CHAPTER 1

Introduction

Physical organic chemistry is the study of the interrelationships between structure and reactivity in organic molecules. It can be seen as the study of organic chemistry using tools of physical chemistry such as chemical equilibrium, chemical kinetics, thermochemistry and quantum chemistry. The term "physical organic chemistry" is commonly attributed to Louis Hammett, who used it as a title for a book in 1940.

The two main themes in physical organic chemistry are structure and reactivity. The study of structure starts from chemical bonding, with special emphasis on the stability of organic molecules due to factors such as steric strain and aromaticity. Other topics in structure include stereochemistry and conformational analysis. Supramolecular structure is also considered in terms of intermolecular forces including hydrogen bonding. Finally, the acid-base chemistry of the molecules is studied in terms of structure, based on resonance and inductive effects and through the use of linear free-energy relations.

The study of reactivity focuses on the mechanisms of organic reactions. It uses chemical kinetics, spectroscopy, isotope effects, and quantum chemistry to determine the sequence of elementary steps involved in a reaction. These elementary steps can be classified in a few
major classes: addition, elimination, substitution, and pericyclic reactions. The mechanisms are commonly expressed in terms of "electron pushing" and potential energy surfaces. Other major topics are photochemistry, the effect of light on the reactivity of organic molecules, and solvent effects on organic reactions.

Structure and reactivity are both involved in the study of reaction intermediates—the transient species involved in reaction mechanisms. The main types of intermediates of interest are carbocations, carbanions, free radicals, and carbenes. Usually, these intermediates are not isolated, but their presence is inferred from stereochemical evidence, spectroscopy, or through the use of chemical traps. In some cases, however, it is possible to isolate these types of molecules at very low temperatures (cryochemistry) or via matrix isolation. It is also possible to create specific derivatives that are stabilized through chemical means such as resonance, as in the case of the triphenylmethyl radical.

1.1 Types of Organic Reactions

Organic reactions are chemical reactions involving organic compounds. The basic organic chemistry reaction types are addition reactions, elimination reactions, substitution reactions, pericyclic reactions, rearrangement reactions, photochemical reactions and redox reactions. In organic synthesis, organic reactions are used in the construction of new
organic molecules. The production of many man-made chemicals such as drugs, plastics, food additives, fabrics depend on organic reactions.

There is no limit to the number of possible organic reactions and mechanisms. However, certain general patterns are observed that can be used to describe many common or useful reactions. Each reaction has a stepwise reaction mechanism that explains how it happens, although this detailed description of steps is not always clear from a list of reactants alone. Organic reactions can be organized into several basic types. Some reactions fit into more than one category. For example, some substitution reactions follow an addition-elimination pathway. This overview isn't intended to include every single organic reaction. Rather, it is intended to cover the basic reactions.

<table>
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<tr>
<th>Reaction type</th>
<th>Subtype</th>
<th>Comment</th>
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<tr>
<td>Addition reactions</td>
<td>Electrophilic addition,</td>
<td>Include such reactions as halogenation,</td>
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<td></td>
<td>Nucleophilic addition, Radical</td>
<td>hydrohalogenation and hydration.</td>
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<td></td>
<td>addition</td>
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<td>Elimination reaction</td>
<td>Include processes such as dehydration and are</td>
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<td>found to follow an E1, E2 or E1cB reaction</td>
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<td></td>
<td>Substitution reactions</td>
<td>With SN1, SN2 and SNi reaction mechanisms</td>
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<tr>
<td></td>
<td>Nucleophilic aliphatic substitution, nucleophilic aromatic substitution,</td>
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nucleophilic acyl substitution,  
electrophilic substitution,  
electrophilic aromatic  
substitution, radical  
substitution  

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<thead>
<tr>
<th>Organic redox reactions</th>
<th>Redox Reactions specific to organic compounds and are very common.</th>
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<tbody>
<tr>
<td>Rearrangement reactions</td>
<td>1,2-Rearrangements, pericyclic reactions, metathesis</td>
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In Condensation reactions a small molecule, usually water, is split off when two reactants combine in a chemical reaction. The opposite reaction, when water is consumed in a reaction, is called hydrolysis. Many Polymerization reactions are derived from organic reactions. They are divided into addition polymerizations and step-growth polymerizations.

In general the stepwise progression of reaction mechanisms can be represented using arrow pushing techniques in which curved arrows are used to track the movement of electrons as starting materials transition to intermediates and products.
1.2 Review of Literature

1.2.1 N-Halo Amides as Oxidizing Agents

N-Halo amides forms a separate branch in chemistry, which is of great synthetic importance. N-Halo amides have been extensively employed as oxidizing agents for organic substrates. In the recent development, N-halo amides are the sources of positive halogen and have been exploited as oxidant for a variety of substrates in both the acidic and alkaline media. The nature of active oxidizing species and mechanism depends on the nature of the halogen atom, the groups attached to the nitrogen and the reaction conditions.

The various N-halo compounds extensively used as reagents in organic chemistry are N-bromophthalimide, N-bromoacetamide, N-chloroacetamide, N-chlorobenzenesulphonamide, N-bromobenzene-sulphonamide, N-chlorobenzamide, N-bromobenzamide, N-chloro-p-toluensulphonamide, N-chloronicotinamide, N-chlorosuccinimide, N-bromo-saccharin, N-bromo-3,5-dinitrobenzamide, N-chlorosaccharin, and N-bromosuccinimide.

1.2.2 N-Halo amides in aqueous medium

Halogens in aqueous solution are still used world-wide as disinfectants. During the process of halogenation, the substances present in water undergo several chemical processes, yielding relatively unstable
intermediate species; their life-times in the medium depend on their structure and on the physico-chemical conditions.

The generation and reactivity of \(N\)-halo amides and their importance in biological systems have been reviewed. The aqueous solution of halogen has a strong oxidizing character. The species responsible for such oxidizing character may be different depending on the pH of the medium. These oxidant species react readily with \(N\)-amides to give the corresponding \(N\)-halo derivatives. The oxidation products depend on the ratio \([X_2 \text{ (aq)}]/[N\text{-compounds}]\) and on the acidity of the medium.

**1.2.3 \(N\)-Halo amides in acid medium**

It has been reported earlier in the case of \(N\)-halo amides that in the absence of mineral acids, \(HOX\) is the reactive oxidant species. In the oxidation with \(N\)-bromo compounds such as \(N\)-bromoacetamide, “positive” bromine is the effective oxidant. Further Mukerji and Banerji have proposed \(HOBr\) as oxidizing species in the study of oxidation of primary alcohol by \(N\)-bromoacetamide in the absence of mineral acid.

The probable reactive species of \(N\)-halo amides in acid solution are \(>NX\), \(HOX\), \(>N^+HX\) or \(H_2O^+X\) and the reactive species in alkaline solution are \(>NX\), \(HOX\) and \(OX^-\). For example, in the case of \(N\)-
chlorobenzamide the actual reacting species in acid medium are as follows.

\[
\begin{align*}
\text{NCB} & + \text{H}_2\text{O} \rightleftharpoons \text{HOCl} + \text{Benzamide} \quad (1) \\
\text{HOCl} & + \text{H}^+ \rightleftharpoons \text{H}_2\text{O}^+\text{Cl} \quad (2) \\
\text{NCB} & + \text{H}^+ \rightleftharpoons \text{NCBH}^+ \quad (3) \\
\text{NCBH}^+ & + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{O}^+\text{Cl} + \text{Benzamide} \quad (4)
\end{align*}
\]

The protonation of HOCl results in a hypochlorous acidium ion \( \text{H}_2\text{O}^+\text{Cl} \), a prime cationic and remote profile of the choice.

### 1.2.4 Oxidation by Some Selected \( N \)-Halo Amides

The oxidations of organic compounds by \( N \)-halo compounds have been reported by several authors.\textsuperscript{100-200} The results from some studies on mechanism of the oxidation of organic compounds by \( N \)-chlorobenzamide (NCB) and \( N \)-bromoacetamide (NBA) are presented here.

### 1.2.5 Oxidation reactions by \( N \)-Chlorobenzamide

The kinetics of the oxidation of about forty two aromatic anils prepared from (i) unsubstituted benzaldehyde and unsubstituted aniline (ii) substituted benzaldehydes and unsubstituted aniline (iii) unsubstituted benzaldehyde and substituted anilines and (iv) substituted benzaldehydes and substituted anilines by \( N \)-chlorobenzamide in aqueous methanol medium have been reported by Kasim et al.\textsuperscript{118} The reaction was enhanced by electron-releasing substituents both in benzaldehydes as well as in
aniline moieties while electron withdrawing substituents retarded the rate. For the series with various substituents in the ring-X (benzaldehyde) and with hydrogen in the ring-Y (aniline), the $\rho$ value is -0.40. For the series with various substituents in the ring-Y and with hydrogen in the ring-X, the $\rho$ value is -2.65. Linear plots were obtained between $\rho(x(y))$ (obtained from Hammett's plot for various substituents in the benzaldehyde moiety) and $\sigma(y)$ (substituent constants for substituents aniline moiety) with a slope of -1.46 and between $\rho(y(x))$, (obtained from Hammett's plot for various substituents in the aniline moiety) and $\sigma(x)$ (substituent constants for substituents in benzaldehyde moiety) with a slope of -1.51. This relationship has been analysed quantitatively in terms of interactive free energy relationship for multiple substituent effects.

The kinetics of oxidation of thiosemicarbazide (TSC), its zinc metal complex and hydrazones by $N$-chlorobenzamide (NCB) have been investigated in aquo-acetic acid (1:1, v/v) medium in the presence of perchloric acid. The hydrazones studied were benzaldehyde, propionaldehyde, acetone and acetophenone thiosemicarbazones. The oxidations followed first order kinetics in [NCB], fractional order dependences in [substrate] and inverse fractional order in [$H^+$]. Addition of the reduced product of the oxidant and variation in ionic strength or the solution have no significant effect on the rates of oxidations. The rates increase with the increase in acetic acid composition of the solvent. The
rate-limiting steps have been identified in all the cases and the rate coefficients of these steps and the related activation parameters have also been evaluated. Validity of the deduced rate laws has been checked by recalculating the rate constants as [substrate] and [H$^+$] are varied.$^{119}$

The kinetics of oxidation of thiosemicarbazide (TSC) its zinc metal complex and hydrazones by $N$-chlorobenzamide (NCB) have been investigated$^{118}$ in water methanol (1:1, v/v) medium in the presence of perchloric acid. The hydrazones studied were benzaldehyde, propionaldehyde, acetone and acetophenone thiosemicarbazones. The reactions show first-order kinetics in [NCB], a fractional order dependence in [substrate] and an inverse fractional to inverse first order in [H$^+$]. Addition of benzamide has no significant effect on the rates of oxidations. Variation in the ionic strength of the medium has little effect on the rates of reactions, but a decrease in the dielectric constant of the medium by increasing the methanol concentration in the solvent increases the rates. The rate-limiting steps were identified in all cases and the rate coefficients of these steps and the related activation parameters were also evaluated. The consistency of the deduced rate laws was checked by recalculating the rate constants as the substrate and H$^+$ concentrations were varied.$^{120}$

Kinetics of oxidation of free and Zn(II)-bound thiocarbohydrazide (TCH) by $N$-bromoacetamide (NBA), $N$-chlorobenzamide (NCB) and $N$-bromobenzamide (NBB) have been studied$^{118}$ in aqueous, water-methanol
and water-acetic acid (1:1, v/v) media in the presence of perchloric acid or buffer. The reactions show first order kinetics in [oxidant] and fractional order each in [substrate] and \([\text{H}^+]\). Addition of the reduced product of the oxidant decreases the rate of NBB oxidation, while it has no effect in NCB and NBA oxidations. Increase in either ionic strength or dielectric constant of the medium increases the rates of oxidation in all the cases. Both Michaelis-Menten type and two-pathway mechanisms have been considered to explain the results. The rate constants are also predicted from the deduced rate laws and the predicted values are in good agreement with the experimental constants providing support to the proposed mechanism. The metal complexation of thiocarbohydrazide has little effect either on the rate of oxidation or kinetic orders.\(^{121a}\)

Kinetics of oxidation of thiocarbohydrazide (TCH) by \(N\)-bromoacetamide (NBA) in buffered aqueous medium and by \(N\)-chlorobenzamide (NCB) in buffered water-methanol medium (1:1, v/v) have been studied\(^ {118}\) under varying conditions. The reactions show first order kinetics in [oxidant], fractional order in [TCH], and inverse fractional order in \([\text{H}^+]\) for both the oxidations. Variation in ionic strength of the medium or addition of the reduced products of the oxidants have negligible effects on the rates of both the oxidations. Decrease in dielectric constant of the medium by increasing the methanol content of the solvent decreased the rate of NCB oxidation. Careful analysis of the results shows that NBA oxidation follows a Michaelis-Menten type
mechanism while NCB oxidation follows a two-pathway mechanism. The constants of the rate limiting steps have been determined at different temperatures by varying [TCH] as well as [H$^+$] at each temperature for both the oxidations. Activation parameters corresponding to these constants have been calculated. The observed rate constants have been recalculated from the rate laws as [TCH] and [H$^+$] were varied. Reasonable agreement between the two sets of values provides support to the suggested mechanisms.$^{121b}$

The oxidation kinetics of thirteen aliphatic acetals of normal aliphatic aldehydes and substituted aliphatic aldehydes with aliphatic and substituted aliphatic as well as with aromatic alcohols by $N$-chlorobenzamide (NCB) in aqueous acetic acid medium follows first order and zero order dependence in [NCB] and [acetal] respectively and yields the corresponding esters as the main product of oxidation. (H$_2$OCl)$^+$ has been postulated as the oxidizing species.$^{121c}$

1.2.6 Oxidation reactions by $N$-Bromoacetamide

Kinetics of oxidation of valeric acid by $N$-bromoacetamide have been studied$^96$ in the presence of acidic solution of Ir(III). A first order dependence with respect to $N$-bromoacetamide and Ir(III) has been observed. Valeric acid exhibits zero order kinetics. Negative effect of acetamide and hydrogen ions while positive effect of mercuric acetate
variation were observed. A general mechanism consistent with the above observations had been proposed.

Kinetics of oxidation of carbohydrazide (ch) by N-bromoacetamide (NBA) in aqueous perchloric acid medium and thiocarbohydrazide (tch) in the free state and in its metal complex by NBA both in the presence and absence of added bromide ion have been investigated in aqueous perchloric acid medium. Oxidation of carbohydrazide showed first order kinetics in [NBA], nearly first order in [ch] and inverse fractional order in [H⁺]. The rate slightly decreased with increase in ionic strength of the medium. Addition of either the reduced product of the oxidant or bromide had no significant effect on the rate of CH oxidation. Oxidation of thiocarbohydrazide in the free and metal-bound states both in the presence and absence of added bromide showed first order kinetics in [NBA] and fractional order in both [tch] and [H⁺]. But the fractional order in [H⁺] for the oxidation of tch in the presence of Br⁻ was almost twice that in its absence. The rate increased with increase in [Br⁻] with a fractional order of about 0.3. Variation in ionic strength of the medium had very negligible effects. Addition of acetamide, the reduced product of the oxidant, had no effect on the rate. Michaelis-Menten type mechanisms have been considered to explain the observed results. Activation parameters have been computed for all the oxidations by measuring rates at different temperatures. Detailed mechanisms of oxidations have also been suggested.
The kinetics of Pd(II) catalyzed oxidation of xylose and lactose by N-bromoacetamide has been investigated in perchloric acid medium in the presence of mercuric acetate. The reaction follows identical kinetics, being first order in each substrate and Pd(II) concentration. First order at low concentration of N-bromoacetamide tends to zero order at high NBA concentration. A negative effect of hydrogen ion was found whereas ionic strength, chloride ion and acetamide do not influence the oxidation rate. The reaction follows first order kinetics with respect to mercuric acetate at its lower concentration but follows zero order at higher concentration. The corresponding acids were identified as end products of the reaction. Various thermodynamic parameters have been computed and recorded.

The kinetics of oxidation of some ortho- and para-substituted benzanilides by N-bromoacetamide (NBA) has been studied in acid medium. The product of oxidation is the corresponding benzoquinone. The rate data for these benzanilides have been correlated with DSP equations. These compounds correlate well with the Swain's F and R parameters. The reaction constants are negative and small in magnitude. In this oxidation reaction the field effects are more pronounced than the the resonance effects. The ortho-substituted benzanilides show a good correlation with a triparametric equation involving the Taft's $\sigma_1$ and $\sigma_R$ and the Charton's $\eta$ values. Based on these observations, a suitable mechanism has been proposed.
The oxidation of phosphinic, phenylphosphinic, and phosphorous acids by \( N \)-bromoacetamide (NBA) in acid solution, results in the formation of corresponding higher oxyacids of phosphorus\textsuperscript{100}. The reaction is first order with respect to NBA, second order in the oxyacid and inverse first in hydrogen ions. The oxidation of deuteriated phosphorus oxyacids showed the presence of a substantial primary kinetic isotope effect. The reaction failed to induce polymerization of acrylonitrile. Added acetamide has no effect on the reaction rate. It has been shown that the 'inactive' tautomer of the phosphorus oxyacids, \( R\text{H}P(O)OH \), participates in the oxidation process. A rate-determining step involving transfer of a hydride ion from the P-H bond to the oxidant has been proposed.

The rate of oxidation of amino acids (AA) by \( N \)-Bromoacetamide (NBA) was studied\textsuperscript{101} in aqueous buffered medium at 35\(^\circ\) C. The rate of disappearance of [NBA] is catalyzed by the \( \text{Br}^- \) produced from the reduction of NBA. Analysis of the autocatalyzed reaction gives the kinetic data for the oxidation of bromide ion by NBA. The protonated NBA reacts with \( \text{Br}^- \) to form \( \text{Br}^2^- \) which rapidly oxidizes amino acids. The rate constant for the reaction between protonated NBA and \( \text{Br}^- \) at 35\(^\circ\) C is estimated\textsuperscript{101}.

The kinetics and mechanism of Rh(III) catalysed oxidation of digol by acidic solution of \( N \)-bromoacetamide (NBA) have been studied\textsuperscript{102}. Kinetic data indicate first order kinetics in both NBA and Rh(III) and zero
order dependence on each of digol and $H^+$ ions. Zero effect of ionic strength variation and chloride ion addition was observed while successive addition of acetamide decreased the rate. A suitable mechanism consistent with the observed kinetics has been suggested.

Studies of the kinetics of oxidation of citric acid and tartaric acid by $N$-bromoacetamide (NBA) in the presence of perchloric acid and iridium trichloride have been reported\textsuperscript{103}. The reactions follow identical kinetics, being zero order in substrate and first order in each NBA, Ir(III) and mercuric acetate. A negative effect of hydrogen ions, acetamide and $Cl^-$ is observed, while ionic strength has no effect on reaction velocity. Various activation parameters were calculated and recorded. A suitable mechanism consistent with the above observations is proposed.

Rates of oxidation of DMSO by $N$-bromoacetamide (NBA) in neutral aqueous solution have been measured\textsuperscript{104} in the presence of acetamide (AA). The order in [DMSO] is one at $[\text{DMSO}] < 0.01 \text{ mol dm}^{-3}$, fractional when $[\text{DMSO}]$ is between 0.01 and 0.5 mol dm$^{-3}$ and zero when $[\text{DMSO}] > 0.5 \text{ mol dm}^{-3}$. Different rate laws are operative under these three conditions though $\text{HOBr}$ is the effective oxidising species in all the cases. The influence of the variation of solvent composition on the reaction rate has been studied by employing methanol-water binaries of various compositions. Thermodynamic parameters for the hydrolysis of NBA and adduct formation between HOBr and DMSO have been evaluated. The activation parameter for the first order decomposition of
the adduct have also been calculated for various solvent compositions ranging from 0 to 80% MeOH (v/v). The free energies of activation increase upon increasing the methanol content of the medium, whereas the enthalpies and entropies of activation show a more complex, but partially compensating behaviour.

The rates of bromination of anisoles (Ale) with HOBr produced in situ by the hydrolysis of $N$-bromoacetamide (NBA) have been measured\(^\text{105}\) in 50% aqueous acetonitrile in the presence of mercuric acetate and acetamide (AA). The formation of an intermediate cyclic adduct between HOBr and anisole which decomposes in a slow step to yield the products, has been proposed to explain the observed results. The thermodynamic parameters for the hydrolysis of NBA and adduct formation steps have been evaluated. The activation parameters for the first order decomposition of the adduct have also been calculated. The corresponding ortho-bromoanisoles have been identified as major components in the products.

The kinetics of iridium(III)-catalysed oxidation of 1,2-ethanediol and 1,4-butanediol by $N$-bromoacetamide (NBA) in $\text{HClO}_4$ in the presence of $[\text{Hg(OAC)}_2]$ as a scavenger for $\text{Br}^-$ have been investigated\(^\text{106}\). The reactions are zero-order with respect to both diols, and first-order in NBA at low NBA concentrations, tending to zero order at high concentrations. The order in Ir(III) decreases from unity to zero at high iridium(III) concentrations. A positive effect on the oxidation rate is
observed for [H\(^+\)] and [Hg(II)] whereas a negative effect is observed for acetamide and [Cl\(^-\)]. Ionic strength does not influence the oxidation rate. (H\(_2\)OBr\(^+\)) is postulated as the oxidizing species. A mechanism consistent with the observed kinetic data is proposed.

Kinetics of oxidation of reducing sugars D-galactose (Gal) and D-ribose (Rib) by N-bromoacetamide (NBA) in the presence of ruthenium(III) chloride as a homogeneous catalyst and in perchloric acid medium, using mercuric acetate as a scavenger for Br\(^-\) ions, as well as a co-catalyst, have been investigated\(^{107}\). The kinetic results indicate that the first-order kinetics in NBA at lower concentrations tend towards zero order at its higher concentrations. The reactions follow identical kinetics, being first order in the [sugar] and [Ru(III)]. Inverse fractional order in [H\(^+\)] and [acetamide] were observed. A positive effect of [Hg(OAc)\(_2\)] and [Cl\(^-\)] was found, whereas a change in ionic strength (\(\mu\)) has no effect on oxidation velocity. Formic acid and D-lyxonic acid (for Gal) and formic acid and L-erythronic acid (for Rib) were identified as main oxidation products of reactions. The various activation parameters have been computed and recorded. A suitable mechanism consistent with experimental findings has been proposed.

The kinetics of the homogeneously Pd(II) catalyzed oxidation of D-mannose (Man) and maltose (Mal) by N-bromoacetamide (NBA) in perchloric acid medium, using mercuric acetate as scavenger for Br\(^-\) ions as well as co-catalyst, have been studied\(^{108}\) in the temperature range 35-
50° C. The reactions exhibit first-order kinetics at low concentrations of sugars (Man and Mal) and NBA, tending to zero-order at high sugar and NBA concentrations. The oxidation rate is directly proportional to [Pd(II)], while inverse fractional order in each of [H+] , [Cl−] and [acetamide] was found. A positive effect on the rate of the reaction was observed on successive addition of [Hg(OAc)2], whereas change in ionic strength (μ) of the medium has no effect on the reaction velocity. Formic acid and arabinonic acid (for both reducing sugars, i.e. Man and Mal) were identified as main oxidation products of reactions. The various activation parameters have also been evaluated. A plausible mechanism from the results of kinetic studies, reaction stoichiometry and product analysis is proposed.

The kinetics of Ir(III)-catalysed and Hg(II)-co-catalysed oxidation of D-glucose (Glu) and D-fructose (Fru) by N-bromoacetamide (NBA) were studied in acidic medium. The reactions follow identical kinetics, being zero order in each sugar concentration. The experimental results show a first-order dependence on NBA and Ir(III) at low concentrations, but tending towards zeroth order at higher concentrations. A negative effect of variation of [H+], [Cl−] and [NBA] was observed whereas the ionic strength (I) of the medium has no influence on oxidation rate. The important feature of the reaction is that it follows a second-order dependence on mercury(II) ion concentration at low concentrations, but it tends towards first order at higher concentrations. Various activation
parameters were calculated and recorded. The corresponding acids were identified as the main oxidation products of the reaction. On the basis of the experimental findings, a suitable mechanism consistent with the observed kinetics was proposed. A comparative study was also made between the kinetic results of the present investigation and those of Ru(III)- and Pd(II)-catalysed oxidations of reducing sugars.

The kinetics and mechanism of the homogeneously Pd(II) catalysed oxidation of D-arabinose (Arb) and D-ribose (Rib) by \( N \)-bromoacetamide (NBA) in perchloric acid medium. using mercuric acetate as scavenger for \( Br^- \) ions as well as co-catalyst have been investigated\(^\text{110a}\) in the temperature range 308-323 K. The kinetic results exhibit first order kinetics at low [NBA] and [sugars] (Arb and Rib), tend towards zero-order at high [NBA] and [sugars]. The oxidation rate is directly proportional to [Pd(II)], while inverse fractional order in each of [H\(^+\)], [Cl] and [acetamide] is observed. A positive effect on the rate of the reaction has been found on the successive addition of [Hg(OAc)\(_2\)], whereas change in the ionic strength (\( \mu \)) of the medium does not influence the reaction rate. Formic acid and D-erythronic acid for the oxidation of both Arb and Rib have been identified as main oxidation products of the reactions. The various activation parameters have also been evaluated. A plausible mechanism involving reaction stoichiometry, product analysis has also been proposed.
The kinetic oxidation of trimethylene glycol (TMG) with Os(VIII) in alkaline \(N\)-bromoacetamide (NBA) in the presence of mercuric acetate as \(\text{Br}^-\) ions scavenger has been studied\(^{110b}\). The reaction is first order in NBA, Os(VIII) and OH\(^-\) while zero order dependence of the reaction on trimethylene glycol was observed. The rate of reaction was independent on addition of acetamide and sodium perchlorate. A solvent isotope effect \((K_{D}(D_2O)/K_{H}(H_2O)) = 2.3-2.7\) and \(2.4-2.8\) for trimethylene glycol) has been observed at \(35^\circ C\). Various thermodynamic parameters have been computed and the corresponding trimethylene glycol was found to be product. A mechanism consistent with the kinetic data has been proposed.

The kinetics of Os(VIII) catalysed oxidation of methyl glycol (MG) by alkaline solution of \(N\)-bromoacetamide (NBA) in the presence of mercuric acetate as \(\text{Br}^-\) ions scavenger has been studied\(^{110c}\). The results show first order kinetics with respect to each of NBA, Os(VIII) and OH\(^-\) while zero order dependence of the reaction on methyl glycol was observed. Negligible effect of addition of acetamide and sodium perchlorate on the reaction rate was observed. On the basis of the experimental findings suitable mechanism consistent with kinetic results has been proposed.

The oxidation\(^{110d}\) of 2-ketoglutaric acid in the presence of \(N\)-bromoacetamide in alkaline medium in temperature range 30-40\(^\circ C\), show first order kinetics with respect to \(N\)-bromoacetamide (NBA) and zero order kinetics with respect to 2-ketoglutaric acid. Hydroxide ions
variations show negative effect while acetamide and sodium perchlorate additions show insignificant effect on oxidation rate. Addition of mercuric acetate (used as Br\(^-\) scavenger) increases the rate which shows that probably Hg(II) acts as catalyst. NBA as such is the reactive species. Products identified are oxalic and malonic acids. Various activation parameters have been calculated and recorded on the basis of the experimental findings, a suitable mechanism has been proposed.

Oxidation of levulinic acid to succinic and formic acids by \(N\)-bromoacetamide (NBA) in perchloric acid media in the presence of mercuric acetate as scavenger and ruthenium(III) chloride as catalyst has been studied\(^{110e}\). Kinetic data have been used to discuss the mechanistic implication of the oxidation.

The kinetics of Ru(III) catalysed oxidation of erythritol (1,2,3,4-tetrahydroxybutane) and dulcitol (1,2,3,4,5,6-hexahydroxyhexane) by \(N\)-bromoacetamide (NBA) in HClO\(_4\) in the presence of Hg(OAc)\(_2\) as a scavenger for Br\(^-\) have been investigated\(^{110f}\). The reactions are zeroth order with respect to both alcohols, and first order at low concentration of NBA tending to zero order at high NBA concentrations. The oxidation rate is directly proportional to [Ru(III)] and a positive effect on the rate is observed for [H\(^+\)] and [Cl\(^-\)] whereas a negative effect is observed for acetamide and ionic strength. D\(_2\)O and Hg(OAc)\(_2\) do not influence the oxidation rate; (H\(_2\)OBr\(^+\)) is postulated as the oxidising species. A suitable mechanism consistent with the observed kinetic data is proposed.
Iridium(III) chloride catalyzed oxidation of maltose and lactose by N-bromoacetamide (NBA) in perchloric acid medium shows first order dependence to NBA and catalyst concentrations both, while the rate is independent of [disaccharides]. Rate is unity with respect to lower \([\text{H}^+]\), reaches up to a maximum and beyond which further addition of acid retards the reaction rate. Acetamide, acetic acid and KCl additions have a negative effect while mercuric acetate addition accelerates the reaction rate. Change in ionic strength of the medium does not affect the reaction rate. Calculation of thermodynamic parameters shows the order of reactivity as lactose>maltose. A suitable mechanism was proposed which explains all the experimental findings.

Kinetic investigations on iridium(III) catalysed oxidation of glycerol by acidic solution of N-bromoacetamide (NBA) in the presence of Hg(OAC)\(_2\) as a scavenger for Br\(^-\) have been studied in the temperature range of 30-45\(^\circ\) C. The reactions exhibit a zero order dependence with respect to polyhydric alcohol and first order at low concentration range of NBA was observed to tend to zero order at its higher concentrations. The influence of Hg(OAc)\(_2\) and ionic strength is insignificant. A negative fractional order in both \([\text{H}^+]\) and \([\text{Cl}^-]\) and a positive fractional order in Ir(III) are observed whereas successive addition of acetamide decreases the rate of oxidation. A suitable mechanism, consistent with the observed kinetic data is proposed and activation parameters are calculated.
The kinetics of ruthenium(III) catalysed oxidation of leucine by \(N\)-bromoacetamide (NBA) in basic medium in the presence of mercuric acetate as a scavenger for any bromide ion formed in the reaction has been reported\(^{113a}\) in the temperature range 30-45\(^\circ\) C. First order kinetics is observed in the case of oxidant NBA, catalyst ruthenium trichloride. The reaction follows first order kinetics in leucine. Increase in \([\text{Cl}^-]\) showed a negative effect, while \([\text{OH}^-]\) showed a positive effect. Successive addition of acetamide exhibited negative effect on the reaction rate. An intermediate complex is formed between the reactive species of NBA and the catalyst ruthenium(III) chloride in the slow and rate-determining step. Insignificant effect of mercuric acetate depicts its role as a scavenger for any bromide ion formed in the reaction and, thus, eliminates the possibility of its involvement either as a catalyst or parallel oxidation by free bromine. Negligible effect of ionic strength has been observed. \(\text{OBr}^-\) and \([\text{RuCl}_3\text{H}_2\text{O}]^{2-}\) have been proposed as the real reactive species of NBA and ruthenium(III) chloride, respectively. Various activation parameters have been computed. A suitable mechanism in agreement with the kinetic observations has been proposed.

Kinetic investigations on Ru(III)-catalyzed oxidation of cyclopentanol and cyclohexanol by acidic solution of \(N\)-bromoacetamide (NBA) in the presence of mercury(II) acetate as a scavenger have been reported\(^{113b}\) in the temperature range of 30-45\(^\circ\) C. Similar kinetics was followed by both the cyclic alcohols. First-order kinetics in the lower
concentration range of NBA was observed to tend to zero order at its higher concentrations. The reaction exhibits a zero-order rate dependence with respect to each cyclic alcohol, while it is first order in Ru-III. Increase in [H+] and [Cl−] showed positive effect, while successive addition of acetamide exhibited negative effect on the reaction rate. Insignificant effect of sodium perchlorate, D2O, and mercury(II) acetate on the reaction velocity was observed. Cationic bromine has been proposed as the real oxidizing species. Various thermodynamic parameters have been computed. A suitable mechanism in agreement with the kinetic observations has been proposed.

The kinetics of Ru(III) catalysed oxidation of glycine and alanine by N-bromoacetamide (NBA) in perchloric acid media in the presence of mercury(II) acetate as a scavenger has been reported in the temperature range of 30 – 45°C. Similar kinetics was followed by both the aminoacids. The reaction rate shows first order kinetics both in oxidant and Ru(III) while order with respect to substrate and [H+] is zero. Increase in [Cl−] showed positive effect while successive addition of acetamide exhibited negative effect on the reaction rate. Insignificant effect of sodium perchlorate, D2O and mercury(II) acetate on the reaction rate was observed. Various thermodynamic parameters have been computed. A suitable mechanism in agreement with the kinetic observations has been proposed.
The kinetics of iridium(III) catalysed oxidation of ethylene glycol and dulcitol by \(N\)-bromoacetamide (NBA) in perchloric acid, in the presence of Hg(OAC)\(_2\) as a scavenger for Br\(^-\) has been studied\(^\text{113d}\) in the temperature range of 30 – 45° C. Similar kinetics was followed by both the polyhydroxy alcohols. The reactions exhibit a zero order dependence with respect to each polyhydroxy alcohol and first order at low concentration range of \([\text{NBA}]\) was observed to tend to zero order at its higher concentrations. The influence of Hg(OAC)\(_2\) and ionic strength is insignificant. A negative fractional order in both \([\text{H}^+]\) and \([\text{Cl}^-]\) and a positive fractional order in Ir(III) are observed whereas successive addition of acetamide decreases the rate of oxidation. A suitable mechanism consistent with the observed kinetic data is proposed and activation parameters calculated.

### 1.3 Glimpses of Oxoacids

#### 1.3.1 General features

In 2-oxoacids (R-CO-COOH), due to the interaction of the pi electron clouds of the carbonyl and carboxyl groups in the 2 and 1 position respectively, each group influences the characteristics of the other group. The studies of the 2-oxoacids are found widely in the literature\(^\text{214-217}\). For instance, 2-oxopropionic acid commonly called pyruvic acid (\(\text{CH}_3\text{-CO-COOH}\)) is involved in the biochemical processes like respiration. Among 3-oxoacids, the well known is the ester of
3-oxobutanoic acid, namely acetoacetic ester which is most useful in the synthesis of various organic compounds.\textsuperscript{218}

In 4-oxoacids, the carbonyl and the carboxyl groups are separated by two carbon atoms and so they possess the characteristics of both compounds without the direct influence of the other group. However, intramolecular catalysis (carboxylic acid group can catalyze the reactions of oxo group) has been reported in the halogenation of 4-oxoacids.\textsuperscript{219} Among the 4-oxoacids, the reaction of levulinic acid (\(\text{CH}_3\text{-CO-CH}_2\text{-CH}_2\text{-COOH}\)) has been studied extensively.\textsuperscript{220,221}

### 1.3.2 Reported methods of preparation of 4-oxoacids

The preparation of 4-oxo-4-phenylbutanoic acid, commonly known as \(\beta\)-benzoylpropionic acid, by the Friedel-Craft’s reaction between benzene and succinic anhydride in the presence of anhydrous aluminium chloride was reported\textsuperscript{222} as early as 1882. Haworth synthesized naphthalene from 4-oxo-4-phenylbutanoic acid.\textsuperscript{223} The Friedel-Craft’s reaction of succinic anhydride with toluene, xylenes, mesitylene and a number of alkylated benzenes were reported to give the corresponding phenyl substituted 4-oxo-4-phenylbutanoic acids.\textsuperscript{224,225} Phenanthrene derivatives\textsuperscript{226,227} were obtained from 4-oxo-4-phenylbutanoic acids which were synthesized by the condensation between succinic anhydride and naphthalene derivatives. Tetralin, \(p\)-cymene, phenanthrene and anthracene
were reacted with succinic anhydride to get the corresponding 4-oxoacids.\textsuperscript{228-230} 4-Oxo-4-(4\textsuperscript{'}-bromophenyl)butanoic acid was prepared from bromobenzene and succinic anhydride under drastic conditions.\textsuperscript{231} The structure of the oxoacid was established by heating it with alkaline potassium permanganate and identifying the resulting 4-bromobenzoic acid. 4-Oxo-4-(3\textsuperscript{'}-nitrophenyl)butanoic acid was prepared\textsuperscript{232} by the nitration of 4-oxo-4-phenylbutanoic acid. Aromatic ethers like anisole, phenetole, \textit{p}-methylanisole, \textit{o}-methylanisole, \textit{p}-chloroanisole and veratrole were condensed with succinic anhydride to get the corresponding 4-oxoacids.\textsuperscript{233} Methyl ethers of dihydric phenols were also condensed with succinic anhydride.\textsuperscript{234} The Friedel-Craft\textquotesingle s succinolylolation of 1,2-dichlorobenzene yielded 4-oxo-4-(3\textsuperscript{'},4\textsuperscript{'}-dichlorophenyl)butanoic acid.\textsuperscript{235}

The following mechanism has been proposed for the condensation between succinic anhydride and aromatic compounds in the presence of anhydrous aluminium chloride.\textsuperscript{236} For the complete reaction, one molecule of succinic anhydride (I) requires two molecules of anhydrous aluminium chloride. It is suggested that one molecule of aluminium chloride is used to open the anhydride ring with the formation of the carboxylic acid salt from one half of the anhydride group and the other half is converted into a carbonyl chloride group (II). This reacts in the usual manner with the second
molecule of aluminium chloride to give the complex (III) which then reacts with the nucleophilic component to form the 4-oxoacid (VI) via the intermediates IV and V.

![Chemical structures](image)

1.3.3 Biological importance of oxoacids

Many of the 4-oxoacids and their esters possess fungicidal, antibacterial, microbial\textsuperscript{237} and anti-inflammatory activities.\textsuperscript{238}

For example, 4-oxo-4-phenylbutanoic acid is involved in human
The 4-oxoacids are also used for protecting the hydroxyl functions in nucleosides. The esters and salts of the 4-oxoacids are also utilized widely in the industrial preparation of insect repellents and plastics.

The 4-oxoacids are very useful in the synthesis of several carboxylic acid and heterocyclic compounds. For instance, the bromo oxoacids are used for preparing imidazothiazoles and pyridazinones. They are the starting compounds in the preparation of β-benzoylacrylic esters.

Structure-activity studies of 3-benzoylpropionic acid derivatives establish the fact that these acids possess immunodulative activity and suppress adjuvant arthritis.

3-Benzoylpropionic acid (4-oxoacid) and its derivatives play an important role in the pharmaceutical chemistry. 3-Benzoyl-propionic acid derivatives are used as antirheumatic agents. A study with three types of 3-benzoylpropionic acid derivatives having a mercapto moiety in their structures shows that substitution on the phenyl ring contributes to the antirheumatic activity.
1.4 Oxidation Studies with Oxoacids

Although a lot of work has been reported on the $\beta$-ketoesters, hydroxyl acids, aldehyde and aromatic ketones, a very little work has been reported so far on the oxidation of oxoacids.$^{252-260}$

Kinetics of oxidation of 4-oxoacids by permanganate in buffer media have been reported.$^{253}$ Oxidation of 4-oxo-4-phenylbutanoic acid and its phenyl substituted compounds by permanganate in different buffer media is first order each in [oxoacid] and $[\text{MnO}_4^-]$. The reactions undergo general acid catalysis. Addition of electrolytes has no significant effect on the reaction rate. Electron releasing substituents in aromatic ring enhance the reaction rates, while electron withdrawing substituents retard the rate. The reaction constant $\rho$ is $-1.08$ at 303 K. The oxidation products have been identified and activation parameters are computed. A mechanism consistent with the kinetic results has been proposed.

The oxidation of substituted and unsubstituted 4-oxoacids by alkaline hexacyanoferrate(III) in sodium carbonate-bicarbonate buffer has been studied.$^{254}$ The reaction is zero order in oxidant, first order with respect to Os(VIII), first order at higher concentrations with respect to both substrate and alkali. The reaction products are identified as benzoic acid and malonic acid by comparing the $R_f$ values with that of the
authentic samples. The presence of electron releasing groups in the benzene ring decreases the rate of oxidation and the presence of electron withdrawing groups enhances the rate. The observed rate constants increase with temperature for all the compounds. The reaction constants are positive and decrease with increasing temperature. Based on the kinetic results and observations, an oxidation mechanism is formulated as given in eqs. (5) – (11).

\[ C_6H_5COCH_2CH_2COOH + OH^- \rightarrow C_6H_5COCH_2CH_2COO^- + H_2O \] (5)

\[ C_6H_5\cdot C=CH_2\cdot CH_2\cdot COO^- + OH^- \xrightleftharpoons{k_1} \]

\[ C_6H_5\cdot C=CH\cdot CH_2\cdot COO^- + H_2O \] (6)

\[ C_6H_5\cdot C=CH\cdot CH_2\cdot COO^- \rightarrow I \] (7)

\[ [Os\cdot O_4(OH)(H_2O)]^{1-} + OH^- \xrightarrow{k_2} [Os\cdot O_4(OH)_2]^{2-} \quad \text{H}_2\text{O} \] (8)
Kinetics of oxidation of unsubstituted and substituted 4–oxoacids by acid permanganate in aqueous acetic acid medium have been studied\textsuperscript{255} at high and low $[\text{H}_3\text{O}^+]$. At high $[\text{H}_3\text{O}^+]$, the reaction is first order each in $[\text{H}_3\text{O}^+]$ and the [oxoacid]. Variation in ionic strength of the reaction medium has no significant effect on the rate of the reaction. But the rate of the reaction is enhanced by lowering the dielectric constant of the reaction medium. Electron releasing substituents in the aromatic ring accelerate the reaction rates and electron withdrawing substituents retard them. The value of the $\rho$ at 303 K (at $[\text{H}_3\text{O}^+] = 1 \text{ M}$) obtained from the Hammett’s plot is -1.49. A mechanism involving the attack of permanganic acid on the enol form of the substrate in the rate determining step has been proposed. The protonation of permanganate ion leads to the formation of permanganic acid. The enolization is proposed to be the necessary step prior to the oxidation of the substrate. The above two processes are assumed following the mechanism suggested for acid oxidation.

\[
\begin{align*}
\text{C}_2 + \text{I} & \underset{k_3}{\xrightarrow{\text{Complex}}} \text{C}_3 + \text{OH}^- \\
\text{C}_3 & \xrightarrow[k_4]{\text{slow}} \text{Os(VI)} + \text{Other products} \\
\text{Os(VI)} + 2\text{Fe(CN)}_6^{3-} & \xrightarrow{\text{Fast}} \text{Os(VIII)} + 2\text{Fe(CN)}_6^{4-}
\end{align*}
\]
catalyzed permanganate oxidation of ketones.\textsuperscript{260-263} The mechanism is given in scheme 2 (eqs. 12-17).

\begin{align*}
\text{MnO}_4^- + \text{H}_3\text{O}^+ & \xrightleftharpoons[k_1]{k_1} \text{HMnO}_4 + \text{H}_2\text{O} \\
\text{C}_8\text{H}_6\text{C} = \text{CH}_2\text{C} = \text{CHH}_2\text{C}_\text{OH} + \text{H}_3\text{O}^+ & \xrightarrow[k_2]{k_2} \\
\text{C}_6\text{H}_5\text{C} - \text{CH}_2\text{CH}_2\text{C}_\text{OH} + \text{H}_2\text{O} & \xrightarrow[k_3]{k_3} \\
\text{C}_8\text{H}_5\text{C} = \text{CH} - \text{CH}_2\text{C}_\text{OH} + \text{H}_3\text{O}^+ &
\end{align*}

(F)

\begin{align*}
\text{C}_8\text{H}_5\text{C} = \text{CH} - \text{CH}_2\text{C}_\text{OH} & \xrightarrow{k_4} \text{C}_8\text{H}_5\text{C} = \text{CH}_2\text{C}_\text{OH} \\
\text{C}_8\text{H}_5\text{C} = \text{CH} - \text{CH}_2\text{C}_\text{OH} & \\
\text{C}_8\text{H}_5\text{C} = \text{CH}_2\text{C}_\text{OH} + \text{Mn} = \text{O} \quad \text{(F)}
\end{align*}

(G)
The kinetics of oxidative decarboxylation of β-benzoylpropionic acid by manganese(III) acetate in aqueous acetic acid medium have been studied. The reaction is first order each in [substrate], [oxidant] and [H⁺] ion. The effects of solvent polarity and temperature on the rate of oxidation have been studied. A suitable mechanism consistent with the experimental results has been proposed.

1.5 Structure-Reactivity Relationships

For justifying and generalizing a particular reaction mechanism for similar reactions, almost all the kinetic studies invoke structure-reactivity relationships which depend on the empirical and qualitative rule that like substances react similarly and that similar change in structure produce similar changes in reactivity. The most successful quantitative correlation between structure and reactivity is given by the Hammett equation, a linear free-energy relationship.

\[ \log k = \log k_0 + \rho \sigma \]  
\[ \log K = \log K_0 + \rho \sigma \]

where \( k \) or \( K \) is the rate or equilibrium constant respectively, for a side-chain reaction of meta- or para- substituted benzene derivatives. The \( k_0 \)
or $K_0$ denotes the corresponding quantity for the parent compound. The substituents constant $\sigma$ is independent of the nature of the reaction and gives a measure of the polar effect of replacing H by a given substituents (in the $m$- or $p$- position). The reaction constant $\rho$ depends on the nature of the reaction and its conditions (reagent, catalyst or temperature) and is independent of substituents. For evaluating $\sigma$ for a given substituents the ionization of benzoic acid in water at $25^0$ C is chosen as the standard process for which $\rho$ was arbitrarily defined as 1.00.

Hammett equation is applied to a given reaction by getting a best straight line, by the method of least squares, between log $k$ or log $K$ and $\sigma$ and the slope of that line gives the value of the reaction constant $\rho$. The success of the Hammett equation is commonly assessed in terms of correlation coefficient ($r$) and the standard deviation ($s$).

To account for the failure of Hammett equation in reactions where the conjugation involving substituents and reaction center is substantially more marked than in the ionization of benzoic acids (cross-conjugation) 271, 272 ‘exalted’ $\sigma$ constants ($\sigma^+$ and $\sigma^-$) are introduced. The $\sigma^-$ values are used for $+R$ substituents (e.g. NO$_2$, CN, COOH, COOMe, and SO$_2$Me) and are based on the ionization of anilinium ions or of phenols in water. The $\sigma^+$ values, introduced by Brown and Okamoto 273 based on the solvolysis of $t$-cumyl chloride in 90% acetone-water at $25^0$ C,
are used for –R substituents (e.g. OMe, Me, OH, NH₂, SMe, and Hal ).

The differences ($\sigma^- - \sigma$) and ($\sigma^+ - \sigma$) give a measure of conjugative ability of a given acceptor and donor respectively. Both $\sigma^+$ and $\sigma^-$ values are sometimes used in the same correlation for a reaction in which an electron-deficient / electron-rich reaction centre can directly conjugate with electron-donating / electron-withdrawing substituents.

On the view that the contribution of the resonance effect of a substituents must vary continuously as the electron-demanding quality of the reaction centre is varied, Wepster²⁷⁴,²⁷⁵ introduced a ‘sliding scale’ of $\sigma$ (unexalted) values, called $\sigma^0$. Taft²⁷⁶ also evaluated similar set of unexalted $\sigma$ constants, called $\sigma^0$, on the basis of ionization of phenylacetic and phenylpropionic acids.

To deal with the influence of –R and +R substituents respectively on reactions that are more or less electron-demanding than the ionization of benzoic acid, Yukawa and Tsuno²⁷⁷ and Yasioka²⁷⁸ formulated the following eqs. (20) and (21) known as Yukawa-Tsuno equations.

\[
\log k = \log k^0 + \rho (\sigma + r^+ \Delta\sigma^+_R)
\]  
²⁰

\[
\log K = \log K^0 + \rho (\sigma + r^- \Delta\sigma^-_R)
\]  
²¹

where $\Delta\sigma^+_R = \sigma^- - \sigma$ and $\Delta\sigma^-_R = \sigma^- - \sigma r^+$ gives a measure of the extent to which cross-conjugation of substituents with reaction centers stabilizes the transition state or product relative to the initial state. The $r^+$ in eq. (20)
can have values varying from 0 to unity and values greater than one is also possible for \( r \) in eq. (21).

A quantitative separation of substituents effect into inductive and resonance contributions by Taft\(^{279,280}\) led to the possibility of a ‘dual substituents parameters’ (DSP) treatment of reaction series, where simple correlations based on Hammett equation fail, in the form of eq. (22)

\[
\log \left( \frac{k}{k^0} \right) = \rho_I \sigma_I + \rho_R \sigma_R
\]

(22)

where \( \sigma_I \) and \( \sigma_R \) are the inductive and resonance substituent constants, and \( \rho_I \) and \( \rho_R \) are the corresponding reaction constants.

### 1.6 Scope of the Present Investigation

A thorough literature survey reveals that only few works on the oxidation of 4-oxoacids have been reported so far.\(^{252-259}\) Although the \( N \)-halo amide oxidation of a large variety of organic compounds have been studied, there seems to be no report on a systematic kinetic study of the oxidation of 4-oxoacids by \( N \)-halo amides.

The present investigation employs \( N \)-halo amide as oxidants, perchloric acid as catalyst and 4-oxoacids as substrates. The choice of this system may be rationalized on the following aspects.
Of the many efficient oxidation systems known those involving positive halogen species as an oxidant are among the most numerous and well studied. The 4-oxoacid has much biological significance associated with it and plays an essential role in the pharmaceutical chemistry. Few examples are; the 4-oxoacids and its derivatives act as antirheumatic agents for human being.\textsuperscript{242} It plays an important role in suppressing adjuvant arthritis.\textsuperscript{243}

Mutations in components of the extraordinarily large \(\alpha\)-ketoacid dehydrogenase multienzyme complexes can lead to serious and often fatal disorders in humans, including maple syrup urine disease.\textsuperscript{246}

In view of these facts, 4-oxoacid is a suitable substrate to be employed in the oxidation studies. This study makes interesting and useful findings in elucidating the mechanism of the 4-oxoacid oxidation process.

A detailed study of the oxidation of 4-oxoacids by \(N\)-halo amides is undertaken with a view to propose the mechanism for the oxidation. The experiments have been focused to explore the following aspects:

\begin{enumerate}
\item To determine the order of the reaction with respect to the reactants namely, the oxoacids and \(N\)-halo amides
\item To determine the catalytic activity of hydrogen ions in the oxidation.
\end{enumerate}
iii) To determine whether the reaction is general acid catalyzed.

iv) To determine the rate of enolization by bromination method.

v) To determine the effect of dielectric constant of the reaction medium on the rate of reaction.

vi) To determine the effect of ionic strength on the reaction rate.

vii) To determine whether the reaction involves the formation of polar (or) free radical intermediates.

viii) To determine the stoichiometry of the reaction and to study the product analysis.

ix) To determine the effect of substituents on the reaction rate and to apply the linear free energy relationship.

x) To determine the reaction constant and isokinetic temperature.

xi) To determine the activation parameters for the oxidation and finally

xii) To propose a suitable mechanism.