Investigations of ternary complexes of Co(II) and Ni(II) with thiodiacetate anion and 1,10-phenanthroline or 2,2’-bipyridine in aqueous solutions

Abstract: A potentiometric titration method (PT) and a stopped-flow kinetic technique monitored by a UV−Vis spectroscopy have been used to characterize the stability of series of Co(II)- and Ni(II)-thiodiacetato complexes, M(TDA), in the presence of 1,10-phenanthroline (phen) or 2,2’-bipyridine (bipy) in aqueous solutions. The stability constants of the binary (1:1), ternary (1:1:1) as well as the resulting hydroxo complexes were evaluated and compared to the corresponding oxydiacetate complexes. Based on the species distribution as a function of pH the relative predominance of the species in the system over a pH range was discussed. Furthermore, the kinetic measurements of the substitution reactions of the aqua ligands to phen or bipy in the coordination sphere of the binary complexes M(TDA) were performed in the 288–303 K temperature range, at a constant concentration of phen or bipy and at seven different concentrations of the binary complexes (0.2–0.5 mM). The kinetic stability of the M(TDA) complexes was discussed in relation to the experimental conditions and the kind of the auxiliary ligands (phen/bipy). Moreover, the influence of the type of primary ligand (thiodiacetate/oxydiacetate) on the substitution rate of the auxiliary ligands was also compared.

Keywords: thiodiacetate complexes, ternary complexes, potentiometric titration, stopped-flow method

1 Introduction

The subject of our continuous interest are oxydiacetate metal complexes since it has been found that they are able to scavenge superoxide free radicals (O_2•^-) [1]. The O_2•^- anion is a well-established precursor of reactive oxygen and nitrogen species (RONS), which are known to contribute to the oxidative stress [2]. The biological studies, including an assessment of mitochondrial activity and cytoplasmic membrane integrity (MTT and LDH tests) revealed that the cobalt(II) oxydiacetate complex can protect effectively a mouse hippocampal cell line (HT22) against RONS, however, its cytoprotective activities strongly depend on the dose used. A lower cytoprotective activity was also found for the nickel(II) oxydiacetate complex. To get a better insight into biological properties of the complexes it is important to explore their behaviour in solutions. The knowledge of the stability constants of the complexes is crucial for determining the concentration of metal ion in a system and for evaluating the ability of the ligands to bind the metal ions. Moreover, the study of the mechanism of ligand or group substitution in the coordination sphere enables the description or prediction of the behaviour of inorganic centres in solutions as well as in biological and industrial processes.

The present study constitutes a continuation of our earlier efforts in characterization of the oxydiacetate complexes in solutions [1,3]. It seems to be worth investigating how the substitution of the ethereal donor atom in the oxydiacetate ligand (ODA) by the sulphur donor atom (the thiodiacetate ligand, TDA) affects the stabilities of the complexes in solutions. As far as we are concerned there are only few reports on physicochemical properties of...
such compounds in solutions. Thus, it was, among others, the reason that prompted us to embark on these studies.

Consequently, the aim of the investigations performed was to study the influence of the metal-sulphur (TDA) and metal-oxygen (ODA) bond properties on the stability of the resulting binary and ternary complexes as well as on the rate of substitution of the examined compounds by nitrogen donor ligands (phen/bipy). The obtained results supported by further biological studies may be helpful to define structural and physicochemical features that should have coordination compounds considered as effective superoxide free radicals (O$_2^-$) scavengers during the treatment of diseases of different aetiologies and for a protection of healthy tissues during the treatment.

In this paper, we report the results of potentiometric (PT) and kinetic studies (the UV stopped-flow method) on physicochemical properties of a series of thiodiacetate Co(II) and Ni(II) complexes, M(TDA) (where TDA denotes thiodiacetate dianion), in the presence of 1,10-phenanthroline (phen) or 2,2’-bipyridine (bipy) in aqueous solutions.

2 Experimental Procedure

2.1 Synthesis

All reagents used for the syntheses were of analytical grade and used without further purification. They were as follows: CoCl$_2$·6H$_2$O (≥98%), NiCl$_2$·6H$_2$O (≥98%), 2,2’-thiodiacetic acid (H$_2$TDA, 98%), 1,10-phenanthroline monohydrate (phen, reagent grade), 2,2’-bipyridine (bipy, ≥98%). The compositions of the compounds were established on the basis of the elemental analysis of carbon and hydrogen (Vario EL analyzer Cube CHNS).

The syntheses of [Co(TDA)(H$_2$O)] and [Ni(TDA)(H$_2$O)$_2$] were carried out according to the procedures described in the literature [4,5]. Thus, to the solution of thiodiacetic acid (H$_2$TDA), obtained by dissolving 9 mmol of H$_2$TDA in 60 mL of water, a stoichiometric quantity of solid Na$_2$CO$_3$ was added. The mixture was stirred at room temperature until the evolution of CO$_2$ ceased. Then, to this solution, a stoichiometric quantity of a salt solution (CoCl$_2$·6H$_2$O or NiCl$_2$·6H$_2$O) was added followed by a stoichiometric quantity of the phen or bipy solution. The compounds crystallized directly from these mixtures after 1 – 5 days at room temperature. Crystalline solids were filtered off and washed with small amounts of cold water and air-dried. [Ni(TDA)(phen)(H$_2$O)]: Yield ca 70%, Anal. Calcd for NiC$_{22}$H$_{32}$O$\cdot$4H$_2$O: C, 46.8%, H, 3.2%, S, 7.2%, N, 6.8%. [Co(TDA)(phen)(H$_2$O)]: Yield ca 70%, Anal. Calcd for CoC$_{22}$H$_{32}$N$_2$O$\cdot$4H$_2$O: C, 47.4%, H, 3.5%, S, 7.9%, N, 6.9%. [Ni(TDA)(bipy)(H$_2$O)]: Yield ca 80%, Anal. Calcd for NiC$_{14}$H$_{22}$O$_2$N$_2$: C, 37.1%, H, 4.9%, S, 7.1%, N, 6.2%. [Ni(TDA)(bipy)(H$_2$O)]$\cdot$4H$_2$O: Yield ca 80%, Anal. Calcd for CoC$_{14}$H$_{22}$O$_2$N$_2$: C, 37.1%, H, 4.9%, S, 7.1%, N, 6.2%. [Co(TDA)(bipy)(H$_2$O)]$\cdot$4H$_2$O: Yield ca 80%, Anal. Calcd for CoC$_{14}$H$_{22}$O$_2$N$_2$: C, 37.1%, H, 4.9%, S, 7.1%, N, 6.2%.

2.2 Potentiometric titration (PT)

Potentiometric titrations were performed in a 30 mL thermostated (298.15  ± 0.10 K) cell using the Cerklo Lab System microtitration unit fitted with a 5-mL Hamilton’s syringe, a pH combined electrode (Schott–BlueLine 16 pH type) and a self-made measuring cell equipped with a magnetic stirrer. The temperature was controlled using the Lauda E100 circulation thermostat. The electrode was calibrated according to IUPAC recommendations [9], whereas the syringe was calibrated by a weight method. All the solutions were prepared immediately before measurements. The compositions of the titrand solutions used in the experiments were as follows: Ni$^{2+}$ or Co$^{2+}$ (1.5 mM), H$_2$TDA (1.5 mM), phen or bipy (1.5 mM) and HClO$_2$ (5.0 mM). The double distilled water of conductivity approximately 0.18 µS/cm was used throughout for the preparation of aqueous solutions. Other reagents used in the experiments were purchased from Sigma-Aldrich.

They were as follows: Co(NO$_3$)$_2$·6H$_2$O (ACS reagent, ≥99.9%), Ni(NO$_3$)$_2$·6H$_2$O (99.999%), 2,2’-thiodiacetic acid (H$_2$TDA,
98%)), 1,10-phenanthroline monohydrate (phen, ACS reagent, 99%), 2,2’-bipyridine (bipy, ≥99%). The solutions (V_0 = 5.0 mL) were potentiometrically titrated with the standardized KOH solution (0.05 M) in the pH range from 2.5 to 11.0. The titrant (KOH) was added to the titrand in increments of 0.01 mL, with a pause of 60 s. Each titration was repeated at least three times in order to check the reproducibility of the data. The stability constants of the complexes were determined using the Hyperquad2008 program [9]. The concentration distribution of various complex species existing in the solution as a function of pH was obtained using the HySS program [11].

2.3 Kinetic measurements

The UV-Vis spectra were recorded in the range of 200-400 nm using the Perkin Elmer Lambda 650 spectrophotometer equipped with the temperature control Peltier Systems, with a scan accuracy of 1 nm and a 1 nm slit width at a 120.00 nm min\(^{-1}\) scanning rate. Kinetic measurements were carried out using the Applied Photophysics SX-17MV spectrophotometer using a stopped-flow technique. The wavelengths were chosen so that the changes in the absorbance of the substrate (the binary complexes) and the product of reaction (the ternary complexes) were as high as possible, i.e. Co-TDA-bipy at 273 nm, Co-TDA-phen at 280 nm, Ni-TDA-bipy at 274 nm and Ni-TDA-phen at 255 nm. To prevent the formation of complexes of different than 1:1:1 [metal:TDA:phen (or bipy)] stoichiometry, for each experiment the concentration of the binary complex solution (0.2 – 0.5 mM) was higher than the concentration of phen or bipy (0.05 mM) solution. The measurements were carried out at five temperatures: 288 K, 293 K, 298 K, 303 K and 308 K, for seven different concentrations of the binary complex (0.5 mM, 0.45 mM, 0.4 mM, 0.35 mM, 0.3 mM, 0.25 mM and 0.2 mM), while the concentration of the phen or bipy ligand was kept constant (0.05 mM each). The reagents were thermostated at the chamber of spectrophotometer for at least 30 min. before each measurement. The rate constants were computed using the “Glint” program based on the global analysis [12].

3 Results and Discussion

The equilibrium constants defined by Eqs. (1) and (2):

\[
pM + qL + rB + sH = M_{p}L_{q}^{1}B_{r}^{1}H_{s}^{1}
\]  

\[
\beta_{pqr} = \frac{[M_{p}L_{q}^{1}B_{r}^{1}H_{s}^{1}]}{[M_{p}][L]^{q}[B]^{r}[H]^{s}}
\]

(where M is the metal ion, L the thiodiacetate ion, B denotes 1,10-phenanthroline or 2,2’-bipyridine, H is the proton and p, q, r, s are stoichiometric coefficients for an reaction) were refined by a least-squares calculation using the computer program Hyperquad2008 (ver. 5.2.19) [10] taking into account the presence of the hydroxide species of cobalt and nickel as well as the autoprotolysis of water. The equilibrium model for interaction of the metal ion (M) with TDA (denoted as L) and phen or bipy (denoted as B) takes into account the formation of the binary (ML) and ternary (MLB) complexes, the hydrolysis of the resulting ternary complexes (MLBH), the protolysis of the divalent metal cations (MH\(^+\)) as well as the autoprotolysis of water (H\(^+\)). The protonation constants of H\(_2\)TDA, log\(\beta_{001}\) (HTDA + H\(^+\) = H\(_2\)TDA) = 3.20 and log\(\beta_{000}\) (2H\(^+\) + TDA\(^2-\) = H\(_2\)TDA) = 7.50 [13] as well as BH, log\(\beta_{001}\) (phen + H\(^+\) = phenH\(^+\)) = 4.9 and log\(\beta_{000}\) (bipy + H\(^+\) = bipyH\(^+\)) = 4.3 [14] were fixed and, consequently, only the stability constants of the species presented in Table 1 were refined. This equilibrium model has given the best fitting of the calculated data to the experimental ones. Thus, the tridentate TDA ligand can be considered as a primary ligand and the B ligand as a secondary one. The representative pH-titration curves for the systems under study are shown in Fig. 1, whereas the speciations as a function of pH, molar ratio M:L:B equal 1:1:1, are shown in Fig. 2.

The diagrams reveal the predominance of the binary complexes up to pH ca. 4. The stability of the Ni-TDA complexes is found to be a little higher than the stability of the Co-TDA complexes. Taking into account a high spin d-electron configuration of the metal ions, Co\(^{2+}\) (d\(^7\)) and Ni\(^{2+}\) (d\(^8\)), in the complexes under study [15], as well as the same composition of the coordination sphere of the central ion, the ligand field stabilization energy provides somewhat higher energetic profit for the nickel(II) complex. Thus, this is probably one of the factors responsible for the higher stability of the nickel(II) complexes.

It is also interesting to note that the binary thiodiacetate Co(II) and Ni(II) complexes in the system under study (M:L = 1:1) are more stable than the corresponding oxydiacetate complexes (M-ODA) [3]. This phenomenon can be explained by the differences in the electronegativity between the central donor atoms of the ODA and TDA ligands (oxygen and sulfur atoms, respectively) and the metal ion in the coordination centres of the complexes (Co\(^{2+}\) or Ni\(^{2+}\)). A more covalent character of the M-S(thioether) bond in M-TDA than the
Figure 1: Potentiometric titration curves of the systems under study at 298.15 K.

Figure 2: Species distributions as a function of pH of 1:1:1 M:L:B calculated form the stability constants listed in Table 1.

Table 1: Logarithms of the stability constants (log$\beta_{pqrs}$) of binary and ternary complexes of Co(II) or Ni(II) with TDA and B (phen or bipy) obtained by adapting the equilibrium model to PT data. The standard deviations are given in parenthesis.

| Number of species | Spesies | log$\beta_{pqrs}$ | $M^{2+} = \text{Co}^{2+}$ | $M^{2+} = \text{Ni}^{2+}$ |
|------------------|---------|-------------------|------------------|------------------|
|                  |         |                   | $B = \text{phen}$ | $B = \text{bipy}$ | $B = \text{phen}$ | $B = \text{bipy}$ |
| 1                | ML      | log$\beta_{1100}$ | 4.55 (±0.02)     | 4.43 (±0.03)     | 4.97 (±0.01)     | 4.96 (±0.02)     |
| 2                | MLB     | log$\beta_{1100}$ | 8.37 (±0.05)     | 7.35 (±0.08)     | 9.15 (±0.02)     | 8.60 (±0.03)     |
| 3                | MLBH-1  | log$\beta_{111-1}$ | -1.86 (±0.08)    | -2.40 (±0.12)    | -0.69 (±0.04)    | -1.54 (±0.04)    |
| 4                | MH-2    | log$\beta_{110-2}$ | -18.31 (±0.04)   | -18.42 (±0.05)   | -19.41 (±0.05)   | -19.36 (±0.04)   |
| 5                | H-1*    | log$\beta_{100-1}$ | -13.95 (±0.05)   | -13.92 (±0.03)   | 13.90 (±0.05)    | 13.90 (±0.10)    |

*The ionization constant of water ($pK_w = -\log\beta_{000-1}$)
M-O(etheral) bond in M-ODA results in a stronger binding of the metal ions. The ternary complexes Co(TDA)(phen), Ni(TDA)(bipy) and Ni(TDA)(phen) predominate in the 4−9.5 pH range. On the other hand, for the Co:TDA:bipy (1:1:1) system the binary complex Co−TDA predominates up to pH ca. 10. Due to the greater basicity of the phen ligand, the complexes with phen are more stable than the corresponding complexes with bipy. The same situation was also observed for the ternary oxydiacetate complexes of Co(II) and Ni(II), M(ODA)(B) (where M denotes Co(II) or Ni(II), B denotes phen or bipy) [3]. The ternary complexes undergo hydrolysis and the resulting hydroxo complex species reach the highest concentration in the 10−11 pH range. This phenomenon is due to the neutralization of the proton coming from the aqua ligand present in the coordination sphere of the metal ions of the ternary complexes. It is worth noting that this finding proves the existence of octahedral coordination geometry of ternary complexes in aqueous solutions. Thus, the coordination sphere of the metal ion comprises one tridentate ligand (TDA$^{2-}$), one bidentate ligand (phen or bipy) as well as one molecule of water. For this reason the formula that reflects the structure of the ternary complexes in solutions should be written as M(TDA)(B)(H$_2$O). However, it is worth emphasizing that the formation of the ternary complexes is not favoured over the corresponding binary ones, as occurs in the case of the oxydiacetate cobalt(II) and nickel(II) complexes [3].

This conclusion can be drawn from the assessment of the relative stability of the ternary and the corresponding binary complexes, according to the following equation [16]:

$$\Delta \log K = \log K_{MLB} - \log K_{ML}$$

$$\log K_{MLB} = \frac{\log \beta_{1110}}{\log \beta_{1100}}$$

where $\log K_{MLB}$ is the logarithm of stability constant represented by the equilibrium ML + B = MLB and $\log K_{ML} = \log \beta_{1100}$.

In these studies the negative values of $\Delta \log K$ were found for all the systems indicating the lack of cooperative interactions between the ligands in the coordination sphere of the metal ion.

The formation of the ternary complexes in aqueous solutions has subsequently been confirmed spectrophotometrically by recording the electronic spectra in the UV region (200−400 nm) for all the substrates (the B ligand, the M-TDA complexes do not absorb in the UV region) and the synthesized products (the ternary complexes, M-TDA-B) of the substitution reaction (Scheme 1). The spectra were compared with the spectrum of a mixture composed of M-TDA and B in the molar ratio 1:1. It was found that the spectra were identical. The representative spectra are depicted in Fig. 3.

To assess the rate of substitution of the aqua ligands in the coordination sphere of the binary M(TDA) complexes with B ligand, the changes in the absorbance of the B ligand during reaction were monitored by using the stop-flow method. It has been found that for all the experiments the approximated curves decrease monoexponentially and the reactions proceed in one step. Based on the global analysis method assuming the A → B model reaction, the values of the reaction rates constants ($k$) were determined. The linear relationship of the substitution reaction versus the concentration of the binary complex as well as the temperature is observed (Fig. 4).

The rate of substitution reaction for the nickel(II) binary complexes with phen or bipy is comparable to each other but for the cobalt(II) binary complexes the substitution with phen proceeds ca. 3–6 times faster than with bipy. The higher reaction rate of phen than bipy is also observed for formation of 1:1 metal-phen (or bipy) species [17]. However, our recent results have
shown that for the oxydiacetate cobalt(II) complex the substitution reaction proceeds unexpectedly faster with the bipy ligand [3]. The kinetic data also confirm a more inter nature of the nickel(II) complexes than the cobalt(II) ones (Fig. 4). Such behaviour correlates very well with the ligand field stabilization energy (the LFSE) that favours to a greater extent the exchange of the coordination water for the high spin d⁸ configuration of the nickel(II) ion than for the cobalt(II) ion (d⁷) in an octahedral coordination environment [18].

4 Conclusions

The potentiometric titration (PT) and the stopped-flow methods have successfully been applied to characterize the stability of series of the thiodiacetate Co(II) and Ni(II) complexes in the presence of 1,10-phenanthroline (phen) or 2,2’-bipyridine (bipy) in aqueous solutions. It has been found that the substitution of the ethereal donor atom in the oxydiacetate ligand (ODA) by the sulphur donor atom (the thiodiacetate ligand, TDA) affects both their thermodynamic and kinetic stability. The more covalent character of the M-S(thioether) bond than the M-O(ethereal) bond is responsible for the formation of a more stable binary and ternary thiodiacetate complexes. However, the M-S(thioether) bond does not favour the cooperative interactions between the ligands in ternary complexes as it does for the oxydiacetate complexes. In both series of the complexes (oxydiacetate and thiodiacetate) the stability constants for the phen ternary complexes are higher than for bipy ones. At a higher pH range (above pH 8) the ternary complexes undergo hydrolysis. The results of the PT measurements suggest that the coordination sphere of the metal ion in the ternary complexes seems to have the same composition in solutions and in solids. Based on the kinetic data (a stopped-flow technique) it has been found that the thiodiacetate nickel(II) complexes are more inert in substitution reactions than the cobalt(II) ones. The substitution reaction rates for the nickel(II) complexes with phen and bipy are comparable, whereas for a more labile cobalt(II) complexes the substitution with the former ligand proceeds faster. Furthermore, the study revealed that the substitution of ODA for TDA in the coordination sphere of nickel(II) results in decreasing the substitution rate of the nickel(II) complexes with phen and bipy. A different situation is observed for the cobalt(II) complexes. In this case, the TDA complexes react slower with bipy, however, contrary to the ODA ones, are more labile in the substitution reaction with phen.

The differences in coordinating properties of the oxydiacetate and thiodiacetate anions towards the Co²⁺ and Ni²⁺ ions are reflected by the behaviour of the complexes in solutions. Investigations aimed at obtaining some information regarding the correlation between physicochemical properties of the complexes under study and their cytoprotective activity against reactive oxygen and nitrogen species are under way.

Acknowledgements: This study was supported by the National Science Centre (grant no. 2011/03/D/ST5/05920).
References

[1] Wyrzykowski D., Inkielewicz-Stępniak I., CZupryniak J., Jacewicz D., Ossowski T., Wożniak M., Chmurzyński L., Electrochemical and Biological Studies on Reactivity of [VO(oda)(H₂O)₂]·H₂O and [Ni(oda)(H₂O)₃]·1.5H₂O Towards Superoxide Free Radicals, Z. Anorg. Allg. Chem., 2013, 639, 1795-1799.

[2] Sayre L.M., Perry G., Smith M.A., Chem. Res. Toxicol., Oxidative stress and neurotoxicity, 2008, 21, 172-188.

[3] Wyrzykowski D., Pranczk J., Jacewicz D., Tesmar A., Pilarski B., Chmurzyński L., Investigations of ternary complexes of Co(II) and Ni(II) with oxydiacetate anion and 1,10-phenanthroline or 2,2'-bipyridine in solutions, Cent. Eur. J. Chem., 2014, 12, 107-114.

[4] Alarcón-Payer C., Pivetta T., Choquesillo-Lazarte D., González-Pérez J.M., Crisponi G., Castiñeiras A., et al., Inorg. Chem. Commun., Structural correlations in nickel(II)–thiodiacetato complexes: molecular and crystal structures and properties of [Ni(tda)(H₂O)]₂, 2004, 7, 1277-1280.

[5] Grirrane A., Pastor A., Álvarez E., Mealli C., Masi D., et al., Thiodiacetate cobalt(II) complexes: synthesis, structure and properties, Inorg. Chem. Commun., 2005, 8, 463-466.

[6] Kopel P., Trávníček Z., Marek J., Mozifšský J., Syntheses and study on nickel(II) complexes with thiodiglycolic acid and nitrogen-donor ligands. X-ray structures of [Ni(bpp)(tdga)(H₂O)]·4H₂O and [en]Ni(μ-tdga)Ni(en)]·4H₂O (tdgaH₂=thiodiglycolic acid), Polyhedron, 2004, 23, 1573-1578.

[7] Grirrane A., Pastor A., Álvarez E., Mealli C., Ienco A., Galindo A., Synthesis and molecular structure of oxydiacetate complexes of nickel(II) and cobalt(II). Theoretical analysis of the planar and non-planar conformations of oxydiacetate ligand and oxydiacetic acid, J. Chem. Soc., Dalton Trans., 2002, 3771-3777.

[8] Martin R.B., Prados R.J., Some factors influencing mixed complex formation, J. Inorg. Chem., 1974, 36, 1665-1670.

[9] Richens D.T., Ligand substitution reactions at inorganic centers, Chem. Rev. 2005, 105, 1961-2002.