IV. RESULTS AND DISCUSSION

It is known that Ce(IV) ammonium sulfate is an one-electron oxidant capable of oxidizing compounds both in H$_2$SO$_4$ and HClO$_4$ media. Of course, the reactivity of Ce(IV) differs in both these media. It can manifest its oxidative ability either in terms of direct e$^-$ transfer as with metal ions or through H abstraction with organic compounds and its reaction with double bonds have to some extent been studied. It is this last aspect that is found to be operational in this present study.

Pyrimidine base with a C$_5$ - C$_6$ double bond exhibits nucleophilicity. The attack of electrophiles towards this reaction center is well documented. Its reactivity bears many important biological significances.

IV.1. Structure and Distribution of Electron density in pyrimidines:

A large amount of experimental evidence shows that the pyrimidines have the diketo (dilactam) structure. This form was found in the X-ray crystallographic studies of these molecules. This structure was also found in uridines and deoxyuridines. Analysis of the IR spectra of these compounds also confirmed the predominance of the diketo structure in the solid state as
well as in solution\(^{33-36}\). Raman spectroscopy studies confirmed the conclusions of IR spectroscopy by showing that uracil and its derivatives possess the dilactam form and the possibility that the lactim forms could predominate in solution was ruled out\(^{87}\). The luminescence properties of uracil and its derivatives also confirmed the diketo structure\(^{88,89}\). It is generally accepted that substitution at C\(_5\) and / or C\(_6\) of the pyrimidine ring does not change significantly the tautomeric equilibrium of the uracils. Thus the 5- and 6-halouracils or thymines or the corresponding nucleosides still exist in aqueous solution as well as in the crystalline state in the diketo form\(^{90}\).

Veillard showed that the proton spin-spin coupling constants \(J_{H_5-H_6}\) pyrimidines were proportional to the \(\pi\)-bond order of the C\(_5\)-C\(_6\) bonds in these molecules\(^{91}\). The high-field shifts observed for H\(_3\) were found to correlate with the high charge densities at this position for all the pyrimidine bases.

The 2-, 4-, and 6-positions of the pyrimidine ring have a marked electron deficiency\(^{80}\). Such active positions were found to be readily attacked by nucleophiles\(^{80}\).
The aromatic '5' - position:

The 5-position of the pyrimidine ring most closely resembles a true aromatic position, being made only slightly $\pi$-electron deficient by induction. If an electrophilic attack occurs at all, then the 5-position is the site of attack. It should also be noted that unless an electron-releasing group such as amino, mercapto etc. are present so as to counteract the $\pi$-electron deficiency of the pyrimidine ring at 2,4 and 6-positions, these are not affected by any electron acceptor (oxidant). From an inspection of the delocalisation of the electrons in the pyrimidine ring, it has been proved beyond doubt that the position 5 is very much more favoured for attack by an electron acceptor (oxidant) as this is the only reported carbon site which is not significantly electron deficient.

Observations on kinetic data pertaining to the attack of Ce(IV) on this $C_5-C_6$ double bond together with other experimental evidences are presented and discussed below:

IV.2. Oxidation of uracils in sulfuric acid medium:

In sulfuric acid medium, Cerium(IV) may be associated with the $\text{HSO}_4^-$ as evidenced by the considerable decrease in the redox potential. Hardwick
and Robertson considered the following equilibria:

\[ 
\text{Ce}^{4+} + \text{HSO}_4^- \rightleftharpoons [\text{CeSO}_4]^{2+} + \text{H}^+ \\
[\text{CeSO}_4]^{2+} + \text{HSO}_4^- \rightleftharpoons \text{Ce(SO}_4)_2 + \text{H}^+ \\
\text{Ce(SO}_4)_2 + \text{HSO}_4^- \rightleftharpoons [\text{Ce(SO}_4]_3^{2+} + \text{H}^+ 
\]

The equilibrium constants for the above reactions were found to be 3500, 200 and 20 respectively.

**Order and Rate law:**

IV.2.(i) **Order with respect to [Ce(IV)]:**

All the experiments were carried out under pseudo first order conditions, [Pyrimidine base] > [Ce(IV)].

It was observed that the plots of log Abs. Vs time were linear for all the pyrimidines studied (Fig.1,2,3,4,7) and the slope of such plots independent of the initial concentrations of Ce(IV). Accordingly, the values of pseudo first-order rate constants (k', s') evaluated from the slope of these plots were found to be independent of the initial concentration of Ce(IV).
Hence, the first order dependence of reaction rate on [Ce(IV)] is established. Beer-Lambert’s law was obeyed in the range of Ce(IV) concentration employed.

IV.2.(ii) Order with respect to [Pyrimidine base]:

Variation of [Pyrimidine base] at a fixed concentration of Ce(IV) was found to enhance the rate of disappearance of Ce(IV) and the corresponding plots of log Abs Vs time were linear (Fig.5, 6, 7, 8,.) and the pseudo first-order rate constants (k’, s^-1) evaluated from these plots were found to increase with an increase in [Pyrimidine base] (Tab.2, 5, 9, 13, 17, 22, 27, 32, 37, 42, 47, 52, 57, 62, 67, 72, 77, 82, 87, 92, 97, 102, 107, 112, 117, 121, 125). This shows that the reaction exhibits first order with respect to [Pyrimidine base]. Plots of k’(s^-1) Vs [pyrimidine base] gave straight lines passing through origin (Fig.9, 19, 21, 23, 25, 27, 29) confirming the first-order dependence of reaction rate with respect to [Pyrimidine base].

This was found to be the case for all the systems studied. Such a kinetic behaviour with no intercept in the plots of k’ (s^-1) Vs. [Pyrimidine base] indicates either the absence of any complex formation between Ce(IV) and pyrimidines or the complex formed is too unstable to be detected.
Complex formation depends on the ratio of the formation constant to the decomposition constant ($K/k$) of the complex. The absence of any kinetic evidence in this work shows that the ratio $K/k$ is negligibly small\textsuperscript{18,19}. Such observations have also been made in the oxidation of mandelic acid\textsuperscript{19} alkenylbenzenes\textsuperscript{21} and thioethers\textsuperscript{23} by Ce(IV)sulfate with no involvement of any complex formation.

**IV.2.(iii) Effect of $[\text{H}_2\text{SO}_4]$:**

The influence of $[\text{H}_2\text{SO}_4]$ on the rate of the reaction was investigated at various initial concentrations of $\text{H}_2\text{SO}_4$ (0.05 M to 2.0 M) with fixed initial concentrations of Ce(IV) and pyrimidine base. It was observed that the rate of disappearance of Ce(IV) was retarded by an increase in the concentration of $\text{H}_2\text{SO}_4$ (Fig. 10, 11, 12, 13, 14; Tab. 3, 6, 10, 14, 18, 23, 28, 33, 38, 43, 48, 53, 58, 63, 68, 73, 78, 83, 88, 93, 98, 103, 108, 113, 118.). This type of kinetic behaviour was found to be obeyed in all the systems studied. Thus an inverse first order dependence of rate on $[\text{H}_2\text{SO}_4]$ is established. Such a rate retarding effect of $[\text{H}_2\text{SO}_4]$ is explainable in terms of the equilibria involving the complexation of $\text{HSO}_4^-$ (from the dissociation of $\text{H}_2\text{SO}_4$) with Ce(IV), as often reported in literature\textsuperscript{94-97}. Infact, the K values for such equilibria have already been evaluated\textsuperscript{92,94,96,98,99}. Hence, it is clear that the competitive complexing
ability of $\text{HSO}_4^-$ vs the organic substrate molecules (the pyrimidines) with Ce(IV) resulting in the equilibrium as follows accounts for the observed decrease in reaction rate with increase in $[\text{H}_2\text{SO}_4]$:

$$\text{Ce} (\text{SO}_4)_2 + \text{HSO}_4^- \rightarrow \text{H} \text{Ce} (\text{SO}_4)_2^-$$

It is to be noted that the active species of the oxidant, Ce(IV) depends on the range of concentration of $[\text{H}_2\text{SO}_4]$ employed. In the present work, it is fair to assume that $\text{Ce}(\text{SO}_4)_2$ and $\text{H} \text{Ce} (\text{SO}_4)_2^-$ are the predominant active specie of the oxidant, Ce(IV), in terms of the range of the sulfuric acid concentration used (0.05 M to 2.0 M).

A comparison of the present experimental conditions with the earlier ones provides evidences in support of the above mentioned active specie of the oxidant.

IV.2.(iv) Influence of $[\text{HSO}_4^-]$:

The effect of $[\text{HSO}_4^-]$ on the reaction rate in the present study was investigated by carrying out the reactions at constant initial concentrations of Ce(IV) and Pyrimidine but with different initial concentrations of $\text{H}_2\text{SO}_4$ and $\text{HClO}_4$ keeping their total concentration the same. Such experiments allow for examining the role of $[\text{HSO}_4^-]$ on $k'(s^{-1})$ as $[\text{H}^+]$ is maintained constant.
by the employed acid mixture\textsuperscript{18,19,93,101} It was noticed that an increase in $[\text{HSO}_4^-]$ achieved by individually varying the initial concentrations of $\text{H}_2\text{SO}_4$ and $\text{HClO}_4$, maintaining a constant total concentration of this acid mixture led to a decrease in the observed $k'(s)$ (Fig 15, 16, 17, Tab 7, 11, 15, 19, 24, 29, 34, 39, 44, 49, 54, 59, 64, 69, 74, 79, 84, 89, 94, 99, 104, 109, 114, 119) This kinetic behaviour was found to be obeyed by all the pyrimidine systems studied A plot of $k(\text{M}^{-1}\text{s}^{-1})$ Vs $[\text{HSO}_4^-]$ yielded a straight line (Fig 17A) Such rate retarding influence of $[\text{HSO}_4^-]$ is attributed to the competitive complexing ability of $\text{HSO}_4^-$ as against the organic substrate molecule, the pyrimidine towards $\text{Ce(IV)}$\textsuperscript{18,19,93} Hence, the following equilibria can be considered accounting for the rate retardation

$$\begin{align*}
\text{Ce(IV)} + \text{HSO}_4^- & \rightleftharpoons \text{CeSO}_4^{2-} + \text{H} \\
\text{CeSO}_4^{2-} + \text{HSO}_4^- & \rightleftharpoons \text{Ce(SO}_4)_2 + \text{H}^+ \\
\text{Ce(SO}_4)_2 + \text{HSO}_4^- & \rightleftharpoons \text{HCe(SO}_4)_2^- \text{ or Ce(SO}_4)_2^{2-} + \text{H}^+
\end{align*}$$

\textbf{IV.2.(v) Role of $[\text{H}^+]$}

It is to be noted that the actual influence of $[\text{H}^+]$ alone on $k'(s)$ is possible to be studied only when $[\text{HSO}_4^-]$ ($\text{HSO}_4^-$ from the dissociation of $\text{H}_2\text{SO}_4$) is strictly held constant This is experimentally achieved by using a mixture of $\text{H}_2\text{SO}_4$ and $\text{NaHSO}_4$, wherein the individual concentration of both
are varied but maintaining their total concentration the same. This ensures the participation of varying concentrations of H⁺ thus enabling an examination of its role on k'(s⁻¹). Thus, the effect of [H⁺] on k'(s⁻¹) in this work has been studied. Results obtained from these experiments indicate that the k' values increase with increase in [H⁺] (Fig. 17B, Tab. 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115). This was observed to be true for all the systems studied.

It is well established that Cerium (IV) species exists as sulfated complexes in sulfuric acid. It has been reported that in the range of acidity used in the present work (0.2 - 2.0 M) the di- and tri-sulfated complexes, Ce(SO₄)₂ and Ce(SO₄)₃²⁻ are predominant. These species will be in a series of equilibria with H⁺ as follows

\[
\begin{align*}
[\text{Ce(SO₄)}₂]²⁻ + \text{H⁺} & \rightleftharpoons [\text{HCe(SO₄)}₃]⁻ \\
[\text{HCe(SO₄)}₃]⁻ + \text{H⁺} & \rightleftharpoons [\text{H₂Ce(SO₄)}₄] \\
[\text{H₂Ce(SO₄)}₄] + \text{H⁺} & \rightleftharpoons [\text{H₃Ce(SO₄)}₅]⁺
\end{align*}
\]

The increase in acid concentration due to the increase in [H⁺] at constant [HSO₄⁻], as is true in this experiment would thus increase the concentrations of protonated forms of Cerium(IV) species. Since the net positive charge of
Ce(IV) will be increased in this way, the transfer of electron from the organic substrate molecules, the pyrimidines to the oxidant, Ce(IV) would take place more readily. Hence, increase of $[H^+]$ increases the rate of the reaction where the electron transfer from pyrimidines to Ce(IV) occurs. In the oxidation of naphthalenes by Ce(IV), a similar rate enhancing influence of $H^+$ was noticed and was attributed to the charge effect as mentioned above.\textsuperscript{26}

Regarding the nature of the active species of the pyrimidine bases, it is the reportedly more stable keto (lactam) form which predominates over the enol (lactim) form.\textsuperscript{104} 

\[ \text{e.g; Uracil} \]

\[ \text{Lactam} \]

\[ \text{Lactim} \]

Based on the electronic charges of the carbonyl oxygens of the nucleobases, it is clear that out of all oxygens of the carbonyl groups of the nitrogenous bases of the nucleic acids only the oxygen of cytosine (not studied in this work) is known to be the most reactive towards protonation.\textsuperscript{85,105} It may be mentioned that there has been no report in which the protonated form of the pyrimidine bases studied is a major species in reactions.\textsuperscript{106}
IV.2.(vi) Rate Law:

Based on the foregoing kinetic observations, it is reasonable to visualize the following reaction sequences:

\[
\begin{align*}
HCe(SO_4)_3^- + \text{Pyrimidine} & \rightarrow \text{Product} \\
Ce(SO_4)_2^- + \text{Pyrimidine} & \rightarrow \text{Product}
\end{align*}
\]

Hence, the rate equation is written as:

\[
\frac{d[Ce(IV)]}{dt} = k_1 [\text{Pyrimidine}] \left[HCe(SO_4)_3\right] + k_1 [\text{Pyrimidine}] \left[Ce(SO_4)_{2}\right] \\
= [\text{Pyrimidine}] \left(k_1 [HCe(SO_4)_3] + k_2 [Ce(SO_4)_2]\right) \\
= [HCe(SO_4)_3] [\text{Pyrimidine}] \left(k_1 + k_2\right)
\]

Thus, the observed dependencies of rate such as first order each with respect to [Ce(IV)], [pyrimidine base] and inverse first order on \([H_2SO_4]\) are in accordance with the above rate equations. Such kinetic observations were
also noticed in earlier studies\textsuperscript{92,94-96} involving the oxidation of a number of organic compounds by Ce(IV).

IV.2.(vii) Effect of $\mu$:

Studies carried out at fixed concentration of $\text{H}_2\text{SO}_4$, pyrimidine and Ce(IV) but with different initial concentrations of NaClO$_4$ indicated the absence of any variation in the values of the observed rate constant. This was found to be so for all the pyrimidines investigated. This clearly points to the participation of a neutral reactant molecule, the pyrimidine base in the reaction. Hence, the result of this experiment is in accordance with the Bronsted - Bjerrum equation\textsuperscript{107}: $\log k = \log k_o + 1.02 Z_A Z_B \sqrt{\mu}$ where $k = \text{rate constant in presence of a particular concentration of NaClO}_4$; $k_o = \text{rate constant in absence of NaClO}_4$; $Z_A$ and $Z_B$, the charge on the reacting molecules and $\mu = \text{ionic strength of the added salt}$.

IV.2.(viii) Stoichiometry:

The stoichiometry of the reaction, [Ce(IV)]: [Pyrimidine base] was determined by estimating the amount of unreacted oxidant as in the kinetic runs, spectrophotometrically by monitoring the change in absorbance of
Ce(IV) at 345 nm. Such experiments repeated with various initial concentrations of the reactants led to the same result indicating a stoichiometry of [Ce(IV)] : [Pyrimidine base] = 2:1. This proves that one bioorganic molecule provides 2 electrons to two molecules of the oxidant.

IV.2.(ix) Evidence for radical intermediates:-

A search for the involvement of radical intermediates in the reaction between Ce(IV) and pyrimidine bases was carried out. Freshly distilled acrylamide monomer when added to deaerated reaction mixture containing Ce(IV), pyrimidines and H$_2$SO$_4$ was found to result in a polymer hinting the intermediacy of radicals in the reaction. It is well known that Ce(IV) is a one-electron oxidant. Hence it is probable that some radical intermediates are involved in the reaction. Oxidation of organic molecules by Ce(IV) involving radicals has already been reported in literature$^{21,25,26,75}$.

IV.2.(x) Reactivity Trend:

For the sake of an unambiguous interpretation, the reactivity trend observed is broadly classified into two categories, one conforming to uracil, thymine, 6-methyluracil and the other to 5-Bromo-, 5-Chloro-, 5-Fluoro-and 5-Iodouracils.
From Table.173, based on k values the following reactivity trend is observed:

Thymine > 6-Methyluracil ≈ Uracil

Thus it is found that at any temperature, thymine (5-methyluracil) reacts appreciably faster (by approximately 6 and 12 times) than both 6-methyluracil and uracil. The reactivity of 6-methyluracil is slightly (≈ 1.5-2 times) more than that of uracil. Of all the above cited three pyrimidines, uracil was found to react with a much slower rate compared to thymine and 6-methyluracil. Due to the inverse dependence of rate on $[H_2SO_4]$ as mentioned previously, in the case of uracil, measurable rate constants could be obtained only at relatively lower $[H_2SO_4]$. Hence, the rate constant values for thymine and 6-methyluracil were obtained at 0.5M $H_2SO_4$ whereas for uracil it was at 0.05M $H_2SO_4$. This comparative reactivity trend may be inferred from Table.173. No reaction was observed with 5-nitouracil. These foregoing observations indicate that the rate of the reaction is more sensitive to the electron availability at $C_5$ of the $C_5$-$C_6$ double bond of the pyrimidine ring. Thus, thymine with an electron releasing - CH$_3$ group at $C_5$ exhibits the highest reactivity. It may thus be inferred that the $C_5$ - $C_6$ double bond is the most probable site of attack by the oxidant, Ce(IV). This is further supported by the absence of any reaction between 5,6-dihydrouracil and Ce(IV). Regarding the oxidative ability of the
ring nitrogens, it is worthwhile to mention here that the N-oxidation of pyrimidines is rather very unlikely\textsuperscript{108}. It may be mentioned here that such N-oxidation was observed only with powerful oxidants such as certain peracids CH$_3$CO$_3$H and m-chloroperbenzoic acid under drastic conditions (higher temperatures)\textsuperscript{108}. Even then the yield was very poor\textsuperscript{109}. However improved yield was noticed with disubstituted pyrimidines. The presence of two electron donating groups was found to be necessary to achieve better yield of N-oxidation\textsuperscript{108}. Taking into account these points and the rather mild reaction conditions of the present work, it is reasonable to suggest the absence of any N-oxidation of the pyrimidine ring with Ce(IV). It has already been documented that the C$_5$ position is more prone to electrophilic attack. In a previous study involving the oxidation of certain pyrimidine bases by permanganate, the nucleophilicity of the C$_5$-C$_6$ double bond as observed in the present study has been reported\textsuperscript{38}. In a very recent work, the double bond attack by Ce(IV) in the oxidation of naphthalenes has been noticed\textsuperscript{26}.

Among the halopyrimidines studied, the following reactivity trend was noticed (Table.173):

5-Iodouracil > 5-Bromouracil > 5-Chlorouracil > 5-Fluorouracil > Uracil

In fact, it was observed that next to thymine, the 5-halopyrimidines reacted faster than 6-methyluracil, the last in the series being uracil.
A theoretical analysis involving the estimation of electron density at C₅ and C₆ of the pyrimidines has been carried out with a view to see the possibility of a relationship between electron density and rate constant, \( k'(s^{-1}) \) values. All the calculations were done at semiempirical MO level with AM1 hamiltonian using MOPAC 6.0 programme, implemented in Micro Vax II computer. The electron density values are depicted in Table 172. The experimentally observed reactivity of 5-halouracils is in accord with the higher nucleophilicity of C₅ over C₆. This is clearly reflected in Table 172 in which the C₅ electron density of the halouracils studied is found to be higher than the C₆ electron density. A correlation was found to exist between the thus theoretically obtained C₅ electron density values and the \( k'(s^{-1}) \) values of the halouracils investigated (Fig.44). This clearly demonstrates the significance of the C₅ position in controlling the reactivity of the pyrimidine ring via electron transfer to the electrophilic species, the oxidant Ce(IV).

IV.2.(xi) Effect of Temperature:

Kinetic investigations were carried out at different temperatures for each system.
Based on Arrhenius equation\textsuperscript{110} \( \log k = \log A - \frac{E_a}{2.303RT} \), the plots of \( \log k \)(obtained from the variation of [pyrimidine base]) Vs. \( 1/T \) were made and straight lines with intercept on the ordinate were obtained (Fig.18,20,22,24,26, 28,30). From the slope of such plots, the values of \( E_a \) were evaluated (Tab. 173) using the Eyring Equation, \( \log k = \log k_{0}T/h \times e^{-\frac{\Delta H^\#}{RT} e^{\frac{\Delta S^\#}{R}}} \) the values of \( \Delta H^\# \) and \( \Delta S^\# \) were computed and are shown in Table.173.

IV.2.(xii) Rate and Activation parameters:

The activation parameters ( \( \Delta H^\#, \Delta S^\# \) and \( \Delta G^\# \)) calculated from the \( k(M^{-1}s^{-1}) \) values obtained at different temperatures are depicted in Table.173.

The Arrhenius form of the rate laws for the oxidations can be given as

\[
\begin{align*}
    k(M^{-1}s^{-1}) &= (6.16 \pm 0.01) \times 10^7 \ \exp[-(13.31 \pm 0.09)/RT] \\
    &\quad \text{for Uracil} \\
    k(M^{-1}s^{-1}) &= (4.72 \pm 0.01) \times 10^8 \ \exp[-(12.73 \pm 0.09)/RT] \\
    &\quad \text{for 5-BrUracil} \\
    k(M^{-1}s^{-1}) &= (3.64 \pm 0.02) \times 10^6 \ \exp[-(10.03 \pm 0.14)/RT] \\
    &\quad \text{for 5-ClUracil}
\end{align*}
\]
k(M⁻¹s⁻¹) = (6.10 ± 0.02) x 10⁹ exp[-(15.08 ± 0.28)/RT]
for 5-FUracil

k(M⁻¹s⁻¹) = (2.58 ± 0.02) x 10⁸ exp[-(10.77 ± 0.02)/RT]
for 5-IUracil

k(M⁻¹s⁻¹) = (2.68 ± 0.02) x 10⁹ exp[-(14.29 ± 0.15)/RT]
for Thymine

k(M⁻¹s⁻¹) = (1.03 ± 0.003) x 10¹⁰ exp[-(16.11 ± 0.04)/RT]
for 6-MeUracil

The reactivity trend observed namely, 5-Iodouracil > 5-Bromouracil > 5-Chlorouracil > Thymine > 5-Fluorouracil > 6-Methyluracil > Uracil, is in accord with the obtained E⁻ and ΔS⁻ values. That is, the highest reactivity of 5-Iodouracil is in conformity with the very less negative ΔS⁻ (in the series) and the smaller E⁻ values. The other compound, 5-Bromouracil with more negative ΔS⁻ and higher E⁻ values comes accordingly next in the reactivity. The 5-Chlorouracil having a lower E⁻ value reacts slower than 5-Bromouracil probably due to its more negative ΔS⁻ value. Thymine which has higher E⁻ value than 5-Chlorouracil accordingly reacts comparatively slower; it may be interesting to see the offset of the increase in the ΔS⁻ value (from 5-Chlorouracil to thymine) by ΔH⁻ value, i.e., the ΔH⁻ becoming more negative in the case of thymine (as per Erying equation) leads to its comparatively...
reduced reactivity. The decreased rate for 5-Fluorouracil (than thymine) is due to the more electronegative fluorine which rather decreases the electron density at C, comparatively. However it is faster than uracil and 6-methyluracil.

Though uracil has a lower $E_\lambda$ value than 6-methyluracil, it reacts comparatively slower due to its more negative $\Delta S^*$ value. The negative $\Delta S^*$ values observed in all the system is indicative of the involvement of a severely structured transition state due to electrostriction. The negative values of $\Delta S^*$ observed reflect a closer penetration or contact of the reactants (possibly due to the electrostatic attractive force between the positive charge on the oxidant and the π-electron cloud in the pyrimidine ring) in the transition state than in the initial stage thus leading to a severe restriction in the geometry of the transition state resulting in electrostriction. Further, it is found that the $\Delta G^*$ values for all the systems are almost the same (Tab. 173) indicating the operation of a similar mechanism in each case. The constant $\Delta G^*$ values may arise from the compensation effect in which the enthalpies have a tendency to compensate each other so that the changes in $\Delta G^*$ are much smaller.
IV.2.(xiii) Isokinetic relationship:

The enthalpy of activation and the entropy of activation were correlated using the equation:

$$\Delta H^\circ = \Delta H_0 + \beta \Delta S^\circ$$

where $\beta$ is the isokinetic temperature. A plot of $\Delta H^\circ$ Vs $\Delta S^\circ$ for all the compounds studied was found to be linear (Fig.45). The isokinetic temperature was found to be 348 K well above the experimental temperature. The existence of a linear relationship between $\Delta H^\circ$ and $\Delta S^\circ$ indicates that similar mechanism is operating throughout the series\textsuperscript{114,115}. The correlations between log $k$ values at 293 K and that at 303 K is shown as a typical example in Fig.46. From the slope value the isokinetic temperature was calculated using the formula:

$$\beta = \frac{T_1 T_2 (1-b)}{(T_1 - b T_2)}$$

Where $\beta$ is the isokinetic temperature and $b$ is the slope. The value of $\beta$ is found to be 378.9K. This temperature is in a fair agreement with that obtained from the slope of $\Delta H^\circ$ and $\Delta S^\circ$ values(348K). This suggests that all the pyrimidine bases are oxidised by the same mechanism\textsuperscript{114,115}. 
IV.2.(xiv) Mechanism:

Taking uracil as a typical example, the following mechanism is proposed:

\[
\text{HN} \quad \text{H} \quad \text{HN} \\
\text{+ Ce(IV)} \quad \rightarrow \\n\text{HN} \quad \text{H} \quad \text{HO} \\
\text{+ Ce(IV)} \quad \rightarrow \\n\text{HN} \quad \text{H} \quad \text{OH} \\
\text{+ Ce(IV)} \quad \rightarrow \\n\text{HN} \quad \text{H} \quad 2\text{Ce(III)}
\]
Thus, the mechanism consists in the reaction of Ce(IV) on C$_5$-C$_6$ double bond initiating the attack at C$_5$ forming a radical cation which subsequently reacts with water in a successive fashion leading to the corresponding glycol as the product. Such type of reactions involving Ce(IV) forming radical cations of the organic substrates are already available in literature$^{21,25,26,116}$ The generation of radical cations in the oxidation of aromatic systems by metal ions has been postulated by a number of research workers$^{117-119}$. In the oxidation of 2,5-diphenylfuran by Ce(IV), a radical cation was proposed as$^{25}$

\[
\text{Ph} - \text{C}=\text{C} - \text{Ph} \xrightarrow{\text{Ce(IV)}} \text{Ph} - \text{C}^{+} = \text{C} - \text{Ph}
\]

Müller et al. examined the oxidation of a series of olefins with Ce(IV) and reported that it does not react with C-H bonds but with the C=C involving a radical$^{121}$ The oxidation of 1,2-diarylethanones by Ce(IV) was postulated involving electron abstraction from the $\pi$-system$^{122}$ In the oxidation of toluenes by Ce(IV), a radical mechanism was found to be operative$^{123}$ A radical cation formation from the $\pi$-system of the aryl groups in the oxidation of aryl alkyl hydrocarbons by Ce(IV) was suggested$^{124,125}$ Evidences in support of this based on a Hammett correlation with $\sigma^+$ were obtained$^{117,119,124,125}$ The oxidation of substituted bibenzyls by Ce(IV) was suggested as proceeding...
through a radical cation formation by electron transfer from the aromatic nucleus\textsuperscript{119,126}. It may be recalled as mentioned earlier that a mechanism involving radical cation in the oxidation of naphthalenes by Ce(IV) has very recently been reported\textsuperscript{26}. The involvement of radical cations of pyrimidines and their subsequent reaction with water has already been implicated in the photohydration of pyrimidines studied by flash photolysis\textsuperscript{127}. In connection with the direct effect of ionising radiation on DNA, recently a pulse radiolytic study of the reaction of SO\textsubscript{4}\textsuperscript{2-} with thymine derivatives has been carried out\textsuperscript{128}. A mechanism involving the intermediacy of radical cations was proposed\textsuperscript{128}.

**IV.3. Oxidation of Uracils in perchloric acid medium:**

It is well established that the oxidation by Ce(IV) is faster in HClO\textsubscript{4} than in H\textsubscript{2}SO\textsubscript{4}. This is attributed to the difference observed in the redox potential of Ce(IV)/Ce(III) in these two acidic media\textsuperscript{16}. In HClO\textsubscript{4}, \(E^{\circ}(\text{Ce(IV)/Ce(III)}) = 1.74\) V vs. NHE, whereas it is lower (1.44 V) in H\textsubscript{2}SO\textsubscript{4}\textsuperscript{16,129}.

It was observed that the reactions of all the pyrimidine bases studied in H\textsubscript{2}SO\textsubscript{4} couldn't be carried out in HClO\textsubscript{4} due to some of them being immeasurably fast. Hence, the results pertaining to the investigations on uracil, 6-methyluracil, uridine, 1,3-dimethyluracil, thymidine and 6-azathymine alone are presented.
Order and rate Law:

IV.3.(i) Order with respect to [Ce(IV)]:

The experiments were carried out under pseudo first order condition, keeping [pyrimidine base] >> [Ce(IV)].

At a fixed [pyrimidine base] and [HClO₄] and μ the effect of varying [Ce(IV)] on rate was studied. The rate of the reaction was monitored by following the disappearance of [Ce(IV)] spectrophotometrically at 345 nm. The pseudo first order plots of log(Abs) Vs time(Fig.30A) were all linear for various [Ce(IV)]. This was found to be so in all the system studied. However, the values of first order rate constant obtained from the slope of such plots decreased as the concentration of Ce(IV) was increased. This can be explained based on the fact that in perchloric acid, Ce(IV) undergoes appreciable hydrolysis, followed by dimerisation:\(^{16}\),

\[
\begin{align*}
\text{Ce(H}_2\text{O)}_6^{4+} & \rightarrow [\text{Ce(OH)(H}_2\text{O})_5]^{3+} + \text{H}^+ \\
2[\text{Ce(OH)(H}_2\text{O})_5]^{3+} & \rightarrow [\text{(H}_2\text{O})_5\text{Ce-O-Ce(H}_2\text{O})_3]^{6+} + \text{H}_2\text{O}
\end{align*}
\]

It is very likely that the relative proportion of the dimeric Ce(IV) species
increases with an increase in the concentration of Ce(IV). The observation of a decreasing rate constant with increasing Ce(IV) concentration indicates that the dimeric species are unreactive kinetically and that only the monomeric Ce(IV) species are reactive\textsuperscript{16,130}.

Similar observations were made in the kinetic study of the oxidation of acetone by Ce(IV) in nitric acid medium\textsuperscript{102}. The existence of Ce(IV) dimers in aqueous media has been proved conclusively, in studies on the extraction of Ce(IV) with diethyl ether\textsuperscript{131}. Hence the active species is the monomeric Ce(IV) one. In HClO\textsubscript{4}, the species Ce(OH)\textsuperscript{3+} arises due to:

\[
\text{Ce(IV)} + \text{H}_2\text{O} \rightarrow \rightarrow \text{Ce(OH)}^{3+} + \text{H}^+
\]

It may be inferred that Ce(OH)\textsuperscript{3+} is also not a kinetically active species due to the observed retardation of the rate with increase in [Ce(IV)]. Thus, it is unequivocally proved that the monomeric Ce(IV) acts as the active species in this work. A similar observation was made in the oxidations of ethanol\textsuperscript{130}, 2,3-butanediol\textsuperscript{132}, 2-propanol\textsuperscript{133}, 2-butanol\textsuperscript{134} and cyclohexanol\textsuperscript{134} concluding that Ce\textsuperscript{4+} was the active oxidant species and not Ce(OH)\textsuperscript{3+}.

However, when the initial rates were plotted against the corresponding
Cerium (IV) concentrations, a straight line plot was obtained showing that the initial rate increased with the increasing Ce(IV) concentration. Such a type of kinetic behavior was reported in the oxidation of methanol$^{16}$, ethanol$^{16}$ and sulfanilic acid$^{135}$ by Ce(IV). The pseudo-first order rate constant ($k'$, s$^{-1}$) obtained, remained constant for various initial concentrations of Ce(IV) showing that the order of the reaction with respect to [Ce(IV)] is unity.

**IV.3.(ii) Order with respect to [Pyrimidine Base]:**

The effect of varying the initial concentration of pyrimidine base was studied at a fixed concentration of Ce(IV), HClO$_4$ and constant $\mu$. For all the systems studied, it was noticed that the plots of log Abs. Vs time at different initial concentrations of pyrimidine base were linear (Fig.30B). The rate constant for the reaction was obtained from the slope of these plots as:

$$\frac{\text{slope x 2.303}}{60} = \frac{k'(s^{-1})}{60}$$

Increase of [pyrimidine base] enhanced the rate of the reaction showing that the reaction follows first order with respect to [pyrimidine base]. This was confirmed by the straight line passing through origin obtained by plotting $k'(s^{-1})$ Vs.[pyrimidine Base] (Fig.31,34,36,38,40,42; Tab.130).
132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170). These figures show that the observed rate constants depend linearly on [pyrimidine base], implying little or no complexation between Ce(IV) and the substrate.

IV.3.(iii) Effect Of [HClO₄]:

The effect of [H⁺] was studied by carrying out the reaction at fixed [Ce(IV)], [pyrimidine base] and μ. For all the systems investigated the plots of log(Abs) vs. time were linear (Tab.131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171) and increase of [HClO₄] was found to enhance the rate of the reaction showing a first order dependence of rate on [HClO₄]. The plot of k'(s⁻¹) Vs [HClO₄] yielded straight line passing through origin (Fig.32) in all the cases studied.

Based on the foregoing kinetic observations, the following rate law is proposed:

\[
\frac{d[\text{Ce(IV)}]}{dt} = k[\text{Ce(IV)}][\text{pyrimidine base}][\text{HClO}_4]
\]
rate

\[ \frac{\text{rate}}{\text{s}^{-1}} = k'(\text{s}^{-1}) = k[\text{pyrimidine base}] \text{[HClO}_4\text{]} \]

[Ce(IV)]

IV.3.(iv) Effect of \( \mu \):

Studies carried out at fixed concentration of HClO\(_4\), pyrimidine base and Ce(IV) but with different concentrations of NaClO\(_4\) indicated the absence of any change in the values of the observed rate constant (\( k', s^{-1} \)) for all the pyrimidines studied. This clearly points to the participation of a neutral reactant molecules, the pyrimidine base in the reaction\(^{116} \)

IV. 3. (v) Stoichiometry:

The stoichiometry of the reaction, [Ce(IV)] [pyrimidine base] was estimated by finding the amount of unreacted oxidant as in the kinetic runs, spectrophotometrically by monitoring the change in absorbance of Ce(IV) \( \text{ab} 345 \text{ nm} \)

Such experiments repeated with various initial concentrations of the reactants led to the same result indicating a stoichiometry of [Ce(IV)] [pyrimidine base] = 2 1 This shows that one bioorganic molecule provides two electrons to two molecules of the oxidant
IV.3.(vi) Evidence for radical intermediates:

Experiments were also carried out making a search for the involvement of radical intermediates in the reaction between Ce(IV) and the pyrimidine bases. Freshly distilled acrylamide monomer when added to deaerated reaction mixture containing Ce(IV), pyrimidine and HClO$_4$ was found to form a polymer hinting the involvement of radicals in the reaction.

IV.3.(vii) Mechanism:

Based on the thus obtained results, the following reaction steps are suggested:

\[
\text{Ce(IV)} + \text{Pyrimidine} \rightarrow \text{Product}
\]

in keeping with the rate law as mentioned earlier. With uracil as a typical example, the mechanism is depicted as
IV.3.(viii) Reactivity Trend:

From Table 174, it is clear that the reactivity trend observed is:

6-methyluracil > uracil > Thymidine > 6-azathymine >
Uridine > 1,3-Dimethyluracil.

The nucleoside thymidine being relatively richer in electron availability than the uridine (due to the absence of any electron releasing group at C₃) reacts faster than uridine and 1,3-dimethyluracil. It may be recalled from the earlier discussion in H₂SO₄ that the reaction rate is accelerated by electron donating groups at C₃ (e.g., thymine). The absence of any rate acceleration in 1,3-dimethyluracil points to the absence of any attack of the oxidant Ce(IV) on the nitrogens N₁ and N₃. This is also supported by the fact that in H₂SO₄, the reaction of 1,3-dimethyluracil with Ce(IV) was immeasurably slow. It may be noted that the same pattern of reactivity as observed in H₂SO₄ is also observed in HClO₄ among uracil and 6-methyluracil and thymine (or thymidine) and uridine. It is to be noted that 6-methyluracil and uracil react faster than both thymidine and uridine. This is due to the presence of the sugar moiety in the latter two compounds making them relatively electron deficient than 6-methyluracil and uracil (containing no sugar units). It is noted that 6-azathymine shows an intermediate behavior of reactivity in the series.
IV.3.(ix) Product Analysis:

This was carried out as outlined earlier for the reactions in H\textsubscript{2}SO\textsubscript{4}. The nature of the product formed in HClO\textsubscript{4} was found to be the same as in H\textsubscript{2}SO\textsubscript{4}. This suggests the formation of the corresponding glycol as the product.

IV.3.(x) Effect of temperature:

The effect of temperature on the rate of the reaction was studied by performing the reaction at different temperatures. Using the \( k (\text{M}^{-1}\text{s}^{-1}) \) values obtained from the variation of [pyrimidine base], the Arrhenius plots were made between log \( k \) Vs \( 1/T \) and from the slope of such plots (Fig.33,35,37,39,41,43) \( E_a \) was determined (Tab.174).

IV.3.(xi) Rate and Activation Parameters:

Based on temperature variation studies using Erying's equation, the values of activation parameters (\( \Delta H^\circ, \Delta S^\circ \) and \( \Delta G^\circ \)) have been computed and are presented in Tab.174.
The Arrhenius form of the rate laws for the oxidations can be given as:

\[
k(M^{-1}s^{-1}) = (5.82 \pm 0.01) \times 10^9 \exp[-(14.47 \pm 0.11)/RT]
\]
for Uracil

\[
k(M^{-1}s^{-1}) = (4.22 \pm 0.01) \times 10^7 \exp[-(12.58 \pm 0.10)/RT]
\]
for 1,3-DimethylUracil

\[
k(M^{-1}s^{-1}) = (1.96 \pm 0.01) \times 10^8 \exp[-(13.00 \pm 0.07)/RT]
\]
for Uridine

\[
k(M^{-1}s^{-1}) = (1.08 \pm 0.01) \times 10^8 \exp[-(11.86 \pm 0.08)/RT]
\]
for 6-MeUracil

\[
k(M^{-1}s^{-1}) = (3.46 \pm 0.01) \times 10^8 \exp[-(12.96 \pm 0.52)/RT]
\]
for Thymidine

\[
k(M^{-1}s^{-1}) = (1.41 \pm 0.004) \times 10^7 \exp[-(11.09 \pm 0.01)/RT]
\]
for 6-Azathymine

The reaction of thymidine which has the highest rate constant value among the pyrimidines in HClO₄ possesses correspondingly lower Eₗ value than the others.

It may be noted that the ΔG° values for the reaction of all the compounds
are almost the same implying that a similar mechanism operates in all the cases. The $\Delta S^\circ$ values are all negative pointing to electrostriction. This reflects that the transition state is a severely structured one. It may be noted that the $\Delta G^\circ$ values for the reactions in $H_2SO_4$ and $HClO_4$ do not differ much indicating probably that there is not a significant change at all in the reaction pathway between the two acidic media. Such a type of behavior has already been reported in literature.

Comparisons of the reactions in aq.$H_2SO_4$ and $HClO_4$ media:

It was observed that the reaction (oxidation) of pyrimidine bases with Ce(IV) in $HClO_4$ is faster than in $H_2SO_4$ and is due to the higher reduction potential of Ce(IV) in $HClO_4$. The reactions were found to proceed with no involvement of any complex formation between Ce(IV) and the pyrimidines but involving radical cations of the pyrimidine bases finally yielding the glycols as the product. The reactivity trend noticed among some of the commonly studied substrates (pyrimidine bases) in both acidic media was found to differ.