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Spiro Skeletons: A Class of Privileged Structure for Chiral Ligand Design

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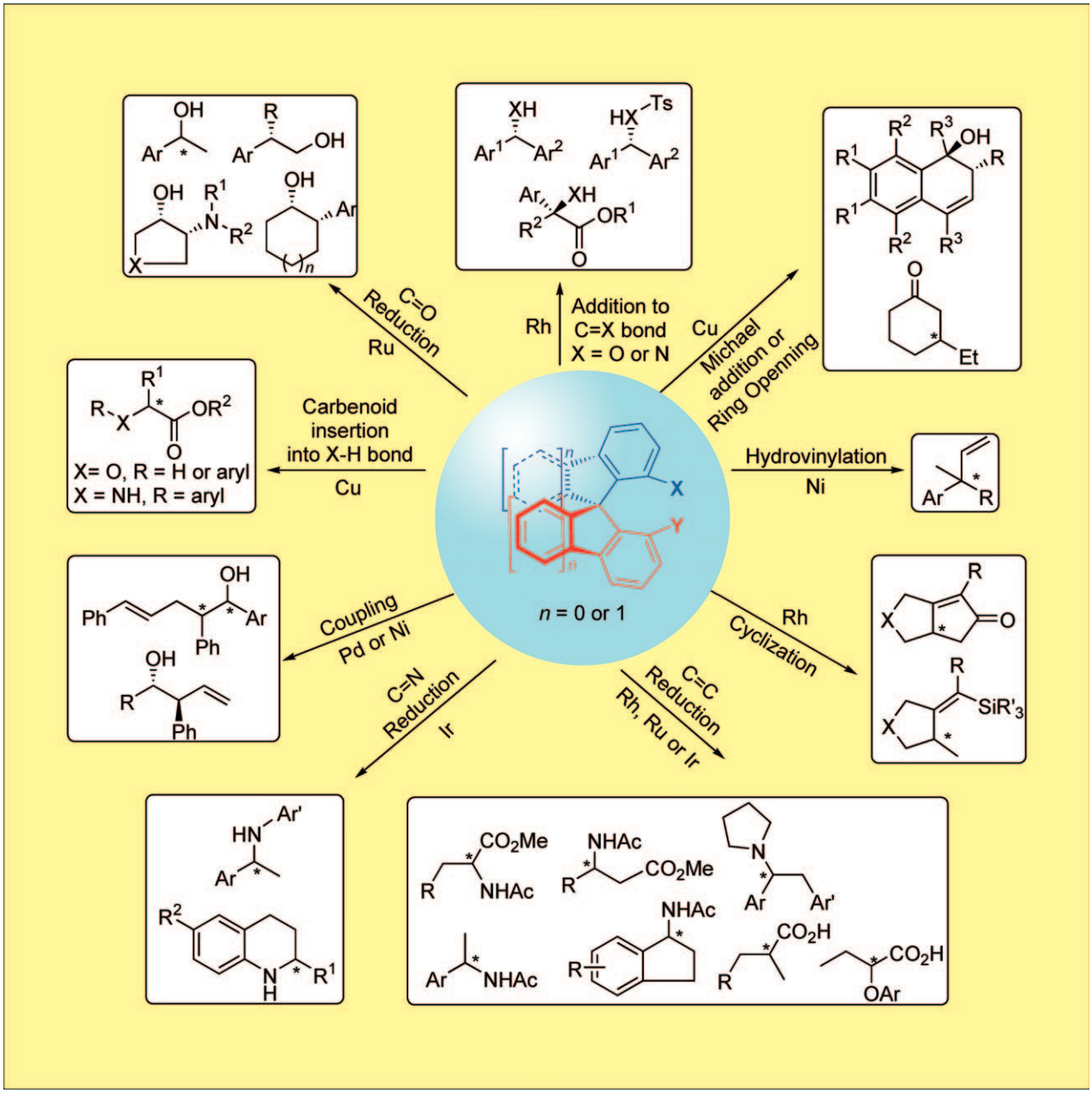

Abstract: This Focus Review highlights the exciting results obtained in the area of asymmetric catalysis using spirobiindane- or spirobifluorene-based chiral ligands. The spiro, mono, and bidentate ligands have been successfully applied in a wide range of transition-metal-catalyzed asymmetric reactions, including hydrogenations, carbon–carbon and carbon–heteroatom coupling reactions, with superior or comparable enantioselectivities to those obtained by using the related ligands bearing other backbones, thus proving that the spiro skeleton is a type of privileged structure for chiral ligand design. It is expected that the spiro concept for chiral ligand design will stimulate the future efforts to understand the features that account for their broad applicability and to apply this understanding to seek new privileged chiral ligands and catalysts.

Keywords: asymmetric catalysis · copper · rhodium · ruthenium · spiro ligands

1. Introduction

Driven by the ever-increasing demand for nonracemic chiral chemicals, the development of efficient methods to provide enantioenriched products is of great current interest to both academia and industry.[1,2] Among the various approaches employed for this purpose, asymmetric catalysis constitutes one of the most general and appealing strategies in terms of chiral economy and environmental considerations. Therefore, the development of highly efficient and enantioselective catalysts is one of the most challenging endeavors for chemists. To achieve highly efficient and enantioselective catalysis of asymmetric reactions, tuning the catalysts to make the perfect match among chiral ligands, metal ions, as well as substrates and so on is the key issue, and the design of chiral ligands plays a central role. Over the past several decades, thousands of chiral ligands and their transition-metal complexes have been developed for various organic transformations. Among these chiral ligands or metal complexes, only a few of them have demonstrated high generality for different reactions. Such ligands or catalysts have been termed as "privileged structures" which offer much more than one might have imagined, creating effective asymmetric induction environments for mechanically unrelated reactions.[3] Some of the representative examples are shown in Scheme 1.

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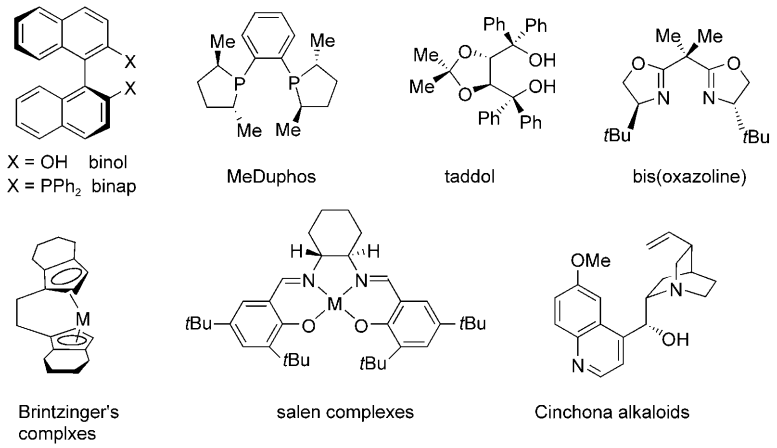
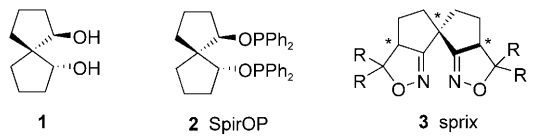
Among the various privileged ligands reported so far, the C_2-symmetric structural feature of the scaffold is predominant with central or axial chirality at a relatively rigid backbone, which would reduce the conformational obscurity of the intermediate or transition state and create an effective chiral environment around the catalytically active center. Molecules containing a spirocyclic framework are quite common in nature. The synthesis of molecules with a spiro structure can be traced back to the late 1890s,[4] and the name "spirocyclane" for bicyclic hydrocarbons having two rings with a common carbon atom (spiro carbon atom) was proposed by von Baeyer in 1900.[5] Owing to the tetrahedral structure of the spiro carbon atom and perpendicular orientation of the two rings, the rotation of the two rings in bicyclic spiro compounds is therefore restricted and as a result gives rise to an axial chirality in spiro compounds with substituents on the rings. The inherent molecular rigidity and the quaternary structure of the bridging carbon atom make the racemization of chiral spiro compounds virtually impossible. These characteristics of spiro compounds, especially C_2-symmetric spiranes, can provide the ideal backbones for chiral ligand design. However, the use of such spirocyclic frameworks to construct chiral ligands has been implemented only recently, probably owing to the difficulty of the synthesis of enantiopure spiro compounds. In this Focus Review, the synthesis and application of a family of chiral ligands based on spirobiindane and spirobifluorene backbones in a variety of transition-metal-catalyzed asymmetric reactions will be highlighted with emphasis on their high generality and advantageous features in asymmetric catalysis in comparison with those of related ligands bearing other backbones.



Scheme 1. Examples of privileged chiral ligands and catalysts.

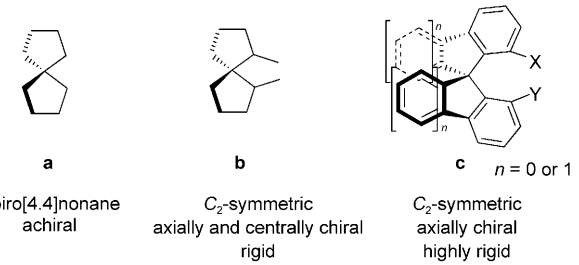
2. The Design and Synthesis of Spirobiindane- and Spirobifluorene-Based Chiral Ligands

In 1992, Kumar utilized the chiral spiro diol *cis,cis*-(+)- or (−)-spiro[4.4]nonane-1,6-diol (**1**, Scheme 2) as a chiral auxiliary in the reduction of ketones with lithium aluminium hydride, giving the corresponding alcohols with good to excellent enantioselectivities.[6] A pioneering work in asymmetric catalysis with spiro backbone based ligands was reported by Chan, Jiang, et al. in 1997, indicating that the chiral phosphinite ligands SpirOP (**2**) derived from chiral spiro diol **1** are highly enantioselective in the rhodium-catalyzed asymmetric hydrogenation of α-dehydroamino acid derivatives.[7] Another type of spiro ligands that should be mentioned is the spiro[4.4]nonane-based bis(isoxazoline) ligands sprix (**3**) reported by Sasai and co-workers.[8] A Pd^{II} complex of **3** demonstrates excellent asymmetric induction in a tandem Wacker-cyclization process, giving a bicyclic compound with 95% *ee* as a single diastereomer. Following these leading efforts, a variety of chiral ligands with spiro backbones have been developed by several research groups and utilized in transition-metal-catalyzed asymmetric reactions.[9]



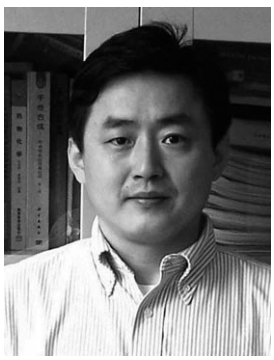
Scheme 2. Representative examples of spiro chiral ligands.

Spiro[4.4]nonane itself is not a chiral molecule (Scheme 3a). The introduction of substituents on spiro cycles results in more than one chiral center in the molecule (Scheme 3b) and increases the difficulty in the synthesis of its optically pure form. On the other hand, spirobiindane (Scheme 3c, $n=0$) and spirobifluorene ($n=1$), which can be regarded as benzo derivatives of spiro[4.4]nonane, only have axial chirality, and their rigid spiro structures make them highly potential backbones for chiral ligands.

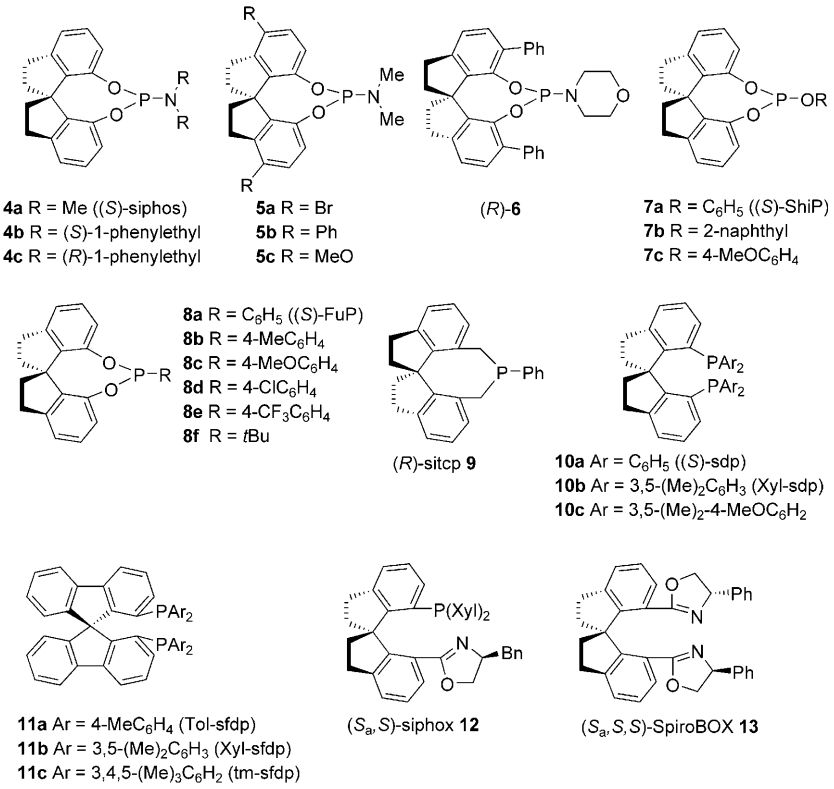


Scheme 3. The concept of spiro ligand design.

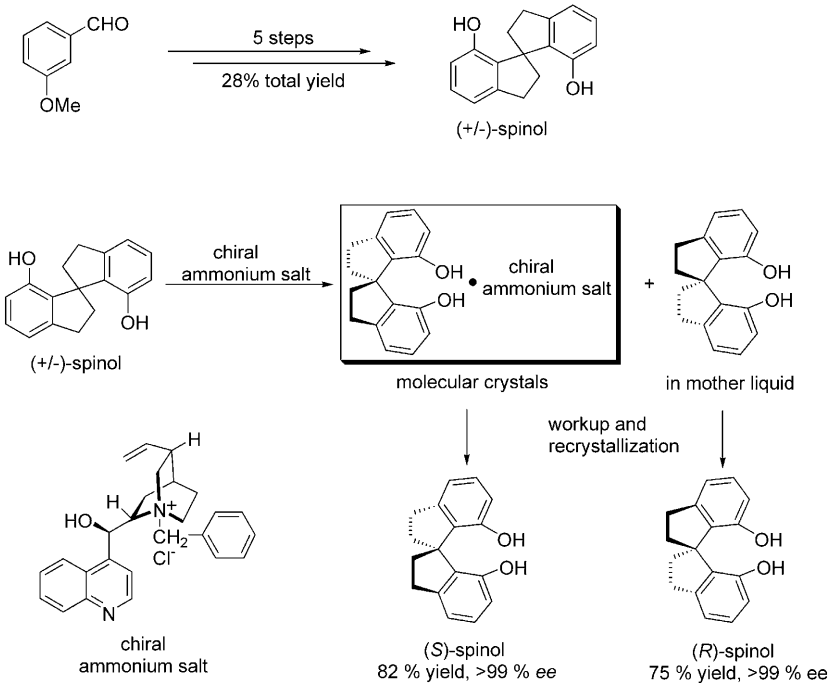
On the basis of the concept mentioned above, Zhou and co-workers have developed a family of chiral ligands (Scheme 4) with benzo spiro[4.4]nonane backbones.[10] The chiral spiro ligands, including mono- and bidentate phosphorus ligands (**4**–**10**), phosphine–oxazoline ligands (siphox, **12**), as well as bisoxazoline ligands (SpiroBOX, **13**) with a 1,1′-spirobiindane backbone, were synthesized from enantiopure 1,1′-spirobiindane-7,7′-diol (spinol) or its derivatives. The racemic spinol can be easily prepared starting from 3-methoxybenzaldehyde by a six-step reaction sequence developed by Birman et al. (Scheme 5).[11] An inclusion complexation strategy[12] is particularly efficient for the optical resolution of spinol among the procedures developed so far,[11,13] in which only 0.55 equivalents of commercially available chiral ammonium salt, *N*-benzylcinchonidinium chloride, is



Kuiling Ding *was born in Henan Province, China. He received his BS from Zhengzhou University (1985) and a PhD from Nanjing University (1990) under the supervision of Professor Yangjie Wu. Dr. Ding became assistant professor at Zhengzhou University in 1990 and full professor at the same place in 1995. He engaged in postdoctoral research with Professor T. Matsuura at Ryukoku University (1993–1994) and was a UNESCO research fellow with Professor K. Mikami at Tokyo Institute of Technology (1993–1994). He joined Shanghai Institute of Organic Chemistry in 1999, where he is currently Professor of chemistry. His research interests include the development of new chiral catalysts and methodologies for asymmetric catalysis.*



Scheme 4. Chiral ligands with privileged spiro backbones.



Scheme 5. Practical synthesis and optical resolution of the key intermediate spinol.

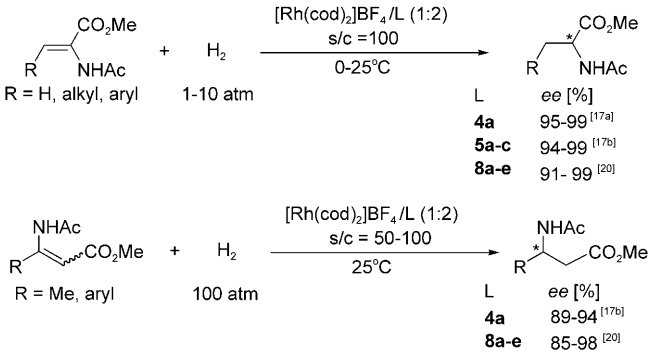
used as the resolving agent (Scheme 5). It should be noted that the above-mentioned procedures for the preparation of racemic and enantiopure forms of spinol can be carried out on a ten-gram scale in the lab. On the other hand, the chiral ligands with a 9,9′-spirobifluorene backbone (sfdp, **11**)[14] were prepared from enantiopure 9,9′-spirobifluoren-1,1′-diol, which has been synthesized and resolved by a procedure developed by Zhou and co-workers.[15] The exciting results achieved recently by Zhou and co-workers with chiral ligands[16] based on these backbones (Scheme 3c) clearly demonstrate that the spiro skeleton indeed makes a difference in a variety of asymmetric catalytic reactions, thus proving that the spiro backbone is a privileged structure for chiral ligand design.

3. Application of Spiro Backbone Based Ligands in Enantioselective Catalysis

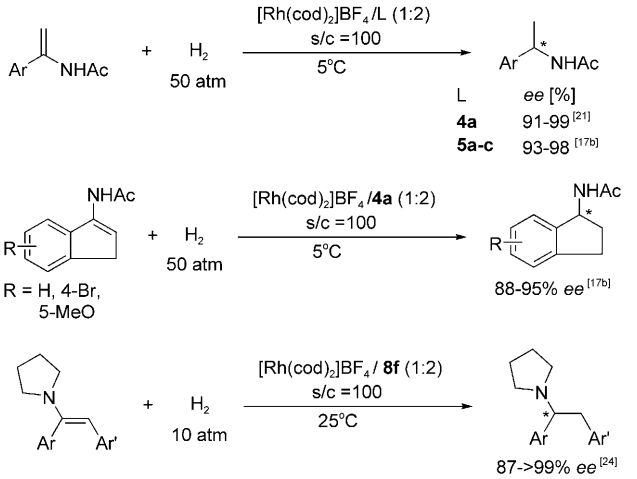
3.1. Enantioselective Hydrogenations

Asymmetric hydrogenation using molecular hydrogen to reduce prochiral olefins, ketones, and imines represents one of the most efficient methods for the production of optically active chiral amino acid derivatives, chiral alcohols, and chiral amines, which are important building blocks for the construction of chiral drugs, agrochemicals, and functional materials.[1,2] The transition-metal complexes of phosphorus ligands including the siphos (**4**, **5**), FuP (**8**), sdp (**10**), and sfdp (**11**) families, as well as the N,P chiral spiro ligands siphox (**12**), proved to be very effective catalysts for the hydrogenation of a broad scope of unsaturated substrates.

As shown in Scheme 6, the Rh^I complexes of monodentate phosphoramidite ligands **4a** and **5a–c** were very effective in the hydrogenation of α-dehydroamino acid derivatives, affording a variety of the corresponding α-amino acid deriva-



Scheme 6. Asymmetric hydrogenation of α- or β-dehydroamino acid derivatives; cod = 1,5-cyclooctadiene.

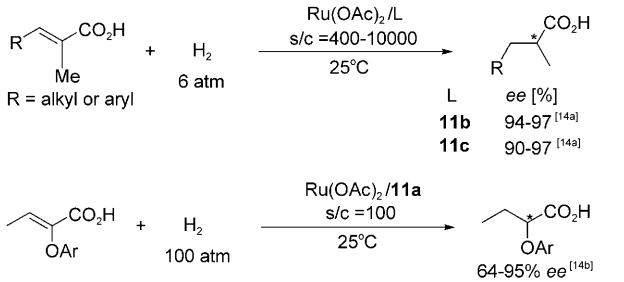


Scheme 7. Asymmetric hydrogenation of acetyl enamides and enamines.

tives with excellent enantioselectivities (94–99% *ee*) under mild conditions.[17] These results are better than or comparable to those achieved with diphosphine ligands[18] and other monophosphorus ligands,[19] showing the excellent enantiocontrol achieved with 1,1′-spirobiindane-based ligands. In the hydrogenation of (*Z*)-methyl-2-acetamido-3-phenylacrylate, FuP ligand **8** was also shown to be effective for enantioselective control. The electronic properties of the substituent at the *para* position of the *P*-phenyl ring demonstrate a dramatic impact on both the reactivity and enantioselectivity of the reaction. The ligand **8c** with an electron-donating 4-MeO group turns out to be the best one in terms of both enantioselectivity (99% *ee*) and reactivity of the catalysis.[20] For the Rh-catalyzed asymmetric hydrogenation of β-dehydroamino acid derivatives, both ligands **4a** and **8a–e** gave very high enantioselectivities (85–98% *ee*) in the corresponding products,[17b,20] despite the need of a higher hydrogen pressure (100 atm). It is noteworthy that the Rh^{I} complexes of ligands **4a** and **8c** can promote hydrogenation of *Z*/*E* mixtures of β-aryl-β-(acylamino)acrylates to afford the corresponding β-amino acid derivatives with high enantioselectivities. This is of practical importance because the β-(acylamino)acrylate substrates are normally prepared as a mixture of *Z* and *E* isomers.

Ligands **4a** and **5a–c** were also found to be highly enantioselective in the asymmetric hydrogenation of α-arylethenyl acetamides; a series of α-arylethenyl amine derivatives were obtained with 91–99% *ee* (Scheme 7).[21] This result was superior to that obtained by using the monophos ligand (90–94% *ee*),[22] thus showing that the 1,1′-spirobiindane backbone confers better enantioselective induction than the 1,1′-binaphthalene backbone in the hydrogenation of α-arylethenyl acetamides. Under the same experimental conditions, *N*-(1,2-dehydro-1-indanyl)acetamides were successfully hydrogenated to 1-aminoindanes with high enantioselectivities.[17b] The asymmetric hydrogenation of enamines is quite challenging because of the absence of a chelating *N*-acyl group in the substrates.[23] It is interesting to find that ligand **8f** with a *t*Bu group on the P atom was an exceptionally outstanding ligand for the asymmetric hydrogenation of (*E*)-1-(1-pyrrolidinyl)-1,2-diarylethenes, yielding the corresponding tertiary amines with excellent enantioselectivities (up to 99.9% *ee*).[24] Other excellent bisphosphine ligands such as binap, josiphos, and sdp (**10**) or monodentate phosphorus ligands, such as monophos, H-mop, siphos (**4a**), and ShiP (**7a**) provided the hydrogenation product with very low enantioselectivities under the same reaction conditions.[24]

The enantioselective hydrogenation of α,β-unsaturated carboxylic acids promoted by transition-metal complexes represents a facile approach to optically active carboxylic acids, one type of versatile intermediates in the synthesis of biologically important compounds. A number of chiral diphosphine ligands have been successfully applied in the ruthenium-catalyzed asymmetric hydrogenation of α,β-unsaturated carboxylic acids.[25] As shown in Scheme 8, the Ru^{II}-diacetate complexes of both sdp (**10**) and sfdp (**11**) ligands with appropriate substituents showed good to excellent enantioselectivities in the asymmetric hydrogenation of tiglic acid, α-methylcinnamic acid, or α-aryloxy unsaturated carboxylic acid derivatives.[14] These results are normally superior to those attained with Ru^{II} complexes of binap or H_8-binap,[25c] which might be attributed to the larger bite angles of the sdp- or sfdp-based Ru complexes.[14a] Among a variety of sfdp ligands **11** examined, **11b** and **11c** with 3,5-dimethyl and 3,4,5-trimethyl substituents on the *P*-phenyl groups gave

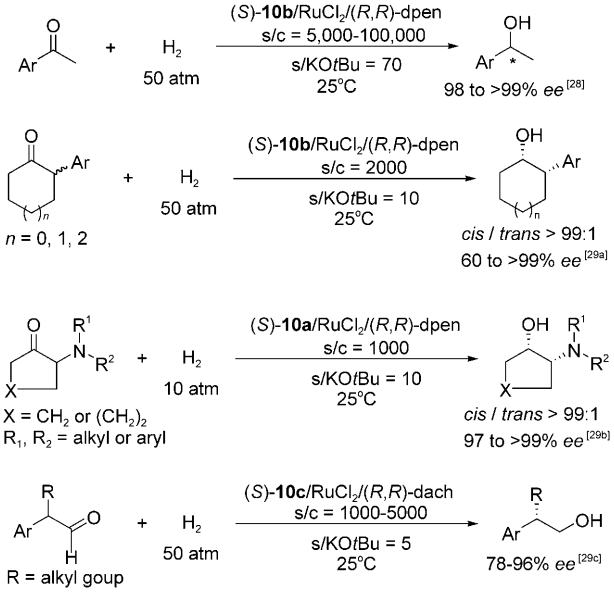


Scheme 8. Asymmetric hydrogenation of α,β-unsaturated carboxylic acids.

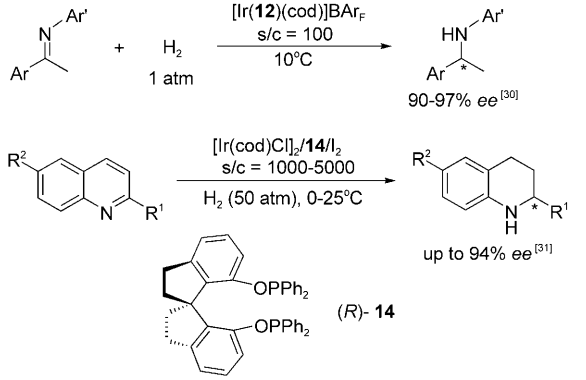
higher *ee* values of the products. A variety of tiglic acid derivatives can be hydrogenated in the presence of **11b**/Ru^{II}, affording excellent enantioselectivities (94–97% *ee*) and good yields (ca. 90%) for various substrates, regardless of the bulkiness of the R group. It is worthwhile to mention that the enantioselectivity of the reaction could be slightly improved as the catalyst loading was reduced from 1 mol% to 0.1 and 0.01 mol%, allowing one to carry out the reaction at a low concentration of catalyst and high concentration of substrates. This is particularly important for a catalyst used on a production scale. Similarly, the catalyst **11c**/Ru^{II} showed excellent enantioselectivities (90–97% *ee*) in the hydrogenation of α-methylcinnamic acid derivatives. More recently, Zhou and co-workers reported that an Ir complex of a siphox P,N ligand (**12**) was extremely efficient for the enantioselective hydrogenation of various α,β-unsaturated carboxylic acids, affording the corresponding optically active aliphatic acids with 90–99% *ee*.[26] In the hydrogenation of α-aryloxy or alkoxy unsaturated carboxylic acids, catalyst **11a**/Ru^{II} is much better than **11c**/Ru^{II}. With the catalyst **11a**/Ru^{II}, a number of crotonic acids substituted by different α-aryloxy groups can be hydrogenated to the corresponding chiral saturated acids in high yields with good to high enantioselectivities.[14b]

The analogous Noyori-type Ru^{II} catalyst[27] generated with ligands (*S*)-**10b** and (*R*,*R*)-1,2-diphenylethylene-1,2-diamine ((*R*,*R*)-dpen) was found to be extremely efficient in the asymmetric hydrogenation of prochiral ketones (Scheme 9), giving the corresponding secondary alcohols with excellent *ee* values.[28] The same type of catalyst also demonstrated excellent stereocontrol in the asymmetric hydrogenation of racemic α-aryl cycloketones or α-amino cycloketones through dynamic kinetic resolution (DKR) under basic conditions, affording the corresponding α-aryl cycloalkanols or α-amino cycloalkanols with excellent *cis*/*trans* stereoselectivities (>99:1) and enantioselectivities (up to 99.9% *ee*).[29a,b] However, the asymmetric hydrogenation of racemic cyclic amino ketones by DKR using Noyori's [$RuCl_2$((*S*)-Xyl-binap)((*R*)-daipen)] (Xyl-binap = 2,2′-bis[di(3,5-xylyl)-phosphino]- 1,1′-binaphthyl; daipen = 1,1-bis(4-methoxyphenyl)-3-methyl-1,2-butanediamine) catalyst gave the corresponding amino alcohol with 82% *ee* and 98% *cis* selectivity.[27b] An analogous catalyst, (*S*)-**10c**/$RuCl_2$/(*R*,*R*)-dach (dach = *trans*-1,2-diaminocyclohexane), was found to be very effective in the asymmetric hydrogenation of racemic α-aryl aldehydes by a DKR process, affording the corresponding optically active primary alcohols with good to excellent enantioselectivities.[29c] This approach represents the first example of asymmetric hydrogenation of aldehydes by DKR.

An Ir^I complex of spirobiindane-based P,N ligand **12** in the presence of sodium tetrakis-3,5-bis-(trifluoromethyl)phenylborate catalyzes the hydrogenation of acyclic *N*-aryl ketimines under ambient pressure with excellent enantioselectivities (up to 97% *ee*; Scheme 10). Therefore, this Ir^I/**12** complex represents one of the best catalysts in the Ir-catalyzed asymmetric hydrogenation of imines developed so far using P,N ligands.[30] The Ir^I complex of (*S*)-sdpo (**14**) demonstrated a very high activity in the asymmetric hydrogenation of quinolines to give the corresponding optically active tetrahydroquinoline derivatives with high enantioselectivity (up to 94% *ee*).[31]



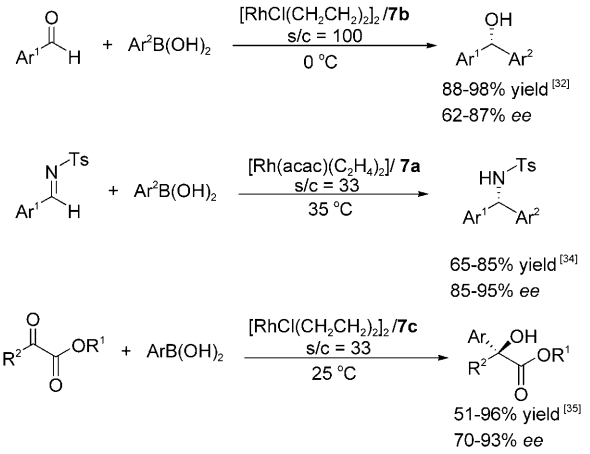
Scheme 9. Asymmetric hydrogenation of ketones and aldehydes.



Scheme 10. Asymmetric hydrogenation of *N*-aryl ketimines and quinolines.

3.2. Enantioselective C–C Bond-Forming Reactions

Catalytic asymmetric carbon–carbon bond-forming reactions represent the most essential tools for the construction of chiral organic molecules. In addition to the excellent performance of the catalysts based on spiro ligands in asymmetric hydrogenations, the metal complexes of spiro mono- or bidentate phosphorus ligands (**4**, **6**, **7**, **9**, and **10**) are also very effective for a variety of asymmetric carbon–carbon bond-forming reactions. As shown in Scheme 11, The Rh^I complex of ligand (*S*)-**7b** with a 2-naphthoxy substituent at the P atom (see Scheme 4) promotes the addition of arylboronic

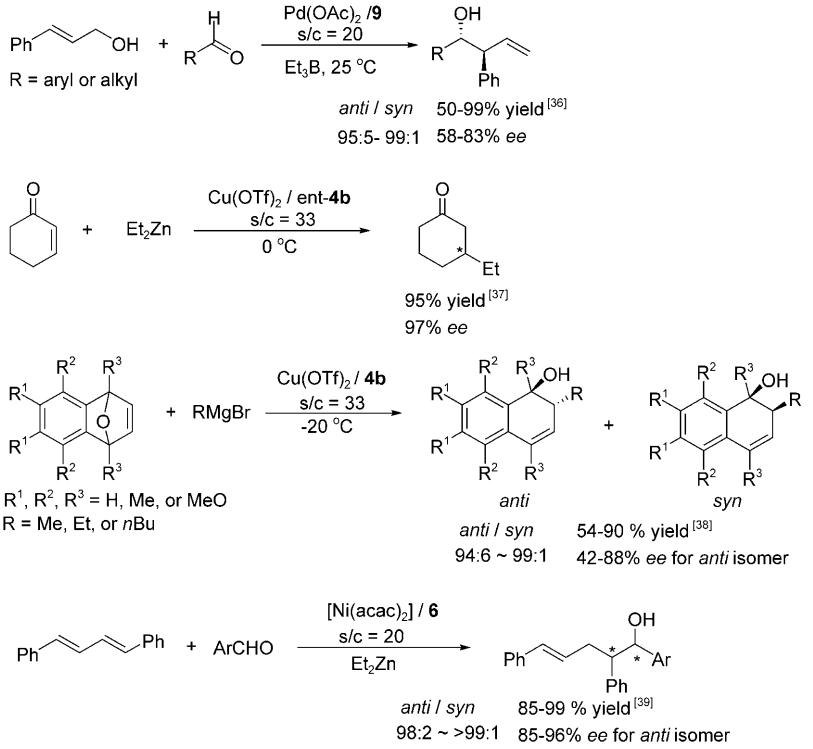


Scheme 11. Asymmetric addition of arylboronic acids to aldehydes, imines, and α-ketoesters.

acids with various aryl aldehydes, affording to the corresponding secondary diaryl alcohols in excellent yields with up to 87% *ee*,[32] which is much better than that obtained by using the (*S*)-MeO-mop ligand.[33] An analogous addition reaction of arylboronic acids to *N*-tosyl aryl imines has been realized by using the (*S*)-**7a**/Rh^{I} catalyst system, providing the corresponding *N*-tosyl methyl amine products in good yields (65–85%) with excellent enantioselectivities (85–95% *ee*).[34] The high enantioselectivity of the catalysis is attributed to the effective asymmetric environment generated by two coordinating spiro phosphite ligands around the rhodium(I) center. Very recently, this methodology was further extended to the addition of arylboronic acids to α-ketoesters, giving the corresponding tertiary α-hydroxyesters in good yields with high enantioselectivities in the presence of Rh^{I}/**7c** as the catalyst.[35]

The allylation of aldehydes using allylic alcohols as the allylation reagent was realized in the presence of Pd^{II}/(*S*)-**9** as the catalyst and Et_3B as the reducing reagent. Accordingly, a series of aromatic, heteroaromatic, and aliphatic aldehydes can be allylated by cinnamyl alcohol to provide the corresponding homoallylic alcohols in good enantioselectivities and excellent diastereoselectivities (Scheme 12).[36] In the Michael addition of diethylzinc to an α,β-unsaturated ketone, the Cu^{II} complex of ligand **4b** was found to be highly efficient, affording the adduct with up to 95% yield and 97% *ee*.[37] The same catalyst was also effective in the catalysis of desymmetrization of *meso* oxabicyclic alkenes using Grignard reagents as the nucleophile, affording ring-opening products with excellent *anti*/*syn* selectivities and good enantioselectivities.[38] The Ni^{II} complex of **6** showed the best performance in catalyzing the asymmetric coupling of dienes with aldehydes, giving chiral bishomoallylic alcohols with excellent diastereo- (*anti*/*syn* 98:2 to greater than 99:1) and enantioselectivities (86–99% *ee*).[39]

Hydrovinylation of vinylarenes represents a very important carbon–carbon bond-forming reaction, but its asymmetric version remains a great challenge, in particular for the construction of all-carbon quaternary stereocenters. The Ni catalyst modified with (*S,R,R*)-**4c** was disclosed to be highly efficient for the reaction of α-alkyl vinylarenes with ethylene under ambient pressure, affording a variety of hydrovinylation products bearing chiral all-carbon quaternary centers in excellent enantioselectivities (70–99% *ee*) with good chemoselectivities (80–89%, Scheme 13).[40] These vinylation products are potentially useful intermediates for the synthesis of versatile optically active molecules, such as chiral carboxylic acids and aldehydes. The Rh^{I} complexes of both the monophosphoramidite ligand siphos (**4a**) and bisphosphine ligand sdp (**10a**) were found to be effective for the asymmetric intramolecular Pauson–Khand reaction of a series of 1,6-enynes, providing the cocyclization products in moderate to excellent yields with good enantioselectivities.[41] In the Rh^{I}-catalyzed silylcyclization of 1,6-enynes, sdp (**10a**) was shown to be superior to other bisphosphine ligands, such as



Scheme 12. Asymmetric alkylation of aldehydes, α,β-unsaturated ketones or *meso* oxabicyclic alkenes.

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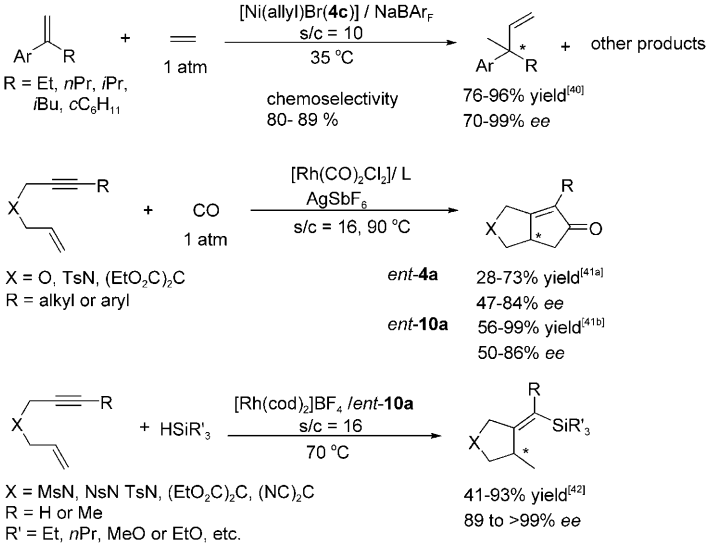
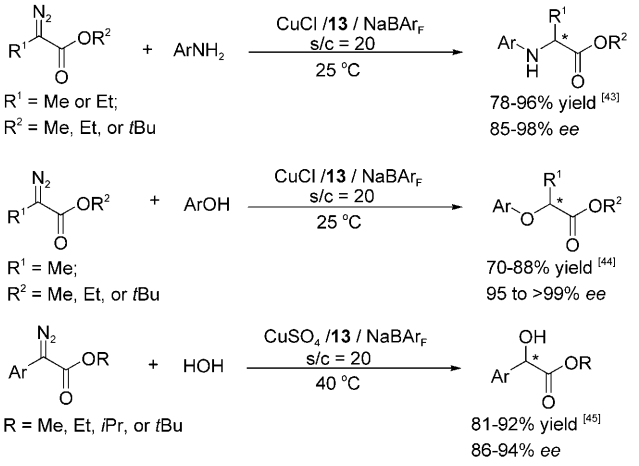


Scheme 13. Asymmetric hydrovinylation and cyclization of olefin derivatives.



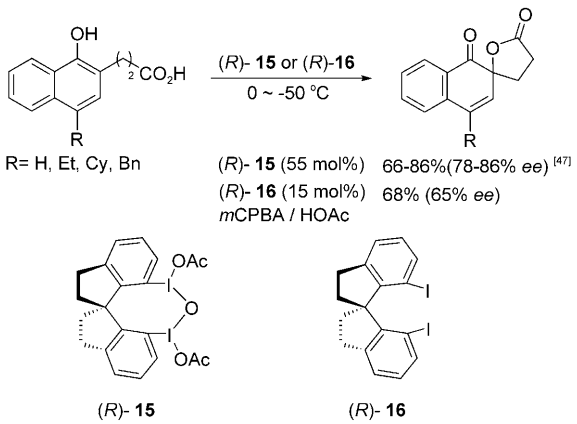
Scheme 14. Asymmetric insertion of α-diazoesters into the N–H or O–H bonds of amines, phenols, or H_2O.

(*S*)-binap, (*R*)-synphos, (*R,R*)-Me-Duphos or (*R,S*)-josiphos, demonstrating good reactivity and excellent enantioselectivity.[42] This methodology provides a facile access to optically active silylalkylidene cyclopentane and pyrrolidine derivatives, along with other functionalized carbocyclic and heterocyclic compounds after subsequent appropriate transformations.

3.3. Enantioselective Carbon–Heteroatom Bong-Forming Reactions

The Cu complexes of bisoxazoline ligands **13** based on a spiro backbone demonstrate exceptionally excellent enantiocontrol in the catalytic asymmetric insertion of α-diazoesters into the N–H or O–H bonds of amines, phenols, or H_2O for carbon–heteroatom bond formation. As shown in Scheme 14, Cu^I complexes of spirobiindane-based bisoxazolines **13** were found to be highly efficient and enantioselective in the asymmetric insertion of α-diazoesters into the N–H bonds of aromatic amines, providing α-amino acid derivatives in 51–96% yields with excellent enantioselectivities (85–98% *ee*).[43] The same Cu complex was also optimized to be an optimal catalyst for the insertion of α-diazoesters into the O–H bonds of a wide range of phenols, affording the corresponding optically active α-aryloxypropionates and the related acids with excellent enantioselectivities (up to 99.6% *ee*),[44] representing the first efficient chiral catalyst for the enantioselective insertion of carbenoids into the O–H bonds of phenols. Parallel to the asymmetric insertions of α-diazoesters into the O–H bonds of phenols, the enantioselective insertion reaction of α-diazoesters with H_2O was realized by using the Cu^{II}/**13** complex as the catalyst. The reaction of a variety of α-diazoesters with H_2O proceeds efficiently to give the corresponding α-hydroxy ester in good yields and enantioselectivities,[45] which represents one of the few catalytic asymmetric procedures using water as a reactant. In addition, the Pd complexes of bisphosphine ligand **10c** and monodentate phosphoramidite ligand **4e** are very efficient catalysts for allylic substitution and hydrosilylation, respectively, affording excellent enantiocontrol in the catalytic reactions.[46]

Very recently, Kita and co-workers reported an elegant enantioselective intramolecular oxidative dearomatization of phenols for the construction of a chiral *ortho*-spirolactone structure using a chiral organoiodine(III) reagent (**15**) based on a 1,1′-spirobiindane backbone (Scheme 15).[47] The high level of the asymmetric induction (up to 86% *ee*) achieved in this reaction was ascribed to the high rigidity of the 1,1′-spirobiindane backbone, which provides the chiral environment around the iodine(III) center throughout the reaction. Furthermore, a catalytic version of this process was also realized in the presence of 15 mol% of 1,1′-spirobiindane-based diiodide **16** using *m*CPBA as a terminal oxidant, affording the corresponding cyclization product with moderate enantioselectivity (65% *ee*).



Scheme 15. Asymmetric intramolecular oxidative dearomatization of phenols.

4. Conclusions and Outlook

In this Focus Review, the exciting results in asymmetric catalysis with spirobiindane-based chiral ligands or reagents, particularly in transition-metal-catalyzed asymmetric reactions, have been highlighted. In many cases for these transformations, the enantioselectivities attained with the spiro ligands are clearly superior to those obtained by using the related ligands having other backbones. These facts have demonstrated that this family of spiro ligands with spirobiindane and spirobifluorene backbones is a privileged class of chiral ligands, and the spiro concept for chiral ligand design represents an important contribution in the area of asymmetric catalysis. It can be expected that the exciting results realized by using these spiro ligands will stimulate future efforts to understand the features that account for their broad applicability and to apply this understanding to seek new privileged chiral ligands and catalysts aiming at high selectivity and activity, ready availability, and broad applicability.

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