Nickel(II) Tetraazamacrocyclic Complexes with Two Pendant Amino Groups: Electrochemical and Kinetic Studies

Bohdan Korybut-Daszkiewicz,*[a] Joanna Taraszewska,[b] and Bohdan Kamieński[a]

Keywords: Electrochemistry / Kinetics / Macrocyclic ligands / N ligands / Nickel

Isomeric 2,9-bis(amionmethyl)-5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradecanenickel(II) and -4,11-dienenickel(II) complexes (**1**–**4**) were studied by cyclic voltammetry. The thermodynamic stability of Ni^{III} was the greatest in complex **4** with a *trans* configuration of the pendant amino groups. On acidification, the Ni^{II}/Ni^{III} redox process was not observed. After alkalisation the redox process was only recovered in complex **4**. The kinetics of the two-step macrocyclic ring isomerisation in 1 M HCl and DCl was studied, as a function of temperature, by UV/Vis and ^1H NMR techniques. The energies of activation for the isomerisation of the cyclam ring from *trans*-V (**5α**) to *trans*-II (**5β**) and from *trans*-II to *trans*-I (**5γ**) were equal to 22.6 and 26.9 kcal mol^{-1}, respectively.

Introduction

Tetraazamacrocyclic polyamines bearing pendant amine groups are especially interesting for studying the influence of axial coordination on the properties of the coordinated metal ion. It was found that such intramolecular donors can profoundly alter the properties of the complexed metal ions.[1,2] The first examples of such ligands were synthesised by Kaden.[1] Complexes of this type found application in the electrocatalysis of processes such as the reduction of CO_2 to CO[3] and hydrogen evolution.[4] They can be also linked to monoclonal antibodies, allowing the specific labelling of macrocycle-conjugated antibodies with radioisotopes,[5,6] and their consequent use as targeting agents in the diagnosis and therapy of cancers and other diseases.

The behaviour of metal complexes with such ligands is spectacular due to the internal pH-dependent equilibrium between the open and chelated forms of the pendant arm. When the pendant amine group is protonated, the diamagnetic, square-planar Ni^{II} complexes are formed. However, at higher pH values, coordination of the amine group leads to the paramagnetic, octahedral complexes. Such a change of structure gives a colour variation that may find analytical application. Due to the active role of the flexible side-chain, the above class of molecules was named scorpiands.[7] The pH-dependent electrochemical behaviour of Ni^{II} tetraazamacrocyclic complexes containing one pendant amino group was studied by Fabbrizzi et al.,[7] by Kimura et al.,[3] and by us.[8]

Nickel(II) complexes of cyclam derivatives substituted with two pendant amino groups are also the subjects of the pH-dependent equilibria. Cyclam dienes functionalised with two pendant arms – *trans*-2,9-bis(aminomethyl)-5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradeca-4,11-dienenickel(II) diperchlorate and its folded *cis* analogue were first synthesised by Korybut-Daszkiewicz,[9,10] and their crystallographic structure determined.[10,11] Recently, Korybut-Daszkiewicz et al.[12] synthesised and characterised isomeric Ni^{II} complexes of *cis*-2,9-bis(aminomethyl)-5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane. The coordination of the two pendant amino groups located on the same side of the tetraazamacrocyclic ring forces the ring to adopt a folded conformation. Protonation of the pendant amino groups resulted in the change of the macrocyclic conformation from folded to planar, and further isomerisation.

This paper is devoted to the study of the pH-dependent electrochemical behaviour of both groups of complexes, and the kinetics of their isomerisation by UV/Vis and ^1H NMR spectroscopy. The schematic structures of studied complexes and their protonated forms are presented in Figure 1.

Results and Discussion

Redox Properties of Complexes

The voltammetric behaviour of complexes **1**–**4** was studied in aqueous solutions containing 0.1 M NaCl as supporting electrolyte. In the negative potential range, reduction of Ni^{II} to Ni^{I} was not observed. The cyclic voltammograms recorded in the positive potential range on the glassy carbon (GC) electrode are shown in Figure 2. In each complex, Ni^{II} was oxidised to Ni^{III} at a potential corresponding to peak *a* and Ni^{III} was reduced to Ni^{II} at a potential corresponding to peak *b*. The redox process Ni^{II}/Ni^{III} in all complexes was reversible. The values of formal potentials E_f, calculated as midpoints between corresponding anodic and cathodic peaks, were 0.70V, 0.66V, 0.60V, and 0.43V for complexes **1**, **2**, **3**, and **4**, respectively.

The voltammetric behaviour of complex **1** at various pH values is shown in Figure 3A. After addition of HCl (pH = 2, curve 2) the current diminished about 25%, in comparison with that in neutral solution, and did not change with time (measurements up to 40 min). The value of E_f shifted

[a] Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw, Poland
Fax: (internat.) + 48-22/6326681
E-mail: bkd@icho.edu.pl
[b] Institute of Physical Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw, Poland

  1434–1948/01/0303–0645 $ 17.50+.50/0

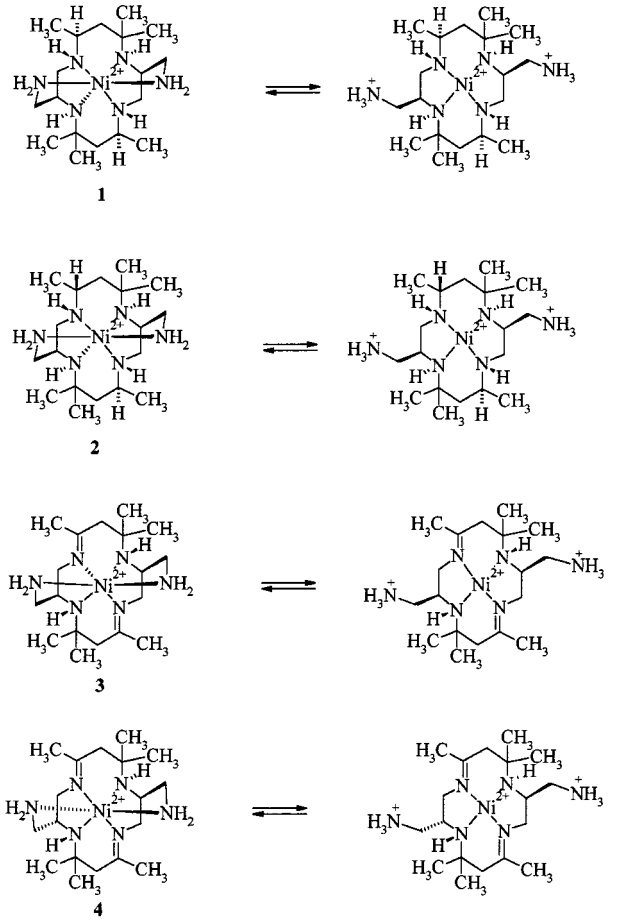


Figure 1. Structures of studied octahedral complexes **1**−**4** and their square-planar protonated forms; the macrocycle in complexes **1**−**3** adopts a folded conformation, and in complex **4** co-planar conformation

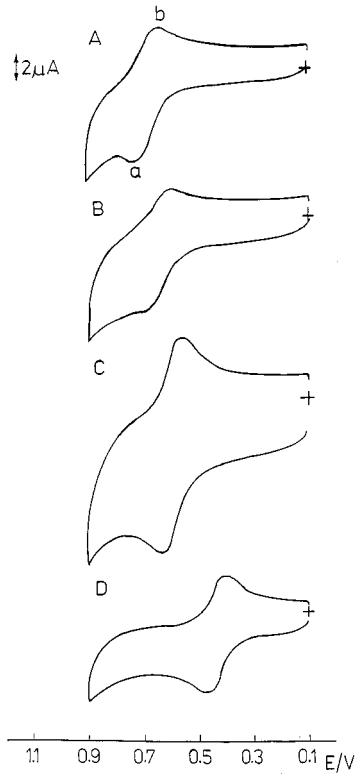


Figure 2. Cyclic voltammograms of $5\cdot10^{-4}$ M complexes **1** (A), **2** (B), **3** (C), and **4** (D) at a GC electrode in aqueous 0.1 M NaCl solution; scan rate 0.05 Vs^{-1}

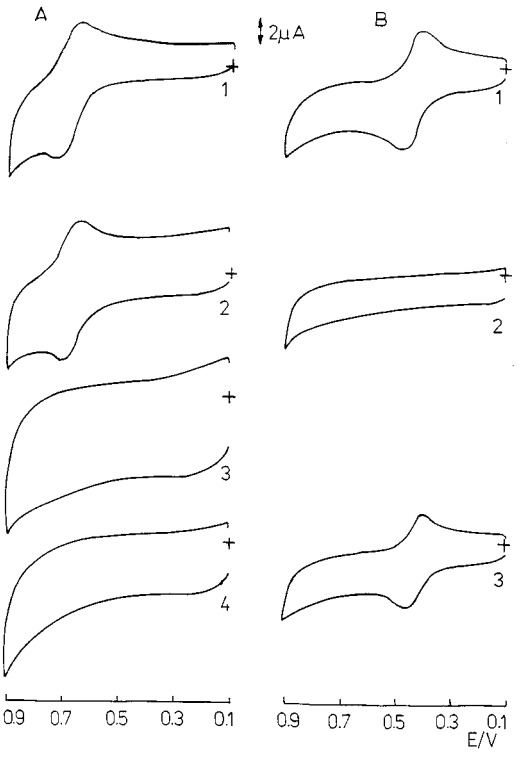


Figure 3. Cyclic voltammograms of $5\cdot10^{-4}$ M complexes **1** (A) and **4** (B) in 0.1 M NaCl as a function of the pH; (A) curve 1: pH = 7; curve 2: pH = 2; curve 3: pH = 1; curve 4: pH = 7; (B) curve 1: pH = 7; curve 2: pH = 3; curve 3: pH = 7

to 0.67 V. Further acidification (pH = 1) caused a rapid decrease of current with time, ultimately resulting in the disappearance of the redox process (curve 3). A subsequent alkalisation of solution did not change the picture even after 2 d (curve 4). The same behaviour was observed for complex **3**. In complex **2** the redox process Ni^{II}/Ni^{III} disappeared already at pH = 3, and did not recover after alkalisation. In complex **4** (Figure 3B) the redox process Ni^{II}/Ni^{III} disappeared at pH = 3, (curve 2) however, it was recovered after the subsequent alkalisation of solution (curve 3).

A comparison of E_f values for the redox process Ni^{II}/Ni^{III} in tetraazamacrocyclic complexes with one and with two pendant amino groups in neutral solutions is presented in Table 1. In tetraazamacrocyclic complexes with one pendant amino group, the most favourable access to the trivalent state was in 6-aminocyclam and the relative stabilization of Ni^{III} was the lowest in *N*-(aminomethyl)cyclam. This is based on the fact that the secondary amines are intrinsically more basic than the tertiary amines, and the interactions of tertiary nitrogen atoms with the metal ion are weaker than those of the secondary amine nitrogen atoms.[13,14]

Table 1. Formal potentials E_f of Ni^{II} tetraazamacrocyclic complexes with one and two pendant amino groups

Complex	E_f ([V] vs.MCE)	Ref.
Ni^{II}-5-AmMe-5,12-diMe-cyclam	0.655	[8]
Ni^{II}-1-AmEt-cyclam	0.740	[7]
Ni^{II}-6-Am-cyclam	0.560	[3]
1	0.700	this work
2	0.660	this work
3	0.600	this work
4	0.430	this work

In complexes **1**−**3**, with two pendant amino groups that are in a folded conformation, the potential of the Ni^{II}/Ni^{III} couple (Table 1) was similar to that in *N*-(aminoethyl)cyclam and 5-aminomethyl-5,12-dimethylcyclam. However, in complex **4**, which is in the *trans* conformation, it was much less positive. From the point of view of the structure of the coordination sphere one can conclude that the thermodynamic stabilization of Ni^{III} is more effective in the *trans* complex, where the macrocycle surrounds the metal ion in a square-planar manner, than in the *cis* analogues with a folded conformation of the amine. A similar effect has been observed by Taraszewska et al.[15] for other nickel azamacrocyclic complexes.

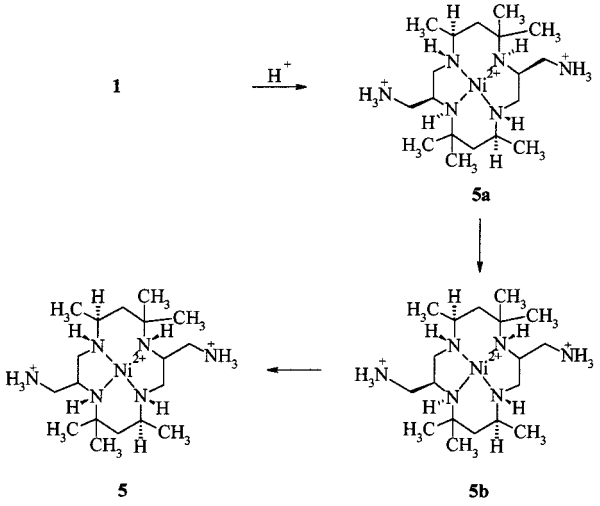
In acidic solutions the behaviour of complexes with two pendant amino groups was different to those with one pendant group. For 5-aminomethyl-5,12-dimethylcyclam studied by us previously[8] at pH = 0.8 we recorded two anodic peaks at potentials 0.65 V and at 0.85 V corresponding to the Ni^{II} oxidation from the complex with a deprotonated and with a protonated amino group, respectively. In more acidic solutions, only a peak at 0.85 V was recorded. Similar behaviour has been described by Fabbrizzi et al.[7] Applying CV with fast scan rates we could record the reduction peak of Ni^{III} from the square-planar complex.[8] In this way we proved experimentally for the first time the existence of Ni^{III} in tetraazamacrocyclic complex in the square-planar form, which is unusual for this type of complex, and has only been observed in some anionic tetraazamacrocyclic complexes.[16] On the basis of the stop-flow experiments we estimated the rate constant of the decoordination of the pendant amino group as equal to 815 s^{-1} (at 25 °C). We observed the reduction of Ni^{II} to Ni^{I}, but the complex of Ni^{I} was not stable.

In complexes with two pendant amino groups studied here, the oxidation of Ni^{II} from the protonated forms was not observed. It may be connected with the presence of many methyl groups in the macrocyclic rings, which forbid the access of axial substituents (solvent or anions), therefore Ni^{III} cannot be formed.

The lack of the redox couple Ni^{II}/Ni^{III} after alkalisation of solutions containing protonated forms of complexes **1**−**3** highlights the fact that the macrocyclic ring cannot be refolded, and coordination of the pendant NH_2 groups to Ni^{II} ion is impossible. It was only possible in complex **4**, which in deprotonated and protonated forms has a planar conformation of the macrocyclic ring with pendant arms in the *trans* configuration. Nevertheless, the octahedral folded complexes **1**−**3** could be regenerated in a basic sodium perchlorate solution.[9,11,12]

Kinetic Studies

As has been described in a previous paper,[12] protonated complex **1** undergoes isomerisation connected with inversion of configuration of N(1) and N(8) nitrogen atoms and simultaneous conformation changes of the six-membered chelate rings. The isomerisation pathway is shown in Scheme 1. The kinetics of isomerisation was followed by UV/Vis and ^1H NMR spectroscopy.



Scheme 1

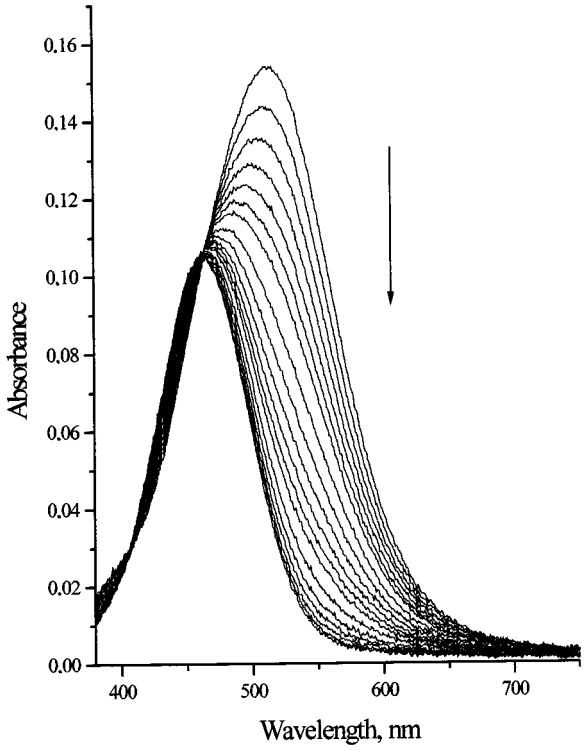


Figure 4. Monitoring of the isomerisation of **5α** into **5β** by UV/Vis spectroscopy; changes of absorption with time recorded for $1 \cdot 10^{-3}$ M complex **1** dissolved in 1 M HCl at 35°C

UV/Vis Studies

Measurements were carried out in solutions of $1 \cdot 10^{-3}$ M of complex **1** dissolved in 1 M HCl in the temperature range 20−45 °C. Changes of absorption with time at 35 °C are shown in Figure 4. The absorption maximum gradually changed from 515 nm, characteristic for complex **5α** (formed from **1** upon protonation) to 462 nm, which is characteristic for isomer **5β**. The steady state was reached after 2.5 h. Absorption changes connected with this isomerisation process were monitored at the wavelength 580 nm. Plots of the absorbance changes vs. time were approximated by the relationship $A(t)/A_o = \exp(-kt)$ for up to 3 half-times, which means that this isomerisation process followed a first-order kinetics. The same procedure was adopted at other temperatures.

Kinetics of isomerisation depended on the acid concentration. A similar experiment carried out in solution acidified with 2 M HCl showed that the kinetics of isomerisation was three times slower ($k = 0.38\ h^{-1}$, 35 °C). In 0.1 M HCl a fast isomerisation to the isomer **5γ** was observed. Such dependence on the acid concentration suggests that the proton dissociation at N(1) and N(8) is the rate determining step in these isomerisation processes. At 35 °C in 0.1 M HCl the inversion of configuration at N(1) and N(8) is fast, and isomer **5γ** is formed in a short time. In 1 M HCl the inversion at the first nitrogen atom is much faster than at second one, therefore we were able to follow the pathway **5α** to **5β**. The isomerisation of **5β** to **5γ** in this medium was followed at higher temperatures by ^{1}H NMR technique (Figure 5).

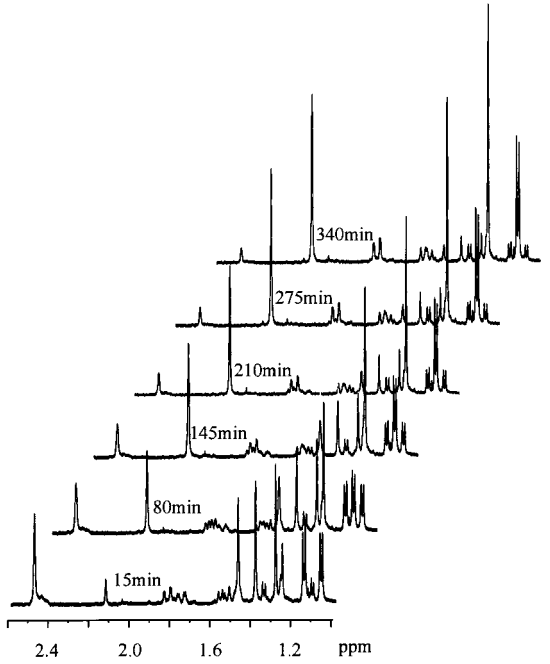


Figure 5. Monitoring of the isomerisation of **5β** into **5γ** by ^{1}H NMR spectroscopy; the methyl group absorption region of the 500 MHz spectra in 1 M DCl solution at 55°C

^{1}H NMR Measurements

The ^{1}H NMR measurements were carried out in $1 \cdot 10^{-3}$ M solutions of complex **5β** in 1 M DCl in the temperature range 40−60 °C. The first spectrum was collected 15 min after dissolution of the sample and the following spectra were measured every 62.5, 32.5, 42.5, 32.5, and 18 min up to 3 half-times at 40, 45, 50, 55, and 60 °C, respectively. The concentrations of the isomer **5β** was followed by integration of 4 proton signal at δ = 2.40−2.53 (overlapping 1 proton multiplet and methyl group singlet) (I_β), and that of the isomer **5γ** by integration of 6 proton methyl group singlet at δ = 2.09−2.16 (I_γ). Plots of the concentration changes vs. time followed a first-order kinetics approximated by the relationship $c(t)/c_0 = \exp(-kt)$ where $c(t)/c_0 = 3I_\beta/(3I_\beta + 2I_\gamma)$.

The values of rate constant k as a function of temperature for both processes are collected in Table 2. The activation energies E_a calculated from this relationship (Figure 6)

Table 2. Dependence of the rate constants of isomerisation on temperature for pathways **5α**−**5β** and **5β**−**5γ** in 1 M HCl and DCl solutions, respectively

Temp. [°C]	**5α**−**5β** k [h^{-1}][a]	**5β**−**5γ** k [h^{-1}][b]
20	0.164	
25	0.336	
30	0.531	
35	1.031	
40	1.785	0.050
45	3.638	0.113
50		0.204
55		0.359
60		0.651

[a] UV/Vis. − [b] ^{1}H NMR.

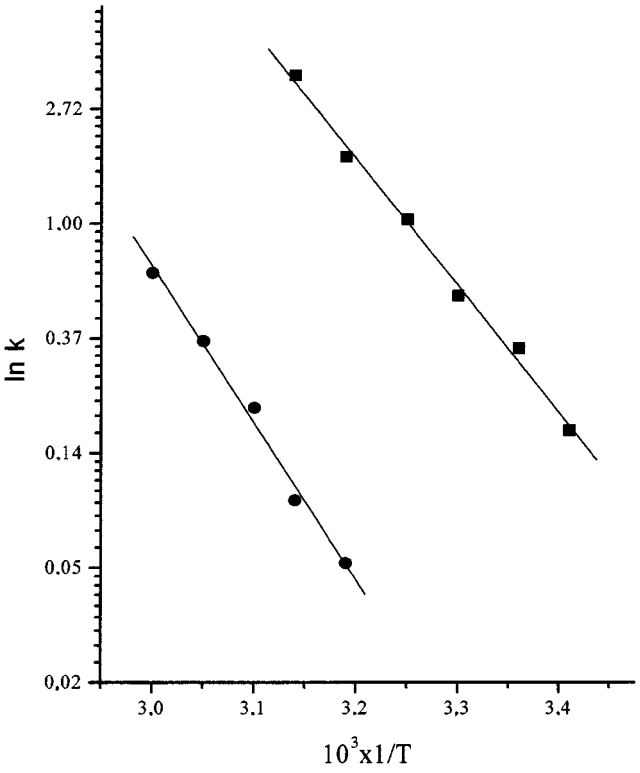


Figure 6. Plots of ln k vs $10^3 \times 1/T$ for the isomerisation of **5α** into **5β** (■) and **5β** into **5γ** (•)

are equal to 22.6 ± 0.7 and 26.9 ± 1.0 kcal mol^{-1} for isomerisation of **5α** into **5β** and **5β** into **5γ**, respectively.

Conclusion

The redox potentials of the Ni^{II}/Ni^{III} couple in complexes **1**−**3**, which are in a folded conformation, were similar to those of complexes with one pendant amino group. However, the thermodynamic stability of Ni^{III} was significantly higher in complex **4**, which exists in a *trans* configuration with a planar conformation of macrocyclic ring. This observation seems to be a general one. The redox process Ni^{II}/Ni^{III} disappeared in acidic solutions and after subsequent alkalisation was recovered only in complex **4** in *trans* configuration.

Protonation of folded complex **1** led to the formation of thermodynamically unstable complex **5α** with a *trans*-V conformation of the macrocyclic ring. Studies in 1 M HCl enabled us to follow the kinetics of stepwise isomerisation of the ring from **5α** through **5β** (*trans*-II) to **5γ** (*trans*-I). The kinetics of isomerisation was followed by UV/Vis and ^{1}H NMR techniques as a function of temperature. The rate constants of the pathway **5α**−**5β** were much higher than those of **5β**−**5γ**. The corresponding activation energies are 22.6 and 26.9 kcal·mol^{-1}, respectively.

Experimental Section

Materials: Complexes **1**−**4** and **5β** were synthesized as described in ref.[12,9,10], respectively. All chemicals were p.a. grade reagents. Triply distilled water was used. The third distillation was carried out from an all-quartz still.

Instrumentation: Cyclic voltammograms of complexes **1**−**4** were measured at a glassy carbon (GC-20) electrode. The counter electrode was a Pt plate. A 1 M aqueous calomel electrode (MCE) was used as the reference electrode. It was connected to the electrolytic cell via an intermediate vessel filled with the solution under investigation. Solutions were deaerated by flushing with pure argon. A measuring system consisting of EPA-20A potentiostat, an EG-20 functions generator (ELPAN Poland) and an *x*,*y* recorder. − The UV/Vis spectra were measured by a Cary 1E (Varian) spectrophotometer. − The 500 MHz ^{1}H NMR spectra were measured in 1 M DCl solutions with a Bruker DRX500 Avance spectrometer.

Acknowledgments

The authors are grateful to Mrs. S. Pawłowska for her great help in electrochemical and UV/Vis measurements. We are indebted to Prof. P. Sobota from Wrocław University for help in estimation of rate constant of de-coordination of a pendant arm by stop-flow method.

[1] T. A. Kaden, *Top. Curr. Chem.* **1984**, *121*, 157−180.
[2] P. V. Bernhardt, G. L. Lawrance, *Coord. Chem. Rev.* **1990**, *104*, 297−343.
[3] E. Kimura, M. Haruta, T. Koike, M. Shionoya, K. Takenouchi, Y. Iitaka, *Inorg. Chem.* **1993**, *32*, 2779−2784.
[4] P. V. Bernhardt, L. A. Jones, *Inorg. Chem.* **1999**, *38*, 5086−5090.
[5] T. A. Kaden, *Pure Appl. Chem.* **1988**, *60*, 1117−1122.
[6] D. Parker, *Chem. Soc. Rev.* **1990**, *19*, 271−291.
[7] P. S. Pallavicini, A. Perotti, A. Poggi, B. Seghi, L. Fabbrizzi, *J. Am. Chem. Soc.* **1987**, *109*, 5139−5144.
[8] J. Taraszewska, G. Rosłonek, B. Korybut-Daszkiewicz, *J. Electroanal. Chem.* **1991**, *297*, 245−255.
[9] B. Korybut-Daszkiewicz, *J. Chem. Soc., Dalton Trans.* **1992**, 1673−1679.
[10] P. Gluziński, J. W. Krajewski, R. A. Koliński, B. Korybut-Daszkiewicz, A. Mishnev, A. Kemme, *Pol. J. Chem.* **1995**, *69*, 350−360.
[11] P. Gluziński, J. W. Krajewski, R. A. Koliński, B. Korybut-Daszkiewicz, A. Mishnev, A. Kemme, *Pol. J. Chem.* **1994**, *68*, 2567−2587.
[12] B. Korybut-Daszkiewicz, P. Gluziński, J. Krajewski, A. Kemme, A. Mishniev, *Eur. J. Inorg. Chem.* **1999**, 263−268.
[13] E. K. Barefield, G. M. Freeman, D. G. Van Derveer, *Inorg. Chem.* **1986**, *25*, 552−558.
[14] M. Ciampolini, L. Fabbrizzi, M. Licchelli, A. Perotti, F. Pezzini, A. Poggi, *Inorg. Chem.* **1986**, *25*, 4131−4135.
[15] J. Taraszewska, G. Rosłonek, Ya. D. Lampeka, I. M. Maloshtan, *J. Electroanal. Chem.* **1998**, *452*, 49−56.
[16] F. V. Lovecchio, E. S. Gore, D. H. Busch, *J. Am. Chem. Soc.* **1974**, *96*, 3109−3118.

Received June 5, 2000
[I00225]