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Novel products of reaction between K[$PtCl_3$(eugenol)] and some pyridine's derivatives

Truong Thi Cam Mai[1], Le Thi Dinh[2], Le Viet Huy[2], Nguyen Thi Thanh Chi[2*]

[1]*Department of Chemistry, Quy Nhon University*

[2]*Department of Chemistry, Hanoi National University of Education*

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Abstract

The interaction between K[$PtCl_3$(Eug)] (M0) and either 4-carboxylpyridine (4-Cpy) or 4-methylpyridine (4-MePy) has been studied for the first time. The structures of unusual resulting complexes, namely [PtCl(Eug-1H)(4-CPy)] (M1), *trans*-[$PtCl_2$(4-MePy)$_2$] (M2), *trans*-[$PtCl_2$(Eug)(4-MePy)] (M3) were determined by means of platinum analysis, IR, ^{1}H NMR spectroscopy and single-crystal X-ray diffraction. In these complexes, the amines coordinate with Pt(II) via the N atom and eugenol (Eug) in M1, M3 coordinates with Pt(II) via ethylenic double bond of the allyl group. In M1, the deprotonated eugenol is bound up with Pt(II) not only at the C=C_{allyl} but also at C atom of the benzene ring to generate the metallacyclic complex. M2 and M3 possess *trans* configuration.

Keywords. Eugenol, platinum(II) complex, 4-carboxylpyridine, 4-methylpyridine.

1. INTRODUCTION

Since *cis*-[$PtCl_2(NH_3)_2$] (Cisplatin) was used in treatment of many cancers such as small cell lung, ovarian, cervical, testicular cancer, etc., thousands of other platinum complexes have been synthesized and evaluated for their anticancer activity [1-2].

The research direction of Pt(II) complexes containing ligand with natural origin has been attracted much attention from researchers all over the world [3-6]. Numerous complexes of Pt(II) bearing eugenol derivatives (eugenol: 4-allyl-2-methoxyphenol, the main component in clove oil, hereafter labeled as Eug) exhibit potential toxicity activities against human cancer cell lines [5-6]. However the complexes of Pt(II) bearing Eug have been approached in 2017 [7] and to the best of our knowledge there has been no publication about Pt(II) complexes containing both Eug and pyridine's derivatives so far.

In this study, we present the results of study on interaction between K[$PtCl_3$(Eug)] and either 4-carboxylpyridine or 4-methylpyridine.

2. EXPERIMENTAL

2.1. Synthesis of complexes

2.1.1. Synthesis of starting complex

K[$PtCl_3$(Eug)] (M0) was synthesized according to the method described in [7].

2.1.2. Interaction of M0 with 4-carboxylpyridine

The reaction of M0 with 4-carboxylpyridine (4-CPy) was performed in different conditions of solvent and molar ratio. Based on the product's characteristics and IR spectra it can be concluded that the products of the experiments are the same and labeled as M1. The highest-efficiency syntheses of M1 was carried out as follows:

4-CPy (24.6 mg, 0.2 mmol) was dropped fast into the mixture of M0 (100 mg, 0.2 mmol) and acetone (10 mL). The reaction mixture was stirred at room temperature (25÷30 ^{o}C). After 10 minutes, 4-CPy was solube and white precipitate of KCl appeared at the same time. The mixture was stirred for an additional 2 hours, then filtered to remove the precipitate and obtain a yellow solution. The solution was added ethanol (3 mL), then slowly evaporating the solvent from the obtained mixture gave a pale yellow powder (M1). Yield: 83 %. M1 is soluble in acetone, slightly soluble in chloroform and ethanol. IR, cm^{-1}: 3421 (υ_{OH}); 3098, 3015 ($\upsilon_{CH\ (aromatic,\ ankene)}$); 2937, 2839 ($\upsilon_{CHaliphatic}$); 1713 ($\upsilon_{C=O}$); 1605, 1561, 1514 ($\upsilon_{C=C}$, $\upsilon_{C=N}$); 522, 485 ($\nu_{Pt\text{-}C,\ Pt\text{-}(C=C),\ Pt\text{-}N}$).

2.1.3. Interaction between M0 and 4-methylpyridine

The reaction of M0 and 4-methylpyridine (4-MePy) was carried out in different experimental conditions (Table 1). The obtained results show that the products depend on the reaction conditions. The detail procedures of experiment 1 and 5 are as follows:

Experiment 1: A solution (5 mL) of 4-MePy (0,3 mmol) was dropped slowly into a solution (10 mL) of M0 (0.2 mmol) within 15 minutes while stirring at room temperature (25÷30 ^{o}C). The mixture was stirred for a further 2 hours, then filtered to get precipitate. Subsequently, the precipitate was washed several times by dilute hydrochloric acid and warm water to afford a pale yellow powder (denoted by M2). Yield: 83 %. M2 is soluble in chloroform, slightly soluble in ethanol and acetone. IR (cm^{-1}): 3090, 3041 ($\upsilon_{CH(aromatic)}$); 2917 ($\upsilon_{CH(aliphatic)}$); 1617, 1500 ($\upsilon_{C=C}$), 514 (υ_{Pt-N}).

Single crystals of M2 were grown by solvent evaporation method as follows: The saturated solution of M2 in chloroform was filtered to obtain a clear solution. The cubic crystals were obtained after slowly evaporating the solvent at the ambient condition for 5 hours. These crystals were used for X-ray diffraction study.

Experiment 5: A solution (10mL) of 4-MePy (0,1 mmol) was added dropwise into a solution (10 mL) of M0 (0.2 mmol) within 60 minutes while stirring at room temperature. The mixture was stirred for an additional 2 hours, then filtered to obtain precipitate. The precipitate was washed several times by dilute hydrochloric acid and warm water to generate a pale yellow powder. The powder is soluble in chloroform and acetone, slightly soluble in ethanol. The ^{1}H NMR spectrum shows that the product is a mixture of two complexes labeled as M2 and M3 of which M2 exists in trace amount.

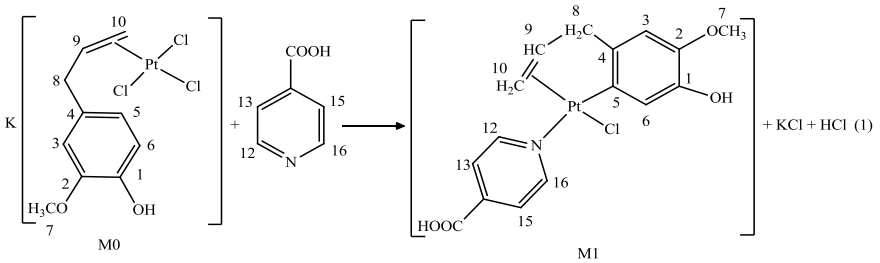
2.2. Instrumentation

Pt was analyzed according to the weight method [5] at Faculty of Chemistry - Hanoi National University of Education. The IR spectra were recorded on IMPACK-410 NICOLET spectrometer in KBr discs in the range 400-4000 cm^{-1}; the ^{1}H NMR spectra were recorded on a Bruker AVANCE 500 MHz, all at 298-300 K, with TMS as the internal standard at Insititute of Chemistry, Vietnam Academy of Science and Technology. Single crystal X-ray diffraction of M2 was measured on Bruker SMART 6000 at 100 K in KU Leuven, Belgium.

3. RESULTS AND DISSCUSION

3.1. Interaction between M0 and 4-carboxylpyridine

According to [7], the interaction between M0 and amine including different aliphatic, aromatic and heterocyclic ones gave *trans*-[$PtCl_2$(Eug)(amin)], the reactions follow the *trans*-effect. Surprisingly, product of reaction between M0 and 4-CPy in the different reaction conditions was not *trans*-[$PtCl_2$(Eug)(4-CPy)] as predicted but [PtCl(Eug-1H)(4-CPy)] (M1), in which deprotonated Eug coordinates with Pt(II) as a bidentate ligand. The reaction equation is described as shown in scheme (1). The similar unusual phenomenon of making chelating complex has been detected for the first time when K[$PtCl_3$(safrol)] reacted with piperidine in ethanol-water solvent, the product was [PtCl(safrol-1H)(piperidine)] but not [$PtCl_2$(safrol)(piperidine)] with a low yield of 20% [8]. However, the yield of making M1 reached herein 83% in the suitable reaction conditions.



Scheme 1: Reaction equation for preparation of [PtCl(Eug-1H)(4-CPy)] (M1)

Percentage of platinum found in M1 by the weight method is 36.96 %, consistent with the value from calculation of 37.75 %. The IR spectrum of M1 (2.1.2) shows characteristic bands for the functional groups in the complex. For example, the presence of 4-Cpy is displayed by intensive band for the C=O group at 1713 cm^{-1}. The value of $\nu_{C=C(allyl)}$ in free Eug of 1640 cm^{-1} [7] whereas that in M1 around 1605÷1514 cm^{-1} indicates that Eug coordinates with Pt(II) via the C=C_{allyl}. The coordination of 4-Cpy with Pt(II) via the N atom and of Eug with Pt(II) via the C=C_{allyl}, C5 are illustrated by the present of some

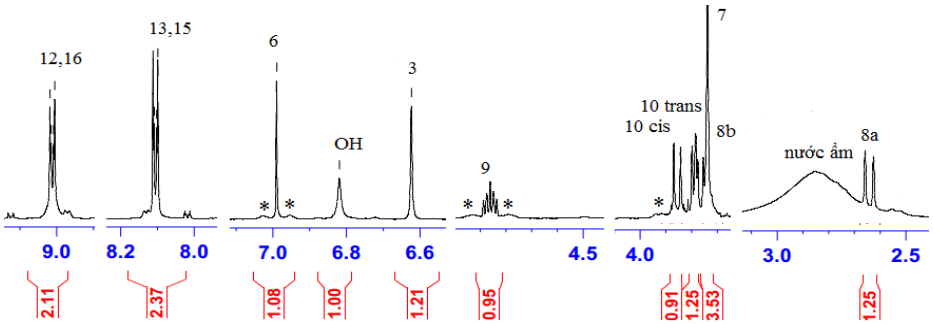


Figure 1: Assigned ^{1}H NMR spectrum of M1 measured in $(CD_3)_2CO$ *(*: ^{195}Pt satellites)*

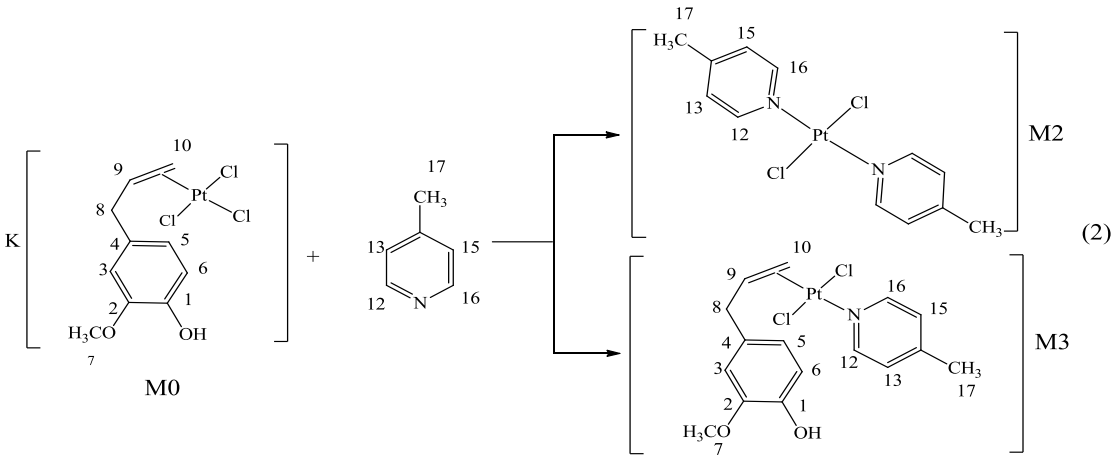
bands at the range of 522÷485 cm^{-1} characterized for the stretching vibration of $\nu_{Pt\text{-}C5}$, $\nu_{Pt\text{-}(C=C)}$, $\nu_{Pt\text{-}N}$.

The assignment of the ^{1}H NMR spectrum is based on their chemical shift, intensity, spin-spin splitting patterns. The result is described in figure 1. In M1, Eug coordinates with Pt(II) via the C=C$_{allyl}$ in an η^2 manner. This coordination can be confirmed by the change in δH9, δH10 compared to those in non-coordinated Eug [7] and the present of the ^{195}Pt satellites from H9, H10 signals (Fig. 1). Additionally, for free Eug, two protons H8 are equivalence (give one signal), but they are in equivalence (give two signals) in P1 [5-8]. In the ^{1}H NMR spectrum of M1, there are only two singlets for H3 and H6 and no signal for H5, the singlet at 6.99 ppm of H6 has two singlet satellites due to the splitting of ^{195}Pt isotope. This proves that Eug undergoes loss of proton H5 and coordinates with Pt(II) via not only the C=C of allyl group but also C5 of benzene ring to form the chelating complex, M1 [5-8]. The coordination of 4-Cpy with Pt(II) in M1 results in a difference between the chemical shifts of H12-H16 in M1 (Fig. 1) and those in free 4-Cpy [9].

3.2. Interaction between M0 and 4-methylpyridine

The result of study on reaction of M0 and 4-MePy is very interesting, the product, which depends on the reaction conditions, is either *trans*-[$PtCl_2$(4-MePy)$_2$] (M2) or *trans*-[$PtCl_2$(Eug)(4-MePy)] (M3) or mixture of M2 and M3. In experiment 1, M0 and 4-MePy were used with the molar ratio of 1:1.5 and high concentration (table 1). The obtained product is only M2, in which 4-MePy replaces not only Cl$^-$ ligand but also Eug ligand in the coordination sphere. Thus, in following experiments, the amount of 4-MePy was used less, concurrently the solution was diluted and dropped more slowly into the M0 solution. This results in a decrease of M2 amount and an increase of M3 in the product. In the experiment 5 with molar ratio of M0: 4-MePy of 2:1, the product is mainly M3 with trace amount of M2. In conclusion, 4-MePy can replace Eug in the coordinaion entiry of Pt(II) in the suitable reaction conditions as described in scheme (2). It is noteworthy that a series of complex K[$PtCl_3$(olefin)] (olefin: eugenol, safrol, methyleugenol, ankyl eugenoxyacetat) react with amine including different aliphatic, aromatic and heterocyclic ones, no amin can replace the olefin in the coordination sphere [5-8].

The percentages of Pt in M2 (product of the experiment 1) and M3 (product of the experiment 5) determined by the weight method are 43.21 % and 38.25 %, which are consistent with the theoretical values of 43.14 % and 37.28 %. The actual value of Pt proportion in M3 is 0.97 % larger than the



Scheme 2: Reaction equation for preparation of M2/M3

Table 1: Some selected experiments for the interaction between M0 and 4-MePy

N°	Reaction time (h)	Time of dropping 4-MePy (h)	Molar ratio of M0:4-MePy	Concentration of M0 (M)	Concentration of 4-MePy (M)	Solvent	Molar ratio of M2:M3
1	2	0.25	1:1.5	0.02	0.06	water	Only M2
2	2	0.5	1:1	0.02	0.02	water	0.4:1
3	2	1	1:1	0.02	0.02	water	0.4:1
4	2	1	1:1	0.02	0.01	water	0.2:1
5	2	1	2:1	0.02	0.01	water	M3 mixed a trace amount of M2

stoichiometry because of a trace amount of M2 in the sample. All the characteristic bands for 4-MePy can be observed clearly in the IR spectrum of M2. Moreover, the Pt-N stretching vibration is shown by band at 514 cm^{-1} proving that 4-MePy has coordinated with Pt(II) via the N atom in M2.

The study on the reaction of M0 and 4-MePy was conducted by ^1H NMR spectroscopy. The ^1H NMR spectrum of M2 displays only one set of signals for 4-MePy but not for Eug (figure 2a). Moreover, the satellites due to spin - spin splitting of ^{195}Pt isotope from signal of $H_{12,16}$ are clear (symbol * in figure 2a). This means that M2 does not contain Eug and ligand 4-MePy coordinates with Pt(II) via the N atom. In the ^1H NMR spectrum of the products of the experiments 2 to 4, two set of signals corresponding to $[PtCl_2(4\text{-MePy})_2]$ (M2) and $[PtCl_2(Eug)(4\text{-MePy})]$ (M3) are clearly observed. Based on the intensive ratio of the signals of the two sets, the molar ratio of M2:M3 can be determined relatively as shown in table 1. In the spectrum of the product of experiment 5 (figure 2b), it seems to have only the set of signals for M3, that for M2 is very small. Hereafter we analyze the spectrum of the product from experiment 2 (figure 2c) as an example. Figure 2c shows a dominant set of signals corresponding to M3 (the protons are labeled H3-H17) and the extra set including three signals at 8.78; 7.13 and 2.43 ppm for $H_{12',16'}$; $H_{13',15'}$ and $H_{17'}$, respectively, of M2. The signals of proton in Eug and 4-MePy in M3 are also change in comparison with those in non-coordinated ligands [7,9], especially H9, H10*trans*, H10*cis* shift dramatically upfield compared to those in free Eug. Additionaly, 2H8 in free Eug are equivalent but they are not in M3. These confirm that Eug coordinates with Pt(II)

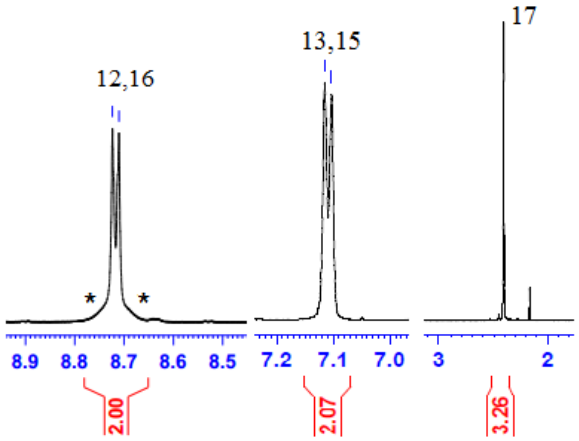


Figure 2a: ^1H NMR spectrum of M2 (the product of experiment 1) measured in $CDCl_3$

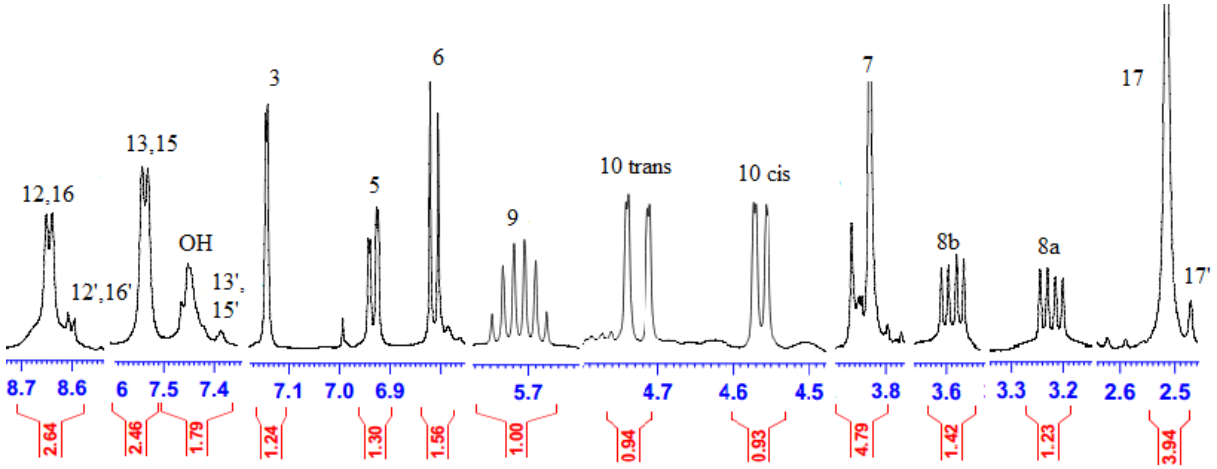


Figure 2b: ^1H NMR spectrum of M3 mixed with M2 in trace amount (experiment 5) measured in $(CD_3)_2CO$

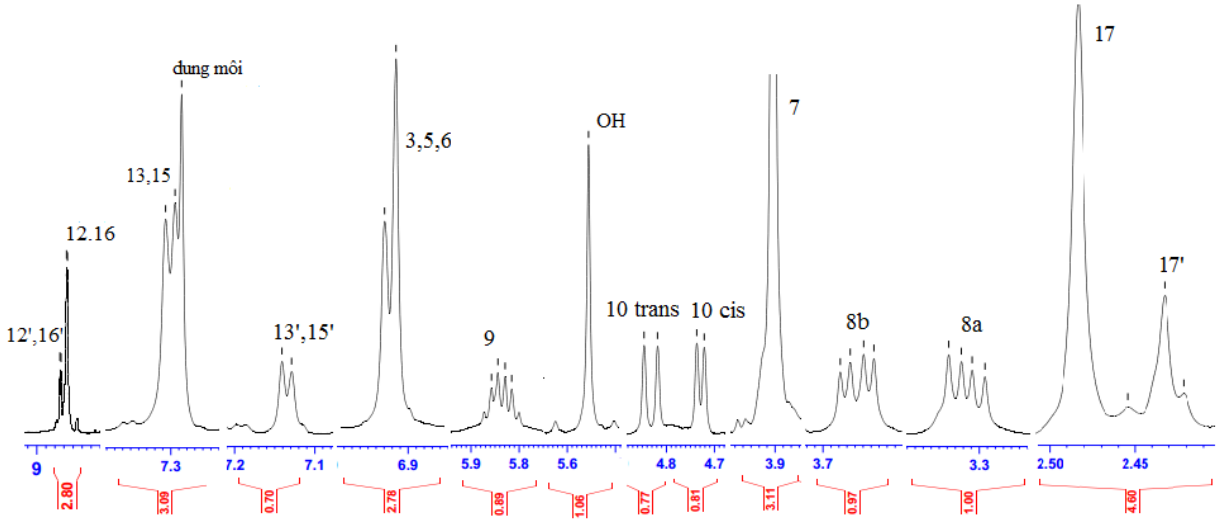


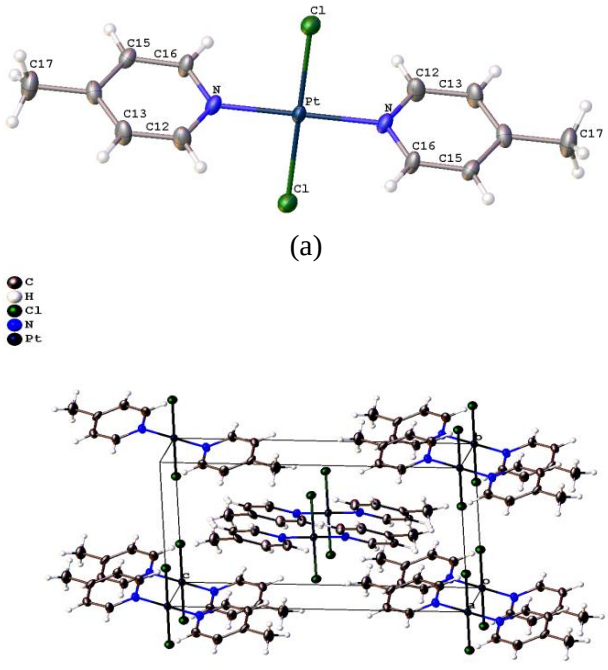
Figure 2c: ^{1}H NMR spectrum of mixture of M2 and M3 (the product of experiment 2) measured in $CDCl_3$

via C=C in a $^{2}\eta$ type in M3 [5-8]. Consequently, basing on the analysis of the Pt percentage, IR spectrum and especialy ^{1}H NMR spectrum, it has not only determined the molar ratio of M2:M3 in products of the examined experiments but also identified the structures of M2 and M3 as shown in scheme (2).

To confirm the structures of M2 and M3, we used single-crystal X ray diffraction method. After many trials, we obtained single crystal of M2 suitable for XRD measurement. The resulting structure of M2 (figure 3a) shows that the complex possesses a square planar geometry, the two 4-MePy ligands coordinate with Pt(II) via N atom and they are in *trans* positions to each other. This structure is completely consistent with that recommended in scheme (2). Crystallography data of M2 (table 2) indicates that M2 was refined with high accuracy (deviation R1/wR2: 0.0271/ 0.0414). The structure of M3 has not been elucidated by XRD method, but it is also able to conclude that M3 has *trans* configuration as described in scheme (2) basing on the *trans* effect and structures of the similar complexes [6,7].

Table 2: XRD experiment details of M2

Molecular formula	$C_{12}H_{14}Cl_2N_2Pt$
Molecular mass	452.24
Crystal system	Monoclinic
Space group	$P2_1/c$
a; b; c (Å)	5.7808(6); 8.1114(11); 14.5506(16)
α; β; γ (°)	90.00; 99.69; 90.00
Volume (Å^3)	672.55(14)
Z	4
Density (mg/mm^2)	2.233
Crystal size (mm^3)	0.1 × 0.09 × 0.07
No. of measured/ independent reflection	2533/1374
Optimized method	Least squares
Deviation R1/wR2	0.0278/0.0429



(a)

(b)

Figure 3: The X-ray structure of M2 (a) and arrangement M2 molecules in the unit cell (b)

4. CONCLUSION

The interaction between $K[PtCl_3(Eug)]$ (M0) and either 4-CPy or 4-MePy has been studied for the first time with the exciting results. The reactions were performed at different conditions for 4-CPy resulting in the same product of [PtCl(Eug-1H)(4-CPy)] (M1). Whereas the product of the reaction of 4-MePy with M0 depends on the molar ratio of M0:4-MePy, it is either *trans*-$[PtCl_2(4\text{-}MePy)_2]$ (M2) or *trans*-$[PtCl_2(Eug)(4\text{-}MePy)]$ (M3) or mixture of M2 and M3. The structures of M1, M2, M3 were determined by the Pt analysis using weight method, IR, ^{1}H NMR spectroscopies and single crystal X-ray diffraction method. The results indicate that 4-CPy and 4-MePy in the three complexes coordinate with Pt(II) via the N atom, Eug in M3 coordinates with Pt(II) through C=C of the allyl group in an $^2\eta$ maner. In M1 complex, deprotonated Eug not only coordinates with Pt(II) via C=C of the allyl group but also via C5 of the aromatic ring to form chelating complex. M2 and M3 complexes adopt *trans* configuration.

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REFERENCES

1. Adnan Salim, Abu-Surrah, Mika Kettunen. *Platinum Group Antitumor Chemistry "Design and development of New Anticancer Drugs Complementary to Cisplatin",* Current Medicinal Chemistry, **13**, 1337-1357 (2006).
2. William M. Motswainyana, Martin O. Onani, Abram M. Madiehe, Morounke Saibu, Jeroen Jacobs, Luc van Meervelt. *Imino-quinolyl palladium(II) and platinum(II) complexes: Synthesis, characterization, molecular structures and cytotoxic effect*, Inorganica Chimica Acta, **400**, 197-202 (2013).
3. Rita Turnaturi, Valentina Oliveri, Graziella Vecchio. *Biotin-8-hydroxyquinoline conjugates and their metal complexes: Exploring the chemical properties and the antioxidant activity*, Polyhedron, **110**, 254-260 (2016).
4. Giovanni Natile, Mauro Coluccia. *Current status of trans-platinum compounds in cancer therapy*, Coord. Chem. Rev., **216**, 383-410 (2001).
5. Tran Thi Da, Young-Mi Kim, Truong Thi Cam Mai, Nguyen Cao Cuong, Nguyen Huu Dinh. *Mono- and dinuclear metallacyclic complexes of Pt(II) synthesized from some eugenol derivatives*, J. Coord. Chem., **63**, 473-483 (2010).
6. Tran Thi Da, Nguyen Thi Thanh Chi, Luc Van Meervelt, Peter Mangwala Kimpende, Nguyen Huu Dinh. *Synthesis, structure and properties of two series of platinum(II) complex containing methyleugenol or chelating methyleugenol and amine*, Polyhedron, **85**, 104-109 (2015).
7. Nguyen Thi Thanh Chi, Tran Thi Da, Nguyen Van Ha, Nguyen Huu Dinh. *Synthesis and spectral characterization of platinum(II) complexes containing eugenol, a natural allylphenol*, J. Coord. Chem., **70(6)**, 1008-1019 (2017).
8. Tran Thi Da, Young-Mi Kim, Nguyen Thi Thanh Chi, Le Xuan Chien, Nguyen Van Minh, Nguyen Huu Dinh. *Formation of Metallacyclic Complexes by Activation of an Aryl C-H Bond in a Platinum-Safrole Analogue of Zeise's Salt*, Organometallics, **27**, 3611-3613 (2008).
9. Tran Thi Da, Nguyen Huu Dinh. *Complex - Synthesis method and structural study*. Science and Technics Publishing House (2007).

Corresponding author: **Nguyen Thi Thanh Chi**
Chemistry Department, Hanoi National University of Education
136, Xuan Thuy road, Cau Giay district, Hanoi, Viet Nam
E-mail: chintt@hnue.edu.vn; Telephone: 0989069204.