INTRODUCTION
ELECTROPHILIC BROMINATION OF AROMATIC SUBSTRATES

Bromination of aromatic substrates has been carried out using a number of brominating agents and in various solvent media.

Molecular bromine as electrophile:

Bradfield et al\(^1\) studied the bromination of aromatic ethers in 50% (v/v) aqueous acetic acid. Kinetics were complicated by the hydrogen bromide produced in the reaction which reacted with bromine establishing the equilibrium,

\[
\text{Br}_2 + \text{Br}^{-} \rightleftharpoons \text{Br}_3^- \quad (K = 50 \text{ at } 18^\circ\text{C})
\]

The observed kinetics followed the rate equation,

\[
\text{rate} = k_2 [\text{Ar}^\cdot \text{H}] [\text{Br}_2^-]
\]

Subsequent kinetic studies of bromination of 2- and 4-chlorophenyl ethers in 75% (v/v) aqueous acetic acid showed mixed second and third order kinetics,

\[
\text{Rate} = k_2 [\text{Ar}^\cdot \text{H}] [\text{Br}_2^-] + k_3 [\text{ArH}] [\text{Br}_2^-]^2
\]

The ratio of second and third order rate was constant.\(^2\)

Robertson et al\(^3\) made an extensive study on the rates of bromination of alkylbenzenes, acetanilide, aceto-p-toluidide, mesitylene, anisole and p-tolylmethyl ether in acetic acid. At high concentrations of bromine (M/40 to M/100) the reaction was found to be of second order in bromine but at low concentration of bromine (M/1000) the order in bromine changed to unity. Hydrogen bromide produced in the reaction exhibited a catalytic effect as an acid and an anticatalytic effect because of Br\(^-\) ions. For less reactive compounds like m-xylene and naphthalene the reactions exhibited up to fourth order kinetics.
The experimental data were interpreted in terms of the following mechanistic steps.

\[
\begin{align*}
\text{ArH} + \text{Br}_2 & \xrightarrow{\text{fast}} \text{ArHBr}_2 \quad \text{..... (I)} \\
\text{ArHBr}_2 & \xrightarrow{k_1} \frac{1}{k_1'} \text{ArHBr} + \text{Br}^- \quad \text{slow ... (II)} \\
\text{ArHBr} & \xrightarrow{k_2} \frac{1}{k_2'} \text{ArBr} + H^+ \quad \text{fast ... (III)}
\end{align*}
\]

Third and higher order reaction is believed to arise from interaction of one or more bromine molecules with the first formed intermediate in step (I) to assist the breakage of \( \text{Br} - \text{Br} \) bond, such as:

\[
\text{ArH} + \text{Br}_2 \xrightarrow{k_1} \text{ArHBr}_2 + \text{Br}^- \quad \text{..... (IV)}
\]

At low concentration of bromine this equilibrium (IV) is less likely.

However, Robertson et al. investigated the effect of catalysts and found the relative catalysed to uncatalysed rates for bromination of \( m \)-xylene in acetic acid with [\( \text{Br}_2 \)] (M/80) and [Catalyst] (M/20) as follows:

\( \text{BCl}_3 (3.1), \text{LiCl} (1.0), \text{H}_2\text{SO}_4 (0.3) \) and \( \text{NaOAc} (0.2) \). Very weak catalysis by \( \text{NaOAc} \), a strong proton acceptor, indicated that equilibrium (III) was not significantly rate determining. The third order kinetics shifted to a second order with increasing concentration of \( \text{HBr} \) due to reduction of free bromine concentration.

Keefer et al. also observed that the kinetics of bromination of mesitylene in acetic acid followed mixed second and third order kinetics. Mason examined the bromination of some polynuclear hydrocarbons such as biphenyl, naphthalene, phenanthrene and benzene. Third order kinetics were obtained except for phenanthrene which gave second order kinetics. This was explained by greater reactivity of phenanthrene as compared to other substrates.
Although the change in kinetic order depended, to a large extent, on the aromatic reactivity, Berliner et al. attempted to find the acid concentration at which kinetic order changes. In 50% acid the bromination of naphthalene followed a second order kinetics and the rate coefficient (at constant ionic strength) showed a dependence on $[\text{Br}]$ in accordance with the equation,

$$k_{\text{obs}} = k_2 K / (K + \text{Br})$$

where $K$ is the dissociation constant for $\text{Br}_2$. The plot $k_{\text{obs}}$ against $K/ (K + \text{Br})$ was found to have an intercept showing the possibility of bromination by $\text{Br}_2$. However this was not found to be meaningful in subsequent work.

Bromination of phenol and anisole in acetic acid has also been reported. While phenol gave a clean second order kinetics with $E_a = 4.8$ K. cal/mole, anisole gave a kinetic order which approximately decreased from third to second order with decreasing concentration of the reactants and increasing temperature. However in 75% aqueous acetic acid the reaction with anisole was second order, the rate being $\sim 1200$ times as fast as in glacial acetic acid.

Bromination of heterocyclic compounds like thiophene also exhibited mixed second and third order kinetics. However in trifluoro acetic acid as solvent the bromination of toluene followed a second order kinetics. The absence of higher order in bromine points to the fact that trifluoro acetic acid with its known facility for hydrogen bonding is very effective in breaking the Br - Br bond, the rate determining step.

In presence of dioxan (the electrophile being dioxandibromide) using benzene as solvent the kinetics of bromination of anisole, phenetole and isopropxy benzene followed the rate law.
Rate = \( k_3 [\text{ArH}] \) \( \text{dioxan dibromide} \)^2

The kinetics order is reduced by adding \( \text{HBr} \).

The effect of catalysts like \( \text{I}_2 \), \( \text{AlCl}_3 \), \( \text{SoCl}_2 \), \( \text{PCl}_3 \), \( \text{PCl}_5 \) and \( \text{SnCl}_4 \) in the bromination of phenanthrene in carbon tetrachloride as solvent was investigated. Iodine was found to be the most effective catalyst. Robertson et al. argued that the mechanism did not involve free bromine, except to produce \( \text{IBr} \). However in the iodine catalysed bromination of mesitylene in carbon tetrachloride and chloroform kinetics followed the rate equation,

\[
\text{Rate} = k_4 [\text{ArH}] [\text{Br}_2]^2 \ [\text{IBr}] + k_4 [\text{ArH}] [\text{Br}_2] [\text{IBr}]^2.
\]

Blake and Keefer re-investigated the problem. The rate was found to be proportional to \( [\text{ArH}] [\text{Br}_2] [\text{IBr}]^2 \). They envisaged a dimer of \( \text{IBr} \) assisting the removal of 3F from \( \text{ArHBr}_2 \). The rate maximum occurred at \( [\text{I}_2]/[\text{Br}_2] = 0.51 \). Subsequent work on iodine catalysed bromination of phenol and anisole gave a rate maximum at \( [\text{I}_2]/[\text{Br}_2] = 0.35 \).

Peroxy acetic acid has also been used as catalyst in bromination of benzene. The kinetic rate law appeared in the form,

\[
\text{Rate} = k_2 [\text{CH}_3\text{CO}_3\text{H}] [\text{Br}_2]
\]

Bromine acetate has been proposed to be the species.

Somaskendan et al. studied the bromination of \( p \)-bromophenol in presence of pyridine using carbon tetrachloride as solvent. The rate of disappearance of bromine was found to increase to reach a limiting value as the concentration of pyridine (Py) was increased. The following mechanism was proposed.
When \([Br_2]_T\) and \(K\) is large, the rate equation takes the form,

\[
v = \frac{k K [ArH] [Py]_T [Br_2]_T}{1 + k [Br_2]_T}
\]

At low concentration of bromine this becomes,

\[
v = k K [ArH] [Py]_T [Br_2]_T
\]

Kuriacose et al. further reported that the bromination of \(p\)-Nitrophenol in acetic acid could be accounted for by the following rate law,

\[
\text{Rate} = k [ArH][Br_2] + k' [ArH][Br_2]^2 + k'' [ArH]^2 [Br_2].
\]

A bromine molecule, a substrate molecule or a solvent molecule has been thought to act as an electrophile in the rate determining step. In subsequent communication the authors have also discussed the influence of \(HBr\).

**Hypobromous acid as electrophile**

Hypobromous acid is approximately 2000 times less reactive than molecular bromine. The bromination of sodium \(p\)-anisate in dilute solutions of phosphate buffers \((pH 7-8)\) by hypobromous acid has been investigated. At pH 7.6 decomposition of \(HOBBr\) is appreciable giving \(Br_2\) so that the rate increase with time but the second order rate coefficients could be calculated in the presence of suspended silverphosphate (which generates hypobromous acid from \(Br_2\) and water). The rate equation appears as

\[
\text{rate} = k_2 [HOBr] [Ar COO].
\]
which is equivalent to,
\[
\text{rate} = k_2 \text{HOBr} [\text{HOBr}] [\text{Ar COO}^-] + k_2 \text{Br}_2 [\text{Br}_2][\text{Ar COO}^-].
\]

The velocity of bromination was found to increase along with the concentration of phosphate buffer but no change occurred when the acid component of the buffer was varied. Bromine phosphate generated by the equilibrium,
\[
\text{HOBr} + \text{H}_2\text{PO}_4^- \rightleftharpoons \text{Br}^- \text{HPO}_4^- + \text{H}_2\text{O}
\]
is thought to be the electrophile.

However, bromine sulphate \(\text{Br}_2\text{SO}_4\) has also been proposed as a possible brominating agent since catalysis by sulphuric acid in the bromination of benzoic acid by \(\text{HOBr}\) is much greater than by perchloric acid of the same strength.

**Bromine acetate as electrophile:**

In the bromination of 4-nitro anisole by \(\text{HOBr}\) in acetic acid, the rate coefficients were not consistent with \(\text{HOBr}\) or \(\text{Br}_2\) as the electrophile but bromine acetate has been proposed to be the species. \(\text{BrOAc}\) has also been proposed as an intermediate species in the bromination of anisole, phenetole, and methyl p-tolyl ether by 2, 4, 6 tribromo N-bromoacetanilide. \(\text{BrOAc}\) is formed via equilibrium,
\[
\text{Ar N Br AC} + \text{HOAc} \rightleftharpoons \text{Ar N HAC} + \text{Br O AC}.
\]
The bromination of biphenyl by \(\text{HOBr}\) in 75% \(\text{HOAc}\) has also been found to obey the rate equation,
\[
\text{Rate} = k_2 [\text{ArH}] [\text{BrOAc}]
\]

**Iodinemono bromide as electrophile:**

Prasad Rao et al found that in the bromination of phenol, substituted phenols and anisoles by \(\text{I}_3\text{Br}\) in presence of \(\text{Hg(OAc)}_2\) the reactions are first order in the \([\text{substrate}]\) and \([\text{Hg(OAc)}_2]\).
fractional order in $[H^+]$ but zero order in $[I_{3r}]$. A mechanism involving initial mercuration has been suggested.

**Bromination by N-bromo compounds:**

Radhakrishnamurty et al. reported bromination of aromatic amines by N-bromosuccinimide (NBS). The reactions followed a second order kinetics. However in the bromination of anisole and p-methyl anisole the kinetic orders have been found to depend on the solvent composition. In pure acetic acid the reactions are zero order in [NBS] while in 75% aqueous acetic acid it is first order in [NBS]. For the bromination of phenol and substituted phenols in acetic acid - NaOAc and aqueous acetic Acid- NaOAc the order in NBS is unity. The composite rate law,

$$\frac{d [ArBr]}{dt} = k' [NBS] [NaOAc] + k'' [NBS] [ArH] + k''' [NBS] [NaOAc] [ArH].$$

...has been proposed to explain the mechanism.

Radhakrishnamurti et al. have studied the bromination of substituted anilides by N-bromo acetamide (NBA). A first order in [NBA], fractional order in [substrate] and first order dependence on $[H^+]$ have been encountered. A mechanism involving a N-bromo intermediate followed by Orton rearrangement has been postulated.

From the above survey it is clear that the bromination of aromatic substrates like toluene and its derivatives, phenols and aromatic aldehydes by N-bromo acetamide has not been studied.

**Oxidation of Amino Acids**

Oxidation of $\alpha$-amino acids by a variety of reagents has received considerable attention.

The Ag(I) catalysed peroxydisulphate oxidation of glycine, L-alanine and L-valine followed a first order kinetics in peroxydi-
sulphate whose dependence on Ag(I) could be expressed as,
\[ k_{\text{obs}} = k_1' + k_2' [Ag^+] \]
where \( k_1' \) and \( k_2' \) are the rate constant for the uncatalysed and Ag(I) catalysed path. Cations like NH\(_4^+\), Na\(^+\) and K\(^+\) inhibited the reaction. A radical chain mechanism has been proposed.

According to Wiberg\(^{35}\) the oxidation of amino acids by Mn (III) acetate followed second order kinetics in [Mn(III)] and was inhibited by added Mn(II). Beg and Kamaluddin\(^{36}\) investigated the oxidation of glycine and DL-\(\alpha\)-alanine by Mn (III) sulphate in H\(_2\)SO\(_4\) in presence of Mn(II) sulphate. A first order dependence on amino acid, second order in [Mn(III)] and inverse effect of [H\(^+\)] as well as [Mn(II)] where encountered. In a separate spectrophotometric investigation\(^{37}\) of Mn(III) sulphate oxidation of DL-\(\alpha\)-amino butyric acid, DL-isovaline, DL-n-valine and L-Leucine they found that at low initial Mn(II) concentration the rate law took the form,
\[ -\frac{d[Mn(III)]}{dt} = k' \frac{[Mn(III)] [Amino acid]}{[H^+]} \]
but at high initial Mn(II) concentration the rate law appeared as,
\[ -\frac{d[Mn(III)]}{dt} = k'' \frac{[Mn(III)] [Amino acid]}{[H^+] [Mn(II)]} \]

Varadrajan and Joseph\(^{38}\) studied the oxidation of Glycine with Mn(III)\(_aq\) in perchloric acid medium. The reaction was of first order in [Mn(III)] and first order in [amino acid]. The rate was proportional to [H\(^+\)] at low temperature where as at higher temperature the acidity effect changed.

An oxidative decarboxylation followed by deamination has been suggested\(^{39}\) in the oxidation of amino acids by MnO\(_4^-\). However in the \(\Gamma^-\) catalysed oxidation of glycine in acid medium Bharadwaj and Nigam\(^{40}\) derived the rate law,
\[
\frac{d[MnO_4^-]}{dt} = \frac{K_2[H^+][MnO_4^-]}{1 + K_2[H^+]} \left( K_1 [G] + K_2 [G] + K_3 [Br\bar{E}] \right)
\]

The values of \( K_1 \), \( K_2 \) and at 45°C were determined. The \( \bar{E} \) catalysis was suggested to operate in two steps i.e. ion pair formation by \( \bar{E} \) and glycine and \( \bar{E} / Br_2 \) cycle.

Navaneeth Rao et al\(^{41}\) found that Ag(I) catalysed Co(III) oxidation of \( \alpha \)-alanine, \( \beta \)-alanine, aspartic acid, glutamic acid and threonine in sulphuric acid was first order in [Co(III)] fractional in [amino acid] and [Ag(I)]. The following mechanism was proposed.

\[
\begin{align*}
\text{CH}_2(\text{NH}_2).\text{COOH} + \text{Ag}^+ &\xrightarrow{\text{fast}} \text{Adduct}^+ \\
\text{Adduct}^+ + \text{CO(OH)}^+ &\xrightarrow{\text{slow}} \text{Adduct}^{+2} + \text{Co(OH)}^+ \\
\text{CH}_2(\text{NH}_2).\text{COO}^- &\xrightarrow{\text{fast}} \text{CH}_2(\text{NH}_2).\text{COO}^- + \text{Ag}^+ + \text{H}^+ \\
\text{CH}_2(\text{NH}_2).\text{COO}^- &\xrightarrow{\text{slow}} \text{HCHO} + \text{NH}_3 + \text{H}^+ + \text{Co(OH)}^+ \\
\text{CH}_2(\text{NH}_2).\text{COO}^- &\xrightarrow{\text{fast}} \text{CH}_2(\text{NH}_2).\text{COO}^- \\
\text{CH}_2(\text{NH}_2).\text{COO}^- &\xrightarrow{\text{slow}} \text{HCHO} + \text{NH}_3 + \text{H}^+ + \text{Co(OH)}^+
\end{align*}
\]

Upadhyaya and Agarwal investigated Os(VIII) catalysed ferricyanide oxidation of some amino acids. \( \alpha \)-Keto acids were reported to be the products. A spectrophotometric evidence for ferrocyanide \( \sim \) amino acid complex was presented.

Oxidation of amino acids by chloramine - T (CAT) has also been studied. Mushrara et al\(^{43}\) found that in alkaline medium the oxidation of leucine was of first order in [CAT], first order in [amino acid] and inverse first order in [OH]. The oxidation of proline has also been reported. Nitriles were identified as products.

Mahadevappa et al\(^{44}\) reported some interesting results on CAT oxidation of alanine and phenylalanine. At low acid concentration (using HCl) the reaction was of first order in
[CAT] and [H^+] but independent of amino acid; but at high [H^+] concentration the reaction showed first order kinetics in [Amino acid] and [CAT] but independent of [H^+]. However the effective oxidising species was not established over a continuous range of pH; as the species generated from chloramine- T are pH dependent.

Srivastave et al. investigated Ag(I) catalyzed oxidation of glycine by Ce(IV) in nitric acid solution. The reaction was first order in [Ce(IV)] and first order in [amino acid]. The rate linearly increased with increase in [Ag^+]. Increasing concentration of acid increased the rate.

Ramalingam et al. studied the kinetics of oxidation of glycine by bromate in aqueous acetic acid sulphuric acid mixtures. A first order dependence each on [substrate], [oxidant] and [H^+] was reported. Increasing proportions of acetic acid accelerated the rate.

Oxidation of some α-amino acids by N-bromosaccharin in aqueous acetic acid medium in presence of Hg(OAc)_2 has been studied. A first order dependence on [oxidant], fractional order in [substrate] and inverse dependence on [H^+] was reported. The following mechanism was postulated.

\[
\begin{align*}
\text{H}_2\text{N} - \text{CH} - \text{COOH} + \text{H}^+ & \rightarrow \text{H}_3\text{N}^+ - \text{CH} - \text{COOH} \\
\text{H}_2\text{N} - \text{CH} - \text{COOH} + \text{C}_6\text{H}_5\text{CO} - \text{SO}_2\text{NHBr} & \rightarrow \text{H}_2\text{N} - \text{CH} - \text{COOBr} + \text{C}_6\text{H}_5\text{CO} - \text{SO}_2\text{NH}_2 \\
\text{H}_2\text{N} - \text{CH} - \text{COOBr} & \rightarrow_{\text{slow}} \text{H}_2\text{N} - \text{CH}^+ + \text{CO}_2 + \text{Br}^- \\
\text{H}_2\text{N} - \text{CH}^+ - \text{R} & \rightarrow \text{R} - \text{CH} = \text{NH} + \text{H}^+ \\
\text{R} - \text{CH} = \text{NH} + \text{H}_2\text{O} & \rightarrow \text{R} - \text{CHO} + \text{NH}_3
\end{align*}
\]
Navaneeth Rao et al. studied the oxidative deamination and decarboxylation of some amino acids by diperiodate cuprate(III) in alkaline medium. An aldehyde product was reported.

Banerjee et al. found that the oxidation of nine α-amino acids by N-bromobenzamide to corresponding aldehyde products followed a second order kinetics with inverse dependence on $[H^+]$. Absence of primary kinetic isotope effect was established. Added benzamide did not effect the rate. A rate determining interaction of the oxidant with Zwitter ion of the amino acid to form an acyl hypobromite derivative was envisaged. Banerjee et al. also reported the oxidation of DL-methionine by N-bromosacetamide to the corresponding sulphone.

Anand Rao reported the peroxydiphosphate oxidation of some amino acids with Ru(III) as catalyst. The formation of 1:1 complex between Ru(III) and amino acid which later interacted with peroxydiphosphate was suggested.

A study of solvent effect and general base catalysis in the N-bromosacetamide oxidation of glycine has been reported. In alkaline medium added carboxylates catalysed the reaction. A zero order in the [substrate] in presence of carboxylates was reported.

Radhakrishnamurty et al. also reported a comparative study of oxidation of amino acids by phenyliodosyl acetate (PIA) and lead tetraacetate (LTA). The effect of substituents and the similarity between LTA and PIA oxidations have been investigated.
The above survey shows that the effect of substituents on the oxidation of di-amino acids by N-bromoacetamide (NBA) has not been investigated although kinetic reports on the NBA oxidation of alcohols and Ketones and dimethyl sulphoxide have been well documented.

**Oxidation of Cinnamic Acids.**

Although oxidation of unsaturated acids by a number of reagents have been reported, there have been only a few attempts on the oxidation of cinnamic acid and its substituted derivatives.

Riber reported the permanganate oxidation of cinnamic acid. Phenyl glyceric acid (m.p. 141°C) was obtained to an extent of 67% yield.

Radhakrishnamurti et al studied the oxidation of substituted cinnamic acids by chromic acid in aqueous acetic acid perchloric acid medium. The reaction followed the rate law,

\[ K_2 = \frac{k \ k_a + k' \ [H^+]}{k_a + [H^+]} \]

Where \( k_a \) is the equilibrium constant for the dissociation equilibrium,

\[ H_2 CrO_4 \xrightarrow{K_a} HCrO_4^- + H^+ \]

and \( k \) and \( k' \) refer to the steps involving \( HCrO_4^- \) and \( H_2 CrO_4 \) respectively. The Hammett plot showed a break with a \( \rho \) value for electron releasing substituents and \( \rho = -0.60 \) for electron withdrawing substituents. The reaction was strongly dependent on the permittivity of the medium.

Lee et al studied the oxidation of a series of substituted methyl cinnamates by \( RuO_4 \). A ruthenium (VI) ester was postulated as the intermediate. The following mechanism was proposed.
Substituent effects \((J^0 = 0.61)\) was consistent with the route being oxidative decomposition of the cyclic ester to carbonyl products. In a subsequent report the rate constants for the sodium per ruthenate oxidation of some substituted cinnamate have been used to compare the activation parameters with that of permanganate oxidation.

There have also been kinetic reports on catalysed oxidations. Radhakrishnamurti et al.\(^6\) reported the \(\text{OsO}_4\) catalysed chromic acid oxidation of cinnamic acid along with other unsaturated acids. A cyclic \(\text{Os(VI)}\) ester was postulated.

The survey shows that the oxidation of substituted cinnamic acids by \(\text{Ce(IV)}\) either in the absence or under the catalytic influence of transitional metal ions such as \(\text{Ru(III)}\) has not been studied.
THE PRESENT WORK

1. Kinetics of bromination of toluene and substituted toluenes by N-bromoacetamide (NBA) in aqueous acetic acid medium in presence of perchloric acid has been carried out to establish the products, kinetic orders, effect of acidity and solvent composition, to study the structural effects, to evaluate the activation parameters and finally to elucidate a plausible mechanism with the proposed brominating species.

2. As a continuing study the kinetics of bromination of phenol and some substituted phenols has also been undertaken to throw light on the mechanism.

3. Kinetics of oxidation of some \( \alpha \)-amino acids by N-bromoacetamide has been investigated to establish the kinetic orders, effect of acidity, effect of structure on reactivity, to evaluate the activation parameters and finally to propose a plausible mechanism.

4. Kinetics of Ru(III) catalysed oxidation of substituted cinnamic acids by Ce(IV) in aqueous acetic acid sulphuric acid medium has been attempted to delineate the probable catalytically active species of Ru(III), to find the effect of structure on reactivity and to propose a suitable mechanism of oxidation.

5. As a continuing study the Ru(III) catalysed oxidation of substituted cinnamic acids by Lead tetra acetate (LTA) has also been attempted to compare the kinetic results of LTA oxidation with Ce(IV) oxidation of these substrates.