Design of Chiral Macrocyclic Complexes Based on trans-Chelation of *n:n* Metal–Bidentate *P,N-* or *N,N-*Ligands

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Chiral self-assembled macrocyclic Pd(II) and Cu(II) complexes with trans-chelation of n:n metal-bidentate P,N- and N,N-ligands have been designed toward the possibility of asymmetric Diels–Alder catalysis.

The design of chiral metallo-supramolecular systems has received considerable attention due to their wide application in the construction of metallocycles.¹ In particular, self-assembly techniques have been attractive as highly efficient methods for constructing supramolecular systems,^{1,2} due to the simplicity of just mixing the necessary organic compounds and some metal ions. However, there are few examples of the use of macrometallocycle as functionalized asymmetric catalysts by themselves without the further addition of some other active metal species.³ We report here the simple design of chiral self-assembled macrocyclic Pd(II) and Cu(II) complexes which require only the trans-chelation of *n:n* metal–bidentate *P,N-* and *N,N-*ligands toward asymmetric catalysis,⁴ in sharp contrast to single-metal catalysts based on cis-chelation or cis-fused self-assembled complexes by additives.

First, we prepared new *P*,*N*-ligands **1** and **3** bearing phosphine and oxazoline moieties in the *m*- or *p*-position,⁵ which can not undergo cis-chelation with a single metal ion. As expected, a 2:1 ratio of **1** or **3** and PdCl₂(MeCN)₂ in C₆D₆ at room temperature for 3–7 h gave trans 2:1 complex **2** or **4**, respectively, as a sole product (Eq 1). Complexations of PdCl₂(MeCN)₂ with new *N*,*N*-ligands **5** and **7** bearing pyridine and oxazoline moieties⁶ were also examined to provide corresponding 2:1 complexes (**6** and **8**), respectively (Eq 2). X-ray analysis of readily available single crystals of **4**, **6**, and **8** unambiguously showed the trans structures (See Supporting Information).



Further complexations of 2:1 complexes (2 and 4) bearing P,N-ligands with additional PdCl₂(MeCN)₂ were examined toward metallocycle formations. The four representative possible 2:2 complexes formed are shown in Figure 1 as a combination of [cis vs. trans] and [head-to-tail vs. head-to-head]. However,

the further addition of $PdCl_2(MeCN)_2$ to 2:1 complex gave 2:2 complex as a sole product in >99% yield (Figure 2). X-ray analysis of 9a and 10a shows the trans-chelating structures in a headto-tail style (See Supporting Information). Notably, 9a and 10a could be obtained directly in quantitative yields by simply mixing a 1:1 molar ratio of PdCl₂(MeCN)₂ and P,N-ligand (1 or 3) in benzene at 80 °C. Exchange of counter anions (Cl⁻) in 9a and 10a by silver salts proceeded in CD₃CN at room temperature for 30 min to give the corresponding OAc, OCOCF3, OTf, BF_4 , and SbF_6 complexes (Figure 2). Interestingly, we obtained a variety of complexes (9c-9f) except for acetate complex 9b via anion exchange from 9a, while only acetate complexes 10b and 10c were obtained from 10a. These behaviors partially might stem from the structural differences between twisted 9 and planar 10 (See Supporting Information). PdCl₂(MeCN)₂ was a good precursor for changing the counter anions in 2:2 complexes, since the direct synthesis of these anion-exchanged complexes from 1, 2, 3, or 4 could not proceed with Pd(OAc)₂, Pd-(OCOCF₃)₂, [(MeCN)₄Pd](BF₄)₂, and so on.



Figure 1. Possible 2:2 complexes.



Figure 2. Trans 2:2 complexes and their anion exchange reactions.

In sharp contrast to *P*,*N*-ligands, expected 2:2 Pd(II) complexes bearing *N*,*N*-ligand **5** could not be obtained under various conditions. For *N*,*N*-ligand **7**, however, a 1:1 molar ratio mixture of PdCl₂(MeCN)₂ and **8** in CDCl₃ at room temperature gave an unknown powdery complex in >99% yield (Eq 3). This new isomer was also obtained directly via complexation of **7** and PdCl₂(MeCN)₂ in 97% yield. Fortunately, X-ray analysis⁷ of this complex proved a new 4:4 complex **11** (Figure 3). Macrocyclic 4:4 complex **11** was a trans-chelating structure in a head-to-head style, and included a 28-membered ring. The shortest distances between Pd(II) centers was Pd(1)–Pd(2) = 4.854 Å with no obvious interactions with each other.



Figure 3. Preparation of macrocyclic trans 4:4 complex 11.

We next synthesized a new macrocyclic compound with the essential structure of 11 to achieve asymmetric catalysis. New bis(oxazolines) ligand 128 with PdCl₂(MeCN)₂ in CD₃CN gave the corresponding trans 2:2 complex 13 (Eq 4). The counter anions in 13 could be changed from Cl to $OCOCF_3$ to give 14. trans 2:2 Cu(II) complex 15 also could be obtained by using CuCl₂ in CH₂Cl₂. Interestingly, 15 had a twisted structure with unambiguous $\pi - \pi$ stacking between two benzene rings at 3.441 Å by X-ray analysis⁷ (Figure 4). Taking advantage of the Lewis-acidity of bis(oxazolines)-Cu(II) catalysts,⁹ we examined the asymmetric Diels-Alder reaction of acrolein with cyclopentadiene in the presence of 5 mol % of 15 (Table 1, Entry 2). The major endo product was obtained in 71% yield but with only 6% ee by macrocyclic Cu(II) catalyst 15, while Pd(II) complex 13 was quite ineffective (Entry 1). Cu(II) catalyst which was prepared in situ from 12 ($10 \mod \%$) and Cu(OTf)₂ ($10 \mod \%$) showed better enantioselectivity than 15 (Entry 3). Moreover, Cu(II) catalyst prepared from 20 mol % of 12 gave the product in 86% yield and 38% ee (Entry 4). Decompositions in dinuclear complexes as seen in X-ray analyses can not be excluded completely under catalysis conditions. However, the results also suggest the possibility of asymmetric catalysis by the self-assembled complexes, since monooxazoline ligand 16 which can not chelate to Cu(OTf)₂ gave racemic product with lower reactivity than macrocyclic complexes (Entry 5).



Figure 4. Preparation of trans 2:2 Pd complex 13 and Cu complex 15.

Table 1. Catalytic asymmetric Diels-Alder reaction

н	CHO + CHO (5 equiv.)	ı(II)		(2 <i>R</i>) H / H CHO + Z	СНО
Entry	Catalyst/mol %	Time /h	Yield /%	Endo:exo	Endo ee/% (config.)
1	13 (5)	5	11	86:14	0
2	15 (5)	5	71	80:20	6 (2 <i>R</i>)
3	12 (10)/Cu(OTf) ₂ (10)	25	82	80:20	23 (2R)
4	12 (20)/Cu(OTf) ₂ (10)	20	86	79:21	38 (2R)
5		20	46	80:20	0

In summary, we have provided simple synthesis of chiral self-assembled macrocyclic complexes with *n*:*n* metal–bidentate *P*,*N*- and *N*,*N*-ligands by intermolecular trans-chelation. Further investigations toward asymmetric catalysis with trans-macrocyclic complexes are now underway.

References and Notes

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