



Kinetics of the reaction of s-carboxymethyl-L-cysteine with palladium(II) chloride*

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Abstract: The influence of the acidity and the Cl^- concentration on the kinetics of the complex formation between s-carboxymethyl-L-cysteine and Pd(II) chloride was studied with a stopped-flow technique in the pH range from 1.5 to 5.0 at 25°C. The reaction mechanism involving $\text{Pd}(\text{H}_2\text{O})_{4-n}\text{Cl}_n$, LH^- , LH_2 and LH_3^+ species was proposed. Fairly good agreement between the computed and experimentally determined rate constants was found.

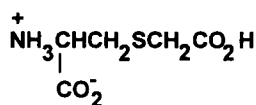
Keywords: s-Carboxymethyl-L-cysteine; palladium (II) chloride; kinetics; stopped-flow.

Introduction

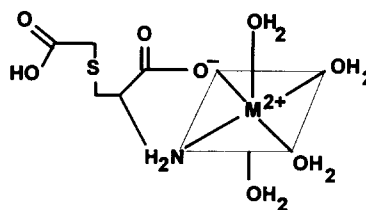
s-Carboxymethyl-L-cysteine (SCMCH₂) belongs to a group of naturally occurring amino acids containing thioether group [1]. SCMCH₂ is a biologically active substance with a mucolytic effect, which was found in urine of cystathioninuric patients [2] and identified as an intermediate in cystamine formation [1].

Only a few studies have been reported concerning the interaction of SCMCH₂ with metal ions, such as Cu(II), Ni(II), Zn(II), etc. [3, 4]. Potentiometric and spectral data suggest that the metal chelate structures depend on the preference of the certain metal ions for certain donor groups. These data provided evidence for the existence of ML, MLH and ML₂ complexes in which the ligand chelates to the metal ion via the α-amino and carboxylate groups of the α-amino acid residue (Scheme 1); the coordination of sulphur atom to the metal ion is also suggested (Scheme 2).

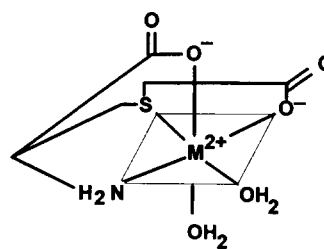
Recently, the spectrophotometric method for determination of N-acetyl-L-cysteine and



SCMCH₂



Structure 1



Structure 2

SCMCH₂ by using palladium (II) chloride (PdCl₂) was developed [5, 6]. It was noticed that the rate of development of the absorption band of the complex depends on the pH and the Cl^- concentration. In the present paper, kinetics of the complex formation between PdCl₂ and SCMCH₂ were studied in order to clarify the mechanism of the reaction.

* Presented at the Fifth International Symposium on Pharmaceutical and Biomedical Analysis, Stockholm, Sweden, September 1994.

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Experimental

Chemicals

All reagents were commercial products of the highest purity available. A freshly prepared 2×10^{-2} M SCMCH₂ aqueous stock solution was used in all experiments. The standard solution of 2×10^{-2} M PdCl₂ was prepared as described elsewhere [5].

Perchloric acid (HClO₄) and sodium hydroxide (NaOH) were used to adjust the pH of solutions. Sodium perchlorate (NaClO₄) was used to maintain the ionic strength. Sodium chloride (NaCl) was used to control the Cl⁻ concentration.

Apparatus and kinetic measurements

The absorption spectra were recorded on a Perkin-Elmer Lambda 5 UV-vis spectrophotometer. For the stopped-flow experiments, the universal rapid kinetic accessory HI-TECH model SFA 12 was fitted to a spectrophotometer. All the reagents (acid, inert salt, NaCl) were added to SCMCH₂ and PdCl₂ solutions at least 20 min prior to mixing. The kinetic experiments were performed by mixing equal volumes of SCMCH₂ and PdCl₂ solutions at $25 \pm 0.1^\circ\text{C}$.

The rate of the complex formation was followed by monitoring the increase of the optical absorbance at 375 nm. Values of k_{obs} were determined by fitting the experimental trace (A vs t) to the function $(A - A_0)/(A_e - A) = f(t)$ (A_0 and A_e are the initial and final absorbancies, respectively) by using a computer program based on the least squares method. All kinetic measurements were reproducible within limits of error of $\pm 5\%$. The quoted values are the average of at least five runs under identical experimental conditions.

Results and Discussion

Absorption spectra

The complex formation between SCMCH₂ and PdCl₂ takes place in aqueous solutions in the pH range from 1 to 8 [6]. Absorption spectra of the solutions which contained equal concentrations of PdCl₂ and SCMCH₂ (4×10^{-4} M), and Cl⁻ ions in the concentration range from 0.002 to 0.6 M at pH 4, are shown in Fig. 1(a-c). The slight shift of the absorption maximum from 380 to 375 nm was observed by lowering the Cl⁻ concentration from 0.6 to

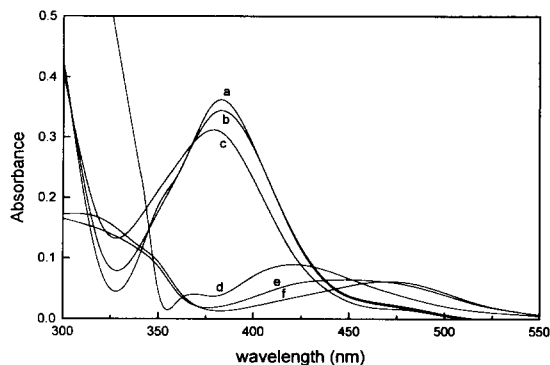
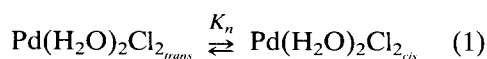
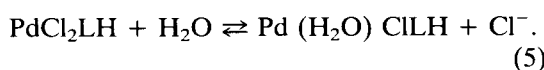
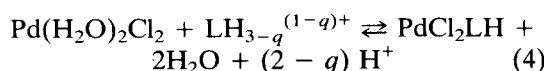
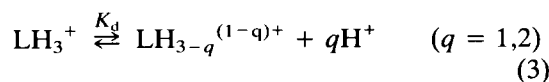
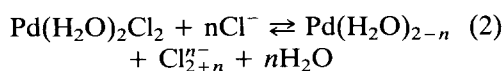


Figure 1

Absorption spectra of Pd(II)-SCMCH₂ complex (a-c) and Pd(H₂O)_{4-n}Cl_n species (d-f) as a function of Cl⁻ concentration: (a) 0.3 M, (b, e) 0.1 M, (c, d) 0.002 M, and (f) 0.6 M; (pH 4.0, [PdCl₂] = [SCMCH₂] = 4×10^{-4} M, $\mu = 0.5$ (NaClO₄)).

0.002 M. Also, the presence of well defined isosbestic points at 305 and 368 nm can be noticed, suggesting that the two complex species are in equilibrium under these experimental conditions. For comparison, the absorption spectra of PdCl₂ solutions in the presence of Cl⁻ ions are given in Fig. 1(d-f). Analysis of the position of the absorption maximum of the complex species according to the ligand field theory indicated the coordination of α -amino and carboxylate groups in Pd(II)-SCMCH₂ complex [7]. Also, the slight hypsochromic shift in the position of the absorption maximum indicates that the equilibrium between Pd(H₂O)ClLH and PdCl₂LH complexes occurs by lowering the Cl⁻ concentration. The absorption spectra at a constant Cl⁻ concentration were also followed in the pH range from 1.5 to 5.0 and did not show any change in the position and intensity of the absorption maximum. These results indicated that the metal chelate structure was not affected by the change of acidity in the pH range from 1.5 to 5.0. It was assumed that only Pd(H₂O)₂Cl₂, Pd(H₂O)Cl₃⁻ and PdCl₄²⁻ species were present when the Cl⁻ concentration was higher than the concentration of Pd(II) [8]. The acidity was high enough to suppress the deprotonation of Pd(II) chloro-aqua complexes [8]. In the investigated range of acidity ($1 < \text{pH} < 5$), the protolytic equilibria of ligand take place [4], and the following reactions occur.





In equation 3, $\text{LH}_{(3-q)}^{(1-q)+}$ are the ionic species of ligand. The charge of all complexes is omitted for simplicity.

Kinetics of the complex formation

Kinetics of the complex formation between SCMCH_2 and $\text{Pd}(\text{II})$ chloroaqua complexes were investigated in the pH range from 1.5 to 5.0. The reaction rate was followed as a function of the ratio between the initial concentrations of the reactants (Table 1). Also, the kinetic runs with equal concentration of $\text{Pd}(\text{II})$ chloroaqua complex and SCMCH_2 fit second-order plots without significant curvature (Fig. 2). These results showed that the rate expression was first-order in $\text{Pd}(\text{II})$ chloroaqua complex and first order in entering ligand

$$\frac{d(\text{complex})}{dt} = k_{\text{obs}} [\text{L}] [\text{Pd}]. \quad (6)$$

The observed rate constant (k_{obs}) was a

Table 1

The observed second-order rate constants (k_{obs}) as a function of initial concentrations of PdCl_2 and SCMCH_2 at 25°C, calculated according to equation 6*

pH	PdCl_2 (M)	SCMCH_2 (M)	$10^{-3} k_{\text{obs}}$ ($\text{M}^{-1} \text{s}^{-1}$)
2.3	4×10^{-4}	4×10^{-4}	2.4 ± 0.2
	2×10^{-4}	2×10^{-3}	2.6 ± 0.3
4.5	4×10^{-4}	4×10^{-4}	0.28 ± 0.03
	5×10^{-4}	1×10^{-4}	0.38 ± 0.04

* $[\text{Cl}^-] = 0.3 \text{ M}$; $\mu = 0.3$ (NaCl).

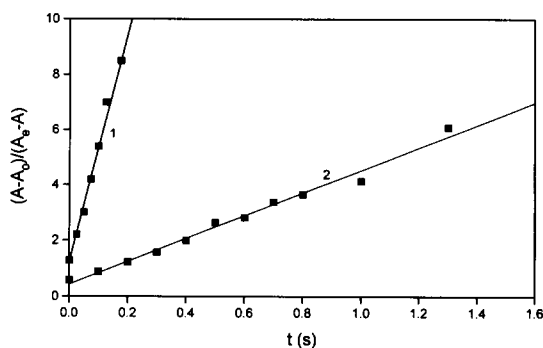


Figure 2

Sample kinetic runs with equal concentrations of $\text{Pd}(\text{II})$ and SCMCH_2 at (1) pH 2.0, and (2) pH 4.5; ($[\text{PdCl}_2] = [\text{SCMCH}_2] = 4 \times 10^{-4} \text{ M}$, $[\text{Cl}^-] = 0.3 \text{ M}$).

function of pH, as well as the Cl^- concentration.

Effects of Cl^- and pH on the reaction rate

The influence of Cl^- ions on the observed rate constant (k_{obs}) at constant ionic strength is shown in Fig. 3. Measurements were per-

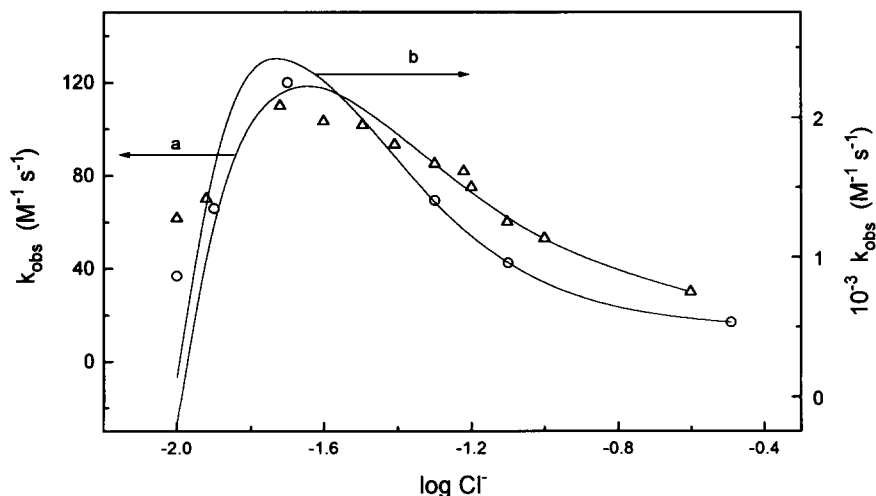


Figure 3

Observed rate constant (k_{obs}) as a function of Cl^- concentration: (a) pH 1.5, $\mu = 0.5$, and (b) pH 4.2, $\mu = 0.42$ (NaClO_4); ($[\text{PdCl}_2] = [\text{SCMCH}_2] = 4 \times 10^{-4} \text{ M}$; 25°C).

formed at pH 1.5 and 4.2 by using solutions that contained equal initial concentrations of Pd(II) chloroqua complex and ligand (4×10^{-4} M). The bell-shaped curves of k_{obs} vs Cl^- concentration were obtained.

The influence of pH on k_{obs} at constant ionic strength was investigated in the presence of low and high concentration of Cl^- ions (0.008 and 0.5 M). Results are shown in Fig. 4. Significant influence of pH on the rate constant was observed at high acidities ($1 < \text{pH} < 2.5$), while at $\text{pH} > 4$ the rate constant remained unchanged. As can be seen in Fig. 4, the pH profile is bell-shaped, with the maximum in the vicinity of the deprotonation of carboxylic group ($\log K_{a_3} = 1.91$ [4]).

The effect of pH on the rate of the complex formation can be explained by the presence of various ionic species of SCMCH₂ ($\log K_{a_2} = 3.33$ and $\log K_{a_3} = 1.91$ [4]). It was assumed that the aquation of Pd(II) was faster com-

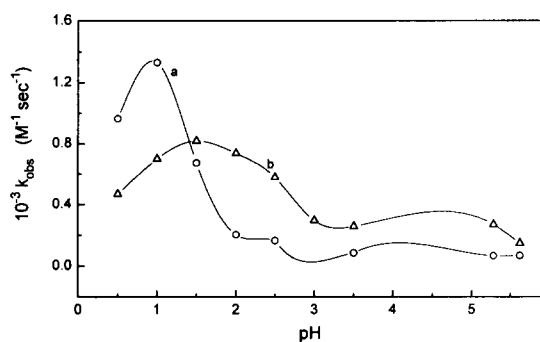


Figure 4
The second-order rate constants for the reaction of the complex formation between PdCl₂ and SCMCH₂ as a function of pH: (a) $[\text{Cl}^-] = 0.008$ M, and (b) $[\text{Cl}^-] = 0.5$ M; $\mu = 0.5$ (NaClO₄). The points were experimentally obtained, while the curves were calculated from equation 11.

$$k_{\text{obs}} \left(1 + \frac{[\text{H}^+]}{K_{a_3}} + \frac{K_{a_2}}{[\text{H}^+]} \right) = \frac{k_1[\text{Cl}]^3 + k_2K_4[\text{Cl}]^2 + k_3K_3K_4[\text{Cl}] + (k_4 - k_{-4})K_2K_3K_4}{[\text{Cl}]^3 + K_4[\text{Cl}]^2 + K_3K_4[\text{Cl}]} \quad (11)$$

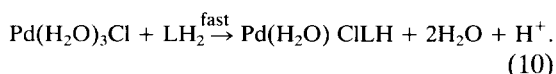
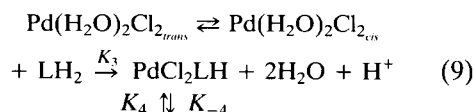
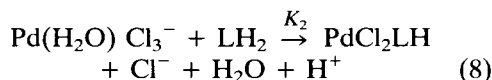
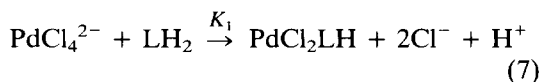
Table 2
Values of the rate constants in reactions 7–10 at 25°C*

pH	μ^\dagger	k ($\text{m}^{-1} \text{s}^{-1}$)			
		k_1	k^2	k^3	$k_4 - k_{-4}$
1.5	0.50	$(1.8 \pm 0.2) \times 10^3$	$(9.4 \pm 0.9) \times 10^3$	$(1.9 \pm 0.2) \times 10^5$	$(4.2 \pm 0.1) \times 10^6$
4.2	0.42	$(1.3 \pm 0.2) \times 10^2$	$(9.1 \pm 0.8) \times 10^2$	$(1.2 \pm 0.1) \times 10^4$	$(2.9 \pm 0.9) \times 10^5$

* $[\text{PdCl}_2] = [\text{SCMCH}_2] = 4 \times 10^{-4}$ M.

\dagger (NaClO₄).

pared to the substitution by ligand [9], and consequently that the equilibrium between Pd(H₂O)_{4-n}Cl_n species was maintained throughout the kinetic run. A scheme that is consistent with the dependence of k_{obs} vs Cl^- concentration is given by the following equations



It was proposed that only the cis form of Pd(H₂O)₂Cl₂ complex reacted with LH₂ form of ligand. Furthermore, in equation 10, the replacement of two molecules of water by ligand was assumed to be fast, and consequently equilibria between the two forms of Pd(II)–SCMCH₂ complexes took place. Decrease of the Cl^- concentration led to the shift of equilibria toward the formation of Pd(H₂O)ClLH complex ($k_{-4} > k_4$).

Taking into consideration equation 3, the same reaction scheme should also be valid assuming that Pd(H₂O)_{4-n}Cl_n species react with LH⁻ and LH₃⁺. If the proposed reaction mechanism is correct, and taking into account equilibria 1–5, the dependence of the observed rate constant on the Cl^- concentration and pH ($1 < \text{pH} < 5$) can be described by the following equation

The symbols in equation 11 are identified in equations 2–10. Also, it can be shown that k_{1-4} are pH dependent rate constants

$$k_n = k'_n + \frac{[H^+]k''_n}{K_{a_3}} + \frac{k'''_n K_{a_3}}{[H]} \quad (n = 1-4), \quad (12)$$

where k'_n , k''_n and k'''_n are rate constants of LH_2 , LH_3^+ and LH^- , respectively.

Reaction constants (k_n) were calculated from the observed rate constants and the corresponding Cl^- concentration by using equation 11. The values of the stepwise $Pd(H_2O)_{4-n}Cl_n$ stability constants were taken from [10]. Results are given in Table 2. The calculated values of k_{obs} are the best fit to equation 11 obtained by using k_{1-4} as variable parameters (Fig. 3).

According to the obtained results, some unusual aspects of the kinetics of the complex formation between $SCMCH_2$ and $PdCl_2$ were noticed. Although the reactions were carried out with a low concentration of ligand, the first-order term, characteristic for the substitution reactions of square planar complexes [11], was either absent or abnormally ineffective in generating the product. The first-order term in substitution reactions of square planar complexes arises from the "solvent path" to the product involving a slow attack by the solvent followed by a rapid displacement of the solvent by the substituting ligand. Under the present reaction conditions the attack of the solvolyzed species by the ligand was slower than solvolysis, giving a second order solvent path. Consequently, the rate law only contains the second-order term (equation 6). The proposed reaction mechanism is in agreement

with the mechanism of substitution reactions for square planar $Pd(II)$ complexes with some bidentate ligands [12, 13]. The ligand attacks all $Pd(H_2O)_{4-n}Cl_n$ species ($n = 1-4$), as demonstrated by the dependence of k_{obs} vs Cl^- concentration. The ligand reacts more rapidly with $Pd(H_2O)_2Cl_2$ and $Pd(H_2O)Cl_3^-$ species than with $PdCl_4^{2-}$, because the water can be more quickly replaced by an attacking ligand than the Cl^- ion. The reaction proceeds with both forms of ligand, protonated and free.

Acknowledgements — The authors would like to thank Dr Sofija Sovilj for critically reading the manuscript. Financial support for this study was granted by the Scientific Fund of Serbia (Yugoslavia).

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[Received for review 22 September 1994;
received in revised form 18 January 1995]