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Asymmetric Catalysis

Directed Orthogonal Self-Assembly of Homochiral Coordination Polymers for Heterogeneous Enantioselective Hydrogenation**

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In the area of heterogeneous asymmetric catalysis, a "self-supporting" strategy for chiral catalyst immobilization was developed recently based on the coordination assembly of a multitopic chiral ligand with catalytically active metal ions.[1] The resulting assemblies have been used as heterogeneous catalysts in a number of asymmetric synthetic reactions, and have demonstrated excellent enantioselectivity and reusability in favorable cases.[2–8] However, covalent bonding was commonly employed for the synthesis of the multitopic chiral ligand, which is often arduous and time-consuming. As a promising and practical alternative to covalent-bonding chemistry, noncovalent interactions (H-bonding and metal coordination) have found wide application in the assembly of numerous complex supramolecular systems.[9,10]

To explore such an approach for facile ligand generation, we envisaged that a bifunctional heteroditopic ligand bearing two orthogonal metal-ligating units might be used to prepare bimetallic assemblies with interesting catalytic properties upon sequential or one-pot reaction(s) with two different metals ions, either or both of which might be catalytically active (Figure 1). Herein, we report for the first time the design and synthesis of a chiral, rigid, heteroditopic ligand **1** that contains a 2,2′:6′,2″-terpyridine (tpy) unit[11] and Feringa's MonoPhos[12] at its ends (Scheme 1), and its selective coordination with Fe^{II} and Rh^{I} ions for the programmed assembly of a class of chiral bimetallic self-supported catalysts. In addition, application of the complexes as recyclable heterogeneous chiral catalysts in the asymmetric hydrogenation of α-dehydroamino acid, enamide, and itaconic acid derivatives shows very high activity (turnover frequency (TOF) up to 4560 h^{-1}) and excellent enantioselectivity (90–97% *ee*).

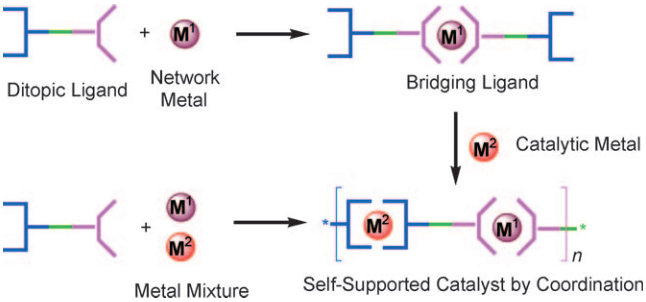
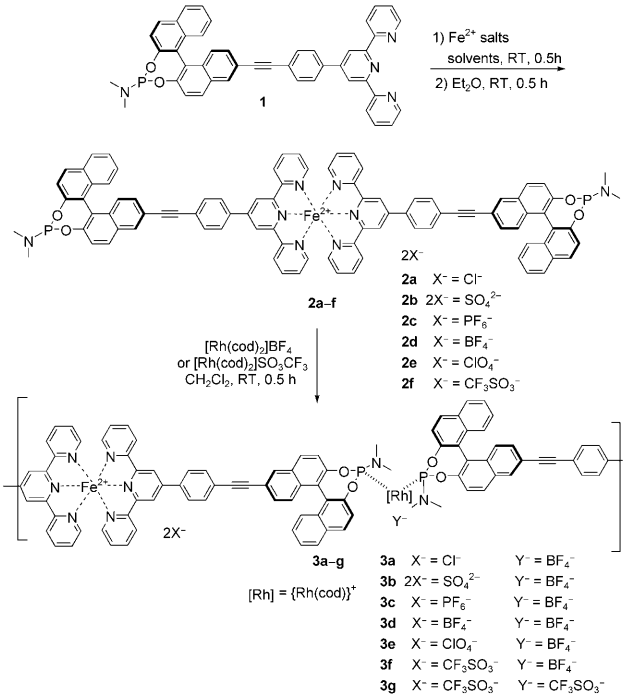


Figure 1. Synthesis of a class of self-supported catalysts through orthogonal coordination of two different metal ions with a single ditopic ligand.



Scheme 1. Synthesis of homochiral self-supported heterobimetallic catalysts **3a–g** through stepwise metal coordination reactions. cod = 1,5-cyclooctadiene.

Tpy is a well-known tridentate ligand that can form stable complexes with a range of metal ions,[13] and is widely utilized as a building block in supramolecular chemistry.[14] On the other hand, MonoPhos is a chiral ligand that is well established in asymmetric catalysis; in particular, its rhodium(I) complex has been shown to catalyze the hydrogenation of some olefins with excellent efficiency.[15] Importantly, incorporation of the soft MonoPhos moiety and the

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harder tpy unit into **1** should allow for selective coordination of the phosphine and tpy domains by discrete metal species, a property valuable for exemplification of the aforementioned strategy.

Ligand **1** was prepared in good overall yield (60%) through a copper-free Sonogashira coupling reaction of 4′-(4-bromophenyl)-2,2′:6′,2′′-terpyridine[16] and bis(methoxymethyl)-protected (*S*)-6-ethynyl-1,1′-binaphthyl-2,2′-diol[5a] with $Ph_2PNiPr_2/Pd(OAc)_2$ as the catalyst,[17] followed by acidic deprotection and further reaction with hexamethylphosphorous triamide (HMPT) in toluene heated at reflux (see the Supporting Information). While many metal ions could have been chosen as the "glue" for linking two ligand **1** molecules via formation of the $[M(tpy)_2]^{n+}$ unit, Fe^{II} was used herein owing to its strong binding affinity towards tpy,[18] low toxicity, cheap availability, and wide use in tpy-containing supramolecular systems.[19]

Thus, treatment of a dichloromethane solution of **1** with 0.5 equiv of an Fe^{II} salt bearing different counterions (Cl^-, SO_4^{2-}, PF_6^-, ClO_4^-, BF_4^-, or $SO_3CF_3^-$) immediately afforded a dark blue-violet solution or suspension (Scheme 1). Further addition of diethyl ether resulted in the gradual precipitation of Fe^{II}-bridged ligands **2a**–**f** as violet-purple powders, which were characterized by UV/Vis and IR spectroscopy, elemental analyses, and/or HRMS. UV/Vis spectra clearly show an overall similar molecular structure for **2a**–**f** (see the Supporting Information), wherein the Fe^{II} ion binds two tpy moieties from two ligand **1** molecules while leaving the MonoPhos sites untouched, thus leading to the effective formation of $[Fe(tpy)_2]^{2+}$-expanded bis-MonoPhos ligands with a chemical reactivity expected to resemble that of MonoPhos.[20] Indeed, self-assembly of **2a**–**f** with a rhodium salt in dichloromethane immediately affords **3a**–**g** as violet-purple precipitates having compositions consistent with the expected structures (Scheme 1). Scanning electron microscopy (SEM) images showed that solids **3a**–**g** are composed of micrometer-sized particles (see Figure 2a), while powder X-ray diffraction patterns indicated that they are amorphous (see the Supporting Information, Figure S2).

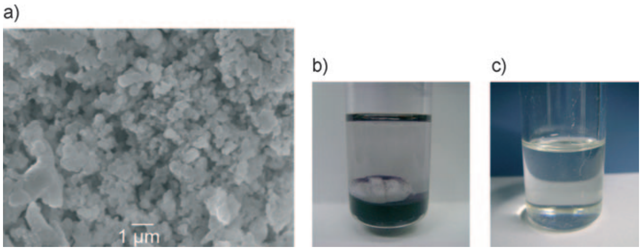
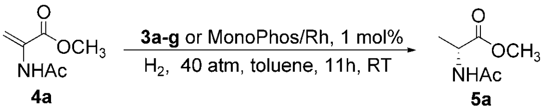


Figure 2. a) SEM image of **3g** (scale bar: 1 µm); b) catalyst **3g** in toluene (solid at the bottom of the reactor); c) supernatant of the reaction mixture filtered after hydrogenation of **4c** using catalyst **3g**.

The Rh^I-containing solids **3** were found to be completely insoluble in toluene (see Figure 2b), thus fulfilling one of the prerequisites for heterogeneous catalysis. Accordingly, **3a**–**g** were initially examined in the hydrogenation of methyl α-acetamidoacrylate (**4a**), under a catalyst loading of 1 mol% in toluene at a hydrogen pressure of 40 atm (Table 1). Encouraging results were obtained using catalysts bearing weakly coordinating anions (**3c**–**g**), wherein the enantioselectivity for **5a** (94–97% *ee*) was comparable to that of their homogeneous counterpart MonoPhos/Rh (97% *ee*) under otherwise identical conditions (Table 1).

Table 1: Enantioselective hydrogenation of compound **4a** under the catalysis of **3a**–**g** or MonoPhos/Rh.[a]



Entry	Catalyst	Conv. [%][b]	*ee* [%][c]
1	**3a**	0	–
2	**3b**	> 99	88
3	**3c**	> 99	97
4	**3d**	> 99	94
5	**3e**	> 99	96
6	**3f**	> 99	96
7	**3g**[d]	> 99	95
8	MonoPhos/Rh[e]	> 99	97

[a] Conditions: [**4a**] = 1.0 M, [**3**] = 1 mol% (with respect to **4a**), $T = 298$ K, $P(H_2) = 40$ atm, $t = 11$ h, toluene solvent. [b] Determined by ^1H NMR spectroscopy. [c] Determined by GC on a Supelco BETA-DEX 120 column. [d] $t = 9$ h. [e] Molar ratio of MonoPhos/Rh = 2:1, $t = 2$ h.

However, catalysts **3a** and **3b** prepared from chloride and sulfate salts of Fe^{II}, respectively, are the exception. While under the catalysis of **3b** full conversion could still be reached with a slightly lowered *ee* value (88%) of **5a** (Table 1, entry 2), no reaction occurred at all after 11 h at room temperature in the case of **3a** (Table 1, entry 1). This is not surprising, considering that the anions in **2a**–**f** are situated at the outer coordination sphere of these $[Fe(tpy)_2]^{2+}(X^-)_2$-type complexes, which are well known to undergo facile anion exchange when another electrolyte is present in the solution. It is likely that during the assembling of **3a**, Cl^- ions in **2a** interchange rapidly with BF_4^- ions in $[Rh(cod)_2]BF_4$ to give **3a,** wherein the Cl^- anions stay nearby or bond directly with the Rh^I centers by virtue of higher affinity, thus leading to inhibition of the catalysis.[21] Such an anionic scrambling may also occur in catalysts **3b**–**g**, and lead to a variation in their chiral induction capabilities, albeit the weakly or noncoordinating nature of the anions does not prohibit the catalysis under the somewhat forcing conditions.

A shift to milder conditions clearly revealed that the anions in **3** exert influence on the catalytic activity as well. Compounds **3c**–**e** and **3g** were effective in the catalytic hydrogenation of **4a** even under an ambient pressure of hydrogen, conducted in a Schlenk tube with a hydrogen gas balloon. The reactions using catalysts **3c**–**e**, **3g**, and their homogeneous counterpart $(MonoPhos)_2/Rh^I$ were monitored by GC analysis, and the reaction profiles are shown in Figure 3. While **3d** and **3e** exhibited a reactivity higher than that of $(MonoPhos)_2/Rh^I$, the reactions with **3c** and **3g** were somewhat slower. It is conceivable that such an activity difference may reflect the subtle variation in catalyst struc-

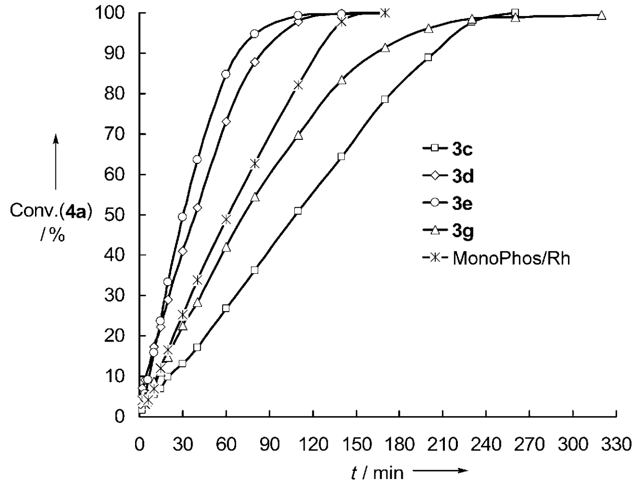


Figure 3. Reaction profiles for the asymmetric hydrogenation of **4a** catalyzed by **3c–e**, **3g**, and $(MonoPhos)_2/Rh^I$. Conditions: [**4a**] = 1.0 M, [**3**] = 1 mol% (with respect to **4a**), $P(H_2) = 1$ atm, $T = 298$ K, toluene = 3 mL.

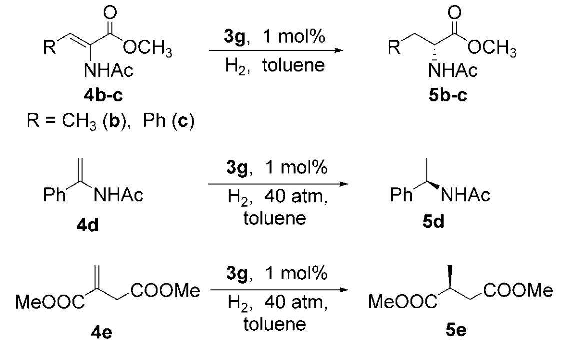
tures, as a result of using different ferrous salts in catalyst preparation. Further testing of **3e** in the same reaction at a catalyst loading of 0.1 mol% under 40 atm of hydrogen resulted in a 76% conversion of **4a** after 10 min, which amounts to a TOF value of 4560 h^{-1} for **3e**.[22] Remarkably, in all cases **5a** was obtained with excellent *ee* values (94–97%).

As shown in Figure 2b and c, the catalysts were insoluble in the reaction mixture and could be easily separated from the solution by filtration upon completion of the reaction. Furthermore, filtration tests using **3e** and **3g** also unequivocally confirmed the heterogeneous nature of the catalysis (see the Supporting Information). Consequently, catalysts **3e** and **3g** were examined for reuse in the hydrogenation of **4a**. Upon completion of each cycle of reaction, the filtration-recovered catalyst was washed with toluene and recharged with the substrate, solvent, and hydrogen for the next run. As can be seen from Table S2 in the Supporting Information, both catalysts could be reused for more than ten cycles without significant loss in the conversion or enantioselectivity. Determination of reaction profiles with recycled **3e** clearly indicated that no loss of activity was observed in the course of catalyst reuse (see the Supporting Information, Figure S3). In particular, catalyst **3g** was used for a total of 15 runs with only a slight deterioration in *ee* values (95–91%).

For each run of the catalyst recycling with **3e**, the product solution was analyzed by inductively coupled plasma–atomic emission spectroscopy (ICP-AES) for potential rhodium and iron leaching (see the Supporting Information). Except for the first run in which the Rh loss amounted to 1.7% (18 ppm) of the total rhodium initially used, no further Rh loss was detected (< 1 ppm) in subsequent recycling runs. The Fe leaching was less regular, however, ranging from 0.8% (9 ppm) for the first run to less than 1 ppm for the 12th run. Considering the long-lasting reactivity and enantioselectivity in the catalyst reuse experiments, we proposed that the initial Rh leaching could have been caused by low-molecular-weight Rh species entrapped in the solid matrix. Since most of the weakly bound rhodium was removed during the first use of the catalyst, the Rh leaching in subsequent runs was negligible.

Catalyst **3g** was also highly enantioselective in the heterogeneous hydrogenation of several other olefinic substrates, including β-methyl- or phenyl-substituted α-dehydroamino acid esters **4b** and **4c**, enamide **4d**, and itaconic acid ester **4e**, which afforded the corresponding products in excellent *ee* values (90–96%) that were comparable or even superior to those obtained with their homogeneous counterpart $(MonoPhos)_2/Rh^I$ under otherwise identical conditions (Table 2).

Table 2: Asymmetric hydrogenation of dehydroamino acid, enamide, and itaconic acid derivatives using catalyst **3g**.[a]



Entry	Substrate	*t* [h]	Conv. [%][b]	*ee* [%][c]
1	**4b**	2	> 99	96 (96)
2[d]	**4c**	20	> 99	94 (56)
3	**4d**	2	> 99	95 (90)
4	**4e**	30	> 99	90 (69)

[a] The conditions were the same as those in Table 1 unless otherwise specified. [b] Determined by ^1H NMR spectroscopy. [c] The *ee* values of **5b** and **5e** were determined by GC on a Supelco GAMMA-DEX 225 column, whereas those of **5c** and **5d** were determined by HPLC on a Chiralcel AD column. In parentheses are the *ee* values obtained using $(MonoPhos)_2/Rh$ under otherwise identical conditions. [d] [**4c**] = 0.2 M, [**3g**] = 1 mol% (with respect to **4c**).

Finally, one-pot assembly of ligand **1**, $[Rh(cod)_2]OTf$, and an Fe^{II} salt ($[Fe(CH_3CN)_2](OTf)_2$ or $Fe(ClO_4)_2 \cdot 6H_2O$) in a molar ratio of 2:1:1 in CH_2Cl_2 at room temperature for 7 h also resulted in the formation of a purple-blue mixture. Upon removal of the solvent, a solid was obtained that was insoluble in toluene and effective in the hydrogenation of **4a** (95 and > 99% conversions in 2 h for the two Fe^{II} salts, respectively), and gave **5a** with excellent *ee* values (both 95%) under a hydrogen pressure of 40 atm.

In summary, a strategy of directed self-assembly of two different metallic ions (Fe^{II} and Rh^I) with a single heteroditopic chiral ligand through in situ orthogonal coordination has been successfully applied in the generation of a new class of heterogeneous chiral catalysts. This strategy has significantly simplified the complexity associated with the catalyst synthesis, and the assembled heterogeneous catalysts were found to be highly efficient, enantioselective, and reusable in the catalysis of the asymmetric hydrogenation of a variety of functionalized olefin derivatives. The present new approach for heterogenization of chiral catalysts will definitely stimulate future research on the facile and rapid creation of chiral catalyst systems on the basis of orthogonal supramolecular interactions.

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[22] For comparison, hydrogenation of the same substrate **4a** in the presence of 0.1 mol % covalently linked tripod self-supported catalyst prepared in this laboratory[8e] was also carried out under the same experimental conditions, and afforded comparable enantioselectivity (98 % *ee*) and activity (with a TOF value of ca. 5000 h^{-1}).