論文の内容の要旨

Kinetically Controlled Stepwise Syntheses of a Heterometallic $Co^{II}Ni^{II}_3$ Complex and a Tetrahedral Chiral-at-Metal Zn^{II} Complex

（速度論的制御を伴った段階的手法による異種金属 $Co^{II}Ni^{II}_3$ 錯体および四面体型 chiral-at-metal Zn^{II} 錯体の合成）

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Introduction

Synthesis of metal complexes is usually based on direct reaction of metal sources and ligands. However, this one-step method is not always useful because kinetic control is difficult. In contrast, stepwise synthesis can provide a variety of structures with high selectivity through kinetically controlled pathways. This method has been widely employed for some inert metal complexes,[1] but rarely used for labile metal complexes. Herein, I report two new methods of highly selective syntheses of relatively labile metal complexes through kinetically controlled, stepwise reactions: (1) a heterometallic tetranuclear $Co^{II}Ni^{II}_3$ complex and (2) an enantiopure tetrahedral chiral-at-metal Zn^{II} complex with achiral ligands.

Heterometallic tetranuclear $Co^{II}Ni^{II}_3$ complex

Heterometallic multinuclear complexes have great potential to exhibit unique chemical and physical properties based on the cooperation of different metal ions.[2] However, most examples previously reported depend on one-step methods or are based only on 4d- or 5d-metal ions. In this work, a new strategy toward an otherwise difficult arrangement of different 3d-metal ions has been achieved by site-selective redox switching and transmetalation (Figure 1).

In my master course study, I have found that the porphyrin-based ligand **L1** can construct a tetranuclear complex, $[Zn^{II}_4\mathbf{L1}_3X_6]$ (X = solvent or counterion), by self-assembly with Zn^{II} ions. This complex possessed chemically inequivalent Zn^{II} sites, which prompted me to initiate the stepwise synthesis of heteronuclear 3d-metal complexes with this structural framework.

First, I introduced Co^{II} as a redox-active component to construct a tetranuclear complex, $[Co^{II}_4\mathbf{L1}_3X_6]$, by self-assembly of **L1** and Co^{II} ions. This complex contained two different Co^{II} centers, one $Co^{II}(bpy)_3$ and three $Co^{II}(bpy)_2X_2$ sites. Then, site-selective oxidation at the $Co^{II}(bpy)_3$ site was found possible by addition of 1 equiv. of oxidant. This site selectivity is due to the stronger coordination field provided by the three bpy ligands of the $Co^{II}(bpy)_3$ site. In the next step, the remaining $Co^{II}(bpy)_2X_2$ sites were site-selectively transmetalated by Ni^{II} ions. This is possible because the thermodynamic affinity of bpy to Ni^{II} is intermediate between Co^{III} and Co^{II}. Finally, site-selective reduction at the $Co^{III}(bpy)_3$ site afforded a

$[\mathrm{Co^{II}Ni^{II}_3}\mathbf{L1}_3\mathrm{X_6}]$ complex. Each complex was well-characterized by ^{1}H NMR spectroscopy and ESI-MS, and some of them by single-crystal XRD and XPS.

Notably, the last complex $[\mathrm{Co^{II}Ni^{II}_3}\mathbf{L1}_3\mathrm{X_6}]$ cannot be synthesized directly from **L1**, Co$^{\mathrm{II}}$, and Ni$^{\mathrm{II}}$ because a Ni$^{\mathrm{II}}$(bpy)$_3$ motif is thermodynamically favored. The synthesis of this complex is not possible without the kinetically controlled stepwise method developed in this work.

Tetrahedral chiral-at-metal Zn$^{\mathrm{II}}$ complex

A metal center of a metal complex can be a chirality center in some cases, which are called chiral-at-metal complexes. The usefulness of chiral-at-metal complexes has been demonstrated in enantioselective catalysis, chiroptical materials, and so on. Therefore, it is necessary to develop an excellent method to synthesize enantiopure chiral-at-metal complexes, desirably with a catalytic center. Historically, separation of enantiomers was initially employed, and it was a little later that diastereoselective synthesis with chiral ligands/counterions was developed as a more efficient method. At last, enantioselective synthesis with a transiently usable chiral reagent was invented, which is useful to obtain complexes free from chiral ligands/counterions (Figure 2).[3]

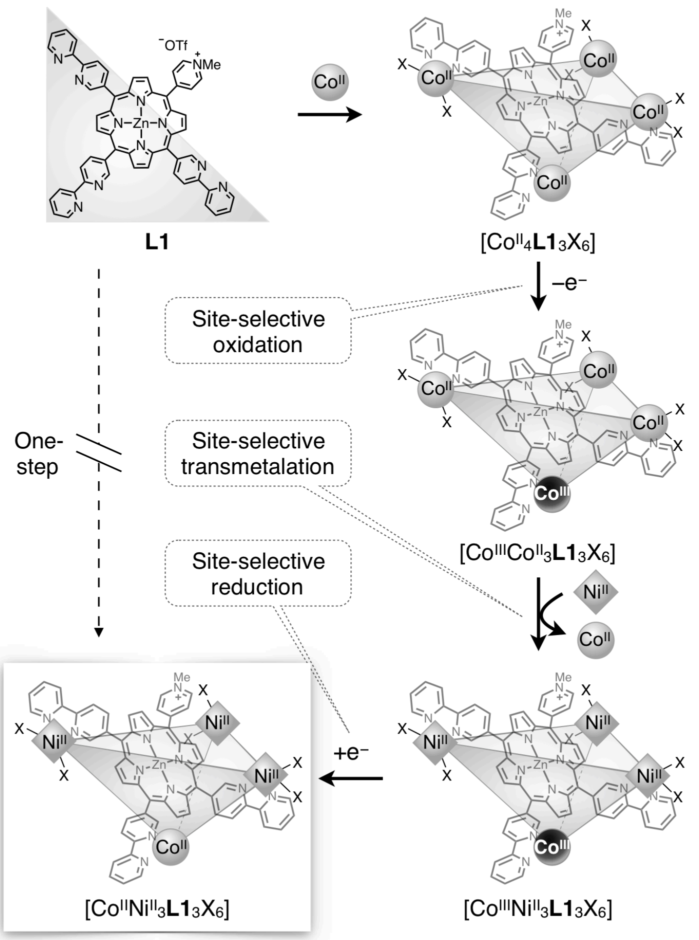


Figure 1. Synthetic scheme of heterometallic tetranuclear Co$^{\mathrm{II}}$Ni$^{\mathrm{II}}_3$ complex.

Note that this development has been focused chiefly on octahedral, relatively inert metal complexes. Although tetrahedral complexes are common in coordination chemistry, enantioselective synthesis has been rarely reported for chiral-at-metal tetrahedral complexes. Therefore, it remains as a challenging task to develop their enantioselective synthetic methods for highly labile tetrahedral chiral-at-metal complexes. It is a key here to avoid fast racemization of the labile tetrahedral complexes.

Herein, I report enantioselective synthesis of a tetrahedral chiral-at-metal complex by kinetically suppressing racemization. In addition, the practical utility of the complex was demonstrated in application to enantioselective catalysis.

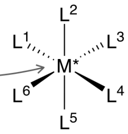
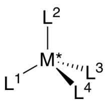
	Octahedral	Tetrahedral
Chirality center		
Separation	✔	✔
Diastereoselective synthesis	✔	✔
Enantioselective synthesis	✔	**Difficult**

Figure 2. Preparation methods for enantiopure chiral-at-metal complex

Design of a tetrahedral chiral-at-metal complex

In this study, I newly designed a tridentate ligand, **L2**, to suppress racemization while leaving one labile site for chirality induction and catalytic application (Figure 3). In the presence of a tridentate ligand, racemization pathways of a tetrahedral complex are limited to dissociation or planarization of the tridentate ligand. To block both pathways, I designed ligand **L2** with strong coordination ability by negatively charged, deprotonated nitrogen donors and with a rigid non-planar structure by steric crowding. In addition, wide bite angles are provided by the 6- and 7-membered chelate rings, in order to favor a tetrahedral geometry.

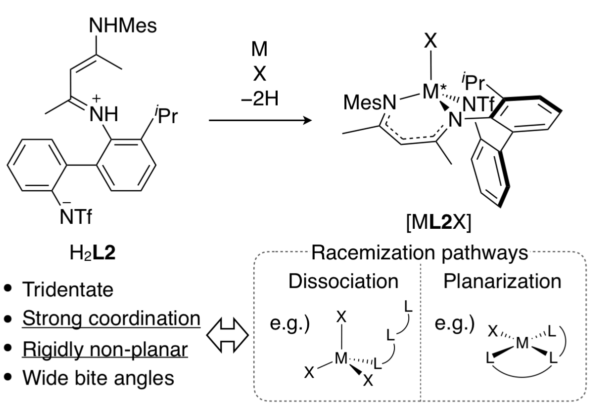


Figure 3. Design of a tridentate ligand **L2** to form a tetrahedral chiral-at-metal complex stable against racemization.

Enantioselective synthesis of a tetrahedral chiral-at-metal $\mathrm{Zn^{II}}$ complex

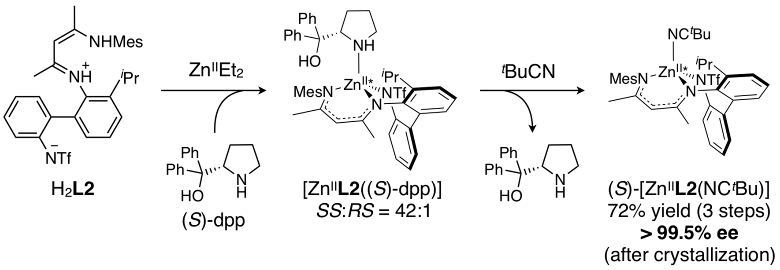


Figure 4. Enantioselective synthesis scheme of (*S*)-[$\mathrm{Zn^{II}}$**L2**(NC^{t}Bu)].

Ligand H_2**L2** was synthesized in 5 steps in 52% overall yield. Enantioselective synthesis of a tetrahedral metal complex using **L2** was conducted in three steps: (1) racemic complexation; (2) asymmetric induction with a chiral ligand; (3) removal of the ligand. $\mathrm{Zn^{II}}$ was used as a metal ion and a weakly acidic chiral monodentate ligand, (*S*)-dpp, was chosen as a chiral auxiliary.

First, complexation of the ligand H_2**L2** with $\mathrm{Zn^{II}Et_2}$ was conducted to give racemic (*R**,*R**)-[$\mathrm{Zn^{II}_2}$**L2**$_2$]. Then, (*S*)-dpp was added to give a diastereomeric mixture of [$\mathrm{Zn^{II}}$**L2**((*S*)-dpp)] in the ratio of *SS*:*RS* = 42:1 (Figure 4). The structure of the *SS* isomer was revealed by ^{1}H-^{1}H NOESY NMR and single-crystal XRD. This isomer exhibited two NH-O hydrogen bonds and one OH-π interaction, which suggest that the high diastereoselectivity may arise from these intramolecular interactions in combination with steric repulsion.

Next, the diastereomeric mixture was treated with an excess amount of pivalonitrile (^{t}BuCN) to replace the (*S*)-dpp ligand. After crystallization in benzene/HMDSO, (*S*)-[$\mathrm{Zn^{II}}$**L2**(NC^{t}Bu)] complex was successfully obtained in 72% yield with enantiopurity of over 99.5% ee. The structure of this complex and the *S* absolute configuration was confirmed by single-crystal XRD.

In this way, enantioselective synthesis of (*S*)-[$\mathrm{Zn^{II}}$**L2**(NC^{t}Bu)] complex was achieved by the three-step sequence. This is the first example of enantioselective synthesis of a tetrahedral chiral-at-metal complex composed of achiral ligands using a chiral ligand as a chiral auxiliary.

Racemization kinetics of the $\mathrm{Zn^{II}}$L2 complexes

The racemization rate of (*S*)-[$\mathrm{Zn^{II}}$**L2**(NC^{t}Bu)] in solution state was examined using ^{19}F NMR (Figure 5). (*S*)-[$\mathrm{Zn^{II}}$**L2**(NC^{t}Bu)] was dissolved in benzene-*d*$_6$, and then the solution was incubated at 24 °C or 70 °C for 0 h or 24 h, followed by addition of a chiral shift reagent. The ^{19}F NMR spectra showed slight racemization in the proportions of 0.02% at 24 °C and 0.35% at 70 °C after 24 h. This result shows exceptional kinetic stability of this complex.

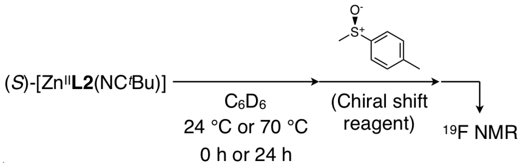


Figure 5. Measurement of the racemization rate for (*S*)-[$\mathrm{Zn^{II}}$**L2**(NC^{t}Bu))].

Interestingly, the intermediate [$\mathrm{Zn^{II}}$**L2**((*S*)-dpp)] diastereomers showed a contrastive behavior. When $\mathrm{Zn^{II}Et_2}$ and (*S*)-dpp were added to H_2**L2** stepwise, the diastereomer ratio gradually changed from 1:1 to 22:1 during heating (Figure 6). A similar experiment with (*S*)-mdp, which have a methoxy group instead of a hydroxy group, showed no changes in the diastereomer ratio from 1:1. These results indicate that the hydroxy group of (*S*)-dpp accelerated stereoinversion temporarily and eventually enabled asymmetric induction.

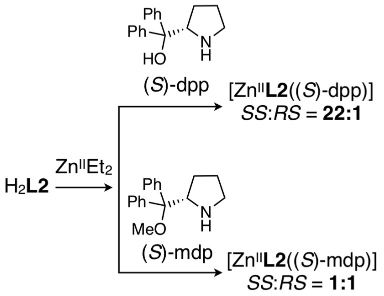


Figure 6. Effect of (*S*)-dpp on stereoinversion.

Application of the $\mathrm{Zn^{II}}$L2 complex to enantioselective catalysis

Catalytic activity of (*S*)-[$\mathrm{Zn^{II}}$**L2**(NC^{t}Bu)] was examined for oxa-Diels-Alder reaction, which is generally catalyzed by Lewis acids. Diene **8** was reacted with aldehyde **9** in the presence of 1 mol% (*S*)-[$\mathrm{Zn^{II}}$**L2**(NC^{t}Bu)] (Figure 7). After acidic treatment, the product (*R*)-**10** was obtained in 78% yield and 88% ee. To examine the cause of enantioselectivity, a catalyst–substrate complex [$\mathrm{Zn^{II}}$**L2**(**9**)] was prepared and analyzed by single-crystal XRD and ^{1}H-^{1}H NOESY NMR. These analyses indicated that the *Si*-face of aldehyde **9** was effectively shielded by the structural framework of $\mathrm{Zn^{II}}$**L2**. The observed enantioselectivity can be well explained by the face-selective attack of diene **8**. This result demonstrates that a tetrahedral chiral-at-metal complex with achiral ligands is practically useful when the racemization rate is extremely slower than that of the reaction.

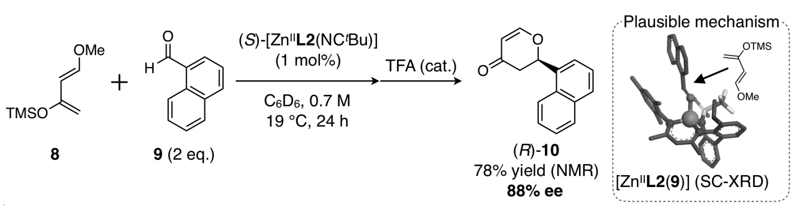


Figure 7. Enantioselective catalysis by (*S*)-[$\mathrm{Zn^{II}}$**L2**(NC^{t}Bu)].

Conclusions

In this work, two metal complexes were synthesized using the kinetically controlled stepwise reactions. Firstly, a Co^{II}–Ni^{II} heterometallic complex was synthesized by site-selective redox switching and transmetalation. Secondly, an enantiopure tetrahedral Zn^{II} complex was synthesized using the rigid tridentate ligand. While both complexes are not accessible by the direct reactions of the ligands and metal ions, the stepwise methods shown here were effective with high selectivity. Notably, although both complexes contain labile metal ions, kinetic control was achieved by the appropriate designs of the systems. These results are expected to expand the structural variety and usability of metal complexes.

References

(1) MacDonnell, F. M.; Kim, M.-J.; Bodige, S. *Coord. Chem. Rev.* **1999**, *185–186*, 535–549. (2) Buchwalter, P.; Jacky, R.; Braunstein, P. *Chem. Rev.* **2015**, *115*, 28−126. (3) Meggers, E. *Chem. Eur. J.* **2010**, *16*, 752–758.