Phosphine-free chiral metal catalysts for highly effective asymmetric catalytic hydrogenation

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In addition to the brilliant chiral phosphorus metal catalysts, chiral phosphine-free metal complexes find increasing application as catalysts for asymmetric hydrogenation. In this account, two types of chiral phosphine-free ligands, N-heterocyclic carbene-based *C*,*N*-ligands and diamine-based *N*,*N*-ligands, in the homogeneous asymmetric hydrogenation of prochiral ketones, imines and quinolines are reviewed.

Introduction

Asymmetric catalysis is the most advanced frontier in recent years as a result of the continuously incremental need for fine chemicals from pharmaceutical, food, cosmetic and chemical industries.[1] Asymmetric hydrogenations, which offer a large quantity of chiral compounds such as chiral alcohol and amine derivatives with the use of a minimal amount of chiral metal catalyst, play more and more important roles in asymmetric catalysis. Chiral phosphorus-containing transition metal complexes have become the dominant choice of catalysts for asymmetric hydrogenation since the homogeneous asymmetric hydrogenation was initiated by Knowles[2] and Horner[3] in the late 1960s.

Although phosphorous metal complexes have achieved great success in asymmetric hydrogenation of unsaturated C=C, C=O, and C=N compounds,[4] some drawbacks still remained. First, most chiral phosphorus-containing catalysts are air-sensitive. The related reactions often need special manipulation with extra equipment in the presence of an inert atmosphere. The other one is the complicated synthetic route to most of the phosphine ligands. The synthesis and modifications of these ligands are often difficult and time-consuming processes. In addition, there are still some limitations to the substrate scope of the phosphorus-containing complex-catalyzed asymmetric hydrogenation. For example, unfunctionalized olefins, imines, and heteroaromatic compounds are all challenging substrates for such a transformation. So, developing molecular oxygen tolerant, phosphine-free ligands for the application of asymmetric hydrogenation is an alternative promising objective in asymmetric catalysis.

To date, three types of phosphine-free chiral ligands and their metal catalysts for asymmetric hydrogenations have been developed. They are a) chiral metallocenes and chiral organolanthanides; b) *N*-heterocyclic carbene (NHC)-containing ligands and their iridium catalysts; and c) chiral diamine ligands and their ruthenium, rhodium and iridium catalysts. The first-type catalysts were reported as early as the 1980s, and have shown excellent enantioselectivities in the hydrogenation of unfunctionalized 1,1-disubstituted, trisubstituted olefins and imines.[4b,5] However, such

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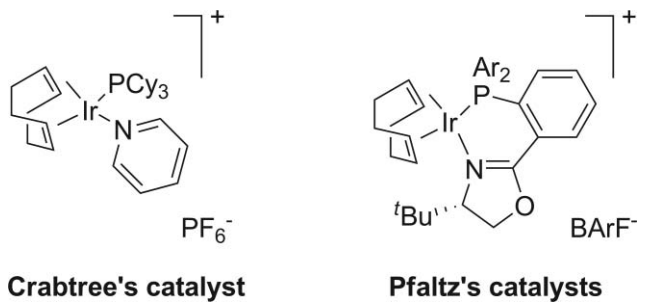
kind of phosphine-free catalysts also suffered from drawback of the extreme air sensitiveness, which might be the reason that limited their widespread applications in asymmetric synthesis. In this review, only the applications of *C*,*N*-ligands and *N*,*N*-ligands in homogeneous asymmetric hydrogenation with molecular hydrogen will be included.

NHC-based chiral ligands and their applications in asymmetric hydrogenation of prochiral olefins

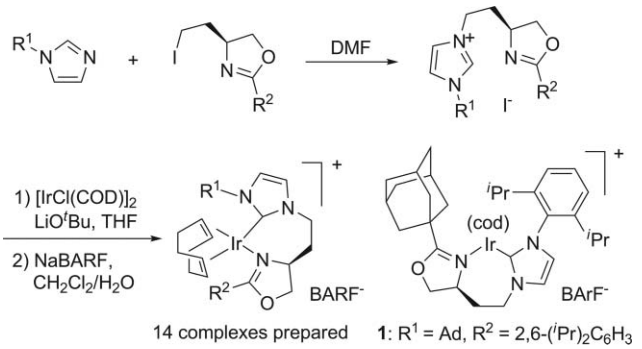
The chemistry of N-heterocyclic carbenes (NHCs) has developed rapidly since the first synthesis of a stable carbene species by Arduengo *et al.* in 1991.[6] Electron-rich NHCs, including those based on the imidazolylidenes, imidazolinylidenes and 1,2,4-triazolylidiene frameworks, have emerged as useful ligands for constructing organometallic catalysts.[7,8] They are often compared to phosphines because of their strong σ-donating and weak π-accepting properties, but complexes containing these carbene ligands tend to be more stable than their phosphine analogues. These carbene complexes have been successfully used in many catalytic transformations, particularly metathesis and C–C and C-heteroatom coupling reactions. Most recently, NHCs have also proven to be highly efficient nucleophilic organocatalysts for asymmetric catalysis.[9] However, the NHC-based catalysts for asymmetric hydrogenation are less studied.

Based on the successful use of Crabtree's catalyst in the hydrogenation of unfunctionalized alkenes,[10] Pfaltz and co-workers recently recognized that chiral phosphine-oxazoline ligands are similar to *cis*-disposed, monodentate, pyridine/phosphine ligand combinations (Scheme 1).[11] Then, they developed a new kind of chiral *N*,*P*-ligand-containing iridium catalysts, which achieved great success in the more challenging asymmetric hydrogenation of unfunctionalized alkenes. As NHCs are frequently regarded as the mimics of phosphines, they are suitable components for the construction of *C*,*N*-analogues of Pfaltz's catalysts.[12]



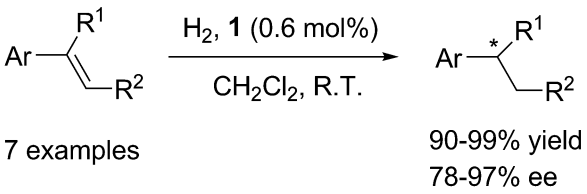
Scheme 1 *N*,*P*-Ir catalysts used in the homogeneous hydrogenation of unfunctionalized alkenes.

The first example of highly effective asymmetric hydrogenation of trisubstituted aryl alkenes catalyzed by NHC–oxazoline ligands was published in 2001 by Burgess group.[13] NHC-oxazoline bidentate ligands were modularly synthesized through a large library of imidazolium salts, which are easily handled, robust, and air-stable materials obtained from small libraries of oxazoline electrophiles and imidazoles (Scheme 2). Then, they made use of these iridium catalysts bearing NHC-oxazoline ligand in the asymmetric hydrogenation of unfunctionalized aryl alkenes. Excellent enantioselectivities (up to 98% ee) were achieved by using iridium



Scheme 2 Synthesis of iridium catalysts bearing NHC-oxazoline ligand.

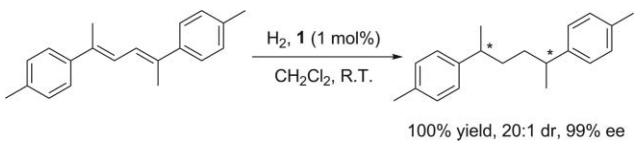
catalyst **1** for the trisubstituted olefins (Scheme 3), while low ee was observed when a terminal olefin was applied. The studies of pressure dependence revealed that the reactions proceeded well when only 1 bar of hydrogen was used in approximately 2 h. These results are comparable with those obtained with chiral phosphine-oxazolines using similar substrates.



Scheme 3 Asymmetric hydrogenation of trisubstituted alkenes with catalyst **1**.

Later, Burgess and co-workers carried out systematic studies with their outstanding iridium catalyst **1** on extending the reaction from simple trisubstituted alkene substrates to aryl-substituted dienes,[14] and to the synthesis of a number of privileged chirons that should be valuable for many natural products such as deoxypolyketides.[15]

In the much more challenging asymmetric hydrogenation of three types of symmetrical aryl-substituted dienes, up to 20 : 1 diastereoselectivity and 99% ee were achieved (Scheme 4).[14] Hydrogenation of (*E*,*E*)-1,4-diaryl-1,4-dimethyl-1,3-dienes gave the best performance in terms of reaction yield and stereoselectivity. The enantioselectivities of the hydrogenation of (*E*,*E*)-1,4-diaryl-2,3-dimethylbuta-1,3-dienes were excellent (97~99% ee) but the yields were moderate because of the formation of the double bond migration by-products. The dienes containing 1,1-disubstituted alkene fragments seemed to be difficult to generate high stereoselective products, and the *meso* product was formed in preference to the enantiomeric product. The activities of the iridium catalyst **1** obtained in this study are better than those obtained from Crabtree's catalyst. Further mechanistic study of the hydrogenation of dienes by an investigation of the reaction kinetics together with density functional theory (DFT)

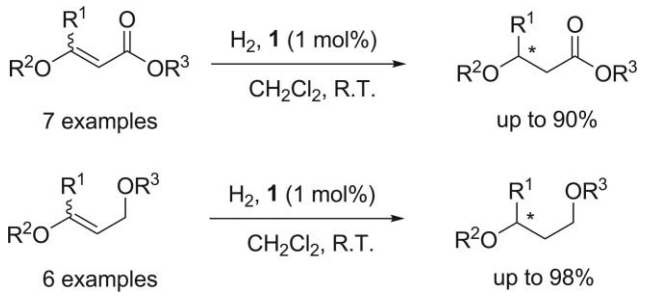


Scheme 4 Asymmetric hydrogenation of a diene with catalyst **1**.

computation revealed that an Ir(III)/Ir(V) pathway is most likely involved.[14c]

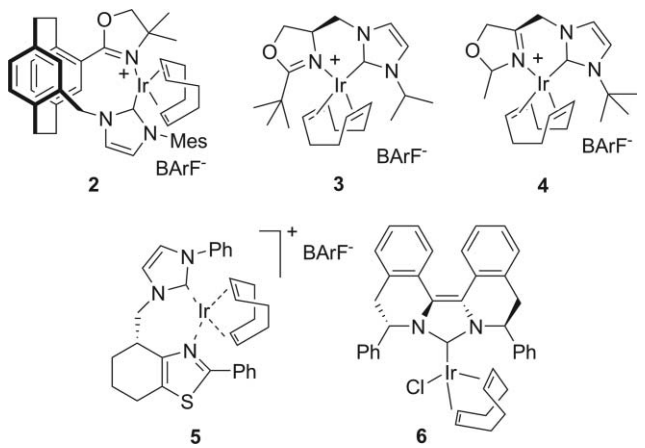
After the development of efficient methodology for the asymmetric hydrogenation of unfunctionalized alkenes and dienes, Burgess and co-workers explored its application to the synthesis of a number of useful chirons, including 1,3-dimethyl-,[15a–c] 1,3-hydroxymethyl-,[15d] 1,2-hydroxymethyl-[15e] and vicinal dimethyl-[15f] synthons, which are usually difficult to obtain with the diphosphine-containing metal catalysts. In most cases, modest to high stereoselectivities (up to 20 : 1 dr) were achieved, and the hydrogenations were found to be catalyst controlled. In addition, several natural products such as (*S*,*R*,*R*,*S*,*R*,*S*)-4,6,8,10,16,18-hexamethyldocosane,[15c] (–)-lasiol and (+)-kalkitoxin[15f] were successfully synthesized by using the NHC-oxazoline catalyst.

Most recently, Burgess and co-workers employed their NHC-oxazoline iridium catalyst to the asymmetric hydrogenation of vinyl ethers (Scheme 5), which are challenging substrates for *P*,*N*-Ir catalysts. Excellent enantiomeric excesses were obtained (ester substrates: up to 90% ee, alcohol substrates: up to 98% ee).[16]



Scheme 5 Asymmetric hydrogenation of vinyl ethers with catalyst **1**.

Besides the excellent work of Burgess's group on asymmetric hydrogenation catalyzed by NHC-containing iridium catalysts, Bolm's, Pfaltz's, Andersson's and Herrmann's research groups made their contributions by using their own NHC-containing catalysts **2** (the first planar chiral carbene-metal complex),[17] **3** and **4** (six-membered chelate ring catalyst),[18] **5**,[19] and monodentate catalyst **6**[20] for the asymmetric hydrogenation of olefins (Scheme 6). Moderate to good enantioselectivities were obtained.

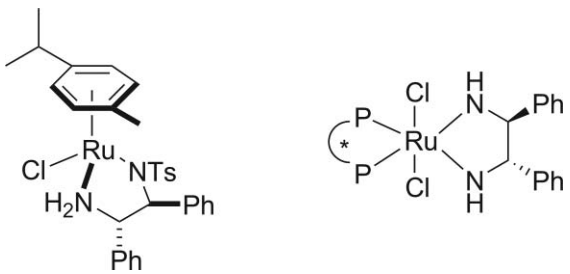


Scheme 6 NHC-containing iridium catalysts used in asymmetric hydrogenation of olefins.

Chiral diamine bidentate ligands and their applications in asymmetric hydrogenation

Nitrogen-containing ligands were rarely used in the 1970s and the 1980s, although some heterogeneous nitrogen-containing chiral systems were applied in asymmetric catalysis.[21] Compared to phosphines, nitrogen-containing ligands present several distinct advantages including high air-stability, easy availability and tailor-made modifications. From the beginning of the 1990s, nitrogen-containing ligands have been attracting more attention in the field of asymmetric catalysis.[22]

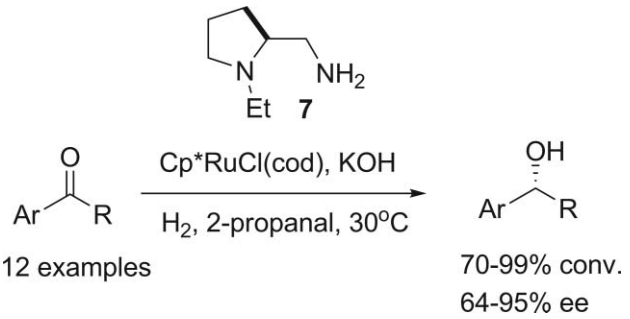
Chiral diamine ligands have been used in the asymmetric transfer hydrogenation more frequently and more successfully than in hydrogenation with molecular hydrogen.[23] The most successful application of chiral diamine bidentate ligand TsDPEN (Ts-DPEN = *N*-(p-toluenesulfony1)-1,2-diphenylethylenediamine) in the Ru-catalyzed asymmetric transfer hydrogenation of simple aromatic ketones was reported by Noyori and co-workers as early as in 1995.[24] Quickly following this primary discovery, chiral TsDPEN found itself powerful ligand in the transfer hydrogenation of imines too.[25] The diamine ligands were also applicable in forming chiral Ru complexes $RuCl_2$(chiral diphosphine)(chiral 1,2-diamine) (Scheme 7), which have proven to be powerful catalysts for asymmetric hydrogenation of a variety of unfunctionalized prochiral ketones with excellent reactivity and enantioselectivity.[26] However, no successful examples of asymmetric hydrogenation were reported by using ligands containing only nitrogen atoms until the beginning of the 21st century.



Scheme 7 Diamine-containing Ru catalysts used in asymmetric reduction of simple aromatic ketones.

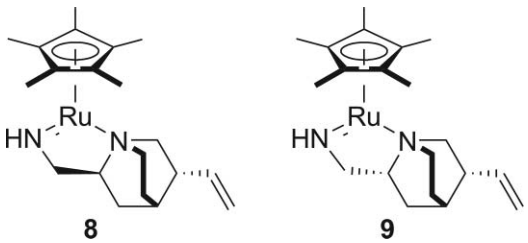
Enantioselective hydrogenation of unfunctionalized ketones

Catalytic asymmetric reduction of prochiral unfunctionalized ketones has been a powerful method to prepare enantiomerically pure secondary alcohols, which are key structural elements in a large number of pharmaceutical products.[1,4] The first publication on phosphine-free chiral transition metal-catalyzed highly effective asymmetric hydrogenation of carbonyl compounds was presented by Ikariya and co-workers in 2001.[27] Chiral diamine ligands **7** derived from L-proline showed good to excellent enantioselectivity (64–95% ee) in the asymmetric hydrogenation of various alkyl aryl ketones (Scheme 8). It was found that the solvent 2-propanol participated in the activation of H_2 based on a metal/NH bifunctional effect to facilitate the hydrogenation. This pioneering work opened up a new path for the asymmetric hydrogenation of simple aromatic ketones.

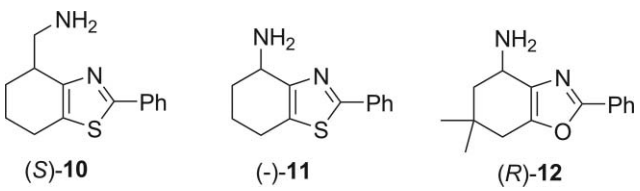


Scheme 8 Asymmetric hydrogenation of ketones with chiral diamine–containing Ru catalyst.

On the basis of Ikariya's finding, Anderson and co-workers recently developed two new RuCp*-1,2-diamine complexes (Scheme 9), derived from the commercially available chiral quincorine-amine and quincoridine-amine.[28a] The former complex was found to be highly active in the hydrogenation of aryl ketones. Modest to good enantioselectivities (44–90% ee) were furnished for most substrates investigated, while the latter one gave much low enantioselectivity with opposite stereoselectivity. A detailed mechanistic investigation demonstrated that the more basic quinuclidine-based complex is approximately 24 times more reactive than Ikariya's catalyst. Similar to Ikariya's finding, the results obtained from computational studies revealed a significantly lower activation barrier for the alcohol-mediated split of dihydrogen, as compared to the nonalcohol-mediated process. Two years later, the same research group developed five- and six-membered chelate chiral thiazole- and oxazole-containing diamines (Scheme 10) for the Ru-catalyzed asymmetric hydrogenation of ketones, while low enantiomeric excesses were obtained but with high activities.[28b]

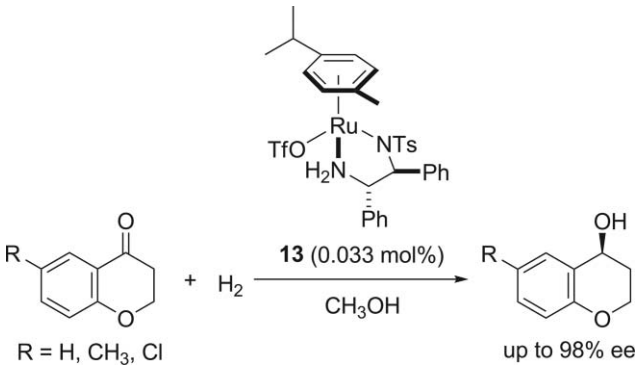


Scheme 9 Ruthenium catalysts derived from quincorine-amine and quincoridine-amine.



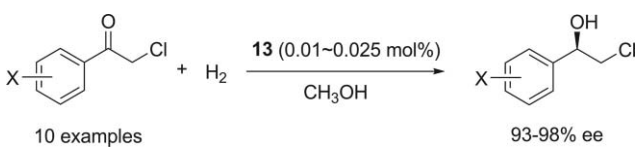
Scheme 10 Chiral thiazole- and oxazole-containing diamine ligands used in the preparation of ruthenium catalysts.

Noyori and co-workers have made important contributions in this area. In 2006, based on their long-term mechanistic investigation, they discovered an effective ruthenium catalyst chiral η^6-arene/Ts-DPEN-Ru(II) complex for asymmetric hydrogenation of simple ketones,[29] which was known as an excellent catalyst only for transfer hydrogenation. It was found that the hydrogenation with such Ru catalyst could be realized simply by switching the conditions from basic to acidic. In the asymmetric hydrogenation of the base-sensitive ketone 4-chromanone, the chiral Ru triflate complex showed high efficiency in methanol under mild conditions, giving the reduced product with 100% yield and 97% ee (Scheme 11). Further mechanistic study demonstrated that such hydrogenation proceeds through a metal–ligand bifunctional mechanism,[30] similar to that of the transfer hydrogenation, and the high catalytic efficiency relies on the facile ionization of the Ru triflate complex in methanol. Most recently, Fang and co-workers investigated the dihydrogen activation process in this Ru-catalyzed hydrogenation of ketones employing density functional theory (DFT) calculations. The results revealed that, while in acidic conditions, the participation of TfO^- in hydrogenation significantly decreased the energy barrier, and TfO^- assisted the deprotonation of protonated η^6-H_2–Ru complex to generate the catalytically active RuH species.[31]

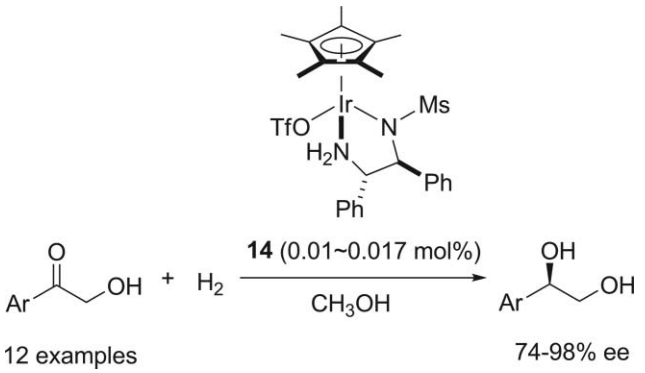


Scheme 11 Asymmetric hydrogenation of 4-chromanones with TsDPEN-Ru catalysts.

Encouraged by these remarkable results, Ohkuma and co-workers further employed such chiral Ru triflate catalysts for the asymmetric hydrogenation of α-chloro-aromatic ketones, which are highly base-labile substrates and had not been hydrogenated with molecular hydrogen before. Hydrogenation of various ketones including a phenolic hydroxyl group-containing substrate proceeded smoothly even on a 206 g scale in methanol, giving chiral chlorohydrins with quantitative yields and excellent enantioselectivities (up to 98% ee) (Scheme 12).[32a] Shortly after this report, they described an iridium triflate complex derived from the same diamine ligand TsDPEN for asymmetric hydrogenation of α-hydroxy aromatic ketones (Scheme 13).[32b] It was found that the reaction could be conducted with a substrate-to-catalyst molar ratio as high as 6000 under 10 atm of H_2, affording various synthetically useful chiral 1-aryl-1,2-ethanediols and the heteroaryl analogues with quantitative yields and excellent enantioselectivities (up to



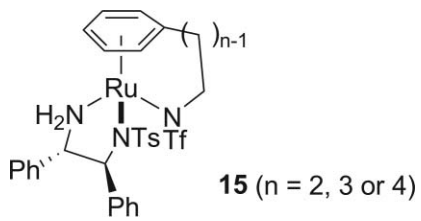
Scheme 12 Asymmetric hydrogenation of α-chloro-aromatic ketones with TsDPEN-Ru catalysts.



Scheme 13 Asymmetric hydrogenation of α-hydroxy aromatic ketones with MsDPEN-Ir catalysts.

99% ee). These results are better than those obtained with chiral diphosphine-containing metal catalysts.

Most recently, Ikariya and co-workers developed novel bifunctional Ru catalysts bearing a triflylamine (NTf) unit linked to a η^6–arene ring for the asymmetric hydrogenation of aromatic ketones (Scheme 14).[33] It was found that a subtle change in the structure of the tether had a significant effect on the catalyst performance. Excellent enantioselectivities (up to 98% ee) were achieved by using the tethered complex with a C_4 side chain.

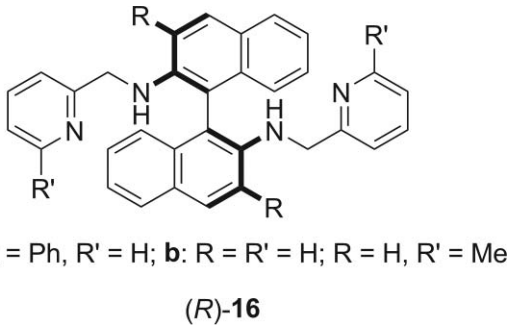


Scheme 14 Triflylamide-tethered arene-Ru(Tsdpen) complexes used in the asymmetric hydrogenation of aromatic ketones.

In addition, several research groups have tried to use metal catalysts generated *in situ* by simply mixing chiral bidentate or tetradentate amine-based ligands with metal (Ir or Ru) precursors for the asymmetric hydrogenation of ketones.[33–35] Very low reactivities and enantioselectivities were often observed.[34,35] One of the most promising example was reported recently by Kitamura and co-workers.[36] Following Noyori's leading concept of a donor–acceptor bifunctional catalyst,[30] they designed and synthesized a tetradentate sp^2N/sp^3N-based ligand bearing C_2-symmetry chiral binaphthyl backbone (Scheme 15). This ligand showed moderate to excellent enantioselectivities (up to 99% ee) in the Ru-catalyzed asymmetric hydrogenation of aromatic ketones.

Enantioselective hydrogenation of imines

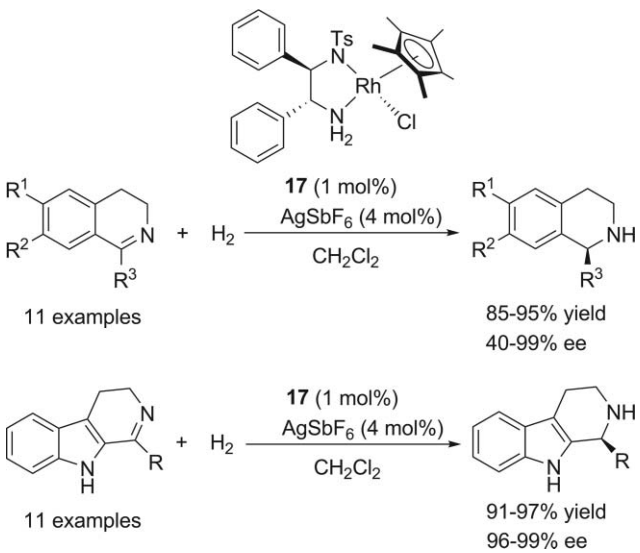
Catalytic asymmetric hydrogenation of imines has drawn much attention recently, since it provides one of the most direct and efficient approaches for attaining optically active amines, which are widely used in pharmaceutical and agrochemical substances.[4] Although great efforts have been made in the last few decades, this area remains a major challenge, in contrast to the relative maturity of asymmetric hydrogenation of olefins or ketones. In contrast to chiral phosphines, the diamine ligands bearing no phosphorus atoms are often recognized to be ineffective in the



Scheme 15 Chiral tetradentate amine-based ligands used in the Ru-catalyzed asymmetric hydrogenation of aromatic ketones.

asymmetric hydrogenation of imine derivatives. This could be due to competitive chelation to the center metal between the amine-based ligand and the amine products, formed after reduction of the corresponding imines. In 2008, Fan's and Xiao's groups independently reported that phosphine-free cationic Ru and Rh complexes bearing chiral diamine ligand TsDPEN were highly effective catalysts for the asymmetric hydrogenation of quinoline derivatives and prochiral imines for the first time, respectively.[37,38]

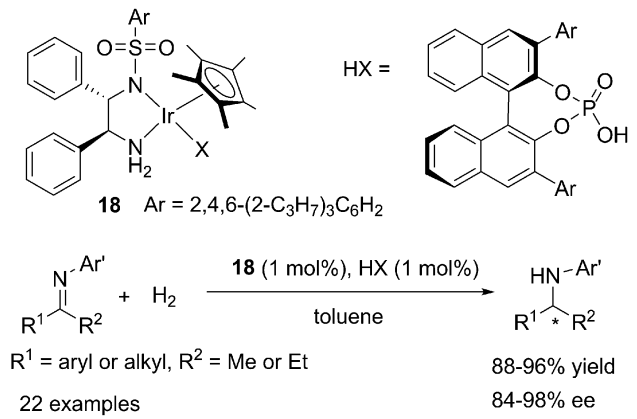
The Rh-TsDPEN complex is a well-known catalyst for the asymmetric transfer hydrogenation of aromatic ketones and imines.[39] Xiao and co-workers successfully realized the asymmetric hydrogenation of cyclic imines by replacing the complex anion chloride with a bulky noncoordinating SbF_6^-.[38] Up to 99% ee and 97% yield were achieved for a range of cyclic imines by the use of η^5-arene-Rh-TsDPEN chloride with the addition of $AgSbF_6$ at ambient temperature(Scheme 16). The unprecedented positive effect of silver salts was also observed by Ikariya in the asymmetric hydrogenation of acyclic imines with similar catalyst systems, but only moderate enantioselective inductions were observed.[40]



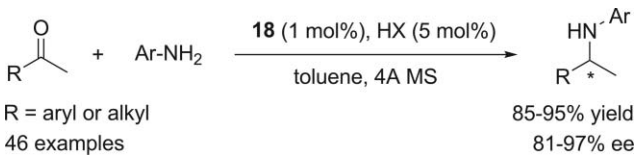
Scheme 16 Asymmetric hydrogenation of cyclic imines with cationic Rh-TsDPEN catalyst.

In contrast to the cyclic imines, acyclic imines proved to be more problematic substrates probably due to the E/Z isomerization.[4,41] Recently, highly enantioselective transfer hydrogenation with Hantzsch ester of acyclic imines or imines *in situ* generated

from ketones and amines was reported by using organocatalysts chiral phosphoric acids.[42] On the basis of these findings and their own results in the reduction of cyclic imines, Xiao and co-workers developed an efficient Ir catalyst featuring a chiral diamine ligand as well as a chiral phosphate counteranion for asymmetric hydrogenation of acyclic imines. It was found that the chiral phosphate anion[43] played a very important role in achieving high stereoselectivity if in a matched manner, and the combination of both the anion and the cation bearing bulky substitutions gave the best results. Additionally, a catalytic amount of the corresponding chiral phosphoric acid was added to improve the yield. Reactions with various imines including N-alkyl ketimines were demonstrated to be highly efficient with the yields between 88–96% and the enantiomeric excesses from 84% to 98% (Scheme 17).[44a] Encouraged by these remarkable results, they further accomplished the cascade asymmetric reductive amination of ketones with anilines using molecular hydrogen.[44b] Excellent yields and enantioselectivities were achieved over a wide range of substrates including some more challenging substrates like aryl ethyl and dialkyl ketones (Scheme 18).



Scheme 17 Asymmetric hydrogenation of acyclic imines with Ir catalyst bearing a chiral phosphate counteranion.



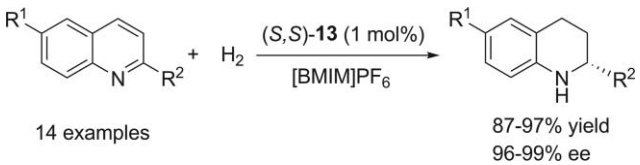
Scheme 18 Asymmetric reductive amination catalyzed by chiral Ir catalyst together with Brønsted acid.

Recently, Andersson and co-workers also reported the Ru-catalyzed hydrogenation of imines with their oxazoline-containing chiral diamine **12**. The *in situ* generated Ru catalyst completely converted several imines to amines in the presence of a base at room temperature, but only two substrates were used for asymmetric hydrogenation with moderate enantioselectivities.[45]

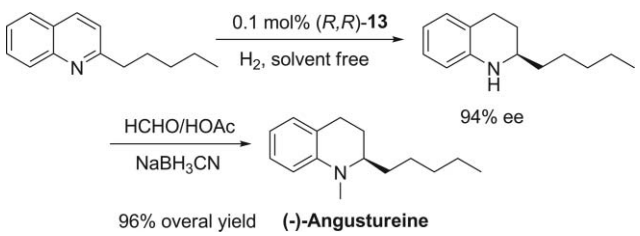
Enantioselective hydrogenation of quinolines

Asymmetric hydrogenation of heteroaromatic compounds provides an attractive and convenient approach to optically pure heterocycloalkanes and their derivatives, which are important organic synthetic intermediates for the synthesis of biologically active compounds.[46] However, a variety of chiral Rh, Ru and Ir complexes, which have been demonstrated to be highly efficient and enantioselective in the hydrogenation of prochiral olefins, ketones, and imines,[4] often failed to give good results in such transformation. Most recently, some appealing results have been achieved in the asymmetric hydrogenation of quinolines with chiral phosphine-containing catalysts since the pioneering work reported by Zhou in 2003.[47,48] Chiral ligands containing only nitrogen as a heteroatom were usually considered not suitable for such transformation due to the potential poisoning of the catalysts by quinolines and/or tetrahydroquinolines.

A breakthrough was made by Fan and co-workers, who firstly reported the asymmetric hydrogenation of 2-alkyl-quinolines by the using of a combination of η^6-arene/TsDPEN-Ru complex **13** and an ionic liquid [BMIM]PF_6 at room temperature.[37] A range of 2-substituted quinolines were efficiently hydrogenated to give tetrahydroquinolines with unprecedented reactivities and excellent enantioselectivities (up to 99% ee) without the need for additives, which are better than those obtained in methanol (Scheme 19). The catalyst recycling was successfully achieved and the catalyst was reused at least eight times without an obvious decrease in reactivity and enantioselectivity. In addition, an ionic catalytic pathway[49] was proposed for this transformation, in which the substrate (C=N bond) was reduced through a stepwise H^+/H^- transfer process. It is different from the concerted mechanism proposed for the reduction of ketones in methanol with the same catalyst system.[29b] In their continuing effort, they found that the Ru catalyst could be successfully applied in a more environmentally friendly solvent-free asymmetric hydrogenation of quinolines.[50] Excellent yields and enantioselectivities were obtained at only 0.02–0.10 mol% catalyst loading, which are unexpectedly better than those obtained in methanol. This practical method was also used for the synthesis of naturally occurring (–)-angustureine on a 2 g scale with high yield (Scheme 20).



Scheme 19 Asymmetric hydrogenation of 2-alkyl quinolines catalyzed by TsDPEN-Ru catalyst **13** in ionic liquid.



Scheme 20 Synthesis of naturally occurring (–)-angustureine.

After this unprecedented discovery, Fan and co-workers developed another type of air-stable iridium catalyst bearing

chiral diamine ligand CF_3TsDPEN (CF_3TsDPEN = *N*-(*p*-trifluoromethylbenzenesulfonyl)-1,2-diphenylethylene-diamine) for the asymmetric hydrogenation of quinolines.[51,52] The reaction proceeded smoothly under a substrate-to-catalyst molar ratio as high as 1000 in undegassed solvent with no need for inert gas protection. As compared with the Ru-TsDPEN, the higher air-stability of the Ir catalyst was probably due to the reason that the iridium hydride complex formed during hydrogenation could reduce oxygen to water in the presence of Brønsted acid.[53] High yields (up to 99%) and excellent enantioselectivities (up to 99% ee) were achieved over a range of 2-substituted quinolines.

Summary and outlook

Developing along with the successful application of the brilliant phosphorous ligands in homogeneous asymmetric hydrogenation, chiral phosphine-free metal complexes have emerged as an alternative type of promising catalysts for such transformation over the past ten years. In addition to the early examples of air-sensitive chiral metallaocenes and chiral organolanthanides, oxygen-tolerant chiral *N*-heterocyclic carbene- and chiral diamine-based catalysts were recently developed for asymmetric hydrogenation. The examples described above have nicely demonstrated the efficiency as well as the potential of these phosphine-free catalysts in the asymmetric hydrogenation reactions.

Comparing to the phosphine ligands, NHCs have similar electronic properties but quite different stereo-conformations. In addition, they are easily available and air-stable. Thus, the design of chiral NHC-based ligands cannot be a simple replacement of phosphine unit with NHCs. As seen from the above, it may be helpful to introduce additional bulky complexation (herein the coordinating oxazoline ring) in the metal center to form more steric hindered catalysts. Although the present application of such type ligands is still limited to the hydrogenation of unfunctionalized olefins, more new highly effective chiral NHC-based catalysts and their application in asymmetric hydrogenation of other type of substrates are expected to appear in the near future. Moreover, the related mechanism is still waiting for further study.

Unlike the chiral phosphine ligands, chiral diamine ligands are frequently employed in asymmetric transfer hydrogenation rather than hydrogenation. This may reflect the compatibility of nitrogen donor atoms with the mechanistic peculiarities of the transfer hydrogenation. But the recent examples described above demonstrated that some metal complexes containing diamine ligands are capable of activating molecular hydrogen. Particularly, metal (Ru, Rh or Ir) complexes bearing tosylated chiral diamines have exhibited excellent performance in the asymmetric hydrogenation of not only simple aromatic ketones but also more challenging substrates like imines and quinolines, which are even better than those obtained from the phosphine-containing catalysts.

Although some appealing progress have been achieved in the asymmetric hydrogenation with the use of chiral N-heterocyclic carbene-based *C*,*N*-ligands and chiral diamine-based *N*,*N*-ligands, the use of chiral phosphine-free catalysts is still in its initial stage. Undoubtedly, the future direction in this emerging field is to continue developing new types of chiral phosphine-free catalysts and expanding the substrate scope.

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