

NOVEL PLATINUM COMPLEXES WITH SCHIFF BASES AND  $\alpha$ -DIOXIMES,  
THEIR PHYSICO-CHEMICAL AND BIOLOGICAL STUDY

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### Abstract

In our research project we prepared the following platinum(II) complexes with Schiff bases and  $\alpha$ -dioximes, such as  $[\text{Pt}(\text{ketone})_2\text{A}(\text{L}_2)]$ , (ketone: 2-heptanone, 2-octanone, 3-octanone; A: hydrazine, phenylhydrazine, *o*-phenylene-diamine; L: 1-naphthylamine, 2-aminopyrimidine, 2-methylimidazole, 2-amino-4-methylpyridine) and  $[\text{Pt}(\text{DioxH})_2\text{L}_2]$ , (DioxH<sub>2</sub>: methyl-phenyl-dioxime, butyl-methyl-dioxime; L: 1-naphthylamine, 2-methylimidazole, 2-amino-4-methylpyridine, lepidine, 2-methylpyridine, *m*-toluidine, dicyclohexylamine, 4-isopropylamine, cyclohexylamine), by the reaction of PtCl<sub>2</sub> in suitable solvent. After a short bibliographical survey, involving the classification and evolution of platinum complexes with possible applications, we analyzed their physico-chemical properties using FTIR, Raman, NMR, UV-VIS spectroscopy, powder X-ray diffraction (XRD), mass spectrometry, thermal analysis (TG, DTG, DTA) and SEM. We also studied the antibacterial effect of complexes on different strains of bacteria. This class of compounds has relevance in biochemistry, some of them are antibacterial agents and potential anti-tumor drugs.

### Introduction

Following the discovery of the anticancer properties of cisplatin, there has been a vast interest in the scientific community to develop metal-based drugs. Cisplatin inhibits the replication of cancer cells by forming covalent cross-links with DNA, which distorts its helical structure and prevents repair and replication, resulting in apoptosis [1].

Besides the biological applications of metal complexes with Schiff base type ligands, they can be used in various dye, drugs, polymer industries and exhibit luminescence properties. In biological applications, they have been studied mainly for their insecticidal, fungicidal, antibacterial, anticancer, and inflammatory activities [2].

Over the past decades, the Pt(II) complexes have been extensively investigated as optoelectronic materials owing to their outstanding photoelectronic properties enabling them for potential applications such as light-emitting devices, chemosensors, and luminescent imaging agents [3].

In this paper we report the synthesis and characterization of novel platinum complexes with Schiff bases and  $\alpha$ -dioximes.

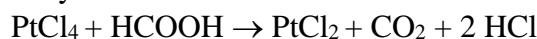
## Experimental

**Used materials:** PtCl<sub>4</sub>, Bu-Me-DioxH<sub>2</sub>, Me-Ph-DioxH<sub>2</sub>, 2-heptanone, 2-octanone, 3-octanone, hydrazine, phenylhydrazine, *o*-phenylene-diamine, 1-naphthylamine, 2-aminopyrimidine, 2-methylimidazole, 2-amino-4-methylpyridine, 2-methylimidazole, lepidine, 2-methylpyridine, *m*-toluidine, dicyclohexylamine, 4-isopropylamine, cyclohexylamine, MeOH, EtOH.

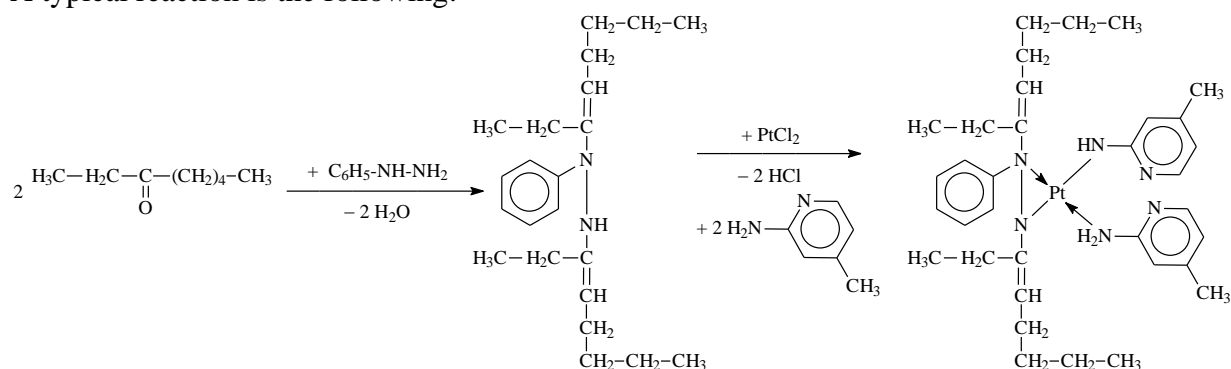
### Methods:

- *Synthesis of [Pt(ketone)<sub>2</sub>A(L<sub>2</sub>)] type complexes*

1.5 mmol PtCl<sub>4</sub> (0.5 g) was reduced with 1 ml formic acid and dissolved in 5 ml distilled water before its use in the complex synthesis:

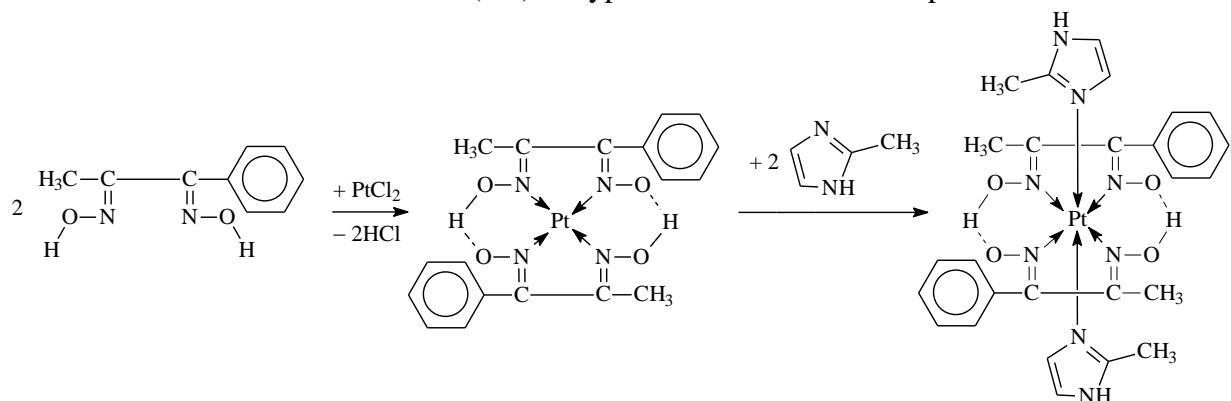


3 mmol ketone (2-heptanone, 2-octanone or 3-octanone) and 1.5 mmol diamine (hydrazine, phenylhydrazine or *o*-phenylene-diamine) were dissolved in 5 ml MeOH, and then refluxed for 1–2 hours. The resulting colored solution was added to the aqueous solution of the reduced platinum salt (PtCl<sub>2</sub>). At last 3 mmol amine (1-naphthylamine, 2-aminopyrimidine, 2-methylimidazole or 2-amino-4-methylpyridine) dissolved in 10 ml MeOH was added. The obtained mixture was refluxed in a water bath for 2–3 hours. After cooling the crystalline complexes were filtered off, washed with MeOH–water mixture (1:1), and finally dried on air. A typical reaction is the following:



- *Synthesis of [Pt(DioxH)<sub>2</sub>L<sub>2</sub>] type complexes*

2 mmol α-dioxime (Bu-Me-DioxH<sub>2</sub> or Me-Ph-DioxH<sub>2</sub>) was dissolved in 20 ml EtOH or MeOH, and then added to the aqueous solution of 1 mmol reduced platinum salt (PtCl<sub>2</sub>). Afterwards 2 mmol amine (1-naphthylamine, 2-methylimidazole, 2-amino-4-methylpyridine, lepidine, 2-methylpyridine, *m*-toluidine, dicyclohexylamine, 4-isopropylamine or cyclohexylamine) dissolved in 5 ml EtOH or MeOH was added. The obtained solution was heated for 2–3 hours on a water bath. After cooling the crystalline complexes were filtered, washed with MeOH–water mixture (1:1). A typical reaction as an example is shown below:



## Results and discussion

Microscopic characterization and yields of the prepared complexes are presented in Table 1.

Table 1. Microscopic characterization, calculated molar masses and yields of the prepared complexes.

Nr.	Compound	Calc. mol. mass	Yield (%)	Microscopic characterization
1.	[Pt(2-heptanone) <sub>2</sub> (hydrazone)(1-naphthylamine) <sub>2</sub> ]	703.83	12	Dark violet irregular microcrystals
2.	[Pt(2-octanone) <sub>2</sub> (hydrazone)(2-amino-pyrimidine) <sub>2</sub> ]	635.71	12	Brown, small triangle-based prisms
3.	[Pt(2-octanone) <sub>2</sub> (Ph-hydrazone)(2-am.-pyrimidine) <sub>2</sub> ]	712.82	50	Dark brown, small triangle-based prisms
4.	[Pt(2-octanone) <sub>2</sub> (o-phenylenediamine)(2-Me-imidazole) <sub>2</sub> ]	685.81	25	Reddish-brown triangle-based prisms (microcrystals)
5.	[Pt(3-octanone) <sub>2</sub> (hydrazone)]	445.50	34	Dark brown triangle-based prisms
6.	[Pt(3-octanone) <sub>2</sub> (Ph-hydrazone)]	522.61	16	Brown irregular microcrystals
7.	[Pt(3-octanone) <sub>2</sub> (hydrazone)(1-naphthylamine) <sub>2</sub> ]	731.88	40	Black triangle-based prisms
8.	[Pt(3-octanone) <sub>2</sub> (Ph-hydrazone)(1-naphthylamine) <sub>2</sub> ]	808.98	14	Black irregular microcrystals
9.	[Pt(3-octanone) <sub>2</sub> (Ph-hydrazone)(2-am.-4-Me-Py) <sub>2</sub> ]	738.89	10	Dark brown triangle-based prisms (microcrystals)
10.	[Pt(Ph-Me-DioxH) <sub>2</sub> (1-naphthylamine) <sub>2</sub> ]	835.82	68	Dark blue triangle-based prisms
11.	[Pt(Ph-Me-DioxH) <sub>2</sub> (2-Me-imidazol) <sub>2</sub> ]	713.65	41	Blue triangle-based prisms (microcrystals)
12.	[Pt(Ph-Me-DioxH) <sub>2</sub> (2-amino-4-Me-pyridine) <sub>2</sub> ]	765.73	50	Dark blue triangle-based prisms (microcrystals)
13.	[Pt(Ph-Me-DioxH) <sub>2</sub> (lepidine) <sub>2</sub> ]	835.82	15	Dark blue triangle-based prisms
14.	[Pt(Ph-Me-DioxH) <sub>2</sub> (2-Me-pyridine) <sub>2</sub> ]	735.70	15	Dark blue triangle-based prisms (microcrystals)
15.	[Pt(Ph-Me-DioxH) <sub>2</sub> (m-toluidine) <sub>2</sub> ]	763.75	41	Dark blue triangle-based prisms
16.	[Pt(Ph-Me-DioxH) <sub>2</sub> (dicyclohexil-amine) <sub>2</sub> ]	912.08	95	Dark blue triangle-based prisms
17.	[Pt(Bu-Me-DioxH) <sub>2</sub> (m-toluidine) <sub>2</sub> ]	723.77	24	Brown, small triangle-based prisms
18.	[Pt(Bu-Me-DioxH) <sub>2</sub> (dicyclohexyl-amine) <sub>2</sub> ]	872.10	31	Blue triangle-based prisms (microcrystals)
19.	[Pt(Bu-Me-DioxH) <sub>2</sub> (4-i-Pr-aniline) <sub>2</sub> ]	779.88	22	Dark violet triangle-based prisms
20.	[Pt(Bu-Me-DioxH) <sub>2</sub> (cyclohexyl-amine) <sub>2</sub> ]	707.81	24	Dark violet triangle-based prisms (longer needle crystals)

*Infrared spectroscopic study*

The mid-IR spectra were recorded with a Bruker Alpha FTIR spectrometer (Platinum single reflection diamond ATR), at room temperature, in the wavenumber range of 4000–400 cm<sup>-1</sup>, and the far-IR range of 500–50 cm<sup>-1</sup>, respectively, on a Bio Rad – FTS 60A, PIKE Gladi ATR spectrometer, with a resolution of 4 cm<sup>-1</sup>. The samples were measured in solid state (in powder

form). The data of the most characteristic IR bands for some selected complexes are presented in Table 2.

Table 2. IR data of selected complexes.

Comp. cm <sup>-1</sup>	2	3	5	6	7	8	10	16	17	19
VO-H	-	-	-	-	-	-	3647 w	3653 w	3224 m	3647 w
VN-H	3284 m	3281 w	3401 w	3223 w	3229 w	3112 m	3216 m	3163 w	3198 s	3200 m
VC-H	2925 s	2923 s	2918 w	2930 m	2945 w	2797 s	3056 m	3060 m	2956 m	2955 vs
VC=C	1618 vs	1615 vs	1690 w	1665 s	1606 m	1606 w	1594 m	1577 w	1614 w	1646 w
VC=N	1566 vs	1559 vs	1561 s	1598 s	1527 s	1528 s	1577 m	1532 s	1586 vs	1585 vs
δCH <sub>2</sub>	1490 m	1457 s	1450 w	1493 m	1459 w	1449 m	1423 m	1443 s	1465 s	1434 s
δCH <sub>3</sub>	1362 s	1357 m	1342 w	1377 w	1387 s	1398 vs	1339 m	1375 s	1377 m	1376 s
VN-N	1206 s	1203 s	1201 m	1244 m	1270 m	1288 m	-	-	-	-
VN-O	-	-	-	-	-	-	1279 m	1281 vs	1204 s	1264 s
VN-OH	-	-	-	-	-	-	1159 m	1145 s	1133 m	1192 vs
τO-H	-	-	-	-	-	-	1016 vs	967 vs	919 vs	1038 s
γC-H	785 s	757 vs	721 w	752 vs	764 vs	764 vs	697 vs	739 vs	684 vs	741 vs
ν <sub>Pt-N</sub>	493 vs	436 m	482 w	503 s	455 s	455 s	485 s	510 m	481 s	509 vs
δ <sub>N-Pt-N</sub>	336 s	328 m	378 m	324 vs	268 s	264 s	326 s	363 s	332 vs	336 vs

(Abbreviations: vs = very strong, s = strong, m = medium, w = weak)

The most important bands for the characterization of complexes are ν<sub>C=N</sub> (1527–1598 cm<sup>-1</sup>) and ν<sub>Pt-N</sub> (436–510 cm<sup>-1</sup>). In the far IR region δ<sub>N-Pt-N</sub> deformation vibrations appear (264–378 cm<sup>-1</sup>) [4]. In case of Schiff bases, if we compare the amine containing complexes, like **7** and **8**, with the amine missing compounds, like **5** and **6**, the ν<sub>C=N</sub> and ν<sub>Pt-N</sub> valence bands are shifted to lower wave-number values in case of the amine containing complexes, which can be explained with the *-I* effect of the amine nitrogen.

#### Mass spectrometry

Mass spectra of the samples were recorded on an Agilent 1200/6410B Triple Quad LC-MS/MS system using electrospray ionization (ESI). In the spectra we could detect the molecular ions and some fragments from decomposition.

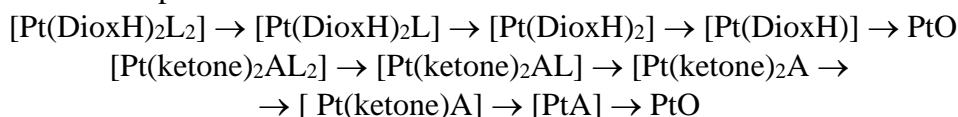
#### NMR spectroscopic study

The <sup>1</sup>H NMR spectra were recorded in DMSO-d<sub>6</sub> in 5 mm tubes at RT on a Bruker DRX 500 spectrometer at 500 MHz, using TMS as internal reference. In the spectra of Schiff bases the aliphatic protons appear at 0.8–2.5 ppm, the aromatic protons appear between 6.7–7.8 ppm and in nitrogen containing aromatic rings at 8–8.6 ppm. In the spectra of dioxime complexes the aliphatic protons appear at 0.9–2.8 ppm, the aromatic protons appear between 6.5–7.7 ppm, in nitrogen containing aromatic rings at 7.8–8.8 ppm and the OH protons appear between 11.3–11.5 ppm.

#### Thermoanalytical measurements (TG-DTG-DTA)

Thermal measurements were performed with a 951 TG and 910 DSC calorimeter (TA Instruments), in Ar or N<sub>2</sub> at a heating rate of 10 K·min<sup>-1</sup> (sample mass of 4–10 mg).

The thermal stability of complexes is limited within the temperature range of 100–140 °C. In the case of  $[Pt(ketone)_2A(L_2)]$  type complexes the first step of the decomposition mechanism is the loss of the amino (L) groups between 100–300 °C, then the *ketone* units leave between 300–415 °C. Finally the diamine (A) unit is lost between 415–530 °C. In the case of  $[Pt(DioxH)_2L_2]$  type complexes the first decomposition step belongs to leaving amino (L) groups, until 270 °C, then the glyoxime units leave. The end of the process is between 420–580 °C. Subsequently, the decomposition of the glyoxime unit is accompanied by big exothermic peaks. This behavior can be explained with the presence of oxygen in the molecule. The general mechanism for decomposition is as follows:



#### UV-VIS spectroscopy

The electronic spectra were recorded with a Jasco V-670 Spectrophotometer in 10% EtOH/water solutions containing the substance in  $10^{-4}$  mol/dm<sup>3</sup> concentration. Using Sørensen buffer solutions the electronic spectra were also recorded as a function of pH, and then the acidity constants were calculated, too. The obtained values were between  $2.2 \cdot 10^{-12}$  –  $3.8 \cdot 10^{-10}$ .

#### Powder X-ray diffraction measurements

The crystal structure of the complexes was studied with powder XRD measurements, carried out on a PANalytical X'pert Pro MPD X-ray diffractometer. As being novel compounds their diffractograms can not be found in the Cambridge database. The dioxime type complexes exhibit crystalline form, the Schiff bases are amorphous, except for  $[Pt(3\text{-octanone})_2(\text{hydrazone})(1\text{-naphthylamine})_2]$  which is crystalline.

#### SEM (scanning electron microscopy) and EDX (energy dispersive X-ray spectroscopy analysis)

The images were taken with a JEOL JSM-5500LV scanning electron microscope. For the study the beam energy was 20 kV in order to obtain the excitation of all the elements and secondary electron detector (SED) were employed for measurement. The morphological study of the sample surface at five significant magnifications 10000x, 5000x, 1000x and 100x were recorded. In case of compound **3** the amorphous form can be observed.

#### Biological study

The antimicrobial effects of complexes were studied on *Staphylococcus aureus* Gram-positive bacterium. The investigations were carried out by Kirby-Bauer disk diffusion method. The complexes were dissolved in DMSO in 10 mmol/l concentration, and 30 µl was applied on sterile paper discs. The diameter of inhibition zones were: **3** – 16.33 mm, **10** – 13.66 mm, **16** – 14.83 mm.

### **Conclusion**

In this work new platinum(II) complexes were synthesized and characterized with physico-chemical and biological methods. Thermal decomposition mechanism was monitored with thermoanalytical measurements.

### **Acknowledgement**

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### **References**

- [1] A. Jain, Coordination Chemistry Reviews 401 (2019) 213067.
- [2] F.N. Sayed, G.G. Mohamed, R.G. Deghadi, Journal of Molecular Structure 1278 (2023) 134904

- [3] T. Liu, Y.N. Chen, D.X. Tan, F.S. Han, *Journal of Organometallic Chemistry* 977 (2022) 122453.
- [4] K. Nakamoto, *Infrared and Raman Spectra of Inorganic and Coordination Compounds. Part B: Applications in Coordination, Organometallic and Bioinorganic Chemistry*, Wiley J., 38, NY 1997.