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The University of Osaka

# Abstract of Thesis

Ｎａｍｅ　（Laurenzo De Vera Alba　）

Title: Structure and Reactivity of Noble Metal Complexes of Saccharide and Glycoside Derivatives Relevant to the Biological Actions
（生物学的作用に関連する糖類および配糖体の誘導体を有する貴金属錯体の構造と反応性）

We have synthesized and characterized new Pt (II) and Pd (II) complexes with hydroxyquinoline bound to an aminosugar via a Schiff base ligand ("Oqn") analogous to the Pt and Pd complexes synthesized in previous studies[1] by Yano *et al*. which have promising anticancer and anti-metastatic effectiveness. The cytotoxic mechanism of these complexes involves interfering with intracellular signaling proteins (in the case of Pd-Oqn) or causing double-strand breaks in the DNA (in the Pt-Oqn complex).[2, 3]

High-quality crystals were obtained for two new Pt and Pd complexes and were analyzed by X-ray diffraction. Together with the previously discovered Pt- and Pd-Oqn complexes, the new complexes of Pt and Pd show the characteristic square planar geometry around the metal center. The Pt and Pd complexes show stacking or dimerization in the solid state assisted by the formation of hydrogen bonds, close metal-metal interaction, and π-π stacking; and inhibited by steric effects of acetylation. Spectral assignments were done through the use of time-dependent density functional theory (TD-DFT) calculations. From the UV-Vis spectral changes of the complexes in solutions mixtures of varying polarity, we have observed aggregation and/or potential dimerization leading to the metal-metal-ligand charge transfer (MMLCT) band in the non-acetylated complexes.

Hydrolysis of the Pt and Pd complexes were measured in aqueous solutions and was found to be inhibited by chloride. Pd complexes hydrolyze much faster than Pt complexes. Hydrolysis initially thought to involve substitution of the chloride ligand with water or hydroxide. In the case of the Pt complex **2**, $^{1}$H NMR studies suggest the formation of a final hydrolysis product composed of an isomerized molecule with Pt coordinating directly to the sugar hydroxyl. This may explain why the reaction is irreversible even upon the addition of excess chloride in solution. Protein interaction with bovine serum albumin (BSA) was measured through fluorescence quenching assay, with complex **4** having the highest affinity to the protein. All complexes show fluorescence quenching and thus are capable of binding to BSA. Overall, the observations herein suggest that, in contact with biological systems, these complexes are readily hydrolyzed and/or bound to protein. There is high possibility that the bioactive species is the hydrolysis product.

A novel Ag(I) complex of acetylsinigrin (Ag·SinAc) was synthesized and crystallized as the first example of a glucosinolate-metal complex. It was found that Ag forms an unstable complex with sinigrin, which rapidly decomposes to form an Ag-aglycone compound by breaking the C-S bond. For the Ag·SinAc complex, the crystal structure shows $\eta^2$-coordination with the ethylene moiety and an overall coordination polymer structure composed of a hollow 1D chain with an Ag-containing central structure. Ag·SinAc degradation into the Ag-aglycone can be induced by heat. Computational studies for heterolytic bond dissociation enthalpies and electron charge transfer using optimized structures show that metals, especially Ag, are able to activate the glycosidic C-S bond through polarization. Additionally, the Ag appears to stabilize the aglycone leaving group. It is proposed that a similar mechanism exists as the role of arginine within the naturally occurring myrosinase enzyme which hydrolyzes sinigrin, in the stabilization of the aglycone leaving group. Thus, the Ag-sinigrin system may be a biomimetic model for the myrosinase-catalyzed decomposition of sinigrin.

様式 7

# 論文審査の結果の要旨及び担当者

氏　名　（ Laurenzo De Vera Alba ）

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## 論文審査の結果の要旨

2021 年 5 月 21 日に De La Salle University (DLSU)にて、Laurenzo De Vera Alba 氏の博士公聴会を行い、発表内容と質疑応答の審査の結果、合格となった。その博士論文タイトルは「Structure and Reactivity of Noble Metal Complexes of Saccharide and Glycoside Derivatives Relevant to the Biological Actions（生物学的作用に関連する糖類および配糖体の誘導体を有する貴金属錯体の構造と反応性)」である。

Alba 氏は、部局間協定にもとづく Double Degree Program (DDP)により本部局の統合理学特別コースに在籍しており、Alba 氏に対するコチュテルの合意にしたがって審査を進めた。DLSU での博士公聴会に先立ち、提出された博士論文に対してそれぞれの大学のカリキュラムに沿う形式で、主査と副査による予備審査を行った。なお、本部局では、化学専攻Ａコースの教授全員による内審を 2021 年 2 月 2 日に行った。

以上の過程を経て、DLSU での博士公聴会の直後に開催された阪大と DLSU の部局間の合同審査委員会により最終的な評価を行い、Alba 氏の研究業績の全体が、既に学術誌での掲載が決定したものも含めて、双方の大学の博士号を授与するに値するという結論に至った。