Chapter I

INTRODUCTION

Kinetics is a part of the science of motion and in chemistry it deals with the rate of chemical reaction, with all factors which influence the rate of reaction, and with the explanation of the rate in terms of the reaction mechanism*. The classic example of a reaction whose mechanism has been exhaustively studied by kinetic methods is the work of Hughes and Ingold in the mid 1930's on nucleophilic aliphatic substitution\(^1\). The theory of elimination reactions has also been developed by the same authors in a way remarkably similar to the way the theory of nucleophilic aliphatic substitution developed.

The expression "substitution" is generally used in organic chemistry to designate reactions in which hydrogen is substituted by another atom or group of atoms. However, in the broader sense of the word, substitution reactions may be defined as reactions in which any atom or group of atoms is replaced by another atom or group of

* There are several mechanisms which are kinetically indistinguishable and the mechanisms deduced from kinetics alone are too vague as to the exact processes taking place.
atoms. In nucleophilic substitution the attacking reagent (the nucleophile) brings an electron pair to the substrate according to the general scheme.

$$Y + R-X \longrightarrow R-Y + X \quad (S_N)$$

where a new bond is formed by co-ordination and old one is broken by heterolysis. Since there is an electron transfer from the substituting agent $Y$ to the centre of substitution in $R$, and from this centre to the expelled group $X$, $Y$ becomes formally one electronic unit more positive and $X$ one more negative. Subject to this no other restriction on the states of electrification of the species involved need be placed. For convenience this type of reaction is symbolised $S_N$. Examples are the Finkelstein reaction, the Menschutkin reaction, the Hofmann degradation, the acid, alkaline and neutral hydrolysis and alcoholysis of alkyl halides and sulphonates. The term "solvolysis" was introduced by Steigman and Hammett$^2$ for kinetically first-order nucleophilic displacements by solvent present in large excess, and considerable attention has been devoted to studying such processes over the past few decades$^3,4$.

Prior to the development of the Hughes-Ingold theory, three different pictures had been put forward to explain the course of nucleophilic substitution reactions$^5$. The first was that substitution
was initiated by an addition process between the substituting agent and the compound substituted to form a molecular compound from which the displaced group was subsequently eliminated. The second theory was based on the idea that the introduction of the replacing group and the expulsion of the replaced group are interdependent features of a single synchronous process. The third picture postulated the prior dissociation of the compound substituted to give a carbocation which would later combine with the substituting agent.

Hughes, Ingold and their coworkers\(^1\) employed the last two modes of reaction mechanisms in developing a comprehensive theory of nucleophilic aliphatic substitution. This theory was remarkably successful in correlating and explaining the large amount of data dealing with reactions of this type. The theory postulates that a nucleophilic substitution being a heterolytic reaction in solution, has two available reaction mechanisms, namely the \(S_N^2\) (Substitution Nucleophilic Bimolecular) and \(S_N^1\) (Substitution Nucleophilic Unimolecular) mechanisms.

The \(S_N^2\) mechanism for an alkyl halide is formulated as

\[ \text{Y} + \text{C-X} \rightarrow \text{Y} - \text{C} - \text{X} \rightarrow \text{Y} - \text{C}^\ominus + \text{X} \]

nucleophile alkyl halide halide ion
In this mechanism the nucleophile approaches the substrate from a position 180° away from the leaving group. The reaction is a one step process. The C-Y bond is formed as the C-X bond is broken. The kinetics of this process must be consistent with a second-order rate expression, first-order in substrate and first-order in nucleophile. Since the attacking species is involved intimately in the rate-determining step, not only will the rate depend on its concentration, but also the chemical nature of the nucleophile.

The $S_{N1}$ mechanism for an alkyl halide is formulated as

$$\begin{align*}
\text{slow} & \\
R-X & \rightleftharpoons R^+ + X^- \\
\text{fast} & \\
R^+ + Y: & \rightarrow R-Y
\end{align*}$$

This mechanism proceeds by rate-determining heterolytic dissociation of the substrate to a tri co-ordinate carbocation* and the leaving group. The dissociation is followed by rapid reaction between the carbocation and the nucleophile. The consequences of this mechanism are that the reaction will exhibit first-order kinetics.

* The tri co-ordinate carbocation has been referred to as carbenium ion $^6$. 
overall, with the rate of decomposition of the substrate being independent of the concentration or nature of the nucleophile. There are many examples of nucleophilic substitution reactions in which the kinetic data do not allow assignment of $S_N^1$ or $S_N^2$ mechanisms. Such behaviour has been described as "borderline". The cause of "borderline" behaviour is a matter of controversy and different viewpoints have been expressed by various workers. Most of the leading physical organic chemists accepted the basic structure of the Hughes-Ingold theory, to mention a few Bartlett, Hammett, Hine, and Brown. The general climate of opinion can perhaps be best expressed in the following words due to streitwieser. "Because of the importance of the concepts involved, the $S_N^1$ hypothesis should be considered as being one of the most important developments in theoretical chemistry. Its general acceptance is marked by the aspects of it, which have appeared in numerous books and texts". This is not to suggest that the acceptance was complete; several workers have suggested modifications of the Hughes-Ingold scheme.

Winstein and coworkers suggested that in addition to the dissociated carbocation and counter-ion of the leaving group, two ion pair intermediates were required to reconcile the available data on kinetics, salt effects and stereochemistry of solvolytic reactions.
The process of ionization generates a carbocation and counter-ion in proximity to each other. This species is called an intimate ion pair. One process available to an intimate ion pair is conversion to a solvent-separated ion pair, in which one or more solvent molecules have inserted between the carbocation and the leaving group. Conversion of the solvent-separated ion pair to "free ions" occur by diffusion of the solvated carbocation and counter-ion away from each other, and is referred to as dissociation.

\[
\begin{align*}
R-X & \rightleftharpoons R^+X^- & \text{ionization} \\
& \rightleftharpoons R^+\mid|X^- & \text{dissociation} \\
\text{intimate} & \text{solvent-separated} & \text{dissociated} \\
\text{ion pair} & \text{ion pair} & \text{ions}
\end{align*}
\]

According to this scheme, attack by a nucleophile or solvent can occur on the covalent substrate, the intimate ion pair or the solvent-separated ion pair, or on the dissociated carbocation. Several lines of evidence supported the essential correctness of this scheme, especially the involvement of more than one ion pair intermediate. The effect of added lithium perchlorate on the rate of solvolysis is anomalous towards certain substrates in producing an initial sharp increase in the solvolysis rate, followed by the expected linear increase at higher lithium perchlorate concentration ("special salt effect")\textsuperscript{14}. Winstein\textsuperscript{15} ascribed this to interaction of
lithium perchlorate with the solvent-separated ion pair to form a solvent-separated carbocation perchlorate ion pair that does not undergo return to the intimate ion pair or covalent substrate. This new ion pair can go on only to product and its formation leads to an increase in solvolysis rate more pronounced than for a simple medium effect.

Sneen and coworkers\textsuperscript{16-19} have undertaken an extensive investigation of the mechanism of nucleophilic substitution at a saturated carbon atom and suggested that the penta co-ordinate transition state of the traditional $S_N2$ displacement is without experimental proof. Ion pair intermediates, on the other hand, are amply supported as having finite existence. Sneen and Larsen\textsuperscript{19} extended their interpretation by suggesting that "all reactions of nucleophilic substitution at a saturated carbon atom proceed via an ion pair mechanism". The Sneen mechanism adopts most elements of the Winstein ion pair scheme. Sneen proposes the following scheme.

\[
\begin{align*}
  RX & \rightleftharpoons R^+X^- & \rightarrow & R^+\mid X^- & \rightarrow & R^+ + X^- \\
  & | & \downarrow & | & \downarrow & |
  SOR & NR & ROS & RN & ROS+SOR & RN+NR
\end{align*}
\]

where the solvent is SOH and $N^-$ is a nucleophilic anion.
Attack by solvent can occur with inversion of configuration at the intimate ion pair stage, with retention of configuration at the solvent-separated ion pair stage, or with recemization at the dissociated-ion stage. Attack by an external nucleophile can occur with inversion at the intimate ion pair stage, or with recemization at the dissociated-ion stage. It is considered that while nominal retention of configuration would occur on attack by nucleophile at the solvent-separated ion pair stage, such a process would not be competitive with solvent collapse. In most secondary systems, including those described as "borderline" attack by nucleophile would occur at the intimate ion pair stage. The "Sneen mechanism" was the subject of great deal of debate and critical summaries have been published\textsuperscript{20-22}. By repeating the original work of Sneen and Larsen\textsuperscript{17,19} on 2-octyl mesylate at constant total salt concentration, which was maintained at 2.0 mol by addition of sodium perchlorate to 0 - 0.3 mol sodium azide, Mclennan\textsuperscript{23} found a rate product correlation in agreement with the classical $S_N^2$ mechanism. The present position is that, as Pross pointed out, the Sneen ion pair mechanism appears to lack general support\textsuperscript{24}.

Schleyer and Bentley\textsuperscript{22,25,26} proposed an alternative ion pair mechanism for the solvolytic reactions which resembles the classical $S_N^2$ mechanism more closely. In their scheme which has been termed $S_N^2$ (intermediate), the first step is the rate-determining, resulting
in the formation of nucleophilically solvated ion pair. The ion pair intermediate then reacts with solvent in a rapid product-determining step. Schleyer and Bentley have suggested that "borderline" behaviour fits readily into this scheme. At the $S_N^2$ end of the spectrum the reaction proceeds through either a classical one-step pathway with strong nucleophiles or through the nucleophilically solvated ion pair for weak nucleophiles. At the $S_N^1$ end of the spectrum, ion pair formation is nucleophilically unassisted. "Borderline" behaviour is consistent with partial nucleophilic assistance in the formation of the ion pair. Thus according to Schleyer and Bentley the major difference between the $S_N^1$ and $S_N^2$ solvolytic pathways may be attributed to the degree of nucleophilic assistance leading to the transition state. Recently a single electron shift stepwise mechanism has been suggested for certain nucleophilic substitution reactions$^{27,28}$.

In the 1,2-elimination reaction of an alkyl halide, dehydrohalogenation involves loss — elimination — of the halogen atom and a hydrogen atom from a carbon adjacent to the one losing the halogen. The reagent required is a base, whose function is to abstract the hydrogen as a proton (The base :$B$ can be neutral or negatively charged; for example $H_2O$ or $OH^-$. The conjugate acid $H:B$ will then be positively charged or neutral: for example, $H_3O^+$ or $H_2O$).
Dehydrohalogenation : 1,2-elimination of HX

\[ :B + \text{H} \cdot \text{C} - \text{C} - \text{H} \cdot \text{X} \rightarrow \text{C} = \text{C}^\cdot + \text{H}:B + :X^- \]

base alkyl halide alkene protonated halide base ion

The halogen leaves the molecule as halide ion, and hence must take its electron pair along. Hydrogen is abstracted by a base as a proton and hence leave its electron pair behind; it is this electron pair that is available to form the second bond — the \( \pi \) bond — between the carbon atoms.

Hughes and Ingold proposed that elimination, like nucleophilic substitution, can proceed by two different mechanisms\(^1\). These mechanisms, they named E2 and E1.

In the E2 mechanism (Elimination Bimolecular), the two groups depart simultaneously, with the proton being pulled off by a base.
The mechanism thus takes place in one step and kinetically second-order: first-order in substrate and first-order in base*. It is analogous to $S_N^2$ mechanism and often competes with it. With respect to the substrate, the difference between the two pathway is whether the species with the unshared electron pair attacks the carbon (and thus act as a nucleophile) or the hydrogen (and thus act as a base). In most cases it has been found that the E2 reaction, like the $S_N^2$, is stereospecific, that is five atoms involved (including the base) must be in one plane, and that H and X must be trans. This conformation of H and X is called anti-periplanar. The dihedral angle between H and X is $180^\circ$. As in the case of $S_N^2$ mechanism, the leaving group may be positive or neutral, and the base may be negatively charged or neutral.

The E1 mechanism is a two step process in which the rate-determining step is ionization of the substrate to give a carbocation which rapidly loses a $\beta$-proton to a base, usually the solvent.

\[
\begin{align*}
1. & \quad \text{slow} & \quad -\text{C-C-X} & \quad \text{fast} & \quad -\text{C-C}^+ + \text{X}^- \\
& \text{H} & \text{H} & \end{align*}
\]

\[
\begin{align*}
2. & \quad \text{solvent} & \quad -\text{C-C}^+ & \quad \text{fast} & \quad \text{C}=\text{C}^-\\
& \text{H} & \end{align*}
\]

* Deviations from integral-order due to base association and salt effects have been observed$^{29}$. 
The E1 mechanism normally operates without an added base. Just as the E2 mechanism is analogous to and competes with $S_N^2$, so is the E1 mechanism related to $S_N^1$. In fact, the first step of E1 is exactly same as that of $S_N^1$ mechanism. The second step differs in that the solvent pulls a proton from the $\beta$-carbon of the carbocation rather than attacking it at the positively charged carbon atom, as in the $S_N^1$ process. It has been shown that E1 reactions can involve ion pairs, just as is true for $S_N^1$ reaction. In a pure E1 reaction, that is, without ion pairs etc., the product should be completely nonstereospecific, since the carbocation is free to adopt its most stable conformation before giving up the proton.

In the E1 mechanism, X leaves first and then H. In the E2 mechanism the two groups leave at the same time. There is a third possibility: the H leaving first, and then the X. This is a two-step process, called the ElcB mechanism (Elimination, Unimolecular of the conjugate base) or the carbanion mechanism, since the intermediate is a carbanion.

\[
\begin{align*}
1. & \quad \text{B:} \quad -\text{C-C-X} \quad \xrightleftharpoons{\text{slow}} \quad -\text{C}=\text{C-X} + \text{H:B} \\
2. & \quad -\text{C}=\text{C-X} \quad \xrightarrow{\text{fast}} \quad -\text{C}=\text{C}^- + \text{X}^-
\end{align*}
\]
This is a second-order mechanism, because both the base and the substrate are present in the rate-determining step. The existence of this mechanism is much less firmly established than that of the E2 or E1 mechanisms. However, recent studies of the reaction of four isomers of butyl iodide with strong organic base tetrakis(dimethylamine), using crossed supersonic nozzle beam technique, revealed the formation of carbanion as the reaction intermediate\textsuperscript{31}. 
Summary of the Present Work*

The work reported in this thesis consists of two parts. **Part A** - deals with the kinetics of solvolysis of α-methyl-α-alkylbenzyl chlorides (alkyl = methyl, ethyl, isopropyl and t-butyl) and their p-methyl and p-bromo substituted compounds in aq. acetone, aq. acetonitrile, aq. dimethyl sulphoxide and methanol. The effect of various salts such as LiClO₄, LiCl, LiBr, NaCl and NaBr on the rates of solvolyses has also been investigated.

The main findings are

1. All the substrates undergo solvolytic reaction by a unimolecular mechanism. The marked drop in the rate of $S_N^1$ solvolysis of the series $(\text{CH}_3)(\text{C}_6\text{H}_5)\text{RC-Cl}$ (where R = methyl, ethyl, isopropyl and t-butyl) has been attributed to steric inhibition of resonance in the carbocation. Evidence for this has been obtained from the plot of log $k_1$ values against Charton's steric constants of alkyl groups and also from the activation parameters of the reaction.

2. Studies on the effect of p-methyl and p-bromo substitution on the rate of α-methyl and α-ethyl substituted compounds show

* Two papers, one based on substitution and the other elimination, have been submitted for publication.
that the minor steric factor due to a change of α-substituent from methyl to ethyl is not affecting the electronic participation from the p-substituent. This observation supports the findings of Brown, by $^{13}$C nmr studies, that fully developed benzylic carbocation is able to overcome the minor steric difficulties in achieving coplanarity with the aromatic ring with only minor costs in energy.

3. The kinetic data for the solvolysis of α-methyl-α-alkylbenzyl chlorides in methanol show that there is ground state stabilization through solvation.

4. Solvolytic rate data of α,α-dimethylbenzyl chloride and its p-methyl substituted derivative in aq. acetone and methanol in presence of added lithium perchlorate show that lithium perchlorate exhibits a special salt effect.

5. The rate data in presence of added lithium chloride, lithium bromide, sodium chloride and sodium bromide for the solvolysis of α,α-dimethylbenzyl chloride and its p-methyl substituted derivative in aq. acetone aq. DMSO and methanol show that a mass-law effect is operative in the solvolytic reactions.
Part B - This section mainly deals with the kinetics of elimination of hydrogen chloride from α-methyl-α-alkylbenzyl chlorides (alkyl = methyl, ethyl, isopropyl and t-butyl) and their p-methyl and p-bromo substituted derivatives in acetonitrile.

The findings are

1. The elimination reaction was found to be quantitative in acetonitrile. The kinetic data of the elimination reaction can be compared with that of substitution reaction. The effect on the rate and activation parameters of elimination reaction, due to changes in the α and p-substituents, is similar to that of substitution reaction. The data show that the elimination reaction in acetonitrile is unimolecular. (E1 elimination)

2. Studies on the kinetics of dehydrochlorination reaction of α,α-dimethylbenzyl chloride in methanol in presence of sodium methoxide show that, under such condition, the reaction is bimolecular (E2 elimination).