ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Kinetics and Mechanism of Ruthenium (III) Catalysed Oxidiaton of L - Cystine by Hexacyanoferrate (III) in Alkaline Medium

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ABSTRACT

The kinetics and mechanism of ruthenium (III) catalysed oxidation of L-cystine by alkaline hexacyanoferrate (III) (HCF (III)) were studied spectrophotometrically at 30°C. The reaction was first order dependent each on [HCF (III)] and [ruthenium (III)] and fractional order dependent on [alkali] and independent of [cystine]. The main product of oxidation was 2-oxoethyldisulfanylacetaldehyde and it was identified and confirmed by Mass spectral studies. Further, no effect of added reaction product was observed. A plausible mechanism was proposed involving $[Ru(H_2O)_5OH]^{2+}$ in the slow step. Thermodynamic parameters for the rate determining step, E_a and $\Delta S^{\#}$ were computed using linear least squares method and are found to be 56.59 ± 0.58 kJ mol^{-1} and -132.60 ± 1.91 J K^{-1} mol^{-1} respectively.

$$\text{Rate} = \frac{kK[\text{Ru}^{\text{III}}]_t\,[\text{HCF(III)}]\,[\text{OH}^-]_t}{1 + K[\text{OH}^-]_t}$$

Keywords: Kinetics, mechanism, Oxidation of L – Cystine, catalysis.

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INTRODUCTION

Sulfur containing amino acids involve in protein synthesis and also play a significant role in metabolism. L-cystine is a covalently linked dimeric non-essential amino acid formed by the oxidation of cysteine. Two molecules of L-cysteine are joined together by a disulfide bridge (S-S) to form L-cystine. Cystine is excreted through urine, and can form a calcus(hard mineral formation) when deposited in the kidney. It is metabolized to form pyruvic acid and is vital for the formation of skin and hair. Cystine reduces damage from free radicals, and repairs nucleic acids in the cells. It also has an anti-aging effect on the body which can reduce the accumulation of age spots.

L-cystine can be oxidized by a variety of oxidizing agents [1-9] and the products formed differ for different oxidants. Thus we believe that the detailed investigation on the kinetics and mechanism of oxidation of cystine is important from the chemical point of view, its selectivity towards the oxidants and the nature of the oxidation product formed.

MATERIALS AND METHODS

The standard solutions of L-cystine in 0.1 mol dm^{-3} NaOH were prepared afresh by dissolving the sample in a requisite volume of sodium hydroxide and its strength was determined iodometrically.

Hexacyanoferrate(III)(E.Merck) was prepared by dissolving the requisite amount of potassium hexacyanoferrate(III) in double distilled water. The solution was standardised by measuring the absorbance using Milton Roy UV-Visible 1201 spectrophotometer at 420 nm(ε =1060±50 $dm^3 mol^{-1} cm^{-1}$). Ruthenium(III) solution was prepared by dissolving ruthenium chloride in 2.0 mol dm^{-3} sulfuric acid (Johnson Matthey, London) and its strength was determined by the titration method suggested by Beamish and Valnoon[10]. All other chemicals used were of AR grade and double distilled water was used throughout the investigation.

A Milton Roy Spectronic - 1201 UV-Visible spectrophotometer; Siskin Julabo-V constant temperature liquid circulatory bath.

All kinetic measurements were performed under pseudo first-order conditions where [cystine] is in excess over [HCF(III)] at a constant ionic strength of 0.3 mol dm^{-3} in alkaline medium in presence of ruthenium(III) at a constant temperature of 30 ± 0.1°C. The progress of the reaction was followed by measuring the absorbance of hexacyanoferrate(III) at 420 nm. As no other species except hexacyanoferrate(III) had any significant absorption at this wavelength under the conditions employed, the absorbance of the solution was taken as a measure of the residual concentration of [HCF(III)] at time ‘t’. Plots of log(absorbance) versus time were found to be linear up to 80% completion of the reaction indicating that the reaction is first order with respect to [HCF(III)]. The pseudo-first order rate constants calculated from the slopes of these plots were denoted by k^{l} and the rate constants were found to be reproducible within ± 5%.

EXPERIMENTAL

The reaction mixture containing excess [HCF(III)] over [cystine] in presence of ruthenium(III) at 0.1 mol dm^{-3} alkali were allowed to react at 30 ± 0.1°C. After 24 hours, the residual [HCF(III)] in each case was determined spectrophotometrically at 420nm. The results obtained indicate that four moles of HCF(III) were consumed by one mole of cystine. The stoichiometry of the reaction was found to correspond to the equation

$$\text{cystine} + 4\ \text{HCF(III)} \xrightarrow{\text{Ruthenium(III)}} \begin{array}{l}\text{2 oxoethyl}\\ \text{disulfanyl}\\ \text{acetaldehyde}\end{array} + 4\ \text{HCF(II)}$$

The reaction product was isolated by a solvent extraction method using an organic solvent diethyl ether and the reaction product was confirmed by mass spectral studies (Fig. 1). The compound displayed a peak at m/z 174 which was obtained by the addition of sodium atom to its molecular mass (m/z 150). In line with these observations, the product of oxidation of cystine by alkaline hexacyanoferrate (III) in presence of ruthenium (III) was confirmed to be 2- oxo ethyldisulfanyl acetaldehyde.

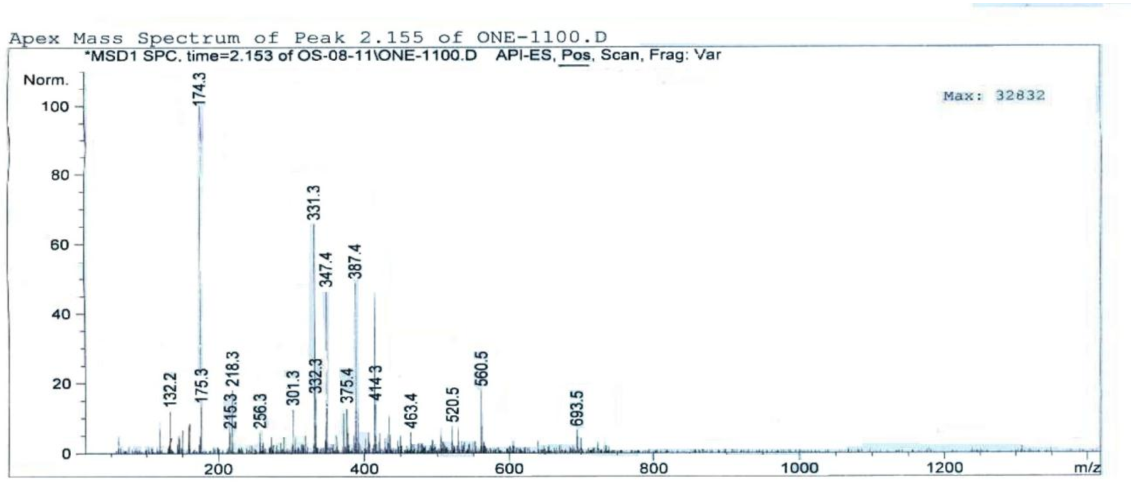


Fig.1 Mass spectrum of 2-oxoethyldisulfanylacetaldehyde

Test for free radicals was carried out by taking cystine, sodium hydroxide and ruthenium(III) in a thumberg tube and acrylonitrile and hexacyanoferrate (III) in the bent tube. After evacuating the system the solutions were mixed by tilting the tube. The reaction mixture was kept aside and even after 24 hours no precipitate was observed indicating the absence of free radicals.

RESULTS AND DISCUSSION

To study the effect of [HCF(III)], it was varied in the range of 1.0-6.0 $X10^{-4}$ mol dm^{-3} and the plot of log(absorbance) versus time was found to be linear indicating the order with respect to [HCF(III)] was unity. The [cystine] was varied in the range of 1.0-6.0X10^{-3} mol dm^{-3} keeping the concentrations of all other reactants constant and the $k^{\prime}$ values remain constant indicating the order with respect to [cystine] to be zero. The effect of [alkali] at three different temperatures 25,30,35 and 40^{0}C on the reaction rate was studied and the pseudo first order rate constants, $k^{\prime}$ values obtained were found to increase with increase in [OH^{-}] (Table.2) and the order with respect to [OH^{-}] was fractional. Further, the plots of 1 / $k^{\prime}$ versus 1 / [OH^{-}] were found to be straight lines with positive intercepts on Y-axis (Fig. 2). To know the order with respect to [ruthenium(III)] on the reaction rate, [ruthenium(III)] was varied in the range of 2.0-7.0X10^{-6} mol dm^{-3} by keeping the concentrations of all other reactants constant. The plot of $k^{\prime}$ versus [ruthenium(III)] was found to be a straight line passing through the origin indicating unit order dependence on [ruthenium(III)].

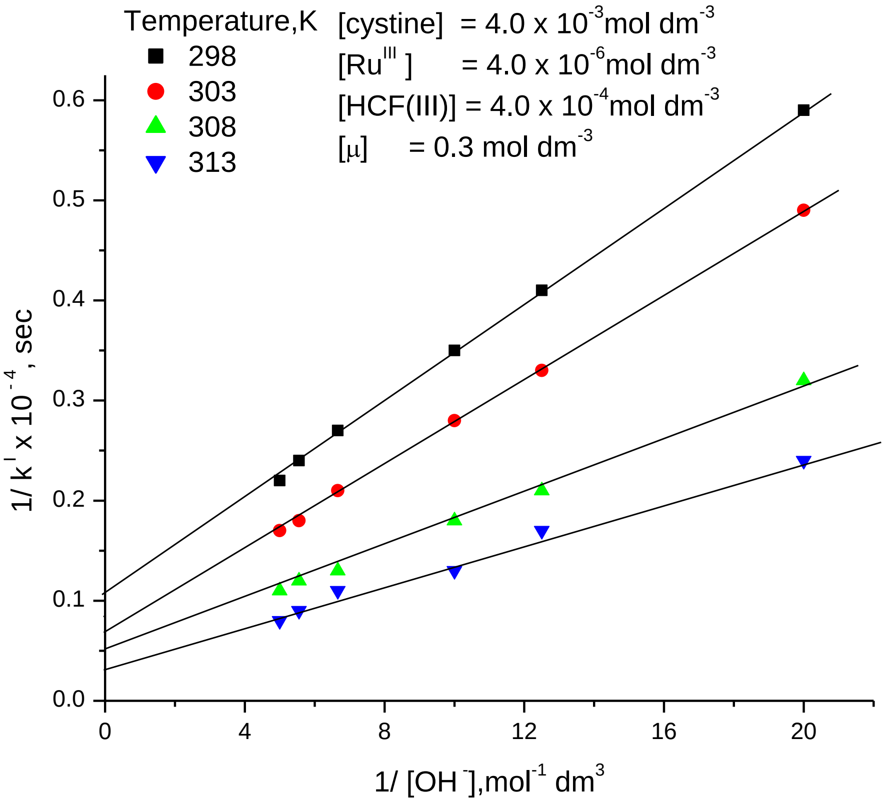


Fig.2 plot of 1/ $k^{\prime}$ versus 1/ [OH^{-}]

To study the effect of hexacyanoferrate(II), one of the products on the rate of reaction, kinetic runs were carried out keeping the concentration of all other reactants constant and varying the concentration of hexacyanoferrate(II). The constancy of rate constants obtained from the slopes of pseudo-first order plots showed that hexacyanoferrate(II) did not have any significant effect on the reaction rate.

Table 2: Effect of [OH$^-$] on the pseudo-first order rate constant (k^{I}) at 298, 303,308 and 313 K

[OH$^-$] (mol dm^{-3})	k^{I} x 10^{4} (sec^{-1}) Temperature,K			
	298	303	308	313
0.05	1.66	2.04	3.07	4.16
0.08	2.43	3.03	4.76	5.88
0.10	2.85	3.45	5.30	7.69
0.14	3.70	4.76	7.69	8.82
0.18	4.16	5.48	8.33	9.96
0.20	4.54	5.88	9.09	11.11

[cystine] = 4.0 x10^{-3} mol dm^{-3}, [Ru^{III}] = 4.0 x 10^{-6} mol dm^{-3}, [HCF(III)]=4.0x10^{-4} mol dm^{-3}, μ = 0.3 mol dm^{-3}

The effect of ionic strength was studied by varying the concentration of $NaClO_4$ from 0.2-0.7 mol dm^{-3}. The pseudo-first order rate constants obtained from log(absorbance) versus time plots showed that increasing the ionic strength(μ) increased the rate of the reaction (Table. 1).

Table 1: Effect of [HCF(III)], [cystine], [Ru^{III}] and ionic strength(μ) on the pseudo-first order rate constant, k at 30 ± 0.1°C

[HCF(III)]x10^{4} (mol dm^{-3})	[cystine]x10^{3} (mol dm^{-3})	[Ru^{III}]x10^{6} (mol dm^{-3})	[OH$^-$] (mol dm^{-3})	μ (mol dm^{-3})	k^{I} x10^{4} (sec^{-1})
1.0	4.0	4.0	0.1	0.3	3.82
2.0	4.0	4.0	0.1	0.3	3.57
3.0	4.0	4.0	0.1	0.3	3.83
4.0	4.0	4.0	0.1	0.3	3.58
5.0	4.0	4.0	0.1	0.3	3.62
6.0	4.0	4.0	0.1	0.3	3.56
4.0	1.0	4.0	0.1	0.3	3.56
4.0	2.0	4.0	0.1	0.3	3.57
4.0	3.0	4.0	0.1	0.3	3.54
4.0	4.0	4.0	0.1	0.3	3.58
4.0	5.0	4.0	0.1	0.3	3.20
4.0	6.0	4.0	0.1	0.3	3.10
4.0	4.0	2.0	0.1	0.3	2.70
4.0	4.0	3.0	0.1	0.3	3.19
4.0	4.0	4.0	0.1	0.3	3.58
4.0	4.0	4.5	0.1	0.3	4.77
4.0	4.0	5.0	0.1	0.3	5.23
4.0	4.0	6.0	0.1	0.3	6.23
4.0	4.0	7.0	0.1	0.3	7.45
4.0	4.0	4.0	0.1	0.2	3.24
4.0	4.0	4.0	0.1	0.3	3.58
4.0	4.0	4.0	0.1	0.4	4.88
4.0	4.0	4.0	0.1	0.5	7.12
4.0	4.0	4.0	0.1	0.6	8.69
4.0	4.0	4.0	0.1	0.7	11.50

L-cystine,[-$SCH_2CH(NH_2)(COOH)$]$_2$ is a sulfur containing amino acid and it possess four pKa values, two corresponding to the carboxylic groups $(COOH)_1$=1.51; $(COOH)_2$=2.79 and the other two for amino groups $(NH_3^+)_1$=8.25; $(NH_3^+)_2$=8.97. The trivalent state is the most stable oxidation state for ruthenium. Ion exchange [11] separation has allowed definite characterization of $[Ru(H_2O)_6]^{3+}$,$[RuCl(H_2O)_5]^{2+}$, cis and trans $[RuCl_2(H_2O)_4]^+$,$[RuCl_6]^{3-}$,$[RuCl_4]^-$and $[RuCl_4(H_2O)_2]^-$. In alkaline medium the following equilibrium exists in accordance with earlier reports.

$$[Ru(H_2O)_6]^{3+} + OH^- \rightleftharpoons [Ru(H_2O)_5OH]^{2+} + H_2O$$

$[Ru(H_2O)_6]^{3+}$ has high CFSE compared to $[Ru(H_2O)_5OH]^{2+}$.The greater the CFSE of a species, the higher will be the activation energy needed for the reaction and hence the hydroxylated species of ruthenium$[Ru(H_2O)_5OH]^{2+}$is presumed to be the reactive species of ruthenium(III),since the rate increases with increasing $[OH^-]$.

Ruthenium (III) is found to substantially catalyse the reaction and the order with respect to [cystine] is found to be zero. Hence it may be presumed that ruthenium (III) assists the redox reaction between hexacyanoferrate (III) and cystine. This is only possible if an intermediate between HCF(III) and ruthenium (III)species is formed prior to its reaction with cystine. Further reaction between the intermediate and cystine is assumed to be fast as the rate of the reaction is independent of [cystine].In view of these observations the following mechanism has been proposed for which all the observed orders in each constituent such as [oxidant],[cystine], [catalyst] and $[OH^-]$ may be well accommodated.

MECHANISM

$$[Ru(H_2O)_6]^{3+} + OH^- \overset{K}{\rightleftharpoons} [Ru(H_2O)_5OH]^{2+} + H_2O \qquad ....(1)$$

$$[Ru(H_2O)_5OH]^{2+} + HCF(III) \xrightarrow[\text{slow}]{k} \text{Intermediate (I)} \qquad ....(2)$$

$$\text{I} + \text{Cystine} \xrightarrow{fast} \text{Products} + [Ru(H_2O)_5OH]^{2+} + HCF(II) \qquad ...(3)$$

The above scheme leads to the rate equation

$$\text{Rate} = k[Ru(H_2O)_5OH^{2+}]_e\,[HCF(III)] \qquad ......(4)$$

$$\text{Rate} = kK[Ru(H_2O)_6{}^{3+}]_e[OH^-]_e[HCF(III)] \qquad ....(5)$$

Since,

$$[Ru^{III}]_t = [Ru(H_2O)_6{}^{3+}]_e + [Ru(H_2O)_5OH^{2+}]_e$$

$= [Ru(H_2O)_6{}^{3+}]_e + K\,[Ru(H_2O)_6{}^{3+}][OH^-]_e$

$= [Ru(H_2O)_6{}^{3+}]_e\,\{1+K[OH^-]_e\}$

Therefore,

$$[Ru(H_2O)_6{}^{3+}]_e = \frac{[\,Ru^{III}\,]_t}{1+K[OH^-]_e} \qquad \ldots(6)$$

Substituting for $[Ru(H_2O)_6{}^{3+}]_e$ in equation (5) the rate law becomes,

$$\text{Rate} = \frac{kK[\,Ru^{III}\,]_t\,[HCF(III)]\,[OH^-]_e}{1 + K[OH^-]_e} \qquad \ldots.(7)$$

The above equation predicts the plot of $1/k^{/}$ versus $1/[OH^-]$ should be a straight line with a positive intercept on y-axis. Exactly similar plots were obtained experimentally when alkali variations were carried out at four different temperatures, 298, 303, 308 and 313K (Fig.1) and the intercepts and slopes of these plots are $1/k[Ru^{III}]$ and $1/kK[Ru^{III}]$ respectively.

Table 3: Calculated values of k at four different temperatures

Temp. (K)	**k x 10^{-1} ($mol^{-1}\,dm^3\,sec^{-1}$)**		
298	22.72		
303	36.76		
308	44.64		
313	71.42		

[Cystine] = 4.0×10^{-3} mol dm^{-3} ; [HCF(III)] = 4×10^{-4} mol dm^{-3}; [Ru^{III}] = 4×10^{-6} mol dm^{-3}

Further, the rate constants of the rate-determining step, k were determined from the intercepts and the values thus obtained are presented in Table.3.From the rate constants of the rate determining step the energy of activation, E_a and entropy of activation, $\Delta S^{\#}$ for the slow step were computed using a linear least squares method and found to be56.59 ± 0.58 kJ mol^{-1} and -132.60 ± 1.91 J K^{-1} mol^{-1} respectively.

CONCLUSION

Based on the nature of the species and the conditions employed for the reaction, the following points may be put forth in support of the proposed intimate mechanism.

1. In the presence of hydroxide ion, $[Ru(H_2O)_6]^{3+}$ is converted to $[Ru(H_2O)_5OH]^{2+}$ with the replacement of H_2O molecule. This is supported by the experimental observation that increase in $[OH^-]$ results in increase in rate of the reaction. Also $[Ru(H_2O)_5OH]^{2+}$ with a lower overall charge on the complex undergoes ligand exchange faster than $[Ru(H_2O)_6]^{3+}$.

2. The attack of HCF(III) on the $[Ru(H_2O)_5OH]^{2+}$species is facilitated because of less steric hindrance of $[Ru(H_2O)_5OH]^{2+}$ compared to $[Ru(H_2O)_6]^{3+}$.

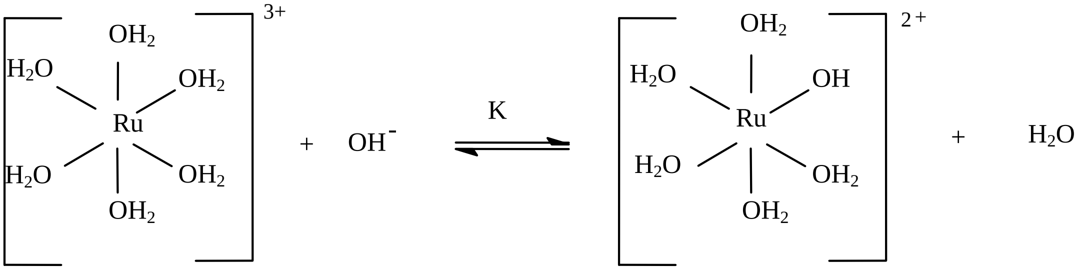
3. Further,$[Ru(H_2O)_5OH]^{2+}$ reacts with HCF(III) to form an intermediate (I) through the formation of Ru-N bond which can be supported by the fact that ruthenium(III) is a boarder line acid and prefers to coordinate through nitrogen.

4. Further the intermediate formed oxidizes cystine to

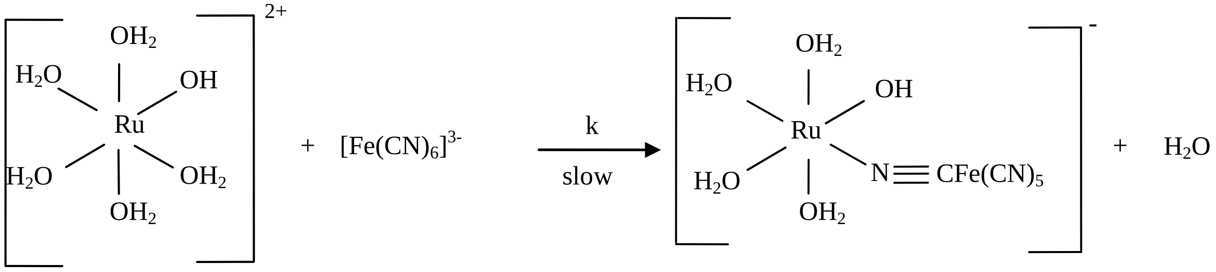
   2-oxoethyl disulfanyl acetaldehyde in several fast steps

In uncatalysed reaction of cystine with HCF(III) the reaction order with respect to both oxidant and substrate was unity, and $[OH^-]$ was found to enhance the rate of the reaction where as in ruthenium(III) catalysed oxidation of cystine by HCF(III), the rate is independent of [substrate] and has unit order dependence on [oxidant] and [catalyst].Further, the product of oxidation was found to be cystine aldehyde in the title reaction while in the former reaction, the product is cysteic acid. In view of these observations the following mechanistic scheme is proposed which is consistent with the kinetic orders and product analysis.

INTIMATE MECHANISM

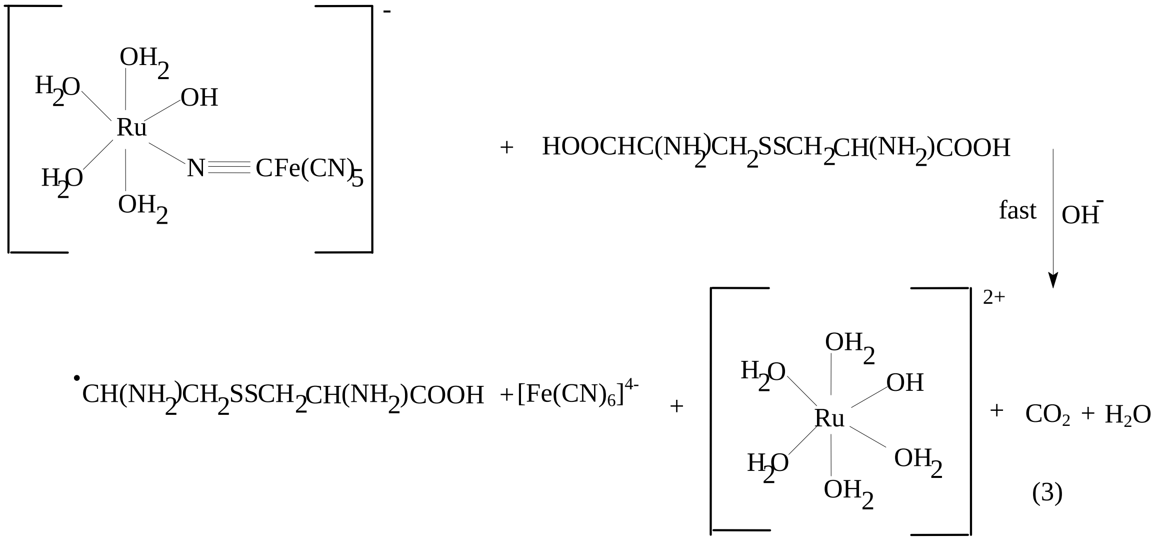


(1)



(I)

(2)



(3)

$$[Fe(CN)_6)]^{3-} \quad {}^{+}CH(NH_2)CH_2SSCH_2CH(NH_2)COOH + \xrightarrow{fast} {}^{\cdot}CH(NH_2)CH_2SSCH_2CH(NH_2)COOH + [Fe(CN)_6]^{4-} \quad (4)$$

$$^{+}CH(NH_2)CH_2SSCH_2CH(NH_2)COOH + H_2O \xrightarrow{fast} OHCCH_2SSCH_2CH(NH_2)COOH + NH_4^{+} \quad (5)$$

fast

$$OHCCH_2SSCH_2CH(NH_2)COOH + [Fe(CN)_6]^{3-} \xrightarrow[OH^-]{} OHCCH_2SSCH_2(NH_2)H\dot{C} + [Fe(CN)_6]^{4-} + CO_2 + H_2O \quad (6)$$

$$OHCCH_2SSCH_2(NH_2)H\dot{C} + [Fe(CN)_6]^{3-} \xrightarrow{fast} OHCCH_2SSCH_2(NH_2)HC^+ + [Fe(CN)_6]^{4-} \quad (7)$$

$$OHCCH_2SSCH_2(NH_2)HC^+ + H_2O \xrightarrow{fast} OHCCH_2SSCH_2CHO + NH_4^+ \quad (8)$$

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