

OXIDATION OF DL-METHIONINE, A SULFUR-CONTAINING AMINO ACID BY DIETHYL AMMONIUM CHLOROCHROMATE

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ABSTRACT

Oxidation of DL-methionine (Met), sulphur-containing amino acid by Diethylammonium chlorochromate (DEACC) in dimethylsulphoxide (DMSO) is leading to produce its consecutive sulphoxide. The reaction is of first-order w. r. t. methionine and DEACC. The addition of an acid enhance the reaction rate, the effect of acidity is expressed by the relation $k_{obs} = a + b [H^+]$. The rate of the oxidation of methionine is recorded in 19 non aqueous solvent medium. The effect of solvent medium is was studied in nineteen different organic solvents. The solvent effect is evaluated by the models of Kamlet and Swain multiparametric equation.

Importance of the cation solvating powers is predominantly seen in the effects of solvent medium. On the basis of results and discussion a suitable mechanism is proposed.

Keywords: Halochromate, Methionine, Oxidation, Sulfoxide.

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INTRODUCTION

Halochromates are used as placid and choosy reagents in synthetic chemistry¹⁻⁵. DEACC is also such a similar reagent available in the literature for the same purpose⁶. It has been a matter of interest of our group in Jodhpur to study the reactions by halo- and dichromates and has emanated a few reports on similar halochromates⁷⁻¹⁰. We have not seen any report on the oxidation aspects of Met by DEACC. Met acts differently from other amino acids with various oxidizing reagents^{11,12} as it contains electron-rich sulfur, which oxidizes at ease. As per our previous record of studies with chromates, we are going to report in the present paper the oxidation kinetics of Met by DEACC in DMSO. We are going to propose a suitable mechanism also.

EXPERIMENTAL

Material and Methods

Chromate oxidant is synthesized by the method available in literature⁶, and purity was confirmed by iodometry. Methionine is a commercially available chemical that is used as received. Because of nonaqueous nature of the solvents, para toluene sulfonic acid is the source of acidity. All the other solvents used are purified by the method of Perrin.¹³

Confirmation of Product Formed

Kinetic conditions are employed for the analysis of the product so formed after the completion of the reactions. It was confirmed by the method available in literature¹⁴, that sulfoxide is formed by the oxidation of Met with DEACC. Availability of the product, sulfoxide is $95 \pm 3\%$ and the oxidation state of chromium is +4, at the ned of reaction after several half-lives.

Experimental Kinetics

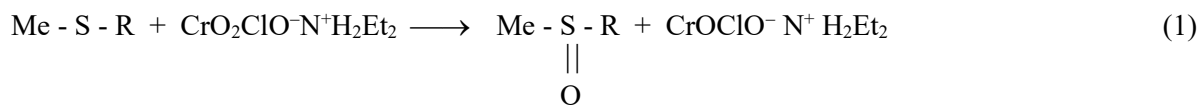
The ratio is maintained 1 : 10 or more (Reactant on Oxidant) to achieve the first-order condition. The solvent medium is DMSO except under solvent effect experiments. A decrease in oxidant concentration is followed on a spectrophotometer at a temperature constantly maintained at ± 0.1 K and at lambda max 380 nano-meters. This lambda is specific for these reactants and products. k-observed, the rate constants, is

calculated by a linear graph of time in seconds versus DEACC concentrations for at least up to 4 half-lives. Only those reactions are done with acid, which are studies for acidity effects.

RESULTS AND DISCUSSION

Stoichiometric Determinations

Reactions of Met with DEACC are done under kinetic conditions and form the sulfoxide as the consequent product, therefore in general, the reaction can be symbolized as given below:



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

The oxidant, DEACC is, undergone a 2 electron change, which is in agreement with some earlier studies by P.C.C. and P.F.C. halochromates^{15,16}. Magnetic vulnerability, E.S.R. and I.R. studies have already shown that both these halochromates are 2 electron oxidants and are reduced to chromium four as oxidation number.

Kinetic Dependence

All the reactions are of unit order w.r.t. oxidant and reductant both. Plots DEACC against time is linear in nature. Rate constants are independent of the starting concentrations of the oxidant. Further, reaction rates increase with the increase in the concentration of reductant. It is evidenced by results recorded in Table-1 and represented by Fig.-1.

Table-1: Rate Constants for the Oxidation of Methionine by DEACC At 298 K

10^3 [DEACC] (mol dm ⁻³)	[Met] (mol dm ⁻³)	[TsOH] (mol dm ⁻³)	$10^4 k_{\text{obs}}$ (mol dm ⁻³)
1.0	0.10	0.00	2.50
1.0	0.20	0.00	5.06
1.0	0.40	0.00	10.2
1.0	0.60	0.00	15.1
1.0	0.80	0.00	20.2
1.0	1.00	0.00	25.2
2.0	0.40	0.00	9.36
4.0	0.40	0.00	10.8
6.0	0.40	0.00	9.54
8.0	0.40	0.00	10.5
1.0	0.20	0.00	5.13*

^a contained 0.001 M acrylonitrile

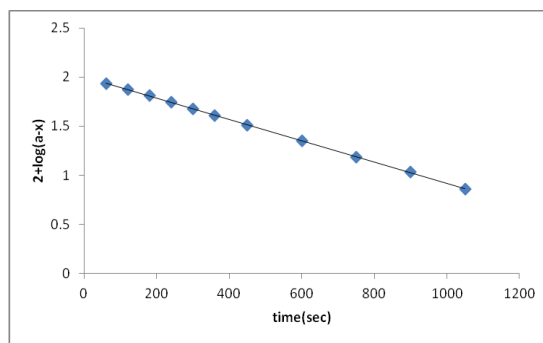


Fig.-1: Oxidation of DL-methionine by DEACC: A typical Kinetic Run

Induced Polymerisation of Acrylonitrile

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, one-electron oxidation, giving rise to free radicals, is unlikely. We 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.

Effect of Acidity

The reaction was studied at different acidities by adding the varying amount of toluene-*p*-sulphonic acid (TsOH) to the reaction mixtures. The reaction is catalyzed by hydrogen ions (Table-2). The dependence of hydrogen ion is expressed by the relation; $k_{\text{obs}} = a + b [\text{H}^+]$. The values of a and b are $2.45 \pm 0.06 \times 10^{-4} \text{ s}^{-1}$ and $4.78 \pm 0.10 \times 10^{-4} \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$ are recorded in that order ($r^2 = 0.9984$).

Table-2: Dependence of the Reaction Rate on Hydrogen-Ion Concentration

	[DEACC] = 0.001 mol dm ⁻³ ;		[Met] = 1.0 mol dm ⁻³ ;		Temp. = 298 K	
[H ⁺]/mol dm ⁻³	0.10	0.20	0.40	0.60	0.80	1.00
Met	2.88	3.51	4.32	5.31	6.21	7.29

On the basis of the acidity effect, it is suggested that the present reaction follows 2 pathways; one depends on acidity, but the other is independent of acid effect. DEACC is protonated by acid and is represented as equation given below:



Effect of Temperature

The rates of oxidation of Met are determined at four different temperatures and the activation parameters were also calculated (Table-3). The log k_2 at different temperatures is linearly related to the inverse of the absolute temperature in all cases (Fig.-2). It indicates the validity of Arrhenius equation.

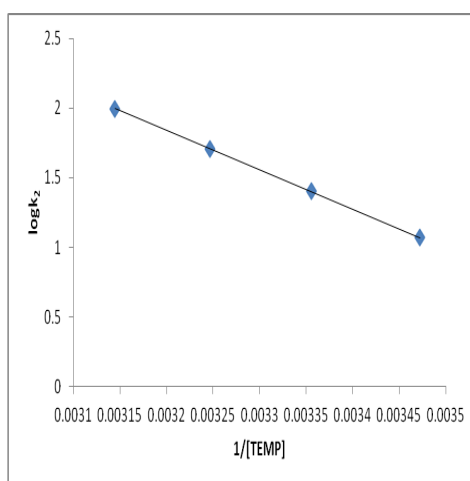


Fig.-2: Oxidation of DL-methionine by DEACC: Effect of temperature

Table-3: Rate Constants and Activation Parameters of the Oxidation of Met by DEACC

10 ⁴ k ₂ / (dm ³ mol ⁻¹ s ⁻¹)				ΔH* (kJ mol ⁻¹)	- ΔS* (J mol ⁻¹ K ⁻¹)	ΔG* (kJ mol ⁻¹)
288K	298K	308K	318K			
11.7	25.2	51.3	98.1	51.5±0.2	123±1	87.8±0.2

Solvent Effect

Rates of oxidation of Met are studied in nineteen organic solvents. Because of the solubility of oxidants in primary and secondary alcohol, the option is restricted. No appreciable reaction is observed with the solvents taken into account. The behavior is almost similar in every medium. The data for rate constants are present in table four.

Table-4: Effect of Solvents on the Oxidation of Methionine by DEACC At 288 K

Solvents	$10^5 k_{\text{obs}}$ (s^{-1})	Solvents	$10^5 k_{\text{obs}}$ (s^{-1})
CHCl ₃	51.3	C ₆ H ₅ CH ₃	12.0
1,2-C ₂ H ₄ Cl ₂	41.7	C ₆ H ₅ COCH ₃	43.7
CH ₂ Cl ₂	39.8	Tetrahydrofuran	20.9
DMSO	117	t-Butylalcohol.	22.4
CH ₃ COCH ₃	33.9	1,4 - C ₄ H ₈ O ₂	18.2
Dimethyl formamide	63.1	1,2- C ₄ H ₁₀ O ₂	13.5
C ₄ H ₈ O	27.5	Carbon Disulphide	5.25
Nitrobenzene	46.8	CH ₃ COOH	26.9
C ₆ H ₆	14.8	C ₂ H ₅ COOC ₂ H ₅	17.4
C ₆ H ₁₂	1.86		

Except that of carbon disulphide, the rate constants are correlated with Kamlet¹⁷ model of LSER., in 18 solvents because of the nonavailability of a full number of data of CS₂.

$$\log k_2 = A_0 + p\pi^* + b\beta + a\alpha \quad (3)$$

In this model,

π^* is defined as solvent polarity,

β is defined as hydrogen bond acceptor basicities

α is the hydrogen bond donor acidity.

A_0 is the intercept term.

It is to be noted here that out of eighteen solvent, twelve are having α as zero point. The data so correlated by this model of Kamlet tri parametric equation is mentioned below:

$$\log k_2 = -3.65 + 1.50 (\pm 0.16) \pi^* + 0.11 (\pm 0.13) \beta + 0.30 (\pm 0.12) \alpha \quad (4)$$

$$R^2 = 0.8845; \quad sd = 0.14; \quad n = 18; \quad \psi = 0.37$$

$$\log k_2 = -3.58 + 1.39 (\pm 0.17) \pi^* + 0.21 (\pm 0.14) \beta \quad (5)$$

$$R^2 = 0.8337; \quad sd = 0.17; \quad n = 18; \quad \psi = 0.43$$

$$\log k_2 = -3.53 + 1.44 (\pm 0.17) \pi^* \quad (6)$$

$$r^2 = 0.8084; \quad sd = 0.17; \quad n = 18; \quad \psi = 0.45$$

$$\log k_2 = -2.77 + 0.46 (\pm 0.31) \beta \quad (7)$$

$$r^2 = 0.1236; \quad sd = 0.37; \quad n = 18; \quad \psi = 0.96$$

In the above equations, n represents the data point taking part in the reaction and ψ represents Exner's mathematical parameters.¹⁸

Triparametric equation of Kamlet¹⁷ justifies 88% of the data of solvents effect, but as per Exner's¹⁸ this correction is not up to the mark. The main role is of solvent polarity, which is explaining alone 80% of the results. Alpha and beeta very minor roles in this process.

Therefore, we fit our data in another model of solvent effect given by Swain¹⁹ and co-workers. This model is based on cation and anion solvating perception of solvents.

$$\log k_2 = aA + bB + C \quad (8)$$

In the above equation;

A is denoted by anion solvating power of the solvent

B denotes cation solvating power.

C termed as intercept.
(A+ B) is represented as solvent polarity.

Results obtained by this equation 8, are summarized below:

$$\log k_2 = 1.18 (\pm 0.05) A + 1.38 (\pm 0.03) B - 3.85 \quad (9)$$

$$R^2 = 0.9927; \text{sd} = 0.04; n = 19; \psi = 0.09$$

$$\log k_2 = 0.99 (\pm 0.46) A - 2.90 \quad (10)$$

$$r^2 = 0.2163; \text{sd} = 0.37; n = 19; \psi = 0.91$$

$$\log k_2 = 1.29 (\pm 0.21) B - 3.46 \quad (11)$$

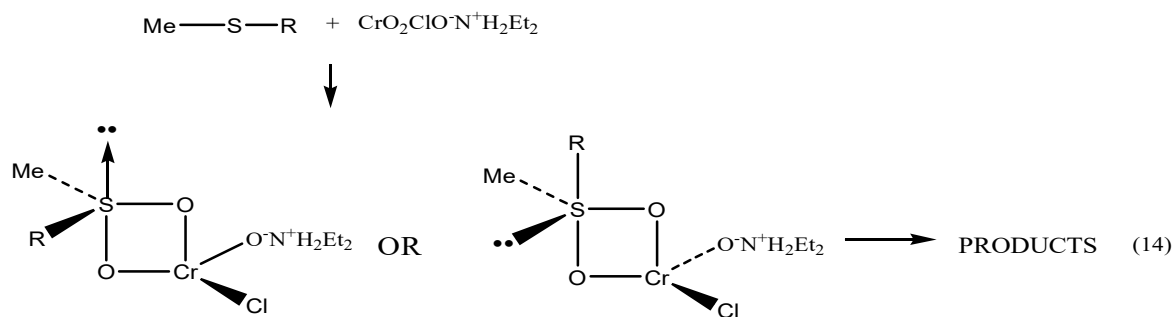
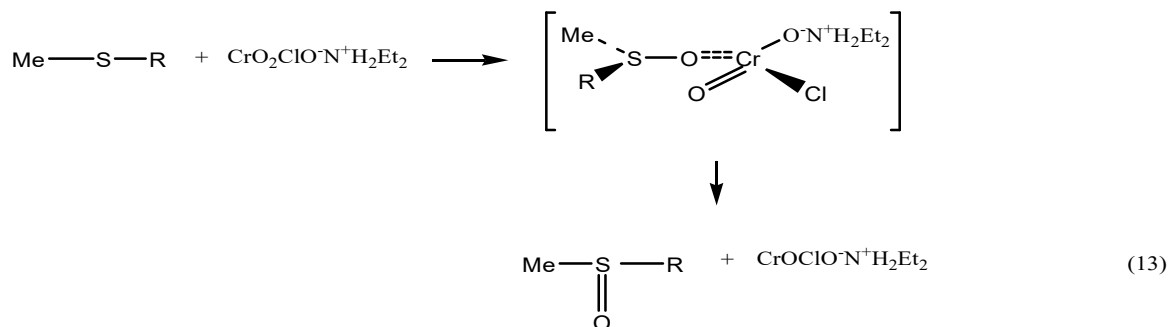
$$r^2 = 0.6854; \text{sd} = 0.23; n = 19; \psi = 0.58$$

$$\log k_2 = 1.31 \pm 0.04 (A + B) - 3.84 \quad (12)$$

$$r^2 = 0.9867; \text{sd} = 0.05; n = 19; \psi = 0.12$$

Oxidation rates of Met in various solvents are correlated extremely well with Swain equation showing a noteworthy part of cation and anion solvating powers. As compared to anion solvating, cation solvating power is playing a bit more prominent role. 98% of the data are explained by solvent polarity. But correlations separately are not good with A and B. as the solvent polarity is showing a prominent role, we correlate the rate of the reaction with relative permittivity, which is not found to be linear ($r^2 = 0.4781$; $\text{sd} = 0.30$; $\psi = 0.74$).

Solvent studies indicate the presence of a transition state which may be a polar higher degree than the reactant. Moreover, the main part of cation and anion solvating power indicating the presence of a dipolar transition state equal to S_N2 reactions. We may also explain the solvent effect with an assumption that DEACC and the complex exist as an ion pair in a nonpolar medium like cyclohexane and be considerably dissociated in more polar solvents.



Scheme-1

Mechanism

As per the non-availability of free radical reaction, the one-electron oxidation process may not be possible in this reaction system. The results so obtained are in relation to the fact that electrophilic oxygen is

transferring from DEACC to the sulphur present in Met. This is happening through an intermediate complex shown in equation thirteen. These types of the mechanistic path have also been suggested in the oxidation of sulphides and iodide by IO_4^- ion²⁰, and oxidation by H_2O_2 ²¹. We can assume and see the electrophilic attack on sulphur of sulphide as a reaction similar to $\text{S}_\text{N}2$. The present solvent effect is also supporting a transition state similar to $\text{S}_\text{N}2$.

It has already been suggested earlier in various reactions by chromium²² six, a cyclic transition state and it may be suggested in this oxidation of Met by DEACC. We may assume that the present cyclic transition state may be in more strain because of the presence of either a single pair of electrons or a $-\text{CH}_3$ group, as shown in reaction fourteen. It has been observed that a cyclic transition state requires a large specific orientation and may be resulted in higher negative entropy of activation than that observed in reaction(Scheme-1).

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 are reactive oxidizing species.

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