THE METHIONINE SULFONE OXIDATION BY PERMANGANATE ION (AUTOCATALYSIS): KINETIC STUDY

Ibrahim Y. Mohammed

Chemistry Department, College of Education for Pure Sciences, University of Mosul, Mosul, Iraq
e-mail: ibrahemawab@uomosul.edu.iq

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Abstract: *A study was conducted on the reaction kinetics of methionine sulfone oxidation in an aqueous solution using potassium permanganate. The kinetic results indicated that the oxidation reaction occurs through two distinct paths: the first pathway is a non-catalyzed reaction, while the second pathway is auto-catalyzed by the product manganese (II) oxide. The rate of the first pathway reaction is determined by the first-order dependence on the concentrations of both methionine sulfone and the oxidizing agent. However, the rate of reaction of the secondary pathway is solely determined by the first-order dependence on the concentration of methionine sulfone, as well as the oxidizing and autocatalytic agent. The thermodynamic characteristics for the two pathways were determined by calculating the reaction rate constant (k) and temperature (T) dependence; this was done at various temperatures within the range of 303-323K. The rate constants of both the non-catalyzed and auto-catalyzed reactions exhibit an increase as the temperature rises. The use of Arrhenius plots facilitated the determination of thermodynamic data for the oxidation reaction by providing linear relationships. The aforementioned findings corroborate the suggested mechanism for the reaction, indicating that the rate-limiting stage of the reaction involves the transfer of a solitary electron from methionine sulfone to the permanganate ion.*

Keywords: *Kinetics, Auto-Catalysis, Oxidation, Methionine*
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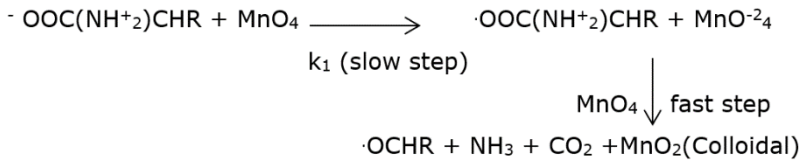
1. Introduction

Methionine is an essential and hydrophobic amino acid that belongs to the group of amino acids containing sulfur. Methionine, being hydrophobic, is typically located within proteins. Contrary to cysteine, the sulfur in methionine does not possess a strong tendency to react with nucleophiles, although it can still react with some electrophilic sites. It often does not partake in the covalent chemical reactions that take place within the active sites of enzymes [1]. The sulfur in methionine is chemically linked through a thiol ether bond. Contrast this terminology with that used for ethers that include oxygen. The sulfur in methionine, like that in cysteine, is susceptible to oxidation. The initial stage, which produces methionine sulfoxide, can be reversed by conventional reducing agents that include thiol groups. The second stage produces methionine sulfone, which is essentially irreversible [2-4].

The process of oxidizing methionine in peptides is frequently linked to the reduction of biological activity. Due to the favorable anti-inflammatory properties exhibited by methionine, its oxidized derivatives, methionine sulfoxide and methionine sulfone, were subjected to testing. The sulfone had greater action than the sulfoxide, while methionine demonstrated the highest activity, suggesting that the anti-inflammatory efficacy is not dependent on the oxidation state of sulfur. Their capacity to scavenge hydroxyl radicals was quantified. Methionine exhibited the highest level of activity, while sulfone showed the lowest level of activity. No association between anti-inflammatory action and the subject in question was identified [5].

The kinetic studies of amino acids by common oxidation have been given a large concern because of their biological significance [6, 7]. One of these studies is the oxidation by permanganate ion, which has shown [8, 9] that these reactions are started by electron transfer from the amino acids to the permanganate ion in

the rate-determining step followed by other fast steps leading to the product as shown in Scheme 1:



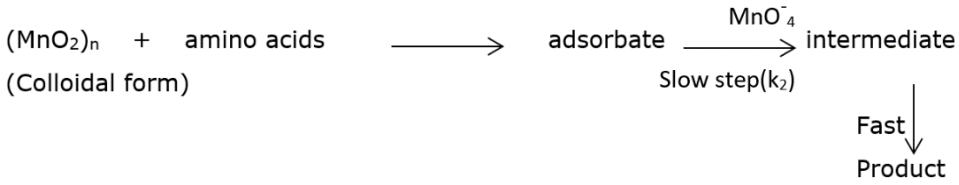
Scheme -1

It has been found that this reaction is first order in the concentration of both amino acids and permanganate ion, as shown by this equation:

$$r = k_1 [\text{amino acids}] [MnO_4^-] \qquad (1)$$

where (k_1) is the rate constant. After that the reaction is auto-catalyzed by (MnO_2), resulting from the reaction, which is present in the solution as colloidal particles that absorb the (amino acids) on its surface and catalyze the oxidation reaction by acting as auto catalytic agent.

The mechanism of autocatalyzed reaction is similar to the non-catalyzed reaction mechanism [10-14], but only between adsorbed (methionine sulfone) and (MnO_4^-) in the solution as summarized in Scheme 2:



Scheme- 2

1) Auto-catalyzed reaction rate can be represented by this equation:

$$r_n = k_2[\text{ adsorbate}] [MnO_4^-] \qquad (2)$$

As well as, the relation between the concentration of adsorbate, colloidal MnO_2, and amino acids at equilibrium can be extracted from the Freundlich adsorption isotherm as shown in this equation:

$$[\text{adsorbate}] / [MnO_2] = a[\text{amino acids}]^b \qquad (3)$$

where (a and b) are adsorption constants.

2) So that autocatalyzed reaction rate can be represented by this equation:

$$r_a = ak_2[MnO_4^-][MnO_2] [\text{amino acids}]^b \qquad (4)$$

According to the above assumption, the total rate for the oxidation reaction by $[MnO_4^-]$ can be represented by this equation:

$$r = k_1 [MnO_4^-][\text{ amino acids}] + ak_2[MnO_4^-][\text{ amino acids}]^b[MnO_2] \qquad (5)$$

Since the reaction is started by the electron transfer from the amino acids to the oxidizing agent. One can anticipate that the electron density at the chiral carbon atom of the amino

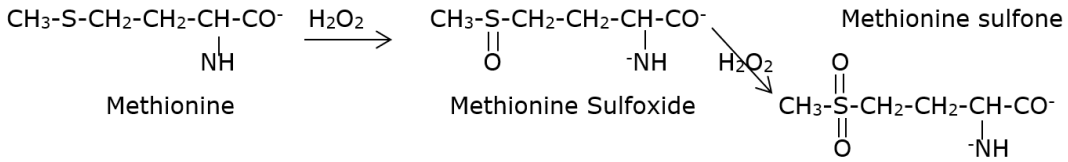
acids plays an important role in the rate of oxidation. Owing to the fact that the electron density at the chiral carbon atom is highly affected by the nature of the R-group attached to it [15-17].

On the other hand, the Arrhenius equation is employed to calculate the thermodynamic parameters, which are utilized in the discussion of the reaction mechanism. Oxidation kinetics has received considerable attention due to the wide range of biological processes in which metal ions participate [18, 19].

2. Experimental part

2.1. Materials. Amino acids (methionine), hydrogen peroxide (H_2O_2), potassium permanganate ($KMnO_4$), K_2HPO_4, KH_2PO_4, in this work, were purchased from Fluka and B.D.H. Chemical Ltd.

2.2. Methionine Oxidation. The process of oxidizing the methionine amino acid is recognized as a significant chemical route responsible for the degradation of protein molecules. Peroxides in a solution can readily oxidize the sulfur atoms present in the methionine residues, resulting in the formation of methionine sulfoxide and methionine sulfone [20-24].



2.3. Treatment of permanganate ion concentration. The concentration of the permanganate ion was determined by accurately measuring its absorbance at a wavelength of 526 nm. This was done by measuring the absorbance of the mixture containing the inorganic product (MnO_2), which absorbs light at the maximum wavelength (λ_{max}) of the permanganate ion (526 nm). In order to get the concentration of [MnO_4^-] at a wavelength of 418 nm, where only the product absorbs light and the following equation can be used:

$$[MnO_4^-] = ((A^{526} – (E_{p.}^{526} \text{ x } A^{418} / E_{p.}^{418})) / E_{R.}^{526} \qquad (6)$$

here, the subscripts R and P represent the reactant and product, respectively.

The extinction coefficient of permanganate ion $E_{R.}^{526}$ is $2.4x10^3$ $mol^{-1}\cdot dm^3\cdot cm^{-1}$. The extinction coefficient for the product at wavelengths 418 nm and 526 nm can be determined by measuring the final absorbance of the reaction mixture at these two wavelengths [25].

2.4. The kinetic measurements. In order to maintain a consistent pH of the medium and prevent the precipitation of manganese dioxide during the reaction, a buffer solution consisting of K_2HPO_4 and KH_2PO_4 was employed. The concentration of the permanganate ion was selected as the species to monitor the rate. This was done by utilizing a spectrophotometer equipped with a digital printer DP 802, which allowed for spectrophotometric tracking using double-beam technology. The cell temperature was regulated by flowing water in its outer jacket using a Juloboo design pT40ps thermostat. The solution's pH was determined using a pH-meter of the Orion type.

The rate constant and activation energies for the reaction were calculated using a linear regression approach, with a minimum accepted correlation coefficient of 0.9120.

3. Results and discussion

3.1. Treatment of the kinetic. Where the methionine sulfone concentration is always ten times greater than the permanganate ion concentration. The kinetic measurements were carried out under pseudo-first-order reaction. The reaction was followed by monitoring the

concentration of permanganate ion spectrophotometrically. At different times the total rates for the reaction were calculated by using this equation, which provides a simple and accurate method for this purpose [26].

$$r_2 = (C_3-C_1) / (t_3-t_1) \qquad (7)$$

where (C) stands for the permanganate ion concentration from using the equation (6).

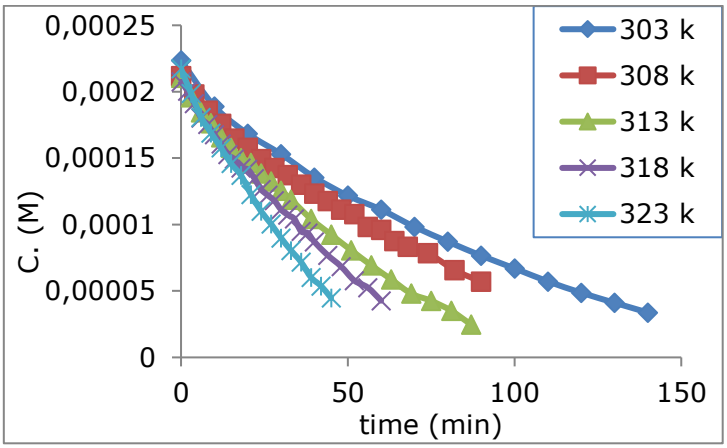


Fig. 1. A plot of concentration versus time for oxidation of Methionine sulfone by permanganate ion.

The calculation rate values for oxidation of methionine sulfone, as representative results, are listed in Table 1.

Table 1. The rate values for oxidation of methionine sulfone by $KMnO_4$ at pH 7.5 and different temperatures.

Temperature k°	time min.	Absorption 418nm.	Absorption 526nm.	C x 10^{-5} mole/dm^3	r x 10^{-6} mol.dm^3.min^{-1}	r/C x 10^{-2} $min.^{-1}$
303	0	0.128	0.563	22.350	0.0	0.0
	80	0.553	0.30	8.720	1.085	1.244
	90	0.593	0.307	7.660	1.010	1.318
	100	0.632	0.292	6.700	0.970	1.448
	110	0.664	0.275	5.720	0.915	1.599
308	0	0.159	0.541	21.170	0.0	0.0
	40	0.516	0.403	12.330	1.563	1.267
	44	0.552	0.397	11.770	1.500	1.277
	52	0.612	0.386	10.790	1.613	1.494
	64	0.681	0.352	8.780	1.600	1.822
	82	0.796	0.323	6.580	1.543	2.269
313	0	0.158	0.538	21.050	0.000	0.000
	15	0.395	0.461	15.790	2.583	1.636
	18	0.436	0.451	15.020	1.917	1.276
	21	0.470	0.449	14.640	1.933	1.321
	24	0.513	0.439	13.860	2.333	1.684
	27	0.536	0.429	13.240	2.167	1.636
	30	0.581	0.422	12.560	2.267	1.805
	33	0.606	0.411	11.880	2.378	2.001
	39	0.664	0.388	10.420	2.200	2.111
	57	0.816	0.336	6.940	2.558	3.686
	63	0.881	0.324	5.880	1.775	3.019
	75	0.977	0.305	4.260	1.075	2.523
	0	0.150	0.529	20.740	0.000	0.000
	16	0.485	0.459	14.930	2.525	1.691
	18	0.519	0.450	14.260	1.925	1.350
	26	0.650	0.428	12.210	2.150	1.761

318	28	0.660	0.420	11.790	2.700	2.290
	30	0.689	0.410	11.130	2.650	2.381
	34	0.760	0.408	10.430	3.100	2.972
	36	0.758	0.385	9.490	2.675	2.819
	40	0.825	0.380	8.700	2.783	3.199
	44	0.874	0.366	7.690	2.313	3.007
	48	0.918	0.355	6.850	2.388	3.485
	52	0.978	0.344	5.780	1.988	3.438
	56	1.020	0.338	5.260	1.888	3.590
323	0	0.166	0.556	21.730	0.000	0.000
	15	0.558	0.466	14.590	3.450	2.365
	18	0.622	0.458	13.700	3.883	2.835
	24	0.726	0.415	11.010	3.683	3.335
	36	0.973	0.373	7.180	3.383	4.712
	39	1.034	0.359	6.020	3.000	4.984

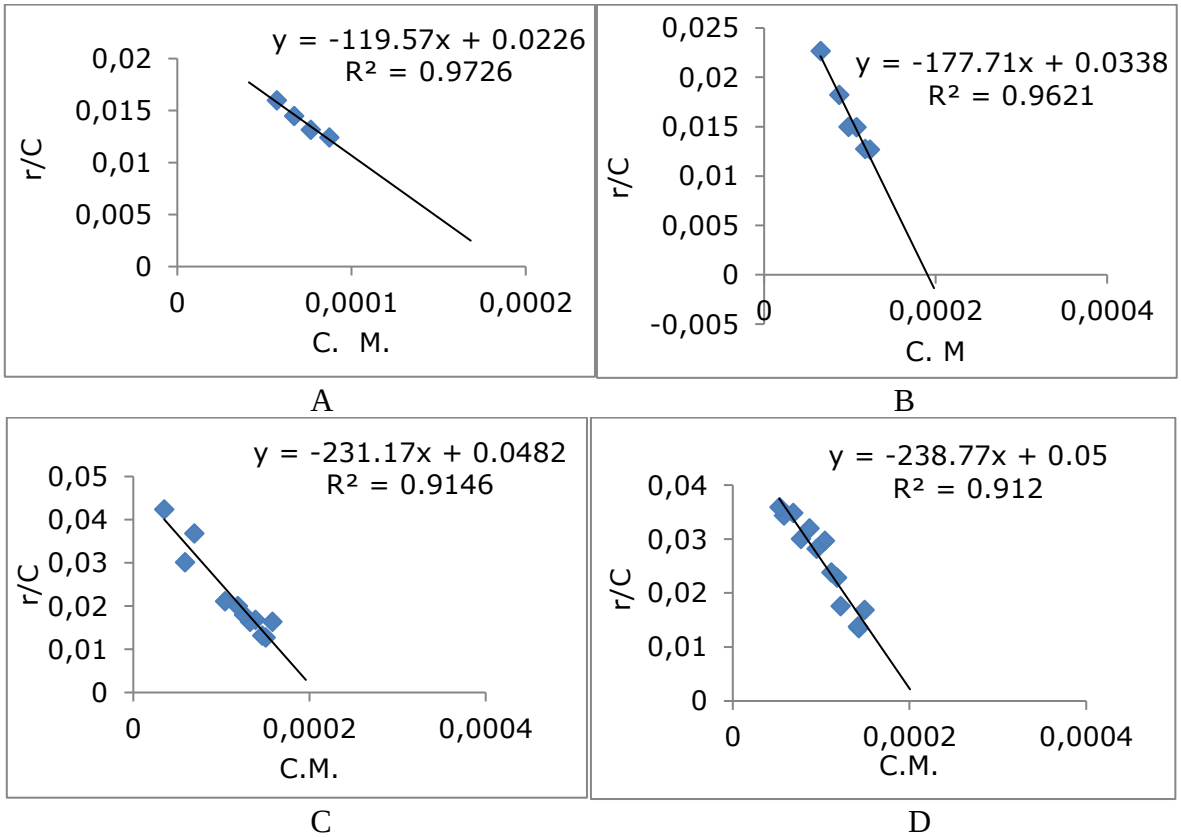
The rate equation (5) at high concentration of methionine sulfone is reduced to equation (8):

$$r = k_1C + k_2C(C_0 - C) \quad (8)$$

where: k_1 = the rate constants for non-catalyzed; k_2 = the rate constants for auto-catalyzed reaction; C = permanganate ion concentration with time; C_0 = permanganate ion concentration at zero time. From equation (8), we can get this equation:

$$r/C = k_1 + k_2C_0 - k_2C \quad (9)$$

A plot between r/C and C gave a linear relationship up to 75% of the reaction as shown in Fig. 2 (A-E). This confirms the validity of equation (9). The k_1 and k_2 values were found from the slope and the intercept and summarized in Table 2.



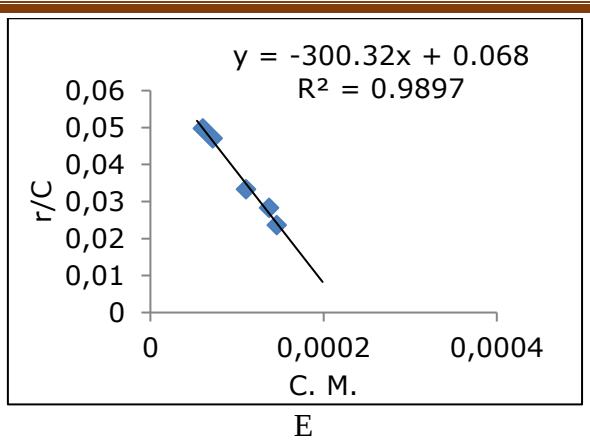


Fig. 2. A plot of r/C versus C for oxidation of Methionine sulfone by permanganate ion.

Table 2. The values of k_1 and k_2 for oxidation of methionine sulfone by $KMnO_4$ at different temperature and pH 7.5

Temperature C°	**Intercept**	**R^2**	**$k_1 \times 10^{-2}$ min.$^{-1}$**	**k_2 M^{-1} . min.$^{-1}$**
30	0.0226	0.9726	8.239	119.570
35	0.0338	0.9621	12.266	177.710
40	0.0482	0.9146	16.379	231.170
45	0.0500	0.9120	16.939	238.770
50	0.0680	0.9897	21.826	300.520

2. Effect of temperature. The temperature dependences of the rate constants are investigated, where the rate of decomposition of permanganate is negligible between 303-323 K. Arrhenius equation applications:

$$\ln k = \ln A - E_a / RT \qquad (10)$$

and a plot of *ln k* against 1/T gave a straight line (as shown in Figs. 3 and 4).

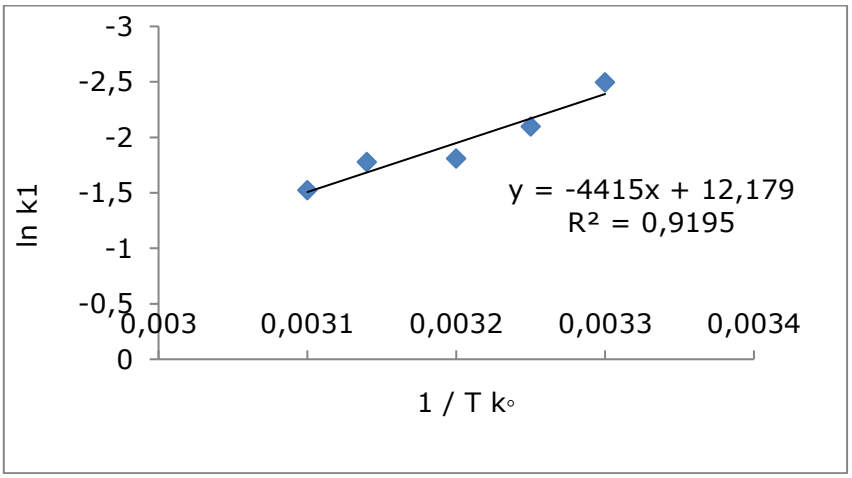


Fig. 3. Arrhenius plots for non-catalyzed oxidation reaction Methionine sulfone.

In the non- and auto-catalyzed reaction, the thermodynamic parameters were obtained from using the following equations, which are gathered in Tables 3 and 4:

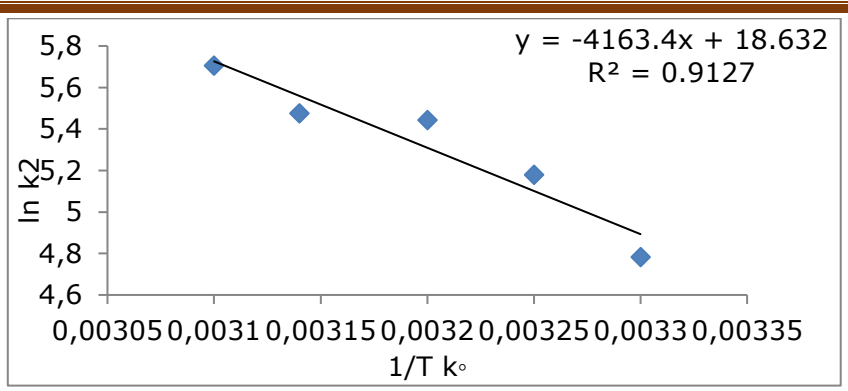


Fig. 4. Arrhenius plots for catalyzed oxidation reaction Methionine sulfone.

$$Ea = -slope \times R \quad (11)$$

$$Ln\ A = Intercept \quad (12)$$

$$\Delta H^* = Ea - nRT \quad (13)$$

$$\Delta S^* = R(\ln A - \ln (K_b.T/h)) \quad (14)$$

$$\Delta G^* = \Delta H^* - T\,\Delta S^* \quad (15)$$

Where A = Frequency factor; K_b = Stefan-Boltzmann constant (1.380×10^{-23} J/k°); h = Plank constant (6.626×10^{-34} J·sec); R = gases constant (8.314 J/K· mol^{-1}).

Table 3. The thermodynamic parameters of activations for non-catalyzed oxidation reaction at pH 7.5

T k°	Ea kJ/mole	A x10^5 min^{-1}	ΔH* kJ/mole	ΔS* J/mole. K°	ΔG* kJ/mole
303			34.187	-143.782	77.753
308			34.145	-143.924	78.474
313	36.706	1.9466	34.104	-144.057	79.194
318			34.062	-144.190	79.914
323			34.021	-144.314	80.634

Table 4. The thermodynamic parameters of activations for auto-catalyzed oxidation reaction at pH 7.5

T k°	Ea kJ/mole	A x 10^8 min.$^{-1}$	ΔH* kJ/mole	ΔS* J/mole. K°	ΔG* kJ/mole
303			32.096	-90.132	59.406
308			32.054	-90.273	59.859
313	34.615	1.2353	32.013	-90.406	60.311
318			31.971	-90.539	60.762
323			31.930	-90.664	61.214

The scientist Ostwald [27] explained that the catalyst is the substance that increases the rate of the reaction without being affected chemically; the rate constant of the non-catalyzed reaction (k_1) is lower than the rate constant of the auto-catalyzed reaction (k_2). In addition, the catalyst affects the amount of activation energy (E_a) and works by providing an alternative mechanism in which the reactions are faster than those mechanisms that do not include its presence, thus reducing the activation energy required for the reaction [28].

In all cases, the activation energies (E_a) for the oxidation showed a decrease in their values as the rate constants increased, which means that the reaction is mainly controlled by the energy barrier of the rate-determining step. Positive values of the enthalpy ΔH* indicate that the

oxidation reaction is of the endothermic type, and the decrease in these values with increasing temperature proves that the increase in temperature increases the rate of oxidation and therefore requires less energy ΔG* for the oxidation reaction to occur. The high values of Gibbs free energy indicate that this reaction is nonspontaneous. Furthermore, the non-spontaneity of the reaction increases as the temperature rises. The negative values of the entropy of activation, ΔS*, suggest that the transition state is more organized than the reaction itself. This outcome aligns with the suggested mechanism whereby the electron is transferred from the methionine sulfone to the oxidizing agent, resulting in the formation of a highly charged intermediate. The transition state exhibits a more organized structure compared to the reactant [29].

3. Conclusion

1. The values of the rate constant in the non-catalyzed reaction (k_1) are fewer than the auto-catalyzed reaction (k_2).
2. The rate constants of reaction in the non-catalyzed (k_1) and auto-catalyzed (k_2) reactions increased with increasing temperature.
3. The non-catalyzed reaction needs much higher energy than an auto-catalyzed reaction.
4. The oxidation reaction is classified as endothermic and non-spontaneous. The negative entropy of activation values indicates that the transition state is more organized than the reaction itself.

5. Conflict of interest

No conflicts of interest exist.

6. Acknowledgments

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