

# Kinetics and mechanistic study of manganese(II)-catalyzed cerium(IV) oxidation of thiamine hydrochloride in aqueous perchloric acid medium by stopped flow technique

D. V. Naik · K. S. Byadagi · S. T. Nandibewoor ·  
S. A. Chimatadar

Received: 2 February 2012 / Accepted: 26 April 2013 / Published online: 5 June 2013  
© Springer-Verlag Wien 2013

**Abstract** The kinetics of the manganese(II)-catalyzed oxidation of thiamine hydrochloride by cerium(IV) in aqueous perchloric acid medium at a constant ionic strength of  $1.10 \text{ mol dm}^{-3}$  was studied spectrophotometrically at 15, 25, 35, and 45 °C by the stopped flow technique. The reaction between thiamine hydrochloride and cerium(IV) in the acid medium exhibits 1:3 stoichiometry. The main products were identified by spot test, IR,  $^1\text{H}$  NMR, and GC–MS studies. The reaction is first order in cerium(IV) and manganese(II) and has less than unit order in thiamine hydrochloride. As the acid concentration increases the rate of reaction decreases. The added product cerium(III) retards the rate of reaction. The active catalyst and oxidant species were identified as  $[\text{Mn}(\text{H}_2\text{O})_4]^{2+}$  and  $[\text{Ce}(\text{OH})]^{3+}$ , respectively. A probable mechanism involving free radicals and the formation of a complex between substrate and catalyst is proposed. The reaction constants, activation parameters, and thermodynamic quantities are calculated and discussed.

**Keywords** Thiamine hydrochloride · Cerium(IV) · Manganese(II) · Oxidation · Catalysis · Kinetics

## Introduction

Thiamine hydrochloride (TH) is known as vitamin B<sub>1</sub>. It was the first member of the vitamin B complex to be isolated and identified as a vitamin. Vitamin B<sub>1</sub> occurs in the outer coats

of the seeds of many plants including cereal grains. Thiamine is fundamentally associated with carbohydrate metabolism. It is phosphorylated in the body to the active coenzyme thiamine pyrophosphate that functions as co-carboxylase for various reactions in carbohydrate metabolism [1]. Thiamine might also serve as a modulator of neuromuscular transmission. It binds to isolated nicotinic cholinergic receptors, and neurotransmission is impaired by pyriethamine, a thiamine antimetabolite [2]. In thiamine deficiency, the oxidation of  $\alpha$ -ketoacid is impaired, resulting in an increase in the concentration of pyruvate in the blood. The requirement for thiamine is related to the metabolic rate and is greatest when carbohydrate is a source of energy [3]. The oxidation kinetics and mechanism of vitamin B<sub>1</sub> are thus important to the process in vitro.

Manganese(II) is important in both animal and plant enzymes and is necessary for photosynthesis. Manganese(II) most probably acts as either catalyst or reductant (the reduction potential [4] of the couple Mn(III)/Mn(II) is 1.51 V in dilute acid). Most of the studies employed manganese(II) as a catalyst [5].

Cerium(IV) is a well-known oxidant in acid media [6] (the reduction potential [4] of the cerium(IV)/cerium(III) couple is 1.70 V) and is stable only in high acid concentrations. In sulfuric acid and sulfate media cerium(IV) forms several sulfate complexes [7]. Similarly in perchloric acid solutions [8, 9] cerium(IV) exists as  $\text{Ce}^{4+}$ ,  $[\text{Ce}(\text{OH})]^{3+}$ ,  $[\text{Ce}(\text{OH})_2]^{2+}$ ,  $[\text{Ce}-\text{O}-\text{Ce}]^{6+}$ , and  $[\text{HO}-\text{Ce}-\text{O}-\text{CeOH}]^{4+}$ . A potentiometric study [10] of cerium(IV) hydrolysis indicates  $[\text{Ce}(\text{OH})]^{3+}$  to be the predominant active species of cerium(IV), in the concentration range  $0.30\text{--}2.0 \text{ mol dm}^{-3} \text{ HClO}_4$ , but its role has not received much attention so far. The oxidation of organic compounds by cerium(IV), in general, proceeds via the formation of an intermediate complex [11]. Among the inorganic substrates

D. V. Naik · K. S. Byadagi · S. T. Nandibewoor ·  
S. A. Chimatadar (✉)  
P.G. Department of Studies in Chemistry, Karnatak University,  
Pavate Nagar, Dharwad 580003, Karnataka, India  
e-mail: schimatadar@gmail.com

which serve as ligands for cerium(IV) are chloride, bromide, and hypophosphite [12].

The oxidation of TH has been performed with ferricyanide [13], hypiodide [14], chlorite [15], and *N*-chlorobenzenesulfonamide [16]. However, there was no report on the oxidation of TH by cerium(IV) in the literature. Thus we tried to study this reaction in sulfuric acid and perchloric acid media. The reaction is facile only in the presence of micro-amounts ( $10^{-6}$  mol dm $^{-3}$ ) of manganese(II) in perchloric acid medium, but not in sulfuric acid. The mechanism may be quite complicated owing to the formation of different cerium(IV) and manganese(II) complexes in the form of active species in the perchloric acid medium. Hence, we have investigated the manganese(II)-catalyzed oxidation of TH by cerium(IV) in order to understand the behavior of the active species of the oxidant,  $[\text{Ce}(\text{OH})]^{3+}$ , and catalyst,  $[\text{Mn}(\text{H}_2\text{O})_4]^{2+}$ , and to propose a suitable mechanism.

## Results and discussion

### Reaction orders

The reaction orders were determined from the slopes of  $\log(\text{rate})_c$  vs.  $\log(\text{concentration})$  plots by varying the concentrations of cerium(IV), TH, perchloric acid, and manganese(II) catalyst, while keeping all other concentrations and conditions constant.

### Effect of [oxidant] and [substrate]

At constant concentration of TH ( $5.0 \times 10^{-2}$  mol dm $^{-3}$ ), perchloric acid ( $1.0$  mol dm $^{-3}$ ), catalyst manganese(II) ( $5.0 \times 10^{-6}$  mol dm $^{-3}$ ), and at constant ionic strength ( $I = 1.10$  mol dm $^{-3}$ ), the cerium(IV) concentration was varied from  $0.50 \times 10^{-4}$  to  $5.0 \times 10^{-4}$  mol dm $^{-3}$ ; the initial rate increased with increase in the cerium(IV) concentration (Table 1). From the plot of  $\log(\text{rate})_c$  vs.  $\log[\text{Ce}(\text{IV})]$ , the order with respect to cerium(IV) concentration was found to be unity.

The substrate TH concentration was varied in the concentration range  $5.0 \times 10^{-3}$ – $5.0 \times 10^{-2}$  mol dm $^{-3}$  at 25°C, keeping all other conditions constant. The initial rate increased with increase in the concentration of TH (Table 1). From the slope of the plot of  $\log(\text{rate})_c$  vs.  $\log[\text{TH}]$ , the order with respect to TH concentration was found to be fractional (0.59).

### Effect of [acid]

At constant ionic strength ( $I = 1.10$  mol dm $^{-3}$ ) and with other conditions remaining constant, the rate was found to

decrease with increasing perchloric acid concentration (Table 1). The order with respect to perchloric acid concentration was determined from the log–log plots of  $(\text{rate})_c$  vs. acid concentrations and was found to be negative fractional ( $-0.40$ ). Cerium(IV) is known to form several complexes in aqueous perchloric acid media [8, 9], such as  $\text{Ce}^{4+}$ ,  $[\text{Ce}(\text{OH})]^{3+}$ ,  $[\text{Ce}(\text{OH}_2)]^{2+}$ ,  $[\text{Ce}-\text{O}-\text{Ce}]^{6+}$ , and  $[\text{HO}-\text{Ce}-\text{O}-\text{CeOH}]^{4+}$ . A potentiometric study of the hydrolysis of cerium(IV) indicates [10]  $[\text{Ce}(\text{OH})]^{3+}$  to be the predominant active species of cerium(IV) in perchloric acid in the concentration range  $0.30$ – $2.0$  mol dm $^{-3}$ .

### Effect of [manganese(II)]

At constant oxidant, reductant, and acid concentration of  $2.0 \times 10^{-4}$ ,  $5.0 \times 10^{-2}$ , and  $1.0$  mol dm $^{-3}$ , respectively, and  $I = 1.10$  mol dm $^{-3}$ , the catalyst manganese(II) concentration was varied between  $1.0 \times 10^{-6}$  and  $10.0 \times 10^{-6}$  mol dm $^{-3}$  (Table 1). The order with respect to manganese(II) concentration was found to be unity. As catalyst concentration increases the rate of the reaction also increases, and the activity of catalyst reaches a maximum when [manganese(II)] is at least  $10.0 \times 10^{-6}$  mol dm $^{-3}$  under the aforementioned experimental conditions.

### Effect of ionic strength and dielectric constant

At constant concentration of reactants and other conditions constant, the ionic strength was varied from  $1.10$  to  $3.40$  mol dm $^{-3}$  by varying the concentrations of sodium perchlorate and the rate was found to increase with increasing ionic strength. A plot of  $\log(\text{rate})_c$  vs.  $\sqrt{I}$  is linear with a positive slope (Fig. 1). The effect of the dielectric constant was studied by varying the volume fraction acetic acid–water ( $\phi$ , see [17]) in the reaction mixture with all other conditions being kept constant. It was found that  $(\text{rate})_c$  increased with decreasing dielectric constant of the medium. In other words, as the acetic acid content in the reaction mixture increases, the pH of the reaction medium decreases and the rate of the reaction  $[(\text{rate})_c]$  increases. No reaction of the solvent occurred during the oxidant under the experimental conditions employed. A plot of  $\log(\text{rate})_c$  vs.  $1/D$  is linear with positive slope (Fig. 1).

### Effect of initially added products

The effect of initially added product cerium(III) was studied in the  $5.0 \times 10^{-5}$ – $5.0 \times 10^{-4}$  mol dm $^{-3}$  concentration range, keeping the ionic strength, reactant concentration, and other conditions constant. It was found that cerium(III) in the concentration range  $5.0 \times 10^{-5}$ – $5.0 \times 10^{-4}$  mol dm $^{-3}$  caused a decrease in rate. The inhibitory effect of initially added product cerium(III) is shown in Fig. 2.

**Table 1** Effect of variation of cerium(IV), thiamine hydrochloride, perchloric acid, and manganese(II) concentrations on the manganese(II)-catalyzed cerium(IV) oxidation of thiamine hydrochloride in aqueous perchloric acid medium at 25 °C and  $I = 1.10 \text{ mol dm}^{-3}$ 

[Ce(IV)] $\times 10^4/\text{mol dm}^{-3}$	[TH] $\times 10^2/\text{mol dm}^{-3}$	[HClO <sub>4</sub> ]/mol dm <sup>-3</sup>	[Mn(II)] $\times 10^6/\text{mol dm}^{-3}$	(rate) <sub>c</sub> $\times 10^7/\text{mol dm}^{-3} \text{ s}^{-1}$	
				Found	Calculated
0.50	5.0	1.0	5.0	1.03	0.99
1.0	5.0	1.0	5.0	2.00	2.01
2.0	5.0	1.0	5.0	3.89	3.99
3.0	5.0	1.0	5.0	5.48	5.41
4.0	5.0	1.0	5.0	7.94	7.88
5.0	5.0	1.0	5.0	9.44	9.76
2.0	0.5	1.0	5.0	1.04	1.00
2.0	1.0	1.0	5.0	1.28	1.29
2.0	2.0	1.0	5.0	2.19	2.25
2.0	3.0	1.0	5.0	2.92	2.97
2.0	4.0	1.0	5.0	3.24	3.35
2.0	5.0	1.0	5.0	3.89	3.99
2.0	5.0	0.1	5.0	9.89	9.81
2.0	5.0	0.2	5.0	7.41	7.37
2.0	5.0	0.4	5.0	5.62	5.67
2.0	5.0	0.6	5.0	4.73	4.53
2.0	5.0	0.8	5.0	4.32	4.12
2.0	5.0	1.0	5.0	3.89	3.99
2.0	5.0	1.0	0.0	Immeasurably slow	
2.0	5.0	1.0	1.0	0.80	0.79
2.0	5.0	1.0	2.0	1.60	1.59
2.0	5.0	1.0	3.0	2.34	2.39
2.0	5.0	1.0	4.0	3.16	3.19
2.0	5.0	1.0	5.0	3.89	3.99
2.0	5.0	1.0	6.0	4.68	4.79
2.0	5.0	1.0	7.0	5.50	5.59
2.0	5.0	1.0	8.0	6.17	6.39
2.0	5.0	1.0	9.0	7.00	7.19
2.0	5.0	1.0	10.0	7.76	7.99

### Test for free radicals

The intervention of free radicals was examined as follows: The reaction mixture, to which a known quantity of acrylonitrile (scavenger) had been added initially, was kept in an inert atmosphere for 2 h at room temperature. When the reaction mixture was diluted with methanol, formation of precipitate resulted, suggesting that free radicals are taking part in the reaction.

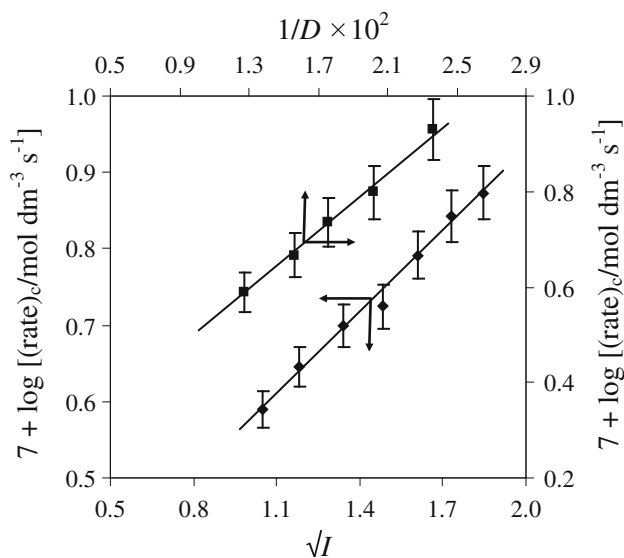
### Effect of temperature

The rate of reaction was measured at different temperatures (15, 25, 35, and 45 °C) under varying acid and TH concentrations by using the stopped flow technique. The initial rate was found to increase with increasing temperature. The

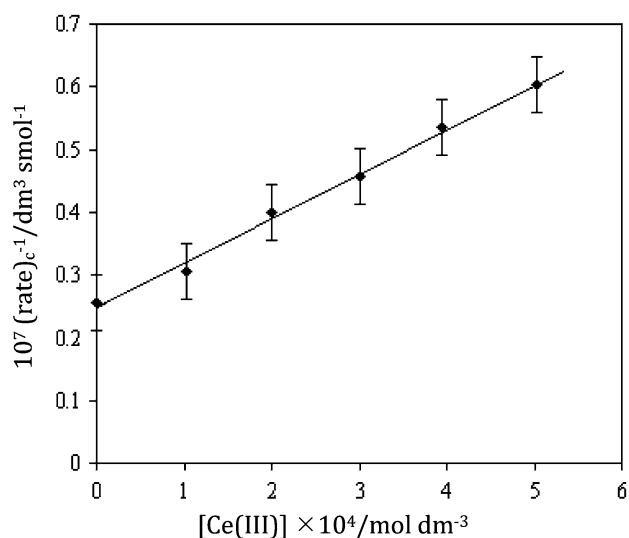
rate constant  $k$  (the slow step),  $K_1$  (the equilibrium constant of the first equilibrium step), and  $K_2$  (the equilibrium constant of the second equilibrium step) were obtained from the plots of  $[\text{Ce(IV)}][\text{Mn(II)}]/(\text{rate})_c$  vs.  $1/[\text{TH}]$  and  $[\text{Ce(IV)}][\text{Mn(II)}]/(\text{rate})_c$  vs.  $[\text{H}^+]$  (Scheme 1; Fig. 3) at four different temperatures (Table 2). The energy of activation  $E_a$  was evaluated from the slope of the Arrhenius plot of  $\log k$  vs.  $1/T$  (Table 2). The enthalpy of activation  $\Delta^\ddagger H$  and the entropy of activation  $\Delta^\ddagger S$  were obtained by using the Eyring equation [18].

$$k = \frac{k_B T}{h} e^{\left(-\frac{\Delta^\ddagger G}{RT}\right)} = \frac{k_B T}{h} e^{-\left(\frac{\Delta^\ddagger H + T\Delta^\ddagger S}{RT}\right)} \quad (1)$$

where  $k$  is the rate constant,  $k_B$  is the Boltzmann's constant,  $R$  is the gas constant,  $h$  is Planck's constant,  $T$  is the



**Fig. 1** Effect of ionic strength and dielectric constant on the manganese(II)-catalyzed cerium(IV) oxidation of thiamine hydrochloride at 25 °C



**Fig. 2** Effect of added product cerium(III) on the manganese(II)-catalyzed oxidation of thiamine hydrochloride by cerium(IV) at 25 °C

absolute temperature, and  $\Delta^\ddagger G$  is the free energy of activation. The linear form of Eq. (1) is

$$\ln \frac{k}{T} = -\frac{\Delta^\ddagger H}{RT} + \frac{\Delta^\ddagger S}{R} + \ln \frac{k_B}{h} \quad (2)$$

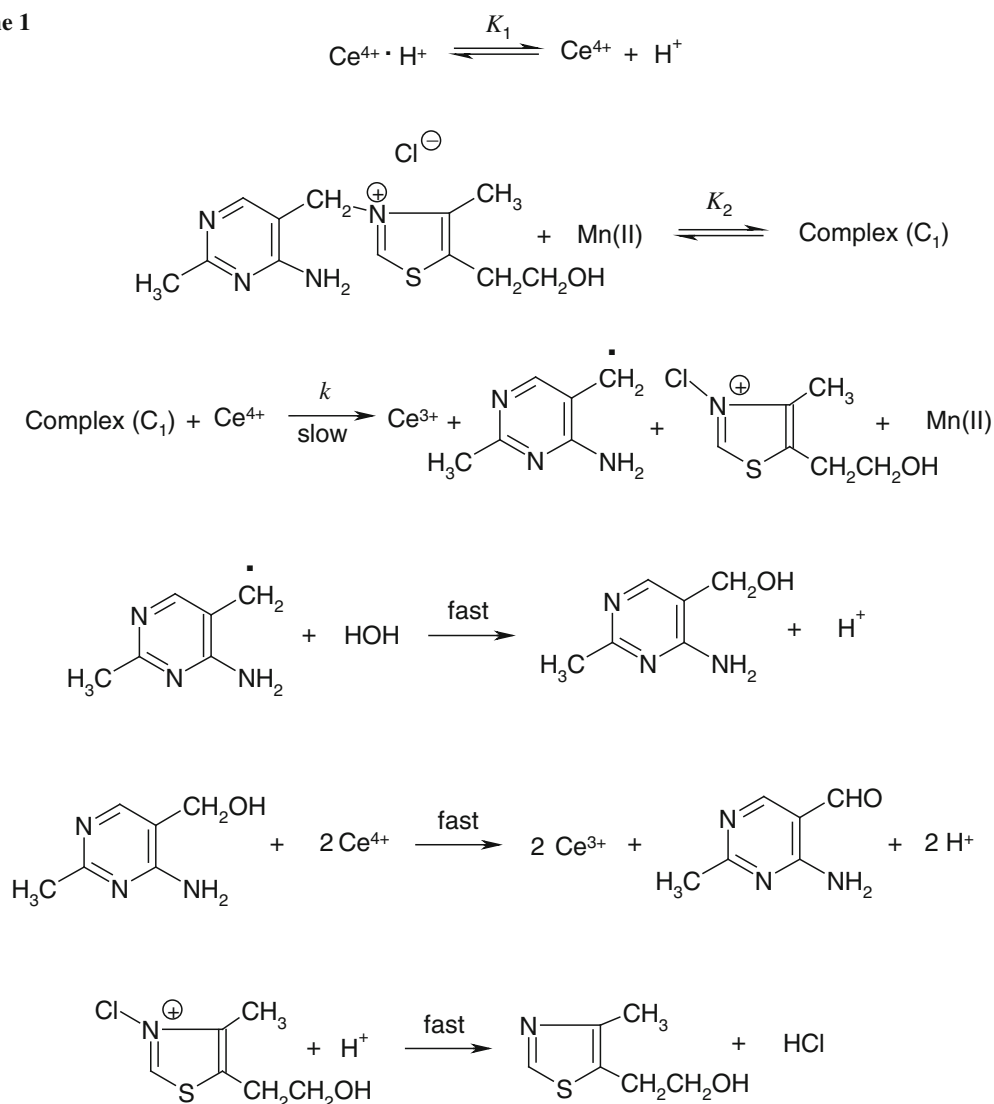
The slope of the plot of  $\log k/T$  vs.  $1/T$  gives the value of enthalpy of activation  $\Delta^\ddagger H$  (Table 2). By using the value of  $\Delta^\ddagger H$  and the rate constant at a particular temperature  $T$  the value of  $\Delta^\ddagger S$  was obtained by simple rearrangement of Eq. (1) (Table 2). Using these values of  $\Delta^\ddagger H$  and  $\Delta^\ddagger S$ , the free energy of activation  $\Delta^\ddagger G_{298}$  is obtained as

$54.29 \pm 0.03 \text{ kJ mol}^{-1}$ . The van't Hoff plot ( $\log K_1$  vs.  $1/T$ ) was drawn and the thermodynamic quantities were calculated (Table 2).

The oxidation of TH by cerium(IV) does not occur to any appreciable extent in the aqueous sulfuric acid and perchloric acid media under the present experimental conditions. The reaction is facile only in the presence of micro-amounts ( $10^{-6} \text{ mol dm}^{-3}$ ) of manganese(II) in aqueous perchloric acid medium, but not in sulfuric acid. In the presence of sulfuric acid the manganese(II) catalyst is inefficient, perhaps owing to the fact that the active species of manganese(II),  $[\text{Mn}(\text{H}_2\text{O})_4]^{2+}$ , does not form in sulfuric acid media. Hence the study was undertaken in aqueous perchloric acid medium. In perchloric acid medium the reaction between TH and cerium(IV) in the presence of manganese(II) has a stoichiometry of 1:3, i.e., 1 mole of TH reacts with 3 moles of cerium(IV) to give the final products cerium(III), 4-amino-2-methylpyrimidine-5-carbaldehyde, and 2-(4-methylthiazol-5-yl)ethanol. The reaction is first order with respect to cerium(IV) and manganese(II) concentrations and less than unit order (0.59) with respect to TH. The effect of hydrogen ions on the rate was studied by adding perchloric acid and it was found that as the perchloric acid concentration increased in the reaction mixture the rate of the reaction decreased. The order with respect to perchloric acid concentration is less than unity and negative. Similar behavior was reported for the oxidation of mandelic acid [19] and mercury(I) [20] by cerium(IV) in perchloric acid medium. Initially added product cerium(III) retards the reaction rate appreciably. Similar results were obtained in the oxidation of tellurium(IV) [21], L-glutamic acid [22], and glycerol [23] by cerium(IV). The experimental result suggest that TH combines with the active species of the catalyst to form a complex, which then reacts in a slow step with 1 mole of cerium(IV) to give the product cerium(III), a free radical derived from TH, and an unstable complex, with generation of the catalyst manganese(II). The free radical derived from TH undergoes hydrolysis to give another intermediate product, 4-amino-2-methylpyrimidine-5-carbinol. This intermediate reacts with 2 moles of cerium(IV) in a further fast step to give the final product cerium(III) and 4-amino-2-methylpyrimidine-5-carbaldehyde. The intermediate complex formed in the rate-determining step combines with  $\text{H}^+$  ions to give the other final product 2-(4-methylthiazol-5-yl)ethanol in further fast step. The experimental results are accommodated in the form of the following mechanism (Scheme 1).

The results indicate the formation of a complex between TH and manganese(II). The spectral evidence for the formation of a complex between the substrate and catalyst was obtained from UV-Vis spectra of TH and thiamine hydrochloride-manganese(II) mixtures in which a hypsochromic shift of 4 nm from 284 to 280 nm was observed. The formation of a complex was also proved kinetically by a

Scheme 1



Michaelis–Menten plot (Fig. 3). Such formation of a complex between substrate and catalyst was also observed in literature [22, 23]. Scheme 1 leads to the rate law Eq. (8) which explains the observed order with respect to cerium(IV), TH, perchloric acid, and manganese(II):

$$\begin{aligned}
 (\text{rate})_c &= k[\text{complex(C}_1\text{)}][\text{Ce(IV)}] \\
 &= \frac{kk_1k_2[\text{Ce(IV)}][\text{TH}][\text{Mn(II)}]}{[\text{H}^+]} \quad (3)
 \end{aligned}$$

The total concentration of thiamine hydrochloride  $[\text{TH}]_t$  is given by

$$\begin{aligned}
 [\text{TH}]_t &= [\text{TH}]_f + [\text{C}_1] \\
 &= [\text{TH}]_f + K_2[\text{TH}]_f[\text{Mn(II)}] \\
 &= [\text{TH}]_f\{1 + K_2[\text{Mn(II)}]\}
 \end{aligned}$$

Therefore,

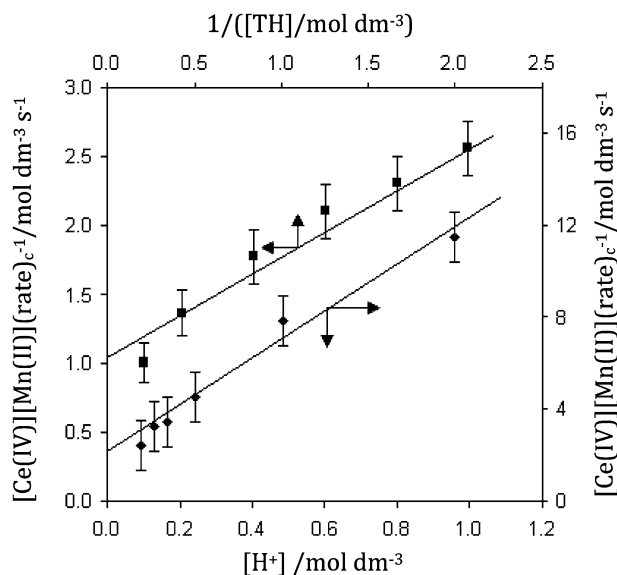
$$[\text{TH}]_f = \frac{[\text{TH}]_t}{1 + K_2[\text{Mn(II)}]} \quad (4)$$

where subscripts t and f stand for total and free, respectively. In the experiment a very low concentration of manganese(II) is used. Hence, the term  $K_2[\text{Mn(II)}]$  may be neglected in comparison with unity in Eq. (4). So,

$$[\text{TH}]_f = [\text{TH}]_t \quad (5)$$

Similarly,

$$\begin{aligned}
 [\text{Mn(II)}]_t &= [\text{Mn(II)}]_f + K_2[\text{TH}][\text{Mn(II)}] \\
 &= [\text{Mn(II)}]_f\{1 + K_2[\text{TH}]\} \\
 [\text{Mn(II)}]_t &= \frac{[\text{Mn(II)}]_t}{1 + K_2[\text{TH}]} \quad (6)
 \end{aligned}$$



**Fig. 3** Verification of rate law Eq. (8) in the form of Eq. (9)

and

$$\begin{aligned} [\text{Ce(IV)}]_t &= [\text{Ce(IV)}]_f + [\text{Ce(IV)}][\text{H}^+] \\ &= [\text{Ce(IV)}]_f + K_1 \frac{[\text{Ce(IV)}]_f}{[\text{H}^+]} \\ &= [\text{Ce(IV)}]_f \left\{ 1 + \frac{K_1}{[\text{H}^+]} \right\} \end{aligned}$$

Therefore,

$$[\text{Ce(IV)}]_f = \frac{[\text{Ce(IV)}]_t}{1 + \frac{K_1}{[\text{H}^+]}} \quad (7)$$

Substituting Eqs. (5, 6, 7) in Eq. (3) and omitting the subscripts, we have

$$\begin{aligned} (\text{rate})_c &= \frac{-d[\text{Ce(IV)}]}{dt} \\ &= \frac{k K_1 K_2 [\text{Ce(IV)}] [\text{TH}] [\text{Mn(II)}]}{[\text{H}^+] + K_1 K_2 [\text{TH}] [\text{H}^+] + K_1 K_2 [\text{TH}]} \end{aligned} \quad (8)$$

The rate law Eq. (8) may be rearranged to Eq. (9) which is suitable for verification.

$$\frac{[\text{Ce(IV)}] [\text{Mn(II)}]}{(\text{rate})_c} = \frac{[\text{H}^+]}{k K_1 K_2 [\text{TH}]} + \frac{1}{k K_2 [\text{TH}]} + \frac{[\text{H}^+]}{k K_1} + \frac{1}{k} \quad (9)$$

According to Eq. (9) the plots of  $[\text{Ce(IV)}] [\text{Mn(II)}]/(\text{rate})_c$  vs.  $1/[\text{TH}]$  and  $[\text{Ce(IV)}] [\text{Mn(II)}]/(\text{rate})_c$  vs.  $[\text{H}^+]$  should be linear and are found to be so (Fig. 3).

I. From the first plot, i.e.,  $[\text{Ce(IV)}] [\text{Mn(II)}]/(\text{rate})_c$  vs.  $1/[\text{TH}]$ , we obtain

$$(\text{Slope})_1 = \frac{[\text{H}^+]}{k K_1 K_2} + \frac{1}{k K_2} \quad (10)$$

**Table 2** Effect of temperature on the manganese(II)-catalyzed cerium(IV) oxidation of thiamine hydrochloride in aqueous perchloric acid medium

Temperature/°C	$k \times 10^{-2}/\text{s}^{-1}$	
Rate constant with respect to slow step of Scheme 1		
15	15.54	
25	19.44	
35	23.12	
45	27.32	
Parameters	Value	
Activation parameters		
$\Delta^{\ddagger}H/\text{kJ mol}^{-1}$	$11.77 \pm 0.46$	
$\Delta^{\ddagger}S/\text{J K}^{-1} \text{mol}^{-1}$	$-142.6 \pm 1.5$	
$\Delta^{\ddagger}G/\text{kJ mol}^{-1}$	$54.29 \pm 0.03$	
log A	$5.7 \pm 0.05$	
Temperature/°C	$K_1/\text{dm}^3 \text{mol}^{-1}$	$K_2 \times 10^5/\text{dm}^3 \text{mol}^{-1}$
Effect of temperature on first and second equilibrium steps of Scheme 1		
15	0.82	26.21
25	0.75	18.46
35	0.56	12.43
45	0.41	8.10
	Values from $K_1$	Values from $K_2$
Thermodynamic quantities with respect to first and second equilibrium steps of Scheme 1		
$\Delta H/\text{kJ mol}^{-1}$	$-18 \pm 3.2$	$-29.8 \pm 1.6$
$\Delta S/\text{J K}^{-1} \text{mol}^{-1}$	$-63.4 \pm 10.6$	$-172 \pm 5$
$\Delta G/\text{kJ mol}^{-1}$	$0.94 \pm 0.23$	$21.5 \pm 0.1$

$$(\text{Intercept})_1 = \frac{[\text{H}^+]}{k K_1} + \frac{1}{k} \quad (11)$$

Therefore,

$$\begin{aligned} \frac{(\text{Intercept})_1}{(\text{Slope})_1} &= K_2 \\ &= \text{Formation constant of the complex}(C_1) \end{aligned} \quad (12)$$

II. From the second plot, i.e.,  $[\text{Ce(IV)}] [\text{Mn(II)}]/(\text{rate})_c$  vs.  $1/[\text{H}^+]$ , we obtain

$$\begin{aligned} (\text{Slope})_2 &= \frac{1}{k K_1 K_2 [\text{TH}]} + \frac{1}{k K_1} \\ &= \frac{1}{k K_1} \left\{ \frac{K_2 [\text{TH}] + 1}{K_2 [\text{TH}]} \right\} \end{aligned} \quad (13)$$

$$\begin{aligned} (\text{Intercept})_2 &= \frac{1}{k K_2 [\text{TH}]} + \frac{1}{k} \\ &= \frac{1}{k} \left\{ \frac{1 + K_2 [\text{TH}]}{K_2 [\text{TH}]} \right\} \end{aligned} \quad (14)$$

Hence,

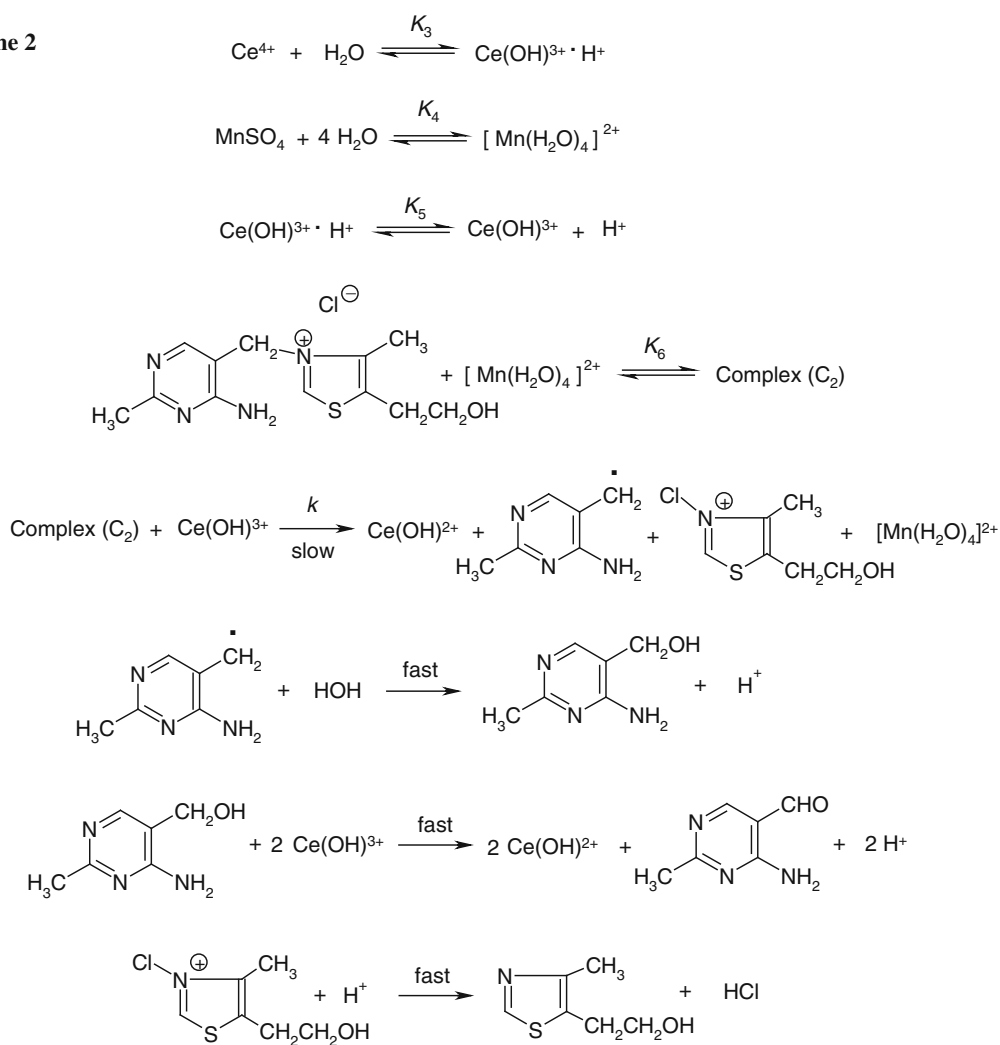
$$\frac{(\text{Intercept})_2}{\text{Slope}_2} = K_1 = \text{Ionization constant of } \text{Ce}^{4+} \cdot \text{H}^+ \quad (15)$$

Substituting the values of  $K_1$  and  $[\text{H}^+]$  in the (intercept)<sub>1</sub> of the first plot, i.e., in Eq. (11), we get the value of  $k$ , the rate constant with respect to the slow step of Scheme 1. By this procedure the obtained values of  $k$ ,  $K_1$ , and  $K_2$  are  $1,944.4 \pm 50 \text{ mol dm}^{-3} \text{ s}^{-1}$ ,  $0.75 \pm 0.04 \text{ dm}^3 \text{ mol}^{-1}$ , and  $18.46 \pm 0.40 \text{ dm}^3 \text{ mol}^{-1}$ , respectively, at  $25^\circ \text{C}$ . The value of  $K_1$  obtained is in reasonable agreement with the literature [20] ( $K_1 = 0.56$ ). Using these values, we calculated rate constants (rate)<sub>c</sub> under different experimental conditions by applying the rate law Eq. (8) and compared the results with the experimental data.

Experimental and calculated values agree reasonably well (Table 1), which fortifies the proposed scheme.

The active species involved in the mechanism can be understood as follows: cerium(IV) is known to form several species in aqueous perchloric acid media [8, 9], such as  $\text{Ce}^{4+}$ ,  $[\text{Ce}(\text{OH})]^{3+}$ ,  $[\text{Ce}(\text{OH})_2]^{2+}$ ,  $[\text{Ce}-\text{O}-\text{Ce}]^{6+}$ , and  $[\text{HO}-\text{Ce}-\text{O}-\text{CeOH}]^{4+}$ . The potentiometric study of the hydrolysis of cerium(IV) indicates that  $[\text{Ce}(\text{OH})]^{3+}$  is the predominant active species of cerium(IV) in perchloric acid [10]. Hence,  $[\text{Ce}(\text{OH})]^{3+}$  is considered as the active oxidant species. The manganese(II) catalyst is understood to be present in the aqueous acid medium mainly as  $[\text{Mn}(\text{H}_2\text{O})_4]^{2+}$  [24]. Manganese(II)-catalyzed oxidation of TH is greatly facilitated in perchloric acid solution and the reason may be that cerium(IV) species such as  $[\text{Ce}(\text{OH})]^{3+}$  and manganese(II)  $[\text{Mn}(\text{H}_2\text{O})_4]^{2+}$  are actively involved.

Scheme 2



The mechanism in Scheme 1 will therefore involve the active species as shown in Scheme 2.

Therefore, in terms of active species, the rate law Eq. (8) takes the following form (Eq. (16)):

$$\begin{aligned} (\text{rate})_c &= \frac{kK_5K_6[\text{Ce}(\text{OH})^{3+}][\text{TH}][\text{Mn}(\text{H}_2\text{O}_4)]^{2+}}{[\text{H}^+]K_5 + K_6[\text{TH}][\text{H}^+] + K_5K_6[\text{TH}]} \\ &= \frac{kK_3K_4K_5K_6[\text{Ce}(\text{OH})^{3+}][\text{TH}][\text{Mn}(\text{H}_2\text{O}_4)]^{2+}}{[\text{H}^+][\text{SO}_4]^{2-} \{ [\text{H}^+] + K_5 + K_6[\text{TH}][\text{H}^+] + K_5K_6[\text{TH}] \}} \end{aligned} \quad (16)$$

The effect of ionic strength on the rate qualitatively accounts for the reaction between two positively charged ions as seen in Scheme 1. The effect of solvent on the reaction rate has been described in detail in the literature [25]. The increase in the acetic acid content in the reaction medium leads to an increase in the rate of reaction which might be due to the presence of ionic species of TH and the dissociated form of the acetate ion. In the present study, the plot of  $\log(\text{rate})_c$  vs.  $1/D$  is linear with a positive slope, which is in the right direction as shown in Scheme 1.

The values of  $\Delta^\ddagger H$  and  $\Delta^\ddagger S$  are both favorable for electron transfer processes. The negative values of  $\Delta^\ddagger S$  indicate that the complex is more ordered than the reactants [5]. The value of  $\Delta^\ddagger S$  is within the range of those expected for radical reactions and has been ascribed to the nature of the electron pairing and unpairing process and to the loss of degree of freedom formerly available to the reactants upon formation of a rigid transition state [26]. The observed modest enthalpy of activation as well as the high value of the rate constant of the slow step indicates that the oxidation presumably occurs via an inner-sphere mechanism. This conclusion is supported by the literature [27].

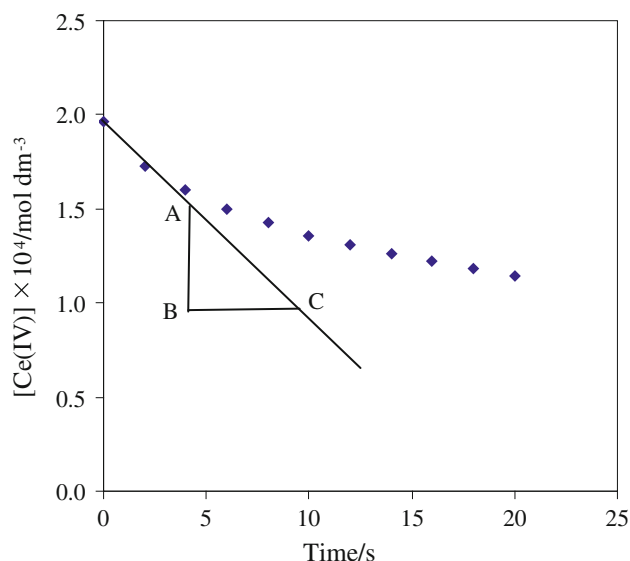
## Conclusion

The reaction is immeasurably slow in perchloric acid at room temperature. However, the reaction is facile in the presence of micro-amounts ( $10^6 \text{ mol dm}^{-3}$ ) of manganese(II). Manganese(II)-catalyzed cerium(IV) oxidation of thiamine hydrochloride (TH) in perchloric acid has a reductant to oxidant stoichiometry of 1:3. The order with respect to both oxidant and catalyst is found to be unity, whereas the order with respect to substrate is less than unity. The products were identified by UV-Vis, GC-MS, IR, and  $^1\text{H}$  NMR spectra. The added product cerium(III) retards the rate of reaction. The active species of oxidant and catalyst are  $[\text{Ce}(\text{OH})^{3+}]$  and  $[\text{Mn}(\text{H}_2\text{O}_4)]^{2+}$ , respectively. The decomposition of the complex is the slow step in the reaction mechanism and is followed by fast steps to give the products.

## Experimental

The solutions were prepared in doubly distilled water and reagent grade chemicals were used. The stock solution of the oxidant cerium(IV) was obtained by dissolving cerium(IV) ammonium sulfate (E. Merck) in  $1.0 \text{ mol dm}^{-3}$  of  $\text{H}_2\text{SO}_4$  and standardized with iron(II) ammonium sulfate solution [28]. A stock solution of TH (HIMEDIA) was prepared by dissolving TH in distilled water. Manganese(II) stock solution was made by dissolving a known weight of  $\text{MnSO}_4$  (sd fine-chem Ltd.) in distilled water. Acetic acid and perchloric acid were obtained from Glaxo Excelar. The former was purified by refluxing with potassium permanganate for 5–6 h and then distilling; a further distillation yielded the fraction of b.p.  $118^\circ\text{C}$  for use. Cerium(III) solution was prepared by dissolving cerium(III) sulfate (BDH) in water. Sodium perchlorate and perchloric acid were used to provide the required ionic strength and acidity, respectively. Sodium perchlorate was prepared by mixing equal volumes of sodium hydroxide and perchloric acid and neutralizing to pH 7.0.

For kinetic measurements a UV-Vis spectrophotometer (Varian CARY 50 Bio) connected to a rapid kinetic accessory (HI-TECH SFA-12) was used. For product analysis, GC-MS data was obtained on a Shimadzu 17A gas chromatograph with a Shimadzu QP-5050A mass spectrometer using EI ionization, IR spectral data was obtained on a Nicolet 5700-FT-IR spectrometer (Thermo, USA),  $^1\text{H}$  NMR data was obtained on a Bruker 300 MHz spectrometer, and for pH measurements an Elico pH meter model LI120 was used.



**Fig. 4** Plot of cerium(IV) concentration vs. time at  $25^\circ\text{C}$



## Kinetic measurements

All kinetic runs were carried out under pseudo-first-order conditions where TH concentration was in excess over cerium(IV) concentration at a constant temperature of  $25 \pm 0.1$  °C. The thermally equilibrated solution of cerium(IV) and TH also contained the required quantities of

perchloric acid, sodium perchlorate, and manganese(II) catalyst because the initial reaction was too fast to be monitored by usual methods. The course of the reaction was followed by monitoring the decrease in absorbance of cerium(IV) in a 1-cm quartz cell placed in the thermostated compartment of a the UV-Vis spectrophotometer at its absorption maximum of 360 nm as a function of time. The

Scheme 3

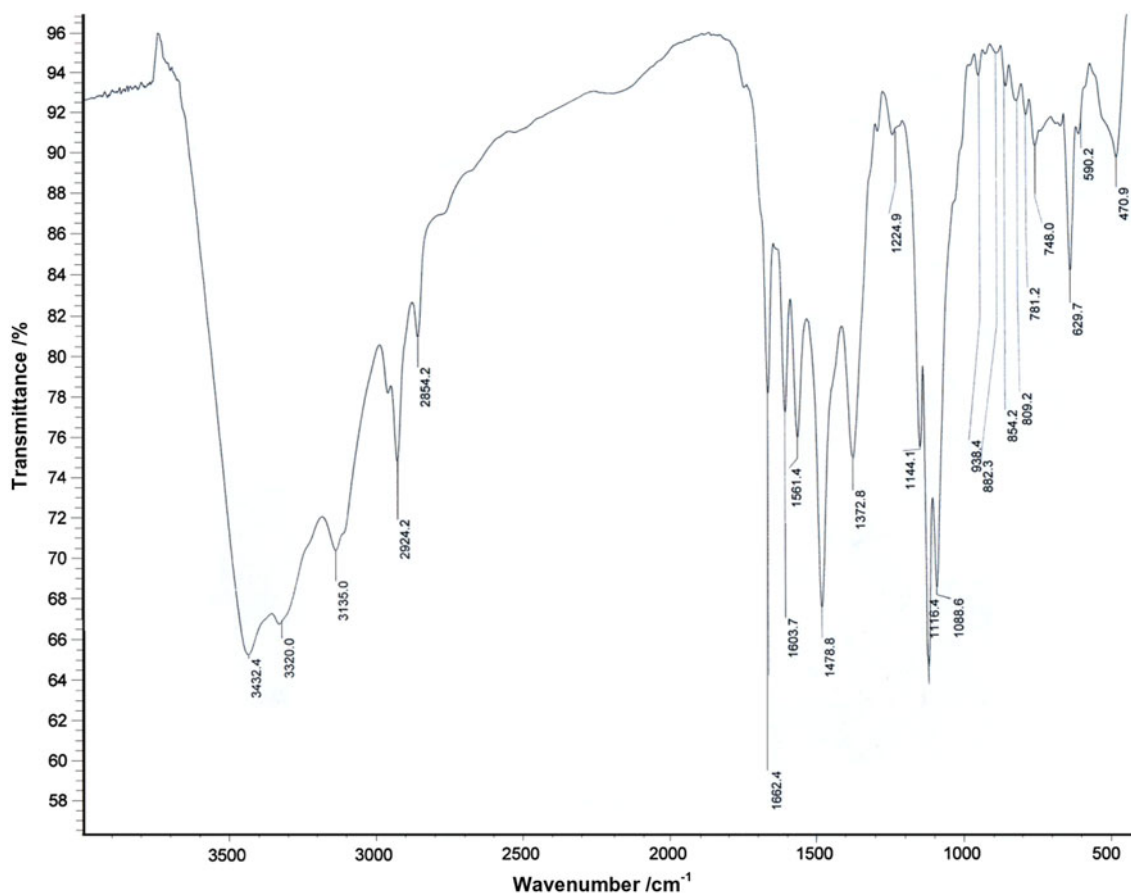
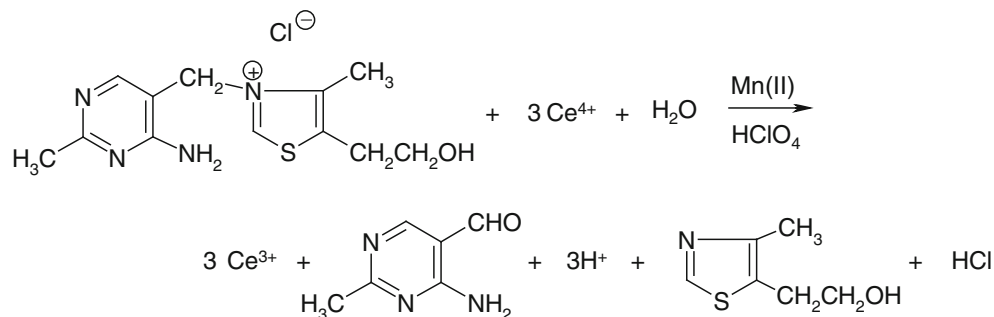


Fig. 5 IR spectra of the product 4-amino-2-methylpyrimidine-5-carbaldehyde

perchloric acid and sodium perchlorate provide the required acidity and ionic strength in the reaction medium. The application of Beer's law under the reaction conditions had been verified at 360 nm in 1.0 mol dm<sup>-3</sup> perchloric acid. The molar absorptivity index of cerium(IV) at 360 nm was found to be  $\epsilon = 3,500 \pm 50 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ . In the present study one of the products cerium(III) retards the reaction; hence, initial rates were determined from a plot of [cerium(IV)] vs. time (Fig. 4) by employing the plane mirror method [29, 30]. The initial rates (rate)<sub>c</sub> obtained were reproducible within  $\pm 5 \%$  and are the average of at least four independent kinetic runs.

#### Stoichiometry and product analysis

Different reaction mixtures with different sets of concentrations of reactants, where cerium(IV) concentration was in excess over TH concentration, at constant ionic strength, acidity, and at constant concentrations of catalyst were kept

for 8 h at room temperature in an inert atmosphere. The unreacted cerium(IV) concentration was assayed by measuring the absorbance at 360 nm. The products were identified and confirmed by UV-Vis, IR, GC-MS, and <sup>1</sup>H NMR spectra as cerium(III), 4-amino-2-methylpyrimidine-5-carbaldehyde, and 2-(4-methylthiazol-5-yl)ethanol. The results showed that 2-methylpyrimidine-5-carbaldehyde was a major product in the reaction. The results indicate that 1 mole of TH reacted with 3 moles of cerium(IV) according to Scheme 3.

The product cerium(III) was confirmed by UV-Vis spectra at 230–260 nm. The products 4-amino-2-methylpyrimidine-5-carbaldehyde and 2-(4-methylthiazol-5-yl)ethanol were identified by spot tests [31]. 4-Amino-2-methylpyrimidine-5-carbaldehyde was identified by IR spectra owing to the presence of the C=O stretch at 1,662 cm<sup>-1</sup> and -NH<sub>2</sub> stretch at 3,432 cm<sup>-1</sup> (Fig. 5). 4-Amino-2-methylpyrimidine-5-carbaldehyde and 2-(4-methylthiazol-5-yl)ethanol were confirmed by GC-MS

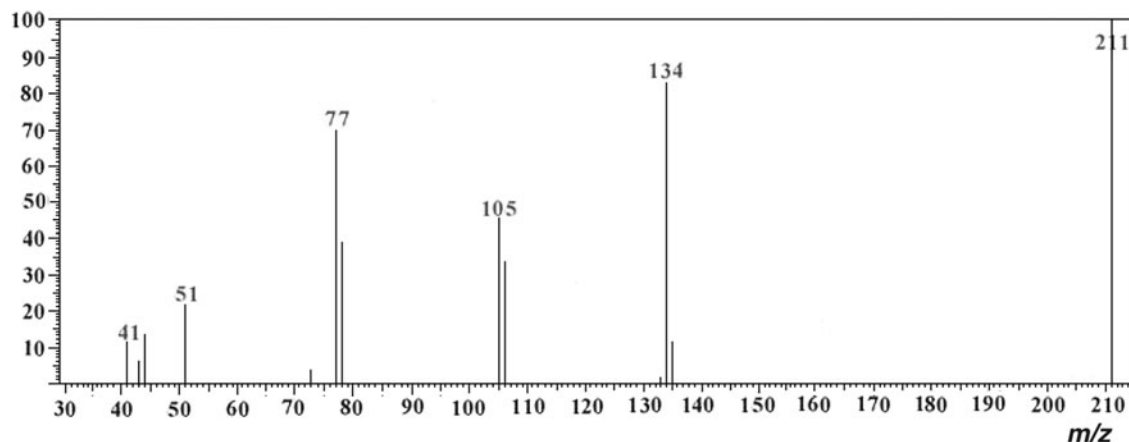
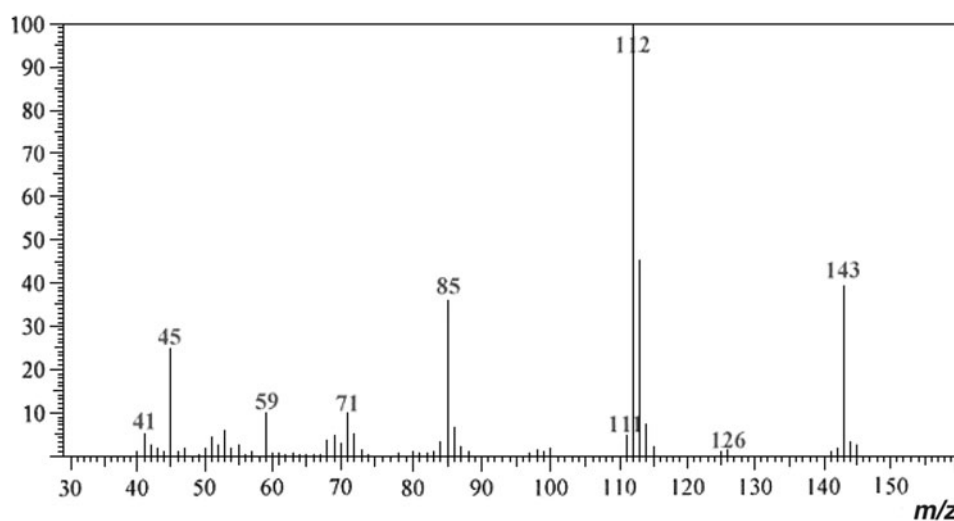


Fig. 6 GC-MS spectra of the product 4-amino-2-methylpyrimidine-5-carbaldehyde

Fig. 7 GC-MS spectra of the product 2-(4-methylthiazole-5-yl)ethanol



spectra owing to the presence of molecular ion peaks at 134 amu (Fig. 6) and 143 amu (Fig. 7), respectively. All other peaks in the GC–MS spectra were consistent with the observed structures. 4-Amino-2-methylpyrimidine-5-carbaldehyde was also confirmed by  $^1\text{H}$  NMR spectra, which were recorded on a Bruker 300 MHz spectrometer using  $\text{DMSO-}d_6$  as solvent and TMS as internal reference. The product showed a singlet at  $\delta = 2.34$  ppm accounting for the three protons of the methyl group at position 2. The amine group appeared as a broad singlet ( $\text{D}_2\text{O}$  exchanged) at 5.33 ppm. The proton at the 6-position and the aldehyde proton appeared as singlets at 8.06 and 9.46 ppm, respectively.

## References

1. Dougherty HW, Pollak PI (1970) Medicinal chemistry, 3rd edn. Wiley-Interscience, New York 30
2. Waldenlind I (1978) Acta Physiol Scand 1:459
3. Marcus R, Coulsfon AM (1991) The pharmacological basis of therapeutics, 8th edn. Pergamon press, New York, Chap 63
4. Day MC, Selbin J (1964) Theoretical inorganic chemistry. Reinhold, New York, p 226
5. Patil RK, Chimatadar SA, Nandibewoor ST (2008) Transit Met Chem 33:625
6. Thabaj KA, Chimatadar SA, Nandibewoor ST (2007) Transit Met Chem 32:902
7. Kharzeoua SE, Senebrennikou VV (1967) Russ J Inorg Chem 12:1601
8. Hardwick TJ, Robertson E (1951) Can J Chem 29:818
9. Datt N, Nagori RR, Meharotra RN (1986) Can J Chem 64:19
10. Baker FB, Newton TW, Khan M (1960) J Phys Chem 64:109
11. Guilbault GG, McCurdy WH Jr (1963) J Phys Chem 67:283
12. Carroll RL, Thomas LB (1966) J Am Chem Soc 88:1376
13. Garger G, Barger F, Todd AR (1935) Nature 136:259
14. Jaronsanti J, Panijan B (1981) Experientia 37:248
15. Kawasaki C, Horio TJ (1954) Pharm Soc Jpn 74:904
16. Mohana KN, Prasad N, Rai KML (2008) Monatsh Chem 139:1203
17. Gamsjäger H, Lorimer JW, Scharlin P, Shaw DG (2008) Pure Appl Chem 80:233
18. Byadagi KS, Naik DV, Savanur AP, Nandibewoor ST, Chimatadar SA (2010) Reac Kinet Mech Cat 99:53
19. Sengupta KK, Aditya S, Ghosh BN (1963) J Indian Chem Soc 40:1823
20. McCurdy WH Jr, Guilbault GG (1960) J Phys Chem 64:1825
21. Dikshitulu LSA, Hanumantaroo DSN (1981) Indian J Chem 20A:784
22. Chimatadar SA, Madawale SV, Nandibewoor ST (2007) Transit Met Chem 32:634
23. Savanur AP, Nandibewoor ST, Chimatadar SA (2009) Transit Met Chem 34:711
24. Amis ES (1996) Solvent effects on reaction rates and mechanism. Academic, New York
25. Entelis SG, Tiger RP (1976) Reaction kinetics in the liquid phase. Wiley, New York
26. Walling C (1976) Free radicals in solutions. Academic, New York, p 38
27. Farokhi SA, Nandibewoor ST (2003) Tetrahedron 59:7595
28. Jeffery GH, Bassett J, Mendham J (2002) Vogel's textbook of quantitative chemical analysis, 6th edn. Longman, Essex, p 426
29. Laidler KJ (1975) Chemical kinetics, 2nd edn. McGraw-Hill, New Delhi, p 16
30. Casado J, Lopez-Quintella MA, Lorenzo-Barral FM (1986) J Chem Educ 63:450
31. Feigl F (1975) Spot tests in organic analysis. Elsevier, New York, p 435