

Effects of Micelles on the Complex Formation of $[PtCl(dien)]^+$ with Biologically Relevant Ligands#

Tanja Soldatović,[1] Vesna Vasić,[2] and Živadin D. Bugarčić*[1]

[1]University of Kragujevac, Faculty of Science, Department of Chemistry, R. Domanovića 12, P. O. Box 60, 34000 Kragujevac, Serbia

[2]Department of Physical Chemistry, Vinča Institute of Nuclear Science, P. O. Box 522, 11001 Belgrade, Serbia

Received June 5, 2006; E-mail: bugarcic@kg.ac.yu

Substitution reactions of $[PtCl(dien)]^+$ (dien = diethylenetriamine) with some biologically relevant ligands, such as L-methionine ((L)-Met), glutathione (GSH), and guanosine 5′-monophosphate (5′-GMP), were studied in aqueous 0.10, 0.05, and 0.01 M $NaClO_4$ solutions at pH 2.5 using UV–vis spectrophotometry. The kinetics and mechanism of the complex-formation reactions were studied as a function of nucleophile concentration and temperature. These reactions were also studied in the presence and absence of micelles of sodium dodecyl sulfate (SDS). The presence of anionic micelles accelerated complex-formation. The largest effect of micelles has been observed in the case of L-methionine. On the other hand, an increase in the ionic strength in the presence of micelles caused a decrease in the rate. The negative entropies of activation support an associative complex-formation mechanism.

The usual approach to elucidate the mechanism of substitution reactions involves the study of the dependence of the reaction rate on reactants concentration, ionic strength, solvent composition, pH, temperature, and pressure. However, some surfactants, which could form micelles in aqueous solutions, may affect the rate of the reactions. Reactions between pairs of cations or pairs of anions may be dramatically accelerated by appropriately charged surfactants or polyelectrolytes. The large rate enhancements can be attributed to a large increase in local concentrations of ions at the micelle–water interface. However, micelle effects on reactivity are not by any means always large and favorable.[1a]

Previously, we investigated the kinetics of the complex formation of different Pd^{II} and Pt^{II} complexes with N- and S-bonding ligands, including some bio-molecules, such as amino acids, peptides and fragments of DNA.[2–9] Recently, we focused on the investigation of the effects of micelle systems on the reactions of Pd^{II} and Pt^{II} coordination compounds with thiols.[10] Although the micelles do not influence the stoichiometry and mechanism of complex formation,[11–15] the reaction rate was found to be strongly dependent on the presence of the surfactant.[12,15] These studies could be important not only from the fundamental point of view, but also from biochemical aspects, i.e., as models for ligand-exchange reactions on the surface of biomembranes or at the interface of a globular protein.

In the present study, we investigated the complex formation of $[PtCl(dien)]^+$ (Eq. 1) with some biologically important ligands, such as guanosine 5′-monophosphate (5′-GMP), glutathione (GSH), and L-methionine ((L)-Met) (Chart 1) in aqueous solutions of 0.10, 0.05, and 0.01 M $NaClO_4$ and at pH 2.5 in the presence and absence of the 0.01 M anionic surfactant dodecyl sodium sulfate (SDS). These reactions were studied at pH 2.5, because at that pH, the largest changes in k_{obsd} as a function of pH (bell shaped) in the presence of SDS were observed.

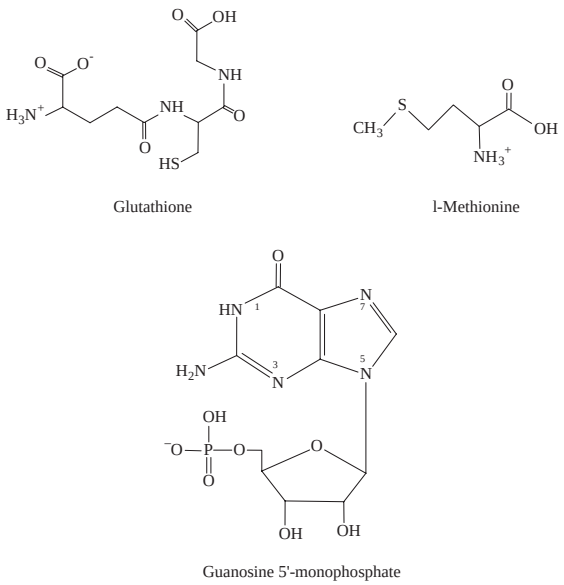


Chart 1.

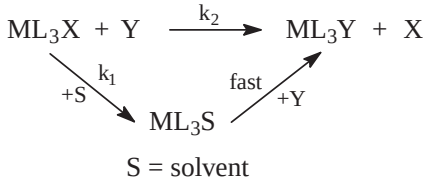
$$[PtCl(dien)]^+ + L \underset{k_1}{\overset{k_2}{\rightleftharpoons}} [Pt(dien)L]^{2+} + Cl^- . \quad (1)$$

L = 5′-GMP, GSH, (L)-Met

Results and Discussion

Substitution reactions of square-planar d^8 metal complexes are, in general, accepted to proceed via to two parallel associative reaction paths.[1b] One involves the rate-determining formation of a solvent ligand complex (k_1-path in Scheme 1) followed by rapid substitution of the coordinated solvent mole-

Published on the web December 13, 2006; doi:10.1246/bcsj.79.1889



Scheme 1.

cule (S). The other reaction involves direct nucleophilic attack by the entering ligand (k_2-path in Scheme 1).

The observed pseudo-first-order rate constants, k_{obsd}, as a function of the total concentration of nucleophile are described by Eq. 2.

$$k_{obsd} = k_1 + k_2[\text{nucleophile}]. \quad (2)$$

The solvolysis rate constant k_1, which is independent of L concentration, can be determined from the intercept of the graph of k_{obsd} vs [L]. The second-order rate constants k_2, which involves the formation of the new complex, can be evaluated from the slope of a plot k_{obsd} vs [L].

The kinetic traces gave excellent fits to a single exponential. k_{obsd}, calculated from the kinetics traces, were plotted versus the concentrations of the entering nucleophiles. A linear dependence of k_{obsd} on the nucleophile concentration was observed for all reactions in the absence and the presence of 1×10^{-2} M SDS (Fig. 1).

Attention has been focused on k_2, which can be measured accurately. Values of k_2 for the displacement of chloride from $[PtCl(dien)]^+$ complexes with nucleophiles were obtained by fitting the experimental data to Eq. 2 and are listed in Table 1.

The Kinetics of the Complex Formation between $[PtCl(dien)]^+$ and L-Methionine in the Presence and Absence of SDS. From Table 1, it can be concluded that L-methionine is the best nucleophile for the $[PtCl(dien)]^+$ complex in the presence and absence of SDS. This can be explained by the positive inductive effect of the methyl group on the sulfur. Also, this is in agreement with previously published results.[8,16] The amino acid, L-methionine ((L)-Met) under our experimental conditions of pH = 2.5 was protonated (the values for the dissociation constants are $pK_{a1} = 2.65$ and $pK_{a2} = 9.08$[17]), and it was present as a positively charged molecule. From a comparison of the reactivity of (L)-Met at pH = 1.0[16] and at pH 2.5 (without SDS), higher reactivity was observed at higher pH due to the higher deprotonation of the ligand.

In the presence of SDS, the complex-formation reaction was accelerated. This could be explained by the presence of a negatively charged micelle surface, which attracted the positively charged (L)-Met and $[PtCl(dien)]^+$. Also, in the presence of micelles, the rate constants increased with a decrease in ionic strength. The highest value of k_2 was observed in 0.01 M $NaClO_4$ (Fig. 2).

The Kinetics of the Complex Formation between $[PtCl(dien)]^+$ and Glutathione in the Presence and Absence of SDS. In the case of glutathione, dissociation of the –COOH group occurs above pH = 2.0 ($pK_{a1} = 2.05$),[17] where formation of zwitterions takes place ($2.05 < pH < 3.40$). The rate constants in the absence of SDS at various ionic strengths have similar values (Table 1). In the presence of SDS, acceleration of the complex-formation reaction was again observed (Fig. 3).

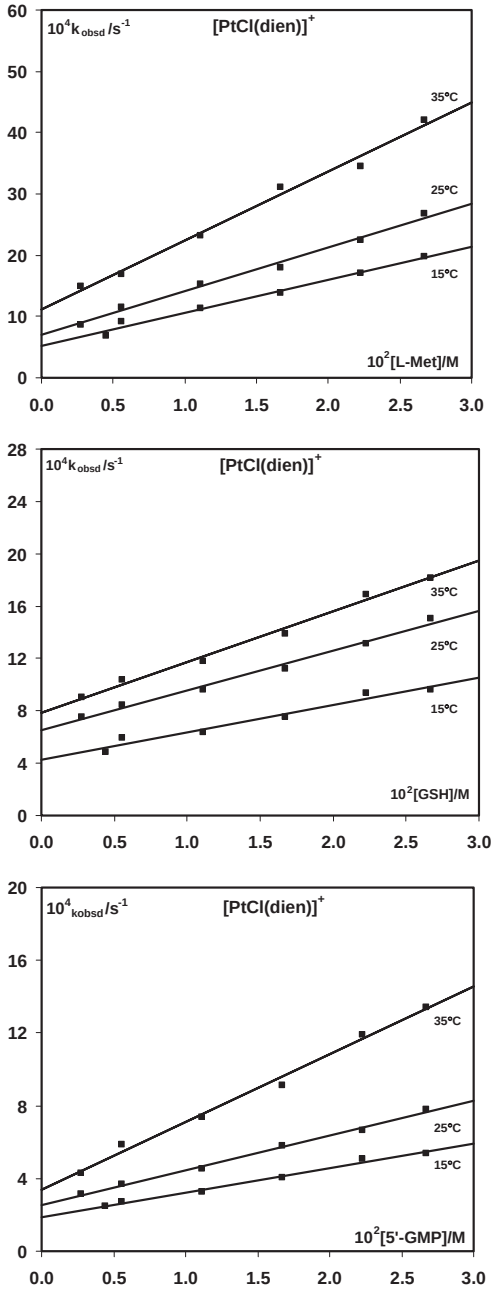


Fig. 1. k_{obsd} as a function of nucleophile concentration and temperature at 0.10 M $NaClO_4$ ionic strength.

The acceleration of the complex formation between $[PtCl(dien)]^+$ and GSH can be explained as a result of the increased concentration of the reactants in the vicinity of the anionic micelles. The anionic micelles provide a dispersed negatively charged surface in solution. As a consequence, a positively charged $[PtCl(dien)]^+$ ions will partition out of the bulk aqueous phase onto the surface of the region of the micelles. On the other hand, at pH = 2.5, positively charged ions of the ligand are still present, and they are attracted by the negatively charge surface of the micelles.

The Kinetics of the Complex Formation between $[PtCl(dien)]^+$ and 5′-GMP in the Presence and Absence of SDS. Under our experimental conditions (pH 2.5), only the

Table 1. Rate Constants and Activation Parameters for the Reactions of $[PtCl(dien)]^+$ with L-Methionine, Glutathione, and 5′-GMP at pH 2.5[a)]

L	I /M	Without SDS				With SDS			
		$10^2\ k_2^{298}$ /$M^{-1}\ s^{-1}$	$10^4\ k_1^{298}$ /s^{-1}	$\Delta H^{\ddagger}$ /kJ mol^{-1}	$\Delta S^{\ddagger}$ /J K^{-1} mol^{-1}	$10^2\ k_2^{298}$ /$M^{-1}\ s^{-1}$	$10^4\ k_1^{298}$ /s^{-1}	$\Delta H^{\ddagger}$ /kJ mol^{-1}	$\Delta S^{\ddagger}$ /J K^{-1} mol^{-1}
(L)-Met	0.01	5.71 ± 0.10	11.94 ± 0.17	—	—	11.59 ± 0.33	11.96 ± 0.54	—	—
	0.05	6.05 ± 0.18	9.51 ± 0.30	—	—	9.30 ± 0.32	9.20 ± 0.53	—	—
	0.10	7.18 ± 0.34	6.92 ± 0.57	24 ± 3	-183 ± 8	8.00 ± 0.28	7.08 ± 0.48	11 ± 3	-232 ± 7
(L)-Met[b)]		4.02 ± 0.20		24 ± 3	-180 ± 4				
(L)-Met[c)]		4.82 ± 0.19							
GSH	0.01	3.27 ± 0.20	8.78 ± 0.32	—	—	6.94 ± 0.14	9.48 ± 0.24	—	—
	0.05	3.14 ± 0.15	7.87 ± 0.24	—	—	5.07 ± 0.09	9.76 ± 0.16	—	—
	0.10	3.03 ± 0.16	6.51 ± 0.27	20 ± 3	-207 ± 8	3.71 ± 0.12	7.45 ± 0.36	17 ± 3	-216 ± 9
GSH[d)]		0.39 ± 0.02		33 ± 4	-170 ± 4				
5′-GMP	0.01	2.17 ± 0.15	8.69 ± 0.24	—	—	3.74 ± 0.16	8.18 ± 0.24	—	—
	0.05	1.99 ± 0.09	8.71 ± 0.15	—	—	3.04 ± 0.15	8.74 ± 0.26	—	—
	0.10	1.91 ± 0.06	2.57 ± 0.10	35 ± 4	-159 ± 12	2.11 ± 0.04	2.50 ± 0.07	13 ± 3	-233 ± 10

a) (L)-Met $pK_{a1} = 2.65$, $pK_{a2} = 9.08$; GSH $pK_{a1} = 2.05$, $pK_{a2} = 3.40$, $pK_{a3} = 8.79$, $pK_{a4} = 9.49$; 5′-GMP $pK_{a1} = 0.30$, $pK_{a2} = 2.33$, $pK_{a3} = 6.14$, $pK_{a4} = 9.59$. b) The results from Ref. 16; I = 0.10 M, pH = 1.0. c) Rate constant obtained by ^{1}H NMR spectroscopy. Ref. 16; I = 0.10 M, pH = 1.0. d) The results from Ref. 16; I = 0.10 M, pH = 1.0.

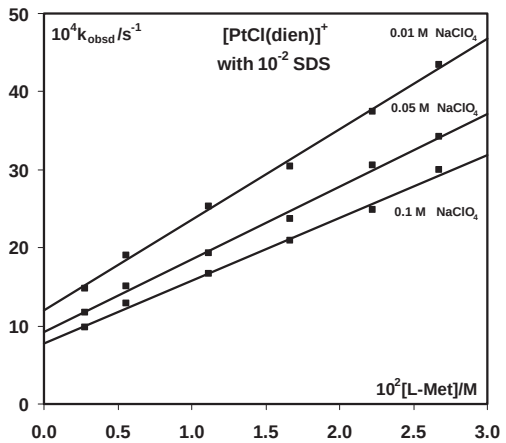


Fig. 2. k_{obsd} as a function of nucleophile concentration at 25 °C in various ionic strengths for L-methionine in the presence of SDS.

N7 position of 5′-GMP will bind to Pt^{II} ($pK_a = 1.2$), since at this pH the N1 position is protonated ($pK_a = 8.88$).[18] Binding through the N7 position in a neutral or weakly acidic medium has been verified.[6,19,20] From a comparison of the reactivity of the nucleophiles that were used (Table 1), it could be concluded that L-methionine is the best nucleophile. Surprisingly, 5′-GMP, which is a N-bonding ligand and coordinated to Pt^{II} via N7,[6] is as good an entering nucleophile as GSH. This could be explained by protonation of GSH in acidic solutions (at pH 2.5). On the other hand, at pH 2.5, the N7 5′-GMP is not protonated. However, at or near neutral pH, although less than 10% of thiols are deprotonated, the N-bonding bases cannot compete with the thiol-containing amino acids and peptides.[7] Therefore, binding primarily takes place through the sulfur donor sites.[8]

In the presence of SDS, there is a small acceleration in the complex formation of $[PtCl(dien)]^+$ with 5′-GMP. At pH > 2.33, the concentration of the negatively charged 5′-GMP increases, while the acceleration decreases.[7,18] The ligand species mostly located in the bulk aqueous phase and negatively charged micelles surface did not attract the species. The rate constants increase slightly with decreasing ionic strength as in the presence of SDS.

The activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ (Table 1) were calculated by using an Eyring equation. All available activation parameters support an associative mechanism. The significantly negative activation entropies suggest that the activation process in the studied systems seems to be strongly dominated by bond making.[1b] The results are in an excellent agreement with similar data reported for related systems.[8,9] In the presence of micelles lower values for $\Delta H^{\ddagger}$ were observed, whereas $\Delta S^{\ddagger}$ has more negative values. This suggests that there is a catalytic effect on the reaction rate in each case.

Dependence of the Rate Constants on Ionic Strength. The rate of the complex formation between $[PtCl(dien)]^+$ and (L)-Met, GSH, and 5′-GMP in the absence and presence of 1×10^{-2} M SDS was investigated as a function of ionic strength (0.01, 0.05, and 0.10 M). The linear dependencies of $\log(k_{obsd}/k^{\circ}_{obsd})$ versus $I^{1/2}$ (k°_{obsd} is the extrapolated value of the rate constant at zero ionic strength) at pH = 2.5 are shown in Fig. 4. It should be noted that at pH = 2.5 L-methionine and the complex are mono cations, and the presence of SDS did not influence the slope of the plots (Fig. 4, plot (a)).

In all cases, it has been observed that, in the presence of micelles, the rate constants increased with a decrease in the ionic strength. The highest value was observed in 0.01 M $NaClO_4$ solutions for the complex-formation. This effect can be explained by the competition between reactant species and Na^+ ions originating from the inert salt $NaClO_4$ for a place on the micelles surface. It has already been mentioned, an increase in the concentration of the inert salt causes a decrease of local concentration of reactants in the vicinity of the micelles surface, and as a consequence, the rate decreases.

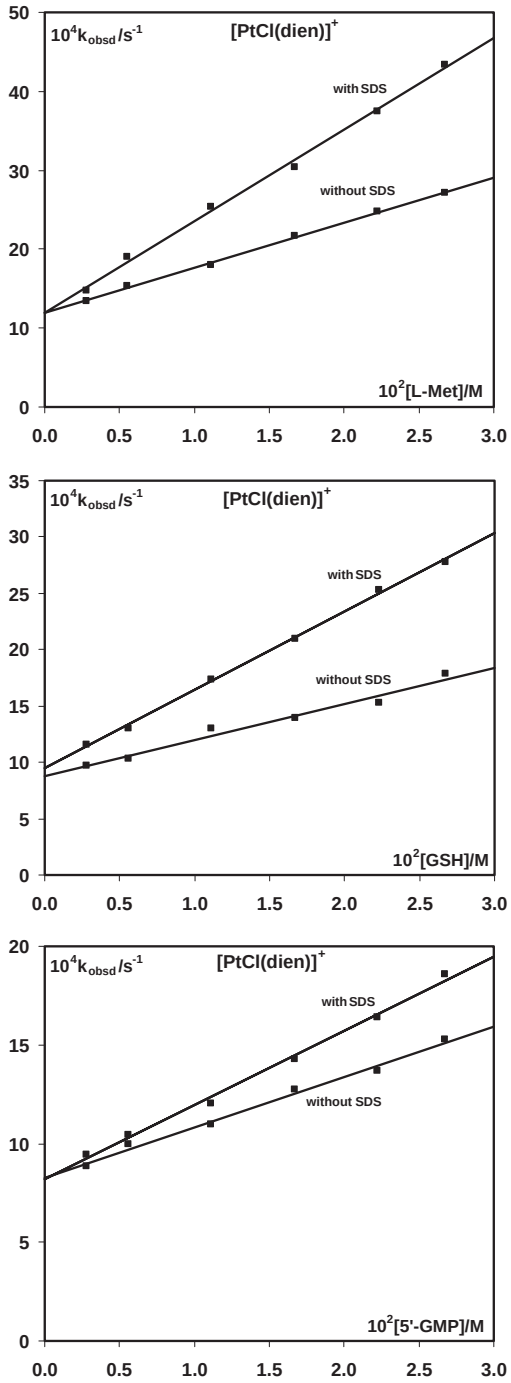


Fig. 3. k_{obsd} for the reactions between $[PtCl(dien)]^+$ and L-methionine, glutathione, and guanosine 5′-monophosphate as a function of nucleophile concentration in the absence and in the presence of 1×10^{-2} M SDS at 25 °C; pH = 2.5; I = 0.01 M $NaClO_4$.

Experimental

The complex [PtCl(dien)]Cl was prepared according to a literature method.[21] Chemical analysis, UV–vis and ^{1}H NMR spectral data agreed with those obtained in previous preparations.[8,9]

Chemicals and Solutions. Ligand stock solutions were prepared shortly before use by dissolving the chemicals L-methionine (Fluka, Assay > 99%), glutathione (Fluka, Assay > 99%), guanosine 5′-monophosphate sodium salt hydrate (Sigma) and dodecyl sodium sulfate (Fluka, Assay > 97%). The other reagents were analytical grade. Highly purified, deionised water was used in the preparation of all solutions.

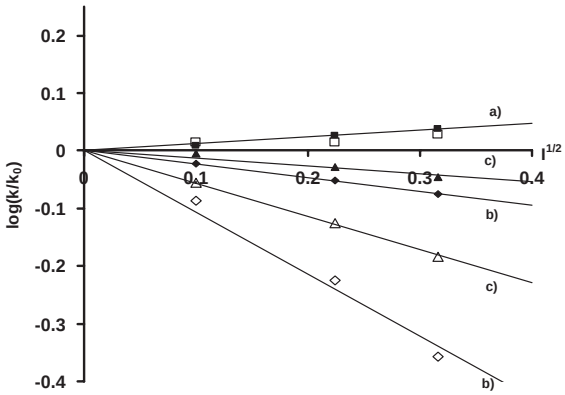


Fig. 4. The effect of the ionic strength in the presence (open symbols) and in the absence (solid symbols) of 1×10^{-2} M SDS on the reaction rate between $[PtCl(dien)]^+$ and a) L-methionine, b) GSH, and c) 5′-GMP at pH = 2.5.

Since it is known that perchlorate ions do not coordinate to Pt^{II} in aqueous solution,[22] the kinetics of the complex-formation reactions were studied in a perchlorate medium. The ionic strength was kept constant with $NaClO_4$ (Merck, pro analyses). The experiments were done at pH 2.5 (adjusted with $HClO_4$ and NaOH). Under these experimental conditions, the $[PtCl(dien)]^+$ was stable, and hydrolysis of the complex was negligible.[23]

Instrumentation. Chemical analyses were performed on a Carlo Erba Elemental Analyzer 1106. UV–vis spectra were recorded on Shimadzu UV 250 and Hewlett-Packard 8452A diode-array spectrophotometers with thermostated 1.00 cm quartz Suprasil cells.

Kinetic Experiments. Spectral changes resulting from mixing solutions of the complex $[PtCl(dien)]^+$ and ligands, were recorded over the wavelength range 220 to 450 nm to establish a suitable wavelength, at which kinetic measurements could be performed. The reaction was initiated by adding 0.5 cm^3 of the Pt^{II} complex solution to 2.5 cm^3 of the ligand thermostated solution into the UV–vis spectrophotometric cell. Complex formation was monitored as the absorbance increase at 260 nm (GSH) and 280 nm (L-methionine), as well as the absorbance decrease at 340 nm (5′-GMP). The kinetic curves were monitored under pseudo-first-order conditions with ligand in at least a 10-fold excess during at least 8 half-lives. The temperature was controlled to ±0.1 °C in the interval from 15–35 °C. All kinetic runs were fitted by a single exponential function, and no subsequent reactions were observed. k_{obsd} was calculated as the average value from two to four independent kinetic runs.

The authors gratefully acknowledge financial support from the Ministry of Science, Technologies and Development of the Republic of Serbia, Projects No. 142008.

Supporting Information

Tables S1–S18 summarized all values for k_{obsd} determined for all reactions at different concentration, temperature, and ionic strength. Figures 1S and 2S show determination of the k_{obsd} for the reaction between $[PtCl(dien)]^+$ and glutathione in the ionic

strength 0.10 M $NaClO_4$ in the absence and presence of SDS. Figure 3S represents UV–vis spectral-changes during the reactions between $[PtCl(dien)]^+$ and L-methionine, in the ionic strength 0.10 M $NaClO_4$ and in the absence of SDS. Figures 4S and 5S show Eyring plots for all reactions at the ionic strength 0.10 M $NaClO_4$ and in the presence and absence of 0.01 M SDS.

References

This paper is dedicated to the 60th birthday of Professor Rudi van Eldik.

1 a) M. L. Tobe, J. Burgess, *Inorganic Reaction Mechanisms*, Addison Wesley Longman Inc., Essex, **1999**, pp. 334–376. b) M. L. Tobe, J. Burgess, *Inorganic Reaction Mechanisms*, Addison Wesley Longman Inc., Essex, **1999**, pp. 30–115.

2 Ž. D. Bugarčić, G. Liehr, R. van Eldik, *J. Chem. Soc., Dalton Trans.* **2002**, 2825.

3 Ž. D. Bugarčić, G. Liehr, R. van Eldik, *J. Chem. Soc., Dalton Trans.* **2002**, 951.

4 Ž. D. Bugarčić, M. M. Shoukry, R. van Eldik, *J. Chem. Soc., Dalton Trans.* **2002**, 3945.

5 Ž. D. Bugarčić, B. Petrović, E. Zangrando, *Inorg. Chim. Acta* **2004**, *357*, 2650.

6 Ž. D. Bugarčić, F. W. Heinemann, R. van Eldik, *Dalton Trans.* **2004**, 279.

7 a) Ž. D. Bugarčić, T. Soldatović, R. Jelić, B. Alguero, A. Grandas, *Dalton Trans.* **2004**, 3869. b) R. W. Hay, D. S. Porter, *Trans. Met. Chem.* **1999**, *24*, 186.

8 T. Soldatović, Ž. D. Bugarčić, *J. Inorg. Biochem.* **2005**, *99*, 1472.

9 B. Petrović, Ž. D. Bugarčić, *Aust. J. Chem.* **2005**, *58*, 544.

10 V. M. Vasić, M. Čakar, J. Savić, B. Petrović, J. Nedeljković, Ž. D. Bugarčić, *Polyhedron* **2003**, *22*, 279.

11 V. M. Vasić, M. S. Tošić, J. M. Nedeljković, *J. Phys. Org. Chem.* **1996**, *9*, 398.

12 M. S. Tošić, V. M. Vasić, J. M. Nedeljković, L. Ilić, *Polyhedron*, **1997**, *16*, 1157.

13 V. M. Vasić, M. S. Tošić, T. Jovanović, L. Vujisić, J. M. Nedeljković, *Polyhedron* **1998**, *17*, 399.

14 V. M. Vasić, J. M. Nedeljković, *J. Serb. Chem. Soc.* **1994**, *59*, 157.

15 V. M. Vasić, M. A. Živanović, M. M. Čakar, J. Z. Savić, J. M. Nedeljković, Ž. D. Bugarčić, *J. Phys. Org. Chem.* **2005**, *18*, 441.

16 B. V. Petrović, Ž. D. Bugarčić, *J. Coord. Chem.* **2001**, *53*, 35.

17 R. M. Smith, A. E. Martel, *Critical Stability Constants*, Plenum Press, New York, NY, **1989**, Vol. 6, 2nd Suppl., p. 20.

18 H. Sigel, S. S. Massoud, N. A. Corfu, *J. Am. Chem. Soc.* **1994**, *116*, 2958.

19 J. Arpalahti, P. Lehikoinen, *Inorg. Chem.* **1990**, *29*, 2564.

20 J. Arpalahti, B. Lippert, *Inorg. Chem.* **1990**, *29*, 104.

21 G. Annibale, M. Brandolisio, B. Pitteri, *Polyhedron* **1995**, *14*, 451.

22 T. G. Appleton, J. R. Hall, S. F. Ralph, C. S. M. Thompson, *Inorg. Chem.* **1984**, *23*, 3521.

23 Ž. D. Bugarčić, B. V. Petrović, R. Jelić, *Trans. Met. Chem.* **2001**, *26*, 668.