



**OXIDATION OF 2-AMINO-4-(METHYLTHIO) BUTANOIC ACID BY  
BENZIMIDAZOLIUM FLUOROCHROMATE IN AQUEOUS ACETIC ACID MEDIUM**

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**ABSTRACT**

The oxidation of 2-amino-4-(methylthio) butanoic acid by benzimidazolium fluorochromate (BIFC) were studied in aqueous acetic acid medium in the presence of perchloric acid. The reaction is first order with respect to BIFC and fractional order dependence with respect to methionine and perchloric acid concentrations. The reaction rate were determined at different temperatures and the activation parameters were computed. The reaction rate decreases with increasing mole fraction of acetic acid in the mixture and specific solvent-solvent-solute interactions were found to predominate. From Kamlet-Taft LSER equation a suitable solvation model also proposed for this oxidation reaction.

**KEYWORDS:** Kinetics, oxidation, 2-amino-4-(methylthio) butanoic acid, chromium (VI).

**INTRODUCTION**

Extensive studies on the mechanism of the oxidation of 2-amino-4-(methylthio)butanoic acid (Met) with several oxidants have been reported.<sup>[1-7]</sup> The sulfur containing essential amino acid is reported to behave differently in comparison to other amino acids towards many oxidants.<sup>[8]</sup> This may well be due to the presence of an electron rich sulfur center, which is easily oxidisable.<sup>[8]</sup> Variety of new chromium(VI) oxidants together with special reaction conditions have been introduced for the chemospecific, regiospecific and stereospecific oxidative degeneration of functional groups in highly sensitive systems.<sup>[9-11]</sup> Benzimidazolium fluorochromate is also one such a recently developed Cr(VI) oxidant<sup>[12]</sup> which is mild, stable and selective oxidant.

In this paper, the kinetics of oxidation of 2-amino-4-(methylthio)butanoic acid by BIFC in aqueous acetic acid mixtures of varying molar compositions are reported. The main aims of this study were to determine mechanism and rate law of the reaction, identify the reactive species and product of this reaction. The observed kinetic results also used to propose a suitable solvation model for this reaction.

**EXPERIMENTAL**

BIFC was prepared by the method described in the literature.<sup>[12]</sup> 2-amino-4-(methylthio)butanoic acid (Loba Chemic), 2,2'-bipyridyl, 1,10-phenanthroline, imidazole (E-merck) and oxalic acid (Qualigens) were used as supplied without further purification and the other

chemicals used in this experiment are all of the AnalaR grade samples.

**Kinetic procedure**

The reaction were performed in aqueous acetic acid medium under pseudo first order conditions (2-amino-4-(methylthio)butanoic acid  $\gg$  Cr(VI)). The progress of the reaction was monitored for at least two half lives by iodometric estimation of unchanged oxidant at regular time intervals. The pseudo-first order rate constant were calculated from the slope of linear plots of log titre *versus* time.

**Products analysis and stoichiometry**

Product analysis was carried out under kinetic conditions. The reaction mixture was allowed to stand for 2 hrs at 30°C, thereafter some sodium bicarbonate was added and the solution was stirred vigorously, followed by the dropwise addition of benzoyl chloride solution until precipitation was completed. The precipitate obtained was identified as benzoyl 2-amino-4-(methylthio)butanoic acid sulphoxide (m.p 183°C) a derivative of 2-amino-4-(methylthio)butanoic acid sulfoxide.<sup>[13]</sup> The formation of the product further confirmed by IR spectrum with a band appeared at 1056  $\text{cm}^{-1}$  ( $>\text{S}=\text{O}$  str band).

The stoichiometry of the reaction was determined by performing the experiment under the conditions of  $[\text{BIFC}] > [\text{Met}]$ . The disappearance of BIFC was monitored until constant titre values were obtained. The

estimation of unreacted oxidant shows that one mole of 2-amino-4-(methylthio)butanoic acid consumed by one mole of BIFC.

## RESULTS AND DISCUSSION

All the oxidation reactions were carried out under pseudo-first order conditions with at least to ten-fold excess of methionine (Met) over [Cr(VI)]. The pseudo-first order rate constants ( $k_{obs}$ ) were given in Table-I. The reaction rate increased linearly with increasing the concentration of Met. The plots of  $\log k_{obs}$  versus  $\log$  [Met] and  $1/k_{obs}$  versus  $1/[Met]$  shows that this oxidation reaction follows Michaelis-Menton type of kinetics. The reaction is catalysed by  $H^+$  ions and the order with respect to  $[H^+]$  is non integral. Addition of  $NaClO_4$  shows the positive salt effect indicating the participation ionic species in the mechanistic path.<sup>[14]</sup>

The added  $Mn^{2+}$  shows a catalytic influence.<sup>[3]</sup> To verify the formation of radicals as intermediates, a free radical scavenger, acrylonitrile (2% aqueous solution) was added in the reaction mixture. No turbidity was developed. Further acrylonitrile had no perceptible effect on the rates show in Table-II rules out a free radical process.

There are different chelating agents<sup>[15-19]</sup> to catalyze the chromium(VI) oxidation of organic substrates. These chelating agents can form a reactive complex with Cr(VI).<sup>[20]</sup> This complex increase the electrophilic activity of the oxidant and thereby enhance the reactivity.<sup>[21]</sup>

To know the catalytic efficiency of chelating agents *viz.*, 1,10-phenanthroline, oxalic acid, 2,2'-bipyridyl and imidazole, the title reaction is carried out in the presence of chelating agents and the rates were given in Table-III.

More pronounced activity in the presence of 1,10-phenanthroline as a catalyst is observed. This may probably due to the formation of more reactive electrophile in between oxidant and 1,10-phenanthroline and the corresponding transition state is well stabilized. The least rate benefit is associated with imidazole.

The temperature dependence of the oxidation of methionine was studied and the activation parameters were evaluated using an Eyring's plot of  $\ln k_{obs}/T$  versus  $1/T$  and the values are

$$\Delta H^\ddagger = 34.22 \text{ kJ mol}^{-1}; \quad \Delta S^\ddagger = -200.87 \text{ J K}^{-1} \text{ mol}^{-1}$$

( $r = 0.991$ ;  $sd = 0.04$ )

### Effect of solvent

The influence of the solvent on the rate of oxidation of 2-amino-4-(methylthio)butanoic acid by BIFC was studied in water-organic solvent mixtures with different mole fractions of the organic co-solvent, *viz.*, acetic acid. The results in Table-IV indicated that the rate constants is remarkably sensitive to the composition of the mixed solvent. The rate constant decreases with increasing mole

fraction of acetic acid in the mixture. The influence of the relative permittivity ( $\epsilon_r$ ) of a solvent on the rate can be described by the equation of Laidler and Eyring.<sup>[21]</sup> A plot of  $\log k_{obs}$  versus  $1/\epsilon_r$  is linear ( $r = 0.976$ ,  $sd = 0.054$ ).

The effect of solvent on reactivity may also be understood from the standpoint of specific and non-specific solvation effects. The specific solute-solvent interactions are short range interactions and are chemical in nature. The intensity of non-specific interactions are measured in terms of bulk solvent parameters like relative permittivity ( $\epsilon_r$ ) and polarizability power ( $\pi^*$ ). This kind of dual dependency of reactivity on the solvent composition is illustrated by the Kamlet-Taft solvatochromic comparison method.<sup>[22]</sup> This method may be used to quantify, correlate and rationalize multiple interaction of solvent effects on reactivity. Thus the rate data were correlated with the solvatochromic parameters in the form of the following LSER equation.

$$\log k = A_0 + S\pi^* + a\alpha + b\beta$$

Where  $\pi^*$  is the measures of ability of the solvent to stabilize a charge by virtue of its dielectric effect,  $\alpha$  is the solvent hydrogen bond donor acidity (HBD) and  $\beta$  is the solvent hydrogen bond acceptor basicity (HBA) in a solute to solvent hydrogen bond. The regression coefficients  $S$ ,  $a$  and  $b$  measure the relative susceptibilities of the solvent dependent solute property. Solvatochromic parameters for the solvent mixtures used in the present study were taken from the literature.<sup>[23,24]</sup>

The rate of oxidation in the solvent mixture studied show satisfactory correlations with solvent *via* this LSER equation and the correlation results obtained are given below.

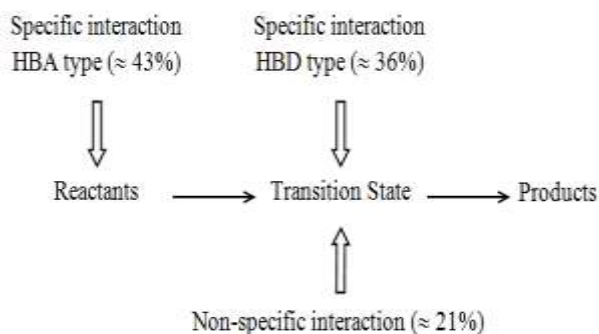
$$\log k_{obs} = -8.38 + 2.57 \pi^* + 4.43 \alpha - 5.44 \beta$$

( $P_\alpha = 36\%$ ,  $P_\beta = 43\%$  and  $P_{\pi^*} = 21\%$ )  
( $R = 0.977$ ,  $sd = 0.07$ )

From the above multiple correlation results, the following conclusions were obtained.

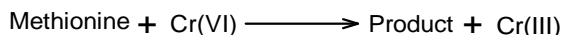
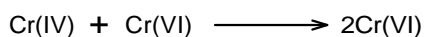
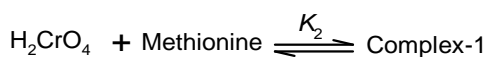
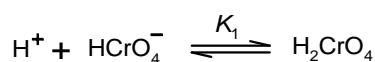
- (i) The rate of reaction is strongly influenced by specific solute-solvent interactions (79%).
- (ii) The positive sign of the coefficient  $\alpha$  suggest that the specific interaction is existing between transition state and the solvent molecules through hydrogen bond donor (HBD) acidity properties.
- (iii) The negative sign of the coefficient  $\beta$  term suggest that the specific interaction is existing between reactant and the solvent molecules through hydrogen bond acceptor (HBA) basicity properties.
- (iv) The solvent dipolarity/polarizability ( $\pi^*$ ) plays a minor role only.

Considering the above results, the following solvation model was proposed.



### Mechanism and Rate law

From the observed kinetic results the following mechanism was proposed. In the Cr(VI) oxidation reactions, the effective oxidizing species is  $\text{HCrO}_4^-$ .<sup>[20]</sup> This  $\text{HCrO}_4^-$  protonates in an equilibrium step to give  $\text{H}_2\text{CrO}_4$ . Further  $\text{H}_2\text{CrO}_4$  associated with methionine molecule to give a binary complex ( $C_1$ ), then this complex ( $C_1$ ) dissociates to yield the product 2-amino-4-(methylthio)butanoic acid sulphoxide in the slow and rate-determining step.



The proposed mechanism was substantiated by the following rate law

$$\text{Rate} = \frac{-d[\text{Cr(VI)}]}{dt} = \frac{K_1 K_2 k_3 [\text{methionine}] [\text{H}^+] [\text{Cr(VI)}]}{\{1 + K_1 [\text{H}^+]\} \{1 + K_2 [\text{methionine}]\}}$$

Observation of high negative entropy values indicates the formation of more ordered binary complex ( $C_1$ ). Michaelis-Menton type of kinetics observed with respect to Met suggesting, dissociation of complex-1 to yield the product in the rate-determining step.

**Table I: Effect of variation of [BIFC], [MET],  $[\text{H}^+]$  and temperature on reaction rates.**

Solvent: AcOH-H<sub>2</sub>O (50% v/v); Temp: 308K.

[BIFC] $10^3$ (mol dm <sup>-3</sup> )	[MET] $10^2$ (mol dm <sup>-3</sup> )	[H <sup>+</sup> ] $10^5$ (mol dm <sup>-3</sup> )	$k_{obs} \times 10^4$ (s <sup>-1</sup> )
0.75	2.00	5.00	3.36
1.00	2.00	5.00	3.42
1.25	2.00	5.00	3.66
1.50	2.00	5.00	3.84
1.75	2.00	5.00	3.17
1.00	1.00	5.00	1.95
1.00	1.50	5.00	2.69
1.00	2.50	5.00	3.98
1.00	3.00	5.00	4.68
1.00	3.50	5.00	4.97
1.00	4.00	5.00	5.48
1.00	4.50	5.00	6.11
1.00	5.00	5.00	6.88
1.00	2.00	2.50	2.52
1.00	2.00	10.00	4.17
1.00	2.00	15.00	4.68
1.00	2.00	20.00	4.69
1.00	2.00	25.00	5.30
1.00	2.00	5.00	2.52 <sup>a</sup>
1.00	2.00	5.00	4.21 <sup>b</sup>
1.00	2.00	5.00	5.05 <sup>c</sup>

a = 303 K, b = 313 K, c = 318 K

**Table II: Effect of variation of  $[\text{MnSO}_4]$ ,  $[\text{NaClO}_4]$  and [acrylonitrile].**

$[\text{BIFC}] = 1.00 \times 10^{-3}$  mol dm<sup>-3</sup>,  $[\text{Met}] = 2.00 \times 10^{-2}$  mol dm<sup>-3</sup>, AcOH-H<sub>2</sub>O = 50-50 (v/v)

$[\text{HClO}_4] = 5.00 \times 10^{-5}$  mol dm<sup>-3</sup>, Temperature = 308 K

$[\text{MnSO}_4] 10^4$ (mol dm <sup>-3</sup> )	$[\text{NaClO}_4] 10^2$ (mol dm <sup>-3</sup> )	$[\text{Acrylonitrile}] 10^4$ (mol dm <sup>-3</sup> )	$k_{obs} \times 10^4$ (s <sup>-1</sup> )
0	–	–	3.42
2.50	–	–	3.55
5.00	–	–	3.97
7.50	–	–	4.41
10.00	–	–	4.89
–	0	–	3.42
–	2.50	–	3.50
–	5.00	–	3.90
–	7.50	–	4.02
–	10.00	–	4.22
–	–	0	3.42
–	–	2.50	3.35
–	–	5.00	3.36
–	–	7.50	3.55
–	–	10.00	3.34

**Table III: Comparison of catalytic coefficients of various chelating agents.**

[BIFC] =  $1.00 \times 10^{-3}$  mol dm<sup>-3</sup>, [Met] =  $2.00 \times 10^{-2}$  mol dm<sup>-3</sup>, AcOH-H<sub>2</sub>O = 50-50 (v/v),  
 [HClO<sub>4</sub>] =  $5.00 \times 10^{-5}$  mol dm<sup>-3</sup>, Temperature = 308 K, [chelating agent]  
 (frequency agent =  $3.50 \times 10^{-3}$  mol dm<sup>-3</sup>)

Catalyst	–	1,10-Phenanthroline	Oxalic acid	Bipyridyl	Imidazole
$10^4 k_{\text{obs}}$ (s <sup>-1</sup> )	0.82	5.32	3.84	3.13	1.80
Rate benefit <sup>a</sup>	–	5.40	3.68	2.82	1.10

$$^a \text{Rate benefit} = \frac{k_{\text{catalysed}} - k_{\text{uncatalysed}}}{k_{\text{uncatalysed}}}$$

**Table IV: Effect of added acetic acid on the oxidation of 2-amino-4-(methylthio)butanoic acid by BIFC at 308 K.**

[BIFC] =  $1.00 \times 10^{-3}$  mol dm<sup>-3</sup>, [Met] =  $2.00 \times 10^{-2}$  mol dm<sup>-3</sup>, [HClO<sub>4</sub>] =  $5.00 \times 10^{-5}$  mol dm<sup>-3</sup>, Temperature = 308 K

Mole fraction of AcOH	0.52	0.70	0.79	0.87	0.96	1.04	1.13	1.22	1.31	1.39
$10^4 k_{\text{obs}}$ (s <sup>-1</sup> )	5.37	4.15	3.85	3.42	3.39	2.39	1.86	1.67	1.53	0.95

## CONCLUSION

The oxidation of 2-amino-4-(methylthio)butanoic acid by BIFC is first order with respect to BIFC and non-integral kinetic order is observed with respect to Met, H<sup>+</sup> concentrations. Kinetic studies demonstrate that Cr(VI)-Met binary complex decomposes in a slow and rate-determining step to give 2-amino-4-(methylthio)butanoic acid sulphoxide as the main product. 1,10-Phenanthroline is used as a most effective catalyst in this conversion. From the Kamlet and Taft LSER regression studies, information on the solvent-reactant and the solvent-transition state interactions is obtained and a suitable solvation model also proposed for this oxidation studies.

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