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Influence of acidity on the reaction between $[PdCl(dien)]^+$ and L-cysteine or glutathione in the presence of sodium dodecyl sulfate micelles

Vesna M. Vasić,[1]* Momir A. Živanović,[1] Mira M. Čakar,[2] Jasmina Z. Savić,[1] Jovan M. Nedeljković[1] and Živadin D. Bugarčić[3]

[1]Vinča Institute of Nuclear Sciences, PO Box 522, 11001 Belgrade, Serbia and Montenegro
[2]Faculty of Pharmacy, University of Belgrade, PO Box 146, 11001 Belgrade, Serbia and Montenegro
[3]University of Kragujevac Faculty of Science, R. Domanovica 12, PO Box 60, 34000 Kragujevac, Serbia and Montenegro

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ABSTRACT: The reaction mechanism and thermodynamic parameters of the complex formation between $[PdCl(dien)]^+$ and sulfur-containing ligands L-cysteine and glutathione (GSH) were investigated in the presence of sodium dodecyl sulfate micelles in the pH range 0.5–3.5. The reaction rates were determined under pseudo-first-order conditions (ligand in excess) in the temperature range 276–299 K by using the stopped-flow technique. A reaction mechanism was proposed that consisted of at least two parallel paths involving protonated and zwitterionic forms of thiols. The pH effects on reaction rate were interpreted in terms of the electrostatic interactions between the negatively charged micelle surface and different ionic forms of the ligand species. The calculation of pH-dependent activation parameters ($\Delta H^{\neq}$ and $\Delta S^{\neq}$) revealed the considerable catalytic effects on the rate of complexation. The entropy of activation is strongly negative in the presence and absence of micelles, which is compatible with an associative reaction mechanism. Copyright © 2004 John Wiley & Sons, Ltd.

KEYWORDS: complex formation; micellar catalysis; sodium dodecyl sulfate; palladium(II); L-cysteine; glutathione

INTRODUCTION

Naturally occurring tripeptides glutathione (GSH) and γ-glutamylcysteinylglycine (γ-Glu-CysH-Gly) and amino acid L-cysteine are sulfur-containing ligands that belong to the group of biomolecules exerting a great role in thiol-dependent biochemical reactions. Glutathione is frequently the most prevalent intracellular thiol with a concentration up to 10 mM and it is the most abundant low-molecular-weight peptide. Glutathione has been adapted through evolution to perform many diverse functions. For instance, GSH protects cells from the toxic effects of reactive oxygen compounds and is an important component of the system that uses reduced pyridine nucleotide to provide the cell with its reducing properties. Glutathione functions in catalysis, metabolism and transport. It participates in reactions involving the synthesis of proteins and nucleic acids and in those that detoxify free radicals and peroxides. However, the intracellular level of GSH is much greater than that of cysteine.[1–3] Recently, it was reported that GSH and L-cysteine are potent enzyme activity reactivators because they recover the metal-ions-induced inhibition of some enzymes.[4,5] These interactions are usually due to the complex formation between thiols and the metal ion bonded to the —SH groups of the active sites of the enzyme.[6]

Both L-cysteine and GSH are highly reactive towards platinum complexes, revealing effective antitumor activity.[7] The interactions between thiols and platinum compounds usually have been associated with resistance and toxicity in the antitumor treatment[7–9] and tripeptide GSH provides a model compound for their study. The Pd(II) complexes with various tridentate ligands are suitable model systems for investigations of the reaction mechanism of Pt(II) anticancer drugs with amino acids because they exhibit $\sim 10^4$–10^5 higher reactivity but their structural and equilibrium behavior is similar.[10] So far, the kinetics of the reactions of several Pt(II) and Pd(II) complexes with sulfur-bonding molecules have been reported.[11–26] Because some platinum complexes have been used as anticancer drugs,[7–9] these interactions are very important from a biological and a medical point of view. This also could be of fundamental importance for understanding the nephrotoxicity of related platinum complexes.[11–14]

Recently, we focused on investigation of the effects of micellar systems on reactions of Pd(II) and Pt(II)

**Correspondence to:* V. M. Vasić, Vinča Institute of Nuclear Sciences, PO Box 522, 11001 Belgrade, Serbia and Montenegro.
E-mail: evasic@vin.bg.ac.yu
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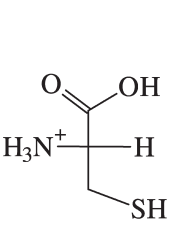
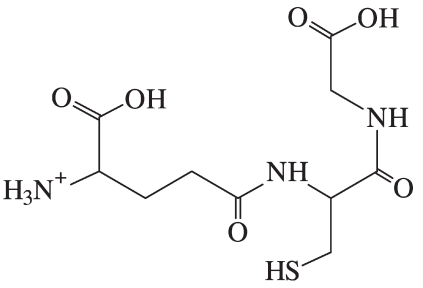
coordination compounds with thiols.[27] Although the micelles do not influence the stoichiometry and mechanism of the complex formation,[27–31] the reaction rate was found to be strongly dependent on the presence of the surfactant. These studies are important not only from a viewpoint of inorganic reaction mechanisms but also from biochemical aspects, i.e. as models of ligand-exchange reactions on the surface of a biomembrane or at the interface of a globular protein.

In the present study the effect of acidity on the rate and thermodynamic parameters of the reaction between $[PdCl(dien)]^+$ and L-cysteine or GSH in the presence of the anionic surfactant sodium dodecyl sulfate (SDS) was investigated.



L-Cysteine



glutathione

EXPERIMENTAL

The complex [PdCl(dien)]Cl was prepared according to a standard procedure.[32] L-Cysteine and GSH were commercial products of the highest purity available. Freshly prepared stock solutions of 1×10^{-2} M L-cysteine (Fluka, 99.5%) and 1×10^{-2} M GSH (Fluka, 99%) in 0.1 M $HClO_4$ (Merck, p.a.) were used in all experiments. More dilute solutions were obtained by appropriate dilution with water. The standard solution of 1×10^{-3} M $[PdCl(dien)]^+$ complex in 0.1 M $HClO_4$ was used in reactions with L-cysteine or GSH. A stock solution of 0.1 M SDS was used in all experiments. The acidity of the solution was controlled by the addition of Britton–Robinson buffer. The ionic strength was kept constant (0.1 M) by the addition of $NaClO_4$. Triply distilled water was used in all solutions and the solutions were purged with nitrogen to remove oxygen.

The absorption spectra were recorded on a Beckman 5260 UV–Vis spectrophotometer in the wavelength range 220–450 nm. The pH values of the solutions were measured by a Metrohm pH-meter (model 713). For the stopped-flow experiments a universal rapid kinetic accessory (Hi-Tech, model SFA 12) was fitted to the spectrophotometer. Kinetic experiments were performed by mixing equal volumes of the $[PdCl(dien)]^+$ complex and thiol solutions. The rate of complex formation was followed by monitoring the increase of absorbance at 250 nm for L-cysteine and at 260 nm for GSH as a function of time for at least eight half-lives. Values of k_{obs} were determined by fitting the experimental trace (A vs. t) to the function $(A_f - A)/(A_f - A_o) = \exp(-k_{obs}t)$ (A_o and A_f are the initial and final absorbancies, respectively). All kinetic measurements were reproducible within limits of error of ± 5%. The quoted values are the average of at least five runs under identical experimental conditions. All reported rate constants were determined at constant temperature in the range 276–299 K.

RESULTS AND DISCUSSION

The pH-dependent equilibrium of complex formation

The formation of the complex between $[PdCl(dien)]^+$ and L-cysteine or GSH in the absence and presence of 1×10^{-2} M SDS was investigated in the pH range 0.5–3.5. The absorption spectra of solutions containing 1×10^{-4} M $[PdCl(dien)]^+$ and 1×10^{-3} M L-cysteine or GSH in the presence of 1×10^{-2} M SDS were followed as a function of acidity. The spectra of both $[Pd(dien)(thiol)]^+$ complexes are similar, with the characteristic absorption maxima at 260 and 390 nm and the shoulder in the wavelength range 300–350 nm (see Fig. 1).

Generally, the presence of 1×10^{-2} M SDS in the investigated acidity range induced a slight bathochromic shift (<5 nm) of the absorption maximum. However, at least two ionic forms of ligands are in equilibrium owing to the dissociation of —COOH groups.[33,34] Consequently, the slight shifts in intensity and position of the absorption maximum with increasing pH indicate the complex formation between different ionic forms of ligands with $[PdCl(dien)]^+$ rather than the influence of micelles on the complex structure.

The equilibrium between the thiol and the complex is therefore pH dependent in both cases, and can be expressed as follows:

$$[PdCl(dien)]_f^+ + L_f \underset{k_b}{\overset{k_f}{\rightleftharpoons}} \text{Complex} \qquad (1)$$

where the subscript 'f' denotes the free, uncomplexed species (L = thiol). The pH-dependent apparent formation constant (K_{app}) is defined using:

$$K_{app} = \frac{[\text{Complex}]_{tot}}{[L_f][Pd_f]} \qquad (2)$$

The $[L_f]$ values for L-cysteine and GSH are given by Eqns (3) and (4), respectively:

$$[L_f] = LH_2^+ + LH = \alpha[LH] \qquad (3)$$

$$[L_f] = LH_3^+ + LH_2 + LH^- = \alpha[LH_2] \qquad (4)$$

$$H_2L^+ + [PdCl(dien)]^+ \overset{K'_{eq}}{\rightleftharpoons} [PdLH(dien)]^{2+} + H^+ + Cl^- \quad (5)$$

$$\Big\downarrow K_{a_1}$$

$$HL + [PdCl(dien)]^+ \overset{K''_{eq}}{\rightleftharpoons} [PdL(dien)]^+ + H^+ + Cl^- \quad (6)$$

$$H_3L^+ + [PdCl(dien)]^+ \overset{K'_{eq}}{\rightleftharpoons} [PdLH_2(dien)]^{2+} + H^+ + Cl^- \quad (7)$$

$$\Big\downarrow K_{a_1}$$

$$H_2L + [PdCl(dien)]^+ \overset{K''_{eq}}{\rightleftharpoons} [PdLH(dien)]^+ + H^+ + Cl^- \quad (8)$$

$$\Big\downarrow K_{a_2}$$

$$HL^- + [PdCl(dien)]^+ \overset{K'''_{eq}}{\rightleftharpoons} [PdL(dien)] + H^+ + Cl^- \quad (9)$$

Scheme 1. Reaction steps for complex formation between $[PdCl(dien)]^+$ and L-cysteine (Eqns (5) and (6)) or GSH (Eqns (7)–(9))

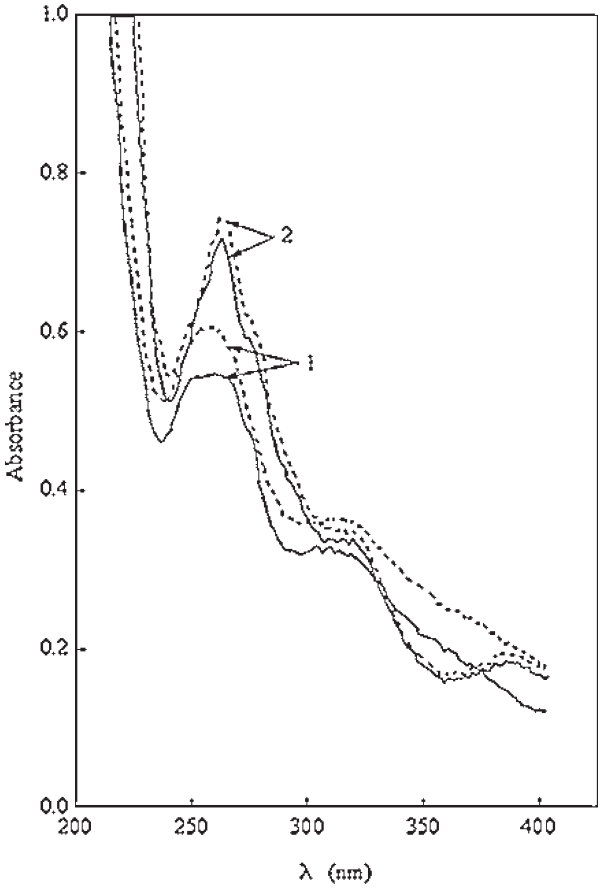


Figure 1. Absorption spectra of solutions containing 1×10^{-4} M $[PdCl(dien)]^+$ and 1×10^{-3} M GSH (1) or L-cysteine (2) in the absence (solid curves) and presence (dot curves) of 1×10^{-2} M SDS at pH 2

where $\alpha = 1 + [H^+]/K_{a1}$ for L-cysteine and $\alpha = 1 + [H^+]/K_{a1} + [H^+]^2/(K_{a1}K_{a2})$ for GSH.

The values of dissociation constants of —COOH groups for L-cysteine and GSH are defined in Scheme 1 ($pK_{a1} = 1.9$ for L-cysteine;[33] $pK_{a1} = 2.05$ and $pK_{a2} = 3.40$ for GSH[34]). Moreover, the —SH group, which is responsible for the complex formation, undergoes dissociation at $pH > 7$ (pK_{SH} values are 8.10 and 8.72 for L-cysteine and GSH, respectively[33,34]). However, the effect of dissociation of the —COOH groups on the equilibrium in the presence of the micelle-forming surfactant must be taken into account in the pH range 0.5–3.5, although they are not responsible for the complex formation. The spectral changes of the complexes at different acidities suggested that two different complex species were formed in the pH range 0.5–3.5 according to Eqns (5)–(9), where H_3^+L and H_2^+L represent the undissociated ionic forms because H_2L and HL are the zwitterions of GSH and L-cysteine, respectively, and HL^- is the GSH ionic form with two dissociated —COOH groups.

The pH-dependent apparent formation constants can be derived by appropriate manipulation of Eqns (2)–(9). It can be shown easily that the equilibrium constants for the complex formation with protonated and unprotonated L-cysteine and GSH can be obtained from Eqns (10) and (11), respectively:

$$[H^+]\alpha K_{app} = \frac{K'_{eq}}{K_{a_1}}[H^+] + K''_{eq} \quad (10)$$

$$[H^+]\alpha K_{app} = \frac{K'_{eq}}{K_{a_1}K_{a_2}}[H^+]^2 + \frac{K''_{eq}}{K_{a_2}}[H^+] + K'''_{eq} \quad (11)$$

Table 1. The pH-dependent apparent (K_{app}) and equilibrium (K'_{eq} and K''_{eq}) constants calculated according to Eqns (10) and (11) for the complex formation between $[PdCl(dien)]^+$ and L-cysteine or GSH at 298 K

pH	L-cysteine	GSH
	$10^5 K_{app}$ (M^{-1})	
1.0	2.0	3.6
1.5	5.9	13.3
2.0	7.7	28.3
2.2	15.8	49.8
2.7	20.5	65.4
K'_{eq}	$(2.3 \pm 0.5) \times 10^4$	$(3.8 \pm 0.3) \times 10^4$
K''_{eq}	$(1.4 \pm 0.9) \times 10^3$	$(2.4 \pm 0.8) \times 10^4$

The values of the pH-dependent formation constants ($K_{app} = k_f/k_b$) were determined spectrophotometrically from equilibrium measurements at different acidities (pH range 1.0–2.7) at 298 K. These values were used to determine equilibrium constants for the complex formation between $[PdCl(dien)]^+$ and thiols according to Eqns (10) and (11). The results are presented in Table 1. It could be also concluded that the ligands are very good nucleophiles for the Pd(II) complex, even in acidic medium, where the sulfur atom is protonated. This is in good agreement with previous published results.[19,20,27]

The pH-dependent kinetics of complex formation

The kinetics of $[Pd(dien)(thiol)]^+$ formation in the presence and absence of 1×10^{-2} M micelle-forming surfactant SDS were followed at different acidities (pH range 0.5–3.5) in the temperature range 276–298 K under pseudo-first-order conditions ($[thiol] \gg [PdCl(dien)]^+$). The experimentally determined rate constants (k_{obs}), calculated from the exponential kinetic curves, followed the simple rate expression common for substitution reactions of square-planar complexes:

$$k_{obs} = k_I[L_f] + k_{II} \qquad (12)$$

where k_I is the second-order rate constant characterizing the direct nucleophilic attack and formation of the new complex, and k_{II} is the solvolysis rate constant, which is independent of thiol concentration.[35]

Linear plots of k_{obs} versus thiol concentration at constant acidity were obtained in all cases. Typical dependence of the observed pseudo-first-order rate constants for the complex formation between $[PdCl(dien)]^+$ and L-cysteine in the presence of 1×10^{-2} M SDS at constant temperature (298 K) on the concentration of excess ligand at various acidities is shown in Fig. 2. The values of k_I and k_{II} were determined from the slope and the intercept of the

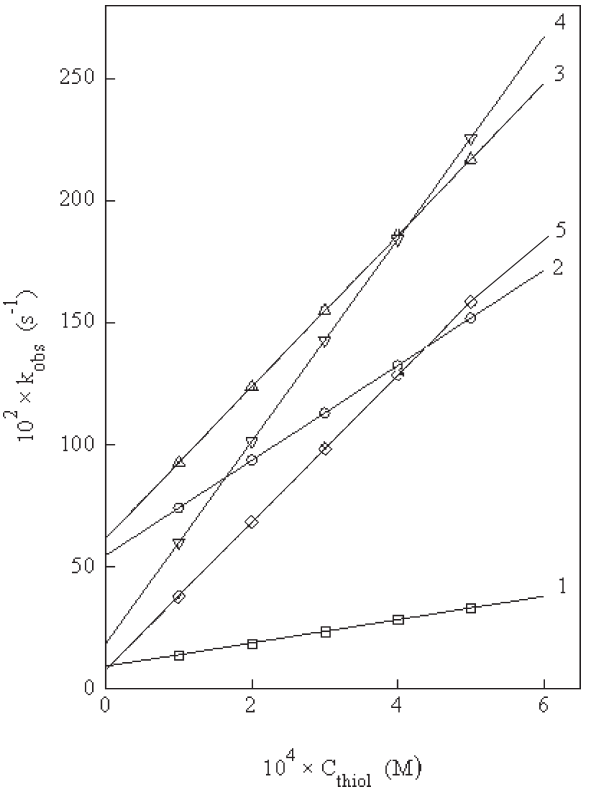


Figure 2. Observed pseudo-first-order rate constants (k_{obs}) for the complex formation between $[PdCl(dien)]^+$ and L-cysteine as a function of excess ligand and acidity in the presence of 1×10^{-2} M SDS at 297K: (1) pH 1.0; (2) pH 1.5; (3) pH 2.0; (4) pH 2.5; (5) pH 3.5; $C_{[PdCl(dien)]} = 1 \times 10^{-5}$ M, $I = 0.1$ N $NaClO_4$

graphs. Tables 2 and 3 contain k_I and k_{II} values for the complex formation between $[PdCl(dien)]^+$ and L-cysteine or GSH as a function of acidity at various temperatures in the absence and presence of 1×10^{-2} M SDS.

The bell-shaped pH profile of the forward rate constants (k_{obs}) was obtained for the reaction of thiols with $[PdCl(dien)]^+$ in the presence of SDS micelles over the investigated temperature range (Fig. 3). The results obtained indicate that the SDS micelles have the strongest effect on the reaction rate at pH$\sim$2, i.e. at the acidity corresponding to the pK_a values of dissociation of the —COOH groups. Also, acceleration of complex formation up to one order of magnitude can be observed in the presence of the SDS micelles compared with results obtained in aqueous medium. Acceleration of the complex formation between $[PdCl(dien)]^+$ and L-cysteine or GSH can be explained as a result of the increased concentration of reactants in the vicinity of the anionic micelles. The anionic micelles provide a dispersed negatively charged surface in solution. As a consequence, the positively charged $[PdCl(dien)]^+$ ions

Table 2. The pH-dependent reaction rate constants (k_I, k_{II})[a] for the complex formation between $[PdCl(dien)]^+$ and L-cysteine at various temperatures in the absence and presence of 1×10^{-2} M SDS

	Water						1×10^{-2} M SDS					
	280 K		288 K		279 K		277 K		288 K		298 K	
pH	$k_I \times 10^{-2}$ ($M^{-1} s^{-1}$)	$k_{II} \times 10$ (s^{-1})	$k_I \times 10^{-2}$ ($M^{-1} s^{-1}$)	$k_{II} \times 10$ (s^{-1})	$k_I \times 10^{-2}$ ($M^{-1} s^{-1}$)	$k_{II} \times 10$ (s^{-1})	$k_I \times 10^{-2}$ ($M^{-1} s^{-1}$)	$k_{II} \times 10$ (s^{-1})	$k_I \times 10^{-2}$ ($M^{-1} s^{-1}$)	$k_{II} \times 10$ (s^{-1})	$k_I \times 10^{-2}$ ($M^{-1} s^{-1}$)	$k_{II} \times 10$ (s^{-1})
1.0	2.59	0.70	3.20	0.71	4.40	0.90	2.78	0.80	3.50	0.99	4.79	0.94
1.5	2.15	0.22	2.65	0.29	3.63	0.27	11.87	3.65	15.38	4.98	19.43	5.48
2.0	2.53	0.27	3.47	0.39	4.10	0.50	19.61	4.48	25.52	5.25	31.00	6.18
2.5	2.71	0.69	3.46	1.15	4.62	1.14	26.60	0.96	33.50	1.00	41.38	1.00
3.5	5.06	2.65	7.33	5.36	9.91	7.29	18.85	1.20	24.13	1.80	30.11	0.80

[a] Experimental error is ± 5%.

Table 3. The pH-dependent reaction rate constants (k_I, k_{II})[a] for the complex formation between $[PdCl(dien)]^+$ and GSH at various temperatures in the absence and presence of 1×10^{-2} M SDS

	Water							1×10^{-2} M SDS					
	276 K		287 K		299 K			277 K		287 K		293 K	
pH	$k_I \times 10^{-3}$ ($M^{-1} s^{-1}$)	$k_{II} \times 10$ (s^{-1})	$k_I \times 10^{-3}$ ($M^{-1} s^{-1}$)	$k_{II} \times 10$ (s^{-1})	$k_I \times 10^{-3}$ ($M^{-1} s^{-1}$)	$k_{II} \times 10$ (s^{-1})	pH	$k_I \times 10^{-3}$ ($M^{-1} s^{-1}$)	$k_{II} \times 10$ (s^{-1})	$k_I \times 10^{-3}$ ($M^{-1} s^{-1}$)	$k_{II} \times 10$ (s^{-1})	$k_I \times 10^{-3}$ ($M^{-1} s^{-1}$)	$k_{II} \times 10$ (s^{-1})
0.5	0.32	0.72	0.70	0.65	1.50	0.96	1.0	4.77	4.58	7.51	3.88	11.61	5.33
1.0	0.48	0.50	1.00	0.32	1.80	0.44	1.5	5.21	4.53	8.52	2.24	13.80	2.82
2.0	0.68	0.68	1.20	0.44	2.40	0.52	2.0	6.80	5.52	10.05	4.52	16.33	7.22
2.5	0.30	0.80	1.00	0.90	2.30	0.12	2.5	3.72	0.97	9.45	1.97	13.35	1.95
3.0	0.15	0.33	0.80	0.55	2.20	0.65	3.0	2.00	0.36	7.61	1.20	12.05	0.90

[a] Experimental error is ± 5%.

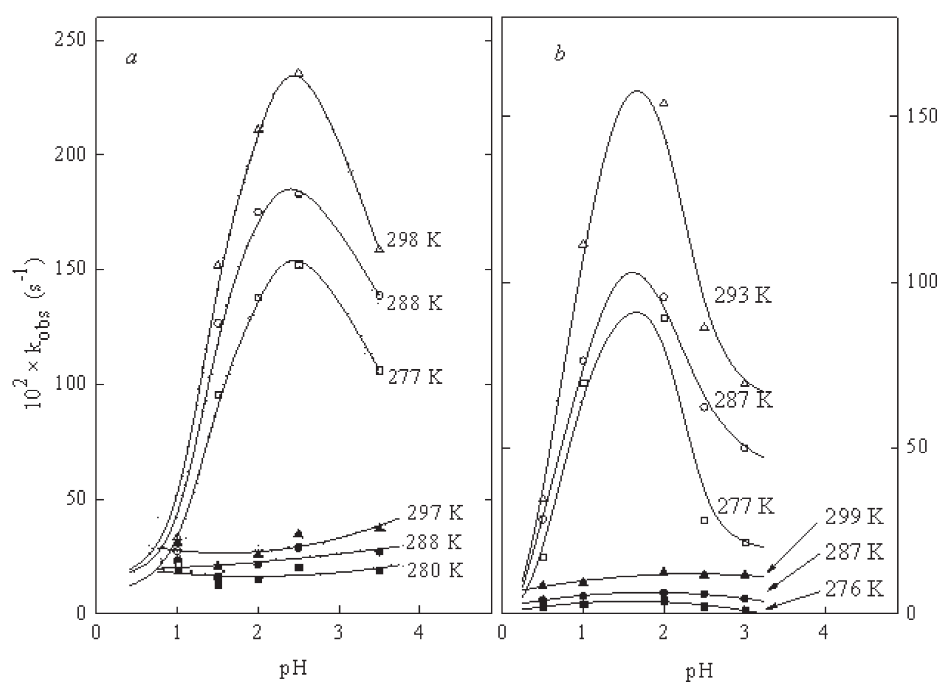


Figure 3. The pH profiles of the observed rate constant (k_{obs}) for the formation of the $[PdCl(dien)]^+$–L-cysteine complex (a) ($c_{thiol} = 5 \times 10^{-4}$ M, $c_{Pd} = 1 \times 10^{-5}$ M) and the $[PdCl(dien)]^+$–GSH complex (b) ($c_{thiol} = 5 \times 10^{-5}$ M, $c_{Pd} = 1 \times 10^{-6}$ M) in the presence (solid symbols) and absence (open symbols) of 1×10^{-2} M SDS at various temperatures

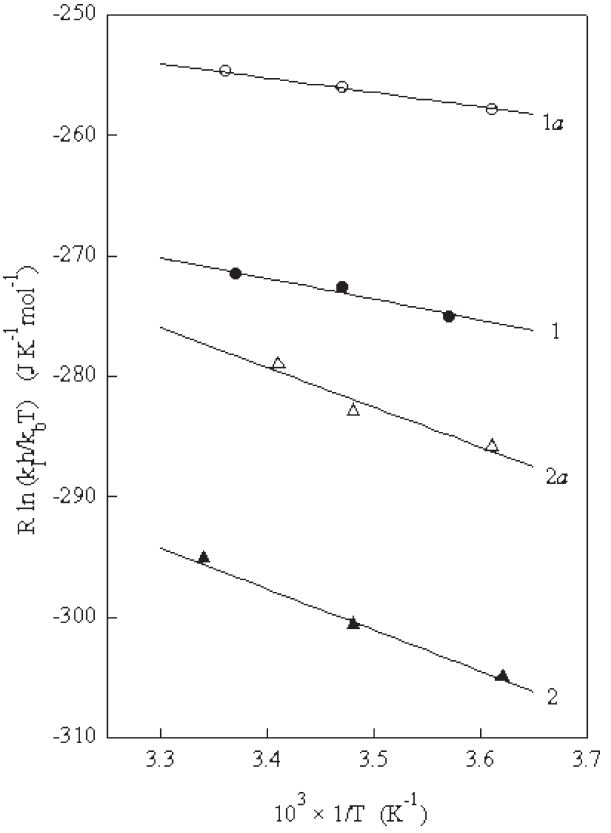


Figure 4. Temperature dependence (Eqn (3)) of the rate constant for the complex formation between $[PdCl(dien)]^+$ and GSH (1) or L-cysteine (2) in the absence (solid symbols) and presence (open symbols) 1×10^{-2} M SDS at pH 2

will partition out of the bulk aqueous phase into the surface region of the micelles. On the other hand, both ligands are protonated below pH 2. Dissociation of the —COOH group occurs above pH 2, where formation of zwitterions takes place. In highly acidic solutions ($pH < 1$) kinetic behavior resembles that of the corresponding homogeneous system due to competition between positively charged reactants and H^+ for a place on the micelle surface.

The pH-dependent thermodynamic parameters

The influence of acidity on the activation parameters for the reaction between $[PdCl(dien)]^+$ and thiols was derived from the temperature dependence of the rate constants obtained in the presence and absence of anionic SDS micelles at various pH values. The forward rate constants (k_I) obtained at different temperatures (results presented in Tables 2 and 3) were used to calculate enthalpies and entropies of activation using the Eyring equation[36]

$$k_I = k_b T/h \exp(\Delta S^{\neq}/R)\exp(-\Delta H^{\neq}/RT) \qquad (13)$$

The typical temperature dependence of the rate constant for the complex formation between $[PdCl(dien)]^+$ and L-cysteine or GSH at pH 2 in the presence and absence of 1×10^{-2} M SDS is shown in Fig. 4. Similar plots were obtained for both ligands in the investigated acidity range. The activation enthalpy and entropy in the absence and presence of 1×10^{-2} M SDS were calculated from the slope and the intercept of the plots and the results are summarized in Table 4. The results indicate the lower values of the reaction enthalpy in the presence of micelles compared with those obtained in the corresponding aqueous solutions. The observed effect is more pronounced in the reaction between $[PdCl(dien)]^+$ and L-cysteine. On the other hand, the presence of micelles does not have significant influence on the entropies of activation of the reaction between $[PdCl(dien)]^+$ and L-cysteine or GSH in the investigated acidity range. However, large negative values of the entropy of activation for both reactions are compatible with an associative mode of activation (I_a or A mechanism).[35,36] This finding indicates that bond-making with the entering ligand is important in the activation processes and that the leaving group is still tightly bound to the metal center in the transition state.

Table 4. Activation parameters for the forward reactions between $[PdCl(dien)]^+$ with thiols in the absence and presence of 1×10^{-2} M SDS

L-Cysteine	Without SDS		With 0.01 M SDS		GSH	Without SDS		With 0.01 M SDS	
pH	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (J mol^{-1} K^{-1})	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (J mol^{-1} K^{-1})	pH	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (J mol^{-1} K^{-1})	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (J mol^{-1} K^{-1})
1.0	18.8 ± 1.6	−131.3 ± 5.6	15.3 ± 2.4	−142.4 ± 8.2	0.5	43.5 ± 0.4	−38.8 ± 1.3	40.2 ± 0.1	−37.0 ± 0.2
1.5	18.1 ± 1.4	−135.1 ± 4.8	13.4 ± 0.2	−137.0 ± 0.8	1.0	36.9 ± 2.5	−59.3 ± 8.9	33.7 ± 5.7	−52.6 ± 2.0
2.0	17.3 ± 3.8	−136.4 ± 13.3	12.8 ± 0.4	−135.0 ± 1.2	2.0	35.1 ± 2.1	−63.3 ± 7.3	32.6 ± 8.3	−53.5 ± 2.9
2.5	19.6 ± 0.7	−128.0 ± 2.5	12.2 ± 0.6	−134.6 ± 1.9	2.5	58.1 ± 6.4	−14.0 ± 2.2	51.6 ± 4.8	−10.6 ± 1.7
3.5	25.5 ± 1.7	−101.5 ± 6.0	13.1 ± 0.5	−134.2 ± 1.6	3.0	77.4 ± 7.5	−78.3 ± 4.0	73.7 ± 7.9	−85.4 ± 2.7

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REFERENCES

1. Jocelyn PC. *Biochemistry of the SH Group*. Academic Press: New York, 1972; 94–95.
2. Friedman M. *The Chemistry and Biochemistry of the Sulfhydryl Group in Amino Acids, Peptides and proteins*. Pergamon Press: New York, 1973; 52–87.
3. Meister A. *J. Biol. Chem*. 1988; **263**: 17205.
4. Clausen AE, Kast C, Bernkop-Schnürch E. *Pharm. Res*. 2002; **19**: 602.
5. Rabenstein DL, Guevremont R, Evans CA. *Met. Ions Biol. Syst*. 1979; 103.
6. Henderson GB, Fairlamb AH, Ulrich P, Cerami A. *Biochemistry* 1987; **26**: 3023.
7. Lippert B. *Cisplatin. Chemistry and Biochemistry of a Leading Anticancer Drug*. Verlag Helvetica Chimica Acta/Wiley-VCH: Zürich/Weinheim, 1999.
8. Wong E, Giandomenico CM. *Chem. Rev.* 1999; **99**: 2451.
9. Reedijk J. *Chem. Rev.* 1999; **99**: 2499.
10. Rau T, van Eldik R. *Metal Ions in Biological Systems*, Sigel A, Sigel H (eds), vol. 32. Marcel Dekker: New York, 1996; 339–378.
11. Jamieson ER, Lippard SJ. *Chem. Rev.* 1999; **99**: 2467.
12. Esposito BP, Najjar R. *Coord. Chem. Rev.* 2002; **232**: 137.
13. Hall MD, Hambley TW. *Coord. Chem. Rev.* 2002; **232**: 49.
14. Teuben JM, van Boom SSGE, Reedijk J. *J. Chem. Soc. Dalton Trans*. 1997; 3979.
15. Teuben JM, Zubiri MRI, Reedijk J. *J. Chem. Soc. Dalton Trans*. 2000; 369.
16. Barnham KJ, Djuran MI, Murdoch PS, Ranford JD, Sadler PJ. *Inorg. Chem*. 1996; **35**: 1065.
17. Frey U, Ranford JD, Sadler PJ. *Inorg. Chem*. 1993; **32**: 1333.
18. Bugarčić ŽD, Liehr G, van Eldik R. *J. Chem. Soc. Dalton Trans*. 2002; 2825.
19. Bugarčić ŽD, Liehr G, van Eldik R. *J. Chem. Soc. Dalton Trans*. 2002; 951.
20. Bugarčić ŽD, Shoukry M, van Eldik R. *J. Chem. Soc. Dalton Trans* 2002; 3945.
21. Pitteri B, Marangoni G, Cattalini L, Bobbo T. *J. Chem. Soc. Dalton Trans*. 1995; 3853.
22. Bugarčić ŽD, Heinemann FW, van Eldik R. *J. Chem. Soc. Dalton Trans*. 2004; 279.
23. Annibale G, Bergamini P, Bertolasi V, Cattabriga M, Lazzaro A, Marchi A, Vertuani G. *J. Chem. Soc. Dalton Trans*. 1999; 3877.
24. Annibale G, Cattalini L, Cornia A, Fabretti A, Guidi F. *Inorg. React. Mech*. 2000; **2**: 185.
25. Pitteri B, Marangoni C, Cattalini L, Visentin F, Bertolasi V, Gilli P. *Polyhedron* 2001; **20**: 869.
26. Pitteri B, Annibale G, Marangoni G, Bertolasi V, Ferretti V. *Polyhedron* 2002; **21**: 2283.
27. Vasić V, Čakar M, Savić J, Petrović B, Nedeljković J, Bugarčić Ž. *Polyhedron* 2003; **22**: 279.
28. Vasić VM, Tošić MS, Nedeljković JM. *J. Phys. Org. Chem*. 1996; **9**: 398.
29. Tošić MS, Vasić VM, Nedeljković JM, Ilić Lj. *Polyhedron* 1997; **16**: 1157.
30. Vasić VM, Tošić MS, Jovanović T, Vujisić Lj, Nedeljković JM. *Polyhedron* 1998; **17**: 399.
31. Vasić VM, Nedeljković JM. *J. Serb. Chem. Soc*. 1994; **59**: 157.
32. Breet ELJ, van Eldik R. *Inorg. Chim. Acta* 1983; **76**: L301.
33. Smith RM, Martell AE. *Critical Stability Constants*, vol. 6, suppl. 2. Plenum Press: New York, 1989; 20–21.
34. Rabenstein DL. *J. Am. Chem. Soc*. 1973; **95**: 2797.
35. Tobe ML, Burgess J. *Inorganic Reaction Mechanisms*. Addison Wesley Longman: Essex, 1999; 70.
36. Wilkins RG. *Kinetics and Mechanism of Reactions of Transition Metal Complexes* (2nd edn). Wiley-VCH Verlag: Weinheim, 1991; 88.