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Synthesis and structure of two platinum(II) complexes containing methyl eugenoxyacetate and 2-aminobenzothiazoles

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Abstract

Two organometallic complexes of Pt(II), *trans*-[$PtCl_2$(Meteug)(Bzt)] (M1) and *trans*-[$PtCl_2$(Meteug)(6-MeOBzt)] (M2) (Meteug: methyl eugenoxyacetate, Bzt: 2-aminobenzothiazole, MeOBzt: 2-amino-6-methoxybenzothiazole), have been synthesized for the first time. The structures of M1 and M2 were determined by analysis of Pt and water of hydration proportion, IR, ^{1}H NMR and ^{13}C NMR spectra. Meteug coordinates with Pt(II) through C=C of the allyl group in both compounds, Bzt and MeOBzt coordinate with Pt(II) via N heteroatom and at *trans* position compared to the allyl group.

Keywords. Methyl eugenoxyacetate, Pt(II) complexes, 2-aminobenzothiazoles, NMR spectroscopy.

1. INTRODUCTION

Since cisplatin, *cis*-[$PtCl_2(NH_3)_2$], was appointed as a cancer chemotherapy drug for different types of cancer such as testicular or ovarian cancer, numerous Pt(II) complexes have been synthesized and examined for their antitumor activities [1, 2]. Beside their medical purpose, Pt and its complexes are known for essential roles in organic synthesis, especially many Pt-olefin complexes are intermediates in transforming olefin into more valuable compounds [3, 4].

Recently, several Pt(II) complexes with the type of K[$PtCl_3$(olefin)], in which the used olefin is natural olefin (e.g. safrole, methyleugenol, alkyl eugenoxyacetate) have been prepared. Based on interaction between these complexes and amines, some series of Pt(II) complexes with the structural analogs of *trans*-[$PtCl_2$(olefin)(amine)] were synthesized and researched for their promising medical application [5-7]. Nevertheless, Pt(II) complexes having these natural olefin and 2-aminobenzothiazole or its derivatives have not been published except for [8]. This study demonstrates the result of synthesizing and characterizing of two new Pt(II) complexes from reaction between K[$PtCl_3$(Meteug)] (Meteug: methyleugenol) and 2-aminobenzothiazole (Bzt) or 2-amino-6-methoxy-benzothiazole (MeOBzt).

2. EXPERIMENTAL

2.1. Synthesis

K[$PtCl_3$(Meteug)] (M0) was synthesized following the procedure described in [6].

Synthesis of trans-[$PtCl_2$(Meteug)(Bzt)] (M1): 150 mg 2-aminobenzothiazole (1.0 mmol) in 5 mL acetone was added gradually into the mixture of 577 mg M0 (1.0 mmol) in 5 mL acetone. The reaction mixture was stirred at room temperature (RT) and filtered off after 2 hours to give away the insoluble part. Subsequently, slowly evaporating the solvent from the reaction mixture at RT after 5 hours gave the yellow powder. The product (denoted by M1) was purified by washing with warm water (3 × 3 mL) and cool ethanol (1 × 3 mL). Yielded 65%. Anal. Calc. For [$PtCl_2C_{20}H_{22}O_4N_2S$]: Pt 29.91 %, H_2O 0 %. Found: Pt 30.05 %, H_2O 0%.

Synthesis of trans-[$PtCl_2$(Meteug)(MeOBzt)] (M2): M2 was prepared starting from 577 mg (1.0 mmol) M0 and 180 mg 2-amino-6-methoxybenzothiazole (1.0 mmol) according to the procedure for the preparation of M1. Yielded 68 %. Anal. Calc. For [$PtCl_2C_{21}H_{24}O_5N_2S$]: Pt 28.59 %, H_2O 0 %. Found: Pt 28.65 %, H_2O 0 %.

2.2. Equipment

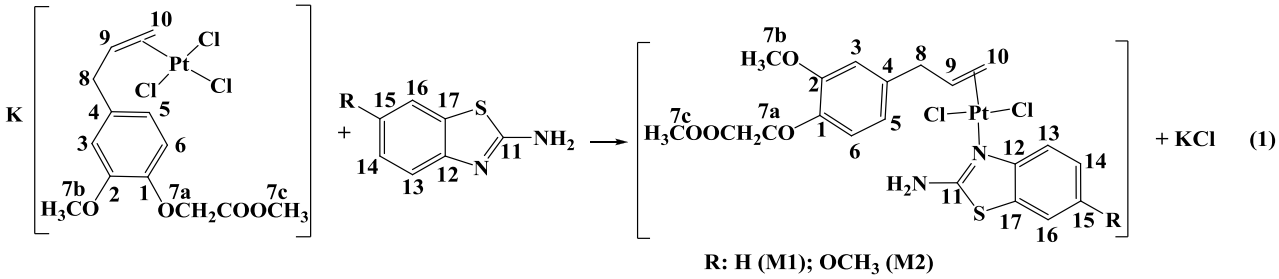
Pt and water of hydration proportion were determined using weight method [9] at Department of Chemistry, Hanoi National University of Education. The IR spectra were recorded on IMPACK-410 NICOLET spectrometer in KBr discs in the range 400-4000 cm^{-1}; The ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AVANCE

500 MHz (all at 298-300 K with TMS as internal standard in suitable solvent) at Vietnam Academy of Science and Technology.

3. RESULTS AND DICUSSION

From the reactions between M0 and Btz or MeOBtz, we obtained M1 and M2 with quite high yields of 65 % and 68 %, respectively. The results from analyzing Pt and water of hydration proportion by weight method (section 2.1) confirm that the chemical formula of M1 and M2 correspond to $[PtCl_2(Meteug)(Btz)]$ (M1) and $[PtCl_2(Meteug)(MeOBtz)]$ (M2).

Btz and MeOBtz can coordinate with Pt(II) through three coordinating centers, N heteroatom, N of NH_2 group and S heteroatom. Theoretically, although a pair of electrons of the S atom has participated in aromatic ring, there is an atom which has participated in aromatic ring, there is still another pair which is capable of coordinating with Pt. Concerning the NH_2 group, a pair of electrons of N atom conjugates with thiazole ring but it is still able to coordinate with Pt via the remaining pair of sp^3 electrons. On the other hand, the N atom of thiazole ring possesses a lone pair of electrons which is sp^2 hybridized, making the N atom be able to coordinate with Pt. Based on analysis of the IR and NMR spectra, it can be determined that in M1 and M2 complexes, both Btz and MeOBtz coordinate with Pt(II) through the N heteroatom as described in equation (1). Additionally, we assume that the products have *trans* configuration, which is reasonable to the *trans* effect. The number for carbons in equation (1) is used for analyzing NMR spectra.



In the IR spectra of M1 and M2, characteristic bands for the functional groups in the compounds can be observed clearly (table 1). For instance, the presence of Meteug in these complexes is confirmed by strong bands for $\nu_{C=O}$ at approximately 1750 cm^{-1} and bands for $\nu_{CHaliphatic}$ from 2951 to 2935 cm^{-1}. Besides, bands for $\nu_{CHaromatic}$ at around 3080 to 3020 cm^{-1} verify the presence of aromatic ring which belongs to Meteug or the coordinated amine. IR spectrum of M2 is shown in Fig. 1 as an example.

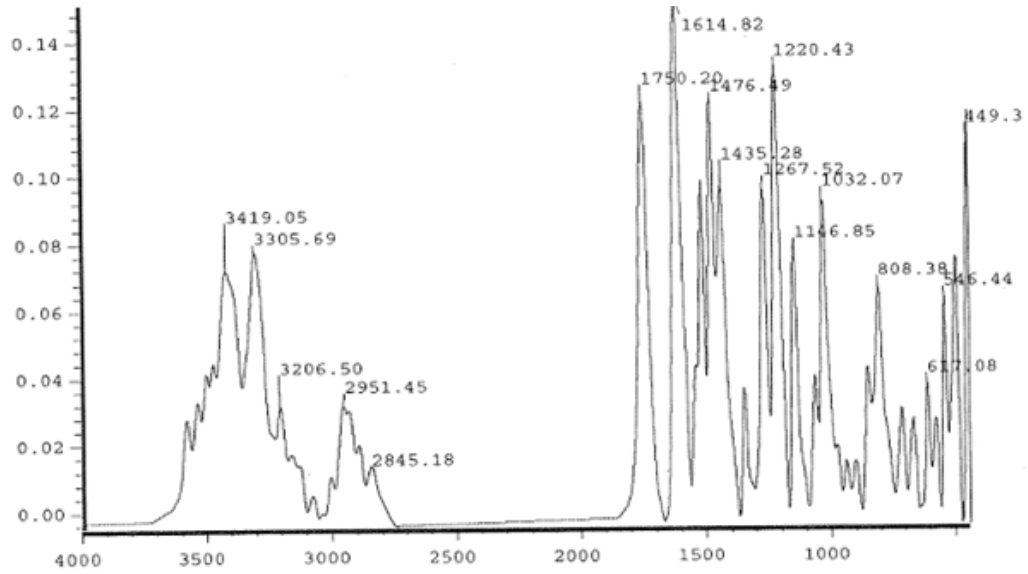


Figure 1: IR spectrum of M2

Table 1: Main bands in IR spectra of M1 and M2 (cm^{-1})

Complexes	ν_{NH}	$\nu_{CH\ aromatic}$	$\nu_{CH\ aliphatic}$	$\nu_{C=O}$	δ_{NH}, $\nu_{C=C}$, $\nu_{C=N}$	ν_{Pt-N}	$\nu_{(Pt-C=C)}$
trans-[$PtCl_2$(Meteug)($C_7H_6N_2S$)] (M1)	3408; 3309	3080; 3025	2935	1748	1616; 1534	588	480
trans-[$PtCl_2$(Meteug)($C_8H_8N_2SO$)] (M2)	3419; 3305	3100; 3020	2951; 2845	1750	1614; 1524	546	449

The analysis of IR spectra proves that Meteug coordinates with Pt(II) through $C=C_{allyl}$ in both complexes M1 and M2. To be specific, wave number of band for $\nu_{C=C\ allyl}$ has decreased from 1640 cm^{-1} in non-coordinated Meteug [10] to around 1616-1524 cm^{-1} in the compounds and concurrently, representative bands for $\nu_{(Pt-C=C)}$ at a range of 480 to 449 cm^{-1} can be visibly detected. The data from table 1 demonstrate that the vibration bands of the NH_2 group in M1 and M2 are mostly not different from ν_{NH} of the non-coordinated amines [9], however bands for ν_{Pt-N} can still be observed in range from 588 to 546 cm^{-1}. It can be concluded that in M1 and M2, Btz and MeOBtz do not coordinate with Pt(II) through N of the NH_2 group but instead, they both coordinate via the N heteroatom. This conclusion can be specified by analyzing ^{1}H NMR spectra of M1 and M2.

In order to analyze ^{1}H NMR spectra, we denote hydrogen atoms of Meteug, Bzt and MeOBzt as in reaction (1). The proton signals are assigned based on their chemical shift (δ), intensity, shape, spin-spin splitting pattern and [8, 9]. The results are listed in table 2 and Fig. 2 shows an assigned ^{1}H NMR spectrum of M1 as an example.

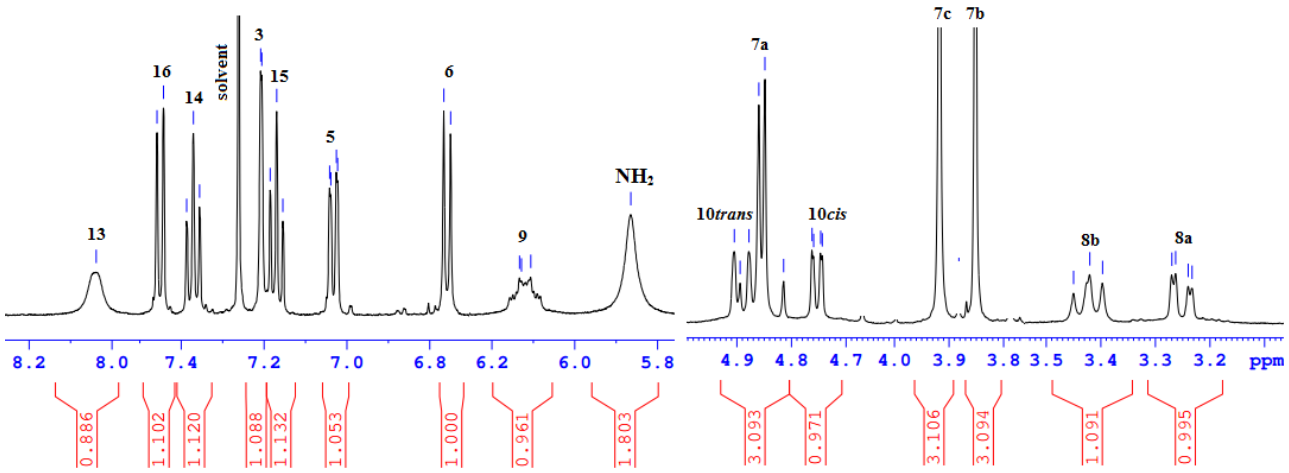
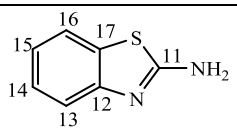
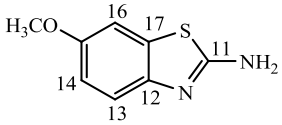


Figure 2: Assigned ^{1}H NMR spectrum of M1

Table 2: ^{1}H NMR signals of Meteug and amines in M1 and M2, δ (ppm), *J* (Hz)

Comp.	H3	H5	H6	H7a	H7b	H7c	H8a	H8b	H9	H10*cis*	H10*trans*
Meteug	7.72	6.67	6.77	4.76	3.79	3.90	3.33		5.94	5.06	5.09
M1 (*)	7.20 d ^4J 1.5	7.03 dd ^3J 8.0 ^4J 1.5	6.76 d ^3J 8.0	4.86/4.85 d ^2J 17.0	3.85 s	3.92 s	3.25 dd ^2J 15.0 ^3J 3.5	3.42 d ^2J 15.0	6.13 m	4.75 dd ^2J 1.5. ^3J 8.0	4.89 d ^3J 14.0
M2 (*)	7.20 d ^4J 2.5	6.94 dd ^3J 8.0 ^4J 2.5	6.80 d ^3J 8.0	4.83/4.82 d ^2J 17.0	3.83 s	3.91 s	3.24 dd ^2J 15.0 ^3J 3.5	3.44 d ^2J 15.0	6.09 m	4.74 dd ^2J 1.5 ^3J 8.0	4.87 d ^3J 13.5

Amine	H13	H14	H15	H16	CH_3	NH_2
	8.04 br	7.37 t ^3J 8.0	7.17 t ^3J 7.5	7.45 d ^3J 7.5	-	5.86 br
	7.90 br	7.03 dd ^3J 8.5 ^4J 1.5	-	6.96 d ^4J 1.5	3.79 s	5.81 br

(*): NMR solvent ($CDCl_3$).

It is shown that proton signals of Meteug in M1 and M2 are entirely different from non-coordinated Meteug [10], which proves the coordination between Meteug and Pt(II). In both complexes, Meteug coordinates with Pt(II) in an η^2 manner. The coordination can be verified by the change in chemical shift of H10*trans* and H10*cis* compared to those in non-coordinated Meteug and the difference between signals of H8, which are the same in non-coordinated Meteug [6]. It is notable that δ of H9 in M1 and M2 increases extremely in comparison to that of free Meteug and M0 (table 2) while in some series of Pt(II) complexes *trans*-[$PtCl_2$(olefin)(amine)] (olefin is not only Meteug but also another arylolefin), it decreases dramatically [5-7]. It can be assumed that the phenomenon is caused by influence from Bzt and MeOBzt.

Signal of protons of the NH_2 group is shown as a broad peak because they are active hydrogens and thus, cause interaction with proton of water in the solvents used for the NMR measurement. The question is that why signal of H13 in both M1 and M2 is also broadened. To answer this, we propose possible structures of M1 and M2 as shown in figure 3 based on coordination ability of Btz and MeOBtz and determine the relative position between H13 and Pt in each case. According to [9], from analyzing NMR spectra of many series Pt(II) complexes, the authors have inferred that when the proton of ligand is under the square planar coordinating plane of Pt(II), its signal tends to be broad. In assumption, the reason could be magnetic induction caused by d^8 electrons of Pt(II).

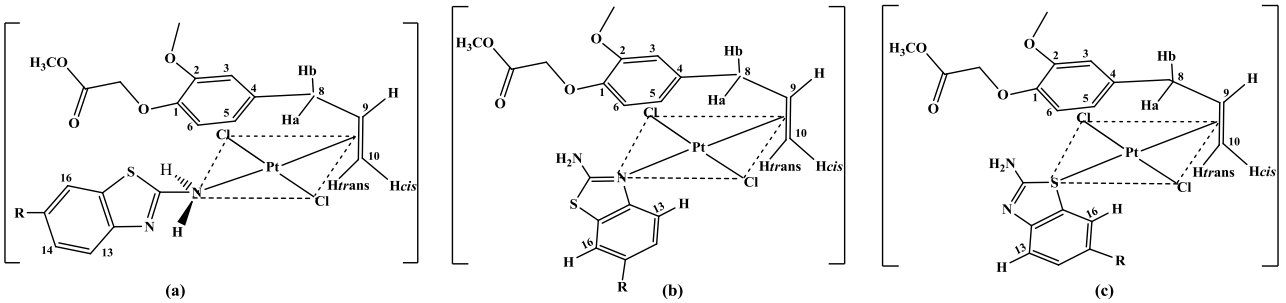


Figure 3: Structures of M1 and M2 when amine coordinates with Pt(II) via: N of NH_2 (a), heteroatom N (b), S (c)

Hypothetically, if Bzt and MeOBzt coordinated with Pt(II) through the N atom of the NH_2 group, there would be no proton under the coordination plane of Pt(II) (figure 2a). Otherwise, if they coordinated with Pt(II) via the N heteroatom and they were perpendicular to the coordination plane (most favorable in terms of the space), H13 would be located under the plane as described in figure 2b and thus, signal of H13 would be broad and signal of H16 would be sharp. Lastly, if Bzt and MeOBzt coordinated with Pt(II) perpendicularly through S (figure 2c), thus signal of H16 would be broad and signal of H13 would be sharp.

Based on the analysis, it is determined that Bzt and MeOBzt coordinate with Pt(II) through the N heteroatom in M1 and M2.

The ^{13}C NMR of M1 further confirms the structure of the complex. The assignment of the ^{13}C NMR signals is based on their chemical shift, experienced rules and reference [9], the assigned ^{13}C NMR spectrum of M1 is shown in figure 4.

From analysis of ^{13}C NMR spectrum of M1, it can be noticed that signals of ^{13}C of Meteug and 2-aminobenzothiazole are absolutely dissimilar to those of non-coordinated form, which confirms the coordination between them and Pt(II). Chemical shift of C9 and C10 of Meteug reduces intensely in comparison with those of non-coordinated Meteug, so it can be totally proved that Meteug coordinates with Pt(II) via C9 and C10 in an η^2 manner.

From the analyzing Pt, water of hydration proportion, IR, ^1H NMR, and ^{13}C NMR spectra, we have determined the structure of M1 and M2 as demonstrated in figure 3b.

4. CONCLUSION

Two organometallic complexes of Pt(II) were synthesized, which are [$PtCl_2$(Meteug)(Bzt)] (M1) and [$PtCl_2$(Meteug)(6-MeOBzt)] (M2). Their structures were determined by elemental analysis, IR, ^1H NMR, and ^{13}C NMR spectroscopies. It is specified that Meteug coordinates with Pt(II) via C=C of the allyl group in both M1 and M2, 2-aminobenzothiazole and 2-amino-6-methoxybenzo-thiazole which have three coordinating centers only

coordinate with Pt(II) through the N heteroatom and at *trans* position compared to the allyl group.

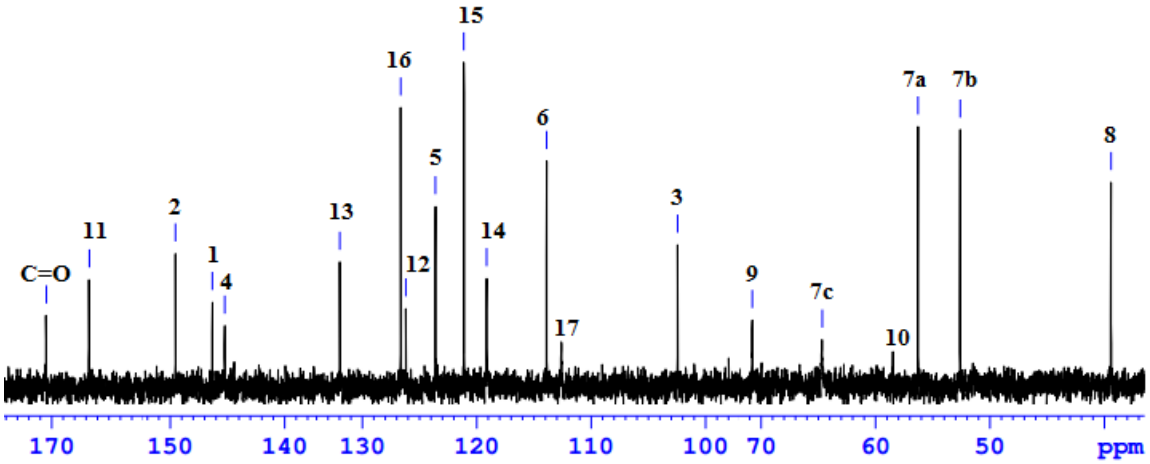


Figure 4: Assigned ^{13}C NMR spectrum of M1

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