II. SCOPE OF THE PRESENT INVESTIGATION

The study of interaction of metal ions with biological systems is of much significance. The use of metal ions and their complexes in non-enzymatic hydrolysis of DNA is documented. Metal ions and their complexes assisted oxidative degradation of the nucleobases assumes importance from their utility in designing a non-evasive dosimetry for the oxidative stress to these biomolecules. In connection with the damage and repair of nucleic acids, the oxidation of nucleic acids and related compounds has received considerable attention. A model study involving a photolytic investigation of the reaction of $\cdot OH$ and $SO_4^-$ with certain pyrimidine bases has been carried out.

It is clear from the preceding chapter that the metal ion oxidant, Ce(IV) is capable of oxidizing a host of organic and inorganic compounds. It is a well known one-electron oxidant. It is soluble in water. Its redox chemistry is less complicated as on reduction it produces Ce(III) which is quite stable and does not spectrally overlap with that of Ce(IV) enabling the disappearance of Ce(IV) to be spectrophotometrically monitored for kinetic measurements (345 nm).
To probe the oxidative damage to the nucleic acid constituents, many pulse radiolytic studies involving $\cdot$OH$^{62}$ and $\cdot$SO$_4$ have been carried out. Recently, laser flash photolytic studies focussing on this aspect relating to the direct effect of ionizing radiation have been reported$^{64}$. However, dark(thermal) reaction studies involving metal ion oxidants are not many in number. Permanganate ion promoted oxidation of nucleobases and certain peroxo compounds (eg: $S_2O_8^{2-}$ and $HSO_5^-$) assisted oxidation of the nucleobases are known$^{41,42}$. It may be worthwhile to mention here the effective part played by Ce(IV) in sequence-selective DNA scission.

DNA hydrolysis by Ce(IV) was found to effectively proceed both in the presence and in the absence of molecular oxygen$^{65-67}$. Synthetic nucleases which rapidly cleave nucleic acids under mild conditions possess many potential applications ranging from the synthesis of custom-designed artificial restriction enzymes to the development of new antitumour agents$^{68}$. Catalysts that cleave DNA oxidatively by generating $\cdot$OH have been used in many innovative studies$^{69-70}$; however, they modify the deoxyribose moiety, forming fragments which can’t be religated$^{71}$. Furthermore, the diffusable hydroxyl radicals can produce multiple cleavage sites. Hydrolytic cleavage suffers from neither of these drawbacks. In this direction, studies aiming at the development of catalysts capable of hydrolytic cleavage of the phosphate diesters are known$^{72}$. In these
cases, Ce(IV) formed from the oxidation of Ce(III) by molecular oxygen was noticed to be an efficient one\textsuperscript{73}. In fact, a facile oxidative cleavage of the phosphate diester bond was achieved with Ce(III) $\text{O}_2$\textsuperscript{72}. A potential use of Ce(IV) for artificial regulation of cell functions has been envisaged\textsuperscript{30}. The use of Ce(IV) in combination with $\gamma$-cyclodextrin complex as an active site of artificial peptidases is reported\textsuperscript{74}. Finally, the construction of complex carbocyclic compounds and its superiority over Mn$^{3+}$ in improving the yield of synthesis are worth mentioning\textsuperscript{75}.

II.1. Objectives:

This work involves an investigation on the kinetic and mechanistic aspects of the reaction (oxidation) of certain nucleobases with Cerium(IV) as an oxidant in aqueous H$_2$SO$_4$ and HClO$_4$ media. Through this present study, it is proposed to investigate the dependence of reaction rate on the concentrations of Ce$^{4+}$ and pyrimidine bases and thus the order of the reaction with respect to these reactants; effect of [H$_2$SO$_4$], [HSO$_4^-$] and [H$^+$] on the reaction rate under appropriate conditions; to study the influence of the nature of the substituent in the pyrimidine ring on the rate of the reaction, effect of $\mu$ and temperature on reaction rate; to evaluate the activation parameters; to find out whether the reaction proceeds through ionic or free radical pathway; to propose a mechanism based on the kinetic and product analysis data.
II.2. Scope :

It is hoped that the results of this study will enable to disseminate the mode of oxidative cleavage (damage) to the biomolecules by the one-electron metal ion oxidant, Ce(IV). A literature search indicated the lack of any report on the reaction of the pyrimidine bases with Ce(IV) which served as the motive for taking up this study. In connection with the modulation of the activities of enzymes in cell functions, the hydrolysis of certain purine nucleotides by Ce(IV) has recently been probed. In understanding the behaviour of the pyrimidine nucleotides (the complementary analogues of the nucleic acids), the work described herein focussing on the reactivity of Ce(IV) towards the pyrimidine bases, the building units of the nucleotides, may serve as an useful model.