

Propositions of PhD thesis

**Hydroxamate-complexes of half-sandwich
platinum metal ions: solution equilibrium studies
and synthesis**

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UNIVERSITY OF DEBRECEN

PhD Program in Chemistry

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I. INTRODUCTION AND THE AIM OF THE WORK

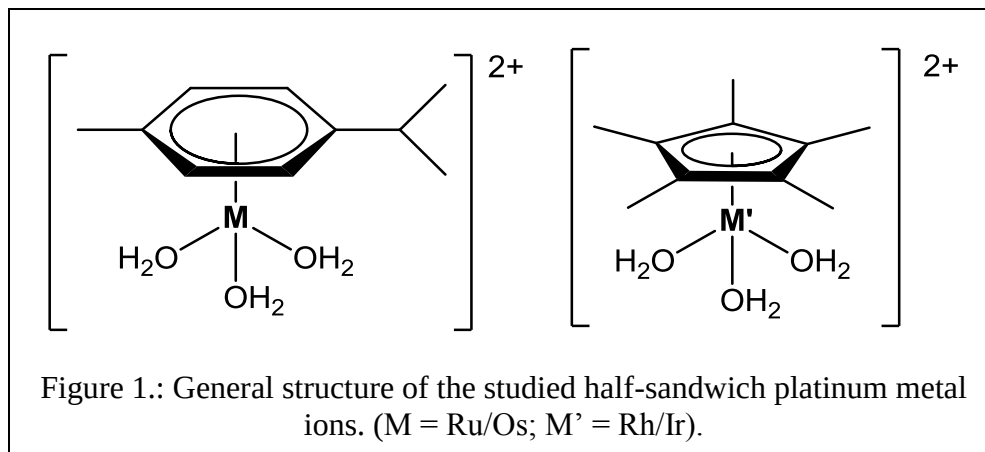
In recent times cisplatin and some other platinum(II) complexes are the only metal compounds used in cancer chemotherapy. They are effective against various types of cancer, but they lack selectivity, which often results in severe side effects. For this reason there has been a continuous research in the past few decades for the development of other effective transition metal complexes with less side effects.

A large number of compounds have been reported with considerable *in vitro* cytotoxicity, but the most promising results have been achieved with ruthenium compounds, namely, three Ru(III)-complexes entered clinical trials. *In vivo* reduction to the corresponding Ru(II)-complex is an important step in their mechanism of action, therefore Ru(II)-compounds have also gained attention. This oxidation state can be stabilized in the so-called half-sandwich type organometallic cations, in which a π -arene ligand (benzene- or cyclopentadienyl derivative) is linked to the metal ion, and the three remaining coordination sites can be occupied by chelating or monodentate ligands (Fig. 1). The physical and chemical properties of these complexes can be tuned by the variation of the metal centre, the aromatic and the chelating ligands, and this makes these compounds more suitable for biological applications. This type of complexes are also common with other platinum metals, namely Os(II), Rh(III) and Ir(III), and numerous examples have been reported in the literature with promising *in vitro* cytotoxicity. For understanding their mechanism of action, it is important to know the stability of these complexes in solution, and the processes that happening to them in biological fluids. Therefore, the hydrolytic behaviour of the half-sandwich platinum metal ions, and their interactions in solution with various chelating and bioligands were studied in detail in the past decade.

Hydroxamic acids are potent chelating ligands which form stable complexes with different metal ions. They have important biological roles and medical uses, for example the hydroxamate-based natural siderophore desferrioxamine B (DFB) is also used as a therapeutic iron chelator. Some hydroxamic acids also possess antitumor activity, of which the most important is the suberoylanilide hydroxamic acid (SAHA), which is an FDA-approved anticancer agent to treat cutaneous T-cell lymphoma. Hydroxamate derivatives which contain an additional donor atom besides the hydroxamate function could also be interesting due to their different complex-forming properties. The most well-known example for this are the aminohydroxamic acids, which contain an additional amino nitrogen donor. With their multiple donor sets these molecules can form oligonuclear complexes as bridging ligands, and this could result in the formation of ringed structures, the so-called „metallacrown” complexes. Similar structures are also common among the half-sandwich platinum metal compounds, and these type of complexes has been studied in detail due to their interesting physical and chemical properties.

Since the half-sandwich platinum metal ions are a promising class of anticancer compounds, and there are also some examples of hydroxamic acids with antitumor effect, combination of them may lead to new compounds with improved antitumor activity. In accordance with this our goal was to study the interaction between these two classes of compounds both in solution and in the solid state, and to screen their *in vitro* cytotoxicity

in selected cancer cell lines. The studied half-sandwich metal ions were the $[(\eta^6\text{-}p\text{-cymene})\text{Ru}(\text{H}_2\text{O})_3]^{2+}$, $[(\eta^6\text{-}p\text{-cymene})\text{Os}(\text{H}_2\text{O})_3]^{2+}$, $[(\eta^5\text{-Cp}^*)\text{Rh}(\text{H}_2\text{O})_3]^{2+}$ and the $[(\eta^5\text{-Cp}^*)\text{Ir}(\text{H}_2\text{O})_3]^{2+}$ cations (see Fig. 1). The structures of the studied hydroxamic acids are depicted in Fig. 2.



The monohydroxamate complexes prepared earlier in our laboratory with the mentioned ruthenium and osmium half-sandwich cations showed no antiproliferative activity, therefore now we continued this work with the aminohydroxamates. With this ligand family the formation of more inert complexes could be expected, which may result in higher cytotoxicity. Furthermore, we extended our solution equilibrium studies to imidazole hydroxamic acids, in order to explore the effect of the amino nitrogen – imidazole nitrogen change on the complex formation processes with the half-sandwich cations.

II. EXPERIMENTAL METHODS

The studied amino- and imidazole hydroxamic acids were prepared according to literature procedures, or with modification of them. **pH-potentiometry** was used for the determination of the protonation constants of the studied ligands, and the composition and stability of their half sandwich platinum metal complexes. The measurements were carried out at $T = 25.0\text{ }^{\circ}\text{C}$ and at constant 0.20 M ionic strength maintained with KCl or KNO_3 . Mettler Toledo DL50 or T50 automatic titrators were used with DGi 114-SC electrode (for the KCl-containing samples) or with a type 6.0255.100 Metrohm double junction electrode (for the nitrate-containing samples). Protonation constants of the ligands and the stability constants of their metal complexes were calculated with the SUPERQUAD and PSEQUAD computer programs, respectively, while the concentration distribution diagrams were calculated with the MEDUSA program.

^1H NMR methods were used for monitoring the complex formation processes in deuterium oxide (and in DMSO-d^6 in one case), at different pH values and temperatures, and at a constant ionic strength. The measurements were performed on a Bruker WP 360 SY, or a Bruker Avance 400 spectrometer, and MestReNova software was used for analysis of the spectra.

ESI-TOF-MS measurements were carried out with samples in aqueous solution in the positive mode, at different pH values and metal ion to ligand ratios. MS analysis of the prepared solid complexes was performed in methanolic solution. The measurements were made with a Bruker micrOTOF-Q ESI-TOF instrument at the Department of Applied Chemistry, University of Debrecen. DataAnalysis program was used for analyzing mass spectra.

The prepared solid complexes were further characterized with **elemental analysis**, **infrared spectroscopy** and **X-ray diffraction** methods. The elemental analysis and IR spectroscopic measurements were made by Dr. Attila Kiss at the Department of Organic Chemistry, University of Debrecen, with a Perkin Elmer FTIR Paragon 1000 PC, and Elementar Vario MICRO CUBE instruments. Single crystal X-ray diffraction measurements were carried out by Dr. Attila Bényei at the Department of Physical Chemistry, University of Debrecen, with a Bruker-Nonius MACH3 diffractometer, using the $\text{Mo-K}\alpha$ radiation ($\lambda = 0.71073\text{ \AA}$). Crystal structures were solved with the SIR-92 program.

Density Functional Theory (DFT) calculations were used in some cases to optimize the geometry of the complexes formed in the investigated systems. The calculations were carried out by Dr. Norbert Lihi and Dr. Mihály Purgel at the University of Debrecen. Gaussian 09 software package was used for the calculations.

In vitro cytotoxicity tests and **cellular uptake study** of the prepared metal complexes were carried out by the group of Prof. Jana Kasparkova, in the frame of an international cooperation. Cytotoxicity tests were made on selected cancer cell lines with the Neutral Red (NR)-method.

III. STUDIED LIGANDS

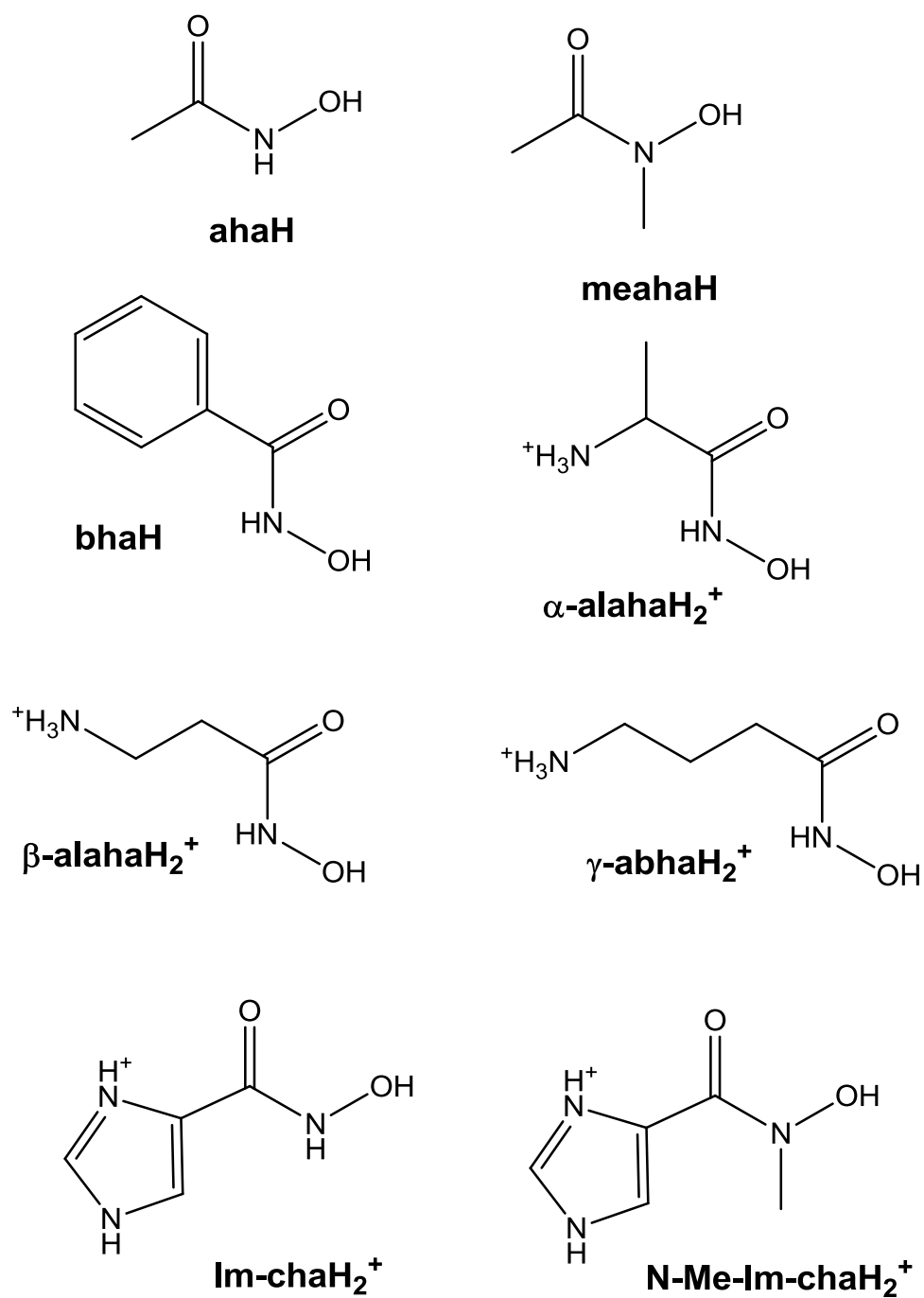


Figure 2.: Structures and abbreviations of the fully protonated forms of the studied ligands.

IV. NEW SCIENTIFIC RESULTS

1. Interaction between half-sandwich platinum metal ions and monohydroxamic acids

1.1. With the secondary hydroxamic acid, meahaH, solution equilibrium studies were carried out with all of the four half-sandwich metal ions. We have found that stable hydroxamate-complexes of $[ML]^+$ composition formed in all of the four systems with similar thermodynamic stability, however, significant difference in the stability can be found when comparing the stability constants of the half-sandwich ruthenium and rhodium complexes (see Table 1.).

Table 1.: Thermodynamic ($\lg\beta$) stability constants of the complexes formed in the half-sandwich metal ion – meahaH systems ($I = 0.20$ M KNO_3 ; $T = 25.0$ °C; 3σ standard deviations are in parentheses).

	$[(\eta^6\text{-}p\text{-cym})Ru]^{2+}$	$[(\eta^6\text{-}p\text{-cym})Os]^{2+}$	$[(\eta^5\text{-}Cp^*)Rh]^{2+}$	$[(\eta^5\text{-}Cp^*)Ir]^{2+}$
$[ML]^+$	10.99(2)	10.06(2)	8.43(1)	10.09(1)
$[MLH_{-1}]$	1.84(4)	3.0(2)	-1.36(6)	2.07(11)
pK_{ML}	9.15	7.06	9.79	8.02

1.2. We have shown that mixed hydroxido complexes with $[MLH_{-1}]$ composition are formed in all cases with the deprotonation of the water molecule occupying the third coordination site of the half-sandwich metal ion. The pK_{ML} value describing this process showed identical trend that can be seen for the hydrolysis of the half-sandwich aqua cations.

1.3. We have demonstrated that the meahaH ligand binds almost all of the half-sandwich ruthenium and rhodium ions in the potentially bioactive $[ML]^+$ species at physiological pH and at 1:1 metal ion to ligand ratio. However, meahaH cannot compete with the strong hydrolytic processes of the half sandwich osmium -and iridium ions at neutral pH (see Fig. 3.).

1.4. With the ahaH ligand we have shown that oligonuclear species are

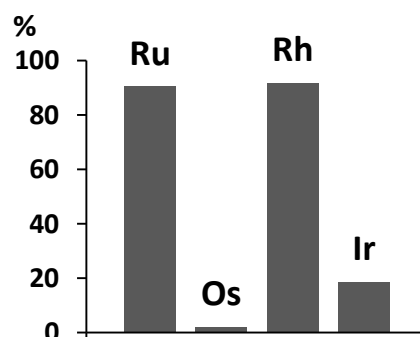


Figure 3.: Fractions (%) of the $[ML]^+$ complexes in the studied half-sandwich metal ion – meahaH systems at pH = 7.4 (1:1 metal ion to ligand ratio, $I = 0.20$ M KNO_3 , $c_M = 2$ mM).

formed during the interaction of the half-sandwich ruthenium and rhodium ions with primary hydroxamates. The hydroxamate nitrogen plays a key role in their formation, also with direct coordination to the metal centres.

1.5. For $[(\eta^5\text{-Cp}^*)\text{Rh}(\text{H}_2\text{O})_3]^{2+}$ we have prepared and characterized the complexes formed with the ahaH and bhaH ligands. We have confirmed the molecular structure of the acetohydroxamate-complex with X-ray diffraction method (see Fig.4.).

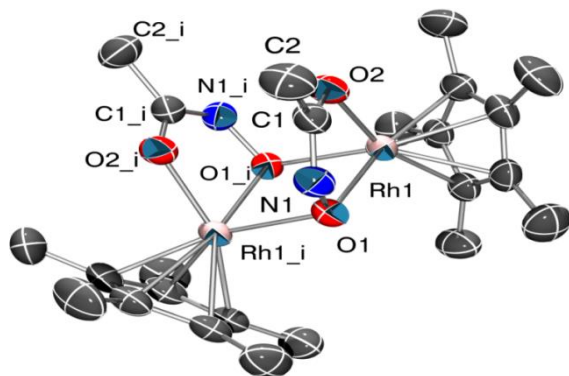


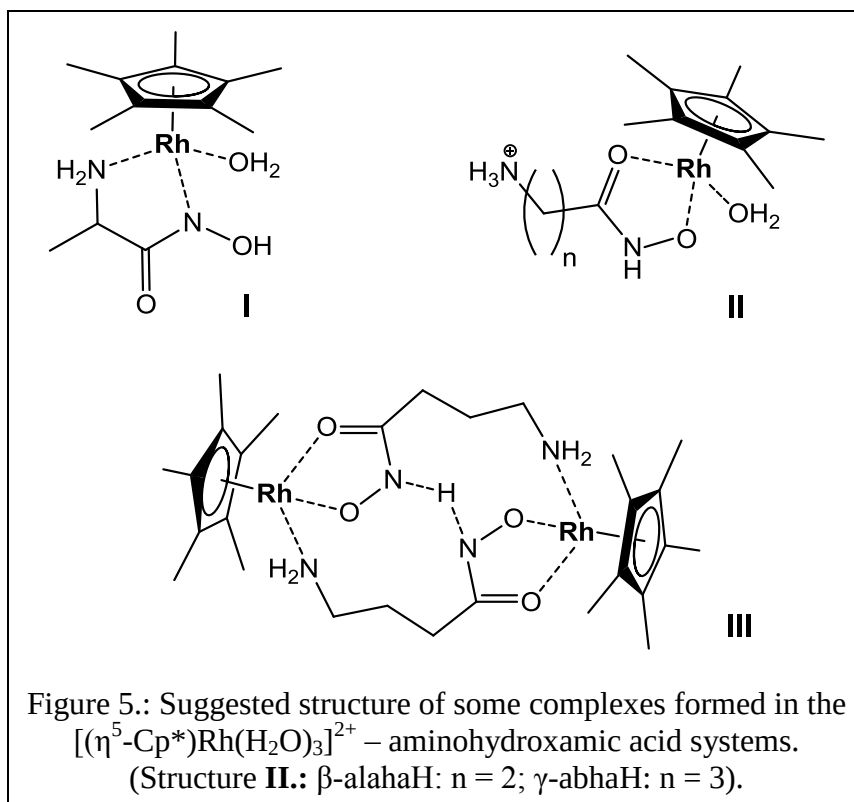
Figure 4.: X-ray structure of the $[(\eta^5\text{-Cp}^*)\text{Rh}]_2(\mu^2\text{-aha})_2]^{2+}$ cation. (Hydrogen atoms are omitted for clarity).

We have found that the structure of these monohydroxamate complexes mainly depends on the presence of other coordinating ligands: in the absence of these other ligands, symmetrical $[\text{M}_2\text{L}_2]$ -type complexes form with bridging hydroxamates between the metal centres. In the presence of monodentate ligands (e.g. chloride ion), however, the results suggest the formation of simple monohydroxamate complexes, in which the monodentate ligand takes the third coordination site of the metal ion.

2. Interaction of the half-sandwich platinum metal ions with amino -and imidazole hydroxamic acids

2.1. We have detected slow complex formation reactions with the half-sandwich ruthenium ion, therefore adequate solution studies with the $[(\eta^5\text{-Cp}^*)\text{Rh}(\text{H}_2\text{O})_3]^{2+}$ cation could only be carried out. To explore the most likely structure of the different rhodium complexes present at different pH values, at first we determined the pH-dependent conditional stability of the possible chelates by the use of model ligands. We have found that the five membered ($\text{N}_{\text{amino}}, \text{N}_{\text{hydroxamate}}$) chelate is the most favoured binding mode in the whole studied pH-range, but its six membered analogue has a comparable stability to the hydroxamate (O,O) chelate.

2.2. We have shown that the half-sandwich rhodium – aminohydroxamate complexes formed with the three studied ligands have different structure and stability, due to the different size of the (N,N) chelate rings. With α -alahaH the $[\text{ML}]^+$ species containing the five membered ($\text{N}_{\text{amino}}, \text{N}_{\text{hydroxamate}}$) chelate, and its deprotonated form (the corresponding mixed hydroxido complex with $[\text{MLH}_{-1}]$ composition) are the predominant species at 1:1 metal ion to ligand ratio (see structure I. in Fig. 5.).



With β -alahaH the dinuclear $[\text{M}_2\text{LH}_{-1}]^{2+}$ complex is the major species in the acidic pH-range even in the equimolar system, due to the comparable stability of the six membered (N,N) chelate and the hydroxamate chelate. With γ -abhaH, however, formation of the $[\text{MLH}]^{2+}$ species containing the hydroxamate (O,O) chelate is more favoured (see structure II. in Fig. 5.). With the two latter ligands $[\text{M}_2\text{L}_2]$ -type complexes are also formed above $\text{pH} = 7$, but with different structures. With β -alahaH the stable dinuclear structure of the $[\text{M}_2\text{LH}_{-1}]^{2+}$ complex is still present in the species formed. With the γ -abhaH ligand (O,O)-chelated species were detected (see structure III. in Fig. 5.) and we have confirmed their structure with DFT calculations as well.

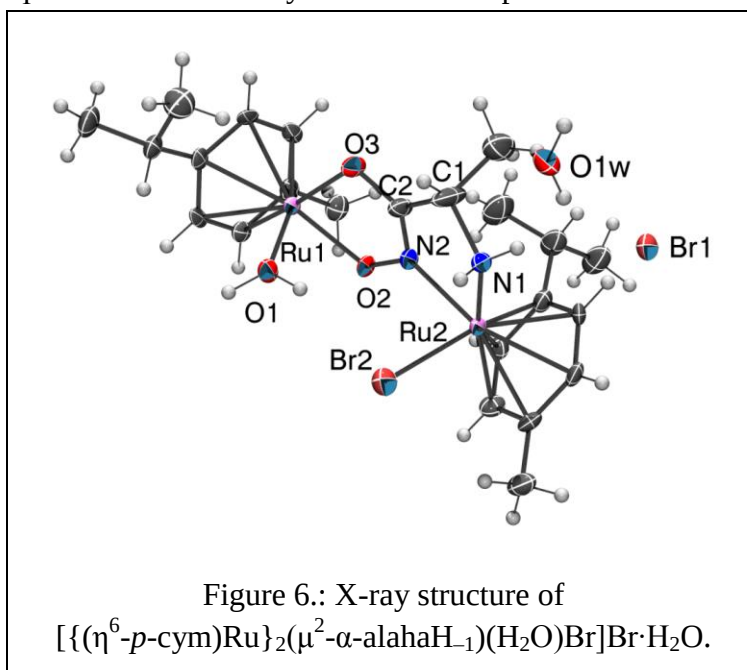
2.3. We have demonstrated that the $[\text{M}_2\text{LH}_{-1}]^{2+}$ complex and its deprotonated forms are the dominant species in the $[(\eta^5\text{-Cp}^*)\text{Rh}(\text{H}_2\text{O})_3]^{2+}$ – aminohydroxamic acid systems at metal ion excess. In these species the aminohydroxamates link two organometallic cations with (O,O)- and (N,N)-chelated rings, and the remaining coordination sites of the metal centres are occupied by water, hydroxide, or chloride (see Figure 6.). Furthermore, the aminohydroxamates bind the half-sandwich rhodium ion up to $\text{pH} = 11$, preventing the hydrolysis of the organometallic cation.

2.4. The $[(\eta^6\text{-}p\text{-cymene})\text{Ru}(\text{H}_2\text{O})_3]^{2+}$ cation shows fast complex formation only with the γ -abhaH ligand. In this system we have identified similar species as with the half-sandwich rhodium ion, but with slightly higher stability. Also, with NMR measurements we have found that the complexes formed in the basic pH range can be present as different isomeric structures simultaneously.

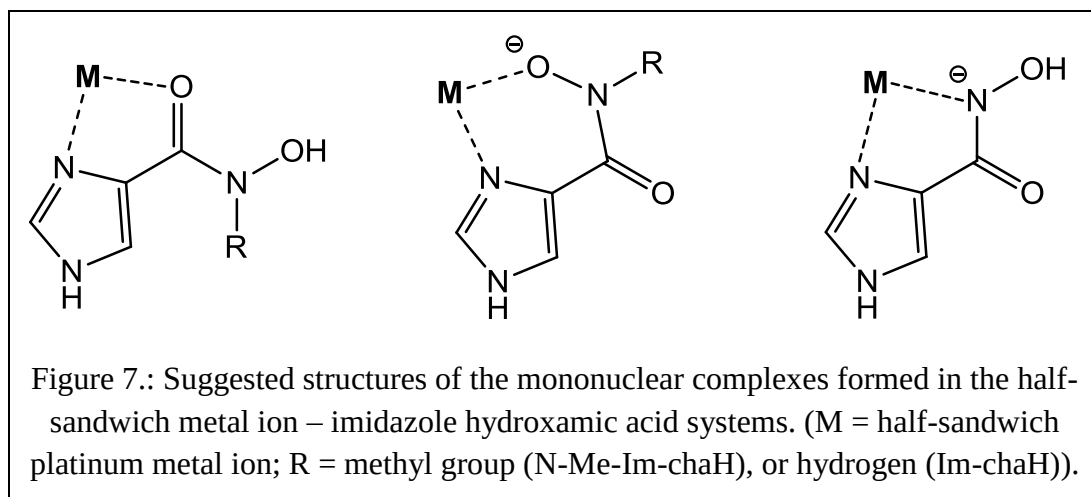
2.5. We have prepared and characterized the $[\{(\eta^6\text{-}p\text{-cym})\text{Ru}\}_2(\mu^2\text{-}\alpha\text{-alahaH}_{-1})]^{2+}$ complex, in the form of two compounds with different counter anions. With X-ray diffraction

method we have also proven their structure detailed in section 2.3., the structure can be seen on Figure 6. We have also prepared the α -alaninehydroxamato complex of the $[(\eta^5\text{-Cp}^*)\text{Ir}(\text{H}_2\text{O})_3]^{2+}$ cation. We have shown that this complex has the same mononuclear structure as described above with the analogous rhodium cation: the ligand coordinates to the metal centre with a five-membered (N,N) chelate ring.

2.6. We have found that the two studied imidazole hydroxamic acids form similar mononuclear complexes with the half-sandwich rhodium ion in the acidic pH-range, at 1:1 metal ion to ligand ratio. The structures of the formed species



can be seen in Figure 7. None of these complexes contain the hydroxamate (O,O) chelate, however, the imidazole N3 nitrogen coordinates to the metal centre in all cases, showing that the imidazole nitrogen is the anchor in which the complex formation starts in these systems.



2.7. We have shown that both imidazole hydroxamic acids form oligonuclear complexes with the half-sandwich ruthenium and rhodium ions in the neutral and basic pH-range. Their composition are similar with the primary and secondary ligand, but their structure are different, depending on the substituent of the hydroxamate-nitrogen. They are probably oligonuclear complexes with fused ring structure, and we have proven this with DFT calculations in the case of the tetranuclear complex formed in the $[(\eta^5\text{-Cp}^*)\text{Rh}(\text{H}_2\text{O})_3]^{2+}$ – N-Me-Im-chaH system.

2.8. Our results show that the studied half-sandwich metal ions form different complexes with the aminohydroxamic acids and the imidazole hydroxamic acids. With the latter ligand family we have not detected the formation of the hydroxamate (O,O) chelate at all, and this suggests that the imidazole group is a more favoured binding site for these organometallic cations, than the hydroxamate function.

3. Biological tests of the prepared metal complexes

3.1. We have tested all of the prepared complexes for their *in vitro* cytotoxicity on selected cancer cell lines, but they proved to be no active in the micromolar concentration range. This result together with earlier studies from our laboratory show that changing the metal (from ruthenium/osmium to rhodium) did not improve the cytotoxicity of the monohydroxamate complexes. Use of the aminohydroxamic acids indeed resulted in more inert complexes, but this modification did not have positive effect either.

3.2. We have also conducted cellular uptake studies with the prepared iridium complex on A2780 cells in comparison with cisplatin. It was found that the cells can uptake the iridium complex much more effectively than cisplatin, and this suggests that the lack of cytotoxicity is probably due to the limited interactions with the biological target molecules within the cell.

V. POSSIBLE APPLICATIONS OF THE RESULTS

We have studied the interaction of half-sandwich platinum metal ions with different hydroxamic acids in solution, and also in the solid state. The *in vitro* cytotoxicity of the prepared complexes was also tested on selected cancer cell lines.

Although our work represents basic research, our results can have practical applications as well. Our results extended the family of half-sandwich platinum metal complexes with potential biological activity, and can help developing new metal-based drugs with the desired thermodynamic and kinetic properties. Besides, the biological tests we have conducted can help to establish structure-activity relationships for anticancer metal complexes.

TUDOMÁNYOS PUBLIKÁCIÓK (PUBLICATIONS)

Az értekezés alapját képező közlemények (articles related to the dissertation):

3. Péter László Parajdi-Lozonczi, Péter Buglyó, Hana Skakalova, Jana Kasparkova, Norbert Lihi and Etelka Farkas: **Half-sandwich type rhodium(III)–aminohydroxamate complexes: the role of the position of the amino group in metal ion binding**, *New Journal of Chemistry*, **42** (2018) 7659-7670. (IF: 3,269 (2016))

2. Péter Buglyó, Péter L. Parajdi-Lozonczi, Attila C. Bényei, Norbert Lihi, Linda Bíró and Etelka Farkas: **Versatility of Coordination Modes in Complexes of Monohydroxamic Acids with Half-Sandwich Type Ruthenium, Rhodium, Osmium and Iridium Cations**, *ChemistrySelect*, **2** (2017) 8127-8136.

1. Péter László Parajdi-Lozonczi, Attila Csaba Bényei, Éva Kováts, István Timári, Tereza Radosova Muchova, Vojtech Novohradsky, Jana Kasparkova and Péter Buglyó: **$[(\eta^6\text{-}p\text{-cymene})\text{Ru}(\text{H}_2\text{O})_3]^{2+}$ Binding Capability of Aminohydroxamates – A Solution and Solid State Study**, *Journal of Inorganic Biochemistry*, **160** (2016) 236-245. (IF: 3,348 (2016))

Az értekezésben nem tárgyalt közlemények (articles not related to the dissertation):

2. Daniele Sanna, Valeria Ugone, Giuseppe Sciortino, Péter Buglyó, Zolt Bihari, Péter László Parajdi-Lozonczi and Eugenio Garribba: **$\text{V}^{\text{IV}}\text{O}$ complexes with antibacterial quinolone ligands and their interaction with serum proteins**, *Dalton Transactions*, **47** (2018) 2164-2182 (IF: 4,029 (2016))

1. Etelka Farkas, Orsolya Szabó, Péter L. Parajdi-Lozonczi and István Pócsi: **Mn(II)/Mn(III) and Fe(III) binding capability of two *Aspergillus fumigatus* siderophores, desferricrocin and N' , N'' , N''' -Triacetylfusarinine C**, *Journal of Inorganic Biochemistry*, **139** (2014) 30-37 (IF: 3,348 (2016))

Előadások (lectures):

5. Parajdi-Lozonczi Péter László, Bényei Attila Csaba, Lihi Norbert, Bíró Linda, Mikó Diána, Horváth Anita, Farkas Etelka és Buglyó Péter: **Félszendvics platinafémissionok monohidroxamát-komplexei: a hidroxamát-N szerepe oldat- és szilárd fázisú kölcsönhatásokban. 51. Komplexkémiai Kollokvium**, Balatonvilágos, Magyarország, 2017. május 29.-31.

4. Péter László Parajdi-Lozonczi, Attila Csaba Bényei, Éva Kováts, István Timári, Tereza Radosova Muchova, Vojtech Novohradsky, Jana Kasparkova and Péter Buglyó: **Organometallic ruthenium- and rhodium aminohydroxamate complexes. 8th International Symposium on Bioorganometallic Chemistry**, Moszkva, Oroszország, 2016. szeptember 4.-8.

3. Parajdi-Losonczi Péter László, Bényei Attila, Godó Attila, Mikó Diána, Horváth Anita, Lihi Norbert, Farkas Etelka és Buglyó Péter: **Félszendvics szerkezetű platinafémionok kölcsönhatása primer és szekunder monohidroxámsavakkal.** 50. *Komplexxémiai Kollokvium*, Balatonvilágos, Magyarország, 2016. május 30. - június 1.

2. Parajdi-Losonczi Péter László, Bényei Attila, Kováts Éva, Timári István, Buglyó Péter, Tereza Radosova Muchova, Jana Kasparkova és Vojtech Novohradsky: **A $[(\eta^6\text{-}p\text{-cimol})\text{Ru}(\text{H}_2\text{O})_3]^{2+}$ kölcsönhatásának vizsgálata aminosavakkal.** I. *Debreceni Röntgendiffrakciós Kerekasztal*, Debrecen, Magyarország, 2016. január 20.

1. Parajdi-Losonczi Péter László, Bényei Attila, Kováts Éva, Timári István és Buglyó Péter: **A $[(\eta^6\text{-}p\text{-cimol})\text{Ru}(\text{H}_2\text{O})_3]^{2+}$ kölcsönhatásának vizsgálata aminosavakkal.** 49. *Komplexxémiai Kollokvium*, Siófok, Magyarország, 2015. május 26.-28.

Poszterek (posters):

3. Péter László Parajdi-Losonczi, Norbert Lihi, Attila Csaba Bényei, Diána Mikó, Anita Horváth, Linda Bíró, Etelka Farkas and Péter Buglyó: **Monohydroxamate complexes of half-sandwich platinum metal ions – A solution and solid state study.** 14th *International Symposium on Applied Bioinorganic Chemistry*, Toulouse, Franciaország, 2017. június 7.-10.

2. Péter László Parajdi-Losonczi, Attila Csaba Bényei, Éva Kováts, István Timári, Tereza Radosova Muchova, Vojtech Novohradsky, Jana Kasparkova and Péter Buglyó: **Organometallic ruthenium- and rhodium aminohydroxamate complexes.** 8th *International Symposium on Bioorganometallic Chemistry*, Moszkva, Oroszország, 2016. szeptember 4.-8.

1. Péter László Parajdi-Losonczi, Attila Csaba Bényei, Éva Kováts, István Timári, Tereza Radosova Muchova, Vojtech Novohradsky, Jana Kasparkova and Péter Buglyó: **Interaction of half-sandwich ruthenium, and –rhodium ions with aminohydroxamic acids.** 13th *European Biological Inorganic Chemistry Conference*, Budapest, Magyarország, 2016. augusztus 28. – szeptember 1.



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Candidate: Péter László Parajdi-Losonczi
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MTMT ID: 10056731

List of publications related to the dissertation

Foreign language scientific articles in international journals (3)

1. **Parajdi-Losonczi, P. L.**, Buglyó, P., Skakalova, H., Kasparkova, J., Lihi, N., Farkas, E.: Half-sandwich type rhodium(III)-aminohydroxamate complexes: the role of the position of the amino group in metal ion binding.
New J. Chem. 42 (10), 7659-7670, 2018. ISSN: 1144-0546.
DOI: <http://dx.doi.org/10.1039/C7NJ04711H>
IF: 3.201 (2017)
2. Buglyó, P., **Parajdi-Losonczi, P. L.**, Bényei, A., Lihi, N., Bíró, L., Farkas, E.: Versatility of Coordination Modes in Complexes of Monohydroxamic Acids with Half-Sandwich Type Ruthenium, Rhodium, Osmium and Iridium Cations.
ChemistrySelect. 2 (26), 8127-8136, 2017. ISSN: 2365-6549.
DOI: <http://dx.doi.org/10.1002/slct.201701858>
IF: 1.505
3. **Parajdi-Losonczi, P. L.**, Bényei, A., Kovács, É., Timári, I., Muchova, T. R., Novohradsky, V., Kasparkova, J., Buglyó, P.: $[(\eta^6\text{-p-cymene})\text{Ru}(\text{H}_2\text{O})_3]^{2+}$ Binding Capability of Aminohydroxamates : A Solution and Solid State Study.
J. Inorg. Biochem. 160, 236-245, 2016. ISSN: 0162-0134.
DOI: <http://dx.doi.org/10.1016/j.jinorgbio.2016.02.032>
IF: 3.348





List of other publications

Foreign language scientific articles in international journals (2)

4. Sanna, D., Ugone, V., Sciortino, G., Buglyó, P., Bihari, Z., **Parajdi-Losonczi, P. L.**, Garribba, E.:
V(IV)O complexes with antibacterial quinolone ligands and their interaction with serum proteins.
Dalton Trans. 47 (7), 2164-2182, 2018. ISSN: 1477-9226.
DOI: <http://dx.doi.org/10.1039/C7DT04216G>
IF: 4.099 (2017)
5. Farkas, E., Szabó, O., **Parajdi-Losonczi, P. L.**, Balla, G., Pócsi, I.: Mn(II)/Mn(III) and Fe(III) binding capability of two *Aspergillus fumigatus* siderophores, desferricrocin and N', Ni, N"-triacytylfusarinine C.
J. Inorg. Biochem. 139, 30-37, 2014. ISSN: 0162-0134.
DOI: <http://dx.doi.org/10.1016/j.jinorgbio.2014.06.005>
IF: 3.444

Total IF of journals (all publications): 15,597

Total IF of journals (publications related to the dissertation): 8,054

The Candidate's publication data submitted to the iDEa Tudóstér have been validated by DEENK on the basis of Web of Science, Scopus and Journal Citation Report (Impact Factor) databases.

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