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THE SYNTHESIS, STRUCTURE OF TWO PLATINUM(II) COMPLEXES BEARING ARYLOLEFIN AND QUINOLIN-8-OL DERIVATIVE

Nguyen Manh Thang, Nguyen Thi Song Huong
and Nguyen Thi Thanh Chi*
Faculty of Chemistry, Hanoi National University of Education, Hanoi city, Vietnam
*Corresponding author: Nguyen Thi Thanh Chi e-mail: chintt@hnue.edu.vn

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Abstract. The reaction of complex $K[PtCl_3(Eug)]$ with HOQCHO or complex $[PtCl(Preug\text{-}1H)]_2$ with HOQ afforded two novel complexes [PtCl(Eug)(OQCHO)] (**C1**) and [Pt(Preug-1H)(OQ)] (**C2**), both obtained in high yields. Their structures were determined using elemental analysis, IR spectroscopy, and ^{1}H NMR spectroscopy. The results confirmed that in both complexes, the amine ligand is deprotonated at the OH group and chelates the Pt(II) center through the N and O atoms. In **C1**, Eug coordinates to Pt(II) *via* the allylic C=C bond, while in **C2**, Preug-1H coordinates to Pt(II) not only through the allylic C=C bond but also via the C5 atom of the benzene ring. Additionally, **C1** exists in two conformational forms in solution due to rotation of the CHO group around the C-C bond, leading to two distinct sets of signals in its ^{1}H NMR spectrum.

***Keywords*:** eugenol, propyl eugenoxy acetate, Pt(II) complexes, ^{1}H NMR.

1. Introduction

Since the worldwide approval of cisplatin in 1979 for the treatment of various human cancers such as testicular, ovarian, and bladder cancer, significant efforts have been devoted to the synthesis of new platinum(II) complexes for cancer chemotherapy. Building on these efforts, two additional platinum-based drugs, carboplatin and oxaliplatin, were subsequently approved by the FDA in 1989 and 2002, respectively. Despite their effectiveness, all three drugs are associated with several undesirable side effects, including nephrotoxicity, ototoxicity, nausea, and vomiting [1]-[4].

To overcome these limitations, researchers have synthesized numerous novel platinum complexes incorporating nature-derived ligands, which have demonstrated promising potential for medical applications. Among these, certain Pt(II) complexes containing 8-hydroxyquinoline (HOQ) and its derivatives have exhibited notable anticancer activities [5]-[8]. However, a significant gap remains in the exploration of Pt(II) complexes that incorporate both arylolefin and HOQ derivatives. For instance,

complexes containing both arylolefin and 2-formyl-8-hydroxyquinoline (HOQCHO) have not been investigated yet.

In this work, we report the synthesis and structural determination of two novel complexes: [PtCl(Eug)(OQCHO)] (Eug: eugenol) and [Pt(Preug-1H)(OQ)] (Preug: propyl eugenoxy acetate). These complexes provide a foundation for further research toward potential medical applications.

2. Content

2.1. Experiments

2.1.1. Synthesis

Starting materials: Complexes $K[PtCl_3(arylolefin)]$ (arylolefin: eugenol, Eug; propyl eugenoxy acetate, Preug) were synthesized from Zeise's salt ($K[PtCl_3(C_2H_4).H_2O]$ and Eug, Preug, respectively according to the previous procedure [9], [10]. The complex $[PtCl(Preug\text{-}1H)]_2$ was synthesized by stirring $K[PtCl_3(Preug)]$ in the mixture of water-acetone [10]. HOQCHO was prepared by oxidation of Me-HOQ with SeO_2 in dioxane/water under reflux conditions [11].

Complexe [PtCl(Eug)(OQCHO)] (C1): **C1** was synthesized by slowly adding a solution of OHCHOQ (34.6 mg, 0.2 mmol) in 3 mL ethanol to a solution of $K[PtCl_3(Eug)]$ (101 mg, 0.2 mmol) in 5 mL ethanol at room temperature, followed by stirring for 3 hours. Subsequently, 5 mL distilled water was added to the reaction mixture, and stirring was continued for an additional hour. The resulting brown precipitate was filtered, washed sequentially with dilute HCl and distilled water, then dried under vacuum. The product was recrystallized in acetone to give a black-brown powder (**C1**) in 80% yield.

Complexe [Pt(Preug-1H)(OQ)] (C2): **C2** was synthesized by slowly adding a solution of HOQ (58 mg, 0.4 mmol) in 2 mL acetone to a mixture of $[PtCl(Preug\text{-}1H)]_2$ (198 mg, 0.2 mmol) and 5 mL of acetone : water (2:3, *v/v*). The reaction mixture was stirred at room temperature, during which the starting complex gradually dissolved, yielding a bright yellow solution after 20 minutes. The solution was stirred further for 2 hours, and the resulting precipitate was filtered, washed sequentially with dilute HCl and distilled water, and then dried under vacuum. The product was recrystallized in acetone : ethanol (3:2, *v/v*) to yield a bright yellow powder (**C2**) in 91% yield.

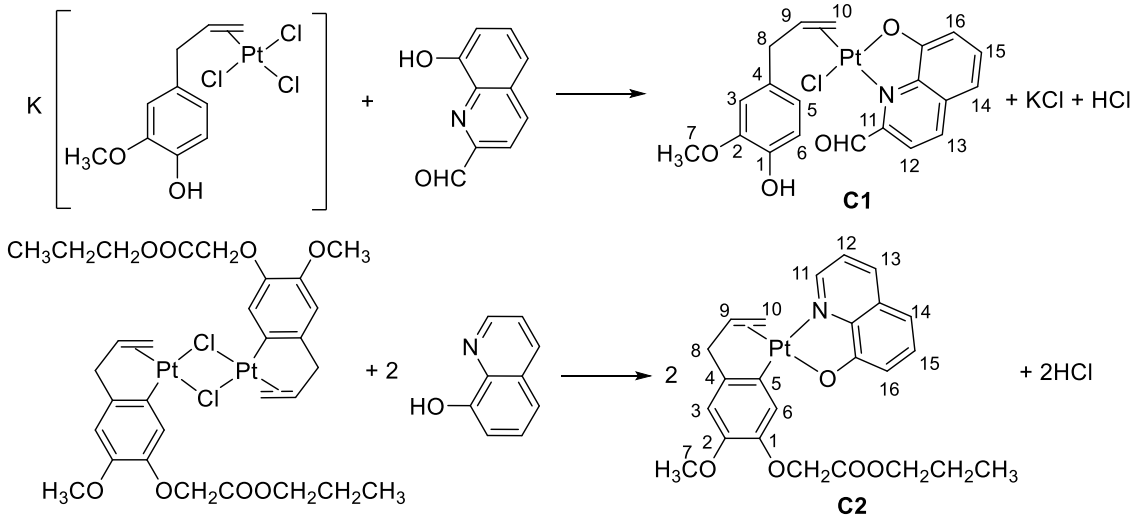
2.1.2. Apparatus and methods

The platinum percentage in complexes **C1** and **C2** was analyzed by the weight method, according to the procedure described in reference [12]. The IR spectra were recorded from KBr discs on an IMPACK-410 Nicolet spectrometer in the range 400 - 4000 cm^{-1}. The ^1H NMR spectra were recorded on a Bruker AVANCE 500 MHz at 298 - 300 K in CD_3COCD_3, and the chemical shifts (δ) were internally referenced using the residual proton-solvent signals relative to tetramethylsilane.

2.2. Results and discussion

2.2.1. Synthesis of the examined complexes

Complex **C1** was synthesized by the interaction of K[$PtCl_3$(Eug)] with HOQCHO in 80% yield. In this reaction, deprotonated HOQCHO (OQCHO) replaced two chloride ligands in the anionic complex K[$PtCl_3$(Eug)], resulting in the formation of the neutral complex **C1**. In **C1**, OQCHO coordinates with Pt(II) through its nitrogen and oxygen atoms. Similarly, the reaction of [PtCl(Preug-1H)]$_2$ with HOQ produced in 91% yield. In this case, the two labile chloride ligands in the diplatinum complex were readily replaced by deprotonated HOQ (OQ), forming the mononuclear platinum chelating complex **C2**. The reaction equations for the synthesis of **C1** and **C2** are shown in Scheme 1, and some of their physical properties are summarized in Table 1.



Scheme 1. Reaction equations for the synthesis of complexes C1 and C2

Table 1. Some physical properties and %Pt of complexes C1 and C2

Comp.	Color	%Pt (Found/Calcd.)	Solubility in some solvent			
			Water	*Ethanol*	*Acetone*	*Chloroform*
[PtCl(Eug)(OQCHO) **C1**	Brown	$\frac{34.72}{34.42}$	Insoluble	Slightly soluble	Soluble	Slightly soluble
[PtCl(Preug-1H)(OQ) **C2**	Bright yellow	$\frac{32.45}{32.39}$	Insoluble	Insoluble	Soluble	Soluble

2.2.2. Structural determination of the examined complexes

Structures of complexes **C1** and **C2** were determined using the weigh method, IR, and ^{1}H NMR spectroscopies. The experimentally determined percentages of Pt in **C1** and **C2** are in good agreement with the values calculated based on the proposed formulas (Table 1).

Table 2. Key bands in the IR spectra of C1 and C2 (cm^{-1})

Comp.	ν_{OH}	$\nu_{CH\ aromatic,\ alkene}$	$\nu_{CH\ aliphatic}$	$\nu_{C=O}$	$\nu_{C=C,\ C=N}$	$\nu_{Pt-X\ (X:\ C,\ N,\ O,\ (C=C))}$
C1	3433	3020	2924 2850	1632	1605 1512	517 467
C2	-	3019 3028	2930 2860	1744	1573 1525	525 465

Characteristic bands for functional groups in complexes **C1** and **C2** are clearly observed in their IR spectra and listed in Table 2. For instance, the presence of Preug-1H in **C2** is confirmed by a strong band at 1744 cm^{-1} for $\nu_{C=O}$ in the -$COOC_3H_7$ group. The absence of a band for ν_{OH} indicates that the OH group of HOQ in **C2** is deprotonated. Additionally, the band for $\nu_{C=C}$ at non-coordinated Eug/Preug appears around 1627 cm^{-1} [6], [7], [13], whereas in **C1** and **C2** it shifts to 1605 ÷ 1512 cm^{-1}. This shift indicates that Eug in **C1** and Preug-1H in **C2** have already coordinated with the Pt(II) *via* the allylic C=C bond. The presence of some bands at 517-465 cm^{-1} in **C1** and **C2** aligns with the coordination of OQCHO/OQ with Pt(II) through the N and O atoms.

Signals in the ^{1}H NMR of **C1** and **C2** were assigned based on their chemical shift (δ), intensity, shape, and value of spin-spin splitting (J) and shown in Table 3.

Table 3. Proton signals in the ^{1}H NMR spectra of C1 and C2 measured in $(CD_3)_2CO$ (δ)

Comp.		H3	H5	H6	H7	H8a	H8b	H9	$H10_{trans}$	$H10_{cis}$	Others
C1	Set 1/ Set 2	6.68 s/ 6.71 ov	6.78 d ^{3}J 8	6.72 d ^{3}J 8	3.86 s	2.88 ov	3.43 dd ^{2}J 15 ^{3}J 7	5.05 m $^2J_{PtH}$ 70	4.08 d ^{3}J 7.5 $^2J_{PtH}$ 60	4.26 d ^{3}J 13 $^2J_{PtH}$ 60	OH: 7.36 s
C2		6.61 s	-	6.97 s $^3J_{PtH}$40	4.54 s	2.70 ov	3.51 dd ^{2}J 15 ^{3}J 7	4.76 m $^2J_{PtH}$ 73	4.13 d $^2J_{PtH}$ 72 ^3J 8	3.55 d ^3J 14	OCH_2: 3.63 s $COOCH_2$: 4.04 m CH_2CH_3: 1.60 m CH_3: 0.83 t ^3J 8
		H11	**H12**	**H13**	**H14**	**H15**	**H16**	**OH**	**CHO**		
HOQCHO		-	8.32	8.05	7.43	7.62	7.28	8.15	10.22		
C1	Set 1	-	9.38 d ^{3}J 8.5	8.38 d ^{3}J 8.5	7.70 d ^{3}J 8	7.91 t ^{3}J 8	7.97 d ^{3}J 8	-	11.2 br		
	Set 2	-	8.91 d ^{3}J 8.5	8.26 d ^{3}J 8.5	7.45 d ^{3}J 8	7.80 t ^{3}J 8	7.73 d ^{3}J 8	-	10.35 s		
HOQ[11]		8.78	7.43	8.15	7.33	7.45	7.19	8.3	-		
C2		8.36 d ^{3}J 5.5	7.53 dd ^{3}J 8.0 ^{3}J 5.5	8.43 d ^{3}J 8.0	7.05 d ^{3}J 8.0	7.44 t ^{3}J 8.0	6.98 d ^{3}J 8.0	-	-		

The ^{1}H NMR spectra of **C1** and **C2** display signals corresponding to all protons present in their structures. However, the spectrum of **C1** reveals two sets of signals with an intensity ratio of 1.5:1 with a similar pattern. The most significant differentiation between

these two sets is observed in the signals of the OQCHO moiety, particularly H12 and the aldehyde proton (Fig. 1). Notably, all signals for the Eug moiety except for H3 are identical in both sets (Table 3). The chemical shifts and shapes of these signals strongly indicate the coordination of Eug with Pt(II) through C9=C10, consistent with our previous studies [7]. Specifically, the signals of H9, H10*trans*, and H10*cis* shift upfield compared to those in free Eug, accompanied by large $^{2}J_{PtH}$ values (60-70 Hz) [7].

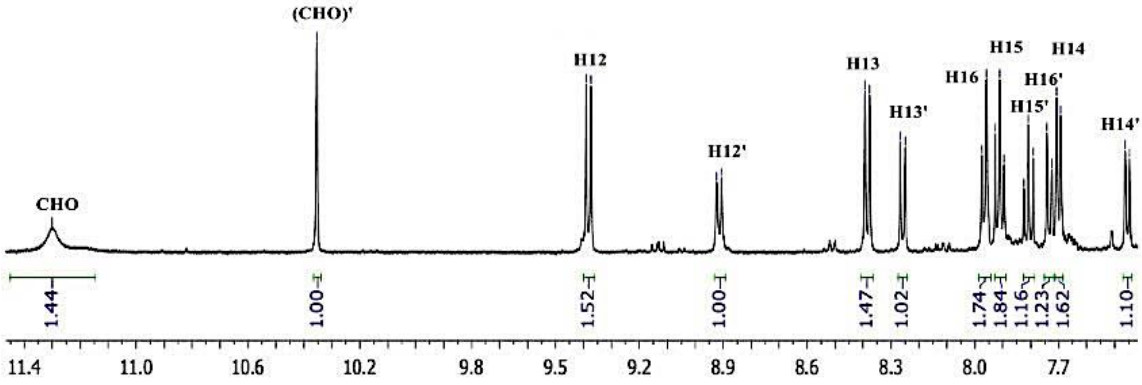


Figure 1. A partial ^{1}H NMR spectrum of complex C1

Similarly, the coordination of Preug with Pt(II) in complex **C2** *via* C9=C10 is evident in the signals of the olefinic protons (Table 3). However, in the spectrum of **C2,** the doublet of H5 is absent, and a singlet at 6.97 ppm appears with two satellites due to spin-spin splitting of ^{195}Pt ($^{2}J_{PtH}$ = 40Hz). This indicates that deprotonated Preug (Preug-1H) coordinates with Pt(II) through both C9=C10 and C5.

In both **C1** and **C2**, no signals for the OH group in the amines are detected. Additionally, all signals exhibit chemical shift change compared to those in HOQCHO/HOQ, confirming the deprotonation of HOQCHO/HOQ at the OH group. Consequently, OQCHO and OQ coordinate with Pt(II) through both the N and O atoms.

The presence of two sets of signals in the spectrum of **C1** can be attributed by the rotation of the CHO group around the C-C bond, leading to spatial difference between the H and O atoms, resulting in two distinct structures (**A** and **B**, Fig. 2). This structural variation explains the significant difference in chemical shifts of H12 and $H_{aldehyde}$ in the two sets. In structure B, the $H_{aldehyde}$ is positioned closer to the Cl ligand, forming a halogen bonding. As a result, the $H_{aldehyde}$ signal is broadened and shifts downfield (δ = 11.2 ppm).

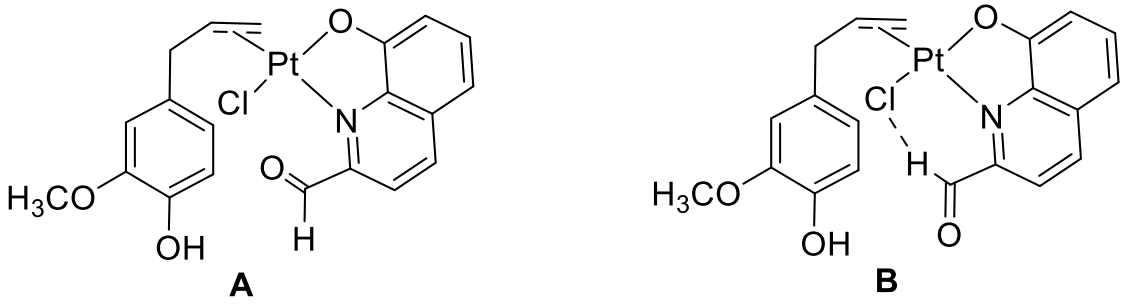


Figure 2. Two conformations of C1 in solution

3. Conclusions

In this study, two new complexes [PtCl(Eug)(OQCHO)] (**C1**) and [Pt(Preug-1H)(OQ)] (**C2**) were successfully synthesized by the reaction of complex $K[PtCl_3(Eug)]$ with HOQCHO or complex $[PtCl(Preug\text{-}1H)]_2$ with HOQ in 80 and 91% yield, respectively. Their structures were characterized by analysis of the Pt percentage, IR, and ^1H NMR spectra. The results confirmed that deprotonated amines (OQCHO/OQ) in **C1** and **C2** coordinate with Pt(II) through the N and O atoms. In both complexes, Eug and Preug-1H coordinate with Pt(II) *via* the $C{=}C_{allyl}$ group. However, in **C2**, Preug-1H also bonds to Pt(II) *via* the C5 atom of the benzene ring, forming a chelating structure. Additionally, in solution, the CHO group in **C1** rotates around the C-C bond, resulting in two distinct sets of signals in its ^1H NMR spectrum. One set corresponds to a structure where the aldehyde proton forms a halogen bond with the Cl ligand, while the other set arises from a conformation where the O atom of the CHO group is close to the Cl ligand.

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