

Kinetics and Mechanism of the Oxidation of DL-Methionine by Imidazolium Dichromate

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ABSTRACT

The oxidation of methionine (Met) by Imidazolium Dichromate (IDC) in dimethylsulphoxide (DMSO) leads to the formation of corresponding sulphoxide compounds. The reaction is found to be first order with respect to IDC. Michaelis-Menten type of kinetics was observed with respect to methionine. The reaction is catalyzed by hydrogen ions. The hydrogen-ion dependence has the form: $k_{obs} = a + b [H^+]$. The oxidation reaction of methionine was studied in nineteen different organic solvents. The solvent effect was studied by using Kamlet's and Swain's multiparametric equations. Solvent effect indicated the importance of the cation-solvating power of the solvent. A suitable mechanism has been proposed.

Keywords: Kinetics, Mechanism, Methionine, Dichromate, Oxidation.

INTRODUCTION

Selective oxidation of organic compounds under non-aqueous conditions is an important reaction in synthetic organic chemistry. For that purpose, a number of different chromium (VI) derivatives have been reported¹⁻³. One of such compounds is Imidazolium Dichromate (IDC)⁴. We have been interested in the kinetic and mechanistic aspects of the oxidation by Cr (VI) species and several reports by halochromates and dichromates have already been reported.⁵⁻¹⁰

It is, known however, that mode of oxidation depends upon the nature of counter-ion attached to the chromium anion. Methionine (Met), a sulphur-containing essential amino acid, is reported to behave differently from other amino acids, towards many oxidants^{11,12}, due to electron-rich sulphur center which is easily oxidisable. There seems to be no report available on the oxidation of methionine by IDC. We report here the kinetics of oxidation of DL-methionine by IDC in dimethylsulphoxide (DMSO) as solvent. A suitable mechanism has also been proposed.

EXPERIMENTAL

Materials:

IDC was prepared by the reported method⁴ and its purity checked by an iodometric method. Methionine (Merck) was used as supplied. Due to non-aqueous nature of the solvent, *p*-toluene sulphonic acid (TsOH) was used as a source of hydrogen ions. Purification of other solvents were carried out by the usual methods of purification¹³.

Product Analysis:

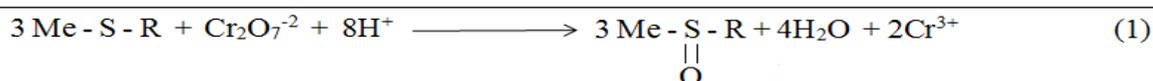
Product analysis was carried out under kinetic conditions. The oxidation of Met by IDC resulted in the formation of corresponding sulphoxide, which was determined by the reported method¹⁴. The yield of sulphoxide was 91%. The oxidation state of chromium in completely reduced reaction mixtures, as determined iodometrically, was +4.

Kinetic measurements:

The pseudo-first order conditions were attained by maintaining a large excess ($\times 10$ or more) of the Met over IDC. The solvent used was DMSO, unless specified otherwise. The reactions were followed, at constant temperatures (± 0.1 K), by monitoring the decrease in [IDC] spectrophotometrically at 355 nm. No other reactant or product has any significant absorption at this wavelength. The pseudo-first order rate constant, k_{obs} , was evaluated from the linear ($r = 0.990 - 0.999$) plots of $\log [IDC]$ against time for up to 80% reaction. Duplicate kinetic runs showed that, the rate constants were reproducible to within $\pm 3\%$. All experiments, other than those for studying the effect of hydrogen ions, were carried out in the absence of TsOH. The second order rate constant, k_2 , was evaluated from the relation shown by formula $k_2 = k_{obs} / [Met]$. Simple and multivariate linear regression analyses were carried out by the least-squares method on a personal computer by using software RegressIt.

RESULTS AND DISCUSSION**Stoichiometry:**

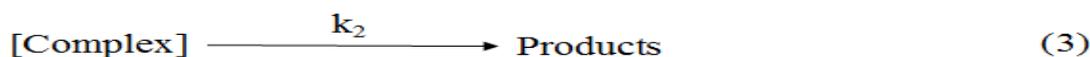
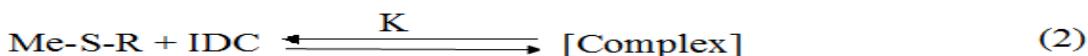
The oxidation of methionine by IDC resulted in the formation of the corresponding sulfoxides. The overall reaction may therefore, be represented as equation (1).



Where R is $\text{CH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{COOH}$

Rate Laws: The reactions were found to be first order with respect to IDC (**Figure 1**). In individual kinetic runs, plots of $\log [\text{IDC}]$ versus time were linear ($r^2 > 0.995$). Further, it was found that the observed rate constant, k_{obs} , does not depend on the initial concentration of IDC. The order with respect to methionine was less than one (**Table-1**). A plot of $1/k_{\text{obs}}$ versus $1/[\text{Met}]$ was linear with an intercept on the rate ordinate (**Figure 2**).

Thus Michaelis-Menten type of kinetics was observed with respect to Met. This leads to the postulation of following overall mechanism (equations 2 and 3) and the rate law (4).



$$\text{Rate} = k_2 K [\text{Me-S-R}] [\text{IDC}] / (1 + K [\text{Me-S-R}]) \quad (4)$$

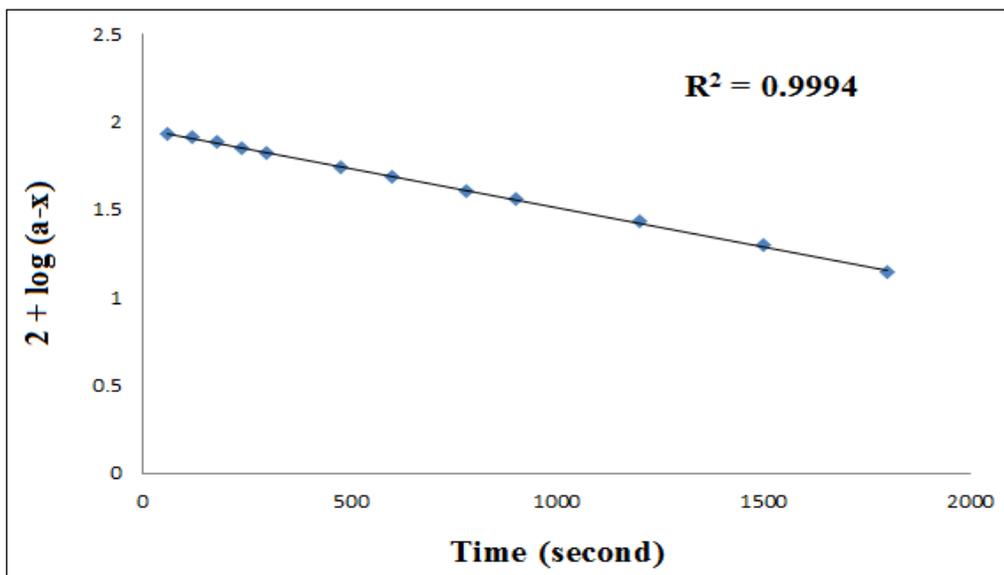


Figure 1: Oxidation of Methionine by IDC: A typical Kinetic Run.

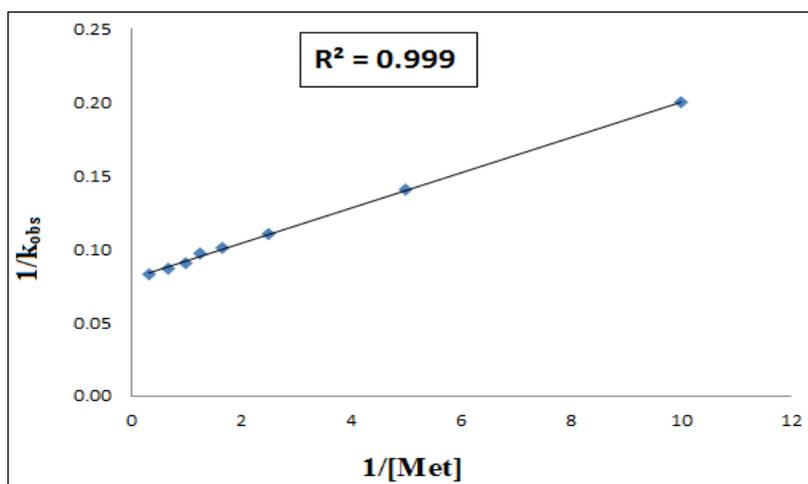
The dependence of k_{obs} on the concentration of methionine was studied at different temperatures and the values of K and k_2 were evaluated from the double reciprocal plots. The thermodynamic parameters of the complex formation and activation parameters of the decomposition of the complexes were calculated from the values of K and k_2 respectively at different temperatures (**Tables-3 and 4**).

Test for free radicals:

The oxidation of Met, in an atmosphere of nitrogen, failed to induce the polymerization of acrylonitrile. Further, the addition of acrylonitrile had no effect on the rate of oxidation (**Table-1**). Therefore, a one-electron oxidation, giving rise to free radicals, is unlikely. To further confirm the absence of free radicals in the reaction pathway, the reaction was carried out in the presence of 0.05 mol dm^{-3} of 2, 6-di-*t*-butyl-4-methylphenol (butylated hydroxytoluene or BHT). It was observed that, BHT was recovered unchanged, almost quantitatively.

Table-1: Rate constants for the oxidation of methionine by IDC at 298 K.

10^3 [IDC] ----- (mol dm ⁻³)	[Met] ----- (mol dm ⁻³)	[TsOH] ----- (mol dm ⁻³)	$10^4 k_{obs}$ ----- s ⁻¹
1.0	0.10	0.00	5.00
1.0	0.20	0.00	7.10
1.0	0.40	0.00	9.06
1.0	0.60	0.00	9.91
1.0	0.80	0.00	10.3
1.0	1.00	0.00	11.0
1.0	1.50	0.00	11.5
1.0	3.00	0.00	12.1
2.0	0.20	0.00	7.18
4.0	0.20	0.00	7.85
6.0	0.20	0.00	6.98
8.0	0.20	0.00	7.74
1.0	0.40	0.00	9.22*
*contained 0.001 M acrylonitrile			

**Figure 2:** Oxidation of Methionine by IDC: A double reciprocal plot.

Effect of acidity: The reaction was studied at different acidities by adding varying amount of p-toluene-sulphonic acid (TsOH) to the reaction mixtures. The reaction is catalyzed by hydrogen ions (**Table-2**). The hydrogen-ion dependence has the form $k_{obs} = a + b [H^+]$. The values for a and b for the oxidation of crotonic acid are $5.175 \pm 0.086 \times 10^{-4} s^{-1}$ and $9.016 \pm 0.141 \times 10^{-4} mol^{-1} dm^3 s^{-1}$ respectively ($r^2 = 0.9996$).

Table-2: Dependence of the reaction rate on hydrogen-ion concentration.

[IDC] = 0.001 mol dm ⁻³ ;	[Met] = 0.1 mol dm ⁻³ ;	Temp. = 298 K				
[TsOH] /mol dm ⁻³	0.10	0.20	0.40	0.60	0.80	1.00
$10^4 k_{obs} /s^{-1}$	6.12	7.01	8.79	10.4	12.5	14.2

Table-3: Formation constants and thermodynamic parameters of the oxidation of IDC-Met complexes.

K (dm ³ mol ⁻¹)				- ΔH*	- ΔS*	- ΔG*	- Eact.
288 K	298 K	308 K	318 K	(KJ mol ⁻¹)	(J mol ⁻¹ K ⁻¹)	(KJ mol ⁻¹)	(KJ mol ⁻¹)
7.35	6.50	5.19	4.20	16.9640	28.6687	6.9905	14.4449

Table-4: Rate constants and activation parameters of the decomposition of IDC-Met complexes.

10 ⁴ k ₂ / (dm ³ mol ⁻¹ s ⁻¹)				ΔH*	- ΔS*	ΔG*	Eact.
288 K	298 K	308 K	318 K	(KJ mol ⁻¹)	(J mol ⁻¹ K ⁻¹)	(KJ mol ⁻¹)	(KJ mol ⁻¹)
7.01	12.9	25.1	49.2	47.0043	-142.1523	90.0798	49.5235

Table-5: Effect of solvents on the oxidation of Methionine by IDC at 308 K.

Solvents	10 ⁴ k ₂ / (dm ³ mol ⁻¹ s ⁻¹)	Solvents	10 ⁴ k ₂ / (dm ³ mol ⁻¹ s ⁻¹)
Chloroform	9.03	Toluene	2.16
1,2-Dichloroethane	10.1	Acetophenone	9.67
Dichloromethane	8.44	THF	3.96
DMSO	25.1	t-Butyl alcohol	4.85
Acetone	7.33	1,4-Dioxane	4.53
DMF	13.6	1,2-Diethoxyethane	2.66
Butanone	5.96	Acetic Acid	5.32
Nitrobenzene	11.1	Ethyl Acetate	3.61
Benzene	2.64	CS ₂	1.32
Cyclohexane	0.33		

Solvent Effect:

The rates of the oxidation of the DL-Methionine were studied in nineteen different organic solvents. The solubility of reagents and reaction of IDC with primary and secondary alcohols limited the choice of solvents. There was no reaction with the solvents chosen for the study. Kinetics was similar in all the solvents. The values of k₂ are recorded in **Table-5**. A perusal of the data shows that the formation constants do not vary much with the nature of the solvents. However, the rate constants, k₂ varied considerably with the solvents. The rate constants, k₂, in eighteen solvents (CS₂ was not considered, as the complete range of solvent parameters was not available for the same) were correlated in terms of the linear solvation energy relationship (5) of Kamlet *et al*¹⁵.

$$\log k_2 = A_0 + p\pi^* + b\beta + a\alpha \quad (5)$$

In this equation, π* represents the solvent polarity, β the hydrogen bond acceptor basicities and α is the hydrogen bond donor acidity. A₀ is the intercept term. It may be mentioned here that out of the 18 solvents, 13 has a value of zero for α. In our correlation analyses, we have used the coefficient of determination (R² or r²), standard deviation (SD) and Exner's statistical parameter¹⁶, ψ, as the measures of the goodness of fit. The results of correlation analyses in terms of equation (5), a biparametric equation involving π* and β, and separately with π* and β are given below by Equations (6) - (9)

$$\log k_2 = -4.40 + 1.53 (\pm 0.15) \pi^* + 0.24 (\pm 0.11) \beta + 0.27 (\pm 0.11) \alpha \quad (6)$$

$$R^2 = 0.898; \text{ SD} = 0.144; n = 18; \psi = 0.32$$

$$\log k_2 = -4.33 + 1.49 (\pm 0.17) \pi^* + 0.21 (\pm 0.13) \beta \quad (7)$$

$$R^2 = 0.855; \text{SD} = 0.165; n = 18; \psi = 0.38$$

$$\log k_2 = -4.29 + 1.55 (\pm 0.17) \pi^* \quad (8)$$

$$r^2 = 0.831; \text{SD} = 0.173; n = 18; \psi = 0.42$$

$$\log k_2 = -3.44 + 0.47 (\pm 0.31) \beta \quad (9)$$

$$r^2 = 0.126; \text{SD} = 0.393; n = 18; \psi = 1.13$$

Here, n is the number of data points. Kamlet's¹⁵ triparametric equation explains *ca.* 89% of the effect of solvent on the oxidation. However, by Exner's criterion¹⁶ the correlation is not even satisfactory (cf. equation 6). The major contribution is of solvent polarity. It alone accounted for *ca.* 83% of the data. Both β and α play relatively minor roles. The data on the solvent effect were analysed in terms of Swain's equation¹⁷ of cation- and anion-solvating concept of the solvents also (equation 10).

$$\log k_2 = aA + bB + C \quad (10)$$

Here, A represents the anion-solvating power of the solvent and B represents the cation-solvating power. C is the intercept term. $(A + B)$ is used to represent the solvent polarity. The rates in different solvents were analysed in terms of equation (10), separately with A and B and with $(A + B)$.

$$\log k_2 = 1.18 (\pm 0.05) A + 1.46 (\pm 0.03) B - 4.57 \quad (11)$$

$$R^2 = 0.992; \text{SD} = 0.041; n = 19; \psi = 0.08$$

$$\log k_2 = 0.98 (\pm 0.47) A - 3.58 \quad (12)$$

$$r^2 = 0.201; \text{SD} = 0.386; n = 19; \psi = 1.05$$

$$\log k_2 = 1.37 (\pm 0.21) B - 4.19 \quad (13)$$

$$r^2 = 0.705; \text{SD} = 0.235; n = 19; \psi = 0.56$$

$$\log k_2 = 1.37 \pm 0.04 (A + B) - 4.57 \quad (14)$$

$$r^2 = 0.986; \text{SD} = 0.052; n = 19; \psi = 0.11$$

The rates of oxidation of DL-Methionine in different solvents showed an excellent correlation in Swain's equation [cf. equation (11)] with the cation-solvating power playing the major role. In fact, the cation-solvation alone accounts for *ca.* 70 % of the data. The correlation with the anion-solvating power somewhat poor.

The solvent polarity, represented by $(A + B)$, also accounted for *ca.* 98 % of the data. In view of the fact that solvent polarity is able to account for *ca.* 98 % of the data, an attempt was made to correlate rate with the relative permittivity of the solvent.

However, a plot of $\log k_2$ against the inverse of the relative permittivity is not linear ($r^2 = 0.621$; $\text{SD} = 0.266$; $\psi = 0.65$).

The observed solvent effect points to a transition state more polar than the reactant state. Further, the formation of a dipolar transition state, similar to those of S_{N}^2 reactions, is indicated by the major role of both anion- and cation-solvating powers.

However, the solvent effect may also be explained assuming that the oxidant and the intermediate complex exist as ion-pair in non-polar solvent like cyclohexane and be considerably dissociated in more polar solvents.

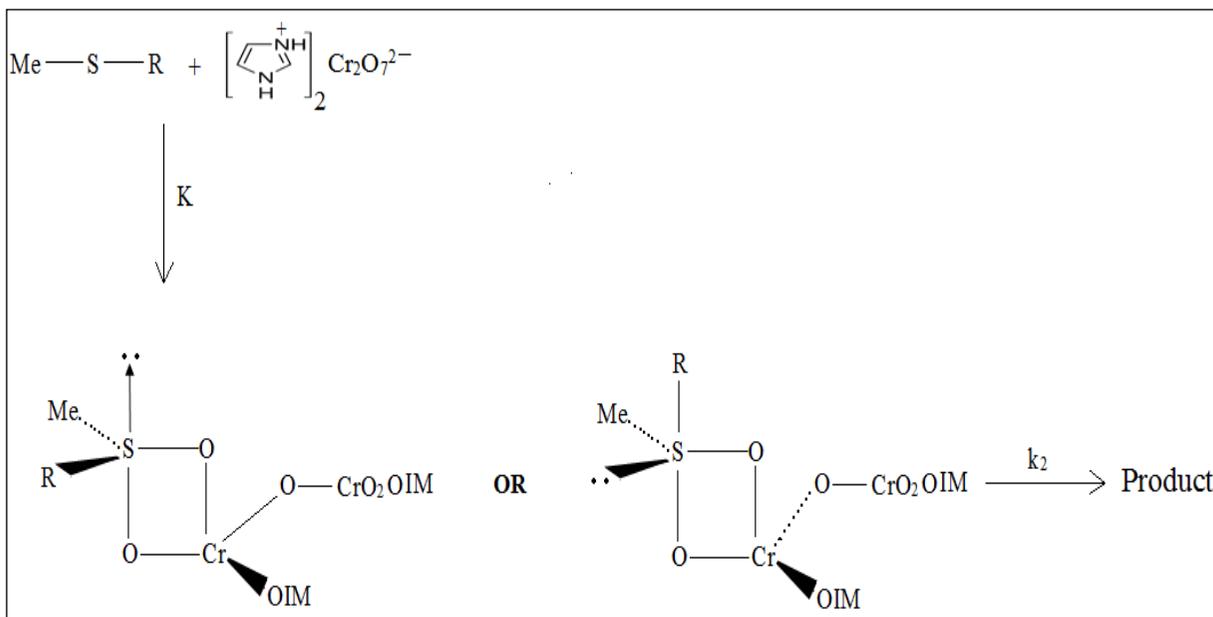
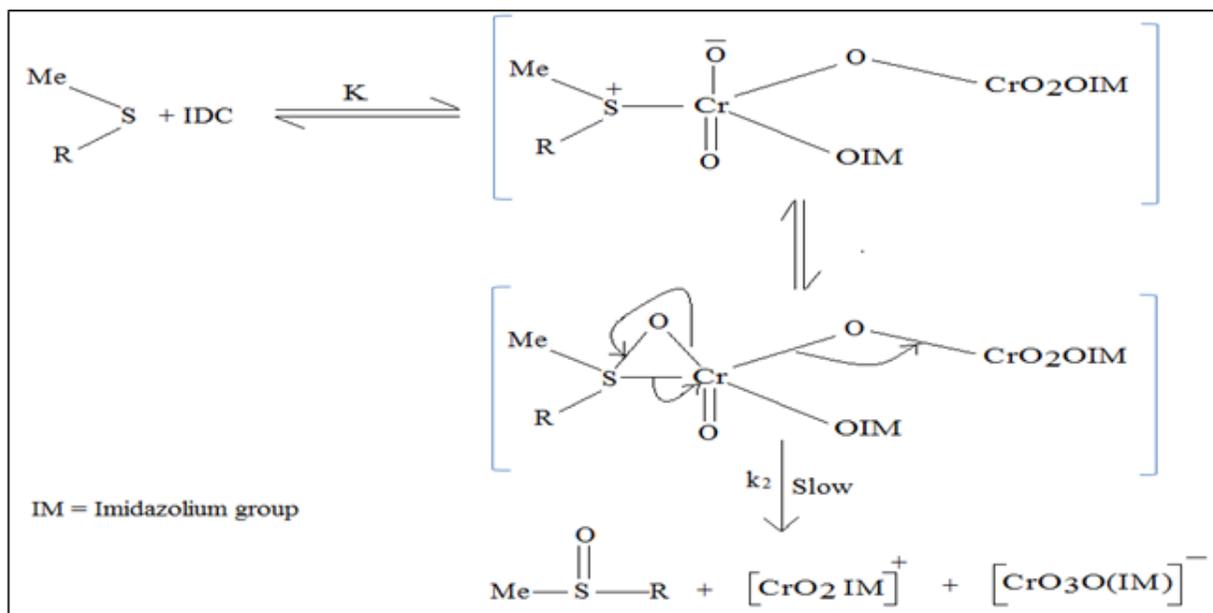
MECHANISM

In view of the absence of any effect of radical scavenger, acrylonitrile, on the reaction rate and recovery of unchanged BHT, it is unlikely that a one-electron oxidation giving rise to free radicals, is operative in this oxidation reaction. The observed Michaelis-Menten type of kinetics observed with respect to methionine, suggests that, there is formation of 1:1 complex of imidazolium dichromate and methionine in a rapid pre-equilibrium (Scheme-I). With present set of data, it is difficult to state the definite nature of the intermediate complex. The experimental results can be accounted for in terms of electrophilic attack of methionine-sulphur at the metal via an intermediate complex.

The transfer of unshared pair of electrons to an empty d -orbital of the metal resulted in the formation of a coordinate bond. The formation of intermediate is likely to undergo a further rapid reaction in which the incipient.

It is of interest to compare here the mode of oxidation of methionine by pyridinium bromochromate (PBC)¹⁸, morpholinium chlorochromate (MCC)¹⁹, tetrakis(pyridine)silver dichromate (TPSD)²⁰ and IDC. The oxidation by PBC and MCC presented a similar kinetic picture, i.e. the reactions are of first order with respect to the reductants. While in the oxidation by TPSD and IDC, Michaelis-Menten type kinetics was observed with respect to the reductants. It is possible that the values of the formation constants for the

reductant-PFC/PBC complexes are very low. This resulted in the observation of second-order kinetics. No explanation of the difference is available presently. Solvent effects and the dependence of the hydrogen ions are of similar nature in all these reactions, for which essentially similar mechanisms have been proposed.



CONCLUSION

The oxidation of DL-methionine involves a rate-determining electrophilic attack of methionine sulfur at the metal *via* an intermediate complex. Both deprotonated and protonated forms of IDC are reactive oxidizing species.

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Don't let the past steal your present.

~ Cherralea Morgen