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A Kinetic Study of the Reaction Between *trans*-[CoCl₂(en)₂]Cl and the Amino Acids Alanine and Valine

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Abstract: A kinetic study is reported on the reaction between the complex *trans*-[CoCl₂(en)₂]Cl and the amino acids alanine and valine. Rate constants (*k*) were measured at several temperatures ranging from 25 to 75°C. Representative *k* (10⁻³ sec⁻¹) values found for valine was 6.34 (25°C), 16.92 (35°C), 55.52 (45°C), 96.97 (55°C), 181.28 (65°C), 319.24 (75°C) and 7.33 (25°C), 20.09 (35°C), 53.82 (45°C), 122.03 (55°C), 214.03 (65°C), 343.13 (75°C) for alanine. The relative large variation in the rate constant as a function of the temperature can be related to the activation energy since, reactions that have lower *E_a* usually present fairly constant rates at different temperatures. The activation energy found for the substitution of alanine into the complex *trans*-[CoCl₂(en)₂]Cl was 66.6 KJ.mol⁻¹ and for valine was 66.8 KJ.mol⁻¹. Both reactions have presented mechanisms of the type SN₁.

Key words: Transition metal, amino acids, kinetic study, substitution reaction, mechanism SN₁.

INTRODUCTION

Amino acids are the main constituents of proteins and have the ability to coordinate to transition metal ions through their amino and carboxylic groups. The complexation of transition metal ions to amino acids and correlated compounds have been reported quite frequently in the last decades (Kothari and Busch, 1969; Fernandes *et al.*, 1997; Rombach *et al.*, 2002; Perret *et al.*, 2002; Hannig *et al.*, 2005; Massabni *et al.*, 2005; Shtyrlin *et al.*, 2005; Jalilehvand *et al.*, 2006; Hao *et al.*, 2007; Estrader *et al.*, 2008). Since, many biological reactions are catalyzed by transition metal ions is relevant to know the reactivity, structure and the kinetics of such reactions. Complexes such as those containing copper (II) or zinc (II) are responsible for the transport of important metal ions in the blood stream. Ternary complex ions of copper (II) as [Cu(his)(thr)] are originated in the blood by means of the reaction with histidine, asparagine, glutamine or threonine. Several examples of the biological importance of these complex ions can be mentioned such as histidine properties to form coordinate covalent bonds with metal ions during the treatment of some genetic disturbs related to copper transportation in the blood stream. Also, interactions between side chains of some amino acids and metallic ions responsible to molecular biological recognition, enzymatic activity, stability of protein structures (Yamauchi *et al.*, 2002).

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Many types of cysteine derivatives form soluble metal complexes and have been suggested as possible detoxifying agents. However, the strong interaction between the thiol group of cysteine and mercury ions accounts for the high toxicity of this metal to the physiological system. For this reason, the investigation of the interaction between cysteine and mercury to form complexes such $[\text{Hg}(\text{Cys})_n]$ has been useful as a tool for the development of detoxifying agents toward mercury poisoning (Jalilehvand *et al.*, 2006).

Transition metal complexes with amino acids and peptides have been shown to have anticancer and antibacterial effects. Complexes such as $[\text{M}(\text{L})(\text{H}_2\text{O})_4]\text{Cl}$ and $[\text{M}(\text{L})_2(\text{H}_2\text{O})_2]$ ($\text{M} = \text{Zn}, \text{Cu}, \text{Ni}$ e Co and $\text{L} =$ acetilacetona substituted with one of the following amino acids: glycine, fenilalanine, alanine, valine or histidine) were investigated by Chohan *et al.* (2006). These complexes have presented octahedral geometry with bactericide and fungicide properties. As an example, $[\text{Zn}(\text{L}_5)_2(\text{H}_2\text{O})_2]$ have shown a very good activity against *Escherichia coli* while $[\text{Zn}(\text{L}_3)_2(\text{H}_2\text{O})_2]$ has presented fairly good results toward *Salmonella typhi* (Chohan *et al.*, 2006). Also, cobalt complexes such as $[\text{Co}(\text{L}_2)(\text{H}_2\text{O})_4]\text{Cl}$ have demonstrated activity against *Cândida albicans*, *Aspergillus flavus*, *Microsporun canis* and *Fusarium solani* while the complex $[\text{Co}(\text{L}_4)(\text{H}_2\text{O})_4]\text{Cl}$ was effective against *Cândida albicans*, *Aspergillus flavus*, *Microsporun canis*, *Fusarium solani* and *Cândida glaberata* (Chohan *et al.*, 2006).

Substitution reactions involving the complex $\text{trans-}[\text{CoCl}_2(\text{en})_2]\text{Cl}$ and the aquo ligand have been reported in the literature in which the rate constant and the activation energy were determined by kinetic measurements for the substitution of aquo ligand into the complex (Jackson and Begbie, 1982; Moura *et al.*, 2006). Since, the reaction presented a mechanism SN_1 , the rate constant depends on the initial concentration of the complex $[\text{CoCl}_2(\text{en})_2]^+$. Then, the rate of the reaction could be determined as a derivative of the curve of concentration as a function of time. The rate constant was then computed by means of the plot $\ln[\text{At}-\text{A}_8]/[\text{A}_0-\text{A}_8]$, where, At is the absorbance of the complex $[\text{CoCl}_2(\text{en})_2]^+$ at time t , A_0 is the absorbance at time $t = 0$ and A_8 is the absorbance after the reaction has gone to completion. The activation energy was determined through the angular coefficient of the plot $\ln(k)/(T^{-1}/\text{K}^{-1})$ (Moura *et al.*, 2006). Taking the facts above into account, this work reports on the kinetic study for the substitution of alanine and valine into the complex $[\text{CoCl}_2(\text{en})_2]\text{Cl}$ in order to determine the rate constants and the activation energy.

MATERIALS AND METHODS

Cobalt chloride (Sigma-Aldrich), alanine (Sigma-Aldrich), valine (Sigma-Aldrich), ethilenodiamine (en, Sigma-Aldrich), hydrogen peroxide (H_2O_2 , Sigma-Aldrich), KBr (Sigma-Aldrich) and hydrogen chloride (Sigma-Aldrich) were used as received. Ether ethylic was distilled prior to use. Cobalt complexes were analyzed by Infrared (IR) on an Bomem 100 instrument. This research was conducted partly at the Faculdade de Ciências Integradas do Pontal of the Federal University of Uberlândia, Ituiutaba (Brazil) and partly at the Centro Universitario da Fundação Educacional de Barretos, Barretos (Brazil) during the year of the 2008.

Synthesis of the complex $\text{trans-}[\text{CoCl}_2(\text{en})_2]\text{Cl}$

The complex $\text{trans-}[\text{CoCl}_2(\text{en})_2]\text{Cl}$ was synthesized following the publish procedure (Moura *et al.*, 2006). Aqueous solution of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ were prepared by adding 5.0 g (0.021 mol) of solute in 20 mL of solvent. Then, 20 mL of 10% ethilenodiamine solution were added together followed by the slow addition of 4.0 mL of 6.0% H_2O_2 . This solution was kept

at 70°C and then 15 mL of concentrated HCl were added. The final volume was evaporated to 1/3 of the initial volume. The precipitate was filtered off, washed with ether ethylic and dried under vacuum with an experimental yield of 20.47%.

Kinetics

Kinetic studies were carried out in temperature steps of 10°C from 25 to 75°C using a concentration rate of 1:2 of the complex trans-[CoCl₂(en)₂]Cl to the amino acid alanine or valine. A Fanem 120/3 water bath was used to keep constant the temperature and a Hach DR/4000 spectrophotometer was employed to measure absorbance of samples collected at controlled time intervals.

RESULTS AND DISCUSSION

The substitution reaction of the complex trans-[CoCl₂(en)₂]Cl with alanine and valine were monitored by measuring absorption spectra in the range of 400-750 nm (Fig. 1A, B). These substitution reactions involving octahedral complexes of cobalt (III) with large ligands such amino acids are characteristic of reactions with mechanism S_N1 as shown in Fig. 2.

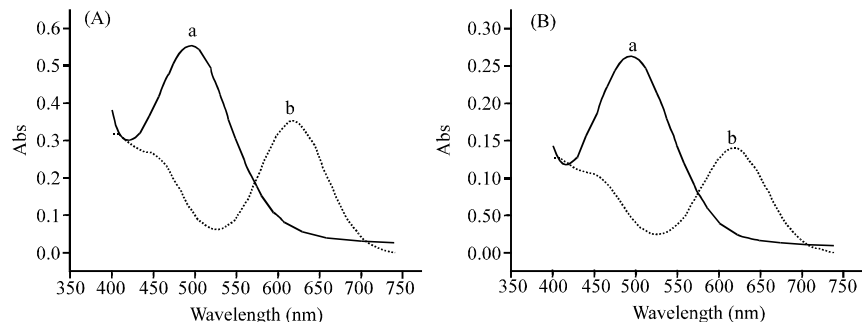


Fig. 1: Spectra of the ion complex trans-dichlorobis(ethylenediamine)cobaltate(III) before (a) and after (b) substitution by (A) alanine and (B) valine

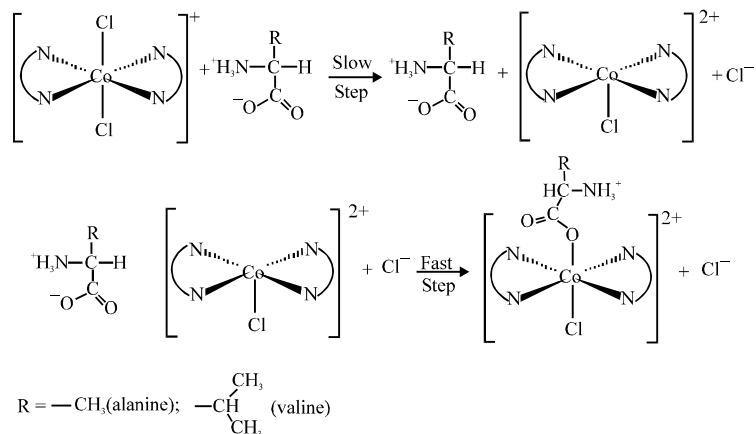


Fig. 2: Substitution reaction of the ion complex trans-dichlorobis (ethylenediamine) cobaltate (III) with amino acid alanine or valine

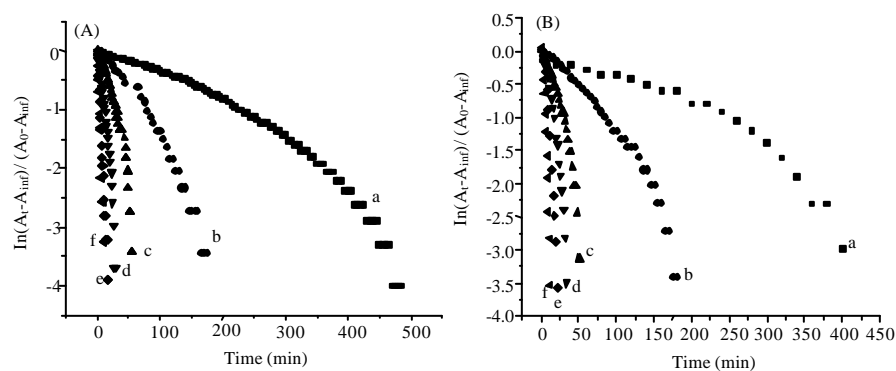


Fig. 3: Kinetic data for the substitution reaction of the ion complex trans-dichlorobis (ethylenediamine) cobaltate (III) with (A) alanine and (B) valine in aqueous solution; absorbance monitored at 605 nm at temperatures of (a) 25, (b) 35, (c) 45, (d) 55, (e) 65 and (f) 75°C

Table 1: Rate constant (k) for the substitution reaction of the ion complex trans-dichlorobis (ethylenediamine) cobaltate (III) with alanine and valine in different temperatures

T(°C)	K (10 ⁻³ sec ⁻¹)	
	Alanine	Valine
25	7.33	6.34
35	20.09	16.92
45	53.82	55.52
55	122.06	96.97
65	214.03	181.28
75	343.13	319.24

Infrared measurements have confirmed the mechanism shown in Fig. 2 by means of the $\nu_{C=O}$ as stretching. By comparing spectra of the free complex with the amino acid substituted complex, a shift from 1621 to 1647 cm^{-1} in $\nu_{C=O}$ was found for alanine as well as a shift from 1612 to 1640 cm^{-1} for valine. Since, the kinetic study was conducted in neutral conditions, is reasonable to claim that the amino acids under investigation act as monodentate ligands as described in the literature (Nakamoto, 1997).

Kinetic studies of the substitution reaction of the complex $\text{trans}[\text{CoCl}_2(\text{en})_2]\text{Cl}$ with alanine and valine.

The kinetic study of the substitution reaction of the complex $\text{trans}[\text{CoCl}_2(\text{en})_2]\text{Cl}$ with alanine or valine was carried out at temperatures of 25, 35, 45, 55, 65, and 75°C. The progress of the reaction was monitored by the suppression of the absorbance at 605nm where the free complex has its maximum of absorption. The rate constants were determined by plotting $\ln(A_t - A_\infty)/(A_0 - A_\infty)$ versus time as shown in Fig. 3A and B. In this plot, A_t is the absorbance at time t, A_∞ is the absorbance after reaction has gone to completion and A_0 is the initial absorbance. The k values were estimated from the angular coefficient of the linear portion of the curves shown in Fig. 3 and are presented in Table 1.

According to a report by Moura *et al.* (2006) the rate constant for the substitution reaction of one chloride ligand by one water molecule in the complex $\text{trans}[\text{CoCl}_2(\text{en})_2]^+$ is about $1.44 \times 10^{-3} \text{ sec}^{-1}$ at 25°C. The value found in this study for the substitution of chloride by alanine was $7.33 \times 10^{-3} \text{ sec}^{-1}$ and for the substitution of chloride by valine was

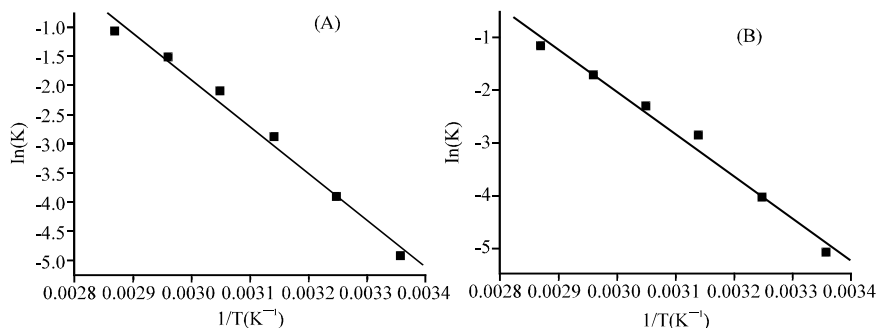


Fig. 4: Plot of Arrhenius equation for the substitution reaction of the ion complex trans-dichlorobis(ethylenediamine)cobaltate(III) with ligands (A) alanine and (B) valine

$6.34 \times 10^{-3} \text{ sec}^{-1}$ at the same temperature of 25°C . These higher values found for the amino acids can be explained by the volume of each ligand since, the substitution of large ligands are favored in mechanism of the type SN_1 .

The activation energy for the substitution reaction of each amino acid was calculated from the angular coefficient of the plot of $\ln(k)$ versus $1/T$ as shown in Fig. 4A and B. The values found were $E_a = 66.6 \text{ kJ.mol}^{-1}$ for alanine and $E_a = 66.8 \text{ kJ.mol}^{-1}$ for valine.

CONCLUSION

Kinetic of the substitution reaction of alanine and valine by chloride in the complex trans- $[\text{CoCl}_2(\text{en})_2]\text{Cl}$ were investigated at different temperatures. The rate constants found for the reaction using alanine were $7.33 \times 10^{-3} \text{ sec}^{-1}$ (25°C), $20.09 \times 10^{-3} \text{ sec}^{-1}$ (35°C), $53.82 \times 10^{-3} \text{ sec}^{-1}$ (45°C), $122.06 \times 10^{-3} \text{ sec}^{-1}$ (55°C), $214.04 \times 10^{-3} \text{ sec}^{-1}$ (65°C) and $343.13 \times 10^{-3} \text{ sec}^{-1}$ (75°C). Those values for the reaction using valine were $6.34 \times 10^{-3} \text{ sec}^{-1}$ (25°C), $16.92 \times 10^{-3} \text{ sec}^{-1}$ (35°C), $55.52 \times 10^{-3} \text{ sec}^{-1}$ (45°C), $96.97 \times 10^{-3} \text{ sec}^{-1}$ (55°C), $181.28 \times 10^{-3} \text{ sec}^{-1}$ (65°C) and $319.24 \times 10^{-3} \text{ sec}^{-1}$ (75°C). Both reactions have presented mechanisms of the type SN_1 . The relative large variation in the rate constant as a function of the temperature can be related to the activation energy since, reactions that have lower E_a usually present fairly constant rates at different temperatures. The activation energy found for the substitution of alanine into the complex trans- $[\text{CoCl}_2(\text{en})_2]\text{Cl}$ was 66.6 KJ.mol^{-1} and for valine was 66.8 KJ.mol^{-1} .

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