

1998年度 総合理学研究所 共同研究報告書

1. テーマ

I. <種々の複素環窒素配位子による銀(I)および金(I)錯体の合成と生理活性>

2. 研究メンバー

代表者 野宮健司 (神奈川県立理学部 教授)

共同研究者 小田宗宏 (明治乳業細胞工学センター 課長)

3. 研究期間 平成10年4月1日 ~ 平成11年3月31日

4. 研究の概要

(1) Two novel polymeric silver(I)-triphenylphosphine complexes with nitrogen-containing heterocycles, $[\text{Ag}(1,2,3\text{-triz})(\text{PPh}_3)_2]_n$ **3** and $[\text{Ag}(1,2,4\text{-triz})(\text{PPh}_3)_2]_n$ **4** (Htriz = triazole) were synthesized from reactions of polymeric precursors $[\text{Ag}(1,2,3\text{-triz})]_n$ **1** and $[\text{Ag}(1,2,4\text{-triz})]_n$ **2** with 3 equiv of PPh_3 in CH_2Cl_2 , respectively. The polymeric precursors **1** and **2** have been obtained as a non-crystalline, colorless powder-solid: **2** showed a wide spectrum of excellent antibacterial activities, but **1** did not. The antimicrobial activities of the complexes **1** - **4**, evaluated by MIC (minimum inhibitory concentration), were compared and key factors affecting them were discussed. The crystal structures of the complexes **3** and **4** were determined by single-crystal X-ray diffraction. The complexes **3** and **4** in the solid-state were helical polymers consisting of AgN_2P_2 cores formed by bridging triazolate anions and two PPh_3 ligands. The complexes **3** and **4** were also fully characterized by elemental analyses, TG/DTA and FT-IR in the solid-state and by various solution NMR (^{31}P , ^{109}Ag , ^1H and ^{13}C) spectroscopies and molecular weight measurements in solution.

(2) Two novel gold(I)-triphenylphosphine complexes with nitrogen-containing heterocycles, $[\text{Au}(1,2,3\text{-L})(\text{PPh}_3)]$ **1** and $[\text{Au}(1,2,4\text{-L})(\text{PPh}_3)]_2 \cdot x\text{H}_2\text{O}$ ($x = 0.5 - 1.0$) **2** (HL = triazole) were synthesized from stoichiometric reactions of a precursor complex $[\text{AuCl}(\text{PPh}_3)]$ with HL in acetone in the presence of aqueous NaOH, and isolated as colorless needles and cubic crystals, respectively. The crystal structures of **1** and **2** were determined by single-crystal X-ray diffraction. **1** and **2** were also fully characterized by complete elemental analyses, TG/DTA and FT-IR in the solid-state and by solution NMR (^{31}P , ^1H and ^{13}C) spectroscopies and solution molecular-weight measurements. **1** consisted of a monomeric 2-coordinate AuNP core both in the solid-state and in solution, while, in contrast, **2** comprised a dimeric $(\text{AuNP})_2$ core through an Au-Au bond in the

solid-state, but a monomeric AuNP core in solution. Within the two gold(I) complexes composed of very closely related nitrogen-containing heterocycles and a common bulky PPh₃ ligand, it was found that the aggregation through the Au···Au interaction in **2** was overruled in **1**. The molecular structures of **1** and **2** were also compared with those of the corresponding silver(I) analogs, [Ag(1,2,3-L)(PPh₃)₂]_n **3** and [Ag(1,2,4-L)(PPh₃)₂]_n **4**, the molecular structures of both of which have been recently determined as helical polymers in the solid-state.

(3) Polymeric silver(I) imidazolate [Ag(imd)]_n (**1**; Himd = imidazole, C₃H₄N₂) showing a wide spectrum of excellent antimicrobial activities against bacteria, yeast and mold, which has been obtained as non-crystalline, colorless powder, was successfully converted to molecular, crystalline complex [Ag(imd)(PPh₃)₃] **2** by a reaction of **1** with 3 equivalents of PPh₃ in CH₂Cl₂. This novel complex **2** was not obtained from reactions in solutions of the precursors [AgCl(PPh₃)₃] and/or [AgCl(PPh₃)₂]₂ with Himd in the presence of NaOH or with sodium salt of imd. On the contrary, the corresponding gold(I) complex [Au(imd)(PPh₃)₃] **3** was formed by a reaction of the precursor [AuCl(PPh₃)₃] and Himd in the presence of NaOH. From a synthetic viewpoint, these facts show the ordering of ligand replacement in these complexes to be Ag-P >> Ag-Cl > Ag-N, while Au-P >> Au-N > Au-Cl. This ordering also exhibits the different reactivity of silver(I) and gold(I) complexes with biological ligands such as proteins, enzymes, nucleic acids and amino acids. The complex **2** was fully characterized by complete elemental analyses, TG/DTA, FT-IR, solution molecular weight measurement and various solution NMR (¹H, ¹³C, ³¹P and ¹⁰⁹Ag) spectroscopies. The complex **2** in solution was present in a rapid equilibrium with the dissociated species of two PPh₃ ligands, *i.e.*, [Ag(imd)(PPh₃)₂]. The ³¹P NMR measurements at low temperature showed that (i) all PPh₃ ligands in **2** in CHCl₃ solution migrated at room temperature between the two isotopes ¹⁰⁹Ag and ¹⁰⁷Ag, in addition to the dissociation of two PPh₃ ligands, and (ii) there were present the 4-coordinate tetrahedral complex **2** and the dissociated complex [Ag(imd)(PPh₃)₂] in solution.

5. 発表論文

- (1) Nomiya, K., Tsuda, K., and Kasuga, N. *C. J. Chem. Soc., Dalton Trans.*, 1653 - 1659 (1998).
- (2) Nomiya, K., Noguchi, R., Ohsawa, K., and Tsuda, K. *J. Chem. Soc., Dalton Trans.*, 4101 - 4108 (1998).
- (3) Nomiya, K., Tsuda, K., Tanabe, Y., and Nagano, H. *J. Inorg. Biochem.*, **69**, 9 -14 (1998).