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SYNTHESIS, CHARACTERIZATION OF Pt(II) COMPLEX OF CAMPHOR 4-PHENYL THIOSEMICARBAZONE

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Abstract

The complex of Pt(II) with camphor 4-phenyl thiosemicarbazone was synthesized and characterized by means of MS, IR, ^{1}H-NMR and UV-VIS spectroscopies. Results showed that, the molecular formula of complex of Pt(II) with camphor 4-phenyl thiosemicarbazone is $[Pt(C_{17}H_{22}N_3S)_2]$. The Pt(II) complex is four coordinate and square planar geometry.

Keywords. camphor 4-phenyl thiosemicarbazone, complex of Pt(II).

1. INTRODUCTION

Platinum-based anticancer drugs are the mainstay of chemotherapy regimens in clinic. Nevertheless, the efficacy of platinum drugs is badly affected by systemic toxicities and drug resistance, and the pharmacokinetics of most platinum drugs is largely unknown [1, 2, 3]. In recent years, platinum complexes with bioactive molecules, natural compounds, targeting groups or nonmaterial's has been interested by chemical and biomedical researchers [4, 5, 6]. The motivation comes from some of the following demands: improve the selectivity or minimize the systemic toxicity of the drugs, enhance the cellular accumulation of the drugs, overcome the tumor resistance to the drugs, visualize the drug molecules in vitro or in vivo, achieve a synergistic anticancer effect between different therapeutic modalities, or to add extra functionality to the drugs [5, 6]. The development of drug delivery systems in the last several decades has provided a variety of methods including the synthesis new Pt(II), Pt(IV) complexes, the incorporation of drugs into liposome's, lipid emulsions, and polymeric micelles to reduce side effects, to increase their solubility, and to prolong circulation time as well [6]. Camphor has bioactivity, it has been used in traditional medicine from time immemorial. The coordination of camphor and platinum could create new compounds with high bioactivity. In this paper, we present the new results of Pt(II) complex with camphor 4-phenyl thiosemicarbazone.

2. CHEMICALS AND METHOD

2.1. Chemicals

Camphor, 4-phenyl thiosemicarbazide, acetic acid and ethanol were purchased from Merck. $K_2[PtCl_4]$ was purchased from Sigma - Aldrich.

2.2. Method

2.2.1. Synthesis of camphor 4-phenyl thiosemicarbazone (H4thiocam)

The H4thiocam was prepared from 4-phenyl thiosemicarbazide and camphor (1 : 1 molar ratio). The H4thiocam was prepared from 4-phenyl thiosemicarbazide and camphor (1 : 1 molar ratio). The mixture of reactants was dissolved in warm ethanol and anhydrous acetic acid was added until pH reached 3-4. This mixture was stirred and refluxed at 70 °C for 6 h. After cooling to room temperature, crystalline product was isolated and washed with water, ethanol-water, and dried over P_2O_5. H4thiocam was obtained as a white powder.

2.2.2. Synthesis of Pt(II) Complex (Pt-4thiocam)

To synthesize Pt-4thiocam, a solution of $K_2[PtCl_4]$ (0.415 g, 0.001 mole) in 50 mL water was added to a solution of camphor 4-phenyl thiosemicarbazone (0.602 g, 0.002 mole) in 100 mL ethanol at 30 °C under stirring for 1 h.The reaction mixture was kept at ~10 °C for 24 h. Afterwards, the precipitate was filtered and washed several times with water, ethanol, and dried over P_2O_5. The Pt-4thiocam was obtained as a dark yellow powder.

2.2.3. Structure determination

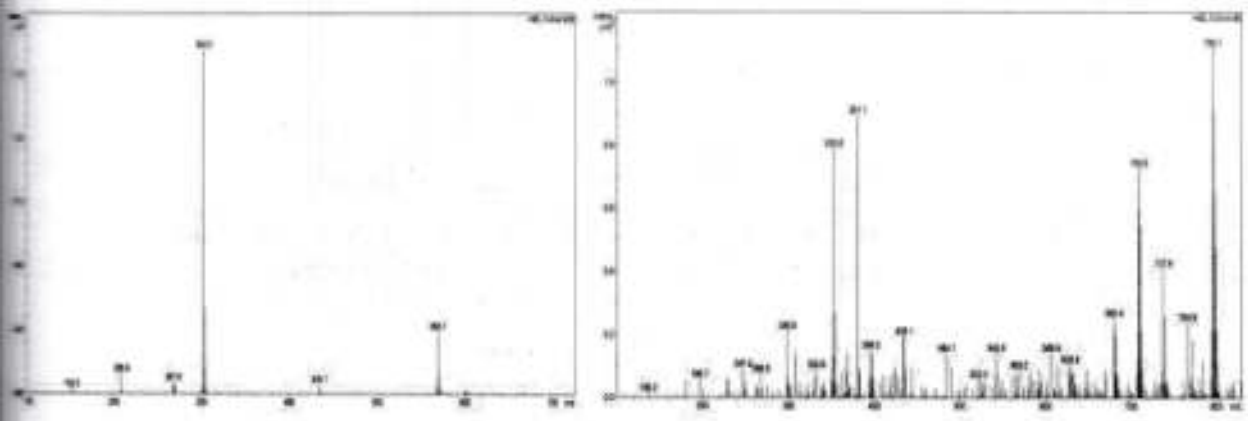
Mass spectroscopy with electro spray ionization technique (ESI-MS) was used in order to confirm the formula of H4thiocam and Pt-4thiocam (Agilent 1100 LC/MSD Trap). IR spectra were recorded with a FTIR Shimadzu spectrophotometer using KBr discs in the frequency range of 4000-400 cm^{-1}. ^{1}H-NMR spectra were obtained with a Bruker 500 MHz spectrometer and the chemical shifts tare given in units of δ relative to TMS as an internal standard using DMSO-d6 as the solvent.

3. RESULTS AND DISCUSSION

ESI/MS data in Table 1. As seen in the MS spectra (Figure 1(a,b)), the appearance of a cluster of peaks with m/z = 302, 303, 304 of H4thiocam (Fig. 1(a)) and a cluster of peaks with m/z =795, 796, 797 of Pt-4thiocam (Fig. 1(b)) were consistent with the molecular formula of ligand $C_{17}H_{23}N_3S$ and the complex $Pt(C_{17}H_{22}N_3S)_2$ calculated from different isotopes.

Table 1. MS data and compound's molecular formula

Sample	m/z,$[M]^+$/ $[M+H]^+$	M	Molecular formula
H4thiocam	302	301	$C_{17}H_{23}N_3S$
Pt-4thiocam	795	795	$Pt(C_{17}H_{22}N_3S)_2$



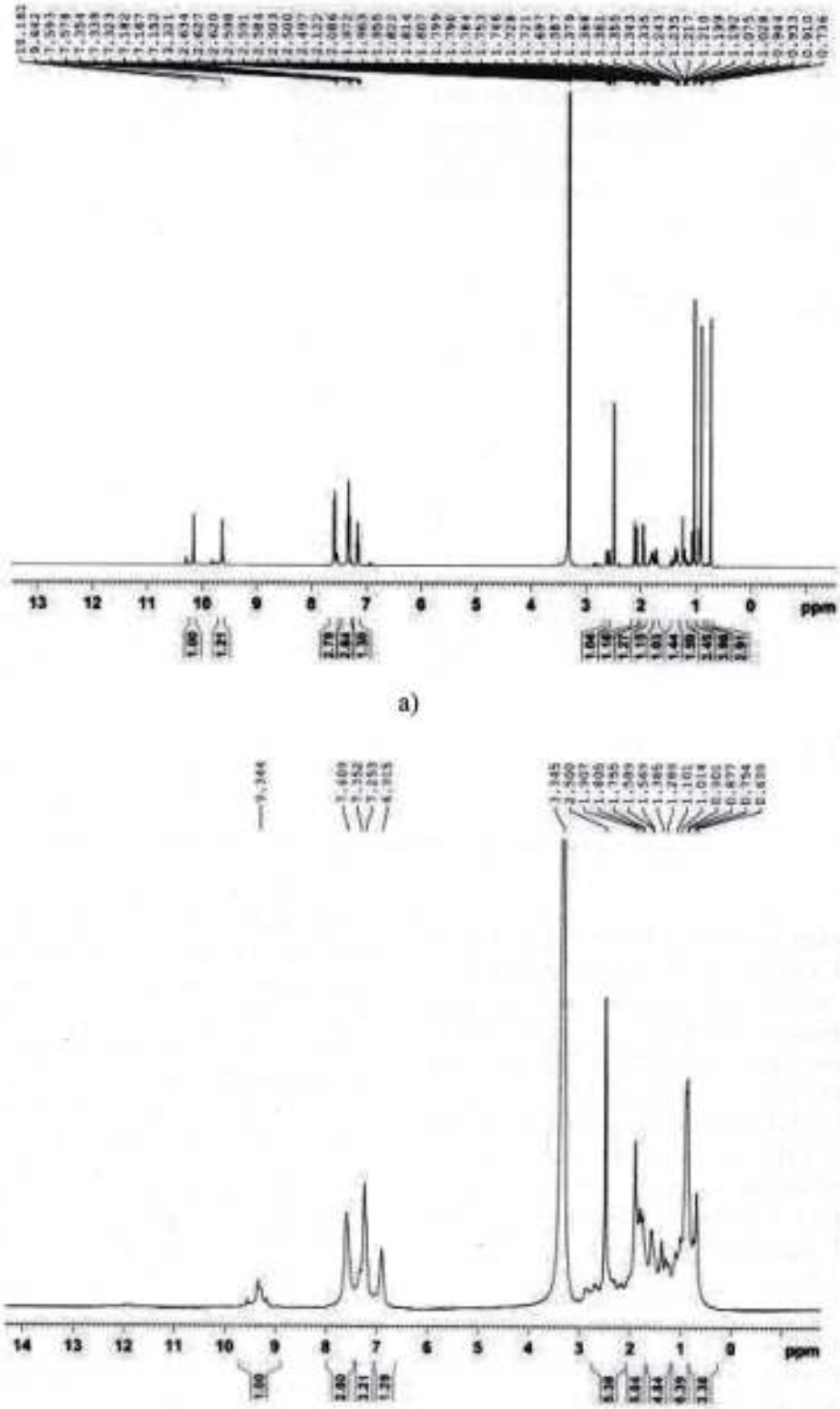
a) b)

Figure 1. Mass spectra of H4thiocam (a) and Pt-4thiocam (b)

The ^{1}H-NMR spectrum of H4thiocam (Figure 2(a)) exhibited a singlet at 10.16 ppm attributed to NH-hydrazine proton. The presence of NH signal indicated the presence of H4thiocam in the thione form. The proton signal on the NH-amide appeared at 9.64 ppm. The signals in range 7.15 to 7.59 ppm were assigned to 5H of benzyl ring. Triplet signals at 0.73 ppm to 1.03 ppm were assigned to 9H of CH_3 groups and signals in range 1.19 to 2.63 ppm were assigned to protons of CH and CH_2. The absence of H signal of NH-hydrazine (NHC=S group) from Pt-4thiocam complex's spectrum (Figure 2(b)) confirmed the deprotonation of the ligand due to coordination with Pt(II) via S and N. The signals of other protons appeared in similar range in ligand's spectrum The NMR results were consistent with IR results.

The IR spectrum of H4thiocam (Fig. 3a) showed absorption bands at 3360 and 3278 cm^{-1} due to stretching frequencies for NH-amide and NH-hydrazine. The band due to the –SH group was not observed in 2500-2600 cm^{-1} and the presence of band at 760 cm^{-1} due to ν(C=S) suggested the existence of thiosemicarbazone in the thione form. The absorptions band for – CN appeared at 1593 cm^{-1}. The IR spectrum of Pt-4 thiocam (Fig. 3b) showed absorption band at 3383 cm^{-1} due to stretching frequencies for NH-amide, while the absorption for NH at region 3000–3200 cm^{-1} was absent. The ν(C=S) band at 760 cm^{-1} in the spectrum of the ligand shifted to 751 cm^{-1} in the spectrum of the complex, indicated that the existence of ligand is in the thiol form and deprotonation on complexation and that Pt(II) coordinated with the thiolate sulfur. The ν(C=N) band of the thiosemicarbazone at 1593 cm^{-1} shifted to 1549 cm^{-1} in the spectrum of the complex, indicated the coordination of the azomethine nitrogen. This result was confirmed by the presence

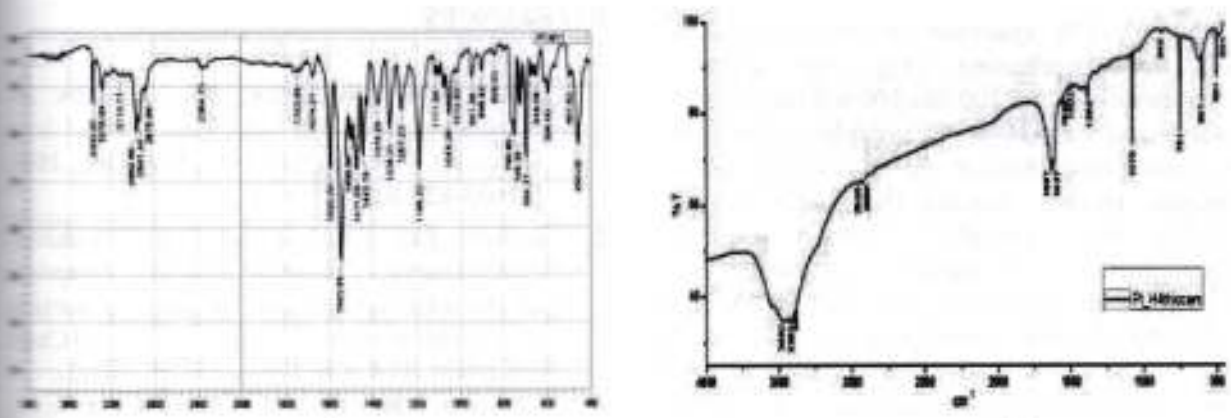
of new bands at 601 and 501 cm^{-1} due to $\nu_{(Pt-N)}$ and $\nu_{(Pt-S)}$. These spectra suggested that after deprotonation the ligand coordinated with the Pt(II) via S and N. Selected IR bands for the ligand (H4thiocam) and complex (Pt-4thiocam) are given in Table 2.



a)

b)

Figure 2. ^{1}H-NMR spectra of H4thiocam (a) and Pt-4thiocam (b)



a) *b)*

Figure 3. IR spectra of H4thiocam (a) and Pt-4thiocam (b)

Table 2. Selected IR bands of the H4thiocam and Pt-4thiocam

ν, cm^{-1} / Compounds	ν_{NH}	$\nu_{CN} + \nu_{Ar}$	ν_{NN}	ν_{CS}	ν_{Pt-X} (X= S, N)
H4thiocam	3360, 3278	1593, 1543	1049	760	-
Pt-4thiocam	3383	1549, 1503	1078	751	601, 501

Based on the above analysis, reasonable structures of H4thiocam ligand and Pt-4thiocam complex are depicted in Fig. 4.

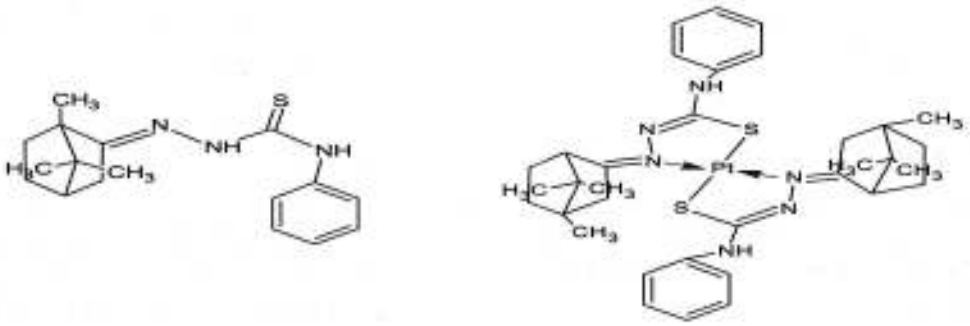
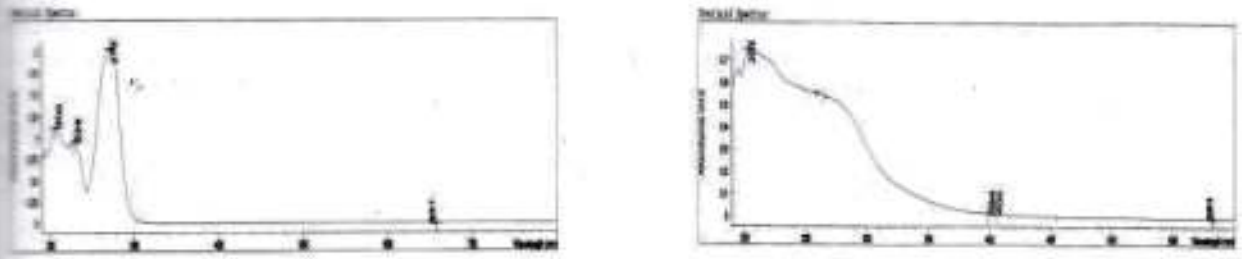


Figure 4. Structures of the H4thiocam and Pt-4thiocam



a) *b)*

Figure 5. UV-VIS spectra of H4thiocam (a) and Pt-4thiocam (b)

The UV-VIS spectrum of the camphor 4-phenyl thiosemcarbazone (Fig. 5a) appeared absorbance only in the 200 nm-300 nm range of the internal ligand transfer, on the complex's spectrum, these absorbencies have a red shift to the longer wavelength region, showing the change of the ligand from free to complex. The spectrum of the Pt(II) complex (Fig. 5b), appeared two absorbencies of the internal ligand transfer and charge transfer at 200 nm - 400 nm. The absorbance with wide, weak intensity in the 400-450nm range is characteristic of the d-d transfer band, corresponding to the square planar geometry. The UV-VIS spectrum of Pt(II) complex with 4-phenyl thiosemicarbazone camphor is consistent with the results of UV-VIS spectra of Pt(II) complexes which were studied by some authors [3, 4].

4. CONCLUSION

In conclusion, the complex of camphor 4-phenyl thiosemicarbazone with Pt(II) was successfully synthesized from $K_2[PtCl_4]$ and camphor 4-phenyl thiosemicarbazone in ethanol-water solvent. The analysis data from MS, IR, ^{1}H-NMR and UV-VIS spectra showed that the molecular formula of complex of Pt(II) with camphor 4-phenyl thiosemicarbazone is $[Pt(C_{17}H_{22}N_3S)_2]$. The Pt(II) complex is four coordinate and square planar geometry.

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REFERENCES

1. Boulikas T., Vougiouka M. *Cisplatin and platinum drugs at the molecular level* (Review). Oncology reports, Nov-Dec; **10(6)**, p.1663-82 (2003).
2. Indrani Pal, Falguni Basuli and Samaresh Bhattacharya, *Thiosemicarbazone complexes of the platinum metals. A story of variable coordination modes,* Indian Acad. Sci. (Chem. Sci.), Vol. **114**, No. 4, pp 255-268 (2002).
3. Aysegül Karaküçük Iyidogan et al, *Novel platinum(II) and palladium(II) complexes of thiosemicarbazones derived from 5-substitutedthiophene-2-carboxaldehydes and their antiviral and cytotoxic activities*, European Journal of Medicinal Chemistry **46**, pp. 5616-5624 (2011).
4. S. Utku, M. Topal, A. Dogen, and M. S. Serin, Synthesis, *characterization, antibacterial and antifungal evaluation of some new platinum(II) complexes of 2-phenylbenzimidazole ligands*, Turkish Journal of Chemistry, Vol. **34**, no. 3, pp. 427-436 (2010).
5. Justin J. Wilson and Stephen J. Lippard, *Synthetic Methods for the Preparation of Platinum Anticancer Complexes*, Chem Rev. 2014 Apr 23; **114(8)**, 4470-4495. Published online 2013 Nov 27. doi: 10.1021/cr400314 (2014).
6. Timothy C. Johnstone, Kogularamanan Suntharalingam, and Stephen J. Lippard, *TheNext Generation of Platinum Drugs: Targeted Pt(II) Agents, Nanoparticle Delivery and Pt(IV) Prodrugs* (Review), Chem. Rev., **116 (5)**, pp 3436–3486 (2016).