	904	902	896	898

Run II

[N - chlorosuccinimide] = 0.0378M
[sodium chloride] = 0.0352M Temperature 25 ° C
[perchloric acid] = 0.1000M

Time (minutes)	0	25	85
Chloride activity (c/m)	904	873	862

It can clearly be seen that N - chlorosuccinimide behaves analogously with N - chloroacetamide and exchange only occurs in the presence of acid.

Pelouze⁵⁵ showed that a concentrated solution of hypochlorous acid gave on treatment with calcium nitrate, chlorine (I) oxide, which he called "hypochlorous acid" in

accordance with the nomenclature of the day. Jakowkin⁵⁶ stated that hypochlorous acid had a normal molecular weight in aqueous solution and he and several other workers demonstrated the volatilisation of hypochlorous acid from solution. Noyes and Wilson⁵⁷ pointed out the fact that the vapour phase contained chlorine oxide and not hypochlorous acid, a fact which has been overlooked by many authors. That the acid volatilizes as Cl_2O is not a contradiction of Clark and Iseley⁵⁸ who reported the reaction

as taking place in sunlight. The simplest explanation of the appearance of chlorine oxide in aspirated solutions of hypochlorous acid is the occurrence of the reaction

although such a statement overlooks the fact that the dehydration reaction requires explanation. About the only explanation possible in accordance with the Lewis - Langmuir theory is indicated by

which means that the water must be formed from a positive hydrogen ion and a negative hydroxyl ion. Unless it is assumed that pairs of electrons are divided in the reaction, the two electrons between the oxygen and the chlorine must go with the oxygen of the negative hydroxyl, leaving only

six electrons with the chlorine atom. The latter would therefore be positive.

Hence if hypochlorous acid is present in solutions of N - chloro compounds it should be possible to detect its presence by aspirating the solution with a stream of nitrogen gas and detecting the chlorine (I) oxide so produced by passing the gas through potassium iodide solutions and also through sodium hydroxide. Such a method is only suitable for solid N - chloro compounds such as N - chloroacetamide owing to the ease with which liquid N - chloro compounds such as N - chloromorpholine may be aspirated from solution (see page 69).

Aspirations of an aqueous solution of N - chlorosuccinimide and radioactive sodium chloride.

Run I

N - chlorosuccinimide (0.189g) was dissolved in 25 ml of aqueous radioactive sodium chloride (0.07M) and nitrogen gas was passed through the mixture at a constant rate, carrying any volatile components through a bubbler containing 0.472N sodium hydroxide (35 ml), followed by a second bubbler containing excess potassium iodide solution. The resulting activities of the sodium hydroxide and the potassium iodide were determined in a liquid counting tube and the radioactivity in these solutions compared with the initial activity of the sodium chloride. The following

results were obtained.

(a) Initial sodium chloride. Total counts in 25 ml. = 7070 c/m. If complete exchange of the halogen atoms was to occur, the expected decrease in the number of counts of this solution would total 4,300.

(b) Total counts in sodium hydroxide solution = 65 c/m. Potassium iodide and excess acetic acid were then added and the total iodine titre was 2.24ml. of sodium thiosulphate (0.0304M).

(c) Total counts in potassium iodide solution = 25 c/m. Iodine titre for the potassium iodide solution was 0.43 ml. of thiosulphate.

The above experiment indicates that activity certainly is appearing in the aspirated gas stream, presumably due to the presence of chlorine (I) oxide formed from hypochlorous acid. Since the hypochlorous acid is continually being removed, the equilibrium:-

is being upset and this explains the relatively large iodine titre of the sodium hydroxide solution which would indicate a reasonable concentration of hypochlorous acid in the initial solution, contrary to the work of Robb⁵⁴ and also to the value of the hydrolysis constant for this reaction found in the present paper.

Run II

N - chlorosuccinimide (0.258) was dissolved in 0.07M radioactive sodium chloride (25 ml.) and a stream of nitrogen gas was passed through the mixture. The gas was then passed through 2N sodium hydroxide (60 ml.) followed by potassium iodide as described in Run I. The activity and chlorine content of these solutions was determined, together with the chloride titre of the reagent mixture and the remaining halide activities (sodium chloride and N - chlorosuccinimide) were determined. The following results were obtained.

Potassium iodide bubbler:= Very little radioactivity was detected in this solution, indicating that all of the volatile halogen containing compounds, if present, must have been absorbed in the sodium hydroxide bubbler. The iodine titre of the potassium iodide solution was equivalent to 0.15 ml. of sodium thiosulphate (0.0304N) and the activity found was < 4 c/m.

Sodium hydroxide trap:= The total number of counts found in this solution was 104.5 c/m, and from the chlorine titre on adding potassium iodide and excess acetic acid (0.67 ml. of 0.0304N) the counts/gm. of chlorine was found to be 14.1×10^4 (c.f specific activity of the original sodium chloride of 11.5×10^4 counts/min./gm.)

Original solution:= The chlorine titre on 5 ml. of the reaction mixture at the end of the aspiration period indicated very little change ($< 1\%$) in the theoretical N - chloro titre. When an aliquot (5 ml.) of this solution was added to silver

nitrate, and the resulting silver chloride filtered off, the filtrate was found to have a total activity of 200 c/m. Specific activity of the chlorine as N - chloro is thus 14.6×10^3 counts/min./gm.) The chlorine titre of the filtrate indicated a small loss of N - chloro titre (approximately 5%). The activity of the chloride ion in the original solution after aspiration, (5,600 c/m), indicated a loss of approximately 1,400 c/m, and this loss can be accounted for by the activity of the N - chlorosuccinimide and the aspirated halogen compounds.

The results of these two experiments indicate that incomplete exchange has taken place between the inorganic sodium chloride and the N - chloro molecule under the influence of an agent which upsets the established equilibrium by removal of a volatile component. The specific activity of the aspirated halogen is almost identical with that of the original sodium chloride, indicating that complete exchange between these two compounds must have occurred in solution. This exchange is presumably the very fast reaction already mentioned between hypochlorous acid and the chloride ion.

The specific activity of the N - chlorosuccinimide halogen was not identical with that of the chloride, and thus complete exchange via the hypochlorous acid molecule had not occurred during the time of observation. From a consideration of the value for the equilibrium constant for the hydrolysis of

N - chlorosuccinimide in water complete exchange would not be expected.

Summary

No evidence of displacement reactions occurring between N - chloro compounds and inorganic chloride has been obtained under widely varying experimental conditions. The apparent exchange which was observed in several experiments could be attributed to an exchange via one or more decomposition or hydrolysis products and experimental evidence has been given to support this theory.

Especially significant has been the observations on the 'catalytic' effect of acids on the apparent exchange and a detailed investigation of the reactions of N - chloro compounds with both hydrochloric and perchloric acids will be given in Chapter 3, where the mechanism of the reactions above will be made clear.

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CHAPTER 2

The Base Strength of N-chloromorpholine and N-chloropiperidine

A knowledge of the possible basic or acidic nature of the chlorine substitution products of ammonia, monochloroamine and dichloroamine is of great practical importance in obtaining a clear understanding of the reactions of these compounds in aqueous solution.

In the water system, the replacement of a hydrogen atom by chlorine has a strong acidifying effect. The acid ionization constant of hypochlorous acid¹, for example, is $3.6 \times 10^{-8} \text{ mole.l}^{-1}$ at 25°C compared with $2 \times 10^{-16} \text{ mole.l}^{-1}$ for water itself. This effect can be compared to that produced by substitution of an acetyl group (ionization constant of acetic acid² = $1.75 \times 10^{-5} \text{ mole.l}^{-1}$), where the result is greatly accentuated by the large amount of resonance in the acetate ion. In the ammonia system, however, the presence of the acetyl group causes a base weakening effect of the same order of magnitude. (Base strength of ammonia³, $1.77 \times 10^{-5} \text{ mole.l}^{-1}$; that of acetamide⁴ = 3×10^{-15}). By analogy, monochloroamine (NH_2Cl) and its alkyl homologues should be very weak bases, with ionisation constants in the region of 10^{-14} to $10^{-15} \text{ mole.l}^{-1}$. Unfortunately, the basic properties of monochloroamine are only manifested to a measurable extent in very acidic solutions where disproportionation rapidly occurs.

Weil and Morris⁵ eliminated this side reaction, obtaining a direct measure of the base strengths of N-chlorodimethylamine and N-chlorodiethylamine. From these results a reasonable estimate of the base strength of monochloroamine was made. Measurement of the ultraviolet absorption spectra of the N-chloro dialkylamines in solutions of varying acidity was employed for the direct determination. As the acid concentration of the solutions of these substances was increased above 0.01M the characteristic absorption bands for the N-chlorodialkylamines diminished in intensity, the changes in the spectrum not being accompanied by corresponding changes in the oxidising titre. Weil and Morris found that the absorption bands could be made to reappear by the addition of alkali, demonstrating that the observed spectrum changes were due to an ionization process given by:

Quantitative analyses by spectrophotometric methods are based on the assumption that Beer's Law, relating absorption to concentration, holds for a mixture of substances as well as for individual compounds. The absorption at a given wave-length for a mixture of compounds is thus:

$$A = A_1 + A_2 + A_3 + \dots + A_n$$

Several methods are available for the analysis of mixtures by spectrophotometric means⁶, the most simple being the interpolation method, which relies on a knowledge

of the total concentration of the components of the mixture, one absorption measurement at one wavelength being sufficient to determine the composition, provided that the extinction coefficients of the various species are known at the wavelength of measurement.

Weil and Morris obtained values of E , the molar extinction coefficient, in the region 220 - 300 $m\mu$ from the transmission data of solutions at pH 10.7. Determinations of the ionisation constants were based upon measurements at 265 $m\mu$ for N-chlorodimethylamine and at 260 $m\mu$ for N-chlorodiethylamine. At these wavelengths the molar extinction coefficients were found to be 366 ± 3 and 312 ± 3 respectively (Metcalf⁷ gives $\lambda_{\max} = 263 m\mu$ and $\epsilon_{\max} = 300$ for both compounds).

Curves were plotted for typical acidified solutions of the N-chloro compounds (Fig. 2.1). From the transmission data, these curves were computed in terms of the "apparent molar extinction coefficient", E^- , which was defined as:

$$E^- = \frac{1}{lM_o} \log \frac{I_o}{I}$$

where l = length of cell.

I_o = incident light intensity.

I = intensity after passing through length of solution.

M_o = total chloroamine concentration, whether as base or ion.

The decreasing absorption with increasing acidity is immediately evident.

The absorption spectra of N-chlorodiethylamine at different acid concentrations. The uppermost curve is at a pH of 10.7. For the others in descending order, $[H^+] = 0.0100, 0.0298, \text{ and } 0.0495$, respectively.

Absorption spectra of N-chlorodimethylamine at different acid concentrations. The uppermost curve is at a pH of 10.7. For the others in descending order, $[H^+] = 0.125, 0.224, 0.322, \text{ and } 0.519$, respectively.

Weil and Morris derived the following equations for use in the determination of the ionization constant. For a solution containing both free base and the ion, the Beer Lambert Law gives

$$\left(\frac{1}{I}\right) \log \frac{I_0}{I} = E_B [B] + E_{BH^+} [BH^+] = E^- M_0 \quad \dots\dots (1)$$

Combining this expression with the relationship

$$M_0 = [B] + [BH^+] \quad \text{gave}$$

$$\frac{[B]}{[BH^+]} = \frac{(E^- - E_{BH^+})}{(E_B - E^-)} \quad \dots\dots (2)$$

for the ratio of the molarity of chloroamine to that of the ions.

(Application of this method to N-chloromorpholine requires $[B] \equiv \text{N-chloromorpholine}$
 $[BH^+] \equiv \text{N-chloromorpholinium ion}$).

At constant ionic strength the dissociation constant for the reaction

may be expressed in terms of concentrations as follows:

$$K_a = \frac{[\text{H}^+][\text{B}]}{[\text{BH}^+]} \quad \text{.....(4)}$$

Combination of this expression with equation (2) gave

$$K_a = \frac{[\text{H}^+][\text{E}^- - \text{E}_{\text{BH}^+}]}{(\text{E}_\text{B} - \text{E}^-)} \quad \text{.....(5)}$$

These authors found that a direct evaluation of the E_{BH^+} terms was unnecessary, rearrangement of equation (5) giving the expression

$$\text{E}_{\text{BH}^+} = \frac{\text{E}^- - K_a(\text{E}_\text{B} - \text{E}^-)}{[\text{H}^+]} \quad \text{.....(6)}$$

Evaluation of E_{BH^+} could thus be accomplished by plotting values of E^- against the function $\frac{(\text{E}_\text{B} - \text{E}^-)}{[\text{H}^+]}$, the axial intercept of the straight line drawn through these points giving E_{BH^+} .

Table 2.1 summarises the values obtained for N-chlorodiethylamine and N-chlorodimethylamine.

Table 2.1

<u>N</u> -chloro compound	E_{BH^+}	K_a mole.l ⁻¹	$\frac{1}{K_a}$ mole.l ⁻¹
dimethylamine	30 ± 5	0.345 ± .015	2.899 ± 0.13
diethylamine	15 ± 5	0.095 ± .003	10.53 ± 0.3

The basic ionization constant, K_b , corresponding to the process

is related to K_a by the equation

$$K_b = \frac{K_w}{K_a}$$

Application of this expression gave for N-chlorodimethylamine $K_b = 2.9 \times 10^{-14} \text{ mole.l}^{-1}$ and for N-chlorodietylamine $K_b = 1.06 \times 10^{-13} \text{ mole.l}^{-1}$, both measured at 25°C.

An estimate of the effect of chlorine substitution on the nitrogen atom can readily be obtained by comparing the basic ionization constants of the dialkylamines with those of the resulting N-chloro compounds. For dimethylamine the change in ionization constant produced by chlorine substitution is from ⁸ 6.0×10^{-4} to $2.9 \times 10^{-14} \text{ mole.l}^{-1}$ (a factor of 5×10^{-11}). For diethylamine it is from ⁹ 1.3×10^{-3} to $1.06 \times 10^{-13} \text{ mole.l}^{-1}$, a factor of 8×10^{-11} . It can therefore be safely assumed that the basic ionization constant of monochloroamine should be approximately $1 \times 10^{-15} \text{ mole.l}^{-1}$ (K_b for ammonia = 1.8×10^{-5}).

A great deal of interest has centred around the reactions of N-chloromorpholine since Carr and England¹⁰ demonstrated that, for the reaction between N-chloromorpholine and phenol in acid solution (hydrochloric acid), the chloride ion played no part in the rate-determining stage. When perchloric acid was used as a catalyst, the third-order rate constant was practically unaffected. On the basis of this

and other evidence, it was concluded that phenol was chlorinated in the rate-determining bimolecular reaction (II), the N-chloromorpholinium ion having been formed in reaction (I).

A similar situation was shown by Brawn and Soper¹¹ to exist for a mixture of phenol and diethylchloroamine in buffered solution. These authors found that the reaction took place mainly by a direct mechanism and not by a preliminary hydrolysis of the chloroamine to hypochlorous acid. The kinetics were interpreted in terms of the interaction of phenoxide ions and diethylchloroammonium cations. From the kinetic data, the acid ionisation constant of the diethylchloroammonium cation was found to be 0.09 mole⁻¹ and its reaction rate towards phenol was approximately 10³ times that of hypochlorous acid (hypochlorous acid is some 10³ times as reactive a chlorinating agent towards phenol as is N-chloroacetanilide)¹².

In his investigations on the kinetics and mechanism of the acid catalysed chlorination by N-chloro compounds, Carr¹³

assumed that the concentration of the N-chloromorpholinium ion ($>\text{NHCl}^+$) was very much smaller than that of the parent N-chloroamine in perchloric acid solutions. Experimental work to be described in this chapter revealed this assumption to be incorrect. Dixon¹⁴ has described the consequences of a precise knowledge of the value of the ionisation constant on the work of Carr, and has re-evaluated this authors work in the light of this new evidence. Thus an accurate value of K is necessary to fully evaluate the chlorinating power of N-chloroamines and amides.

EXPERIMENTAL

EXPERIMENTAL

Three distinct methods were used to determine an accurate value of the equilibrium constant, K , defined as

$$K = \frac{[>NHCl^+]}{[>NCl][H^+]}$$

for the reaction of N-chloromorpholine and the related N-chloroamine, N-chloropiperidine with acids.

(A) Spectroscopy. Unlike the N-chloroamines investigated by Weil and Morris (*loc.cit*), solutions of N-chloromorpholine in perchloric acid failed to exhibit significant spectral change, making the application of this method impractical.

The results obtained for solutions of N-chloromorpholine ($8.44 \times 10^{-4}M$) in varying strengths of acid are given in Table 2.2. A graph of these results (Fig.2.2.) can be compared with that obtained for N-chlorodiethylamine (Fig. 2.1).

TABLE 2.2

Influence of acid strength on the absorption spectrum of N-chloromorpholine at 25°C.

All Solutions contained $8.44 \times 10^{-4}M$ N-chloromorpholine.

Wave-length λ°	Optical Density				
	H ₂ O	0.459M HClO ₄	0.931M HClO ₄	1.41M HClO ₄	1.69M HClO ₄
2100	0.675	0.642	0.649	0.622	0.630
2150	0.463	0.451	0.462	0.458	0.470
2200	0.313	0.309	0.321	0.330	0.340

FIG. 2 .2

Wave-length $\text{\AA}$	Optical Density				
	H_2O	0.459M HClO_4	0.931M HClO_4	1.41M HClO_4	1.69M HClO_4
2250	0.221	0.219	0.229	0.241	0.254
2300	0.176	0.175	0.183	0.195	0.202
2350	0.172	0.166	0.172	0.181	0.185
2400	0.194	0.187	0.187	0.190	0.188
2450	0.230	0.220	0.217	0.211	0.204
2500	0.263	0.250	0.243	0.231	0.220
2550	0.288	0.274	0.262	0.246	0.230
2600	0.298	0.281	0.269	0.249	0.231
2650	0.290	0.275	0.260	0.240	0.221
2700	0.269	0.254	0.240	0.220	0.204
2750	0.236	0.223	0.211	0.194	0.178
2800	0.198	0.187	0.176	0.162	0.149
2850	0.160	0.150	0.141	0.129	0.120
2900	0.124	0.116	0.109	0.101	0.093
2950	0.095	0.089	0.083	0.078	0.070
3000	0.071	0.065	0.061	0.057	0.051
3100	0.039	0.034	0.032	0.032	0.027

It can readily be seen that the characteristic N-chloro peak at 2600 $\text{\AA}$ decreased as the perchloric acid concentration was increased; this effect being reversed by the addition of alkali. From a knowledge of subsequent results, the small drop in optical density can be attributed to the value of

the equilibrium constant K_a , and possibly also to the value of E_{BH^+} being comparable with that of E_B itself. Large acid concentrations (greater than 1 M) would be necessary to obtain a significant change in the spectrum, a condition which would cause appreciable decomposition of N-chloromorpholine.

N-chloropiperidine was also investigated and the behaviour of this compound in perchloric acid exactly paralleled that exhibited by the chloroamine investigated by Weil and Morris. A plot of $(E_B - E^-)/[H^+]$ against E^- was found to be linear (Fig. 2.3.), the intercept giving $E_{BH^+} = -2 \pm 2$.

Table 2.3. summarises the results.

Table 2.3.

Values of K_a for N-chloropiperidine at 25°C.

Note: $E_{\text{N-chloropiperidine}} = E_{BH} = 356$

H^+	O.D. at 2600Å	E^-	$E_B - E^-$	$E^- - E_{BH^+}$	$\frac{E_B - E^-}{[H^+]}$	$K_a \text{ mole.l}^{-1}$
0.0198	0.713	309	47	307	2380	0.132
0.0425	0.615	267	89	265	2090	0.127
0.0627	0.551	239	111	237	1870	0.127
0.0990	0.353	206	150	204	1520	0.135
0.1975	0.239	141	215	139	1090	0.128
0.2882	0.183	109	247	107	857	0.1250
0.4251	0.132	79.5	276	77.5	650	0.119
0.6267	0.102	62.3	294	60.3	470	0.129

FIG. 2.3.

FIG. 2.3.

Mean value of $K_a = 0.128 \pm 0.003 \text{ mole.l}^{-1}$. From this result, K , the equilibrium constant for the reaction:

as defined by $K = \frac{[\text{>NClH}^+]}{[\text{NCl}][\text{H}^+]} = \frac{1}{K_a}$ was determined, the

value being $7.85 \pm 0.18 \text{ mole.l}^{-1}$.

The basic ionization constant K_b , corresponding to the process

is related to K_a by the equation $K_b = \frac{K_w}{K_a} = 7.85 \times 10^{-14} \text{ mole.l}^{-1}$.

The effect of chlorine substitution on the nitrogen atom can be appreciated by comparison with the value of $1.58 \times 10^{-3} \text{ mole.l}^{-1}$ for the K_b of piperidine itself¹⁵.

Because of the unsuitability of this technique for N-chloromorpholine the following method was adopted to obtain results for this compound.

(B) Aspiration. At a constant nitrogen flow rate the amount of N-chloromorpholine which could be aspirated from solution was found to be directly proportional to the concentration remaining in solution.

Nitrogen gas from a cylinder was passed through a

constant pressure regulator, and then through an accurately calibrated flow meter (Fig.2.4), the volume of nitrogen being finely controlled by a sensitive needle valve.

From the flow meter the nitrogen was bubbled through the reaction mixture contained in a 250 ml., B-24 stoppered flask immersed in a constant temperature water bath. The exiting nitrogen, containing N-chloromorpholine, was bubbled through an acidified potassium iodide solution containing starch and a known volume of standard sodium thiosulphate. The time taken for the 'N-chloromorpholine-liberated' iodine to react with the sodium thiosulphate present was accurately measured by the reappearance of the blue starch complex.

Figure 2.5 illustrates the results obtained for typical experiments carried out with both aqueous and perchloric acid solutions of the N-chloromorpholine using a flow rate of 64 millilitres of nitrogen/min. The approximate linear relationship between titre and time breaks down if the amount of the N-chloro compound removed becomes too great, the resulting curve being difficult to interpret satisfactorily. Consequently, no more than 5% of the N-chloro compound was removed from solution during the evaluation of the equilibrium constant.

To ensure that the nitrogen contained no impurities a control experiment was carried out by bubbling the nitrogen through acidified potassium iodide, no iodine being liberated after five hours.

FIG. 2.4.

FIG. 2.5.

The N-chloromorpholinium ion, formed by the action of acid on N-chloromorpholine, is not volatile and consequently cannot be removed from solution with nitrogen. The difference between the graph obtained for the amount of the N-chloro compound actually removed from solution and that expected from the standard graphs plotted for aqueous solutions gives a measure of the amount of the N-chloromorpholinium ion present in solution.

A solution of N-chloromorpholine of known concentration $[a]$ was prepared in standard perchloric acid $[b]$ and the solution was aspirated, a graph of the resulting sodium thiosulphate titre as a function of time being constructed. From this graph the apparent N-chloromorpholine concentration $[x]$ was determined by reference to the standard graphs.

(Note: $[x] < [a]$, $[b] \gg [a]$).

$$\text{Then } K = \frac{[a] - [x]}{[x][b]} = \frac{[\text{NHCl}^+]}{[\text{NCl}][\text{H}^+]}$$

The results of the aspiration experiments with N-chloromorpholine are summarised in Table 2.4.

The salt effect was investigated by aspirating N-chloromorpholine from solutions of sodium perchlorate, the correction to be applied amounting to less than 3%.

Table 2.4

Values of $K = \frac{[>NHC1^+]}{[H^+][>NCl]}$ for N-chloromorpholine

All measurements at 25°C.

$[H^+]$	$[NClM]_{init}$	$[NClM]_{EQBM}$	$K_{-1} \text{ mole}^{-1}.l.$
0.223	0.0573	0.0511	0.540
0.319	0.0396	0.0336	0.560
0.795	0.0396	0.0275	0.551
1.276	0.0396	0.0232	0.553
1.276	0.0453	0.0268	0.542

Mean value = 0.549 $\text{mole}^{-1}.l.$

Application of this method to N-chloropiperidine yielded results in close agreement with those obtained by the spectroscopic method. The results for N-chloropiperidine are given in Table 2.5.

Table 2.5

Values of K for N-chloropiperidine at 25°C.

$[H^+]$	$[NClP]_{init}$	$[NClP]_{EQBM}$	$K \text{ mole}^{-1}.l.$
0.0503	0.0418	0.0300	7.83
0.101	0.0418	0.0232	7.93
0.223	0.0673	0.0249	7.64

Mean Value of K = 7.80 $\text{mole}^{-1}.l.$

Confirmation of the value of the equilibrium constant for N-chloromorpholine came from a study of distribution coefficients.

(C) Distribution. If to a system of two liquid layers, made up of two immiscible or slightly miscible components, is added a quantity of a third substance soluble in both layers, then the substance is found to distribute itself between the two independent layers in a definite manner. If C_1 and C_{11} are the concentrations in the layers I and II respectively, then at a constant temperature

$$\frac{C_1}{C_{11}} = \text{constant } (K_d)$$

Distribution measurements break down if the solute is prone to association or dissociation in either of the solvents, the same molecular weight having to be observed in both solvents. This method has found many applications in the study of equilibria. Dawson¹⁶ applied this method in his evaluation of the reaction.

using carbon disulphide and water as the two liquid phases.

Application of this method to the measurement of the equilibrium existing between N-chloromorpholine and perchloric acid yielded excellent results, the distribution being made between water and carbon tetrachloride, neither perchloric acid nor N-chloromorpholinium perchlorate being

soluble in the latter solvent.

A solution of N-chloromorpholine was prepared in 50 ml of the appropriate aqueous solvent (water, perchloric acid or a solution of sodium perchlorate), and this solution was placed in a 100 ml round bottom B-14 flask. Carbon tetrachloride (50 ml) was then added, together with a small glass-enclosed magnet. The bulb of the flask was immersed in a constant temperature water bath, agitation of the two liquid phases being accomplished with a powerful magnet attached to a high speed motor suspended above the reaction flask. Equilibrium was attained in approximately three hours, the two phases being analysed by titrating the iodine liberated, on the addition of acidified potassium iodide, with a standard sodium thiosulphate solution.

Table 2.6 gives the values of the distribution constant (K_d) for solutions of N-chloromorpholine in water, sodium perchlorate and perchloric acid. The values of K_d in sodium perchlorate (Figure 2.6) demonstrate the 'salting out effect', corrections for which have been applied to the values obtained in the evaluation of the equilibrium constant in perchloric acid.

The agreement between these values and those obtained by aspiration is good.

FIG 2.6.

Table 2.6

Values of K for N-chloromorpholine determined by distribution.

All measurements at 25°C

Aqueous Solvent	Na ₂ S ₂ O ₃ titre		$K_d \left(\frac{CCl_4}{H_2O} \right)$	$K (mole^{-1}.l.)$
	CCl ₄ phase	Aqueous phase		
H ₂ O	53.72	7.30	7.36	-
NaClO ₄ (0.200M)	42.80	5.60	7.65	-
NaClO ₄ (0.400M)	43.70	5.60	7.91	-
NaClO ₄ (0.700M)	43.80	5.45	8.05	-
NaClO ₄ (1.010M)	41.11	4.98	8.26	-
NaClO ₄ (1.276M)	43.60	5.22	8.37	-
HClO ₄ (0.319M)	41.20	6.18	6.65	0.542
HClO ₄ (0.398M)	38.80	6.00	6.47	0.561
HClO ₄ (0.506M)	39.97	6.36	6.29	0.538
HClO ₄ (0.500M)	57.00	9.12	6.26	0.557
HClO ₄ (0.795M)	38.82	6.85	5.68	0.555
HClO ₄ (1.276M)	40.80	8.37	4.89	0.559
HClO ₄ (0.319M) + NaClO ₄ (0.956M)	33.20	4.66	7.12	0.536

Mean value of K = 0.550 mole⁻¹.l.

Application of the distribution method to the evaluation of K for N-chloropiperidine gave results comparable to those obtained by spectroscopy and aspiration. Because of the greater affinity of this compound for the organic phase, the value of the distribution coefficient for the system carbon tetrachloride:water was 124 ± 9 (c.f. 7.3 for N-chloromorpholine). Consequently, the salt effect was more pronounced as can be seen by the values listed in Table 2.7. The value of the equilibrium constant was obtained by plotting K as a function of ionic strength and extrapolating to zero (Figure 2.6).

Table 2.7

Values of K for N-chloropiperidine determined by distribution

All measurements at 25°C.

Aqueous solvent	$K_d \frac{(\text{CCl}_4)}{(\text{H}_2\text{O})}$	K mole ⁻¹ .l.
H ₂ O	124	
0.198M HClO ₄	38.7	10.11
0.320M HClO ₄	25.6	11.40
0.472M HClO ₄	17.25	12.60

Value at zero ionic strength 8.28 ± 0.3 mole⁻¹.l.

SUMMARY

(1) Two methods have been developed for the accurate measurement of the equilibrium constant for the protonation of N-chloromorpholine and related compounds.

(i) Aspiration:- applicable only if the N-chloroamine is a relatively volatile liquid at the temperature of measurement.

(ii) Distribution:- Suitable for any N-chloro compound which is fairly soluble in a water immiscible solvent.

(2) The value of the equilibrium constant for the reaction $>NCl + H^+ \rightleftharpoons >NHCl$ has been found for both N-chloromorpholine and N-chloropiperidine, the values being $0.554 \text{ mole}^{-1}.l$ and $7.80 \text{ mole}^{-1}.l$ respectively. A knowledge of these constants is of importance in obtaining a clear understanding of the variations in the rate of reactions of the N-chloroamines with compounds such as phenol under acid conditions.

(3) The basic ionization constants of N-Chloromorpholine and N-chloropiperidine can readily be obtained from the equilibrium constants given above. Thus K_b for N-chloropiperidine = 7.85×10^{-14} and for N-Chloromorpholine $0.554 \times 10^{-14} \text{ mole.l}^{-1}$.

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CHAPTER 3

The Action of Hydrochloric Acid on N-chloromorpholine and N-chloropiperidine

The value of chloroamines as chlorinating agents has long been established, but as Chattaway¹ and Orton² showed, the nature of the halogenating agent to which they gave rise was determined by the nature of the halogen acid added, in accordance with the simplified equation:

Orton and King³ showed that the chlorination by halogenoamines in the presence of hydrochloric acid involved free chlorine, controlled by the amount of hydrochloric acid present and the equilibrium:-

A modification of this method was shown by Hughes⁴ to be applicable for N-chloroacetanilide, the production of chlorine being a two step process according to the following equations:-

and finally in the presence of phenol:

The above series of reactions are known as the Orton-Hughes Mechanism.

Carr⁵ studied the acid catalysed reaction between several N-chloro compounds and phenol in an attempt to discover the applicability of the Orton mechanism. He found that N-chloroacetamide and N-chlorosuccinimide reacted by the above mechanism, hydrochloric acid being specific in causing a considerable increase in the observed rate of reaction. The kinetics of N-chloromorpholine chlorination, however, proved to be quite different, the rate being dependent on the phenol concentration and independent of the chloride ion concentration. Hydrochloric acid and perchloric acid were therefore equally good catalysts. Carr proposed a rate expression which he associated with the mechanism:

where (6) was shown to be rate determining.

This mechanism cannot be generalised, however, Dixon⁶ having demonstrated that the chlorination of benzyl alcohol by N-chloromorpholine proceeded largely by the Orton mechanism, the reaction not going in the presence of perchloric acid. Benzyl alcohol is much less reactive than phenol and any chlorination by the "Carr" mechanism is much slower than in the case of phenol.

The full understanding of the efficiency of different N-

chloro compounds as chlorinating agents in the presence of acids requires a precise knowledge of both the equilibrium hydrolysis constant and the equilibrium constant K_2 .

Much work has been done on the measurement of the equilibrium hydrolysis constants of halogenoamines, defined as $K_H = \frac{[:NH][HOCl]}{[:NCl]}$. The methods used include:-

- (a) distillation and solubility measurements⁷
- (b) absorption spectroscopy^{8,9}
- (c) displacement of the equilibrium by the removal of the hydrolysis products¹⁰
- (d) kinetic measurements¹¹

Very little information exists on the measurement and final values of K_2 , defined as $K_2 = \frac{[:NH][Cl_2]}{[:NCl][H^+]^2[Cl^-]}$. This function can readily be derived from equations 1 and 2 in the "Orton-Hughes" mechanism.

K_2 can be directly related to K_H by the relationship $K_H = K_2 \cdot K'$ where K' is the equilibrium constant for the hydrolysis of chlorine, that is $K' = \frac{[H^+][Cl^-][HOCl]}{[Cl_2]}$. Because of the importance of N-chloro compounds as chlorinating agents it was necessary to provide more information on the above functions, and the present chapter describes the work carried out on this aspect, particular reference being made to N-chloromorpholine and the related compound N-chloropiperidine. The treatment of N-chloroacetanilide and other amides and imides will be included in Chapter 4.

EXPERIMENTAL

EXPERIMENTAL

(A) Measurement of the equilibrium chlorine concentration by spectroscopy.

Robb¹² attempted to measure the chlorine concentration existing in equilibrium with hydrochloric acid solutions of N-chloroacetamide and N-chlorosuccinimide by studying the ultraviolet absorption spectrum of the reaction mixtures in the region 3000Å to 3600Å. Under such acid conditions, chlorine exhibits a characteristic peak at approximately 3250Å. Unfortunately, the N-chloroacetamide solutions were subject to considerable decomposition, the presence of nitrogen trichloride being suspected which interfered with the normal chlorine spectrum. Figure 3.1 illustrates the spectrum of chlorine in both water and acid solution, the presence of water causing hydrolysis to hypochlorous and hydrochloric acids according to the equilibrium.

(The hydrolysis equilibrium constant of this reaction has been measured by many workers, the most recent being due to Cornick and Yuan-Tsen Chia¹³ who accurately determined the value from 0° - 45° using a conductivity method. Their value, $3.944 \pm 0.020 \times 10^{-4}$ at 25°C, being used to calculate the amount of unhydrolysed chlorine existing in aqueous solution Figure 3.2).

Examination of hydrochloric acid solutions of N-chloro-

FIG. 3.1.

FIG. 3.2.

morpholine indicated a complete absence of any measurable chlorine peak at $3250\text{\AA}$, no decomposition to nitrogen trichloride being exhibited, even in concentrated acid.

Fortunately, chlorine solutions in hydrochloric acid possess a characteristic spectrum below $2900\text{\AA}$,¹⁴ due to the formation of the trichloride ion by the reaction

The presence of this trichloride ion was unfortunately neglected in the work of Robb (loc.cit.).

The value of the equilibrium constant for the formation of the trichloride ion was accurately calculated by Sherrill and Izard¹⁵ from the effect of hydrochloric acid on the solubility of chlorine in water. A more precise value has been obtained by Zimmerman and Strong¹⁶ as a result of spectroscopic measurements. They give

$$K_3 = \frac{[\text{Cl}_3^-]}{[\text{Cl}_2][\text{Cl}^-]} = 0.191 \pm .016 \text{ at } 25^\circ\text{C}.$$

(A graphical relationship between the trichloride ion concentration and the free chlorine existing in solutions containing chloride ion is depicted in Figure 3.3). Before the work of these authors, the absorption spectra of aqueous chlorine and the trichloride ion had not been properly separated in pure water and even in concentrated sulphuric acid there being considerable contribution to the net absorption spectrum of chlorine by the Cl_3^- ion. This effect is

especially prominent at wavelengths less than $2800\text{\AA}$.

The spectrum of the trichloride ion exhibits a characteristic peak at $2280\text{\AA}$, the value of the E_{max} being sufficiently large to enable the detection of very low chlorine concentrations in hydrochloric acid. Table 3.1 lists the values found in the present work for the extinction coefficient of the trichloride ion at 25°C . Measurements were made by adding the chlorine solution, kept in a burette, directly into the silica cells (1 cm or 0.2 cm) maintained at 25°C in a thermostated cell holder.

Analysis of the chlorine concentration was accomplished by adding 10 ml aliquots to potassium iodide and titrating the liberated iodine with standard sodium thiosulphate. Alternate optical density and analytical measurements were made on each sample, the average values being given in the table. By this method the error due to chlorine loss was substantially reduced.

Table 3.1

E_{max} for Cl_3^- at $2280\text{\AA}$
(E of Cl_2 at $2280\text{\AA} = 127.5$)

HCl M	Cell thickness (cm)	E Cl_2	O.D	$E_{\text{max}} \text{Cl}_3^-$
0.574	1.0	4.96×10^{-4}	0.074	14,005
0.745	0.2	5.95×10^{-3}	2.150	13,684
0.745	1.0	2.39×10^{-4}	0.417	14,396
0.745	1.0	4.24×10^{-4}	0.728	14,190

HCl M	Cell thickness (cm)	Cl_2	O.D	$E_{\text{max}} \text{Cl}_3^-$
2.330	0.2	1.09×10^{-3}	0.866	14,000
2.330	0.2	9.50×10^{-4}	0.842	15,320
3.480	0.2	8.49×10^{-4}	0.988	14,384
5.000	0.2	2.36×10^{-4}	0.316	13,569
5.000	0.2	5.10×10^{-4}	0.752	14,973

The mean value of E_{max} (14,280) was accepted for future calculations.

The experimental procedure adopted for the estimation of the equilibrium chlorine concentration by this method relied on the stability of the trihalide ion in solution. The optical density at $2280\text{\AA}$ of a solution of chlorine ($8.75 \times 10^{-4}\text{M}$) in hydrochloric acid (0.574M) was found to be stable over a period of 70 minutes, the maximum change in optical density being no more than $\pm 2\%$.

Solutions of N-chloromorpholine were prepared in the appropriate strength hydrochloric acid and the optical density at $2280\text{\AA}$ was recorded as a function of time to equilibrium. All measurements were made at 25°C . The equilibrium optical density was used to calculate the trichloride ion concentration, and hence the chlorine concentration by the application of the equilibrium constant $K_3 = 0.191$ at 25°C . Figure 3.4 illustrates the nature of the spectra obtained, the increase in absorption in the region $2100\text{\AA} - 2600\text{\AA}$ as a

FIG. 3.3.

FIG. 3.4.

function of acid strength being clearly evident.

Proof that the equilibrium involves hydrochloric acid was obtained by examination of the spectrum after the addition of sodium hydroxide to a solution of N-chloromorpholine in hydrochloric acid in which the equilibrium chlorine concentration had been achieved. The spectrum almost immediately returned to that of the original N-chloromorpholine. The addition of morpholine had an identical effect.

Assuming that the reactions involved are:

$$K_1 = \frac{[\text{NClMH}^+]}{[\text{NClM}][\text{H}^+]} = 0.554 \text{ mole}^{-1} \cdot \text{l.}$$

(writing NClM for N-chloromorpholine)

$$K'_1 = \frac{[\text{NH}_2^+][\text{Cl}_2]}{[\text{NClMH}^+][\text{Cl}^-][\text{H}^+]}$$

the equilibrium

$$K_3 = \frac{[\text{Cl}_3^-]}{[\text{Cl}_2][\text{Cl}^-]} = 0.191$$

then the absorbing species existing in solution are

(i) N-chloromorpholine - this compound possess a characteristic u.v. spectrum (Figure 3.5) with a peak at 2600Å.

(11) N-chloromorpholinium ion - solutions of N-chloromorpholine in perchloric acid exhibited very little spectral change (page 66), the extinction coefficient of this material being neglected.

(111) hydrochloric acid - negligible absorption in the region of measurement, $2100\text{\AA} - 3000\text{\AA}$.

(iv) morpholinium ion ($:\text{NH}_2^+$) - the spectrum of morpholine hydrochloride (Figure 3.5) showed no definite absorption in the ultra-violet region, apart from limited end absorption. The optical density contribution of this species can also be neglected.

(iv) molecular chlorine - Figure 3.1 illustrates the spectra of solutions of chlorine in both sulphuric and perchloric acids. The extinction coefficients obtained in the latter acid were used for the present work owing to the incomplete dissociation of sulphuric acid.

$3.92 \times 10^{-3}\text{M}$ chlorine in HClO_4 (1M)

Wavelength $\text{\AA}$	2100	2200	2300	2400	2500
E	336	141	66	37	22

(vi) trichloride ion (Cl_3^-) - The large value of the extinction coefficients of this ion enabled very small concentrations to be detected in solution.

Solutions of N-chloromorpholine in hydrochloric acid were analysed as follows, all measurements referring to a constant wavelength. ($2280\text{\AA}$ unless otherwise stated).

$$\text{O.D.} = E_{\text{Cl}_3^-} [\text{Cl}_3^-]_E + E_{\text{NClM}} [\text{NClM}]_E + E_{\text{Cl}_2} [\text{Cl}_2]_E \quad (4)$$

where $[Cl_3^-]_E$ = trichloride ion concentration at equilibrium
 $[NClM]_E$ = equilibrium N-chloromorpholine concentration
 $[Cl_2]_E$ = equilibrium chlorine concentration.

Now the $[Cl_2] = \frac{[Cl^-]}{0.191}$ in solutions of hydrochloric acid

in which hydrolysis to hypochlorous acid can be ignored.

The chloride ion concentration for any run may be considered constant since $[Cl^-] \gg [NClM]$.

From equation (2), the N-chloromorpholine concentration at equilibrium can be related to the initial concentration

$[NClM]_I$ by the equation

$$[NClM]_E = [NClM]_I - [Cl_2]_E - [Cl_3^-]_E - [NClMH^+]_E$$

$$\text{from (1)} \quad [NClM]_E = [NClM]_I - \frac{[Cl_3^-]_E}{0.191[Cl^-]} - [Cl_3^-]_E - KH^+[NClM]_E$$

$$\therefore [NClM]_E(1 + KH^+) = [NClM]_I - \frac{[Cl_3^-]_E}{K_3[Cl^-]} - [Cl_3^-]_E$$

Rearrangement of (4) gives

$$O.D. = E_{Cl_3^-} [Cl_3^-]_E + E_{Cl_2} \frac{[Cl_3^-]_E}{K_3[Cl^-]} + \frac{E_{NClM}}{1+KH^+} \left([NClM]_I - \frac{[Cl_3^-]_E}{K_3[Cl^-]} - [Cl_3^-]_E \right)$$

where $K = 0.554 \text{ mole}^{-1}.l.$ and $K_3 = 0.191 \text{ mole}^{-1}.l.$ (5)

Substitution of the values of the extinction coefficients measured at 2280Å:-

$$E_{Cl_3^-} = 14,280$$

$$E_{NClM} = 161$$

$$E_{Cl_2} = 83$$

followed by rearrangement leads to the equation

$$O.D = [Cl_3]_E \left\{ 14,280 + \frac{435}{[Cl^-]} - \frac{161}{1+K[H^+]} \left(1 + \frac{1}{K_3[Cl^-]} \right) \right\} + \frac{161[NClM]_I}{1+K[H^+]} \quad (6)$$

The total chlorine concentration ($\Sigma Cl_2 = [Cl_2]_E + [Cl_3]_E$),

which is equal to the equilibrium morpholinium ion concentration, was calculated by application of (3).

Combination of (1) and (2) gives

$$K_2 = KK'_1 = \frac{[NClMH^+]}{[NClM][H^+]} \cdot \frac{[NMH_2^+][Cl_2]}{[NClM^+][Cl^-][H^+]} \\ = \frac{[NMH_2^+][Cl_2]}{[NClM][H^+]^2[Cl^-]} \quad (7)$$

Substitution of the calculated values in (7) gave the equilibrium constant for the formation of chlorine by the interaction of hydrochloric acid and N-chloromorpholine in aqueous solution at 25°C. A summary of these results is given in Table 3.2.

Even though these values exhibit considerable variation, the order of K is indicated. The variation can be attributed to a combination of the following:-

- (a) loss of chlorine from solution and the instability of the trichloride ion.
- (b) decompositions of N-chloromorpholine under acid conditions.
- (c) bubble formation in the 0.2 cm cells used for the optical measurements. This difficulty was found hard to overcome in the thermostatically heated cells.

The mean value of the constants given in Table 3.2 ($9.46 \times 10^{-4.1} \text{ mole}^{-2.12}$) leads to a value of $K_1' = 17.06 \times 10^{-4} \text{ mole}^{-1.1}$.

Table 3.2.

Values of K_2 for N-chloromorpholine at 25°C.

$[\text{NClM}]_I \times 10^4 \text{M}$	$[\text{H}^+] \text{M}$	$[\text{Cl}^-] \text{M}$	O.D	$10^4 K_2 \text{ mole}^{-2.12}$
37.70	0.400	0.400	1.025	9.65
10.33	0.476	0.600	0.600	10.20
39.80	0.487	0.487	1.390	11.50
39.80	0.628	0.628	1.550	9.13
39.30	0.727	0.727	1.800	6.47
10.67	0.745	0.745	0.905	9.88
10.65	0.795	0.319	0.455	10.82
10.33	0.795	0.600	0.770	12.30
10.33	0.795	0.600	0.778	9.65
10.58	0.795	1.000	1.310	10.18
38.60	0.850	0.850	2.565	9.00
39.80	1.000	1.000	3.125	6.80

$[\text{NClM}]_I \times 10^4 \text{M}$	$[\text{H}^+] \text{M}$	$[\text{Cl}^-] \text{M}$	O.D	$10^4 K_2 \text{ mole}^{-2} \cdot \text{l}^2$
10.65	1.012	0.600	0.860	10.88
39.30	1.034	1.034	3.125	5.90
37.40	1.256	1.256	5.000	9.58

Solutions of N-chloropiperidine in hydrochloric acid (0.62M) did not exhibit the characteristic trichloride absorption at 220 - 230 μ , the spectrum being modified by the formation of the N-chloropiperidinium ion. However, the presence of a new species was indicated by slightly increased extinction coefficients at wavelengths below 260 μ . If chlorine was present in solutions of N-chloropiperidine and hydrochloric acid then the concentration must be considerably less than in the N-chloromorpholine case.

An alternative method of investigating the equilibrium chlorine concentration involved the removal of the free halogen and the analysis of the remaining N-chloro compound by titration or spectroscopy. Experiments investigating this method will now be described..

(B) Measurement of the equilibrium N-chloro concentration after the removal of chlorine.

Chlorine reacts readily with allyl alcohol and it was thought that it should be possible to add this compound to a solution containing N-chloromorpholine and hydrochloric acid.

Subsequent addition of potassium iodide and acetic acid should liberate iodine from the chloroamine only, enabling the titration of this species without interference from molecular chlorine.

The thiosulphate titre obtained after adding potassium iodide to solutions of N-chloromorpholine in perchloric, hydrochloric or acetic acids containing allyl alcohol or allyl ethyl ether showed considerable variation. In the absence of the allyl compound the N-chloromorpholine titre was found to be independent of

- (i) the amount of acid added
- (ii) the potassium iodide concentration
- (iii) the nature of the acid
- (iv) the order of addition of the acid or potassium iodide to the chloroamine.

However, when N-chloromorpholine in water was added to a solution of allyl alcohol (or allyl ethyl ether) followed by acid and potassium iodide, the titre was found to have decreased by approximately 20-30 %. Reversal of the order of addition of the iodide and acid also decreased the titre but to a lesser degree (10%). The titre was found to be almost independent of the amount of the allyl compound added.

The above phenomena can be simply explained. When the hydrochloric acid is added before the iodide, chlorine is produced, which reacts with the allyl compound present. When the iodide is added first, followed by the subsequent

addition of acid, the discrepancy in expected titre can be explained by accepting the presence of a reactive compound which readily attacks the unsaturated allyl compound. Such a compound is iodine monochloride, its existence in solution being confirmed by the following experiments.

N-chloromorpholine was dissolved in perchloric acid and potassium iodide was added. The sodium thiosulphate titre of this solution was found to be 18.83 ml. N-chloromorpholine was then mixed with perchloric acid and potassium iodide, and this solution added to solutions containing, 0.1, 0.2 and 0.3 ml of redistilled allyl ethyl ether. The sodium thiosulphate titres of the resulting mixtures were found to be 18.11, 17.47 and 15.66 ml. respectively. Free iodine in potassium iodide was found to be perfectly stable in the presence of allyl ethyl ether and allyl alcohol, no change in titre being detected even after the addition of perchloric, hydrochloric and acetic acids.

Iodination by a chloroamine and an iodide is not new. Bradfield, Orton and Roberts¹⁸ in 1928 described the preparation of iodine monochloride by the slow addition of hydrogen iodide to an acetic acid solution of dichloramine-T, the reaction taking place being

The first reaction of hydrogen iodide liberating iodine

The hydrochloric acid so formed reacts with another mole of

the chloramine, producing molecular chlorine, which immediately reacts with the iodine to form the monochloride. An alternative more satisfactory method described by these authors, was to add sodium iodide to an acetic acid solution of the dichloramine-T, little or no liberation of free iodine occurring.

White and Robertson¹⁹ investigated the addition of iodine monochloride to many unsaturated compounds, demonstrating that the termolecular mechanism of halogen addition previously demonstrated for bromine and iodine was also applicable to their monochloride. There is an extensive literature on the use of iodine monochloride for the quantitative measurement of unsaturation but kinetic studies are lacking. The influence of hydrochloric acid on the addition of iodine monochloride has been quantitatively examined, the ion ICl_2^- being stable in aqueous solution²⁰. Very little information exists for the reaction in organic solvents. The marked change on colour produced when hydrochloric acid is added to iodine monochloride in acetic acid indicates formation of HICl_2 , the presence of hydrochloric acid thus stabilizing the compound and preventing hydrolysis²¹, while also reducing the rate of addition of the monochloride to unsaturated compounds. This phenomenon explains the greater drop in titre in the presence of perchloric acid than in hydrochloric acid when potassium iodide was added to the acid solutions of N-chloromorpholine containing allyl compounds. A general comparison of the rates of addition of

the halogen species is given in Table 3.3, indicating the efficiency of iodine monochloride as a halogenating species.

Table 3.3.

I_2	IBr	ICl	Br ₂	BrCl
1	3×10^3	10^5	10^4	4×10^6

Comparison with chlorine is not possible owing to the different mechanism for this halogen, however, the addition of iodine monochloride, like that of chlorine, is not reversible.

Final confirmation of the presence of iodine monochloride in solutions of N-chloromorpholine to which potassium iodide and acid had been added was obtained from the following two experiments.

(1) Jones and Richardson²² have shown that 2,4 dihalogenophenols, 3-nitro-p-cresol and 3- and 6-hydroxy-2-naphthoic acids give excellent yields of the mono-iodo derivatives when treated with iodine monochloride, whereas highly reactive compounds such as phenol, p-cresol and β -naphthol undergo both iodination and oxidation.

To N-chloromorpholine (0.5 gm.) dissolved in dilute acetic acid was added 2 : 4-dichlorophenol (0.5 gm.) On the slow addition of a solution of potassium iodide the initial brown colour disappeared and white crystals separated from solution. M.P 61-5-62.5°C. M.P. of 2,4 dichloro-6-iodophenol 62°C.²³. M.P. of original 2 : 4 dichlorophenol 45°C.

A mixed melting point with authentic 2 : 4-dichloro-6-iodophenol confirmed the presence of this material. The iodo compound was also isolated when potassium iodide in acetic acid was added to a solution containing N-chloromorpholine and hydrochloric acid. When a solution of 0.0244 M. iodine monochloride was allowed to react with allyl ethyl ether (0.025M) the reaction was rapid, the iodine monochloride titre as a function of time being illustrated below

t (min)	0	1	3	5	8.2	26.5
titre(ml of 0.037N thio/5 ml)	6.58	2.54	1.55	1.01	0.61	0.08

These results lead to a value of $k_3 = 1.91 \times 10^4 \text{ l.g.mole}^{-1} \text{ min}^{-2}$. 70% of the reaction was completed in 3 minutes at 25°C. Iodine monochloride does not react with morpholine itself.

(2) The ultra violet and visible spectra of a solution of N-chloromorpholine (0.00312M) in acetic acid (2M) containing potassium iodide was compared with solutions of commercial iodine monochloride (E.D.H.) dissolved in the same strength acid (Figure 3.6). The similarity of the two spectra can readily be appreciated. Included, for comparison, is the spectrum of a solution of iodine in excess potassium iodide and acetic acid.

The conclusion from the experimental work outlined above is that the iodometric titration of acid solutions of N-chloromorpholine containing halogen acceptors such as allyl alcohol and allyl ethyl ether is subject to considerable

error arising from the high reactivity of the in-situ produced iodine monochloride, a fact which could possibly explain many of the experimental anomalies found by Body²⁴.

The use of aniline to remove the chlorine was also investigated, the reaction giving hydrochloric acid which would be expected to react with a further aniline molecule to form the hydrochloride, thus, not affecting the overall acidity of the solution. Difficulty was encountered in this method, the solution turning very dark. Subsequent iodometric analysis was impossible.

Irrespective of the errors introduced by iodine monochloride formation, the use of allyl alcohol and allylethyl ether as a very approximate method of measuring the equilibrium constant, was still useful. Table 3.4. gives a list of values of K_2 found by this method.

Table 3.4

Values obtain for K_2 by removing chlorine with allyl compounds.

$[NClM]_{Initial}$ M	$[HCl]$ M	$[NClM]_{EQBM}$ M	$[Cl_2]_{EQBM}$ M	$10^3 K_2$ mole ⁻² .l ² .
3.54×10^{-2}	0.837	2.60×10^{-2}	0.94×10^{-2}	5.8
3.17×10^{-2}	0.837	1.92×10^{-2}	1.25×10^{-2}	1.4
1.95×10^{-2}	0.415	1.78×10^{-2}	1.75×10^{-3}	2.4
8.53×10^{-2}	0.637	7.65×10^{-2}	8.81×10^{-3}	3.9

(C) E.M.F. Measurements. The measurement of low concentrations of halogens in solution by utilisation of a

platinum and a glass electrode has been suggested by Bell²⁵, the method being found suitable for the detection of bromine in solution down to $10^{-9}M$. In the present work a calomel electrode was found to be superior to the glass electrode for the measurement of chlorine, provided due care was paid to the preparation of this electrode. The precautions taken by Hills and Ives²⁶ were adopted. All the glass vessels were thoroughly washed with chromic acid and hydrochloric acid/ethanol²⁷ cleaning solutions, followed by distilled water before oven drying. At a temperature of approximately $60^{\circ}C$ the reaction flask was filled with a 1% solution of Dow-Corning Silicone Fluid No.200 in redistilled carbon tetrachloride, emptied, drained and heated at $165^{\circ} \pm 10^{\circ}C$. for two hours. Repeated washings with carbon tetrachloride removed the excess unbound silicone. This procedure was only repeated following acid cleaning when the silicone film had been destroyed. The precautions necessary for the preparation of suitable calomel have been described (Chapter.7).

To avoid losses of chlorine from solution the electrodes and reaction vessel were fitted with matched ground glass joints (Figure 3.7) The calomel electrode consisted of redistilled mercury in the bottom of the vessel, covered by a thin layer of mercury/calomel prepared by shaking together a mixture of mercury (50 gm.) and calomel (2 gm.) in a flask the required mixture forming as a thin continuous film on the mercury surface where it could be readily removed intact.

FIG. 3. 5.

FIG. 3. 6.

A solution of the required strength hydrochloric acid made electrical contact with the solution through a side arm fitted with a capillary jet (E). Electrical contact with the mercury of the calomel electrode was made through a platinum wire (A) sealed through the central glass tube. External contact with this platinum wire was made via a copper wire (C) immersed in mercury (B). At the end of each measurement with constant strength acid, a small quantity of the salt bridge solution was allowed to run out of (E) by opening stop cock (D). The size of the capillary (E) was such that no diffused chlorine could be detected by colourimetric analyses in the calomel electrode solution after each experiment.

The platinum electrode was extremely simple, consisting of a platinum wire (A) connected to a copper wire (C) by means of a mercury pool (B).

E.M.F. measurements were made with a Muirhead D972A D.C. Potentiometer which was calibrated with a Pye Cadmium Cell (1.086 volts at 20°C. Temp. Coefficient 0.00004/°C). Electrical balance was detected with a sensitive mirror galvanometer (Type A. S. 4; Tinsley and Co.) The accuracy of voltages measured was ± 0.1 millivolts.

The oxidation potentials of these two electrodes for the measurement of chlorine in chloride solution are given below for ions of unit activity and gas pressures of one atmosphere. The potentials are designated by E^0 , measured in absolute volts, and all values are given for 25°C.

Normal calomel electrode ($\text{KCl} = 1 \text{ mole.litre}^{-1}$)

$$E^\circ = -0.2802 \text{ volts}$$

Pt, $\text{Cl}_2(\text{g})$; Cl^- electrode

$$E^\circ = -1.3595 \text{ volts}$$

Under standard conditions the reactions will proceed in the directions indicated below

The overall reaction

$$\text{From } \Delta F^\circ = -nFE^\circ$$

$$= \frac{-(96,500)(1.0793)}{4.184}$$

$= -24,800 \text{ cal}$, it can be seen that the reaction will be spontaneous in the direction written

Furthermore $\Delta F^\circ = -RT \ln K$ from which mathematical rearrangement leads to

$$E = E^\circ - \frac{RT \ln Q}{nf}$$

where Q represents the activity quotient, that is, the ratio of the activities of the products to the activities of the reactants at any specified activities.

Thus for the reaction

$$E = E^{\circ} - \frac{RT}{nF} \ln \frac{(\text{aHg}_2\text{Cl}_2)^{\frac{1}{2}}}{\text{aHg} \cdot (\text{aCl}_2)^{\frac{1}{2}}}$$

$$E = E^{\circ} - \frac{RT}{nF} \ln \frac{1}{(\text{aCl}_2)^{\frac{1}{2}}}, \quad \text{the activity of the solids}$$

being unity. Furthermore, in dilute solution (a condition which applies in the present work) the activity may safely be assumed to equal the concentration, thereby giving

$$E = E^{\circ} - \frac{RT}{nF} \ln \frac{1}{\text{Cl}_2^{\frac{1}{2}}} \quad (n = 1)$$

$$= E^{\circ} + \frac{RT}{2F} \ln [\text{Cl}_2]$$

$$= E^{\circ} + 0.02955 \log [\text{Cl}_2]$$

and thus the E.M.F. at any fixed acid strength is directly proportional to the chlorine concentration.

The experimental procedure for measuring the chlorine concentration in solutions of N-chloromorpholine and N-chloropiperidine in hydrochloric acid was as follows.

A calomel electrode containing the same strength acid (XM) as used in the reaction mixture was prepared, and the electrode allowed to stand in a constant temperature water bath, together with 45.0 ml. of hydrochloric acid ($\frac{50}{45} \times M$) contained in the reaction flask. At zero time an aqueous solution of N-chloromorpholine (5 ml) was added to the three necked vessel. After placing the electrodes in the solution the E.M.F. was measured as a function of time until equilibrium was attained.

For each acid strength (XM) used, a calibration curve of

E.M.F. as a function of the chlorine concentration was previously obtained by adding 5 ml, 4 ml, 3 ml, 2 ml and 1 ml of an aqueous solution of chlorine to 45 ml of hydrochloric acid ($\frac{50}{45}XM$), water being added to make a total volume of 50 ml. The E.M.F. of each of these solutions was measured on the attainment of the thermal equilibrium (Figure 3.8). No correction for hydrolysis had to be made in the acid solutions used since even at the lowest concentration, $X = 0.316M$ only 0.44% hydrolysis occurs. The chlorine concentration was accurately measured by adding aliquots of the aqueous solution potassium iodide and titrating the liberated iodine with standard sodium thiosulphate. All chlorine solutions were delivered from an accurately calibrated burette. The chlorine concentration as a function of time for the reaction between N-chloromorpholine and hydrochloric acid (XM) could then be obtained by reference to the standard graphs given above. However, greater accuracy was obtainable by utilisation of the equation

$$E = E_0 + \frac{RT}{2F} \log_{10} [Cl_2] \quad (8)$$

Examination of this equation shows that the slope of a graph of the chlorine concentration as a function of E.M.F. should be equal to $\frac{RT}{2F}$ (theoretically 0.02955 at 25°C), thus from the slopes of the standard graphs values of this quantity ranging from 0.0298 to 0.0303 were obtained, the maximum error from the theoretical value being approximately + 2%.

The value of E^0 for each acid strength was obtained by

substituting the values of E , $\frac{RT}{2F}$ and $\log_{10}[\text{Cl}_2]$ in equation (8) for three values of E , through which the graph passed. The value of E_0 used was the average of the three calculated values.

The equations used are given below.

[HCl]	Equation
0.316 M	$E = 1.1224 + 0.02980 \log_{10} \text{Cl}_2$
0.491 M	$E = 1.1236 + 0.02997 \log_{10} \text{Cl}_2$
0.602 M	$E = 1.1223 + 0.02984 \log_{10} \text{Cl}_2$
0.875 M	$E = 1.1257 + 0.03033 \log_{10} \text{Cl}_2$

The results obtained by application of the E.M.F. method to the measurement of the chlorine concentrations existing in solutions of N-chloromorpholine and hydrochloric acid follow. All measurements were made at 25°C.

A measure of the approximate error likely to be introduced in the results by loss of chlorine through evaporation was obtained by dissolving a known concentration of chlorine in 0.617N hydrochloric acid and measuring the E.M.F. as a function of time. Table 3.5 summarises the result (also Fig. 3.9).

Table 3.5

Loss of Chlorine from 0.617M hydrochloric acid

Time (min)	E.M.F.	$[\text{Cl}_2] \times 10^4 \text{M}$	% loss of Cl_2
0	1.0605	69.9	-
5	1.0601	68.4	2.2

FIG 3.7.

FIG. 3.8

Time (min)	E.M.F.	$[\text{Cl}_2] \times 10^4 \text{M}$	% loss of Cl_2
10	1.0600	68.1	2.6
17	1.0600	68.1	2.6
26	1.0599	67.6	3.3
43	1.0597	66.8	4.3
60	1.0596 ₅	66.0	5.6
85	1.0594	64.8	7.3
110	1.0593	63.9	8.6
182	1.0590	63.0	9.9
200	1.0589	62.3	11.0
250	1.0585	60.9	13.0
295	1.0583	60.2	14.1

N-Chloromorpholine

Run 1

[Hydrochloric acid]	0.491M
[N-chloromorpholine]	$2.80 \times 10^{-3} \text{M}$.

Time (min)	E.M.F.	$[\text{Cl}_2] \times 10^4 \text{M}$
3.0	1.0015	8.43
4.0	1.0059	1.18
5.0	1.0090	1.50
6.0	1.0116	1.83
6.5	1.0125	1.96
7.0	1.0135	2.12
9.0	1.0167	2.71

FIG. 3.9.

Time (min)	E.M.F.	$[\text{Cl}_2] \times 10^4 \text{M}$
10.0	1.0179	2.97
12.0	1.0196	3.40
16.0	1.0222	4.14
18.0	1.0227	4.32
19.0	1.0232	4.47
30.0	1.0247	5.01
33.0	1.0249	5.08
60.0	1.0249	<u>5.08</u>

Run 2.

$[\text{Hydrochloric acid}] = 0.491 \text{ M}$
 $[\text{N-chloromorpholine}] = 4.78 \times 10^{-3} \text{ M}$

Time (min)	E.M.F.	$[\text{Cl}_2] \times 10^4 \text{M}$
2.0	1.0031	0.95
3.0	1.0095	1.68
4.0	1.0136	2.14
5.0	1.0166	2.69
6.0	1.0191	3.27
7.0	1.0210	3.78
8.0	1.0224 ₅	4.22
10.0	1.0246	4.98
12.0	1.0262	5.62
14.0	1.0271	6.03

Time (min)	E.M.F.	$[\text{Cl}_2] \times 10^4 \text{M}$
16.0	1.0279	6.41
21.0	1.0288	6.87
60.0	1.0288	<u>6.87</u>

Run 3.

[Hydrochloric acid]	0.491 M
[N-chloromorpholine]	$6.305 \times 10^{-3} \text{M}$

Equilibrium chlorine concentration = $7.96 \times 10^{-4} \text{M}$ after 33 min.

Run 4.

[Hydrochloric acid]	0.491 M
[N-chloromorpholine]	$7.525 \times 10^{-4} \text{M}$

Equilibrium chlorine concentration = $2.39 \times 10^{-4} \text{M}$ after 57.0 min.

Run 5.

[Hydrochloric acid]	0.491 M
[N-chloromorpholine]	1.163×10^{-3}

Equilibrium chlorine concentration = $3.06 \times 10^{-4} \text{M}$ after 40 min.

Run 6.

[Hydrochloric acid]	0.602 M
[N-chloromorpholine]	$8.02 \times 10^{-4} \text{M}$

Time (min)	E.M.F.	$[\text{Cl}_2] \times 10^4$
2.5	0.9875	0.30
4.0	0.9960	0.58
5.0	0.9992	0.75
6.0	1.0017	0.91
7.0	1.0039	1.08
8.0	1.0057	1.24
9.0	1.0073	1.40
10.0	1.0084	1.52
11.0	1.0095	1.66
13.0	1.0115	1.94
14.0	1.0123	2.06
16.0	1.0135	2.25
18.0	1.0148	2.50
20.0	1.0156	2.66
25.0	1.0171	2.98
28.0	1.0176	3.10
39.0	1.0187	<u>3.38</u>

Run 7.

[Hydrochloric acid] 0.602 M

[N-chloromorpholine] $5.01 \times 10^{-3} \text{M}$

Equilibrium chlorine concentration = $11.17 \times 10^{-4} \text{M}$ after
20 min.

Run 8.

[Hydrochloric acid] 0.602 M

[N-chloromorpholine] $2.24 \times 10^{-3} \text{M}$

Equilibrium chlorine concentration = $7.08 \times 10^{-4} \text{M}$ after 29.0 min.

Run 9.

[Hydrochloric acid] 0.316 M

[N-chloromorpholine] $4.17 \times 10^{-3} \text{M}$

Time (min)	E. M. F.	$[\text{Cl}_2] \times 10^4$
3.0	0.9930	0.45
4.0	0.9984	0.69
5.0	1.0023	0.93
6.0	1.0055	1.19
7.0	1.0074	1.38
8.0	1.0092	1.59
9.0	1.0109	1.82
10.0	1.0120	1.82
11.0	1.0131	2.15
12.0	1.0141	2.32
13.0	1.0150	2.49
17.0	1.0169	2.88
19.0	1.0173	2.97
22.0	1.0182	<u>3.19</u>

Run 10

[Hydrochloric acid]	0.316 M
[N-chloromorpholine]	$5.82 \times 10^{-3} \text{M}$

Equilibrium chlorine concentration $4.05 \times 10^{-4} \text{M}$ after
26 min.

Run 11.

[Hydrochloric acid]	0.316 M
[N-chloromorpholine]	$10.96 \times 10^{-3} \text{M}$

Equilibrium chlorine concentration $5.47 \times 10^{-4} \text{M}$ after
19 min.

Run 12.

[Hydrochloric acid]	0.617 M
[N-chloromorpholine]	$7.33 \times 10^{-3} \text{M}$

Time (min)	E.M.F.	$[\text{Cl}_2] \times 10^4$
2.0	1.0168	2.92
3.0	1.0225	4.52
4.0	1.0262	6.02
5.0	1.0291	7.53
6.0	1.0310	8.72
7.0	1.0326	9.86
8.0	1.0338	10.81
9.0	1.0347	11.60
10.0	1.0353	12.14
11.0	1.0360	12.82

Time (min)	E.M.F.	$[Cl_2] \times 10^4$
12.0	1.0364	13.22
14.0	1.0370	13.85
16.0	1.0373	14.18
18.0	1.0375	14.40
20.0	1.0375	<u>14.40</u>

From these results the values of K_2 and K_1' for the reaction between N-chloromorpholine and hydrochloric acid were calculated. A summary of the results is given in Table 3.6. The variation of K_2 with acid strength is clearly evident, a similar phenomena being noted by Dixon and Carr in their studies on the chlorination by the N-chlere compounds.

Table 3.6

$[HCl]_M$	$[NClM]_{init} \times 10^3 M$	$\Sigma [Cl_2]_{eqbm.} \times 10^4 M$	$10^4 K_2^* \text{ mole}^{-2} l^2$	$10^4 K_1' \text{ mole}^{-1} l.$
0.316	4.17	3.19	9.25 (8.38)	16.70
0.316	5.82	4.05	9.05 (9.60)	16.34
0.316	10.96	5.47	9.06 (9.11)	16.35
0.491	0.75 ₃	2.39	10.90 (9.40)	19.71
0.491	1.16	3.06	10.70 (9.23)	19.35
0.491	2.80	5.08	10.80 (9.51)	19.52
0.491	4.78	6.87	11.18 (9.74)	20.20
0.491	6.31	7.96	10.80 (9.72)	19.52
0.602	0.80 ₂	3.38	13.38 (11.29)	24.20

$[HCl] M$	$[NClM]_{init}$ $\times 10^3 M$	$\Sigma [Cl_2]_{eqbm.}$ $\times 10^4 M$	$10^4 K_2^*$ mole $^{-2.12}$	$10^4 K_1'$ mole $^{-1.1}$
0.602	2.24	7.08	17.70 (15.00)	32.00
0.602	5.01	11.17	17.30 (14.69)	31.25
0.617	7.33	14.40	17.60 (14.98)	31.81

*Corrections have been made for Cl_3^- formation and the presence of the N-chloromorpholinium ion. The values in brackets are uncorrected.

Values of the equilibrium constant were also obtained by investigating the reverse reaction between morpholine and chlorine in hydrochloric acid (Fig. 3.10; Fig. 3.11). The longer time needed for the attainment of chemical equilibrium in these cases introducing errors due to loss of chlorine by evaporation.

Run 13.

$[Morpholine]$	$3.79 \times 10^{-3} M.$
$[Cl_2]$	$3.74 \times 10^{-3} M.$
$[HCl]$	0.491 M

Time (min)	E. M. F.	$[Cl_2] \times 10^3$
2.0	1.0446	2.296
3.0	1.0419	1.879
4.0	1.0399	1.611
6.0	1.0362	1.213
7.0	1.0350	1.107

FIG. 3-10.

FIG. 3-12.

Time (min)	E.M.F.	$[\text{Cl}_2] \times 10^3$
9.0	1.0327 ₅	0.927
11.0	1.0313	0.832
14.0	1.0294	0.718
17.0	1.0283	0.661
20.0	1.0276	0.627
30.0	1.0261	0.559
35.0	1.0256	0.537
43.0	1.0251	0.518
51.0	1.0245	0.493
65.0	1.0245	0.493

$$K_2 = 7.31 \times 10^{-4} \text{ mole}^{-2.1^2}$$

$$K_1' = 13.22 \times 10^{-4} \text{ mole}^{-1.1.}$$

Run 14.

[Morpholine]	$2.13 \times 10^{-3} \text{ M}$
$[\text{Cl}_2]$	$2.15 \times 10^{-3} \text{ M}$
[HCl]	0.491 M

Time (min)	E.M.F.	$[\text{Cl}_2] \times 10^3$
0.0	1.0438	2.173
2.5	1.0386	1.694
3.0	1.0376	1.352
4.0	1.0357	1.170
5.0	1.0344	1.054

Time (min)	E. M. F.	$[Cl_2] \times 10^3$
6.0	1.0330	0.950
7.0	1.0317	0.860
8.0	1.0305	0.783
9.0	1.0297	0.736
10.0	1.0288	0.687
12.0	1.0272	0.607
14.0	1.0260	0.555
16.0	1.0250	0.512
21.0	1.0230	0.441
26.0	1.0220	0.408
35.0	1.0208	0.372
60.0	1.0194	0.334
70.0	1.0194	0.334

$$K_1' = 10.92 \times 10^{-4} \text{mole}^{-1} \cdot l.$$

$$K_2 = 6.07 \times 10^{-4} \text{mole}^{-2} \cdot l^2.$$

Run 15.

$$[\text{Morpholine}] \quad 3.67 \times 10^{-3} M$$

$$[Cl_2] \quad 3.68 \times 10^{-3} M$$

$$[HCl] \quad 0.602 \quad M$$

Time (min)	E. M. F.	$[Cl_2] \times 10^3$
2.5	1.0445	2.472
3.0	1.0433	2.254
4.0	1.0416	1.959

FIG. 3.41.

Time (min)	E. M. F.	$[Cl_2] \times 10^3$
5.0	1.0400	1.746
6.0	1.0385	1.556
7.0	1.0374	1.429
8.0	1.0363	1.312
9.0	1.0355	1.233
10.0	1.0347	1.159
11.0	1.0340	1.099
12.0	1.0335	1.057
13.0	1.0330	1.016
14.0	1.0326	0.986
16.0	1.0318	0.927
25.0	1.0305	0.839
30.0	1.0301	0.815
40.0	1.0301	0.815

$$K_2 = 12.6 \times 10^{-4} \text{mole}^{-2.12}$$

$$K'_1 = 22.80 \times 10^{-4} \text{mole}^{-1.1.}$$

Run 16.

[Morpholine]	$3.465 \times 10^{-3} M.$
$[Cl_2]$	$3.465 \times 10^{-3} M$
[HCl]	0.316 M

Time (min)	E. M. F.	$[Cl_2] \times 10^3$
2.5	1.0390	1.590
3.0	1.0373	1.394

Time (min)	E.M.F.	$[\text{Cl}_2] \times 10^3$
4.0	1.0342	1.097
5.0	1.0320	0.926
6.0	1.0300	0.793
7.0	1.0281	0.685
8.0	1.0267	0.615
9.0	1.0250	0.539
10.0	1.0239	0.495
15.0	1.0195	0.352
20.0	1.0168	0.286
25.0	1.0155	0.259
30.0	1.0156	0.257

$$K_2 = 7.20 \times 10^{-4} \text{mole}^{-2.1^2}$$

$$\underline{K'_1 = 13.08 \times 10^{-4} \text{mole}^{-1.1.}}$$

In the absence of hydrochloric acid, the reaction between morpholine hydrochloride and chlorine is interesting in that the equilibrium lies almost quantitatively to the right according to the equation.

This was demonstrated (a) Spectroscopically. A solution of morpholine hydrochloride ($4.83 \times 10^{-3}\text{M}$) was added to an equal volume of chlorine water ($4.83 \times 10^{-3}\text{M}$) and the ultra-violet

spectrum measured as a function of time. The spectrum was stable three minutes after mixing and was shown to be identical to that of N-chloromorpholine ($2.39 \times 10^{-3}M$). Thus the reaction had proceeded 99.3% to completion. A repeat experiment gave 100.2% conversion to N-chloromorpholine in three minutes.

(b) by E.M.F. 0.111M sodium chloride (90 ml) was added to a standard flask and the solution allowed to attain thermal equilibrium in a constant temperature water bath ($25^{\circ}C$). Morpholine hydrochloride (5 ml of $4.83 \times 10^{-2}M$) was added followed by an aqueous chlorine solution (5 ml of $7.14 \times 10^{-2}M$). The E.M.F. was found to be stable at 1.0224V after three minutes.

The E.M.F. of standard solutions of chlorine in 0.100M sodium chloride are given in Table 3.7.

Difficulty arises with the calculations owing to the hydrolysis of chlorine in the presence of sodium chloride according to the equation

The plot of $\log_{10} Cl_2$ as a function of E.M.F. had a slope of 0.0496 instead of the conventional 0.0296.

If the amount of chlorine which hydrolyses is denoted by X then

$$\frac{X^2(0.1 + X)}{(Cl_2 - X)} = 3.94 \times 10^{-4}$$

giving the actual concentration of chlorine present ($Cl_2 - X$) (Table 3.7).

Table 3.7

Apparent and actual chlorine concentrations as a function of E.M.F. in 0.1 M NaCl at 25°C.

E.M.F.	Apparent $[\text{Cl}_2] \times 10^4$	Actual $[\text{Cl}_2] \times 10^4$
0.9627	2.125	0.075
1.0020	6.205	0.755
1.0120	11.590	2.190
1.0124	12.400	2.450
1.0276	24.850	7.550
1.0321	31.000	10.500
1.0431	57.900	25.800

The plot of $\log_{10} [\text{Cl}_2]_{\text{actual}}$ as a function of E.M.F. had a slope of 0.0291.

Considering the reaction between chlorine and morpholine hydrochloride already cited, if all the morpholine hydrochloride was chlorinated the excess chlorine concentration should equal

$$(3.57 - 2.415) \times 10^{-3} \text{M.}$$

$$= 1.155 \times 10^{-3} \text{M}$$

and the hydrochloric acid produced should be $4.830 \times 10^{-3} \text{M}$.

Letting $[\text{HOCl}] = X$

$$\text{gives } [\text{H}^+] = X + 4.830 \times 10^{-3} \text{M}$$

$$[\text{Cl}^-] = 0.1 + X + 4.830 \times 10^{-3} \text{M.}$$

$$[\text{Cl}_2] = 1.155 \times 10^{-3} - X$$

then

$$\frac{X(0.1 + 4.83 \times 10^{-3} + X)(4.83 \times 10^{-3} + X)}{1.155 \times 10^{-3} - X} = 3.94 \times 10^{-4}$$

Solving for X gives 5.06×10^{-4} , making the equilibrium chlorine concentration $6.49 \times 10^{-4}M$. From the graph the E.M.F. = 1.0225, which compares well with the value 1.0224 found experimentally, indicating that the original reaction proceeded completely to the right, producing N-chloromorpholine in quantitative yield.

Data relating to the rate of chlorine formation in the reaction between N-chloromorpholine and hydrochloric acid was obtained by plotting the chlorine concentration as a function of time for each acid strength used. (Figures 3.12, 3.13, 3.14).

Consideration of the reaction in which chlorine was produced by interaction of the N-chloromorpholinium ion and the chloride ion.

leads to a rate of chlorine production

$$\begin{aligned} \frac{d(Cl_2)}{dt} &= k [NClMH^+][Cl^-] \\ &= kK [NClM][H^+][Cl^-] \\ &= k_{111} [NClM][H^+][Cl^-] \end{aligned} \quad (10)$$

$$\text{where } K = \frac{[NClMH^+]}{[NClM][H^+]} = 0.554$$

From (10) it can be seen that the rate of chlorine production is dependent on the concentration of N-chloromorpholine, the hydrogen ion and the chloride ion. From the slopes of the graphs of chlorine concentration as a function of time, values of k_{111} were obtained, k_{111} being the third order rate

FIG 3.13.

FIG 3.14.

constant of any chlorination reaction of N-chloromorpholine proceeding exclusively through molecular chlorine and free of side effects due to chlorination by the N-chloromorpholinium ion itself.

$$\text{Hence } k_{111} = \frac{\text{slope}}{[\text{NClM}][\text{H}^+][\text{Cl}^-]} \quad (11)$$

This equation is only applicable for the initial stages of the reaction where the N-chloromorpholine concentration may be regarded as equal to the initial concentration and the graph of the chlorine concentration as a function of time can be considered linear. The data obtained by application of (11) will be more accurate for the lower strength acids because of the lower chlorine concentrations existing at equilibrium. The values of k_{111} found for N-chloromorpholine are summarised in Table 3.8.

Table 3.8

$\frac{[\text{HCl}]_1}{\text{mole.l}^{-1}}$	$\frac{[\text{NClM}] \times 10^3}{\text{mole.l}^{-1}}$	$\frac{d[\text{Cl}_2]}{dt} \times 10^7$ mole.l ⁻¹ .sec ⁻¹	$k_{111} \times 10^4$ mole ⁻² .l ² sec ⁻¹
0.316	4.170	3.58	8.83
0.316	5.820	5.52	9.50
0.316	10.960	9.91	9.05
0.491	0.753	1.45	7.99
0.491	1.163	2.31	8.25
0.491	2.800	4.94	7.31
0.491	4.780	8.75	7.58
0.491	6.305	11.07	7.28

$[HCl]$	$[NClM] \times 10^3$	$\frac{d[Cl_2]}{dt} \times 10^7$	$k_{111} \times 10^4$
mole.l ⁻¹	mole.l ⁻¹	mole.l ⁻¹ .sec ⁻¹	mole ⁻² .l ² sec ⁻¹
0.602	0.802	2.56	8.83
0.602	2.240	6.32	7.79 ₅
0.602	5.012	16.50	9.12
0.617	7.331	24.83	9.37

These values of k_{111} may be satisfactorily compared with those obtained by Dixon²⁸ from his investigation of the hydrochloric acid catalysed chlorination of anisole and benzyl alcohol by *N*-chloromorpholine. Dixon obtained strong evidence for the Orton-Hughes mechanism but unfortunately there appears to exist in both cases a number of significant side effects for which allowance had to be made. The necessity to use a different solvent in the case of anisole made comparison between the two sets of k_{111} values differ but it was significantly clear that they were of a similar magnitude.

Thus

	$PhCH_2OH$	$PhOCH_3$
$[HCl]$	1.028M	1.032M
Solvent	water	10% dioxan
k_{111}	1.30×10^{-3}	2.09×10^{-3}

Dixon showed that for anisole, 10% dioxan increased the value of k_{111} by approximately 60%.

Several runs were carried out in which the chloride ion concentration was varied independently of the hydrogen ion

concentration, this procedure necessitating the calibration of the electrodes for each system used.

Thus

$$[H^+] = 0.320M.$$

$$[Cl^-] = 0.498M. \quad @ 25^{\circ}C$$

$[Cl_2] \times 10^4 M$	6.31	18.91	31.50	3.46
E. M. F.	1.0301	1.0443	1.0498	1.0220

and

$$[H^+] = 0.320M$$

$$[Cl^-] = 0.602M \quad @ 25^{\circ}C$$

$[Cl_2] \times 10^4$	1.46	2.92	6.23	18.71	31.10
E. M. F.	1.0128	1.0210	1.0292	1.0431	1.0495

Run 17

$$[H^+] = 0.320M$$

$$[Cl^-] = 0.498M$$

$$[N\text{-chloromerpholine}] = 5.21 \times 10^{-3}M$$

Time (min)	E. M. F.	$[Cl_2] \times 10^4$
2.0	1.0014	0.74
3.0	1.0075	1.18
4.0	1.014	1.58
5.0	1.0141	1.94
6.0	1.0164	2.31
7.0	1.0185	2.71
8.0	1.0198	2.98
9.0	1.0210	3.27
10.0	1.0220	3.52
12.0	1.0232	3.84

Time (min)	E. M. F.	$[Cl_2] \times 10^4$
14.0	1.0242	4.16
17.0	1.0251	4.43
20.0	1.0256	4.61
33.0	1.0260	4.75
40.0	1.0259	4.74 ₅

Equilibrium $[Cl_2] = 4.75 \times 10^{-4} M.$

$$K_2 = KK'_1 = 10.99 \times 10^{-4} \text{mole}^{-2.1^2}$$

$$\therefore K'_1 = 19.80 \times 10^{-4} \text{mole}^{-1.1.}$$

Slope of graph of $[Cl_2]$ as a function of time = $6.57 \times 10^{-7} \text{mole.l}^{-1}.\text{sec}^{-1}$; giving $k_{111} = \frac{\text{slope}}{[NClM][H^+][Cl^-]} = \underline{7.90 \times 10^{-4} \text{mole}^{-2.1^2}}.$

Run 18 $[H^+] = 0.320M$
 $[Cl^-] = 0.498M$
 $[N\text{-chloromorpholine}] = 8.43 \times 10^{-3}M$

Equilibrium $[Cl_2] = 6.01 \times 10^{-4}M$
 $K_2 = KK'_1 = 9.69 \times 10^{-4} \text{mole}^{-2.1^2}$
 $\therefore K'_1 = \underline{17.80 \times 10^{-4} \text{mole}^{-1.1.}}$

Slope of the graph of $[Cl_2]$ as a function of time = $10.3 \times 10^{-7} \text{mole.l}^{-1}.\text{sec}^{-1}$; thus $k_{111} = \underline{7.82 \times 10^{-4} \text{mole}^{-2.1^2}}.$

Run 19 $[H^+] = 0.320M$
 $[Cl^-] = 0.602M$
 $[N\text{-chloromorpholine}] = 8.25 \times 10^{-3}M$

Time (min)	E.M.F.	$[Cl_2] \times 10^4$
1.5	1.0020	0.60
2.0	1.0070	0.91
2.5	1.0109 ₅	1.27
3.0	1.0138	1.59
4.0	1.0179	2.27
5.0	1.0210	2.94
6.0	1.0230	3.51
7.0	1.0247	4.00
8.0	1.0250	4.13
9.0	1.0270	4.88
10.0	1.0277	5.16
11.0	1.0282	5.40
12.0	1.0288	5.65
13.0	1.0290	5.75
20.0	1.0302	6.37
30.0	1.0302	6.37

Equilibrium $[Cl_2] = 6.37 \times 10^{-4} M$

$$K_2 = KK_1' = 9.03 \times 10^{-4} \text{ mole}^{-2.12}.$$

$$\therefore K_1' = 16.30 \times 10^{-4} \text{ mole}^{-1.1}.$$

Slope of graph of $[Cl_2]$ as a function of time = 11.31×10^{-7}
 $\text{mole.l}^{-1}.\text{sec}^{-1}.$

$$\therefore \underline{k_{111} = 7.14 \times 10^{-4} \text{ mole}^{-2.12}.$$

<u>Run 20</u>	$[H^+]$	$= 0.320M$
	$[Cl^-]$	$= 0.602M$
	$[N\text{-chloromorpholine}]$	$= 4.2 \times 10^{-3}M$

Equilibrium chlorine concentration $= 4.39 \times 10^{-4}M$.

$$K_2 = KK_1' = 9.72 \times 10^{-4} \text{mole}^{-2}.l^2.$$

$$\therefore K_1' = 17.50 \times 10^{-4} \text{mole}^{-1}.l.$$

Slope of graph of $[Cl_2]$ as a function of time $= 5.95 \times 10^{-7}$
 $\text{mole}.l^{-1}.\text{sec}^{-1}.$

$$\therefore \underline{k_{111} = 7.37 \times 10^{-4} \text{mole}^{-2}.l^2.}$$

N-chloropiperidine

Solutions of N-chloropiperidine in hydrochloric acid were shown to contain measurable amounts of chlorine by the E.M.F. method. The results of a typical run are given below. All measurements at 25°C

[<u>N</u> -chloropiperidine]	$6.943 \times 10^{-3} \text{ M.}$
[Hydrochloric acid]	0.618 M.

Time (min)	E.M.F.	$10^6 [\text{Cl}_2] \text{ mole.l}^{-1}$
3	0.8899	0.016
6	0.9018	0.041
8	0.9260	0.26
9	0.9336	0.47
10	0.9408	0.83
11	0.9476	1.40
12	0.9526	2.06
13	0.9560	2.67
14	0.9594	3.47
16	0.9630	4.59
18	0.9661	5.83
20	0.9685	7.01
22	0.9700	7.87
32	0.9742	10.88
39	0.9760	12.51
48	0.9771	13.61
58	0.9779	14.48
70	0.9782	14.82
∞	0.9782	14.82

The results obtained by varying both the N-chloropiperidine and the hydrochloric acid concentrations are summarised in Table 3.9. The graphs of the chlorine concentration as a function of time (Figure 3.15 and 3.16) demonstrate the linear relationship existing during the initial stages of the reaction. The errors in these series of experiments are more marked due to the lower concentration of chlorine being measured.

Table 3.9

Values of k_{111} , K_2 and K_1^1 for N-chloropiperidine.

$[HCl]$ mole.l ⁻¹	$[NC1P]_{init}$ $\times 10^3$ mole.l ⁻¹	$10^5 [Cl_2]_{eqbm}$ mole.l ⁻¹	$10^7 K_2^*$ mole ⁻² .l ²	$10^7 K_1^1$ mole ⁻¹ .l	$10^5 k_{111}^e$ mole ⁻² .l ² sec ⁻¹
0.618	6.94	1.48	6.95	0.89	3.91 (2.27×10^{-5})
0.618	7.01	1.19	4.42	0.57	4.41 (2.56×10^{-5})
0.618	9.74	1.91	8.25	1.06	4.30 (2.50×10^{-5})
0.876	3.39	1.71	8.57	1.11	3.62 (2.46×10^{-5})
0.876	7.06	2.78	10.90	1.39	3.19 (2.49×10^{-5})
0.876	9.11	3.91	16.80	2.15	3.12 (2.45×10^{-5})

* Corrections have been made for the presence of the trichloride ion and the N-chloropiperidine ion (The value of $K = 7.80$ mole⁻¹.l was used).

e Values of k_{111} in brackets are those obtained by assuming a value of $[NC1P]$ equal to $\frac{[NC1P]_{init}}{1 + K[H^+]}$ in the equation

$$k_{111} = \frac{d[Cl_2] / dt}{[NC1P][H^+][Cl^-]}$$

The E.M.F. method proved to be the only method suitable for the measurement of the low concentration of chlorine existing in hydrochloric acid solutions of N-chloropiperidine. The values of k_{111} found by E.M.F. measurements can be compared with the similar function obtained by examining the kinetics of the reaction between N-chloropiperidine and phenol in the presence of hydrochloric acid. Thus Dixon gives the following values of k_{111} at 25°.

[HCl]	[NC1P]	[PhOH]	$10^3 k_{111}$ $l^2 \cdot mole^{-2} \cdot sec^{-2}$
0.516	0.0162	0.0268	5.20
0.516	0.0077	0.0268	6.27
0.516	0.0083	0.0268	5.64
0.0083 + 0.46M KCl	0.0083	0.0268	2.17

Dixon accepted the Carr mechanism as the predominant one in the above reaction, the Orton-Hughes mechanism just begining to appear as a significant complicating factor. The discrepancy in the values of k_{111} as a function of acid strength prevented Dixon from investigating this compound any further.

Attempts to remove the molecular chlorine existing in equilibrium with hydrochloric acid solutions of N-chloromorpholine and N-chloropiperidine were unsuccessful, the N-chloro compound

itself being readily aspirated under the experimental conditions employed. The presence of the unchanged N-chloroamine in the gas stream was confirmed by ultra-violet spectroscopy. The use of the standard colour tests to measure the chlorine concentrations in solution were unsatisfactory as the N-chloro species interfered and in many cases gave a colour reaction itself. For example N-chloromorpholine, dissolved in water, gave a deep yellow solution with O-tolidene and a similar reaction with dimethyl-p-phenylene diamine.

Summary and Conclusions.

Values have been obtained for the equilibrium constant of the reaction between hydrochloric acid and N-chloromorpholine and N-chloropiperidine, reactions in which molecular chlorine has been shown to play an important part. A knowledge of the numerical value of the equilibrium constant is of great importance in explaining many of the unsolved problems relating to the N-chloroamines. Of special importance is the problem of the apparent exchange reaction which was found to occur between N-chloromorpholine and $^{36}\text{Cl}^-$ in the presence of acid (Chapter 1). The results of typical experiments with N-chloromorpholine and HCl^{36} are illustrated below to show the form the reaction takes.

(1)	<u>N</u> -chloromorpholine	0.1604 M.
	HCl^{36} total	0.050 M. Temp. 0°C.
	Time (min)	Counts/min in Cl^-
	0	473
	6	393

Time (min)	Counts/min in Cl^-
10	330
14	270
19	197
24	159
27	134
eqbm	132

(2) [N-chloromorpholine] 0.197 M
 $[\text{HCl}^{36}]$ 0.026 M. Temp. 20°C.

Time (min)	counts/min Cl^-
0	433
1.5	335
3.0	239
4.5	152
6.0	106
7.5	83
9.0	74

A plot of $\log_{10}$ counts/min for the chloride ion as a function of time usually gave a good straight line.

This reaction is now known to occur through the formation in solution of molecular chlorine.

The mathematics of the kinetics of the reaction between ^{36}Cl labelled hydrochloric acid and N-chloromorpholine is complex (Dixon, personal communication) and much more work will have to be done under strictly controlled conditions to enable solution of this problem. It was obvious from the results outlined in

Chapter 1 that a simple exchange of the form below did not occur.

A possible mechanism which would explain the complexity of the kinetics is as follows.

together with possibly a small amount of true displacement taking place. What is now known, however, is the value of the equilibrium constants for the reactions outlined above and it should therefore be possible to afford a solution.

A summary of the numerical constants derived in this Chapter follows.

$$(1) \quad K_2 = \frac{[\text{NH}_2^{+}][\text{Cl}_2]}{[\text{NCl}][\text{H}^{+}]^2[\text{Cl}^{-}]}$$

N-chloromorpholine $9.46 \times 10^{-4} \text{ mole}^{-2.12}.$

N-chloropiperidine $9.31 \times 10^{-7} \text{ mole}^{-2.12}.$

$$(2) \quad K_1^1 = \frac{[\text{NH}_2^{+}][\text{Cl}_2]}{[\text{NClH}^{+}][\text{Cl}^{-}][\text{H}^{+}]}$$

N-chloromorpholine $1.706 \times 10^{-3} \text{ mole}^{-1.1}$

N-chloropiperidine $1.20 \times 10^{-7} \text{ mole}^{-1.1}$

$$(3) \quad k_{111} = \frac{d\text{Cl}_2/dt}{[\text{NClH}][\text{H}^{+}][\text{Cl}^{-}]}$$

N-chloromorpholine $8.33 \times 10^{-4} \text{ mole}^{-2.12} \cdot \text{sec}^{-1}.$

N-chloropiperidine $3.76 \times 10^{-6} \text{ mole}^{-2.12} \cdot \text{sec}^{-1}$

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CHAPTER 4

The Reaction of N-chloro-amides and N-chloro-imides with Hydrochloric Acid

PART 1

N-chloroacetanilide

During the period which has elapsed since Bender¹ discovered N-chloroacetanilide and its rearrangement to chloroacetanilides in the presence of hydrochloric acid, a vast volume of work has appeared on this subject. Investigations have been carried out in aqueous and non-aqueous solution, together with a study of the thermal rearrangement occurring in the dry state. Experiments concerned primarily with the reaction theory have been attempted and a large volume of literature has been devoted to the tabulation of the rates of the reaction between N-chloroacetanilide (acetylchloroaminebenzene) and hydrochloric acid.

Armstrong² contended that something more than a mere interchange of radical position was taking place and shortly after, it was found that hydrochloric acid was a specific catalyst for the reaction although Rivett³ found a very slow transformation in the presence of sulphuric and other acids.

Orton and Jones⁴ considered that the reaction proceeded through a reversible reaction of the N-chloroacetanilide with hydrochloric acid yielding acetanilide and chlorine, the o and p

chloroacetanilides then being formed by a direct attack of the chlorine on the acetanilide molecule, thus

Further support for this mechanism comes from the observation that the ratio of o to p-chloroacetanilide is the same, whether obtained from a mixture of acetanilide and chlorine or from a mixture of N-chloroacetanilide and hydrochloric acid⁵, although Ingold⁶ draws attention to the inadequacy of these observations to differentiate between the Orton mechanism (that mechanism outlined by equations above) and an intramolecular rearrangement:-

Soper⁷ showed that reaction (1) was wholly rate determining in aqueous solution, the rate of isomerisation being just equal to the rate of production of chlorine. Chattaway and Orton⁸ isolated both acetanilide and chlorine from mixtures of N-chloroacetanilide in hydrochloric acid. The possibility that hypochlorous acid is an intermediate in the chlorine formation is seen from their experiments on substituted nitrogen chlorides with acids on which hypochlorous acid has no action. The suggested reactions were:

the second reaction postulated has been shown to be rapid in both directions,⁹ the first two equilibria thus being equivalent to

so that arguments for the Orton mechanism are equally applicable to this alternative mechanism, the only distinction being based on kinetic investigations.

Research with Cl-36, labelled material¹⁰ has shown that 60% of the chlorine came into radioactive equilibrium with the chloride ion in solution, before reacting to form chloroacetanilide. This is in agreement with the theory that the mechanism involves a steady state chlorine concentration, but definitely excludes a real equilibrium between chlorine and the reactants. The idea of a steady-state chlorine concentration was also advanced by Orton and King¹¹ who determined the relative amounts of C- and N- chlorinated products from the reaction between acetanilide and chlorine. A similar decision arose from the research of Orton, Soper and Williams¹².

At this stage, Olson, Halford and Hornel¹³, correcting for the chloride ion concentration produced during the experiment, concluded that all of the N-chloro compounds which reacted came into radioactive equilibrium with the catalyzing chloride

ions, and therefore, must have passed through the free molecular chlorine stage. The rate of the rearrangement was followed by determining the loss of oxidising power (using iodide ion) of the solution, the production of chlorine involving no such loss. The rate work thus involved the acceptance of several assumptions:

- (a) the steady state chlorine concentration had been attained.
- (b) no side reactions occurred.
- and (c) The amount of free chlorine in solution was small in relation to the [N-chloroacetanilide].

The kinetics of the reaction in aqueous solution have been extensively studied by many workers¹⁴ who determined the concentration of N-chloroacetanilide as a function of time and demonstrated the first order properties of the reaction.

$$\text{thus } v = k_{\text{obs}} [\text{N-chloroacetanilide}]$$

Soper¹⁵ combined the hydrolysis constant of N-chloroacetanilide with that of chlorine and the rate of C- and N- chlorination in an attempt to demonstrate that the production of chlorine was the slow rate determining step in the reaction scheme originally proposed by Orton.

Olson and Hornel¹⁶ showed that in aqueous solution N-chloroacetanilide disappears by two paths. In one path the hydrogen ion and chloride ion react with N-chloroacetanilide to build up a steady state (as distinguished from an equilibrium) concentration of chlorine and acetanilide. These

substances then react to form ortho and para chloroacetanilide, regenerating hydrogen and chloride ions. It was also noted that the addition of "chlorinatable" substances such as acetanilide or acetnaphthalide increased the rate of the reaction by decreasing the amount of chloride ion fixed as chlorine. In the second path the *N*-chloro compound condensed to form a new compound which the authors failed to identify, catalysis for this reaction involving only the hydrogen ion. The form of the graphs obtained by Olson and Hernel show that they are in complete agreement with the chlorine intermediate mechanism first proposed by Orton, the concentration of chlorine building up from nothing to its steady state value and then gradually falling. There is no doubt that this steady state is what authors had in mind when they discussed an equilibrium.

The influence which various factors had on the steady state concentration of chlorine gave a partial explanation at least, of a number of phenomena observed by previous investigators. Thus an increase in the concentration of *N*-chloroacetanilide, chloride ion or hydrogen ion increased the rate of formation of chlorine but had no effect on the rate of disappearance of chlorine, and so the steady state concentration should be increased. An increase in the concentration of substances like alcohol increases the activity of the ions but decreases the activity of the *N*-chloroacetanilide by making it more soluble, the change in rate, therefore, depending on the predominant effect. The addition of "chlorinatable" substances like acetanilide was shown by Olson and Hernel to have no effect

on the rate of production of chlorine but a marked effect on the rate of its disappearance, resulting in a decrease in the steady state concentration. The observed rate of disappearance of total oxidising power was stated by Olson and Hornel as being proportional to the first power of the activity of N-chloroacetanilide and of hydrogen ions if the concentration of chlorine was kept constant. The rate should also be proportional to the activity of the chloride ions if the above condition is fulfilled and the amount disappearing by side reactions is small. These workers concluded that when one of the above reactants is present to only a small extent, the effect of depletion of this constituent due to the steady state condition of chlorine and acetanilide becomes very noticeable. Furthermore, they stated that in their experiment the building up of the steady state concentration of chlorine and acetanilide decreased the concentration of chloride ion to less than one half of its initial value in spite of the production of chloride ions by side reactions, and this effectively checked the further disappearance of N-chloroacetanilide by these paths. The addition of acetanilide increased the concentration of chloride ion, explaining how the addition of this component is effective when the chloride ion concentration is small. For the reactions:

Olson and Hornel give the results illustrated in Table 4.1.

The approximate values of k_3 were obtained from the 'chloroanilide graph' by assuming that the concentration of chlorine was stationary at some value of t .

Table 4.1

$t(\text{min})$	$[\text{Cl}^-]_t$	$[\text{Ncl}]$	$[\text{Cl}_2]$	k_3/k_1	$[\text{Cl}^-]_{\text{actual}}$
30	0.0086	0.0339	0.0066	1.275	0.0020
60	0.0119	0.0271	0.0077	1.370	0.0042
90	0.0147	0.0207	0.0080	1.320	0.0067

Hughes¹⁷ suggested that the hydrogen and chloride ions did not react simultaneously, the suggested steps being:

where the second reaction is rate determining. The arguments advanced by Robinson, Ayling and Barker¹⁸ can still be applied, since the energy of activation now applies to the bimolecular second reaction and hence an ionic interpretation is still valid. Actually Richardson and Soper¹⁹ confirmed the ionic interpretation by examining the kinetics of the conversion of N-chloroacetanilide by hydrogen bromide into *o*- and *p*-bromoacetanilide. They found the rate obeyed the expression:-

$$\text{Rate} \propto [\text{chloroamine}][\text{H}^+][\text{Br}^-]$$

which cannot be expressed in an alternative molecular form because two acids were supplying the proton in their experiment, while only one contained the outstandingly reactive bromide anion. Analogously, it is considered that the reaction between

hydrochloric acid and N-chloroacetanilide proceeds through an ionic mechanism.

Hughes regards reaction 1 (page 135) as a bimolecular nucleophilic substitution by halide ion at the chlorine atom of a chloroammonium ion, a type of S_N2 substitution at a chlorine instead of at carbon atom:

It follows by the principle of microscopic reversibility, that reaction (2) is a bimolecular nucleophilic substitution by the acylanilide molecule at one halogen atom in the halogen molecule. Clearly then, reaction (1) is not a hydrolysis as it is sometimes loosely called, but Soper and Pryde¹⁴ showed that in aqueous solution it is accompanied by a comparatively unimportant side reaction of the nature of a hydrolysis furnishing hypochlorous acid which then reacts with hydrochloric acid giving molecular chlorine. The mechanisms of this slow hydrolytic process is unknown, although the possibility of it being an S_N2 type substitution cannot be discarded.

However it could be an S_N1 - type substitution:

It is therefore possible to speak of hydrochloric acid as a specific catalyst for the rearrangement.

Carr²⁰ showed that the effect of the addition of acetanilide,

and the form of the rate expression

$$N = k_a \text{NClA}^a \text{H}^+{}^a \text{Cl}^-$$

are sufficient to reject mechanisms involving hydrolysis as a first step. Soper²¹ found that in glacial acetic acid N-chloro-2:4-dichloroacetanilide gave very little chlorine with hydrochloric acid, except in the presence of water. He interpreted this result as being evidence for the reactions:

The Orton mechanism requires the presence of hydrogen and chloride ions which may not be present in sufficient concentration in glacial acetic acid. Hypochlorous acid and acetanilide have been obtained from aqueous solutions of N-chloroacetanilide^{22,23} but the amounts of both these compounds were small.

In the light of the evidence outlined, the Orton mechanism as modified by Hughes is accepted today and any preliminary hydrolysis to hypochlorous acid must be regarded as insignificant. On the other hand, the proposal that other mechanisms exist, even if it is not fully understood what they are, can be unequivocally supported. For example, the existence of a homolytic mechanism is made clear by effects of light in promoting the transformation of N-chloroacetanilide²⁴. A summary of rearrangements by light is given in an earlier work²⁵.

The development of the E.M.F method of chlorine measurement in the presence of chloride ions gives an ideal method for the investigation of the chlorine concentration which exists in

equilibrium with N-chloroacetanilide in hydrochloric acid solutions. In particular, the present work was undertaken to measure the steady state chlorine concentration.

EXPERIMENTAL

The Acid Catalysed Rearrangement of *N*-chloroacetanilide.

Before attempting to measure the concentration of molecular chlorine existing in solutions of *N*-chloroacetanilide and hydrochloric acid it was necessary to measure accurately the concentration of the *N*-chloro compound as a function of time. This was achieved by mixing aqueous solutions of *N*-chloroacetanilide and hydrochloric acid, both maintained at 25°C in a thermostated water bath. At known time intervals, suitable aliquots were withdrawn and added to aqueous potassium iodide, the amount of *N*-chloroacetanilide and chlorine present being determined by titrating the liberated iodine with standard sodium thiosulphate (0.00516N) solution.

The results of two typical runs are given below, Figure 4.1 showing the plot of $\log_{10}$ titre as a function of time.

Run 1.

[<i>N</i> -chloroacetanilide]	$11.91 \times 10^{-4}M$
[Hydrochloric acid]	0.618M Temp 25°C
[Sodium thiosulphate]	0.00516N

Time (secs)	Vol. of thio (V)ml	$\log_{10} V.$	% of <i>N</i> -chloroacetanilide remaining
60	4.52	0.6551	98.0
300	3.80	0.5798	82.5
540	3.20	0.5051	69.5
900	2.51	0.3997	54.3
1260	1.99	0.2989	43.1
1560	1.66	0.2201	36.0
2010	1.25	0.0969	27.1
2520	0.88	-0.0555	19.1

Run 2.

[N-chloroacetanilide]

$11.61 \times 10^{-4} M$

[Hydrochloric acid]

0.315

M Temp $25^{\circ}C$

Time (sec)	Vol. of this (V) ml	$\log_{10} V$	% of N-chloroacetanilide remaining
60	4.43	0.6464	98.5
300	4.29	0.6325	95.3
915	3.87	0.5877	86.0
1560	3.48	0.5416	77.4
2760	2.80	0.4472	62.2
3900	2.37	0.3747	52.6
4920	1.97	0.2945	43.7
8280	1.20	0.0792	26.6
9000	1.02	0.0086	22.6

In Figure 4.1 titration figures have been used for [NClacetanilide]. From the slopes of these graphs, the two values obtained for the rate constant k are:

Run 1. $k_{obs} = 2.83 \times 10^{-4} \text{sec}^{-1}$

Run 2. $k_{obs} = 7.34 \times 10^{-5} \text{sec}^{-1}$

When these two functions are divided by the corresponding $[HCl]^2$ they yield values of k_{111} equal to $7.13 \times 10^{-4} \text{sec}^{-1} \cdot \text{mole}^{-2} l^2$ and $7.39 \times 10^{-4} \text{sec}^{-1} \cdot \text{mole}^{-2} l^2$ respectively. Thus the kinetic expression is:

$$v = k_{111} [N\text{-chloroacetanilide}] [HCl]^2$$

or more correctly

$$v = k_{111}[\text{N-chloroacetanilide}][\text{H}^+][\text{Cl}^-]$$

agreeing with similar functions determined by other authors¹⁴.

Measurement of the chlorine concentration

Application of the method of E.M.F measurement to the determination of the chlorine concentration existing in hydrochloric acid solutions of N-chloroacetanilide gave the results tabulated below. The concentration of the N-chloro compound present at each measurement has been included, after being corrected for the chlorine concentration.

Run 3.

[Hydrochloric acid] 0.618 M.

[NC1A] = [N-chloroacetanilide] $12.58 \times 10^{-4} \text{M}$ Temp 25°C

Time (sec)	E.M.F	$[\text{Cl}_2] \times 10^5$	$[\text{NC1A}] \times 10^4$	$\frac{\text{NC1A}}{\text{Cl}_2}$
90	0.9931	4.68	11.47	24.5
120	9940	5.02	11.20	22.4
150	9940	5.02	10.92	21.8
180	9940	5.02	10.60	21.2
210	9935	4.83	10.45	21.6
240	9931	4.68	10.25	21.9
270	9928	4.57	10.05	22.0
300	9922	4.37	9.79	22.4
330	9918	4.23	9.58	22.7
360	9912	4.04	9.42	23.3
390	9907	3.89	9.21	23.7
480	9892	3.46	8.65	25.0

Time (sec)	E.M.F	$[Cl_2] \times 10^5$	$[NClA] \times 10^4$	$\frac{NClA}{Cl_2}$
540	0.9881	3.18	8.34	26.1
600	9871	2.95	8.11	27.5
660	9862	2.75	7.69	28.0
900	9829	2.13	6.63	31.1
1080	9802	1.73	5.89	34.0
1200	9787	1.54	5.50	35.7
1380	9762	1.27	4.91	38.7
1620	9737	1.05	4.27	40.8
1860	9710	0.85	3.66	43.1
2340	9660	0.58	2.66	46.0
3240	9546	0.24	1.24	51.6

Run 4.

[Hydrochloric acid] = 0.315 M

[NClA] = 12.58×10^{-4} M. Temp 25°C

Time (sec)	E.M.F	$[Cl_2] \times 10^5$	$[NClA] \times 10^4$	$\frac{NClA}{Cl_2}$
90	0.9738	1.03	12.34	120.0
120	0.9762	1.24	12.27	98.9
150	0.9778	1.41	12.18	86.5
180	0.9781	1.44	12.07	83.9
210	0.9785	1.48	12.03	81.5
240	0.9786	1.50	11.97	79.9
270	0.9786	1.50	11.93	79.6
300	0.9786	1.50	11.84	79.0
330	0.9784	1.477	11.77	80.0

FIG. 4. 2.

Time (sec)	E.M.F	$[Cl_2] \times 10^5$	$[NClA] \times 10^4$	$\frac{NClA}{Cl_2}$
360	0.9782	1.45	11.62	80.9
420	0.9780	1.43	11.66	81.6
480	0.9776	1.38	11.49	83.5
540	0.9771	1.33	11.38	85.7
600	0.9769	1.31	11.28	86.4
960	0.9743	1.07	10.61	99.1
1500	0.9706	0.81	9.71	120.0
1800	0.9680	0.66	9.21	139.8

This run was duplicated, the two graphs being illustrated in Figure 4.2. The result of plotting the $\log_{10}[Cl_2]$ as a function of time is shown in figure 4.3 for several experiments.

From the graphs it can be seen that the variation is large, especially in the case of the 12.58 and $12.20 \times 10^{-4}M$. N-chloroacetanilide solutions in $0.618M$ hydrochloric acid. The explanation of this variation being the possible presence of traces of impurities in solution. However, in spite of these differences, an overall picture of the mode of chlorine build up can be obtained.

Reference to the graphs of the chlorine concentration as a function of time shows the initial rapid increase, followed by a steady state value which persists for only a short length of time. Then follows a gradual fall in concentration, the plot of $\log_{10}[Cl_2]$ being linear during this stage.

The Ratio of the N-chloroacetanilide concentration to that

of the chlorine increases with time after the maximum chlorine concentration has been achieved. This result is the opposite to that found by Olson and Hornel (loc.cit.) although the initial concentrations used by these authors were vastly different.

PART 2. N-chloroacetamide and N-chlorosuccinimide

Carr (loc.cit) extended the work on N-chloro compounds in an attempt to prove that the Orton-Hughes mechanism as found for N-chloroacetanilide was valid for N-chlorosuccinimide and N-chloroacetamide. Preliminary investigation showed that the reaction between N-chlorosuccinimide, hydrochloric acid, and phenol was kinetically first order, the rate of the reaction being given by

$$\frac{-d[\text{NCIS}]}{dt} = k_{\text{obs}} [\text{NCIS}]$$

where $[\text{NCIS}] = \text{N-chlorosuccinimide}$

The study of such a mechanism is simpler than in the case of N-chloroacetanilide for the following reasons.

(a) there is little possibility of an intramolecular rearrangement occurring since the imide (or amide in the case of N-chloroacetamide) formed would be chlorinated only with difficulty, and not simply by molecular chlorine in solution.

(b) N-chlorination of the phenols would be avoided.

(c) the reactivity of the chlorine acceptor could be more readily varied over a wider range, facilitating a more detailed study of the reaction.

The experimental work undertaken by Carr was directed to determining if the following mechanism was acceptable.

where the forward reaction of (1) is rate determining. A study of the catalysis by perchloric acid was also carried out since the perchlorate ion was considered to have no important nucleophilic properties. The results obtained indicated that the reaction was still first order, although the rate was considerably reduced.

The results of Carr's experiments are tabulated below. All runs were carried out at 25°C.

$[HCl]_M$	$k_{obs}(\text{sec}^{-1})$	Variation %
2	4.96×10^{-4}	5
1.5	2.68×10^{-4}	3
1	1.28×10^{-4}	4
0.5	4.17×10^{-5}	5
0.25	1.48×10^{-5}	4

In all cases, at least 80% of the reaction was studied and the N-chlorosuccinimide titre eventually dropped to zero. Doubling the phenol concentration was found to have no effect on the first order rate constants.

$[HClO_4]$	$k_{obs}(\text{sec}^{-1})$
2	1.76×10^{-6}
1.5	1.6×10^{-6}
1.0	1.4×10^{-6}
0.5	1.08×10^{-6}
0.25	0.5×10^{-6}

The products of the reactions were found to be ortho -

and para chlorophenols and succinimide. However, under the acid conditions prevailing throughout the reaction, hydrolysis takes place, and subsequently succinamic and succinic acids are formed.

Carr found that the reaction occurring between N-chloroacetamide, hydrochloric acid, and phenol was identical to that found for N-chlorosuccinimide, thus

$$\frac{-d[\text{NClA}_c]}{dt} = k_{\text{obs}}[\text{NClA}_c]$$

(where $[\text{NClA}_c] = \text{N-chloroacetamide.}$)

The results found for this compound are given below.

$[\text{HCl}] \text{ M}$	$k_{\text{obs}} (\text{sec}^{-1})$	Variation
2.0	12.8×10^{-4}	3%
1.5	6.37×10^{-4}	5%
1.0	2.51×10^{-4}	3%
0.5	0.64×10^{-4}	4%
0.25	0.18×10^{-4}	6%

The phenol concentration was found to have no effect on the first order constants, provided that this concentration was in excess of that of the N-chloro compound. Solutions of N-chloroacetamide containing perchloric acid and phenol showed a markedly different rate of decomposition from that found for

N-chlorosuccinimide, the reaction being slow initially but showing a gradual increase in rate, the graph of log concentration against time eventually becoming linear. Carr assumed that the results were probably due to the hydrolysis:-

Robb²⁶ has shown that any decomposition of N-chloroacetamide by hydrolysis to hypochlorous acid, in the pH range 5 - 13, corresponds to only a small part of the total decomposition. He also assumed that the main decomposition suffered by N-chloroacetamide in hydrochloric acid solution was associated with the formation of nitrogen trichloride, formed by the following reactions :-

There is no literature confirmation of this reaction to produce nitrogen trichloride. Bodenstein²⁷ has shown that

is the main decomposition undergone by monochloroamine in water.

Hence for both N-chlorosuccinimide and N-chloroacetamide, the acid-catalysed chlorination occurs by a mechanism analogous to the "Orton" mechanism.

$$K = \frac{[\text{:NClH}^+]}{[\text{:NCl}][\text{H}^+]}$$

The reaction was observed to be first order which is explicable only if reaction (a) is rate determining. This results in

$$\begin{aligned} \frac{-d[\text{:NCl}]}{dt} &= k [\text{:NClH}^+][\text{Cl}^-] \\ &= kK [\text{:NCl}][\text{H}^+][\text{Cl}^-] \end{aligned}$$

and since $[\text{H}^+]$ and $[\text{Cl}^-]$ are constant throughout the reaction, the observed rate is first order.

The rates of the hydrochloric acid catalysed chlorination by N-chloroacetanilide, N-chloroacetamide and N-chlorosuccinimide become progressively slower and are in the ratio of approximately 12 : 2 : 1. A discussion of the electronic theory as applied to this result is given by Carr (loc.cit.), based on the polarisation effects due to the presence of $-\overset{\text{O}}{\underset{\text{O}}{\parallel}}\text{C}-\text{CH}_3$ groupings which

exert a mesomeric effect $:\text{N}-\overset{\text{O}}{\underset{\text{O}}{\parallel}}\text{C}-\text{CH}_3$, resulting in a decreased

basicity of the nitrogen atom.

Robb attempted to measure spectroscopically the concentration of chlorine existing in equilibrium with solutions of N-chlorosuccinimide and N-chloroacetamide in hydrochloric acid in an endeavour to evaluate the hydrolysis constants for these two compounds. In the case of N-chloroacetamide he claimed that the expected chlorine peak at 325 mμ was overshadowed by a peak at

335 $m\mu$ due to the presence in solution of nitrogen trichloride. The pungent smell existing in such solutions was claimed by Robb to be due to this material. It is the present author's contention that this compound will only be formed with N-chloroacetamide in the presence of alkaline impurities²⁸. Figure 4.4 illustrates the ultraviolet absorption graph of pure N-chloroacetamide ($1.48 \times 10^{-3}M$) in both water and hydrochloric acid (0.618M). The absence of any peak at 335 $m\mu$ was evident. (These graphs are comparable to the one obtained for a chloroform solution of the N-chloro compound²⁹).

In the case of N-chlorosuccinimide no such side reaction was found to occur and Robb obtained the value of $4.5 \times 10^{-5} \text{mole}^{-1}$ at 20°C for K_1^a , defined by

$$K_1^a = \frac{\{a_{Cl_2}\}_E^2}{(a_{:NCl})_E (a_{H^+})_E^2} = \frac{[Cl_2]_E^2}{[:NCl]_E (a_{H^+})_E^2} \quad \text{approximately}$$

$$\text{where } [:NCl]_E = [:NCl]_{\text{initial}} - [Cl_2]_E,$$

$$[:NH]_E = [Cl_2]_E$$

$$\text{and } [H^+]_E = [Cl^-]_E = [HCl]_E = [HCl]_{\text{initial}} - [Cl_2]_E$$

The work to be described utilises the E.M.F method of chlorine measurement in the study of hydrochloric acid solutions of N-chlorosuccinimide and N-chloroacetamide. From these measurements the rate of production of chlorine and the final equilibrium constant were calculated. An investigation of the reverse reaction between the parent amide and chlorine will be outlined.

EXPERIMENTAL

N-chloroacetamide

In a typical run the following results were obtained.

Run 5.

$$\begin{aligned} [\text{NClA}_c] &= [\text{N-chloroacetamide}] = 4.005 \times 10^{-3} \text{M} \\ [\text{Hydrochloric acid}] &= 0.618 \text{ M. Temp } 25^\circ\text{C} \end{aligned}$$

Time (min)	E.M.F.	$[\text{Cl}_2]^* \times 10^5$
1.5	0.9751	1.17
2	0.9820	1.99
2.5	0.9863	2.77
3	0.9893	3.49
3.5	0.9918	4.23
4	0.9930	4.64
4.5	0.9941	5.06
5	0.9950	5.42
5.5	0.9959	5.81
6	0.9963	5.99
7	0.9970	6.32
8	0.9977	6.67
10	0.9980	6.83
11	0.9981	6.88
12	0.9982	6.94
13	0.9983	6.99
16	0.9985	7.10
18	0.9986	7.13
20	0.9987	7.21
30	0.9989 ₅	7.35

Time (min)	E.M.F.	$[Cl_2]^* \times 10^5$
68	0.992	7.49
100	1.0017	9.09
150	1.0016 ₅	9.08

*The chlorine concentrations given in all these tables refers to the total chlorine concentrations i.e. $[Cl_2] + [Cl_3^-]$ where $[Cl_3^-] / [Cl_2][Cl^-] = 0.196$

At equilibrium therefore, $[Cl_2] = 9.09 \times 10^{-5}M$ and substitution of this value in the equation

$$K_1 = \frac{[Cl_2][:NH]}{[:NCl][H^+][Cl^-]} = \frac{[Cl_2]^2}{[:NCl][H^+]^2}$$

(since $[Cl_2] = [:NH]$ at equilibrium and $[H^+] = [Cl^-] \gg Cl_2$) gives $K_1 = 5.52 \times 10^{-6} \text{mole}^{-1}.l.$

Similar duplicated runs were carried out using different concentrations of hydrochloric acid and the N-chloro compound. The results are tabulated below, all measurements at 25°C. No correction has been made for Cl_3^- formation.

$[HCl]M$	$[N\text{-chloroacetamide}] \times 10^3$	$[Cl_2]_E \times 10^5$	$K_1^* \times 10^6 \text{mole}^{-1}.l.$
0.315	3.181	3.96	5.04
0.315	4.005	4.24	4.57
0.315	10.830	8.50	6.79
0.618	3.181	8.03	5.43

$[\text{HCl}]_M$	$[\text{N-chloroacetamide}] \times 10^3$	$[\text{Cl}_2]_E \times 10^5$	$K_1^* \times 10^6 \text{ mole}^{-1.1}$
0.618	4.005	9.09	5.52
0.618	10.830	14.89	5.43

* To correct these values for Cl_3^- formation, divide the values of K_1 obtained in 0.618M hydrochloric acid by 1.121 and those in 0.315M acid by 1.062. These same correction factors also apply in the case of N-chlorosuccinimide.

Figures 4.5 and 4.6 illustrate the chlorine concentration as a function of time for the above experiments.

Combination of the mean value of K_1 , $5.46 \times 10^{-6} \text{ mole}^{-1.1}$ with the accepted value of the hydrolysis constant of chlorine³⁰ ($3.94 \times 10^{-4} \text{ mole}^{2.1-2} = K^1$) gives for the equilibrium hydrolysis constant of N-chloroacetamide -

$$K_H = K_1 K^1$$

$$= 21.5 \times 10^{-10} \text{ mole.l}^{-1} \text{ at } 25^\circ\text{C.}$$

N-chlorosuccinimide

The results obtained by measuring the E.M.F as a function of time for solutions of N-chlorosuccinimide in hydrochloric acid are summarised in Table 4.2 and Figure 4.7.

Table 4.2

Values of K_1 for N-chlorosuccinimide at 25°C.

FIG. 4.5.

$[HCl]_M$	$[N\text{-chlorosuccinimide}]$	$[Cl_2]_E \times 10^5$	$K_1 \times 10^5$ mole ⁻¹ .l.
0.316	8.267×10^{-4}	3.96	2.00
0.316	1.477×10^{-3}	5.35	2.02
0.618	1.066×10^{-3}	9.30	2.35
0.618	1.996×10^{-3}	15.71	3.52
0.618	3.144×10^{-3}	19.36	3.33

The reverse reaction, that is the one between succinimide and chlorine in the presence of hydrochloric acid, was studied by the same method of E.M.F measurements. The hydrochloric acid concentration was adjusted so that when 90 ml was diluted to 100 ml the final strength was 0.618 M. To 90 ml of this acid was added 5 ml of a solution of chlorine in water and 5 ml of a solution of succinimide. The strengths of these last two compounds were made equal and were such that when 5 ml was diluted to 100 ml the desired concentration was achieved. All solutions were thermostated at 25°C before mixing. The chlorine solution was delivered below the level of the hydrochloric acid with a long-tipped micro burette to avoid loss of molecular chlorine by vapourisation. The analysis of the chlorine with a potassium iodide solution was done in the same way. The following results were obtained (Figure 4.8).

Run 6.

$[Succinimide]$	$= 51.1 \times 10^{-4} M$
$[Chlorine]$	$= 51.1 \times 10^{-4} M$
$[Hydrochloric\ acid]$	$= 0.618 \quad M$

FIG. 4.6.

Time (min)	E.M.F	$[Cl_2] \times 10^4$
0	1.0538	51.10
2.5	1.0429	21.83
3.5	1.0402	17.73
4.5	1.0362	13.02
5.0	1.0320	9.42
6.5	1.0289	7.41
8.5	1.0252	5.57
10.0	1.0231	4.74
13.0	1.0202	3.79
17.0	1.0178	3.15
20.0	1.0160	2.74
25.0	1.0149	2.52
Equilibrium	1.0130	2.17

At equilibrium, therefore, the following species will be present.

$$\begin{aligned}
 [Cl_2]_E &= 2.17 \times 10^{-4} M \\
 [S]_E = [\text{Succinimide}]_E &= 2.17 \times 10^{-4} M \\
 [HCl]_E &= 0.618 M \quad (\text{since } [H^+] = [Cl^-] \gg [Cl_2]) \\
 [NClS] = [N\text{-chlorosuccinimide}]_E &= [Cl_2]_{\text{initial}} - [Cl_2]_E \\
 &= 48.93 \times 10^{-4} M
 \end{aligned}$$

$$\begin{aligned}
 \text{Then } K_1 &= \frac{[Cl_2]_E [S]_E}{[NClS]_E [H^+]_E [Cl^-]_E} \\
 &= \frac{[Cl_2]_E^2}{[NClS]_E [H^+]_E^2}
 \end{aligned}$$

$$= 2.52 \times 10^{-5} \text{ mole}^{-1.1}.$$

a value in close agreement with those obtained by studying the reverse reaction. Thus the equation for the reaction between N-chlorosuccinimide and hydrochloric acid can be represented by the general type

and is a true reversible reaction with the equilibrium lying largely to the left.

Run 7.

[Succinimide]	= $3.72 \times 10^{-3} \text{ M}$
[Chlorine]	= $4.72 \times 10^{-3} \text{ M}$
[HCl]	= 0.618 M

Time (min)	E.M.F	$[\text{Cl}_2] \times 10^3$
0	1.0550	4.72
1	1.0471	3.02
3	1.0417	1.99
5	1.0387	1.58
7	1.0370	1.39
11	1.0350	1.19
19	1.0340	1.10
30	1.0336	1.07
Equilibrium	1.0331	1.03

Hence at equilibrium

$$[\text{S}]_E = [\text{S}]_{\text{orig}} - [\text{Cl}_2]_{\text{used}} = .03 \times 10^{-3} \text{ M}$$

$$[\text{Cl}_2]_{\text{E}} = 1.03 \times 10^{-3}\text{M}$$

$$[\text{NClS}]_{\text{E}} = [\text{Cl}_2]_{\text{used}} = 3.69 \times 10^{-3}\text{M}$$

$$[\text{H}^+] = [\text{Cl}^-] = 0.618\text{M}$$

$$\text{giving } K_1 = 2.19 \times 10^{-5} \text{mole}^{-1.1}$$

The average value of K_1 obtained from the above results was $2.56 \times 10^{-5} \text{mole}^{-1.1}$. (Assumption of an activity coefficient of 1.009 for 2 M hydrochloric acid enables the recalculation of Robbs value for

$$K_1^a = \frac{[\text{Cl}_2]^2}{[\text{NClS}](a_{\text{H}^+})^2} \quad \text{at } 20^\circ\text{C}$$

and this becomes $K_1 = 4.57 \times 10^{-5} \text{mole}^{-1.1}$.)

Application of the equation for the determination of the equilibrium hydrolysis constant gives $K_H = 1.01 \times 10^{-8}$ at 25°C . (Robb gives $K_H = 1.83 \times 10^{-8}$ at 20°C).

The presence of unchanged N-chlorosuccinimide and N-chloroacetamide in hydrochloric acid solutions was confirmed by chromatographing such mixtures on Whatman No.1 papers using the ascending technique. The mobile solvent was n-butanol saturated with water, and the position of the N-chloro compound was ascertained by spraying the paper with a solution of potassium iodide and acetic acid containing a drop of starch. Blue spots on a white background indicated the presence of the N-chloro compound. Standards used were hexane solutions of both N-chlorosuccinimide and N-chloroacetamide. Addition of a compound such as allyl ethyl ether to solutions of N-chloroacetamide and

N-chlorosuccinimide in hydrochloric acid produced drastic changes in the measured E.M.F values, demonstrating the removal of the chlorine from solution by reaction with the unsaturated ether. The drop in iodine titre of such a solution was in agreement with the removal of chlorine only, the remaining halogen being tied up as the N-chloro group and hence titratable on the addition of potassium iodide to the reaction mixture. In a typical experiment the following results were obtained.

$$\begin{aligned} [\text{N-chlorosuccinimide}] &= 1.065 \times 10^{-3} \text{ M} \\ [\text{HCl}] &= 0.618 \text{ M} \end{aligned}$$

At equilibrium the E.M.F was 1.0020 volts, corresponding to a chlorine concentration of $9.301 \times 10^{-5} \text{ M}$. On the addition of allyl ethyl ether the E.M.F fell rapidly, and subsequent addition of KI to 10 ml of the solution liberated iodine which was equivalent to 3.74 ml of 0.00516N sodium thiosulphate. Thus the N-chloro titre at equilibrium was equivalent to a concentration of $9.65 \times 10^{-4} \text{ M}$. The expected value, based on the E.M.F measurement was $9.72 \times 10^{-4} \text{ M}$.

Examination of the graphs obtained by plotting the chlorine concentration as a function of time for both N-chloroacetamide and N-chlorosuccinimide will show that they do not all pass through the origin, the phenomenon becoming more pronounced as the rate of reaction became slower. The only explanation offered for such discrepancies is the presence of some impurity, possibly present in the N-chloro material itself, which can react with chlorine. Thus, until the impurity has been 'saturated'

with chlorine, no free halogen will be present in solution. Because of the low values measured, such an explanation is deemed very probable by the present author, the slower the reaction rate the longer it will take to produce enough chlorine to react with the 'impurity' and consequently the longer will be the observed dead time of the reaction.

A plot of the chlorine concentration as a function of time for the initial stages of the reaction between N-chlorosuccinimide and hydrochloric acid appears linear (Fig. 4.7), the gradients being given in Table 4.3; together with values of the rate constants calculated from them.

Table 4.3

[HCl]M	[NClS] x 10 ⁴	Slope = 10 ⁵ [Cl ₂]/t mole.l ⁻¹ min ⁻¹	10 ⁵ k _{obs} [*] sec ⁻¹	10 ⁴ k ₁₁₁ [*] mole ⁻² . l ² sec ⁻¹	% of re- action studied.
0.316	8.27	0.131	2.64	2.65	34
0.316	14.77	0.217	2.45	2.46	37
0.618	10.66	0.443	6.92	1.81	48
0.618	19.96	0.772	6.45	1.69	55
0.618	31.44	1.271	6.74	1.77	51

*Carr defines k_{obs} as follows:

$$\frac{-d[\text{NClS}]}{dt} = k_{\text{obs}} [\text{NClS}] \text{ which from equation (1)}$$

also equals $\frac{d[\text{Cl}_2]}{dt}$

thus $k_{\text{obs}} = \frac{d[\text{Cl}_2]}{dt} / [\text{NClS}]$, assuming that the $[\text{NClS}]$ does

not change greatly during the run.

④

The kinetic expression

$V = k_{111} [\text{NClS}][\text{H}^+][\text{Cl}^-]$ was shown by Carr to represent his results, although the agreement was not exact. The values of k_{111} , which can be called the 'Orton-Hughes' mechanism constants are thus equal to $k_{\text{obs}}/[\text{H}^+][\text{Cl}^-]$

The values obtained by Carr for these functions are tabulated below. Extrapolated values for the hydrochloric acid strengths of 0.316 and 0.618M are included for comparison.

Table 4.4

Values of k_{obs} and k_{111} obtained by Carr for N-chlorosuccinimide in hydrochloric acid plus phenol at 25°C.

$[\text{HCl}]_M$	$10^5 k_{\text{obs}}$	$10^4 k_{111}$
0.25	1.48	2.37
* 0.31 ₆	1.95	1.95
0.50	4.17	1.67
* 0.61 ₈	5.40	1.41
1.0	12.7	1.27
1.5	26.8	1.19
2.0	49.6	1.24

* Extrapolated from a graph of k_{obs} VS $[\text{H}^+]$ constructed with Carr's results.

The results for the same reaction between N-chloroacetamide and hydrochloric acid are given in Table 4.5. However the agreement between these values is not as good as those obtained for the corresponding N-chlorosuccinimide case.

The agreement between the values of k_{111} obtained by Carr in his investigation of the chlorination of phenol by N-chlorosuccinimide and N-chloroacetamide in the presence of hydrochloric acid, and those obtained in the present paper by measuring the rate of chlorine production are excellent. This agreement being firm proof that the chlorination of phenol does in fact proceed through molecular chlorine and not through some other species. When the reactivity of the chlorine acceptor was greatly reduced by using benzoic acid instead of phenol, the reaction was found by Carr to proceed much more slowly, the kinetics no longer being first order.

Table 4.5

Values of k_{obs} and k_{111} for the reaction between N-chloroacetamide and hydrochloric acid at 25°C.

$[HCl]_M$	$[NClA_c]$ $\times 10^3 M$	Slope $10^5 [Cl_2]/t$ mole.l ⁻¹ min ⁻¹	$10^5 k_{obs}$ sec ⁻¹	$10^4 k_{111}$ mole ⁻² . l ² .sec ⁻¹	% of reaction studied
0.316	3.18	0.175	0.92	0.92	43
0.316	4.01	0.32	1.33	1.34	27
0.316	10.83	0.34	0.50	0.51	27
0.618	3.18	1.43	7.49	1.96	62
0.618	10.83	4.16	6.40	1.67	58

$[\text{HCl}]_M$	$[\text{NOClA}]_C$ $\times 10^3 M$	Slope $10^5 [\text{Cl}_2]/t$ $\text{mole.l}^{-1}\text{min}^{-1}$	$10^5 k_{\text{obs}}$ sec^{-1}	$10^4 k_{111}$ $\text{mole}^{-2} \cdot \text{l}^2 \cdot \text{sec}^{-1}$	% of re- action studied
*0.25			1.79	2.86	
0.316			2.50**	2.51**	
*0.50			6.39	2.55	
0.618			9.25**	2.42**	
*1.0			25.2	2.52	
*1.5			63.7	2.82	
*2.0			128.0	3.21	

* From the work of Carr

**

Extrapolated values from the results of Carr.

Examination of Table 4.4 shows the gradual fall off in the numerical value of k_{111} with increasing acid strength, a phenomenon noted by Carr. No reason has been advanced for this result. In particular, rate expressions in which $[\text{H}^+]$ was replaced by a_{H^+} or by the acidity function h_0 were shown by Carr to be no improvement since the value of a_{H^+} decreases in the acid range studied³¹ and h_0 is the same for both hydrochloric acid and perchloric acid in this range³². Attempts to explain the anomaly by assuming the presence of a primary salt effect were also unsuccessful, the graphs of $\log_{10} k_{111}$ as a function of $\sqrt{\mu}/(1 + \sqrt{\mu})$ not being linear. There appears to be no satisfactory rate expression which will summarise the experimental results, the best expression being:

$$V = k_{111} [NClS][H^+][Cl^-]$$

A summary of the values of k_{111} obtained for different N-chloro compounds is given in Table 4.6., together with the method of measurement. It should be realised, however, that since the rate determining stage of the Orton mechanism involves the reaction between the protonated N-chloro compound and the chloride ion, then k_{111}/K is a more accurate measure (where K is the equilibrium constant for the reaction $NCl + H^+ \rightleftharpoons NClH^+$) of the power of chlorination³⁴.

Table 4.6.

Values of k_{111} at 25°C.

<u>N</u> -chloro compound	[HCl]	$10^4 k_{111}$ mole ⁻² . l ² sec ⁻¹	Method of Measurement	Ref.
<u>N</u> -chloroacetanilide	0.618	15.60	Rearrangement	33
<u>N</u> -chloroacetanilide	0.618	7.13	Rearrangement	P 146
<u>N</u> -chloroacetamide	0.618	2.42	Phenol chlorina- tion	Carr
<u>N</u> -chloroacetamide	0.618	1.82	E.M.F	P 168
<u>N</u> -chlorosuccinimide	0.618	1.41	Phenol chlorina- tion	Carr
<u>N</u> -chlorosuccinimide	0.618	1.76	E.M.F	P 166
<u>N</u> -chloroguanidine	0.618	13.50	E.M.F	P 222
<u>N</u> -chloroguanidine	0.551	18.40	Phenol chlorina- tion	Carr
<u>N</u> -chloromorpholine	0.618	8.78	E.M.F	P 120
<u>N</u> -chloromorpholine	0.522	7.69 (9.9)*	Benzyl alcohol chlorination	Dixon 34
<u>N</u> -chloropiperidine	0.618	0.042 (0.25)*	E.M.F	P 127

* The values in brackets are those obtained by application of the correction factor

$$k_{111} = k_{111}^1 (1 + K[H^+]) \text{ derived by Dixon}^{35}, \text{ and}$$

the values of K used were, for N-chloromorpholine and N-chloropiperidine respectively, 0.550 and 7.85.

(N.B. Dixon estimated a value of $5 \times 10^{-4} \text{ litre}^2 \cdot \text{mole}^{-2} \text{ sec}^{-1}$ for the k_{111} value of N-chloropiperidine but it is difficult to see how he arrived at this figure).

Unfortunately the value of K is not known for N-chlorosuccinimide, N-chloroacetamide or N-chloroacetanilide (the value for N-chloroguanidine will be shown to be $0.196 \text{ mole}^{-1} \cdot \text{l}^{-1}$) but it is not expected, from a consideration of the electronic effects that the values will be as large as that obtained for N-chloromorpholine³⁴.

Attempts were made to calculate the value of K for N-chlorosuccinimide and N-chloroacetamide by solving a series of simultaneous equations, involving K and the equilibrium constant K_1^1 . This approach proved unsuccessful, the values of K obtained being - 0.25 and - 0.103 respectively. Details of this method of evaluating K are given in the next Chapter (page 218). Indications from this result are that the values of K are small. (The assumption which has to be made to enable this method to be used is that the equilibrium constant does not vary with acid concentration).

S U M M A R Y

(1) Confirmation of the 'steady state' hypothesis for the chlorine concentration existing in equilibrium with solutions of

N-chloroacetanilide in hydrochloric acid has been obtained.

(2) A mean value of $7.26 \times 10^{-4} \text{ mole}^{-2.12} \text{ sec}^{-1}$ has been found for the value of k_{111} defined by

$$V = k_{111} [\text{N-chloroacetanilide}] [\text{H}^+] [\text{Cl}^-]$$

(3) For N-chlorosuccinimide and N-chloroacetamide the values of k_{111} were found to be 2.08×10^{-4} and $1.28 \times 10^{-4} \text{ mole}^{-2.12} \text{ sec}^{-1}$ respectively. The agreement between these values and those found by Carr as a result of an investigation of the chlorination of phenol are excellent.

(4) The values of the equilibrium constant $K_1 = \frac{[\text{Cl}_2][\text{:NH}]}{[\text{:NCl}][\text{H}^+][\text{Cl}^-]}$ for the reaction

have been found to be $2.64 \times 10^{-5} \text{ mole}^{-1.1}$ for N-chlorosuccinimide and $5.46 \times 10^{-6} \text{ mole}^{-1.1}$ for N-chloroacetamide.

(5) It can safely be assumed from the results obtained that the values of K for N-chloroacetamide and N-chlorosuccinimide are less than that of N-chloromorpholine and are probably also less than the corresponding value found for N-chloroguanidine, ($0.196 \text{ mole}^{-1.1}$).

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CHAPTER 5

N-chloroguanidine

INTRODUCTION

Guanidine is the strongest known organic base aside from the quaternary ammonium bases, a fact attributed to the symmetrical distribution of charge in the guanidinium ion, as illustrated below:-

The value of K_b for guanidine is too large to be measured accurately. The free base is difficult to obtain, although the salts of guanidine can be readily obtained pure, especially the carbonate which crystallizes well. Marchwald and Struwe¹ prepared guanidine in a pure state by mixing alcoholic solutions of guanidine perchlorate and potassium hydroxide, evaporating the solvent in vacuo over phosphorous pentoxide and isolating the product (after filtering off the potassium perchlorate). Guanidine forms very hygroscopic crystals which decompose at high temperatures to give melamine, the tri-polymer of cyanamide. Solutions of guanidine in water are stable and it is a monoacidic base almost as strong as the caustic alkalis, forming salts with weak acids such as boric and silicic acids.

The structure of the guanidine cation has been shown by Lecher and Graf² to be (1) and not (11)

By purely chemical methods it is impossible to distinguish between the two alternatives above, but if alkyl guanidines are used, which are similar to guanidine in behaviour, the distinction becomes possible as was readily demonstrated by Lecher and Graf using N,N,N',N' - tetramethyl - N'' - ethyl guanidine and pentamethyl guanidine.

X-ray crystal analysis³ shows that in the crystal the three nitrogen atoms are symmetrically spaced about the carbon atom, each at a distance of 1.18 Å from it, and that the whole cation lies in one place. The distance between the nitrogen atoms and the carbon atoms is even less than for a normal double bond (N-C, 1.48; N=C, 1.28; N=C, 1.14 Å); and this must be due to the fact that all the nitrogen atoms are involved in resonance.

On the basis of formal resemblance it might be expected that nitrated amidines and guanidines would possess the undesirable property of nitrated acid amides as far as hydrolytic tendencies are concerned, and this expectation is borne out in practise. Thus many guanidines have established positions as explosives, the main one of

these being nitroguanidine which is formed by treatment of guanidine nitrate with concentrated sulphuric acid.

The nitro group in nitroguanidine was originally thought to be in the 2-position⁴ (III), but Thiele⁵ suggested 1-nitroguanidine (IV) as the most likely structure, chiefly because of the acidic property displayed by solubility in alkali. The older structure is more likely, however, because it has been found⁶ that when strongly alkaline solutions of nitroguanidine are chilled, immediately nitroguanidine is precipitated and not the salt. Potentiometric titration of a freshly prepared alkaline solution confirmed that no acidic function was present. However, when dilute alkaline solutions of 2-nitroguanidine were allowed to age, a true

acidic function was detected, and on acidification at least 70% of the original nitroguanidine could be recovered.

This behaviour was explained by assuming that a slow tautomeric conversion of the highly symmetrical 2-nitroguanidine (III) to the sodium salt of 1-nitroguanidine (IV) occurs in

alkaline solution. The second alteration which was noted in alkaline solution was the slow decomposition of nitro-guanidine to nitro urea, nitric acid, urea, carbon dioxide and ammonia, an observation which stresses the instability of this type of compound in solution.

The only other types of substituted guanidines which have been the subject of much study are the alkyl derivatives, which are readily made by the action of alkylamines on cyanide, or by fusing together 'dicyanodiamide' with the alkylamine salt⁷, reactions which are analogous to the preparations available for guanidine itself. The monoalkyl guanidines are as strong bases as the parent substances, but the dialkyl derivatives are distinctly weaker².

The existence of an N-chloro derivative of guanidine was first reported by Kamenski⁸ in 1878. The pale yellow crystals which he isolated were prepared by dissolving guanidine carbonate in a little excess glacial acetic acid and adding bleaching powder until a deep red solution resulted. Kamenski recorded N-chloroguanidine as being soluble in hot benzene and water, and insoluble in ligroin, and on heating, the product decomposed in a capillary tube at approximately 150°C. When equimolecular proportions of bromine and guanidine carbonate were mixed, yellow crystalline needles were isolated by Kamenski which were identified as N-bromoguanidine. If three moles of bromine were used, the product was found to be $\text{CH}_5\text{N}_3 \cdot \text{HBr} \cdot \text{Br}_2$ which crystallised

as dark red prisms. The corresponding iodine compound $\text{CH}_5\text{N}_3\cdot\text{HI} \cdot \text{I}_2$, crystallised in prisms with the colour of iodine itself.

Goerdeler and Willig⁹ suggested that the analysis, colour, and melting point of the N-chloroguanidine prepared by Kamenski pointed to the compound being impure 'azochloramide' :-

which had been shown to exist as yellow crystals by Schmelkes¹⁰ who prepared this compound from guanidine salts and hypochlorite under carefully controlled acidic conditions. The correct structure of the N-bromo derivative of guanidine has also been the subject of speculation, Goerdeler and Willig maintaining that once again Kamenski had incorrectly interpreted experimental results and that the most likely structure of this compound was azobromamide. Taube¹¹ describes the existence of N-bromoformylguanidine, and it has been shown by Goerdeler and Willig that salts of disubstituted guanidine react normally with sodium hypochlorite, yielding N-chloro compounds according to the following equation:

The unsatisfactory literature existing on the subject of N-chloroguanidine, together with the present day

uncertainty as to the structure of this compound, prompted further research on the preparation and properties of the substance and these researches will now be outlined.

Sydall¹² carried out a large number of experiments using solutions of sodium hypochlorite and guanidine hydrochloride and he found that the nature of the products varied considerably, according to the proportions used. A chilled solution of the hydrochloride in acetic acid, when treated with a large excess of hypochlorite, gave an orange oil which formed an orange crystalline powder on shaking with water. This compound was found to be insoluble in water, cold benzene, and petroleum ether, and closely resembled a product isolated by England¹³ when he added bleaching powder to a solution of guanidine hydrochloride contained in a mixture of glacial acetic acid and enough water to just dissolve the solid material. The yellow crystals isolated by England were found to be almost insoluble in water and an iodometric estimation of the N-chloro titre could only be determined by taking up the solid in an organic solvent. Such an estimation gave the molecular weight, based on the N - Cl titre, as approximately 127, and this agreed well with the theoretical value of 127.97 for a guanidine molecule with two N-chloro groups, that is:-

The ultraviolet absorption spectrum of this compound was determined by the present author (see fig. 5.1.), together with a redetermination of the molecular weight, and the new value, 112, indicates decomposition during the storing period of several months.

When 4N sodium hypochlorite (11ml.) was added to guanidine hydrochloride (2gm.) a yellow solution resulted which slowly deposited yellow-white crystals which reverted to a yellow mass overnight. This product was soluble in benzene but was not precipitated with petroleum ether (c.f. Kamenski). Attempts to purify these compounds by recrystallisation were unsuccessful, much decomposition taking place. Sydall persisted with the reaction of hypochlorite on the hydrochloride and many coloured precipitates ranging from purple to pale yellowish white were isolated. On warming a sample of the pale cream crystals over a bunsen, the conversion to yellow took place almost explosively, with the evolution of white fumes which Sydall failed to identify. Analysis of the crude white material gave an equivalent weight of 84, whilst a similar analysis carried out on a sample of the yellow crystals gave the value as 104. Since the theoretical equivalent weight of N-chloroguanidine (46.76) is far less than either of these values, Sydall suggested that condensation with the resultant loss of gaseous chlorine had occurred.

A brief glance at the above experiments, together with

a knowledge of the sparse literature existing on the problem of N-chloroguanidine will quickly show that the chemistry of halogen substituted guanidines is far from complete, and that much more research must be undertaken. It was with the intention of providing some of this information that the following work on the preparation, properties and reactions of N-chloroguanidine was undertaken.

EXPERIMENTAL

EXPERIMENTAL

PART 1

Preparation and Analysis of N-chloroguanidine

(A) Action of calcium hypochlorite on guanidine salts.

The experiments of Sydall and England utilising the reaction between calcium hypochlorite and guanidine hydrochloride in various acetic acid solutions were repeated without success.

When ice-cold solutions of these two compounds were mixed, the initial mixture remained colourless for several minutes and finally turned a deep yellow, no crystals separating after several days. It was noted that when the solutions changed colour a large volume of gas evolved which smelt strongly of chlorine monoxide (Cl_2O) and presumably resulted from hypochlorous acid formation in solution. Because of the relative insolubility of calcium hypochlorite in water, and the decomposition which is undergone in solution, this method was abandoned.

(B) Action of molecular chlorine on guanidine hydrochloride.

When equimolecular solutions of morpholine and chlorine are mixed it has been found that the ultraviolet absorption spectrum indicates almost instantaneous reversion to N-chloromorpholine in practically constant theoretical yield. ($> 99\%$). However, when a similar experiment was repeated with piperidine, the reaction was found to be slow and did not go to completion (see page 302).

When similar experiments were carried out using solutions of guanidine hydrochloride and chlorine, a reaction was found to take place, but even after a period of several hours the spectrum was still changing, indicating the existence of a slow reaction. During the course of this reaction the colour of the solution slowly turned to yellow and it was assumed that decomposition was taking place.

The results of the ultraviolet spectrum studies carried out on this reaction are well illustrated in Figure 5.2. The absence of the twin peaks as found in the compound isolated by England is apparent and hence the presence of this compound as one of the products can be discounted. The absence of any peak at $2600\overset{\circ}{\text{A}}$, which is the normal wave length for the N-chloro group to absorb, should be noted.

When the above experiment was repeated using guanidine carbonate in place of the hydrochloride an identical result was obtained, the reaction being relatively slow and decomposition occurring as before.

(C) Chlorination of guanidine salts utilizing t-butyl hypochlorite

The alkyl hypochlorites have been little studied on account of their explosive properties, since Sandmeyer¹⁴ prepared the first two members of the series. The alkyl hypochlorites are yellow, mobile, volatile liquids with strong and irritating odours. They give off vapours which

- 185a -

FIG. 5.1.

FIG. 5.2.

attack the eyes and mucous membranes violently, and the primary and secondary compounds are unstable, decomposing explosively when exposed to light. The tertiary hypochlorites, on the other hand, are remarkably stable, and tertiary butyl hypochlorite, for example, can be distilled without change and if not exposed to light, may be kept for months at room temperature with scarcely any decomposition. When exposed to light, or heat, they decompose as follows:-

In 1923 tertiary butyl hypochlorite was first described by Chattaway and Backeburg¹⁵. Subsequently Halford, Irwin and Hennion¹⁶ and also Emling, Vogt and Hennion¹⁷ demonstrated that halohydrins, ethers, and esters of halohydrins could be produced by chlorination of an ethylenic compound. Teeter, Bachmann and Bell¹⁸ showed that t-butyl hypochlorite reacted readily with a wide variety of substances containing replaceable or active hydrogen, such as alcohols, acids, aliphatic unsaturated hydrocarbons, phenols, rubber and saturated and unsaturated fatty acid esters.

The first instance of t-butyl hypochlorite being used successfully in the preparation of H-chloro compounds was

reported by Colton, Jones and Audrieth¹⁹ who investigated the preparation of hydrazine from this reagent and urea. It was well known from previous investigations²⁰ that urea and alkali hypochlorites reacted to give hydrazine, and the yield was found to be dependent on three factors.

- (a) mole ratio of urea to t-butyl hypochlorite.
- (b) presence of alkali.
- (c) use of an inhibitor such as gelatin.

Hydrazine had also been prepared by the action of hypochlorite on ammonia²¹ and it had been shown that monochloroamine was the first product. Colton, Jones and Audrieth demonstrated spectrophotometrically that N-chloro-urea was the initial product of the reaction of urea and t-butyl hypochlorite.

A mechanism for the formation of hydrazine from urea and hypochlorite in basic solution was long ago proposed by Schestakoff²², suggesting that a typical Hofmann rearrangement takes place²³, the reaction is-

being the first stage.

Although attempts to isolate N-chloro urea were unsuccessful, the spectrum of solutions containing both urea and t-butyl hypochlorite definitely indicated the formation of a compound containing the N-chloro linkage having a peak of $\epsilon_{\text{max}} = 244$. It was immediately apparent that this peak

was not due to urea, dichlorourea or t-butyl hypochlorite²⁴, and any possibility of it being monochloroamine, formed by hydrolysis, could be discounted, since monochloroamine has a molecular extinction coefficient of 416 at 2450A²⁵.

Final proof of the existence came from a sample of N-chlorourea prepared by the method of Behol and Detoeuf²⁶ which, although only containing 3% of active chlorine, exhibited an absorption maximum at 2450A when measured in aqueous solution. The N-Cl linkage has been shown to absorb in the vicinity of 2400-2600A, Monochloroamine 2450A, N-chlorodimethylamine 2630A²⁷, N-chlorodiethylamine 2620A²⁷, N-chlorophthalamide 2465A²⁸ and N-chlorosuccinimide 2459A.

The success of t-butyl hypochlorite in the above reaction prompted the following experiments with N-chloroguanidine, N-chloromorpholine and N-chloropiperidine.

(i) Chlorination of Morpholine.

When solutions of morpholine and t-butyl hypochlorite in water were mixed, the reaction was found to be almost instantaneous (less than 3 minutes for 100%) and the product was N-chloro morpholine in quantitative yield. The result of this experiment is shown in Figure 5.3, together with the absorption spectrum of the hypochlorite (which compares favourably with the literature).

(ii) Chlorination of piperidine.

After mixing equimolar solutions of piperidine and the hypochlorite the ultraviolet absorption spectrum (Figure 5.3) of

the mixture indicated that complete reaction had occurred in less than five minutes, the spectrum being extremely stable as a function of time. Hence t-butyl hypochlorite succeeds as an N-chlorinating agent for piperidine, whereas chlorine in water, (or more correctly a mixture of chlorine and hypochlorous acid) failed to give rapid quantitative yields. Solutions of t-butyl hypochlorite in sodium hydroxide were equally successful in chlorinating morpholine and piperidine and these results are also illustrated in the figure.

It will be noted that the hypochlorite concentration used is in excess of the morpholine and piperidine concentrations, and allowance for the absorption due to this has been made in calculating the yields of the corresponding N-chloro compounds. However the graphs exhibit the composite spectra.

(111) Chlorination of guanidine salts.

When equimolar (1.69×10^{-3}) solutions of guanidine hydrochloride and t-butyl hypochlorite were mixed, the resultant spectrum of the mixture was not constant and gradually changed with time as can be seen by reference to Figure 5.4. This result is similar to that obtained with molecular chlorine. As the guanidine is chlorinated, hydrochloric acid is simultaneously produced and the presence of this compound could be significant in explaining the resultant instability of the N-chloroguanidine.

FIG. 5.3.

FIG. 5.4.

In an endeavour to avoid the formation of a strong acid, guanidine carbonate was substituted for the hydrochloride in the above reaction with notable success.

Figure 5.4 illustrates the ultraviolet absorption spectrum obtained when solutions of guanidine carbonate and t-butyl hypochlorite were mixed. The spectrum was completely reproducible and constant after three minutes, no further change being observed over a period of several hours. When potassium iodide was added to the mixture only a faint yellow colouration was obtained but on the addition of dilute acetic acid iodine was liberated. In sodium hydroxide solution an identical result was obtained. The absence of any peaks in the spectrum should at once arouse suspicion, but it must be remembered that N-chloroacetamide, the chemistry of which is well established, exhibits an almost identical spectrum, having no peaks in the range 210-350m μ .

Because of the accessibility of sodium hypochlorite and the lack of the unpleasant properties associated with the tertiary alkyl hypochlorite, chlorination by this compound was next attempted. This step, at this stage, was prompted by the success of the chlorination of guanidine using alkaline t-butyl hypochlorite. N-chloroguanidine has been isolated from mixtures of guanidine carbonate and the alkyl hypochlorite but the sodium hypochlorite method, which will now be discussed, gave greater yields and a purer product.

(D) Chlorination by sodium hypochlorite.

Guanidine carbonate (3.6 gms.) was dissolved in water (15 ml.) and the mixture placed in an ice bath. To this solution was added drop-wise with stirring 2M sodium hypochlorite (10 ml.) over a period of 45 minutes. On cooling, the clear solution deposited white crystals which were filtered at the pump and stored at 0°C in a vacuum desiccator over silica gel.

Analysis. Volume of sodium thiosulphate (0.03344N) needed to titrate the iodine liberated on the addition of potassium iodide and acetic acid to a solution of the crystals (.01224g) in water = 7.77 ml.

If the compound is assumed to be N-chloroguanidine, the resulting percentage purity = 99.26%.

Melting point. The compound was found to explode violently at 62-63°C (This temperature was completely reproducible and the range for ten different preparations was 61-63.5°C.).

On standing at room temperature, the white crystals gradually reverted to a pale yellow and finally a deep orange material. This compound will be discussed later. All attempts to carry out an elemental analysis on the sample of N-chloroguanidine were unsuccessful due to the gradual change to the orange compound which was found to be dependent only on heat, light having no effect.

In an effort to prove conclusively that the isolated compound was in fact N-chloroguanidine, Kjeldahl nitrogen

determinations were attempted, but it soon became apparent that N-chloroguanidine would not revert quantitatively to ammonium salts in solution and this fact was supported by the literature and also by the fact that Kjeldahl determinations, carried out on guanidine carbonate itself, failed to give the correct nitrogen percentage, the values obtained from four determinations. (51.4, 82.2, 52.5 and 66.8%) indicating the lack of reproducibility of the results. Sprout, Gilfillan and Wilson²⁹ give a method of digestion which is applicable to nitro, nitroso and azo compounds utilizing the decomposition of the compound with hydroiodic acid, followed by digestion with concentrated sulphuric acid, in the presence of a catalyst³⁰ to convert the nitrogen to ammonium sulphate; this method was also tried without success. All the methods which proved unsuccessful with N-chloroguanidine yielded excellent results when applied to the analysis of nitrogen in inorganic ammonium salts.

Attempts at determining the molecular weight of N-chloroguanidine failed to give results. The methods tried included:

(1) Depression of freezing point of benzene.³¹ - this method was unsatisfactory due to the insolubility of both N-chloroguanidine and the orange decomposition product in this solvent. Other organic solvents also proved unsatisfactory. Whenever the N-chloro compound was found to be slightly

soluble, decomposition was noted to have occurred.

(11) Isothermic methods³² - these methods require a long period for equilibrium to be established with the result that considerable decomposition of the N-chloro compound occurred during equilibrium.

The ultraviolet absorption spectrum of N-chloro-guanidine (Figure 5.5), can be compared with the spectrum of guanidine carbonate (Figure 5.4). The absence of peaks should be noted, and also the similarity of the spectrum of the isolated compound with that of the solutions prepared by mixing guanidine salts and

(a) tertiary-butyl-hypochlorite (see page 190)

(b) aqueous solutions of chlorine (see page 184).

Paper chromatography of N-chloroguanidine. In an endeavour to determine the homogeneity of the N-chloro-guanidine, and to identify the orange decomposition product, samples of these compounds were run on Whatman No.1. paper using butanol saturated with water as the mobile phase and employing the ascending technique.

The N-chloro compounds (N-chloroguanidine and the orange product) were detected by spraying the paper with acidified potassium iodide (1%) containing starch, blue spots on a white background being obtained. Ordinary guanidine derivatives (e.g. guanidine hypochloride) were detected by spraying the paper with pentacyanoaminoferrate (PCNAF) reagent³³, guanidines giving red to yellow spots

with this reagent the sensitivity of detection being 0.5 - 10 μ g. The following results were obtained:

(1) Pure N-chloroguanidine:- Three spots were present having the following R_f values.

(a) 0.165 (red) no reaction with KI

(b) 0.550 (red) reacts with KI

(c) 0.785 (purple) reacts with KI. This last spot was present in only trace amount.

(2) Yellow compound obtained by warming N-chloroguanidine:- Two spots appeared having R_f values.

(a) 0.165 (red) no reaction with KI

(b) 0.785 (purple) reacts with KI

(3) Guanidine hydrochloride:- found to have an R_f value of approximately 0.2, this compound gave a red spot with PCNAP reagent.

(4) Guanidine carbonate:- Would not run well on paper, the spot (red) extending from the origin to an R_f of approximately 0.2.

(5) Mixture of N-chloroguanidine, yellow compound and guanidine hydrochloride:- three spots were obtained having R_f values of:

(a) 0.179 (red) no reaction with KI

(b) 0.564 (red) reacts with KI

(c) 0.790 (purple) reacts with KI

When hydrochloric acid solutions of N-chloroguanidine were run, the same compounds as above were isolated.

From the results of the above experiments it can readily be seen that N-chloroguanidine, in solution, is slowly converted to the orange material (R_f 0.79) and guanidine hydrochloride (R_f 0.18 - 0.20). This orange material was found to contain guanidine hydrochloride and hence it is doubtful whether it is a pure compound (although the possibility of the hydrochloride being formed by reaction in solution must not be dismissed).

(6) N-chloroguanidine in aqueous solution containing radioactive sodium chloride (Cl - 36) :-

A solution of N-chloroguanidine, left in contact with radioactive sodium chloride for eight hours was run on a chromatogram, and the positions of the radioactive products were detected by scanning at 0.5 cm intervals with a thin mica window Geiger counting tube (EW.3H), collimated with a 2 mm slit.

The result of this experiment is illustrated in Figure 5.6. On spraying, the position of the activity was found to coincide with the positions of guanidine hydrochloride, N-chloroguanidine and the orange material, indicating that all three contained radioactive chlorine. The large amount of activity at the origin is due to radioactive sodium ^{chloride} which only migrates slightly.

A fact worth noting at this stage is that when aqueous silver nitrate is added to N-chloroguanidine, the solution immediately turns purple. If such a solution is run on a

FIG. 5.5.

FIG. 5.6.

paper chromatogram no spots are obtained with either spray reagent. A discussion of the significance of this finding, together with an explanation of the results of the other chromatographic experiments will be postponed until the orange compound has been described in detail.

Having accepted the fact that the white material, prepared by the action of sodium hypochlorite on guanidine carbonate, is in fact N-chloroguanidine, a detailed description of the experiments carried out with this compound will now be given.

Acid catalysed chlorinations of phenol by N-chloroguanidine.

An investigation of the chlorination of phenol in both perchloric and hydrochloric acids by N-chloroguanidine was undertaken in an endeavour to discover the method by which this compound chlorinates. The unusual structure of N-chloroguanidine (which still remains uncertain) should render the results of such a study very valuable when taken into consideration with the other properties exhibited by this compound.

The titre of aqueous solutions of N-chloroguanidine were found to be relatively stable over a period of several hours as can be seen in Table 5.1. Slight coloration of the solutions was noted after four hours, the N-chloro titre at the end of this time remaining unchanged.

TABLE 5.1

[N-chloroguanidine] = 0.0214M. Temp 25°C.

Volume taken 5 ml.

Time (min)	0	15	30	45	60	120	180	240
Volume thio (0.271N)	7.92	7.87	7.91	7.90	7.92	7.86	7.87	7.85

Carr³⁴ found that solutions of N-chlorosuccinimide were unstable when left for a period of several days, and this observation was compared with the suggestion of Robb (loc cit.) that nitrogen trichloride is probably formed from solutions of N-chlorosuccinimide in water.

The titre of a solution of N-chloroguanidine and phenol showed a gradual decrease with time, illustrating that a reaction occurs between these two compounds in nearly neutral solution. Robb reports a similar decomposition for N-chlorosuccinimide and phenol which he attributed to a direct reaction between the phenoxide ion and the N-chloro group. Also, Hurst and Soper³⁵, showed that chlorination of phenol could be accomplished with N-chloroacetanilide, partly by preliminary hydrolysis to hypochlorous acid and partly by direct interaction with the phenoxide ion.

(A) Catalysis by hydrochloric acid.

1.101M hydrochloric acid (50 ml.) was pipetted into a blackened flask standing in a thermostat controlled at 25°C ± 0.02°C by a toluene-mercury thermoregulator. When thermal equilibrium had been attained, 0.21M phenol solution (10 ml.) was added, and the mixture thoroughly shaken.

This was followed as soon as possible by 0.535M N-chloro-guanidine (40 ml.), which had been standing in the thermostat for at least thirty minutes

Aliquots (5 ml.) were withdrawn from the reaction mixture and run into a flask containing acidified potassium iodide, the reaction taking place being -

This solution was immediately titrated with standard sodium thiosulphate (0.0271N.) using freshly prepared starch solution as an indicator. 'A'-grade pipettes and burettes were used throughout.

The sources of error in this experiment are few. The only component, the concentration of which has to be known with any precision, is the hydrochloric acid, which was prepared from constant boiling acid³⁶.

The N-chloro concentration was measured throughout the run and hence the initial precision was not critical. It will be demonstrated later that the phenol concentration need only be in excess of that of the N-chloroguanidine, the absolute value being unimportant for the kinetic interpretation. (Carr estimates that the errors arising from timing, pipetting and burette reading do not exceed 1%).

Run 1.

$$[\text{NC1G}] = 0.0214 \text{ M.}$$

$$[\text{C}_6\text{H}_5\text{OH}] = 0.0210 \text{ M.}$$

$$[\text{HCl}] = 0.5505 \text{ M. Temp. } 25^\circ\text{C} \pm 0.02^\circ\text{C}$$

Note: N-chloroguanidine = $[\text{NC1G}]$

$[\text{NC1G}]$ titre, titration figures are used throughout for $[\text{NC1G}]$

Time (secs)	Titre	Log ₁₀ titre	$k_{\text{obs}} \times 10^4 \text{ sec}^{-1}$
0	7.90	0.8976	_____
60	7.44	0.8716	10.00*
180	7.04	0.8476	4.61
360	6.32	0.8007	6.00
600	5.50	0.7404	5.80
660	5.32	0.7259	5.58
960	4.50	0.6532	5.58
1320	3.63	0.5599	5.97
1680	2.99	0.4757	5.39
2460	1.90	0.2788	5.82
3060	1.38	0.1399	5.35
3720	0.92	1.9638	6.15
4440	0.62	1.7924	5.49
6000	0.24	1.3802	6.08

*Neglected when finding average value of k_{obs} as measurement of $\Delta \log \text{NC1G}$ uncertain.

The k_{obs} values tabulated above were calculated as follows.

A graph was constructed of $\log_{10}$ titre against time (see Fig 5.7). The reaction rate can thus be expressed as

$$\frac{-d[\text{NC1G}]}{dt} = k_{\text{obs}} [\text{NC1G}]$$

Values of k_{obs} were calculated from the integrated equation $k_{\text{obs}} = \frac{2.303}{\Delta t} \log_{10} \frac{[\text{NC1G}]_1}{[\text{NC1G}]_2}$

where Δt is the time interval in seconds between the pairs of experimental results.

The recorded value of k_{obs} was found by averaging the values tabulated. This gave $k_{\text{obs}} = 5.65 \times 10^{-4} \text{ sec}^{-1}$

The graphical value of $k_{\text{obs}} = 5.67 \times 10^{-4} \text{ sec}^{-1}$

A repeat experiment using the same concentrations as above gave $k_{\text{obs}} = 5.73 \times 10^{-4} \text{ sec}^{-1}$, indicating that the reproducibility is satisfactory.

Run 2.

$$[\text{NC1G}] = 0.0201\text{M.}$$

$$[\text{C}_6\text{H}_5\text{OH}] = 0.0210\text{M.}$$

$$[\text{HCl}] = 0.276\text{M.} \quad \text{Temp. } 25^\circ\text{C.}$$

Time (secs)	Titre	$\log_{10}$ titre	$k_{\text{obs}} \times 10^4 \text{ sec}^{-1}$
0	7.27	0.8615	-
60	7.18	0.8561	2.07
240	7.04	0.8476	1.09
540	6.76	0.8299	1.36
960	6.31	0.8000	1.64
1440	5.90	0.7709	1.40

Time (secs)	Titre	$\log_{10}$ titre	$k_{\text{obs}} \times 10^4 \text{sec}^{-1}$
1815	5.58	0.7466	1.49
2100	5.33	0.7267	1.61
2640	4.91	0.6911	1.52
3180	4.59	0.6618	1.25
4020	4.05	0.6075	1.49
4620	3.67	0.5647	1.65
5160	3.46	0.5391	1.10
6180	2.92	0.4654	1.66
8160	2.20	0.3424	1.43
9180	1.90	0.2788	1.44
10800	1.47	0.1673	1.59
13020	1.05	0.0212	1.52

Comparison of the values obtained for this run indicate the effect of changing the acid concentration.

The average value of k_{obs} from the table = $1.49 \times 10^{-4} \text{sec}^{-1}$. A graph of $\log_{10} \text{titre}$ Vs time for this experiment gave the value of k_{obs} as $1.48 \times 10^{-4} \text{sec}^{-1}$.

The values obtained in a duplicate experiment were in good agreement (within 2%) of the value obtained above.

Run 3.

Time (secs)	Titre	Log ₁₀ titre	k _{obs} x 10 ⁴ sec ⁻¹
0	7.58	0.8794	-
60	7.33	0.8651	5.50
240	6.67	0.8241	5.25
720	5.06	0.7042	5.75
900	4.65	0.6675	4.70
1080	4.12	0.6149	6.75
1440	3.37	0.5276	5.59
1800	2.72	0.4346	5.96
2700	1.64	0.2146	5.63
3400	1.07	0.0316	5.70
3720	0.90	1.9542	4.85

Comparison of the value of k_{obs} obtained from the above experiment (5.57 x 10⁻⁴sec⁻¹), with that obtained when the phenol concentration was 0.021M shows that doubling the phenol concentration has no significant effect on the first order rate constant.

From the results obtained for k_{obs} it is possible to calculate the value k₁₁₁ from the relationships.

$$\frac{-d [\text{NClG}]}{dt} = k_{\text{obs}} [\text{NClG}]$$

$$(k_{\text{obs}} = \frac{2.303}{\Delta t} \log_{10} \frac{[\text{NClG}]_1}{[\text{NClG}]_2})$$

and $\frac{-d [\text{NClG}]}{dt} = k_{111} [\text{NClG}] [\text{H}^+] [\text{Cl}^-]$ giving

$$k_{111} = \frac{k_{\text{obs}}}{[\text{H}^+] [\text{Cl}^-]}$$

This last equation will only hold if the $[H^+]$ and $[Cl^-]$ concentrations are in excess of the other species present and can be considered constants.

Values of k_{111} for the reaction between N-chloro-guanidine and phenol in hydrochloric acid are given below.

$[Hcl]$ M	$10^4 k_{obs} sec^{-1}$	$10^3 k_{111} mole^{-2} l^2 sec^{-1}$
0.551	5.65	1.86
0.276	1.49	1.95

Catalysis by perchloric acid.

Run 4.

Time (min)	0	5	30	103	170	243
Titre of thiosulphate.	7.33	7.27	7.29	7.29	7.25	7.23
Time (min)	400	763	1384			
Titre of thiosulphate.	7.23	7.20	7.17			

Hence no appreciable reaction occurs between N-chloro-guanidine and phenol in the presence of perchloric acid, indicating the catalytic effect of hydrochloric acid and showing the dependence of the rate on the chloride ion concentration. This result is exactly analogous to the effect found by Carr with N-chlorosuccinimide and N-chloroacetamide.

The effect of increasing the perchloric acid concentration can be seen in Run 5.

Run 5.

Time (secs)	120	780	3480	6300	18480	38400
Titre	7.30	7.31	7.30	7.26	7.12	6.86
Log ₁₀ titre	0.8633	0.8639	0.8633	0.8609	0.8525	0.8363

A small drop in titre was detectable, and from the slope of the graph of log₁₀ titre plotted as a function of time (see Fig. 5.8), the approximate value of $k_{\text{obs}} = 1.48 \times 10^{-6} \text{ sec}^{-1}$ was obtained. These values can be compared with those obtained by Carr for the reaction between N-chlorosuccinimide and phenol under similar conditions.

From the result of this series of experiments the similarity in reactivity between N-chloroguanide and N-chlorosuccinimide has been demonstrated, indicating the unreactivity of the N-chloroguanidinium ion as a chlorinating agent of the N-chloromorpholine type. Further experiments with the chlorinated guanidine were performed in an endeavour to understand more of its properties.

III Thermal Decomposition of N-chloroguanidine.

The position of the chlorine atom in the N-chloroguanidine molecule has been the subject of much conjecture, the two possibilities being illustrated below.

It has been shown previously³⁷ that ald-chloroimines (RCH = NCl) readily undergo thermal decomposition, nitriles and hydrogen chloride being identified as primary products. Because of the thermal instability of N-chloroguanidine an investigation of this compound was undertaken using similar techniques to those applied by Hauser, Gillaspie and LeMaistre³⁸ for the ald-chloroimines.

The products obtained in the thermal decomposition of ald-chloroimines are accounted for by the two reactions, (1) and (11).

The extent of the primary decomposition (1) was calculated from the amount of nitrile obtained, or from the hydrogen chloride in the gaseous products plus that used up in the secondary reaction (11). By inspection of equation (11) it can be seen that the amount of hydrogen chloride used should be equivalent to the free chlorine produced. The decomposition at elevated temperatures appeared to follow the same course as that at lower temperatures. However, at the lower temperatures, the life of the chloroimine is relatively long, and there is consequently more opportunity for hydrogen chloride to come in contact with unchanged chloroimine, producing more secondary products at

the expense of the primary decomposition products.

A glance at the N-chloroguanidine structure will indicate that the reaction (1) above cannot occur, the production of a nitrile being virtually impossible. However, if hydrogen chloride is formed by a reaction of the type -

then a reaction of type (11) above could proceed as follows:-

and hence a study of the thermal decomposition products of N-chloroguanidine by the method adopted by Hauser et. al. (loc. cit.) for ald-chloroimines should prove valuable.

The apparatus used for the thermal decomposition studies is illustrated in Fig. 5.9.

The bulb (c) was allowed to come to thermal equilibrium at the decomposition temperature of N-chloroguanidine (65°C) by placing it in an oil bath kept at temperature by a mercury-toluene regulator. A known weight of the N-chloro compound was then introduced into the apparatus on the small glass shovel (A) which was held rigid by means of the springs (B). Taps (D) and (E) were then opened and the complete apparatus was flushed with nitrogen to remove the air. The bottom of bubbler (G) was filled with small glass balls, followed by the absorbing liquid (either potassium iodide or sodium hydroxide).

When all the air had been displaced by nitrogen, Tap D was closed and the shovel A was inverted, allowing the N-chloroguanidine to come into contact with the hot bulb (c). Immediate decomposition was found to occur and the gases were collected in the bubbler. Before the contents of (G) sucked back past the safety bulb (F), tap E was closed and the complete apparatus allowed to cool to room temperature. Taps D and E were again opened and the apparatus flushed once more with nitrogen, removing the gaseous products to the bubbler where they were absorbed. Note: It was found necessary to join the sections of the apparatus with springs owing to the very high pressures developed when N-chloroguanidine decomposed.

Exp. A.

Bubbler containing potassium iodide.

Wt. of N-chloroguanidine = 0.0599 gms.

Volume of sodium thiosulphate (0.0346N) to titrate iodine liberated = 0.8 ml.

The residue in flask C was a very pale yellow solid. This solid was dissolved in water (10 ml.) and 0.0986N silver nitrate (20 ml.) was added and the solution boiled to coagulate the precipitated silver chloride. The silver halide was filtered off and the excess silver nitrate was titrated with 0.1157N potassium thiocyanate³⁹. Volume required = 13.47 ml.

The amount of silver nitrate used was equivalent to

trap (G) and the N-chloroguanidine exploded. Solutions were treated as follows:-

(a) Sodium hydroxide (10 ml.) was acidified with dilute acetic acid and potassium iodide was added. No chlorine was found to be present. If gaseous chlorine had been absorbed by the sodium hydroxide a certain percentage of chloride ion would have been formed, together with some sodium hypochlorite which would have been detected on the addition of acid.

(b) Sodium hydroxide (10 ml.) from the bubbler was acidified with 6N nitric acid and 0.0986N silver nitrate (10 ml) was added. The excess silver nitrate was titrated with 0.1157N potassium thiocyanate (8.01 ml) using ferric ammonium sulphate as indicator.

(c) a 10 ml aliquot of the sodium hydroxide solution was boiled with ammonium hydroxide to reduce any chlorine. The solution was then acidified with nitric acid and treated as in (b). Volume of thiocyanate for the back titration was 8.10 ml.

(d) 10 ml. of the sodium hydroxide solution was titrated with standard 0.0791N sulphuric acid (10.6 ml.) indicating that a total volume of 5.60 ml. of sodium hydroxide had been neutralised by the decomposition gases.

(e) No N-chloro compounds were detected in flask (C). From these results it was found that 27.6% of the total chlorine was present in the sodium hydroxide bubbler

0.0147 gms. of chloride ion and this represents 24.6% of the total. It is obvious from this result that a large amount of chlorine must escape as gaseous hydrogen chloride and this theory was tested by replacing the potassium iodide in the bubbler with silver nitrate.

Exp. B

Weight of N-chloroguanidine = 0.0560 gm.

0.1 AgNO₃ (25 ml) was placed in the bubbler and the amount remaining after decomposition was found to be 23.95 ml. The N-chloro titre of the residue in the flask (0.28 ml. of .0346N thio.) indicates that no significant amount of any N-chloro group remains after thermal decomposition.

The contents of flask C were made up to 50 ml. with water and aliquots (25 ml.) were titrated with 0.0986N silver nitrate (1.80 ml.). Hence the chlorine balance is as follows:-

(i)	As Cl ⁻	in residue	59.6%
(ii)	As Cl ⁻	in gaseous product	17.4%
(iii)	As N-Cl	in residue	0.8%
(iv)	As Cl ₂	in gaseous product	5.2%
TOTAL			<u>83.0%</u>

indicating that a large percentage of the chlorine was unaccounted for. This experiment was repeated.

Exp. C.

Weight of N-chloroguanidine = 0.1006 gm.

0.0944N sodium hydroxide (50 ml.) was placed in the

(c.f 22.6% in Exp. B.) If all the chloride in the sodium hydroxide solution was present as hydrogen chloride, the volume of sodium hydroxide neutralised should only have been 3.14 ml. (c.f. the 5.60 ml. found). Consequently the indications are that either:-

- (i) another acidic gas other than hydrogen chloride was evolved in the thermal breakdown of N-chloroguanidine
- or (ii) a second gas containing chlorine was produced which reacted with sodium hydroxide to give chloride ion. Chlorine is the answer which immediately springs to mind but this can be ruled out from the absence in solution of any hypochlorite.

This experiment was repeated in an endeavour to check on the above results.

Exp. D.

Weight of N-chloroguanidine = 0.0980 gm.

Bubbler contained 0.0944N sodium hydroxide (50 ml.)

A summary of the results of this experiment is given below, the experimental methods applied being the same as for Exp. C.

- (a) The percentage of the total chlorine found in the sodium hydroxide solution was 23.4%.
- (b) If all the chlorine in the sodium hydroxide was collected as hydrogen chloride, the volume of sodium hydr-

oxide neutralised should be 2.63 ml. Actual volume found = 5.40 ml., indicating the presence of another highly acidic gas.

(c) No sodium hypochlorite was present in the alkali trap.

(d) Total volume of 0.0986N silver nitrate required to titrate the residue in the reaction flask was 8.0 ml. The percentage of the total chlorine found in this vessel was 76.0%.

The total recovered chloride ion (99.1% theoretical) indicates that all the chlorine originally bound to the nitrogen atom in N-chloroguanidine has been converted to a form which reacts with silver nitrate directly to form silver chloride or alternatively is very readily hydrolysed by alkali or acid into a compound of similar behaviour. The fact that the percentage of chloride ion existing in the sodium hydroxide trap was greater than that found in the silver nitrate bubbler indicated that a hydrolysis of acidic gaseous component had occurred, yielding chloride ion. It can safely be deduced that not all of the halide is evolved as hydrogen chloride itself, a large percentage existing as other acidic vapours, possibly nitrogen trichloride.

The absence of any chlorine as a gaseous product is interesting as it eliminates the possibility of the hydrogen chloride, produced in an initial reaction, attacking the N-chloroguanidine molecule to yield guanidine hydrochloride and molecular chlorine.

The proportions of the products varied in the different experiments, the percentages of chloride appearing in the gaseous state and that remaining in the reaction flask not being constant. The absence of any chlorine in the products could indicate that reactions of the type illustrated below might possibly be occurring, all the chlorine being tied up as inorganic chloride.

Even though the possibility of these two compounds existing is open to conjecture, a very likely reaction product is melamine which is known to be produced when guanidine itself is heated, the reaction involving the loss of three molecules of ammonia:

The tendency to form an unsaturated six-membered ring

similar to that of benzene doubtless supplies the driving force. With N-chloroguanidine, the products would presumably be monochloroamine and melamine.

Whatever the complete mode of decomposition, the products are probably complex and cannot be easily stereotyped, the amounts of the various compounds varying from experiment to experiment.

The important factors which emerge from this section are that N-chloroguanidine is extremely unstable to heat and decomposes explosively to form several gaseous products, none of which can be identified as molecular chlorine.

IV The equilibrium existing between hydrochloric acid and N-chloroguanidine.

The application of E.M.F. measurements to the study of the equilibrium chlorine concentration existing in solutions of N-chloro compounds and hydrochloric acid has already been described in detail (see pages 98n- 105) N-chloroguanidine has been shown to closely follow N-chlorosuccinimide and N-chloroacetamide in the mode of chlorination of phenol, the reaction having been shown to be kinetically of the first order, being independent of the phenol concentration.

Experiments will now be described in which the chlorine concentration is measured as a function of time for the reaction between N-chloroguanidine and hydrochloric acid, and the results will be compared with those already obtained for other N-chloro compounds.

Run 1.

$$[\text{N-chloroguanidine}] = 2.068 \times 10^{-3} \text{M}$$

$$[\text{hydrochloric acid}] = 0.618 \text{M} \quad \text{Temp. } 25^{\circ}\text{C.}$$

Time (min)	E.M.F. (volts)	$[\text{Cl}_2] \times 10^4$
1.5	1.0050	1.17
2.0	1.0080	1.57
2.5	1.0119	2.00
3.0	1.0140	2.35
3.5	1.0159	2.72
4.0	1.0174	3.05
5.0	1.0200	3.73
6.0	1.0220	4.35
7.0	1.0233	4.81
8.0	1.0248	5.40
9.0	1.0259	5.88
10.0	1.0266	6.21
12.0	1.0279	6.83
14.0	1.0287	7.30
19.0	1.0299	8.01
21.0	1.0301	8.13
23.0	1.0302	8.19
∞	1.0302 ₅	8.19

The inherent errors in these results are identical to those already described for the experiments with N-chloro-

morpholine and are largely due to the precision with which the E.M.F. can be measured.

Run 2.

$$[\text{N-chloroguanidine}] = 3.10 \times 10^{-3} \text{M}$$

$$[\text{hydrochloric acid}] = 0.618 \text{M} \quad \text{Temp. } 25^{\circ}\text{C.}$$

Time (min)	E.M.F. (volts)	$[\text{Cl}_2] \times 10^4$
1.5	1.0092	1.62
2.0	1.0122	2.04
2.5	1.0150	2.54
3.0	1.0170	2.96
3.5	1.0190	3.45
5.0	1.0229	4.67
6.0	1.0249	5.44
8.0	1.0275	6.65
13.0	1.0309	8.65
20.0	1.0320	9.42

Run 3.

$$[\text{N-chloroguanidine}] = 3.67 \times 10^{-3} \text{M}$$

$$[\text{hydrochloric acid}] = 0.618 \text{M} \quad \text{Temp. } 25^{\circ}\text{C.}$$

Time (min)	E.M.F. (volts)	$[\text{Cl}_2] \times 10^4$
2.0	1.0141	2.37
3.0	1.0185	3.32
3.5	1.0206	3.91
4.0	1.0220	4.35

Time (min)	E.M.F. (volts)	$[Cl_2] \times 10^4$
5.0	1.0245	5.28
6.0	1.0261	5.97
7.0	1.0277	6.76
9.0	1.0297	7.88
11.0	1.0310	8.72
14.0	1.0320	9.42
26.0	1.0328	10.02

The results of the above experiments are plotted in Fig.5.10, indicating the rate of formation of chlorine as a function of time. Once again the graphs are seen to be linear for approximately 40-50% of the reaction, enabling a rough estimation of the rate of chlorine production.

Identical experiments were carried out in 0.316M hydrochloric acid (see Fig. 5.11), the results being summarised in Table 5.2.

TABLE 5.2

Equilibrium chlorine concentrations for the reaction between N-chloroguanidine and 0.316M hydrochloric acid at 25°C.

$[N\text{-chloroguanidine}] \times 10^4$	7.72	16.86	16.86	43.7
$[Cl_2] \text{ eqbm} \times 10^4$	2.13	2.69	3.14	3.02

Treatment of results

The reactions taking place in solution are assumed to

FIG. 5.11.

be as follows:-

for which the following equilibrium constants can be written :-

$$K = \frac{[\text{NHC1}^+]}{[\text{NCl}][\text{H}^+]} ; K' = \frac{[\text{NH}_2^+][\text{Cl}_2]}{[\text{NHC1}^+][\text{H}^+][\text{Cl}^-]} \text{ and } K_3 = \frac{[\text{Cl}_3^-]}{[\text{Cl}_2][\text{Cl}^-]}$$

only the value of K_3 being already known⁴⁰. The values of K and K' can readily be obtained by setting up two simultaneous equations:-

Letting the initial N-chloroguanidine concentration

$$\begin{aligned} [\text{NCl}] \text{ init} = a \text{ and the equil } [\text{NCl}] &= x = (\text{N-chloroguanidine}) \\ [\text{NHC1}^+] &= y = [\text{N-chloroguanidinium ion}] \\ [\text{Cl}_2] &= z \\ [\text{Cl}_3^-] &= w \end{aligned}$$

The measured chlorine concentration is $\text{Cl}_2 + \text{Cl}_3^-$ and will be designated by v . Hence $v = z + w$ and $a = x + y + z + w$.

Now since

$$\frac{[\text{Cl}_3^-]}{[\text{Cl}_2][\text{Cl}^-]} = 0.192 = K_3$$

then it follows that

$$z = \frac{v}{1 + K_3 \text{Cl}^-}$$

From the equilibrium constant K $\frac{y}{x} = \frac{[\text{NHC1}^+]}{[\text{NCl}]} = K [\text{H}^+]$

and since $y + x = a - z - w$

then
$$x = \frac{a - v}{1 + K [H^+]}$$

and consequently a function K_2 can be derived where

$$K_2 = \frac{[Cl_2][NH_2^+]}{[NCl][H^+]^2[Cl^-]} = \frac{z \cdot v}{\frac{a - v}{1 + K [H^+]} [H^+]^2 [Cl^-]} = K K'$$

making the substitution for z gives

$$K_2 = \frac{\frac{v}{1 + K_3 [Cl^-]} \cdot v}{\frac{a - v}{1 + K [H^+]} [H^+]^3} \quad \text{since } [Cl^-] \approx [H^+]$$

by equating this function for varying values of $[H^+]$ the value of K can be readily obtained, leading immediately to the values of K_2 which are listed in Table 5.3. Values of

$$K_1 = \frac{[Cl_2]^2}{[NCl][H^+]^2} \quad \text{as used for } \underline{N}\text{-chlorosuccinimide and}$$

N-chloroacetamide have been included for comparison in two cases. Calculations involving K_1 make no allowance for the formation of N-chloroguanidinium ion or the trihalide ion. Nor do they correct for the protonation of guanidine itself. This factor becomes important because of the basic strength of guanidine as compared to the other two N-chloro compounds which are comparatively weak bases.

TABLE 5.3

$[\text{N-chloroguanidine}]$	$[\text{HCl}]$	$K_2 = \frac{[\text{NH}_2^+][\text{Cl}_2]}{[\text{NCl}][\text{H}^+]^3}$ mole ⁻² l ²
7.724×10^{-4}	0.316	2.56×10^{-3}
1.686×10^{-3}	0.316	1.62×10^{-3}
1.686×10^{-3}	0.316	2.28×10^{-3} (7.18×10^{-4})*
2.068×10^{-3}	0.618	2.28×10^{-3} (14.10×10^{-4})*
3.100×10^{-3}	0.618	1.74×10^{-3}
3.666×10^{-3}	0.618	1.60×10^{-3}
		Mean 2.01×10^{-3} mole ⁻¹ l.

* Values calculated using $K_1 = \frac{[\text{Cl}_2]^2}{[\text{:NCl}][\text{H}^+]^2}$

Examination of the above table indicates a wide variation in the value of the equilibrium constant. This spread is due to the instability of the N-chloro compound in acid solution, giving rise to discrepancies in the measured chlorine concentration.

The value of K (defined by $K = \frac{[\text{NHC1}^+]}{[\text{NCl}][\text{H}^+]}$) for N-chloroguanidine was found to be $0.196 \text{ mole}^{-1} \text{ l.}$, and this value can be compared with the indentical functions already derived for the other N-chloro compounds given in Table 5.4.

TABLE 5.4

N-chloro compound	$K = \frac{[NHC1^+]}{[NCl][H^+]}$	Ref.
<u>N</u> -chloromorpholine	0.554	40
<u>N</u> -chloropiperidine	7.906	41
<u>N</u> -chlorodiethylamine	10.530	42
<u>N</u> -chlorodimethylamine	2.899	42

From the reactions $NCl + H^+ \rightleftharpoons NHC1^+$,
 and $NHC1^+ + Cl^- + H^+ \rightleftharpoons NH_2^+ + Cl_2$, an
 approximate rate expression $v = k_{111} [NCl][H^+][Cl^-]$ can be
 written. More precise equations containing k_{111} have been
 derived⁴³, but the accuracy of the measurement of chlorine
 for the reaction between N-chloroguanidine and hydrochloric
 acid does not warrant detailed calculation, consequently
 only qualitative measurements of the value of k_{111} were
 derived:-

$$v = k_{111} [NClG] [H^+] [Cl^-] = k_{obs} [NClG] \text{ since } [H^+] \text{ which } = [Cl^-] \text{ remains constant.}$$

i.e $\frac{d[Cl_2]}{dt} = k_{obs} [NClG]$ and by assuming that the N-chloro-
 guanidine concentration remains constant over the early
 stages of the reaction, the value of k_{obs} can be calculated.

From the slopes of the graphs of the chlorine concen-
 tration plotted as a function of time (Fig.5.10 and Fig.5.11)
 the values of $k_{obs} [NClG]$ were obtained, and hence values of

k_{111} using

$$k_{111} = \frac{k_{\text{obs}}}{[\text{H}^+][\text{Cl}^-]} = \frac{k_{\text{obs}}}{[\text{H}^+]^2} \quad \left(\text{Note } k_{\text{obs}} = \frac{d[\text{Cl}_2]}{dt} / [\text{NClO}] \right)$$

and this should be the third order rate constant of any chlorination by N-chloroguanidine which proceeds exclusively through chlorine. The values of k_{111} are given in Table 5.5 indicating the great variability due to the instability of N-chloroguanidine in solution. Because of the very low chlorine concentrations measured, the possibility of impurities affecting the result was always present and must be accepted.

TABLE 5.5

[N-chloro- guanidine] mole .1 ⁻¹	[HCl] mole .1 ⁻¹	10 ⁵ slope mole .1 ⁻¹ min ⁻¹	10 ⁴ k _{obs} sec ⁻¹	10 ³ k ₁₁₁ 1 ² . mole ⁻² . sec ⁻¹
7.724 x 10 ⁻⁴	0.316	0.86	1.85	1.85 *
1.686 x 10 ⁻³	0.316	1.12	1.11	1.11
1.686 x 10 ⁻³	0.316	1.12	1.11	1.11
4.370 x 10 ⁻³	0.316	1.53	0.58	0.58
2.068 x 10 ⁻³	0.618	7.80	6.29	1.65
3.100 x 10 ⁻³	0.618	8.67	4.67	1.23
3.666 x 10 ⁻³	0.618	10.00	4.59	1.20

As can be seen from the graphs, the initial 50% of the reaction gives an approximate linear plot of chlorine concentration against time and this phenomenon has been explained for N-chloromorpholine in hydrochloric acid (see page 105).

* Neglected when the mean value $1.35 \pm .26 \times 10^{-3} \text{ l}^2 \cdot \text{mole}^{-2} \cdot \text{Sec}^{-1}$ was calculated (this figure reduces to $0.81 \pm .15 \times 10^{-1} \text{ l}^2 \cdot \text{mole}^{-2} \cdot \text{min}^{-1}$).

The value of k_{111} obtained by this method is in agreement with the mean value of $1.90 \times 10^{-3} \text{ l}^2 \cdot \text{mole}^{-2} \cdot \text{sec}^{-1}$ obtained from the chlorination of phenol.

V Yellow decomposition product of N-chloroguanidine.

When samples of N-chloroguanidine were left at room temperature, changes in colour were found to occur, the original white powder reverting slowly to a deep orange. This reaction was found to proceed explosively if slight heat was applied. The orange powder, unlike the original N-chloroguanidine, was found to be practically insoluble in water.

Several samples of the orange material (X) were analysed for N-chloro groups by the addition of dilute acetic acid and potassium iodide with the following results.

TABLE 5.6

wt of sample	0.0109g.	0.0109g.	0.0109g.	0.0109g.
Vol of this 0.027	4.31 ml	4.76 ml	7.16 ml	4.80 ml.

indicating the variation in the N-chloro titre. The conversion of the white material to X is slow, and the analyses given above were carried out on samples of N-chloroguanidine left at room temperature for several days.

Other properties of compound X were investigated as follows:-

(a) Chemical Analysis. Three different samples were analysed ⁴⁴ and the results are compared in Table 5.7. The theoretical percentages of the elements present in N-chloroguanidine have been given for comparison.

TABLE 5.7

	C%	H%	N%	Cl%	O%	Total
Sample 1	12.96	3.84	42.87	35.93	-	95.60
Sample 2	12.47	4.05	43.28	36.28	1.05	97.13
Sample 3	12.88	4.32	45.08	37.27	0.00	99.55
<u>N</u> -chloroguanidine	12.84	4.31	44.93	37.91	0.00	99.99

From an examination of these results, it can be ascertained that in the reversion of N-chloroguanidine to compound X, no loss of elements occurs, indicating the absence of the evolution of gaseous products such as molecular chlorine or hydrogen chloride.

This observation is supported by the fact that no appreciable loss of weight occurs when N-chloroguanidine reverts to the orange material.

By boiling a sample of X with sodium hydroxide for 15 minutes, neutralising with nitric acid, and titrating the chloride produced with standard silver nitrate, values identical to those obtained by Campbell⁴⁴ were obtained. This indicated that all of the halogen in X exists either as halide ion or as readily hydrolysable chlorine.

(b) Melting Point. Whereas N-chloroguanidine explodes at 61-63°C when heated in a capillary tube, X was found to decompose with frothing at 143-144°C (c.f. yellow crystals isolated by England M.P. 134-135°C.)

A sample of the orange powder was continuously extracted with carbon tetrachloride in a Bolten extractor, yielding pale yellow crystals of M.P. 161-162°C. These crystals were more soluble in water than X and were found to give no precipitate with acidified silver nitrate.

From the results of these experiments, taken in conjunction with those obtained from the paper chromatography work, it was obvious that the orange material was not a pure compound but existed as a mixture of guanidine hydrochloride and compounds such as azochloroamide. The deep orange colour was presumed to be due to the presence of the strong chromophore-N=N-, the colour being intensified by the presence of -NH₂ groups acting as auxachromes⁴⁵.

The yellow compound, extracted from the carbon tetrachloride, was found to liberate iodine from acidified potassium iodide, and a quantitative estimation yielded the following result:

Weight of substance 0.0149 gms

Volume of thio (.0345N) = 9.49 mls.

If the compound is azochloroamide $(\text{NH}_2-\text{C}-\text{N} = \text{N}-\text{C}-\text{NH}_2)$
 $\quad \quad \quad \parallel \quad \quad \quad \parallel$
 $\quad \quad \quad \text{NCl} \quad \quad \quad \text{NCl}$

then 1000ml of N thio = $\frac{M.W}{4} = 45.754$ gms

∴ 9.49 ml of .0345N thio = 0.0149₈ gms.

It is assumed from the analytical results and the melting point, that the yellow compound is azochloroamide, and that X was a mixture of this compound, guanidine hydrochloride and possible other products in small amounts. If X contained 55% of azochloroamide, then the analytical figures given in Table 5.7 would be explained if an average value of 4.78 ml was adopted for the volume of thiosulphate equivalent to 0.0109 gms.

Such a mixture could be formed by a reaction of the type $4(\text{NH}_2)_2\text{C} = \text{NCl} \rightarrow \text{NH}_2-\text{C}-\text{N} = \text{N}-\text{C}-\text{NH}_2 + 2\text{NH}_2-\text{C}-\text{NH}_2 \cdot \text{HCl}$
 $\quad \quad \quad \parallel \quad \quad \quad \parallel \quad \quad \quad \parallel$
 $\quad \quad \quad \text{NCl} \quad \quad \quad \text{NCl} \quad \quad \quad \text{NH}$

the percentage of azochloroamide in such a mixture being 49%.

Conclusions and Summary.

A detailed investigation of the preparation, properties and reactions of N-chloroguanidine has been carried out and these reactions have been compared, where applicable, to the corresponding reactions of other N-chloro compounds. In particular, the following significant

results emerged from the experimental work:-

- (1) A preparation of N-chloroguanidine was devised and this compound has been isolated in a pure state for the first time. N-chloroguanidine exists as a white crystalline solid which decomposes explosively at 61-63°C.
- (2) A chromatographic investigation has been outlined and the R_f values have been evaluated for guanidine hydrochloride, N-chloroguanidine and azochloroamide using butanol-saturated water as the mobile phase.
- (3) N-chloroguanidine was found to chlorinate phenol in the presence of hydrochloric and perchloric acids, and the similarity in the reactions of this compound and N-chlorosuccinimide has been demonstrated. In particular, the unreactivity of the N-chloroguanidinium ion is amply illustrated by the slowness of the reaction between N-chloroguanidine and phenol in perchloric acid, compared with the analogous experiments carried out with N-chloromorpholine.
- (4) The thermal decomposition has been investigated and the possible nature of the products has been discussed. The important point emerging from this work was the lack of any chlorine in the gaseous products, a compound which could readily have been formed by a reaction of the type:-

in the solid state (c.f. the vigorous reaction which takes place when hydrogen chloride gas is passed over pure anhydrous N-chloromorpholine.)

(5) The equilibrium constant defined by

$$K_2 = \frac{[NH_2^+][Cl_2]}{[NClG][H^+]^2[Cl^-]}$$

was found to be applicable for the N-chloroguanidine case and values have been measured at 25°C for several acid concentrations, a mean value of $2.01 \times 10^{-3} \text{ mole}^{-1} \cdot \text{l.}$ being obtained.

By solving a series of simultaneous equations, the equilibrium constant for the reaction:-

was found to be $0.196 \text{ mole}^{-1} \cdot \text{l.}$, compared with the identical function for other N-chloro compounds, in particular N-chloromorpholine (0.553) and N-chloropiperidine (7.90).

(6) Utilisation of the E.M.F. method of chlorine measurement led to values for the rate of production of chlorine in the reaction between N-chloroguanidine and hydrochloric acid. Because of the low values measured, and the obvious presence of impurities in the N-chloroguanidine owing to the impossibility of purifying this unstable compound, the rate constants obtained are of only qualitative value.

(7) N-chloroguanidine was found to be unstable at room temperature, reverting to a deeply coloured compound (X) which was identified as a mixture of azochloroamide and guanidine hydrochloride, with the possibility of other products being present in small amounts. When silver nitrate was added to a solution of N-chloroguanidine in

water, the mixture slowly turned purple, and paper chromatography of this mixture illustrated the absence of the N-chloro group (existing as N-chloroguanidine or as compound X) and of guanidine hydrochloride. The conclusion being that the silver nitrate removed the chlorine from N-chloroguanidine as the chloride, presumably by some hydrolysis reaction, demonstrating the instability of N-chloroguanidine in solution as opposed to a compound such as N-chloromorpholine which is relatively stable in the presence of silver nitrate. Aqueous solutions of N-chloroguanidine are acidic and it is therefore unlikely that the purple colouration could be due to the presence of silver hydroxide or oxide formed by the reaction of silver nitrate with hydroxide ions in solution.

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CHAPTER 6

Cyanide displacement reactions on

Halides

The reaction between alkyl halides and metal cyanides is well known and takes place to furnish either cyanides (b) or isocyanides (a) :

The relative proportions of the two products appear to depend largely on the metal cyanide used. Isocyanide is the principal product of the action of the lower alkyl halides on silver cyanide. Mercuric and zinc cyanides also yield a high proportion of isocyanides by reaction with alkyl iodides.¹

The alkali cyanides, on the other hand, give nitriles as the principal product of the interaction with alkyl halides and this method has widely been adopted for the preparation of simple nitriles.

The ease with which this reaction proceeds depends largely upon the relative mobility of the halogen on the negative group, this in turn being determined by the nature of the compound of which it forms a part and the position of the negative residue in the molecule.

The halogen is replaced with great difficulty in certain types of compounds, in such cases it is often necessary to heat the halogenated compound with the metal cyanide at a comparat-

ively high temperature for a long period. To this class of compounds belong many halogenated aliphatic hydrocarbons and, with very few exceptions, aromatic hydrocarbons in which the halogen is attached to a nuclear carbon atom. In these cases the reaction is often facilitated by the addition of a catalyst such as cuprous cyanide. Several examples are given below:

(1) reaction of potassium cyanide with chloromethylimidazole to form cyanomethylimidazole

(11) Monochloroacetone reacts with potassium cyanide in alcoholic solution to form cyanoacetone, $\text{CNCH}_2\text{COCH}_3$ ²

Reactions in alcoholic solutions are often complicated because of the reaction $\text{ClCN} + \text{KCN} + \text{HOC}_2\text{H}_5 \rightarrow \text{C}_2\text{H}_5\text{OC}(\text{NH})\text{CN} + \text{KCl}$

which was shown by Nef³ to take place in solutions where the possibility of cyanogen chloride formation was known to occur.

The kinetics of the reaction between methyl iodide and potassium cyanide in aqueous solution were investigated in 1959 by Marshall and Moelwyn Hughes⁴ and this was the first detailed study of these reactions undertaken, although kinetic studies on the reaction in solution of simple alkyl iodides with cyanide ions are numerous but fragmentary^{5, 6, 7}. The reaction $\text{CH}_3\text{I} + \text{CN}^- \rightarrow \text{CH}_3\text{CN} + \text{I}^-$ was carried out in a special reaction vessel in the absence of vapour and was found to be irreversible, bimolecular and free from complications. The Arrhenius equation

governing the rate was found to be $\ln k_2(1\text{-mol}^{-1} \text{ sec}^{-1}) = 26.284 - 19,990/RT$. These workers showed that during the course of the displacement no isocyanide was formed.

In principle, at least, six reactions can take place :

Reaction (1) was found to go to completion and reaction (2) does not occur under the conditions of the experiment. The known rates of reactions (3) and (4) as measured by Moelwyn-Hughes⁵ are so much less than (1) as to be negligible, this fact being consistent with the impossibility of differentiating between the constants calculated from the rate of liberation of iodide ion and those calculated from the rate of consumption of cyanide ion. The hydrolysis of acetonitrile (reaction 5) would not effect the kinetic analysis but would possibly effect the static analysis of the products. Marshall and Moelwyn-Hughes showed that hydrolysis was small, even at 85°. The hydrolysis of the cyanide ion, reaction (6), if rapid, could possibly have established equilibrium throughout but a solution containing 150 millimoles/litre of potassium cyanide showed that the extent of the hydrolysis was less than 1%.

A summary of the results found by the above workers is given in Tables 6.1 and 6.2 where the effect of adding potassium

nitrate is well illustrated.

Such reactions as these are clearly classifiable as bimolecular substitutions and seem suitable for the study of carbon isotope fractionation in the formation of carbon-carbon bonds.

Table 6.1

Variation of k_2 with temperature

T(°K)	293.26	300.05	305.32	309.87	314.40	318.46	323.00	327.43
$k_2 10^4 (1. \text{ mole}^{-1} \text{ sec}^{-1})$ obs.	3.27	7.21	13.3	21.7	33.8	50.3	82.2	127.0
k_2 Calc	3.36	7.44	13.1	21.6	33.9	51.2	79.7	122.0

Table 6.2.

The effect on the rate constants at 318.46°K of varying the KCN concentration and of adding KNO_3

KCN (m moles/l)	30.22	49.92	50.0	50.0	99.54	80.0
KNO_3 (m moles/l)	0	0	0	10	0	100
$10^3 k_2 (1. \text{ mole}^{-1} \text{ sec}^{-1})$	5.02	5.07	4.92	5.15	4.94	5.09

Lynn and Yankwich⁹ investigated the reactions of sodium cyanide with some alkyl iodides in both aqueous and aqueous ethanolic solution. The values of activation parameters obtained by these workers are in general correspondence to those reported for similar ion-molecule reactions, and in good agreement with the Arrhenius parameters reported by Marshall and Moelwyn-Hughes⁸. For methyl iodide cyanization in aqueous solution, the difference of about 3.5 e.u. in the entropies of activation in the two

solvent systems (water and 50% water/ethyl alcohol) is in the direction, and of the same magnitude, which would be expected for a simple dielectric effect¹⁰. For a cyanide ion radius of 1.05°A and using values for the dielectric constants of water/ethanol mixtures interpolated from the data of Akerlof¹¹, Lynn and Yankwich demonstrated that the effects of solvent on k_2 , attributed solely to variations in the entropy of activation, corresponded to a radius for the activated complex of approximately 4.0°A .

The reaction between N-chloro compounds and cyanides has been little investigated since the original work of Slosson¹² on acylhalogenamine derivatives and the Beckman rearrangement. Slosson found that acyl halogen anilides do not form any cyanogen derivatives with potassium cyanide according to the equation :

but are always reduced to the acyl anilides. On the other hand, undoubted nitrogen chloride derivatives, like the chlorodialkylamines, R_2NCl , easily give cyanamides under exactly similar conditions.

In order to test the generality of Berg's reaction, Slosson prepared piperidyl cyanide (N-cyanopiperidine) as follows.

Six grams of N-chloropiperidine¹⁴ were dissolved in alcohol and treated with finely powdered cyanide (3 gm). The reaction took place immediately and the alcohol was heated to boiling.

After distilling off the alcohol, taking up the residue with ether, and drying it over potassium hydroxide, the cyanide was distilled in vacuum (30 mm) between 122 and 124°C. It was found to be a colourless, fragrant oil, insoluble in water. The material was identified positively by converting it into piperidyl urea and comparing it with authentic piperidyl urea made by Cahour's method¹⁵. A mixture of the two preparations melted at the same temperature (103°).

The only other existing literature on reactions of this type is that of Henry and Dehn¹⁶ who prepared N-cyanomorpholine from N-chloromorpholine by the method of Slosson. They reported N-cyanomorpholine as being a colourless liquid, boiling at 124°C at 18 mm.

In an endeavour to obtain more information on the mechanism of the reactions between N-chloro compounds and cyanide ion the following experimental work was undertaken. Special interest centres around this work because of the apparent success the cyanide ion has in bimolecular substitution reactions with the halogen atom bound to nitrogen, remembering the failure of attempts to displace this halogen atom with chloride ion under similar experimental conditions.

EXPERIMENTAL

Analytical Procedures

(1) Analysis of cyanide

(a) The determination of cyanide was based upon the reaction :

At the start the cyanide is in excess and the addition of silver nitrate the solution remains clear owing to the formation of the non-dissociated ion $\text{Ag}(\text{CN})_2^-$. After the ratio of the cyanide to silver has been reduced to two, the next drop of silver nitrate causes the precipitation of silver cyanide,

marking the equivalence point of the reaction. Because of the slowness of the dissolution of silver cyanide in excess potassium cyanide the method outlined above was modified by utilizing the formation of another non-dissociated compound of silver, that with ammonia, which ionizes slightly according to the equation

If ammonia is added to the solution of cyanide before the titration with silver nitrate begins, no precipitate of silver cyanide forms at the point where the drop of silver nitrate from the burette strikes the solution because silver cyanide is soluble in ammonia. However, by taking advantage of the fact that silver iodide will dissolve in potassium cyanide solution but not in ammonia, the end point can still be located. By adding potassium iodide therefore, a precipitate of silver

iodide forms on the next drop of silver nitrate beyond that needed to make the ratio of cyanide to silver 2 : 1. Moreover, the physical character of the silver iodide precipitate is such that it immediately redissolves in the cyanide solution on mixing. The equivalence point is marked by the formation of silver iodide which appears as a cream precipitate. The end point is claimed to be one of the sharpest obtainable in the entire field of volumetric analysis.

Because two molecules of potassium cyanide react with one atom of silver in this reaction, the equivalent weight of potassium cyanide is twice the molecular weight.

(b) An alternative method, that of potentiometric titration, was utilized when cyanide concentrations of $< 0.02M$ were to be measured. The silver iodide method described above, was found to give slightly higher results due to the quantity of silver iodide necessary to give a visual end point of sufficient reproducibility.

A silver wire was placed in a beaker containing the cyanide solution, connected to a beaker containing a calomel electrode immersed in saturated potassium chloride via a salt bridge containing 2M potassium nitrate. Silver nitrate (standardised with chloride and potassium chromate indicator¹⁷) was added to the cyanide solution from a burette and the mixture was stirred with a magnetic stirrer. The E.M.F. was measured with a Cambridge pH meter (Fig. 6.1)

A comparison of the available methods of cyanide estimation is given in Table 6.3.

Table 6.3

Volume of silver nitrate (0.0999N) for 20ml of potassium cyanide

Ammonium hydroxide and iodide : 10.40 10.47 10.43

Potentiometric titration : 10.21 10.26 10.30

(2) Analysis of mixtures of cyanide and chloride. If a displacement reaction of the type

takes place then it is obviously necessary to be able to measure the concentration of at least one (and preferably two) of the components as a function of time.

(a) Chloride can be used instead of iodide for the detection of the end point, but once again the disadvantage of the slow rate at which silver cyanide dissolves in excess potassium cyanide makes itself apparent. When ammonium hydroxide and iodide was added to solutions of cyanide to which chloride had been added the cyanide end point could still readily be detected, no interference from chloride being noticed.

The best method of determining the concentration of the two species was found to be by potentiometric titration, utilising the apparatus previously described. Stokes and Woolf¹⁸ have described the determination of small amounts of iodide in the presence of chloride by a similar method. Equal success was found in the present work with cyanide and chloride. Two large E.M.F. changes were observed during the titration, the first being due to the formation of the $\text{Ag}(\text{CN})_2^-$ complex and the second to the end point of the titration of the chloride ion. Thus, if the

volume of silver nitrate for the first E.M.F. change is X ml. and the total volume of silver nitrate to the second E.M.F. change is Y ml, then the volume of silver nitrate equivalent to the chloride present is thus (Y - 2X) ml.

The results of several experiments on cyanide-chloride mixtures are listed in Table 6.4, experiments carried out at temperatures from 0°C to 40°C gave good agreement between theoretical and practical.

Table 6.4

Volume of cyanide added (ml)	Wt of KCl added (gm)	Volume of silver nitrate(0.0999N) for cyanide	Total volume of silver nitrate	KCl found
20	0.1052	10.40	35.68	0.1109
20	0.0711 (NaCl)	10.47	33.02	0.0705
20	0.0695	10.50	30.39	0.0699

Preparation and properties of N-cyanomorpholine.

(1) By the method of Slosson¹²

N-chloromorpholine (3 gm) was added to a solution of potassium cyanide (1.5 gm) in absolute ethyl alcohol (100 ml) and the mixture was warmed to 50°C on a water bath. The ethyl alcohol was removed under vacuum at room temperature and the residue was distilled in a micro, all glass apparatus. The fraction boiling at 124°C (18 mm) was collected.

Found : C, 53.34; H, 7.47; N, 22.64; Cl, 0.00; Calculated from $C_5H_8N_2O$: C, 53.5; H, 6.6; N, 24.99.

Gas chromatography of this product gave only one peak. The

ultra-violet absorption spectrum of N-cyanomorpholine is illustrated in Fig. 6.2. The absence of any significant peak in the region of 2600Å is worth noting.

(2) By the reaction of N-chloromorpholine with potassium cyanide in aqueous solution.

0.174M N-chloromorpholine (50 ml) was added to 50 ml of 0.18M potassium cyanide and the mixture was left at room temperature for several hours. When the N-chloro titre was reduced to zero the solution was continuously ether extracted for 24 hours. The ether layer was dried with sodium sulphate and filtered. The ether was removed under vacuum at 30°C leaving a pale yellow oil which was distilled at 18 mm, the fraction boiling at 120-125°C being collected. This fraction was further distilled and the fraction boiling at 124°C collected and analysed.

Found: C, 52.99; H, 6.82; N, 24.00

A gas chromatogram of this product yielded a peak of identical R_f to the sample prepared by the method of Slosson, and this result, together with the analysis above, indicates that N-cyanomorpholine can be prepared by the reaction of N-chloromorpholine and potassium cyanide in aqueous solution. The natural assumption at this stage is that the reaction taking place is a simple displacement:-

Experiments were carried out in an endeavour to prove this

FIG. 6.2.

hypothesis, at the same time obtaining quantitative data for the kinetics of the apparent displacement reaction.

The experimental procedure adopted was to mix the solutions of N-chloromorpholine and potassium cyanide which had reached thermal equilibrium in the constant temperature bath. At the moment of mixing the clock was started and aliquots were withdrawn at known time intervals and added to ice water, the concentration of cyanide being determined by potentiometric titration. Because of the length of time necessary to carry out the potentiometric titration and to clean the apparatus for the next reading, it was found impossible to obtain enough samples over the initial period of the reaction by the normal pipetting technique. Consequently a Y-tube, as developed by Burns¹⁹, was used for some fast runs. In this technique, 5 ml of each component was placed in one arm of the tube and the Y-tube was placed in the water bath supported by a glass rod. When thermal equilibrium was attained the tube was inverted and the contents were mixed into a 15 ml B.14 stoppered test-tube kept in the constant temperature bath. At the time of inverting, the clock was started. Each reading for a kinetic run required one tube. The contents of the stoppered test-tubes were poured into ice water and titrated as described.

In the early experiments, both the cyanide titre and the chloride titre were determined but the correspondence between these two results was so good that the concentration of one only needed to be found since the value $Cl^- + CN^- = \text{constant}$.

All experiments were performed at 25°C unless otherwise

FIG. OF Y-TUBE

stated.

Run 1.

[N-chloromorpholine] = 0.0579M = a

[potassium cyanide] = 0.0510M = b

Y-tube technique used. Total volume of reaction mixture
= 10 ml

[AgNO₃] = 0.010N

Time	Vol. AgNO ₃	b - x	x	a - x	$\ln \frac{a}{a-x}$	$k_1 \times 10^3$ (sec ⁻¹)	$k_2 \times 10^2$ (mole ⁻¹ . sec ⁻¹)
0	26.30	0.0510	-	0.0579	-	-	-
120	21.60	0.0419	0.0091	0.0488	0.1655	1.380	2.68
240	19.19	0.0372	0.0138	0.0441	0.2700	1.125	2.25
420	14.57	0.0282	0.0228	0.0351	0.5008	1.191	2.43
600	10.59	0.0205	0.0305	0.0274	0.7467	1.244	3.21
900	6.80	0.0132	0.0378	0.0201	1.0578	1.175	3.60
1200	4.73	0.0092	0.0418	0.0161	1.2809	1.067	3.75

Mean value of $10^3 k_1 = 1.197 \pm 0.098 \text{ sec}^{-1}$

* The values of k_1 were calculated from the equation

$$k_1 t = \ln \frac{a}{a-x}$$

Derived from $x = a(1 - e^{-k_1 t})$

A plot of the values of $\ln \frac{a}{a-x}$ as a function of time should be linear and pass through the origin if the reaction obeys 1st order kinetics. (See Fig 6.3).

⑨ The values of k_2 were obtained by application of the second order equation $k_2 t = \frac{x}{a(a-x)}$, applicable when the concentrations of a and b are equal. When the concentrations of N-chloromorpholine and potassium cyanide were different the equation used was

$$k_2 t = \frac{2.303}{(a-b)} \log_{10} \frac{b(a-x)}{a(b-x)}$$

Run 2.

[N-chloromorpholine] = 0.0547M

[potassium cyanide] = 0.0526M

Y-tube technique used.

Time (secs)	Vol. AgNO_3	$k_1 \times 10^3 (\text{sec}^{-1})$	$k_2 \times 10^2$ ($\frac{\text{mole}^{-1}}{\text{sec} \cdot \text{l.}}$)
120	22.60	1.165	2.283
240	20.20	1.029	2.117
360	17.68	1.031	2.300
480	15.21	1.068	2.550
600	13.40	1.052	2.683
780	10.60	1.083	3.121
960	8.17	1.132	3.713
1200	6.21	1.095	4.150
1620	3.60	1.088	5.450

Mean value of $10^3 k_1 = 1.083 \pm 0.042 \text{sec}^{-1}$.

The values of $\ln \frac{a}{a-x}$ as a function of time are illustrated in Fig. 6.3.

Run 3.

[N-chloromorpholine] = 0.0530M

[potassium cyanide] = 0.0525M

Y-tube technique.

Time(secs)	180	300	420	660	840	1080	1800
$k_1 \times 10^3 (\text{sec}^{-1})$	1.080	0.925	0.997	1.012	1.043	1.053	1.032
$k_2 \times 10^2$ (mole ⁻¹ sec ⁻¹ .l)	2.244	2.003	2.335	2.743	3.145	3.722	5.670

$$\text{Mean value of } 10^3 k_1 = 1.020 \pm 0.046 \text{ sec}^{-1}$$

The effect of varying the concentration of the cyanide and N-chloromorpholine concentration will now be illustrated.

Run 4.

[N-chloromorpholine] = 0.0931M

[potassium cyanide] = 0.0525M

Y-tube technique

Time(secs)	120	240	360	480	600	720	840
$k_1 \times 10^3 (\text{sec}^{-1})$	0.900	0.897	0.875	0.898	0.885	0.862	0.833
$k_2 \times 10^3 (\text{mole}^{-1} \text{sec}^{-1}.l)$	Values increase rapidly.						

$$\text{Mean value of } 10^3 k_1 = 0.878_6 \pm .023 \text{ sec}^{-1}$$

89% of reaction studied.

At the completion of the reaction (when the cyanide titre had reached zero) the remaining N-chloromorpholine was titrated with standard sodium thiosulphate and the volume required

(23.00 ml) can be compared with the theoretical value of 23.52 ml. indicating that some decomposition has taken place but the overall stoichiometry is good.

Run 5.

[N-chloromorpholine] = 0.0544M

[potassium cyanide] = 0.111 M

Y-tube technique

Time(sec)	120	240	360	540	600	720	930	1500
$k_1 \times 10^3$ (sec ⁻¹)	2.057	1.745	1.855	2.092	2.158	2.083	2.267	2.083

k_2 Values of k_2 again increase rapidly with time.
90% of reaction studied.

Mean value of $10^3 k_1 = 2.043 \pm 0.155 \text{ sec}^{-1}$

Run 6.

[N-chloromorpholine] = 0.0264M

[potassium cyanide] = 0.0263M

Y-tube technique

Time (sec)	120	240	420	600	780	1020	1500
$k_1 \times 10^3$ (sec ⁻¹)	0.719	0.654	0.662	0.596	0.665	0.660	0.677
$k_2 \times 10^2$	2.870	2.730	2.890	2.702	3.317	3.517	4.420

70% of reaction studied

Mean value of $10^3 k_1 = 0.662 \pm .034 \text{ sec}^{-1}$

When a run was carried out with identical concentrations to those used in run 6, in the presence of potassium chloride (0.0580M), the reaction was found to follow the same rate, indi-

cating no significant effect of salt on the kinetics and Mechanism of the reaction.

In an endeavour to determine if the rate of disappearance of cyanide paralleled that of the N-chloro compound, several experiments were carried out in which the rate was measured by the change in N-chloro titre as a function of time. An aliquot of the reaction mixture (5 ml) was added to acidified potassium iodide and the liberated iodine was titrated with standard sodium thiosulphate (0.0344N).

Note: Iodine reacts quantitatively with potassium cyanide giving cyanogen iodide, a fact which can be utilised for the accurate estimation of aqueous solutions of cyanide. When iodine in potassium iodide was added to potassium cyanide the colour immediately disappeared, a reaction which was rapidly reversed by the addition of dilute acids. Consequently, the presence of the dilute acetic acid necessary for the estimation of N-chloromorpholine with potassium iodide prevents interference by the cyanide ion.

Run 7.

$$[\text{N-chloromorpholine}] = 0.0560\text{M.}$$

$$[\text{potassium cyanide}] = 0.0545\text{M.}$$

Time (sec)	Vol. of $\text{Na}_2\text{S}_2\text{O}_3$	$k_1 = \frac{\ln \frac{a}{a-x}}{t}$ $\times 10^3 (\text{sec}^{-1})$	$k_2 \times 10^2$ ($\text{sec}^{-1} \text{mole}^{-1} \text{l.}$)
0	32.60		
70	30.30	0.953	1.75
240	25.90	0.931	1.88

Time (sec)	Vol. of $\text{Na}_2\text{S}_2\text{O}_3$	$k_1 = \frac{\ln \frac{a}{a-x}}{t}$ $\times 10^3 (\text{sec}^{-1})$	$k_2 \times 10^2$ $(\text{sec}^{-1} \text{mole}^{-1} \cdot \text{l})$
420	21.18	1.012	2.26
660	15.71	1.095	2.88
900	11.77	1.129	3.50
1200	8.02	1.162	4.52
1500	5.80	1.149	5.49
1740	4.32	1.155	6.65
2100	3.05	1.127	8.20

$$\text{Mean value of } 10^3 k_1 = 1.079 \pm .085 \text{ sec}^{-1}$$

A duplicate run gave identical results. The agreements with the results obtained by following the disappearance of the cyanide ion are good, pointing to a 1 : 1 correspondence in the disappearance of the N-chloromorpholine and potassium cyanide.

Run 8.

$$\begin{aligned} [\text{N-chloromorpholine}] &= 0.0560\text{M} \\ [\text{potassium cyanide}] &= 0.116 \text{ M} \end{aligned}$$

Followed by titrating an aliquot (10ml) with standard sodium thiosulphate (.03435N).

Time (sec)	60	230	425	600	780	960	1155
Vol. thio	29.43	22.45	14.90	9.88	6.34	4.10	2.67
$k_1 \times 10^3 (\text{sec}^{-1})$	1.740	1.645	1.834	2.000	2.111	2.166	2.170

$$\text{Mean value of } 10^3 k_1 = 1.952 \pm 0.198 \text{ sec}^{-1}$$

When the N-chloromorpholine titre was reduced to zero an

aliquot (10ml) of the reaction mixture was titrated with standard silver nitrate (0.1N) using the potassium iodide/ ammonium hydroxide method. The volume required, 2.97 ml, agrees favourably with the theoretical value of 3.00 ml. Another sample (10 ml) was titrated potentiometrically for chloride ion in the presence of cyanide and the value found, 5.48ml, was in good agreement with that calculated assuming that the chlorine had been replaced by cyanide in the N-chloromorpholine molecule (5.60ml).

From the results of this experiment, the indications are that the cyanide replaces the chlorine quantitatively, and any other products, if present, must be in very low concentration.

The best method of obtaining an overall picture of the effect of varying the reaction species is by reference to Table 6.5, in which all the experiments carried out with N-chloromorpholine and potassium cyanide in aqueous solution are tabulated.

Table 6.5

All reactions at 25°C

[NC1M]	[KCN]	[KCl]	$k_1 \times 10^3$ (sec ⁻¹)	$\frac{k_1 \times 10^2}{[KCN]}$
0.0579	0.0510 ^W	-	1.197	2.35
0.0547	0.0526*	-	1.083	2.06
0.0530	0.0525*	-	1.020	1.95
0.0543	0.0545*	0.0580	1.064	1.96
0.0560 [@]	0.0545	-	1.079	1.98
0.0931	0.0525*	-	0.879	1.67

[NC1M]	[KCN]	[KCl]	$k_1 \times 10^3$ (sec ⁻¹)	$\frac{k_1 \times 10^2}{[KCN]}$
0.0544	0.1110*	-	2.043	1.85
0.0264	0.0263*	-	0.662	2.51
0.0264	0.0263*	0.0580	0.663	2.51
0.0550 ^②	0.0546	-	1.074	1.97
0.0548 ^②	0.0545	0.1102	1.072	1.97
0.0560 ^②	0.1160	-	1.952	1.68

* Studied by Y-tube technique and following KCN

② Studied by following N-chlorotitre

Possible effect of hydrogen cyanide

Hydrogen cyanide is an extremely weak acid and is formed readily in solution by the hydrolysis of potassium cyanide according to the following equation -

$$\text{Now } K_a^{20} = 7.2 \times 10^{-10}; \quad K_w = 10^{-14}$$

$$\text{and } K_h = \frac{[\text{HCN}][\text{OH}^-]}{[\text{CN}^-]} = \frac{K_w}{K_a} = 1.39 \times 10^{-5}$$

Denoting the degree of hydrolysis by x , then

$$K_h = \frac{x^2}{(1-x)V} \quad \text{where } (V = \frac{1}{C})$$

and using this equation the percentage hydrolysis was calculated as a function of the potassium cyanide concentration.

[KCN]	% Hydrolysis
.001	11.05
0.01	3.65
0.02	2.60
0.03	2.15
0.04	1.85
0.05	1.68
0.08	1.32
0.10	1.15

The reaction of amines with hydrogen cyanide has been virtually unexplored, and the literature suggests that amines and hydrogen cyanide do not react, even to the limited extent of forming salts in alcoholic solution²¹. However, Erickson²² investigated this type of reaction, and showed that hydrogen cyanide reacts readily with aliphatic and heterocyclic amines. In the presence of small amounts of aliphatic amines, especially tertiary amines, the reaction occurring was the polymerization of hydrogen cyanide²³ which was catalysed by alkaline material. If the amine was present in molar excess over the cyanide, the polymerisation was avoided and with some primary and secondary amines (diethylamine, piperidine) addition of the amine to the triple bond of hydrogen cyanide occurred, giving unstable substituted formamidines and their hydrochlorides.

However, morpholine differs from the other amines in that,

as it reacts with hydrogen cyanide, much ammonia is evolved and a compound $C_{10}H_{17}O_2N_3$ is formed. It supplies one mole of hydrogen cyanide and two moles of morpholine on hydrolysis and these facts limit the possibilities to I or II

I

II

From infra-red studies, (I) was indicated as the correct structure from consideration of an absorption band at 2242cm^{-1} characteristic of the $\text{C} \equiv \text{N}$ group. The reaction of morpholine with hydrogen cyanide no doubt gives the formamidine as the first product, two molecules of this compound then reacting to give ammonia and di-4-morpholenylacetonitrile (I). This latter compound is stable when dry but generates hydrogen cyanide in the presence of moisture, a reaction very similar to the behaviour of the dialkoxyacetonitriles²⁴.

Because of the possibility of N-chloromorpholine hydrolysing in solution to yield morpholine and hypochlorous acid according to the equation -

then a consideration of the possible effect of hydrogen cyanide on the reaction between N-chloromorpholine and potassium cyanide

is of obvious importance, especially in non-aqueous solution where the generation of hydrogen cyanide by the action of water on tri-4-morpholenylacetonitrile is unlikely to occur.

Solutions of cyanides in water are basic and the change in pH of a mixture of N-chloromorpholine and potassium cyanide was utilised to study the disappearance of cyanide from solution. A Radiometer pH meter (23C) was standardised against Radiometer buffer of pH 6.5 ± 0.02 and the pH of the reaction mixture was measured at intervals, the mixture being uniformly stirred throughout the measurements.

$$[\text{N-chloromorpholine}] = 0.1048\text{M.}$$

$$[\text{potassium cyanide}] = 0.1040\text{M Temp } 18.5^{\circ}\text{C}$$

$$\text{pH of potassium cyanide } (.104\text{M}) = 11.06 \text{ (calculated } 11.07)$$

Time (min)	1	3	5	12	17	25	34	46	65	120
pH	11.12	11.05	10.94	10.61	10.41	10.21	10.02	9.89	9.72	9.32

The pH continued to drop slowly, indicating the removal from solution of the cyanide ion.

The possibility that a reaction was occurring between morpholine and potassium cyanide was eliminated by mixing these two compounds and titrating the cyanide at known time intervals, the results are given below

$$[\text{Morpholine}] = 0.154\text{M}$$

$$[\text{potassium cyanide}] = 0.113\text{M Temp } 25^{\circ}\text{C}$$

Time (min)	1	7	16	56	100	15.5 hrs
Vol. $\text{A}_{\text{g}}\text{NO}_3$ (0.021N)	25.80	25.78	25.81	25.72	25.75	25.80

The results of this experiment also eliminates the possibility that a reaction of the type

was occurring, a reaction which is common with heterocyclic amines containing oxygen. (Erickson (loc.cit.) reports that a mixture of morpholine (87g) and hydrogen cyanide (13.5g) gave after two months 39% of dimorpholinoacetonitrile. When the reaction time was shortened to two weeks 62% of the product was recovered. The compound was found to readily hydrolyse in dilute acid to hydrogen cyanide).

Effect of added morpholine.

If an equilibrium involving morpholine forms part of a reaction mechanism governing the formation of N-cyanomorpholine by the action of potassium cyanide on N-chloromorpholine, then it would be expected that the addition of excess morpholine would have a considerable effect on the rate. This assumption was tested at several temperatures and with widely varying component concentrations with the following results.

N-chloromorpholine was found to be quite stable in the presence of excess morpholine and the N-chloro group could still be titrated by addition of an aliquot of the mixture to a solution of potassium iodide acidified with dilute acetic acid. However, when morpholine was added to concentrated solutions of

iodine in potassium iodide, orange crystals deposited which were found to be unstable to heat, decomposing at approximately 240°C . An analysis gave H, 3.09%; C, 15.08%; N, 3.00% and I, 66.30%. Knorr refers to a tri-iodide complex of morpholine without discussing the physical properties or preparative conditions. The orange material was found to be unstable to acids, readily liberating iodine which could be titrated with sodium thiosulphate. The analytical results, combined with the physical properties would indicate that the material was a mixture, probably of N-iodomorpholine and morpholine tri-iodide. When dilute solutions of iodine in potassium iodide, were added to morpholine, no such precipitate formed, the iodine giving the theoretically expected titre with standard sodium thiosulphate. When N-chloromorpholine itself was added to aqueous potassium iodide a yellow colouration was immediately produced but in the presence of morpholine this reaction did not occur.

[N-chloromorpholine] = 0.052M.

[morpholine] = 0.604M.

Time (min)	1	7	15	61	240
Vol thio(0.0343 ₅ N)	29.00	29.45	29.30	29.28	29.31

Morpholine (4.7569g.) and N-chloromorpholine (0.6826g.) were dissolved in water (50ml) and the mixture placed in a constant temperature water bath. 0.226M potassium cyanide solution (50ml) was then added and the clock was started, aliquots (10ml) were withdrawn at known intervals and titrated with

sodium thiosulphate (0.03435N).

Run 9.

[Potassium cyanide] = 0.1130M = b

[N-chloromorpholine] = 0.0561M = a

[morpholine] = 0.545 M

Temp 25°C.

Time (sec)	Vol thio (.0343 ₅)	$k_1 \times 10^3$	$k_2 \times 10^3$
0	32.60	-	-
60	28.60	2.183	20.30 ^②
270	22.79	1.325	12.92
390	18.80	1.405	14.37
660	15.75	1.095	11.47
960	12.01	1.038	11.45
1640	7.69	0.878	10.34
2100	5.79	0.821	10.13
2760	3.82	0.776	10.00

Mean $11.53 \times 10^{-3} \text{ mole}^{-1} \text{ sec}^{-1.1}$

②

Neglected when calculating the average value of k_2

Run 10

[N-chloromorpholine] = 0.0504M = a

[potassium cyanide] = 0.0452M = b

[morpholine] = 0.497 M

Temp. 25°C

Time (sec)	Vol. thio.	$k_1 \times 10^3$	$k_2 \times 10^3$
60	27.49	0.973	24.37
315	24.05	0.631	15.59
630	20.99	0.535	14.27
900	18.90	0.488	13.88
1410	16.13	0.425	13.48
2415	12.71	0.345	12.92
3600	10.38	0.289	12.52
6000	7.88	0.218	11.96
9660	6.19	0.165	11.25

Mean value of $k_2 = 13.23 \pm 1.29 \times 10^{-3} \text{ sec}^{-1} \text{ mole}^{-1} \text{ l.}$

It can be seen that under these conditions the variation in k_2 is very considerably reduced, whilst the values of k_1 now show a tendency to fall off as a function of time. Further experiments were carried out under different experimental conditions of temperature and concentration and these runs will now be described.

Run 11.

[N-chloromorpholine] = 0.0551M
 [potassium cyanide] = 0.0282M
 [morpholine] = 0.977 M Temp. 25°C

Time(sec)	60	330	630	930	1410	1820	2280	3000	4530
$k_1 \times 10^3$ (sec^{-1})	0.730	0.424	0.355	0.307	0.278	0.238	0.217	0.183	0.139
$k_2 \times 10^3$ ($\text{sec}^{-1} \text{ mole}^{-1} \text{ l.}$)	-	17.70	16.40	14.97	14.90	14.50	15.22	14.70	14.75

Mean value of $k_2 = 14.84 \pm 10.23 \times 10^{-3} \text{sec}^{-1.1}$. (neglecting first two values). (graphical value = 14.82 ± 0.28)

A function of k_2 for Run 11 is plotted in Figure 6.4.

The above value of k_2 was completely reproducible and was not affected by large increases in the morpholine concentration.

A run identical to the above was followed by titrating the excess potassium cyanide with standard silver nitrate (0.01N) and identical results were obtained. The difficulty with this method is the interference by the reaction between morpholine and silver nitrate producing silver oxide, two end points being detectable, the first due to the titration of the cyanide present and the second due to the morpholine.

Run 12.

[N-chloromorpholine]	= 0.1395M
[potassium cyanide]	= 0.0289M
[morpholine]	= 0.978 M Temp 25°C

Time(sec)	70	300	480	720	1050	1560	2190	2820
$k_1 \times 10^3$ (sec^{-1})	2.49	1.73	1.55	1.45	1.36	1.270	1.18	1.11
$k_2 \times 10^3$ ($\text{sec}^{-1.1}$ mole $^{-1.1}$)	18.2*	12.92	11.71	11.30	10.90	10.40	9.85	9.35

Mean value of $k_2 = 10.92 \pm 1.2 \times 10^{-3} \text{sec}^{-1} \text{mole}^{-1.1}$

* Neglected.

(graphical value = 10.76 ± 0.58)

The individual values of k_2 appear to drift badly but the

FIG. 6.3.

FIG. 6.4.

graph of $\log_{10} \frac{b(a-x)}{a(b-x)}$ as a function of time indicates the approximately linear relationship which exists.

Run 13.

[N-chloromorpholine]	= 0.0535M
[potassium cyanide]	= 0.0504M
[morpholine]	= 0.900 M Temp 40°C $\pm$ 0.02°C

Time (sec)	60	300	480	660	900	1260	1680	2340	3600
$k_2 \times 10^3$ (sec ⁻¹ mole ^{-1.1})	47.71	35.82	34.03	33.32	32.07	32.48	29.62	27.81	25.60
$k_1 \times 10^3$ sec ⁻¹	2.33	1.51	1.31	1.18	1.03	0.918	0.773	0.640	0.494

Mean value of $k_2 = 31.34 \pm 3.20 \times 10^{-3} \text{sec}^{-1} \text{mole}^{-1.1}$.

Run 14.

[N-chloromorpholine]	= 0.0519M
[potassium cyanide]	= 0.0504M
[morpholine]	= 0.900 M Temp 5.0 $\pm$ 0.02°C

Time(sec)	60	840	2340	3600	4500	6480	9780	14580	23580
Vol. thio. (.0348)	29.00	26.99	23.67	21.43	19.90	17.77	14.80	12.30	9.00
$k_1 \times 10^3$ (sec ⁻¹)	0.494	0.125	0.0989	0.0915	0.0905	0.0809	0.0720	0.0610	0.0507
$k_2 \times 10^3$ (sec ⁻¹ mole ^{-1.1})	9.60	2.45	2.17	2.10	2.14	2.05	2.02	1.89	1.89

Mean value of $k_2 = 2.089 \pm 0.17 \times 10^{-3} \text{sec}^{-1} \text{mole}^{-1.1}$.

Run 15

[N-chloromorpholine] = 0.0581M
 [potassium cyanide] = 0.0995M
 [morpholine] = 0.9 M Temp 45°C

5 ml aliquots titrated

Time(sec)	45	205	350	480	705	840	1020	1165	1320	1710
Vol.thio (0.0304N)	15.1	8.9	7.15	4.65	3.05	2.45	1.90	1.55	1.26	0.83
$k^2 \times 10^3$ sec ⁻¹ .mole ⁻¹ .l.	53.3	45.2	36.0	42.6	39.4	38.2	36.8	36.2	35.2	32.8

Mean value of $10^3 k_2 = 37.1 \pm 1.9 \text{ sec}^{-1} \text{ mole}^{-1} \text{ l.}$

The first two values were neglected when calculating the average value. The value obtained from the graph of $\log_{10} \frac{b(a-x)}{a(b-x)}$ plotted as a function of time was $37.4 \times 10^{-3} \text{ sec}^{-1} \text{ mole}^{-1} \text{ l.}$

It can be seen that the addition of morpholine has a marked effect on both the rate and the mechanism of the reaction, the rate constants obtained exhibiting in the main, second order characteristics although variations are apparent from run to run. Figure 6.5 illustrates the line of the graph of $\log_{10} k_2$ plotted as a function of $\frac{1}{T^\circ A}$, the slope giving 5660 cal/mole for the value of the energy of activation.

Obviously, morpholine must play a major part in the reaction mechanism, without actually entering into the rate constant itself as judged from the absence of any effect by widely varying the morpholine concentration whilst keeping the concentrations of the other components constant. If the effect is

FIG. 6.5.

FIG. 6.6.

due solely to alkalinity changes produced by the addition of the base, morpholine, then piperidine, which should behave similarly to morpholine, should exhibit an identical effect.

Effect of added piperidine.

Piperidine ($K_b = 1.3 \times 10^{-3}$) is a considerably stronger base than morpholine ($K_b = 2.44 \times 10^{-6}$) and the effect of increasing the base strength was investigated by carrying out the reaction between N-chloromorpholine and potassium cyanide in the presence of excess piperidine.

Run 16.

[<u>N</u> -chloromorpholine]	= 0.0572M
[potassium cyanide]	= 0.0573M
[piperidine]	= 0.9 M Temp. 25°C

Time (sec)	Vol. thio (0.0319N)	a - x	$k_1 \times 10^3 (\text{sec}^{-1})$	$k_2 \times 10^3$ ($\text{sec}^{-1} \text{mole}^{-1.1}$)
0	18.00	0.0572		
60	17.08	0.0544	0.815	15.00
240	14.11	0.0450	0.996	19.80
420	11.39	0.0362	1.090	24.20
600	9.20	0.0293	1.110	27.81
780	7.68	0.0245	1.080	29.97
960	6.58	0.0210	1.045	30.57
1200	5.49	0.0175	0.985	33.14
1500	4.51	0.0144	0.920	34.73
1890	3.65	0.0116	0.845	36.42
2400	2.91	0.0093	0.756	37.60
3300	2.10	0.0067	0.650	40.00

When the N-chloro titre was reduced to zero the reaction mixture was ether extracted, the combined ether fractions dried with anhydrous sodium sulphate, and the ether removed under vacuum at room temperature. A gas chromatogram of the residue indicated that the product consisted largely of N-cyanopiperidine, only a small percentage of N-cyanomorpholine being present. This result can best be explained by considering the effect of N-chloromorpholine on piperidine.

Utilising the small difference in the absorption spectra of N-chloromorpholine and N-chloropiperidine in the region 2200 - 2500^oA it was shown that N-chloromorpholine rapidly (3 min) chlorinated piperidine. This fact was confirmed by the addition of perchloric acid to the mixture, the spectrum exhibiting a large change in O.D at 2600^oA, a characteristic of N-chloropiperidine but not of N-chloromorpholine. The fact that N-chloromorpholine chlorinates piperidine confirms the result that N-chloropiperidine is the more stable N-chloro compound. This conclusion is confirmed by considering the reactions of the two N-chloro compounds with phenol in the presence of hydrochloric and perchloric acids.

When potassium cyanide is added to a mixture of piperidine and N-chloromorpholine the first reaction is the chlorination described above, followed by a displacement reaction of the cyanide ion on the N-chloro group. However, complications are present due to the presence in solution of cyanogen chloride, a factor which will be discussed in detail later.

[N-chloromorpholine] = 0.0572M
 [potassium cyanide] = 0.0573M
 [morpholine] = 0.45 M
 [piperidine] = 0.45 M Temp. 25°C

5 ml aliquots titrated. 90% of reaction studied

Time(sec)	Vol.thio. (0.0319N)	$k_1 \times 10^3 (\text{sec}^{-1})$	$k_2 \times 10^3 (\text{sec}^{-1} \text{ mole}^{-1} .1)$
60	17.30	0.654	11.70
220	15.70	0.595	11.40
540	11.90	0.764	16.70
840	9.36	0.778	19.20
1200	7.13	0.773	22.40
1500	5.72	0.763	25.00
1800	4.87	0.731	26.50
2160	4.00	0.698	28.50
2460	3.50	0.665	29.60
2940	2.89	0.621	31.20
3480	2.40	0.579	32.80
4320	1.83	0.530	35.90
Mean		0.680	

A gas chromatogram of the liquid products indicated that N-cyanopiperidine was the predominant component. The trend of the numerical value of the constants closely resembled that obtained in Run 16, the values of k_2 slowly increasing as a function of time, the value of k_1 initially rising and finally decreasing. It is obvious that a mixed mechanism occurs.

Reactions in non-aqueous solvents.

If reactions involving hydrolysis are responsible for the discrepancies in the expected second order rate constants obtained for the reaction between N-chloromorpholine and potassium cyanide, then an investigation of the rate constants in non-aqueous solvents should indicate if reactions of the type

are present in the rate determining stages or are involved in any way in the overall reaction mechanism.

Run 18.

Solvent 40% ethyl alcohol

[<u>N</u> -chloromorpholine]	= 0.0572M
[potassium cyanide]	= 0.0572M
[morpholine]	= 0.9 M Temp 25°C

Time (sec)	Vol. thio (0.0319N)	$k_1 \times 10^3$ (sec ⁻¹)	$k_2 \times 10^3$ (sec ⁻¹ mole ⁻¹ .1)
40	17.20	1.220	12.40
210	15.25	0.791	8.60
390	13.73	0.694	8.00
700	11.86	0.598	7.45
1080	10.10	0.540	7.31
1640	8.49	0.458	6.78
2520	6.86	0.383	6.45
3180	5.92	0.352	6.42
3840	5.35	0.318	6.22
4920	4.54	0.304	6.05
6660	3.65	0.240	5.91

90% of the reaction studied

A gas chromatogram of the liquid products of this reaction showed only one peak due to N-cyanomorpholine.

N-chloromorpholine was found to be extremely stable in both aqueous methyl alcohol and absolute methyl alcohol solutions.

N-chloromorpholine = 0.045M Solvent = 100% MeOH

Time (min)	0	15	38	84
Vol. thio (0.0318N)	33.12	33.08	33.05	33.03

Run 19.

Solvent 100% methyl alcohol

[N-chloromorpholine] = 0.0513M

[potassium cyanide] = 0.0513M Temp. 25°C

Time (sec)	Vol. thio (0.0319N)	$k_1 \times 10^3$ (sec ⁻¹)	$k_2 \times 10^3$ (sec ⁻¹ mole ⁻¹ .1)
0	16.20	-	-
70	14.30	1.745	37.0
240	11.42	1.461	33.9
360	9.97	1.340	33.8
570	8.33	1.162	32.3
730	7.47	1.061	31.4
900	6.76	0.968	30.3
1110	6.10	0.881	29.2
1290	5.62	0.820	28.4
1500	5.21	0.756	27.5
2250	4.21	0.600	24.7

Run 20.

Solvent - 100% methyl alcohol

[N-chloromorpholine]	= 0.0540M
[potassium cyanide]	= 0.0858M Temp. 25°C

The results of this run are plotted in Fig. 6.6, together with the results of Run 19. The values of the second order rate constants obtained were

$$\text{Run 19 :- } 3.09 \times 10^{-2} \text{ sec}^{-1} \text{ mole}^{-1} \text{ l.}$$

$$\text{Run 20 :- } 3.09 \times 10^{-2} \text{ sec}^{-1} \text{ mole}^{-1} \text{ l.}$$

showing excellent agreement. When Run 19 was repeated in the presence of N-cyanomorpholine (0.06M) the values of the rate constants remained unchanged. The important fact which emerges from the kinetics of the experiments carried out in alcohol solution is the constancy of the values of k_2 , a result which could only be obtained in aqueous solution on the addition of excess morpholine.

The effect of excess morpholine on the reaction in methyl-alcohol was investigated as follows.

Run 21.

Solvent - 100% methyl alcohol

[N-chloromorpholine]	= 0.0532M
[potassium cyanide]	= 0.0862M
[morpholine]	= 0.575M Temp 25°C

$$k_2 = 3.69 \times 10^{-2} \text{ sec}^{-1} \text{ mole}^{-1} \text{ l.}$$

The results of this experiment are also plotted in Fig.

6.6., indicating that the second order rate constants have become more stable. A side reaction is obviously present in non-aqueous solution but not to such a large extent. The possible nature of this will now be discussed.

Presence of cyanogen chloride.

Among the characteristic reactions of cyanogen halides are those with primary and secondary amines, a hydrogen atom attached to the nitrogen being replaced by a CN group according to the equation

This reaction being quite general although all amines do not react with equal ease. Primary and secondary aliphatic amines react readily whilst negative substituents in the aromatic ring diminish the reactivity of an aromatic amine in proportion to their number and also their degree of negativity.

Alkyl residues attached to nitrogen forming part of a ring may be exchanged by the CN group by the action of cyanogen bromide²⁵. In most cases a second reaction involving the rupture of the nitrogen ring also takes place.

The resulting brominated compound reacts with the unconverted cyclic base to form a quarternary compound.

Cyanogen bromide reacts vigorously with N-methyl morpholine in ether solution, fission of the ring occurring²⁶.

The kinetics of the reactions of cyanogen halides with bases in aqueous solution has been studied by Griffith, Jobin

and McKeown²⁷. These workers studied the reactions of cyanogen iodide and bromide with sodium hydroxide, ammonia, carbonates and amines and it seemed plausible to assume that each of the amine reactions (including that of ammonia) was in the first stage a simple addition process.

forming the halide of a very weak base or ampholyte which then rapidly reacts with a second molecule of a stronger base as below.

During the course of the present investigation an ether solution of morpholine was added dropwise to cyanogen chloride kept at -15°C . An immediate reaction took place, white crystals being deposited which were removed by suction filtration and identified as morpholine hydrochloride M.P. $169-174^\circ\text{C}$; lit 174. Analysis Cl 28.59%, theoretical 28.72%. The ether solution was concentrated and gas chromatographed, the only peak appearing being due to N-cyanomorpholine.

It has been accepted²⁸ that cyanogen chloride behaves as Cl^+ and CN^- and there are few, if any reactions, in which cyanogen chloride behaves as a cyanide. Neither cyanogen chloride nor the iodide solutions in benzene or nitrobenzene gave precipitates with silver perchlorate in seven days. Cyanogen iodide and silver perchlorate in benzene gave a preci-

pitrate of silver cyanide, no silver iodide being formed.

During the investigation of the destruction of cyanide in waste waters, Eden and Wheatland²⁹ observed that, even in strongly alkaline solution, the first product of the reaction of a cyanide with a hypochlorite was cyanogen chloride which then undergoes hydrolysis³⁰, possibly with the formation of a cyanate. The rate of formation of cyanogen chloride was extremely rapid, but hydrolysis, as was shown by Price et al., proceeds at a measurable rate, given by the equation

$$\frac{-d[\text{CNCl}]}{dt} = k_1 [\text{CNCl}][\text{OH}^-]$$

The value of k_1 being $600 \text{ l.mole}^{-1} \cdot \text{min}^{-1}$, at 25°C . The hydrolysis of cyanogen chloride in aqueous solution is catalysed by hydrochloric acid and retarded by sodium chloride. The reaction proceeding as follows³¹:-

The hydrolysis in buffered (pH 11) solution was shown by Eden and Wheatland to follow a pseudo first order reaction both in the presence and absence of hypochlorite.

Thus when a hypochlorite (or chlorine) is added to a solution containing an alkali cyanide the first product is cyanogen chloride

In the presence of an excess of hypochlorite, further reaction with cyanogen chloride or cyanate occurs in ways which differ according to the pH value of the solution.

At pH 11, for instance, an excess of hypochlorite has an apparently catalytic effect in greatly accelerating the hydrolysis of cyanogen chloride.

In the present work cyanogen chloride was prepared by mixing equimolar (0.14M) solutions of hypochlorous acid and potassium cyanide. When aliquots of this solution were added to potassium iodide no iodine was liberated, even in the presence of dilute acid (acetic or hydrochloric).

Solutions containing cyanide and hypochlorous acid were found to go yellow with time, and on adding sodium hydroxide and back titrating, the expected cyanogen chloride was not found, indicating severe decomposition.

When aqueous solutions of cyanogen chloride were added to silver nitrate no precipitate was obtained (Williams³² notes that a 3% solution of cyanogen chloride in water, diethyl ether or ethyl alcohol gave a precipitate with silver nitrate, the reaction proceeding less rapidly with fresh solutions).

The presence of cyanogen chloride in both aqueous and methanolic solutions of N-chloromorpholine and potassium cyanide was confirmed by application of the test developed by Falkof, Witten and Gehauf³³ which offers advantages in sensitivity and specificity over the conventional methods. The test depends on the ability of cyanogen chloride to split the pyridine ring to form a derivative of glutaconic aldehyde which in turn is made to couple with a derivative of pyrazolone (in this work, 1-phenyl-3-methyl-5-pyrazolone) to form a highly coloured

(magenta to deep blue) compound.

The solution to be tested for cyanogen chloride was aspirated with nitrogen, the gaseous mixture then being passed through absorption tubes containing white silica gel which contained a paste of pyridine and 1-phenyl 3-methyl 5-pyrazolone. The presence of cyanogen chloride was indicated by the rapid colouration of the silica gel, the original white colour turning magenta and finally deep blue. The results are given in Table 6.6.

The presence of cyanogen chloride was further confirmed by use of sodium sulphide paper³⁴. Cyanogen chloride gives sulphocyanide which, when treated with a drop of hydrochloric acid followed by 1% ferric chloride yields a deep red colouration.

Table 6.6.

Solution aspirated	Effect on absorbent
Aqueous NC1M	No colouration
NC1M in MeOH	No colouration
NC1M in EtOH	No colouration
NC1M + KCN in H ₂ O	Magenta to deep blue
NC1M + KCN in MeOH	Magenta to blue
NC1M + KCN in EtOH	Magenta to blue
NC1M + KCN in H ₂ O, morpholine added to absorbant	No colouration
Aqueous KCN	No colouration

Product Analysis

Several experiments were carried out in an endeavour to

obtain information on the nature of the products for the reaction between N-chloromorpholine and potassium cyanide under varying solvent conditions.

(1) N-chloromorpholine (0.6773 g., .00557 moles) and potassium cyanide (0.3639 g., .00559 moles) were dissolved in anhydrous methyl alcohol, the volume of sodium thiosulphate (0.0318N) required to titrate the liberated iodine (on addition of potassium iodide and dilute acid) after three days was 1.8ml / 5ml (if no reaction had taken place titre would be 17.4ml/5ml).

The methyl alcohol was removed at 35°C under vacuum and sucked almost to dryness. The solid and liquid residues remaining were washed several times with anhydrous ether, the combined ether solutions were heated at 30°C under vacuum (17mm) leaving a small quantity of a pale yellow liquid which was identified by gas-liquid chromatography as N-cyanomorpholine.

The white solid was analysed as follows.

wt. of sample 0.0482g.

Volume of AgNO_3 (0.0578N) = 9.65 ml (if the sample was pure potassium chloride the expected titre would be 11.12ml). No cyanide was found in the solid residues.

A microanalysis carried out on the solid product gave Cl, 41.91%; H, 0.53%; C, 0.72%; N, 0.00%. KCl requires Cl 47.55%.

Morpholine hydrochloride, a compound which could be formed by the action of cyanogen chloride on morpholine, readily sublimes at 150°C but any attempt to sublime this material from the product above failed.

Note: Small discrepancies in the percentage of potassium chloride formed could be due to the impurities present in the analar potassium cyanide initially, approximately 3.7%, but the actual value found was too large to be accounted for by this fact.

(2) Potassium cyanide (0.3639g), N-chloromorpholine (0.6773g) and piperidine (5 ml) were dissolved in anhydrous methyl alcohol (100 ml.) and the mixture was maintained at 25°C. After 18 hours the N-chloro titre for 5 ml of the reaction mixture was less than 0.1 ml of thiosulphate (0.0318N). The solution was treated as in (1). The liquid residue was identified as N-cyanopiperidine.

Analysis of solid: wt of sample 0.0584 g.

Vol of AgNO_3 (0.0578N) = 13.0 ml.

(if pure KCl the expected titre was 13.5 ml).

No cyanide was present.

(3) Potassium cyanide (2.7452 g) and N-chloromorpholine (4.9916 g) were dissolved in distilled water and the mixture left for 48 hours. At the end of this period the water was removed at 40°C under vacuum (17 mm) using a rotary film evaporator, leaving a white solid (3.1398 g) and a small quantity of a colourless liquid which was removed by extraction with ether.

(a) liquid residue identified by gas liquid chromatography as N-cyanomorpholine. Analysis C, 53.28; H, 7.36; N, 24.92; O, 14.85; Cl, 0.00. Required for $\text{C}_5\text{H}_8\text{N}_2\text{O}$ C, 53.55; H, 7.19; N, 24.98; O, 14.27%.

(b) Solid residue - white crystalline powder soluble in water. Analysis. C, 1.25; H, 9.72; Cl, 40.62%.

It is obvious from these experiments that the sole liquid product of the reaction between N-chloromorpholine and potassium cyanide in both aqueous and non-aqueous solvents is N-cyano-morpholine. The solid residue never satisfies the requirements of potassium chloride, possibly due to impurities present in the original potassium cyanide. No morpholine hydrochloride could be identified in the solid products although organic material is unquestionably present.

A summary of the results of all kinetic runs is given in Table 6.7.

Table 6.7

Kinetic runs with N-chloromorpholine and potassium cyanide

Temp.	Sol-vent	[NClM]	[KCN]	[Morpholine]	$k_1 \times 10^3$ sec ⁻¹	$k_2 \times 10^2$ sec ⁻¹ mole ⁻¹ .1
25 *	H ₂ O	0.058	0.051	-	1.197	increases Mean 2.4
25 *	H ₂ O	0.055	0.053	-	1.083	increases
25 *	H ₂ O	0.053	0.053	-	1.020	increases
25	H ₂ O	0.056	0.055	-	1.079	increases
25 *	H ₂ O	0.093	0.053	-	0.879	increases
25	H ₂ O	0.056	0.116	-	1.952	increases
25 *	H ₂ O	0.054	0.111	-	2.043	increases
25 *	H ₂ O	0.026	0.026	-	0.662	increases
25	H ₂ O	0.056	0.113	0.545	decreases	decreases slowly 1.15
25	H ₂ O	0.050	0.045	0.497	decreases	decreases slowly 1.32

Temp.	Sol-vent	[NC1M]	[KCN]	[Morpholine]	$k_1 \times 10^3$ sec ⁻¹	$k_2 \times 10^2$ sec ⁻¹ mole ⁻¹ .1
25	H ₂ O	0.055	0.028	0.977	decreases	1.48
25	H ₂ O	0.140	0.029	0.978	decreases	decreases slowly 1.10
5°C	H ₂ O	0.052	0.050	0.900	decreases	0.21
40°C	H ₂ O	0.054	0.050	0.900	decreases	3.13
45°C	H ₂ O	0.058	0.0998	0.900	decreases	3.74
25°C	H ₂ O	0.057	0.057	0.45M Piperidine 0.45M Morpholine	0.680	increases
25°C	H ₂ O	0.057	0.057	0.900 Piperidine	decreases slowly 1.09	increases
25°C	40 % EtOH	0.057	0.057	0.900	decreases rapidly	decreasing slowly ~0.6
25°C	100% MeOH	0.051	0.051	-	"	decreasing slowly 3.1
25°C	100% MeOH	0.054	0.086	-	"	3.1
25°C	100% MeOH	0.053	0.086	0.575	"	3.7

* Studied by measuring rate of disappearance of cyanide.

The important points emerging from the preceding experimental work can be summarised as follows.

1. In the absence of excess morpholine, the disappearance of cyanide ion (or of N-chloromorpholine) appears to follow first order kinetics for any one run. Variations of the potassium cyanide, and to a lesser extent the N-chloromorpholine concen-

trations, causes a pronounced change in the apparent first order rate constant.

2. In the absence of morpholine, rate constants based on the second order calculation increase rapidly during the course of the run. The presence of sodium chloride in concentrations up to 1.0M, had no effect on the rate constants.

3. In the presence of excess morpholine, the first order rate constants throughout the experiment decreased rapidly whilst the second order constants exhibited only a slow decline with time.

4. In the presence of excess morpholine the second order constants did not appear to be so dependent on changes in the cyanide ion concentration,

5. It was found that increasing the morpholine concentration above 0.5 molar had little effect on the rate constants.

6. Solutions of N-chloromorpholine and potassium cyanide in water were found to contain cyanogen chloride. The only volatile liquid product which could be isolated from such a mixture was N-cyano morpholine, no morpholine, N-chloromorpholine or morpholine hydrochloride could be detected at equilibrium

7. For runs carried out at different temperatures ($5^{\circ}\text{C} - 45^{\circ}\text{C}$) and in the presence of excess morpholine, the plot of $\log_{10} k_2$ against $1/T_A$ was a straight line. From the graph the energy of activation was found to be 5,660 cal./mole.

8. N-chloromorpholine was found to chlorinate piperidine rapidly in neutral solution, thereby explaining the presence of N-cyano-piperidine in reaction mixtures containing N-chloromorpholine, potassium cyanide and excess piperidine.

9. In non-aqueous solution the reaction between N-chloromorpholine and potassium cyanide appeared to follow second order kinetics, although the individual values of k_2 throughout a run still decreased slowly. Values of k_1 fell rapidly. The values of k_2 in ethanol solution did not depend on the cyanide ion concentration. The addition of excess morpholine to ethanolic solutions of the reaction mixture produced only a slight change in the second order rate constant.

10. Cyanogen chloride could be detected in ethanol solutions of N-chloromorpholine and potassium cyanide but the concentration of this compound was far less than existed in aqueous solutions.

CONCLUSIONS

The reaction between N-chloromorpholine and potassium cyanide in non-aqueous solution follows second order kinetics and the mechanism is suspected to be the direct reaction between the cyanide ion and the chlorine atom of the N-chloro compound.

k_2 for this reaction was approximately $3.1 \times 10^{-2} \text{ sec}^{-1} \text{ mole}^{-1}$. but more work on this important problem appears to be desirable as this would seem to be one of the few reactions known of a

direct displacement of a chlorine atom attached to nitrogen.

In aqueous solution a mixed mechanism consisting of several concurrent paths is thought to occur. The most likely reactions are the following.

Dixon (personal communication) considers that the series of reactions below might play a part.

Eden, Hampson and Wheatland³⁵ have studied the reaction between hypochlorite and cyanide and have shown it to be very dependent on pH. At pH values above 10 the reaction is slow but it is extremely rapid in solutions of pH 8 - 9.5. The initial pH of a solution of N-chloromorpholine and potassium cyanide is approximately 11, but the pH rapidly changes with time as the cyanide is consumed. The initial reaction

takes place very rapidly at all pH values. The slow step at high pH values is the hydrolysis of CNCl in the presence of OH⁻ to give cyanate according to the following equation

No trace of cyanate could be found in the reaction products so

it can only be assumed that the main reaction between CNCl and morpholine occurs at a faster rate and is thus favoured.

The addition of morpholine slows the reaction down and stabilises the numerical values of the second order constants. This is to be expected on examining the equation,

Morpholine suppresses the hydrolysis of N-chloromorpholine so the main reaction then proceeds by mechanism 1 which leads to roughly second order kinetics.

By the application of rate equation and mathematical approximations, Dixon has shown that the mechanism outlined above does fit the results and that the residual mechanism is between 1st and 2nd order but more work is required before numerical values can be given to the rate constants for the different steps.

Suggestion for future work.

An investigation of the reaction between N-chloromorpholine and hydroxide ion in aqueous solution.

Henry and Dehn¹⁶ claim to have made N-hydroxy morpholine by the action of 30% hydrogen peroxide on an aqueous solution of morpholine kept at 0°C . Their product has a B.P. of $101 - 102^\circ\text{C}$ at 16 mm and was a clear liquid. When their synthesis was repeated a compound having identical physical properties was obtained, but gas chromatography (Figure 6.7) showed a mixture

of two compounds. The present work was undertaken in an attempt to elucidate the nature of these compounds and ultimately investigate the reaction between N-chloromorpholine and hydroxide ion in aqueous solution.

It is also known from the literature that N-chloromorpholine reacts with alcoholic potassium hydroxide, a dehydrohalogenation reaction taking place according to the equation.

FIG. 6.7.

Properties of the N-hydroxymorpholine mixture are outlined below.

1. Clear liquid
2. B.P. 101°C @ 16 mm

3. In dilute solutions of hydrogen peroxide the amount of the lower boiling compound predominated. The compound corresponding to peak II in the gas chromatogram had the higher B.P and lower ether solubility.
4. The mixture reduced silver nitrate but after reaction, the relative amounts of the two compounds remained unchanged.
5. Both compounds could be isolated unchanged from 6N hydrochloric acid and 6N sodium hydroxide. 60% sulphuric acid destroyed both compounds.
6. Reaction with bromine followed by gas chromatography showed that no double bonds were present in the molecule.

From these results it appeared that the two compounds in the mixture were related, possibly in an analogous manner to the N-hydroxy compound of piperidine,

When a solution of N-chloromorpholine (0.57g) in 2N sodium hydroxide (20ml) was left for several hours a compound having the same R_f value as N-hydroxymorpholine was isolated by ether extraction. The kinetics of this reaction was investigated and the results follow.

Chloride and hydroxide ion concentrations were measured in the same solution potentiometrically. The accuracy of detection was $\pm 0.5\%$

$$[\text{NaClM}] = 0.0759\text{M} = a$$

$$[\text{NaOH}] = 0.0755\text{M} = b \quad \text{Temp } 25^\circ\text{C}$$

Time (sec)	$[\text{NaClM}]^*$ (a-x)	x	$[\text{Cl}^-]^*$	$k_2 \times 10^4$ $\text{sec}^{-1} \text{mole}^{-1} \text{l.}$
300	0.0754	.0005	-	2.92
1410	.0740	.0019	-	2.40
1680	-	-	.0016	
4680	.0723	.0036	-	1.40
4920	-	-	.0045	
8580	.0701	.0058	-	1.27
8760	-	-	.0075	
12360	.0680	.0079	-	1.24
19700	.0637	.0122	-	1.28
23500	-	-	.0174	
30300	.0583	.0176	-	1.31
30900	-	-	.0176	
34500	.0572	.0187	-	1.25
37800	-	-	.0194	
78500	.0421	.0338	-	1.34
79000	-	-	.0328	
90300	.0396	.0363	.0366	1.34
104000	.0367	.0392	-	1.35
194820	.0245	.0514	-	1.42
540500	.0117	.0642	.0620	1.35

* Iodometric titration

* potentiometric titration

From these results the rate appeared to follow second order kinetics with a mean value of $k_2 = 1.32 \times 10^{-4} \text{sec}^{-1} \text{mole}^{-1}$. At the end of the experiment the loss in hydroxide titre was found to exactly equal the increase in chloride titre of the solution. The change in the ultraviolet absorption spectrum of the solution was in accordance with the above observations, N-hydroxymorpholine exhibiting very little absorption in the region of 2600A (Figure 6.8)

Much more work needs to be done on this type of reaction but the indications are that it is quite promising and opens up a new field of N-chloro chemistry.

FIG. 6.8.

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PREPARATION AND PURIFICATION OF MATERIALS

N - chloroacetanilide Prepared by the method of Barnes and Porter¹.

To an ice cold solution of acetanilide (15g.0.11 moles) and sodium carbonate (16.8g.0.2 moles) in water (3 l.) was added slowly with stirring, 150 ml. of sodium carbonate solution (1.0N) containing between 1.6 and 1.8×10^{-3} equivalents of chlorine/ml., which was kept at 5 °C. The white needles were removed by filtration and vacuum dried at room temperature. The crude material was recrystallised from a solution of acetone (1 vol.) and petroleum ether (9 vol.) Yield: 14.8 gms. (80%) M.P. 90.5-91° (literature 91)². The purity was further checked by weighing out a convenient amount, dissolving it in 30% acetic acid, and titrating the liberated iodine on addition of potassium iodide, with standard sodium thiosulphate.

e.g. Weight of <u>N</u> - chloroacetanilide	= 0.1141gms.
Titre of 0.0990N thiosulphate	= 13.63ml.
Purity	= 100.0%

Acetone Commercial quality acetone was distilled over magnesium perchlorate after drying with sodium sulphate. The dried material was stored over calcium sulphate and delivered via a sintered tube.

B.P 56.0-56.5 °C., n_D^{25} 1.3564 (literature 56.2 °C., 1.3566⁴)

Lithium Chloride B.D.H. Lithium chloride was recrystallised three times from distilled water and oven dried at 100°C. Solutions of lithium chloride in acetone were prepared as required.

N - chlorosuccinimide Prepared by the method of Bender⁵, as modified by Tscherniac⁶.

An ice cold solution of succinimide (4.95g.) dissolved in a mixture of water (15 ml.) and glacial acetic acid (6 ml.) was added with rapid stirring to an ice cold solution (50 ml.) of 1.0M sodium hypochlorite. The compound was pure white, with melting point 150 °C (literature⁷: 150 °C). Yield: 4.8g. (72%). Purity as found by iodometric titration was 99.6%. If necessary the compound was recrystallised by continuous extraction with dry carbon tetrachloride.

N - chloroacetamide Prepared by the method of Orton and Bradfield⁸.

Acetamide (35g.) and sodium bicarbonate (50g.) were suspended in ice cold water (80 ml.) and chlorine was passed through the rapidly stirred solution. M.D. Carr⁹ noted that difficulty was experienced with this preparation, and a varying factor effecting the formation appeared to be present under apparently strictly reproduced conditions. In the present work, instead of a mass of N - chloroacetamide and sodium chloride being formed, what was in fact produced were a few crystals, and approximately 20 ml. of a deep yellow, extremely corrosive, pungent, liquid, which was

denser than the remaining solution. When this yellow liquid, and the remaining filtrate, were isolated from the solid material present and allowed to warm slightly, evolution of gas occurred, and a white mass of crystals collected. The yellow oil was identified as N- dichloroacetamide and the reaction taking place as¹⁰:-

The N - chloroacetamide was recrystallised from chloroform. M.P. was 110.5-111 °C (c.f. literature¹¹ 111-112 °C).

Yield: Quantitative. Purity by iodometric titration was found to be 99.8%. It was noted that N - chloroacetamide which had been recrystallised from benzene was found to be only 97% pure and melted at 104-106 °C, hence decomposition appears likely in this solvent.

A more satisfactory method of preparing N - chloroacetamide was that of M.Ch.Manguin¹². Acetamide (59g.) was dissolved in water (100 ml.) and Zinc oxide (40g.) was added to the solution which was kept at -5 °C (ice and salt), whilst 1 mole of chlorine (71g.) was passed through the rapidly stirred solution. The chlorine was absorbed with surprising facility, and the zinc oxide gradually disappeared, leaving crystals of N - chloroacetamide.

Radioactive lithium chloride Cl-36 was available as 6×10^{-3} M. hydrochloric acid having ^{an} activity of approximately 6×10^3 counts/min/ml. in a thin walled liquid counter (type M6H as supplied by 20th Century Electronics Ltd.). To this hydrochloric acid (12 ml.) was added 1.038N hydrochloric acid (5 ml.) and the solution was then neutralised with 0.902N lithium hydroxide after adding phenolphthalein. The mixture was gently heated to remove the water and then fused to decompose the organic material present. This last step was carried out in a silica flask. Since lithium chloride is only sparingly soluble in acetone¹³, and almost insoluble when fused, a small quantity of water (3 ml.) was added to the residue in the flask and a current of warm air was drawn over the gently heated solution until dryness was reached. Dry acetone (100 ml.) was then added, and the resulting stock solution of lithium chloride (approximately 0.056M) was stored in a desiccator over silica gel to exclude moisture.

Dioxan Commercial dioxan (2.5 litres) was refluxed with concentrated hydrochloric acid (40 ml.) and water (200 ml.) for approximately 12 hours, meanwhile bubbling nitrogen through the mixture to exclude air. After cooling, sodium hydroxide pellets were added with shaking until no more would dissolve, the aqueous layer was then removed and a further quantity of sodium hydroxide (100g.) was added to the dioxan, and the mixture was allowed to stand overnight. Any further aqueous layer was then removed, the dioxan transferred to a

flask containing ferrous sulphate (200g.), and the resulting mixture left for 24 hours with occasional shaking. The dioxan was then filtered and distilled from sodium hydroxide under an atmosphere of nitrogen.

B.P 101°C (literature¹⁴ $101.3 - 101.5^{\circ}\text{C}$) n_d^{25} 1.4199
(literature¹⁵ 1.4202)

Methyl alcohol Magnesium (5g.) and iodine (0.5g.) were placed in a 2l. round bottom flask, and methyl alcohol (60 ml.) added. The mixture was warmed under reflux until the iodine disappeared; methyl alcohol (900 ml.) was then added and the mixture was refluxed for 30 minutes before distillation.

B.P $64.5-64.6^{\circ}\text{C}$ (lit. ¹⁶ $64.5-64.75^{\circ}\text{C}$) n_d^{25} 1.3264 (lit.¹⁷ 1.3276)

Hydrochloric acid "Analar" hydrochloric acid was found to contain traces of an impurity which gave large extinction coefficients at a wavelength of 220-235 $m\mu$ when mixed with chlorine (see page 86). Consequently all hydrochloric acid solutions used throughout the present work were prepared from constant boiling hydrochloric acid.¹⁸

Sodium thiosulphate A.R. reagent sodium thiosulphate was used. The solutions were stored in brown bottles, and restandardised periodically with A.R. potassium iodate. Without the aid of chloroform as a stabilisation agent, it was noted that the percentage drop in strength of a 0.035M solution was approximately 0.5% per week.

Starch Solution Analar water soluble starch (1g.) was mixed to a thin paste with water and added with stirring to boiling distilled water (100 ml.), the resulting mixture being boiled for a further two minutes. Fresh solutions were prepared as required.

Potassium iodide Analar reagent free from traces of iodine was used.

Perchloric acid Analar reagent was used throughout and solutions were standardised with sodium hydroxide using phenolphthalein as indicator.

Allyl ethyl ether This compound was prepared by the action of sodium ethoxide on the allyl halide.

Sodium metal (18g.) was dissolved in absolute ethyl alcohol (120 ml.) and to the resulting sodium ethoxide in ethanol was added dropwise allyl chloride (50g.). The solution was refluxed for 30 minutes and then fractionated, the fraction boiling between 60 and 76 °C being collected. This fraction was then distilled using a 24 inch vigreux vacuum jacketed fractionating column, the fraction boiling between 62 and 62.5 °C being collected. This fraction was washed with water to remove traces of alcohol, and finally dried over anhydrous sodium sulphate, before distilling from a mixture of quinol and ferrous sulphate in an atmosphere of nitrogen. The resulting allyl ethyl ether was stored in a blackened vessel under nitrogen to eliminate

the formation of peroxide impurities.

Yield: 20.9g. (35% theoretical)

B.P 62-62.5 °C (lit.¹⁹ 66-67 °C; 62.5 °C and 64 °C)

²⁰
 $n_d = 1.3851$ (lit. ²⁰ n_d 1.3856)

Carbon tetrachloride B.D.H. technical carbon tetrachloride was purified by the method described in Vogel²¹, utilizing a solution of potassium hydroxide and rectified spirit dissolved in water to remove the carbon disulphide present (approximately 4%). After drying over calcium chloride, the liquid was distilled in an all glass apparatus.

B.P 76.5-77 °C (lit.²¹ 76.8 °C); ²⁵ n_d 1.4570 (lit. ²² ²⁵ n_d 1.4573)

Morpholine As supplied by L. Light and Co., Ltd. Distilled in an all glass apparatus, the fraction boiling in the range 128.5-129.5 °C being collected. The purified material was analysed by titration with standard hydrochloric acid to an end point with bromothymol blue indicator.

Morpholine hydrochloride Purified morpholine (30g.) was neutralised with concentrated hydrochloric acid (40 ml.) and the resulting solution was evaporated until darkening occurred. The mixture was cooled, when morpholine hydrochloride crystals started to separate. These crystals were collected at the pump and recrystallised from a mixture of ethyl alcohol and ether (1:2) after refluxing with animal charcoal.

M.P 174-175 °C (lit.²³ 175-176 °C)

Calomel Prepared by the method outlined by Hills and Ives²⁴. Excess 2 N. hydrochloric acid was added rapidly with stirring to a diluted solution of pure mercurous nitrate in dilute nitric acid standing over a pool of mercury. The precipitate was allowed to settle, the electrolyte was decanted off and replaced by fresh 2 N hydrochloric acid and vigorous mechanical stirring was continued for a further 6 hours. This procedure was repeated, and the calomel washed by decantation, first with the same strength acid and then with distilled water. The calomel was finally filtered at the pump, washed with water until the washings gave no test for chloride and then drained and dried in a vacuum desiccator. The purified material was stored over phosphorus pentoxide. Note: It is important that the acid used in the preparation be not less than 1-2N, because of the possibility of basic salt formation²⁵.

Sodium Hypochlorite Commercial 4N sodium hypochlorite as supplied by the Ados Chemical Co. Ltd. was used throughout the present work. The solution was kept at 2 °C in the absence of light, and was found to maintain its strength for approximately eight months under these conditions.

When purer sodium hypochlorite was required for spectroscopic studies it was prepared by dissolving sodium hydroxide (100g.) in distilled water (200 mls) and cooling the mixture at 5 °C. Crushed ice (500g.) was then added, followed by chlorine until the increase in weight was 72g. The solution was made up to 1 litre and kept at 0 °C. The concentration

of the resulting solution was found to be 2N with respect to sodium hypochlorite.

Chlorine Commercial chlorine as supplied by I.C.I.

Australasia Ltd., was used, and this was scrubbed with water and dried with concentrated sulphuric acid before use.

t-butyl hypochlorite The procedure reported by Chattaway and Backeberg²⁶ with modifications outlined by Irwin and Hennion²⁷ was used to prevent the necessity of low temperature baths.

A solution of sodium hydroxide (40g.) in water (350 ml.) was prepared and the solution cooled to room temperature. t-butyl alcohol (37g.) was then added, together with sufficient water to produce a homogenous solution. A stream of chlorine was passed through the rapidly stirred solution until the formation of the second phase was complete (3 hours). The upper oily layer was separated, washed with sodium carbonate until neutral to congo red, washed four times with water, dried over calcium chloride and finally distilled in an all glass apparatus, the fraction boiling between 79 and 79.5 °C being collected.

Yield: 45g. (84% theoretical). Purity as determined by iodometric titration using acetic acid and potassium iodide was 99.3%.

(t-butyl hypochlorite is a pale yellow, mobile liquid with a characteristic, irritating odour. It is very stable, and kept for months at - 10 °C when unexposed to the light²⁸).

It violently attacks the eyes and the mucous membrane)

Hypochlorous acid A solution of chlorine (1) oxide in carbon tetrachloride was prepared by the method developed by Bowen²⁹.

Dry chlorine gas was bubbled through pure dry carbon tetrachloride (100 ml.) kept at 0 °C until the concentration of chlorine reached 50g./litre. The flask was allowed to warm to room temperature (20 °C) and yellow mercury (11) oxide (22g.) was added with rapid stirring.

Stirring was continued for 45 minutes, after which interval nearly all of the dissolved chlorine had been consumed. The solution was filtered through a coarse fluted filter paper, and stored in the dark at 0 °C. The initial yield of chlorine (1) oxide was 85% but filtering reduced it to 67%.

The chlorine oxide solution in carbon tetrachloride (100 ml.) kept at 0 °C; was extracted with ice cold water (150 ml.) for three minutes.

The resulting hypochlorous acid solution was analysed by the method of Spinks³⁰ which is based upon the fact that liberation of iodine by the reaction between either chlorine oxide or hypochlorous acid and a solution of potassium

iodide is accompanied by the consumption of hydrogen ions according to the equations

whereas chlorine reacts without the consumption of acid.

The purity of the resulting hypochlorous acid solution (0.2M) was 100.0%. The stability of such a hypochlorous acid solution was investigated, and in 9 hours at 25 °C, the solution had decomposed by 3%.

Potassium cyanide "Analar" B.D.H. potassium cyanide was used for the greater percentage of the work without further purification, since Marshall and Moelwyn-Hughes³¹ found that purification of potassium cyanide by shaking with ethyl alcohol and washing with ether, followed by drying in a vacuum desiccator had no effect on the rate constant found using untreated potassium cyanide. For work in non-aqueous solvents this latter method of purification was adopted to remove water.

Guanidine carbonate Analar reagent was used without further purification.

Guanidine hydrochloride B.D.H. Laboratory reagent was recrystallised from a mixture of ethyl alcohol and ether.
M.P. 140°C .

(found: Cl, 37.75%: Required Cl, 37.2%)

Chloramine -T B.D.H. Laboratory reagent was recrystallised from distilled water and analysed by iodometric titration until a purity of better than 99.5% was attained.
M.P. 176° (decomp.) (literature³² $175-180^{\circ}$ (decomp.)

Phenol Analar reagent phenol was dried in a vacuum desiccator, and from this, solutions were prepared and analysed as follows:-

An aliquot of the phenol solution was added to a known volume of standard potassium bromate. Excess potassium bromide and hydrochloric acid was added, and the solution left to stand for at least 2 minutes. The reactions:-

being quantitative. The excess bromine was estimated by adding an excess of potassium iodide solution and titrating the liberated iodine with standard sodium thiosulphate. Estimations were carried out in iodine flasks to avoid loss of bromine.

Sodium hydroxide Analar reagent was used and standard

solutions were analysed by titration against hydrochloric acid solutions prepared from constant boiling acid. Phenolphthalein was used to detect the end point.

Acetamide As supplied by L. Light and Co. Ltd., and recrystallised from acetone. This chemical was found to be extremely deliquescent and was stored in a vacuum desiccator over silica gel.

M.P. $81.5-82^{\circ}\text{C}$ (literature³³ 82°C)

Succinimide Succinimide supplied by L. Light and Co. Ltd., was recrystallised from a mixture of ethyl alcohol (2) and ether (1) and stored in a vacuum desiccator over silica gel.

M.P. $124.5-125.5^{\circ}\text{C}$ (literature³⁴ $126-127^{\circ} : 125-126^{\circ}$)

Piperidine Reagent grade piperidine (L. Light and Co. Ltd.,) was distilled in an all glass apparatus and the fraction boiling between 105.5 and 106.5° was collected.

(literature³⁵ -106.4°C)

4-nitrobenzalchloroimine Prepared by the method outlined by Hauser, Hauser, and Gillaspie³⁶ utilising the action of cold monochloroamine³⁷ on the aldehyde.

1.75N ammonium hydroxide (114 ml.) was diluted with water (86 ml.) and this solution was added to 4N sodium hypochlorite (50 ml.) and crushed ice (150g.). This solution was shaken vigorously with a mixture of 4-nitrobenzaldehyde

(6g.) in ethyl acetate (60 ml.). A yellow mass separated which on further shaking coagulated. The N-chloro compound was filtered at the pump and recrystallised from ethyl alcohol. Analysis by the normal iodometric method gave the purity as 99.5%.

M.P. 211-212° (decomp.) (literature³⁸ 213° decomp.)

N-chloropiperidine Several methods have been outlined in the literature for the preparation of this compound. Bally³⁹ describes methods involving the action of bleaching powder on piperidine and also a reaction between chlorine in aqueous alkali, or chloroform with piperidine. The action of alkali hypochlorites on piperidine was the subject of work carried out by Delepive⁴⁰.

The N-chloropiperidine used in the present work was prepared as follows:-

Piperidine (30g.) kept at 0 °C, was added dropwise with stirring to an ice cold solution of 4N sodium hypochlorite (200 ml.) which had been saturated with sodium chloride. The resulting mixture was placed in a separating funnel kept at 0 °C, and after several hours the upper layer of N-chloropiperidine was collected and dried over anhydrous sodium sulphate. The N-chloropiperidine was distilled as described for N-chloromorpholine, and the resulting colourless oil, which possessed an extremely pungent odour was analysed iodometrically. Purity 99.93%.

$$^{25}n_d = 1.4717 \quad (\text{no literature value available})$$

Allyl chloride Commercial quality material (L. Light and Co. Ltd.,) was distilled from ferrous sulphate and the fraction boiling in the range 44-46° C was collected.

$$\begin{array}{cc} 25 & 25 \\ n_d = 1.4116 & (\text{literature}^{41} \quad n_d = 1.4119_3) \end{array}$$

Iodine monochloride B.D.H. laboratory reagent was used without further purification.

N-chloromorpholine Morpholine reacts with aqueous solutions of sodium hypochlorites to give the corresponding N-halogen substituted compound⁴² and this reaction was utilised by Henry and Dehn⁴³ in preparing N-chloromorpholine from sodium hypochlorite and morpholine. This method has been described as a quantitative preparation, and as expected, the yields obtained by this method were often correspondingly high, although in several cases⁴⁴, ether extraction of the resulting solution was often necessary to obtain a satisfactory yield of the N-chloro compound.

Carr and Browne⁴⁵ developed a method involving the direct chlorination of morpholine hydrochloride in a solution buffered between pH8 and pH9 with potassium bicarbonate. D.R. Eddy (loc. cit.) found that the yield obtained by this method was very poor owing to the difficulty of being able to decide when all the morpholine hydrochloride was chlorinated. After a variable time interval, the rate of absorption

of chlorine was found to increase, and, beyond this point, the N-chloromorpholine produced appeared to suffer decomposition in the presence of the excess chlorine, and a dark yellow liquid remained, typical of the polymerised dehydromorpholine⁴³. Body developed a method involving the chlorination of morpholine by potassium hypochlorite, formed by the action of chlorine on potassium carbonate in solution, the greater solubility of potassium carbonate enabling the preparation to be carried out under near saturation-point conditions, yet reducing the total volume of solution required. Body maintained that these conditions should greatly facilitate the separation of N-chloromorpholine by automatically salting it out of solutions as soon as it is formed. The quantities of the various reagents used were calculated on the basis that the chlorine content of the solution should be in slight excess, ensuring that all the morpholine is in fact chlorinated, thus preventing it from becoming an impurity in the final product. It is the present author's view that this reasoning is not entirely correct, since owing to the enormous solubility of morpholine in water, then contamination of the N-chloro compound with morpholine is impossible, and an excess of chlorine will cause only unwanted decomposition⁴⁵.

In the present paper N-chloromorpholine was prepared by a modification of the method of Henry and Dehn (loc. cit.) which gave consistently high yields, usually in excess of 80% theoretical.

Morpholine (39g.) dissolved in water (50 ml.) and kept at 0°C, was added dropwise with stirring to an ice cold solution of 4N sodium hypochlorite (250 ml.) which had been previously saturated with sodium chloride, the total addition taking approximately 2 hours. The resulting solution was placed in a separating funnel and left over-night at 0°C., when it was found that two layers formed. The resulting N-chloromorpholine, which was the oily upper layer, was dried with sodium sulphate and purified by low temperature, high vacuum static distillation. The product was condensed in traps immersed in liquid air.

The pure N-chloromorpholine was found to be a colourless oil having an extremely pungent odour and possessing strong lachrymatory properties. The purity of the compound was found by iodometric titration in the usual manner. The N-chloromorpholine used was always greater than 99.7% pure. The boiling point of N-chloromorpholine was determined by the Siwoloboff method (Fig.7.1.) B.P. 149.3°C. The refractive index was found to be; n_d^{25} 1.4707 (no literature value available).

Potassium cyanide C-14 Supplied by the Radiochemical Centre, Amersham, England, and prepared by heating barium carbonate, potassium, and ammonium chloride in a sealed tube at 640°C ⁴⁶.

FIG. 7.1.

Technical data: Specific activity $6.6\mu\text{curies/mgm.}$
Radiochemical purity 99%
Chemical purity 100%
(argentimetric titration)

The crystalline product was received in glass ampoules sealed under vacuum and no deterioration of the compound was observed.

Cyanogen chloride This chemical was prepared by the reaction of chlorine with potassium zinc cyanide⁴⁷.

Zinc sulphate pentahydrate (13.2g.) and potassium cyanide (12g.), each in 60 ml. of water, were mixed at 0°C , in a three necked flask provided with a stirrer and an inlet bubbler. Chlorine was passed through the vigorously stirred solution until the initial precipitate had almost disappeared (about 60 min.). The flask was then connected in series with drying tubes (calcium chloride and magnesium perchlorate) and a liquid air trap, and the cyanogen chloride was removed from solution by gently warming the flask at 70°C . The removal of the product was assisted by carrying out the distillation under a slow stream of nitrogen.

The crude cyanogen chloride was purified by refluxing over mercury and a mixture of calcium carbonate and magnesium oxide for several hours, followed by fractionation.

B.P. 12.5°C (literature⁴⁸ 13.0°C)

Monochloroacetone Commercial monochloroacetone (L. Light and Co. Ltd.) which was very dark in colour was distilled in

an all glass apparatus under an atmosphere of nitrogen. The product rapidly started to darken but the physical constants remained the same over a period of several days after distillation.

B.P. 119-119.5 °C (literature⁴⁹ 119 °C)

Potassium chloride B.D.H. Analar reagent was used.

N-cyanomorpholine Prepared by the general method outlined for similar compounds by Slosson⁵⁰.

N-chloromorpholine (3gm.) was added to a solution of potassium cyanide (1.5g.) in absolute ethyl alcohol and the mixture warmed on a water bath. The ethyl alcohol was removed under vacuum and the residue was distilled in a micro distillation apparatus, the fraction boiling between 124 and 124.5 °C, at 18 mm. being collected.

(found: C, 52.99: H, 6.82: N, 24.00: Cl, 0: Calc.

for $C_5H_8N_2O$: C, 53.5: H, 6.6: N, 24.99)

N-hydroxymorpholine A preparation of this compound has been outlined by Henry and Dehn (loc. cit.) and is given below, but the possibility of the product not being homogeneous has been discussed in the section on the reaction of alkali with N-chloromorpholine (page 282).

30% hydrogen peroxide (23 ml.) was added dropwise with stirring to a solution of morpholine (17.5ml.) kept at 0 °C, and the mixture was left for 14 hours. As soon as the

reaction mixture was allowed to warm to room temperature, an exothermic reaction took place, and the solution went a deep amber colour, the temperature of the solution exceeding 120°C . Henry and Dehn state that they obtained a similar result if the solutions were originally mixed at room temperature, but that the reaction proceeded quietly if the reagents were cooled first.

After the exothermic reaction was completed, the mixture was distilled in an all glass apparatus through a vigreux column, the fraction which came over at $101-102^{\circ}$ at 16 mm. being collected. (c.f. Henry and Dehn $101-102^{\circ}$ @ 16 mm.)
Found: C, 47.24: H, 8.96: N, 14.62: O, 27.44 Calc.
for $\text{C}_4\text{H}_9\text{NO}_2$, C, 46.6: H, 8.79: N, 13.59: O, 31.03)

Methyl cyanide (Acetonitrile) B.D.H. Laboratory reagent was used without further purification.

$$^{20}_{\text{nd}} = 1.3432 \text{ (literature}^{51} \text{ }^{16.5}_{\text{nd}} = 1.3459)$$

I-phenyl-3-methyl-5-pyrazolone Recrystallised from a mixture of ethyl alcohol and water (2:1).

M.P. $126-126.5^{\circ}\text{C}$ (literature⁵² 127°C)

Iodine Standard solutions of iodine were prepared by dissolving the required amount of "Analar" iodine in potassium iodide solutions, and standardising with sodium thiosulphate and starch.

Pentacyanoaminoferate (PCAF) This compound which is used as a spray reagent for guanidines⁵³ was prepared as follows:-

Sodium nitroprusside (10g.) was dissolved in concentrated ammonium hydroxide (40 ml.) and the mixture kept at 0 °C for 24 hours. The solution was filtered and absolute ethyl alcohol added to the clear filtrate until a precipitate formed. The precipitated pentacyanoaminoferate was stored in vacuo over concentrated sulphuric acid.

The spray reagent was prepared by adding 20% sodium hydroxide (5 ml.) to pentacyanoaminoferate (15 ml. of 1% solution) and 1 drop of 30% hydrogen peroxide. This reagent is only stable for 24 hours.

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A P P E N D I X

The following symbols and formulae appear in the text.

:NCl or >NCl general formula for an N-chloro compound.

:NH or >NH parent base.

:NH₂⁺ or >NH₂⁺ ion of a base in an acid.

:NHC1⁺ or >NHC1⁺ ion of an N-chloro compound in an acid.

NC1M N-chloromorpholine

M.W. 121.573

NC1MH⁺ N-chloromorpholinium ion,

NMH Morpholine; M.W. 87.124.

NC1P N-chloropiperidine,

M.W. 119.600

NC1PH⁺ N-chloropiperidinium ion

NPH piperidine; M.W. 85.151.

NC1G N-chloroguanidine, (NH₂ - C - NH₂);
M.W. 93.524.

N C1S N-chlorosuccinimide

M.W. 133.541.

NC1A N-chloroacetamide, (CH₃CONHC1);
M.W. 93.519

NC1A_c N-chloroacetanilide, C1NCOCH₃
M.W. 169.617

>NCN N-cyano compound

>NOH N-hydroxy compound

$$K = \frac{[:\text{NHC1}^+]}{[\text{NCl}][\text{H}^+]} = \frac{1}{K_a}$$

$$K_H = \frac{[:\text{NH}][\text{HOC1}]}{[:\text{NCl}]}$$

$$K^1 = \frac{[\text{H}^+][\text{Cl}^-][\text{HOC1}]}{[\text{Cl}_2]}$$

$$K_2 = \frac{[:\text{NH}][\text{Cl}_2]}{[:\text{NCl}][\text{H}^+][\text{Cl}^-]}$$

$$K_1^1 = \frac{[:\text{NH}_2^+][\text{Cl}_2]}{[:\text{NClH}^+][\text{Cl}^-][\text{H}^+]}$$

$$K_2 = KK_1^1$$

$$\begin{aligned} \frac{d\text{Cl}_2}{dt} &= k[:\text{NClH}^+][\text{Cl}^-] \\ &= kK[:\text{NCl}][\text{H}^+][\text{Cl}^-] \\ &= k_{111}[:\text{NCl}][\text{H}^+][\text{Cl}^-] \end{aligned}$$

NOTE

$$1000 \text{ ml of N thio} = \frac{:\text{NCl}}{2}$$