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Metal Complexes Incorporating Monoanionic Bisoxazolinate Ligands: Synthesis, Structures, Reactivity and Applications in Asymmetric Catalysis

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The present contribution reviews the synthesis, structures, reactivity and applications in asymmetric catalysis of metal complexes containing monoanionic bisoxazolinate ligands. The anionic and bidentate bisoxazolinate ligand, which may be seen as a nitrogenated version of the acetylacetonate unit and may also be closely related to the diketiminate bidentate ligand, appears to exhibit a rich and versatile coordination chemistry with various metal centers. These excellent coordination properties, combined with the ready accessibility of chiral bisoxazolinate ligands in an enantiomerically pure form, has opened the way to various applications in asymmetric catalysis involving this class of bidentate ligands. Thus, the use of chiral bisoxazolinate ligands in asymmetric catalysis constitutes a central part of this review.

Introduction

Chiral oxazolines are among the most widely used ligands in asymmetric catalysis.[1] The success of this "privileged" class of ligands in numerous metal-complex-catalyzed transformations may be related both to their ready accessibility and the possibility of using them as building blocks for the design of multidentate ligands, thereby allowing access to various chelating ligands with finely tuned coordination properties.[2] In addition to these attractive features, the intrinsic skeleton of the chiral oxazoline unit is expected to favor a high level of asymmetric induction as it incorporates a stereogenic center that is usually located on the carbon next to the metal-coordinated nitrogen. The latter feature, which is of obvious importance in asymmetric catalysis, is also largely responsible for the widespread use of these ligands in this field. Thus, since the earliest studies on the use of chiral oxazolines in catalysis, ligands incorporating an oxazoline with various donating groups include bisoxazolines,[3] trisoxazolines,[4] and oxazoline ligands with an additional chiral element attached to their skeleton or with a characteristic structure.[5]

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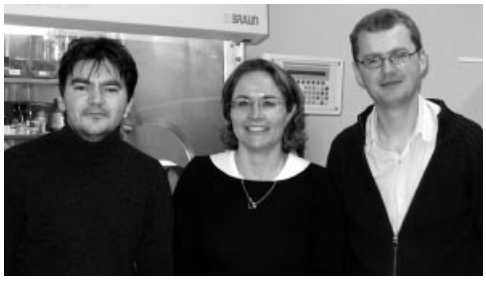
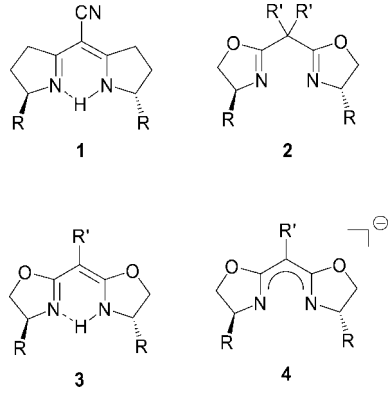


Samuel Dagorne (left) obtained his undergraduate degree in chemistry at the Université de Rennes I (Rennes, France) in 1994. In 1995, he joined the group of Professor Richard F. Jordan at the University of Iowa (Iowa City, IA, USA) and graduated with a Ph.D in 1999 on the chemistry of chiral zirconocenes and group 13 compounds. In 1999, he became a member of the group of Professor Richard R. Schrock (Massachusetts Institute of Technology, Cambridge, MA, USA) as a postdoctoral fellow working on molydenum alkylidene chemistry. He joined the CNRS in october 2000 as a Chargé de recherche and is currently at Université Louis Pasteur. His research interests mainly concern the synthesis and reactivity studies of highly electrophilic group 13 species.
Stéphane Bellemin-Laponnaz (right) studied chemistry at the Université Joseph Fourier (Grenoble, France) and at the Université Louis Pasteur (Strasbourg, France). In 1994, he joined the group of Professor John A. Osborn at the Université Louis Pasteur to obtain his doctorate in 1998 studying the chemistry of rhenium oxo compounds. In 1999, he became a member of the group of Professor Gregory C. Fu (Massachusetts Institute of Technology, Cambridge, MA) as a postdoctoral fellow working on kinetic resolution and phosphametallocene chemistry. Since October 2000, he has been a Chargé de recherche CNRS at the Université Louis Pasteur. His research centres on asymmetric catalysis with highly symmetric ligands and N-heterocyclic carbenes.
Aline Maisse-François (middle) was born in 1974. She studied chemistry at the Université de Franche-Comté (Besançon, France) and Université Louis Pasteur (Strasbourg). In 1995 she joined the group of Dr. M. Pfeffer (ULP, Strasbourg) to obtain her doctorate in 1999 in organometallic chemistry. Then she became a member of the group of Pr. G. Suess-Fink (Université de Neuchâtel) as a postdoctoral associate working on catalysis with ruthenium clusters. Since September 2000, she has been Maître de Conférences at the Université Louis Pasteur.

Among the above class of ligands, neutral C_2-symmetric bisoxazoline ligands have been the most studied as C_2-symmetric chelates have become landmark ligands for use in asymmetric catalysis since the pioneering work of Kagan in this area.[6] In general, bisoxazoline ligands in which one carbon atom links two oxazoline rings are the most frequently used (Scheme 1). Such entities, which can be structurally related to the semicorrin ligands **1** developed by Pfaltz and co-workers,[7] are neutral bidentate ligands of the type **2** and **3**. While derivatives **2** and **3** may be used as L_2 chelates, monoanionic bisoxazolinates **4** that act as LX^- chelates may be obtained by deprotonation of **3**. Such anionic bidentate ligands may be seen as a chiral, nitrogenated version of the acetylacetonate (acac) unit, which is known to exhibit a rich and versatile coordination behavior with various metal centers.[8] Over the last few years, the use of chiral bisoxazolinate ligands of type **4** for coordination to metal centers has received a growing attention as the derived complexes may be of interest in asymmetric catalysis. In this regard, remarkable catalytic systems have already been developed based on this ligand structure. In addition, several recent reports on the coordination chemistry of bisoxazolinate to various metal centers have provided an insight into the structural trends that might be expected for this class of complexes.



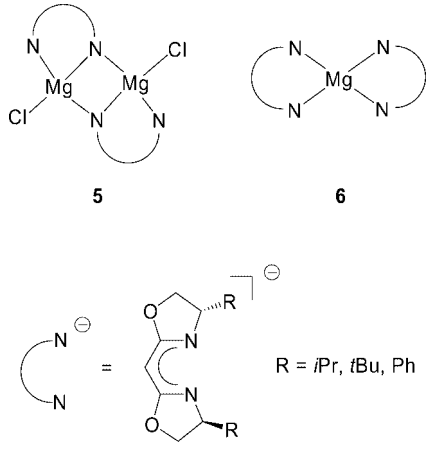
Scheme 1.

Although the coordination chemistry and the potential applications in catalysis of metal complexes bearing neutral bisoxazolines have been reviewed previously,[9] those of bisoxazolinato ligands has not been the subject of a similar survey despite the interesting results reported over the past few years with these monoanionic ligands. The present contribution thus reviews metal complexes incorporating monoanionic bisoxazolinate ligands of type **4** that have been prepared and structurally characterized thus far and the catalytic applications involving these metal complexes. A special emphasis will also be given to their use in asymmetric catalysis.

Group 1 and 2 Metal Complexes

To date, coordination of the bisoxazolinate ligand to group 1 and 2 metals has been the subject of very few reports. Bisoxazolinatolithium salts, for example, which can be easily generated by reaction of neutral bisoxazolines of type **3** with Brönsted bases such as *n*BuLi and amidolithium salts, have been mainly used as convenient starting materials for subsequent salt metathesis reactions with various metal halides, thereby allowing access to the corresponding bisoxazolinate metal complexes. However, to date, no structural data are available on group 1 bisoxazolinate metal complexes.

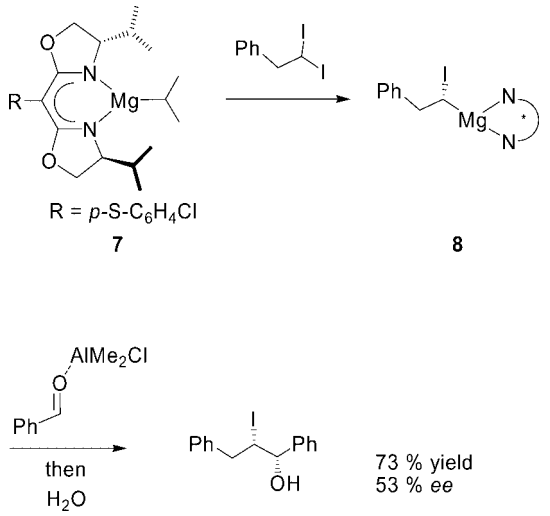
As for group 2 derivatives, reports on these complexes have thus far been restricted to magnesium derivatives. An initial report by Singh concluded, on the basis of NMR, IR, and cryoscopic data, that bisoxazolines readily react with R_2Mg or RMgCl to form the corresponding dinuclear magnesium complexes **5** by an alkane elimination (Scheme 2).[10] The use of two equivalents of bisoxazolines was reported to yield the homoleptic bis(bisoxazolinato)-magnesium complex **6** (Scheme 2).



Scheme 2. Proposed structures of complexes **5** and **6**.

More recently, Hoffmann et al. have elegantly illustrated the potential use of chiral bisoxazolinatomagnesium complexes in enantioselective synthesis.[11] Thus, for example, the chiral alkylmagnesium complex **7**, which can be readily prepared by treatment of the corresponding chiral bisoxazoline with iPr_2Mg, can be used to differentiate the enantiotopic iodine atoms of 1,1-dihaloalkanes by a halogen/metal exchange reaction (Scheme 3).

The kinetically controlled iodine/magnesium exchange between **7** and a 1,1-dihaloalkane preferentially affords the diastereomer **8**, which was proposed to be configurationally stable at –78 °C on the basis of careful monitoring experiments and can be trapped by a combination of $AlMe_2Cl$ and benzaldehyde to afford the corresponding iodohydrins in good yield (73%) and with a reasonable *ee* (53%). The chiral bisoxazolinatomagnesium complex **7** was also used for an enantioselective halogen/metal exchange reaction of a racemic bromoiodo compound, thus providing access to an enantiomerically enriched bromohydrin, albeit in low *ee*, by a kinetic resolution process (33% yield, 18% *ee*, Scheme 4). The unreacted enantiomer of the racemic bromoiodo compound could be re-isolated in 62% yield with 8% *ee*.

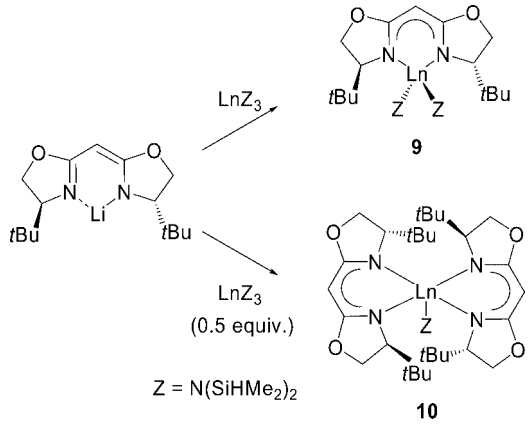


Scheme 3. Reaction of a 1,1-diiodoalkane with complex **7**.

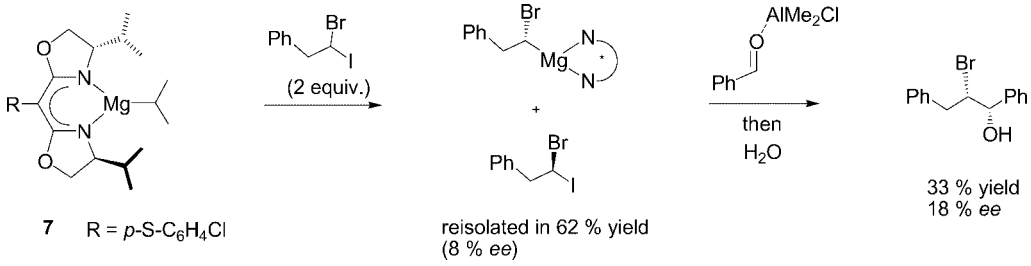
From a reactivity point of view, these studies show that the basicity of the monoanionic bisoxazolinate ligand can greatly influence the outcome of the reaction between the neutral bisoxazoline and iPr$_2$Mg. Thus, while the reaction of the simple bisoxazoline (BOX-iPr$_2$)H with iPr$_2$Mg yields a statistical mixture of iPr$_2$Mg, the mono-bisoxazolinato, and the bis(bisoxazolinato)magnesium complexes (Scheme 5), that of the arylthio-substituted bisoxazoline yields the mono-bisoxazolinatomagnesium complex quantitatively (Scheme 5). This difference in reactivity may be ascribed to the less basic character of the arylthio-substituted bisoxazolinate with respect to (BOX-iPr)$^-$.

Group 3 Transition Metal Complexes

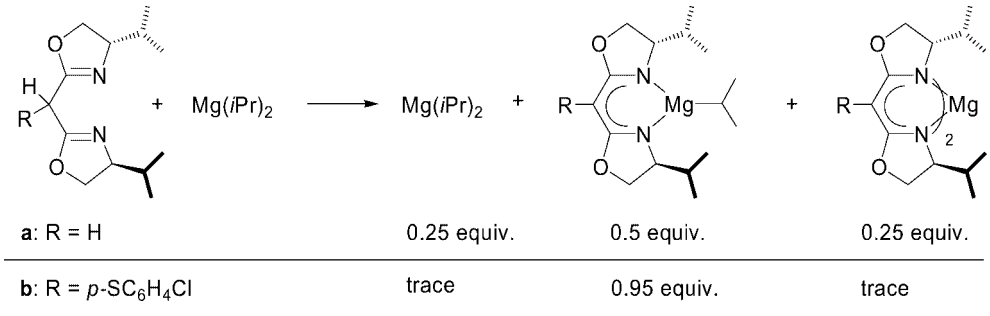
The use of nitrogen-based chelating ligands for coordination to rare earth metals (including scandium and yttrium) has been increasing over the last years, with the diketiminate bidentate ligand being a ligand of choice in this area.[12] It is therefore easily understood that bisoxazolinates have become of interest for coordination to group 3 metal complexes. In this regard, Anwander and collaborators first synthesized lanthanide complexes incorporating bisoxazolinate ligands.[13] The precursors Ln[N(SiHMe$_2$)$_2$]$_3$(thf)$_2$ (Ln = Y, La) were found to react smoothly with one or two equivalents of a lithium bisoxazolinate salt to give the corresponding chiral complexes **9** or **10** in good yields (Scheme 6). Yttrium and lanthanum were chosen for this study because



Scheme 6. Synthesis of lanthanide complexes **9** and **10** (Ln = Y, La).



Scheme 4. Kinetic resolution of 1,1-bromoiodoalkane.



Scheme 5. Reaction of ligand **a** or **b** with Mg(iPr)$_2$.

they are representative of small and large lanthanides, respectively. The yttrium derivative **9** was characterized by an X-ray crystallographic study (Figure 1). The complex lies on a C_2-symmetric axis and the metal center adopts a distorted tetrahedral structure. The silylamide ligands are oriented away from the bulky *tert*-butyl groups, thereby minimizing the steric interactions. The bis(bisoxazolinato) complexes **10** were characterized by classical techniques, although no X-ray study was reported. Attempts to synthesize the homoleptic complexes $Ln(Box)_3$ failed, presumably for steric reasons.

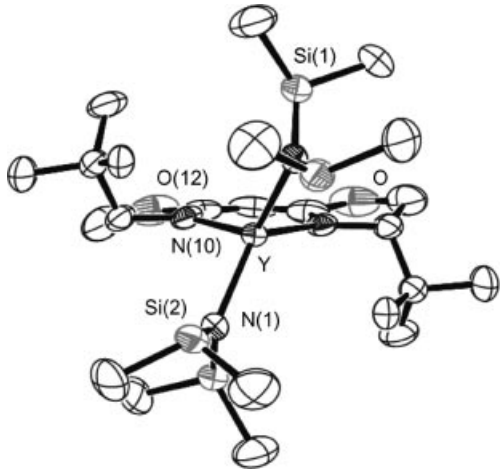
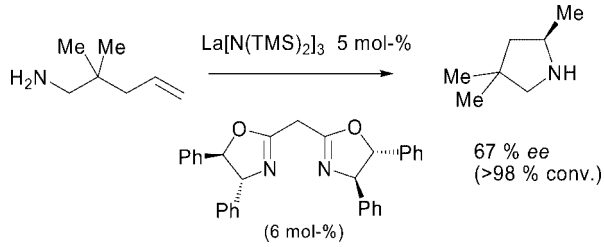


Figure 1. Molecular structure of **9**. Selected distances [Å] and angles [°]: Y–N(1) 2.222(6), Y–N(10) 2.288(5); N(10)–Y–N(10)′ 82.0(2), N(1)–Y–N(1)′ 126.4(2).

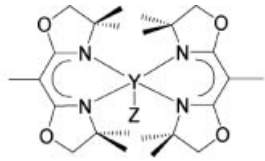
The ready and straightforward accessibility of chiral bisoxazolinato lanthanide complexes has prompted studies of their potential in enantioselective catalysis. In this area, Marks et al. have already thoroughly shown the usefulness of this new class of chiral complexes as catalysts for the enantioselective intramolecular hydroamination reaction − a formal addition of an N–H bond across a C=C double bond.[14] In the 1990s, chiral *ansa*-lanthanocenes were found to be efficient catalysts for this reaction, with *ee* values of up to 74% being reported for the formation of five-membered rings[15] and *ee* values of up to 67% for six-membered rings.[16] However, these chiral *ansa*-metallocene derivatives were found to racemize in the presence of amines, which lowers the enantioselectivity and also hampers accessibility to the substrate. In the search for a new catalyst class that may outperform chiral lanthanocenes, various lanthanide bisoxazolinate complexes were tested.[17]

Different screening experiments showed that lanthanide mono-bisoxazolinate complexes $(Box)Ln[N(TMS)_2]_2$ effectively catalyze the enantioselective intramolecular hydroamination with good rates and enantioselectivities (up to 67% *ee*; Scheme 7), which constitutes a rare example of an enantioselective hydroamination by non-Cp lanthanide complexes. Interestingly, and unlike the trend observed in metallocenes derivatives, the enantioselectivities were found to increase with the ionic radius of the metal, with the best results being observed for the chiral lanthanum derivatives. As for the bis(bisoxazolinato) lanthanide compounds, these were also found to catalyze the reaction, with similar enantioselectivities but lower activity.



Scheme 7. Intramolecular hydroamination/cyclization with a chiral bis(oxazolinato)lanthanide catalyst generated in situ.

More recently, Carpentier et al. have reinvestigated the chemistry of bis(bisoxazolinato) lanthanide complexes such as **10** and synthesized new chiral and achiral bis(bisoxazolinato)yttrium and -lanthanum complexes.[18] The aim of their studies was to probe the potential of these complexes as initiators of the ring-opening polymerization (ROP) of (D,L)-lactide and (D,L)-β-butyrolactone. Along the way, the molecular structure of the achiral dimethylbisoxazolinate derivative **11** was established by X-ray crystallography; this is the first solid-state structure reported for a bis(bisoxazolinato) lanthanide compound (Figure 2). The geometry at the metal center in **11** is distorted trigonal bipyramidal, with the apical sites being occupied by two bisoxazolinate nitro-



11
Z = N(SiHMe$_2$)$_2$

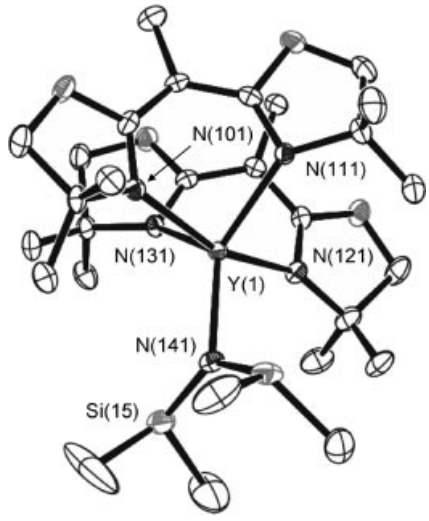
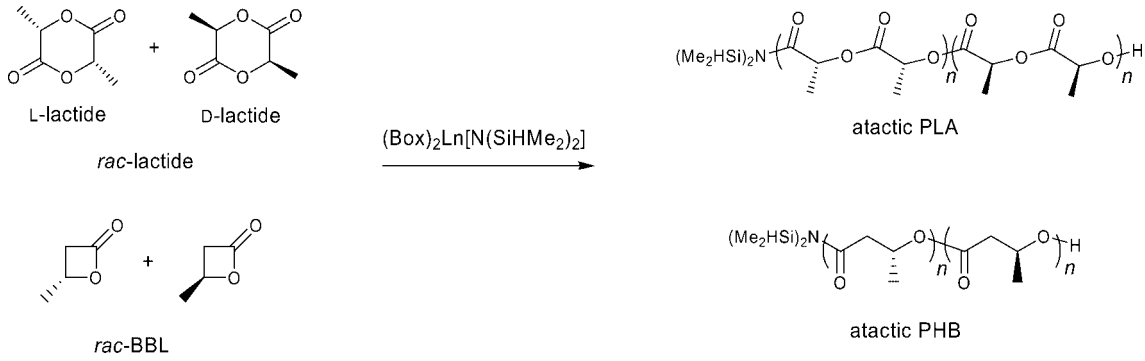


Figure 2. Molecular structure of **11**. Selected distances [Å] and angles [°]: Y(1)–N(111) 2.253(2), Y(1)–N(121) 2.389(2), Y(1)–N(131) 2.325(2), Y(1)–N(111) 2.336(2), Y(1)–N(101) 2.388(2); N(121)–Y(1)–N(141) 99.35(7).



Scheme 8. Ring-opening polymerization of *rac*-lactide and *rac*-β-butyrolactone.

gens. As expected, a significant delocalization of the ligand's negative charge is indicated by an elongation of the N–C and a decrease of the C–C bond lengths of the bisoxazolinate chelating backbone with respect to those in the neutral bisoxazoline analogs.

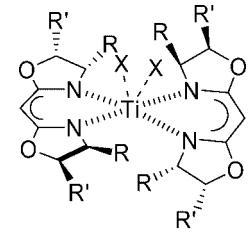
The prepared complexes were found to be highly active and productive in the ROP of (D,L)-lactide and (D,L)-β-butyrolactone, with turnover frequencies of up to 31200 h^{-1} and turnover numbers of up to 2400 (at room temperature; Scheme 8). These polymerizations proceed in a controlled manner and give polymers with relatively narrow polydispersities (M_w/M_n = 1.08–1.44). However, in all cases, and regardless of the nature of the chelating bisoxazolinate ligand, the microstructure of the polymer exhibits no stereoregularity − only atactic polymers are produced.[19]

Group 4–7 Transition Metal Complexes

Ti Complexes

Taking advantage of the ready accessibility of enantiomerically pure bisoxazolines, an enantioselective reduction of ketones catalyzed by Ti^{IV}/chiral bisoxazolinate systems (using a silane as a stoichiometric hydride source) has recently been reported by Cozzi et al.[20] Once again, the main driving force for this work was the design and synthesis of alternative catalysts to the chiral Ti metallocenes originally developed by Buchwald, which were shown to be quite effective catalysts of the aforementioned reduction but whose isolation requires a tedious resolution process. The titanium(IV)/chiral bisoxazolinate catalytic systems were generated in situ by reaction of a chiral bisoxazoline with *n*BuLi followed by addition of a titanium(IV) (TiX_4) precursor. Since two equivalents of bisoxazolinates were used, the titanium complex was proposed to be an octahedral complex of the general formula [$(Box)_2TiX_2$] (**12**; Scheme 9).

According to their studies, the best results were obtained using ligand **13**, TiF_4, and $(EtO)_3SiH$ as the hydride source. Under these conditions, the reduction of various aryl alkyl ketones proceeds with enantiomeric excess of up to 85% (Scheme 10). However, in the present case, the *ee* values are, in general, lower than those observed with chiral titanium metallocenes.



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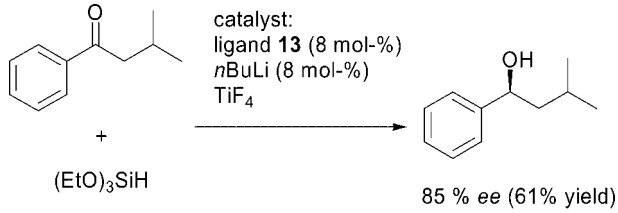
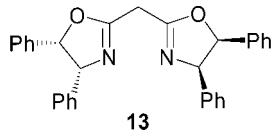
Scheme 9. Proposed structure of the titanium precatalyst.





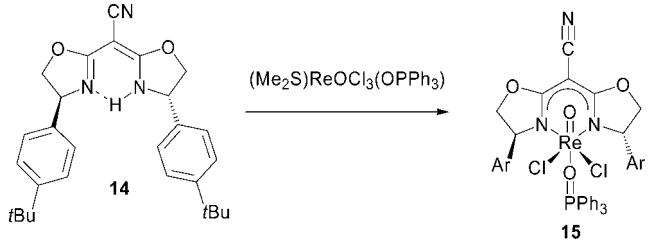
13

Scheme 10. Enantioselective reduction of isovalerophenone catalyzed by a chiral bisoxazolinatotitanium complex generated in situ.

Thorough theoretical investigations together with some NMR monitoring experiments were also carried out to gain insight into the mechanism of the Ti^{IV}/chiral bisoxazolinate-catalyzed reaction.[21] DFT calculations performed for two possible reaction pathways, one involving a Ti^{IV} hydride as the active catalytic species and the other one a Ti^{III} hydride species, concluded that the energetically favored mechanism involves a Ti^{IV} hydride as the active species. These computational results apparently matched the experimental NMR spectroscopic data, since no formation of paramagnetic species could be detected. However, it is noteworthy that a titanium(III) hydride complex has been proposed as the active species in the case of chiral titanium metallocene catalysis.[45]

Re Complexes

A chiral bisoxazolinato(oxido)rhenium(V) complex [(CN-BOX)(PPh_3O)$ReOCl_2$] (**15**; Scheme 11 and Figure 3) that was found to catalyze the enantioselective hydrosilylation of ketones and imines has also been synthesized and structurally characterized recently. Initial studies by Toste et al. showed that the Re^V complex [$(Ph_3P)_2Re(O)_2I$] efficiently catalyzes the hydrosilylation of ketones.[22] Based on mechanistic studies of the latter system, they anticipated that the use of a chiral and monoanionic bidentate ligand may open the way to an enantioselective catalytic system. While classical monoanionic bisoxazolinates do not react with [$(Ph_3P)_2Re(O)_2I$], the more acidic cyanobisoxazolines, first reported by Corey and Wang in 1993, do.[23] Thus, the reaction of cyanobisoxazoline **14** and [$(Me_2S)ReCl_3O(OPPh_3)$] affords complex **15** (Figure 3 and Scheme 11). The metal possesses a distorted octahedral geometry in which the oxido ligand is *trans* to the Ph_3PO ligand.[24] This chiral Re^V species is an active catalyst for the enantioselective phosphanyl imine reduction,[25] with good to excellent enantiomeric excesses (>99% *ee*) for aromatic imines (including heteroaromatic), α-imino esters, and α,β-unsaturated imines (Scheme 12). We also note that these reactions were carried out without the need for rigorous exclusion of air and moisture, thus rendering this catalytic system particularly attractive.



Scheme 11. Synthesis of the rhenium complex **15** from the cyanobisoxazoline **14**.

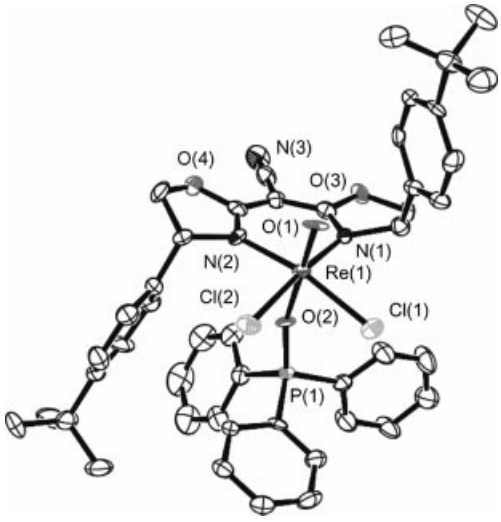
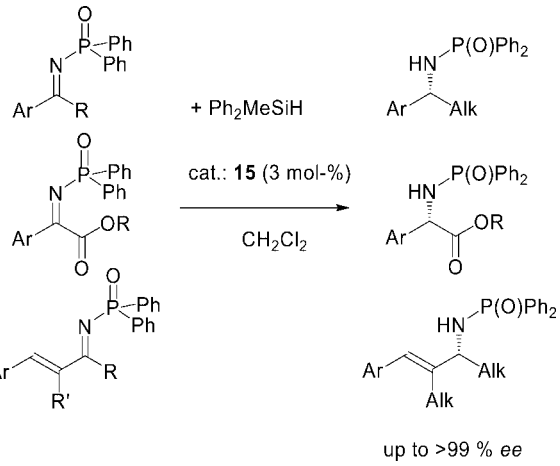


Figure 3. Molecular structure of **15**. Selected distances [Å] and angles [°]: Re(1)–O(1) 1.672(5), Re(1)–O(2) 2.131(6), Re(1)–N(1) 2.068(7), Re(1)–N(2) 2.045(7), Re(1)–Cl(1) 2.378(3), Re(1)–Cl(2) 2.368(2); N(1)–Re(1)–N(2) 90.1(3), O(1)–Re(1)–O(2) 174.7(3).

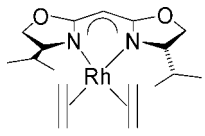


Scheme 12. Enantioselective imine reduction with rhenium precatalyst **15**.

Group 9–12 Metal Complexes

Rh Complexes

Bisoxazolinate ligands have also been found to be suitable for coordination to rhodium. In 1994, Brown et al. reported the synthesis and solid-state structure of the bisoxazolinato complex [(BOX-*i*Pr)$Rh^I(\eta^2\text{-ethene})_2$] (**16**; Figure 4).[26]



16

(BOX-Ph)Rh^I-(η-ethene)$_2$ (**17**)

(BOX-*t*Bu)Rh^I-(η-ethene)$_2$ (**18**)

Figure 4. Structure of the Rh complexes **16**–**18**.

The most interesting feature of **16** is that both ethenes are displaced from the ideal perpendicular geometry in a rotatory or "rolling" fashion by about 10°. This distortion occurs with little or no energetic cost according to theoretical calculations. More recently, the related Rh^I complexes [(BOX-Ph)$Rh^I(\eta^2\text{-ethene})_2$] (**17**) and [(BOX-*t*Bu)$Rh^I(\eta^2\text{-ethene})_2$] (**18**) have also been characterized and found to exhibit similar distortions to those observed for **16**.[27] Interestingly, the Rh^I complex **18** disproportionates to Rh^0 and the Rh^{II} species [(BOX-*t*Bu)$_2Rh^{II}$] (**19**), whose identity was unambiguously established by X-ray crystallography (Figure 5).

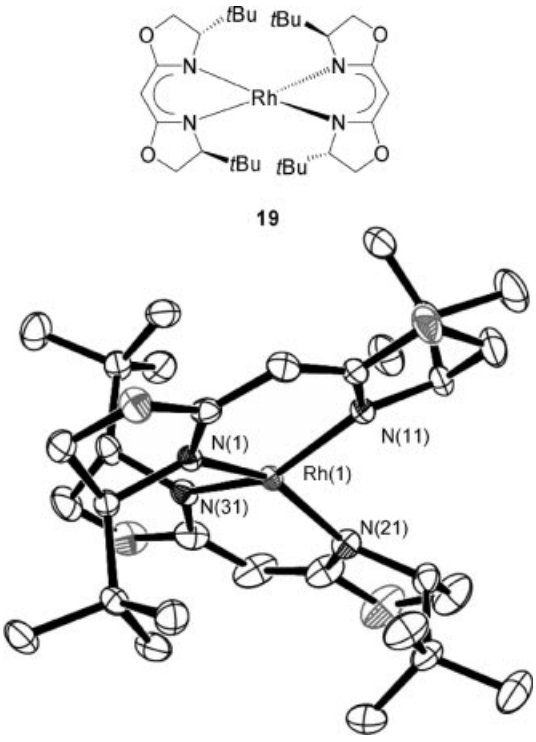


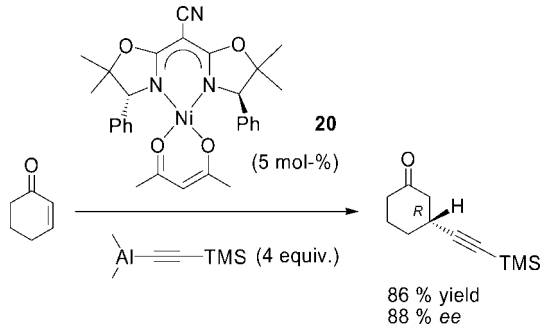
Figure 5. Molecular structure of **19**. Selected distances [Å] and angles [°]: Rh(1)–N(1) 2.041(2), Rh(1)–N(11) 2.0511(18), Rh(1)–N(21) 2.049(2), Rh(1)–N(31) 2.037(2); N(1)–Rh(1)–N(11) 90.14(10), N(21)–Rh(1)–N(31) 89.80(10).

Rh^{II} complexes are especially rare owing to the relative instability of the +II oxidation state. In light of this, complex **19** is the first example of a fully characterized mononuclear Rh^{II} complex obtained by disproportionation of a rhodium(I) complex species into Rh^0 and Rh^{II}, thus illustrating the excellent stabilizing properties of bidentate bisoxazolinate ligands. As shown in Figure 5, unlike other structurally characterized Rh^{II} complexes, which are square planar, the coordination geometry of the Rh center in **19** is approximately halfway between square planar and tetrahedral. On the basis of DFT calculations, this unusual, distorted orientation of the ligands around Rh^{II} apparently stems from an electronic preference rather than steric influences.

Group 10–12 Metal Complexes

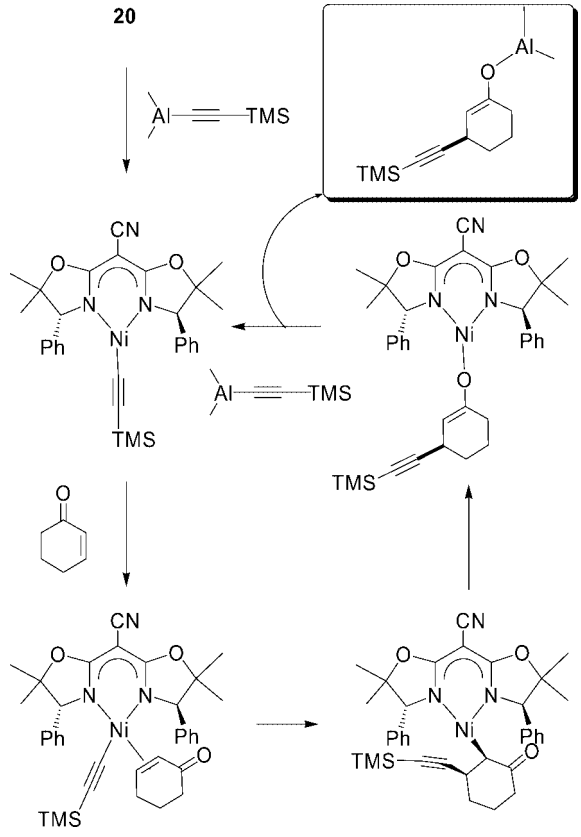
Ni Complexes

The first example of an asymmetric conjugate addition of an alkynyl group to a cyclic α,β-enone was recently reported by Corey et al. using the well-defined chiral bisoxazolinatonickel complex **20** as a catalyst and an aluminum derivative as alkynyl source (Scheme 13).[28] This unprecedented Ni^{II}-catalyzed reaction proceeds with good yields (up to 86%) and *ee* values (up to 88%) under mild conditions.

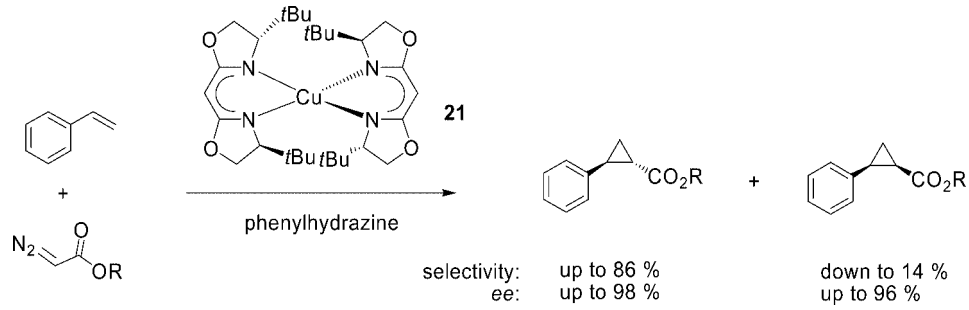


Scheme 13. Nickel-catalyzed asymmetric alkylynation of cyclohexenone.

To rationalize the observed results, the authors proposed a mechanism involving the carbometalation of the α,β-enone by an alkynylnickel intermediate (Scheme 14). Complex **20** constitutes the only reported example of a bisoxazolinatonickel complex. It is noteworthy that the outcome of this catalysis is quite different when performed with Ni(acac)$_2$ as the catalyst, where a coupled diacetylene, presumably derived from a bis(alkynyl)nickel(II) complex, was obtained as the major product. As conjectured by Corey et al., the fact that the bisoxazolinato ligand binds more tightly than the acac ligand most likely precludes the formation of this undesired bis(alkynyl)nickel(II) species.



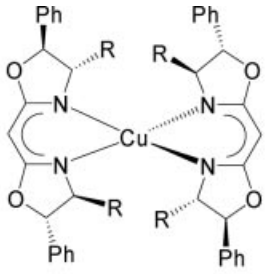
Scheme 14. Proposed mechanism for the Ni-catalyzed conjugate addition of TMS–C≡C–$AlMe_2$ to 2-cyclohexenone.



Scheme 15. Copper-catalyzed cyclopropanation of styrene.

Cu Complexes

While numerous examples of neutral chiral bisoxazolines/Cu catalytic systems have been investigated since the late 1980s due to their great utility in asymmetric catalysis, the use of copper complexes incorporating monoanionic bisoxazolinate ligands is much less common and only a few derivatives have been fully characterized. In this area, Masamune et al. first reported in 1990 the synthesis of several chiral bisoxazolinatocopper(II) complexes of the type [(BOX-R)$_2$Cu] (**21**) that are able to catalyze the asymmetric cyclopropanation of olefins with *ee* values of up to 98% for the cyclopropanation of styrene with alkyl diazoacetate (Scheme 15).[3a] These cyclopropanation reactions, however, usually proceed with poor to moderate *cis*/*trans* diastereoselectivity.



22
R = -CH$_2$OSi(Me$_2$)(*t*Bu)

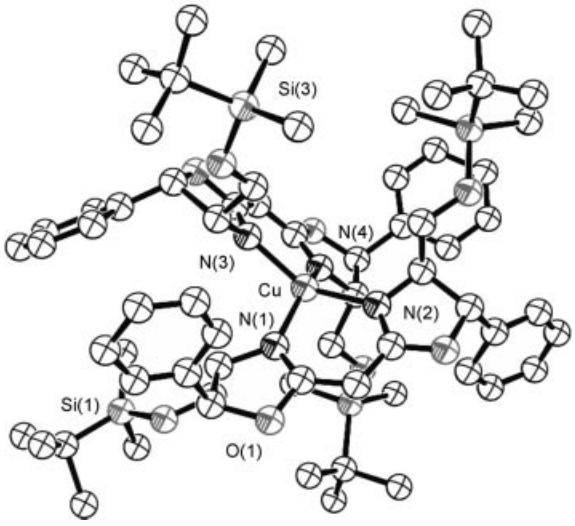


Figure 6. Molecular structure of **22**. Selected distances [Å] and angles [°]: Cu–N(1) 1.93, Cu–N(2) 1.96, Cu–N(3) 1.96, Cu–N(4) 1.91; N(1)–Cu–N(2) 91.6, N(3)–Cu–N(4) 90.8.

A little later, the first X-ray structure of a bisoxazolinatocopper(II) complex, namely [(BOX-CH$_2$OSi*t*BuMe$_2$)$_2$Cu] (**22**), was reported by Lehn et al. and showed the effective chelating ability of the bisoxazolinate unit toward Cu^{II}.[29] As illustrated in Figure 6, the copper atom in **22** adopts a distorted tetrahedral geometry, which may be ascribed to an increase of the ring strain between the R substituents of each bisoxazolinate ligand as they approach the Cu metal center. Precatalyst **22** was used in the asymmetric cyclopropanation of silyl enol ethers but gave poor yields and enantioselectivities.[30]

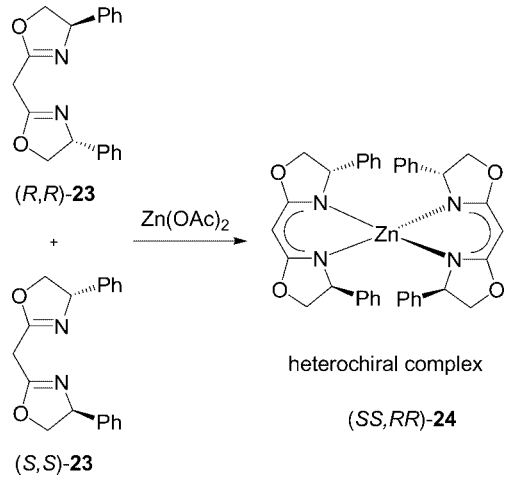
Zn Complexes

While initial spectroscopic studies by Singh suggested that the bisoxazolinate ligand might be suitable for coordination to Zn^{II}, the potential interest and usefulness of bisoxazolinatozinc complexes have only been discovered quite recently.[31] Thus, bis(bisoxazolinato)zinc [(BOX)$_2$-Zn^{II}] complexes have been prepared in an elegant manner by Takacs et al. by chiral self-discrimination of enantiomeric bisoxazoline ligands. The reaction of a racemic mixture of phenyl-substituted BOX ligands (*R*,*R*)-**23** and (*S*,*S*)-**23** with Zn(OAc)$_2$ leads to the sole formation of the heteroleptic and tetrahedral Zn complex (*RR*,*SS*)-**24** (Scheme 16).[32]

This strong preference for (*RR*,*SS*)-**24** is most likely dictated by the steric interactions between the pendant aryl groups, as illustrated by its molecular structure (Figure 7).

This approach is an effective strategy for the development of modular metal complexes based upon self-assembly of subunits (such as bisoxazolinates) around a metal complex. Thus, using this modular approach, a library of chiral bidentate P,P-ligands **25** has been synthesized and the derived chiral diphosphane ligands found to be suitable for asymmetric palladium-catalyzed allylic amination reactions with excellent yields and *ee* values (Scheme 17).[33]

The most interesting feature in the above approach is that it is a remarkably flexible and effective strategy for catalyst design. In a similar strategy, the synthesis of single-enantiomer, chiral donor–acceptor zinc complexes incorporating bisoxazolinate pseudo racemates **26** has also been performed, thereby further illustrating the chiral self-dis-



Scheme 16. Synthesis of the heterochiral complex **24**.

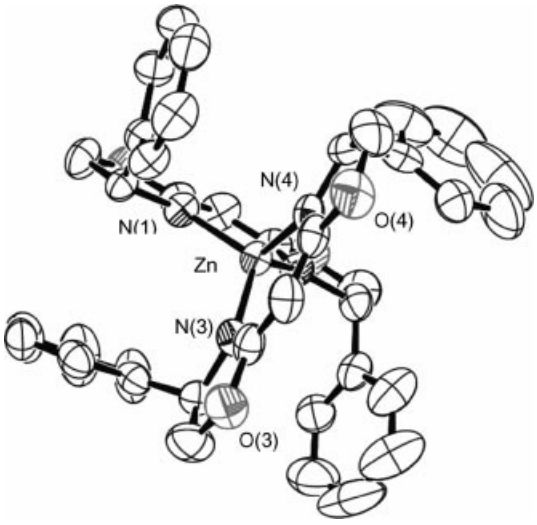
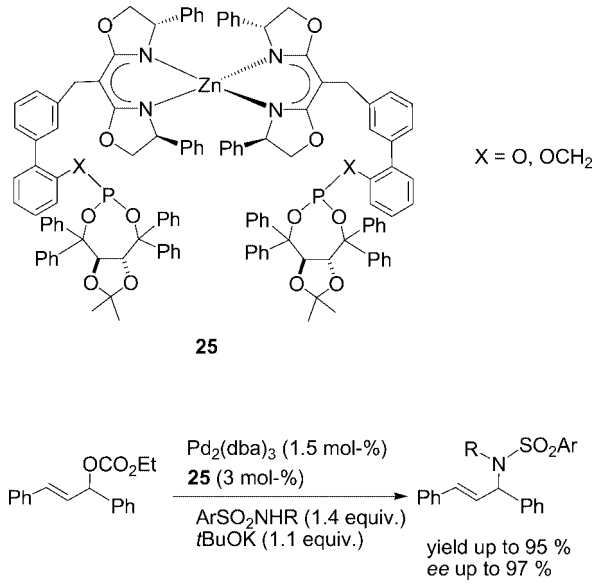


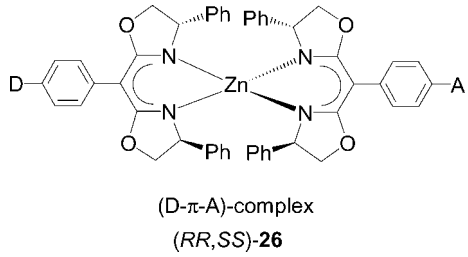
Figure 7. Molecular structure of **24**. Selected distances [Å] and angles [°]: Zn–N(1) 1.971(3), Zn–N(2) 1.973(3), Zn–N(3) 1.975(3), Zn–N(4) 1.976(3); N(1)–Zn–N(2) 94.21; N(3)–Zn–N(4) 93.56.

crimination approach (Scheme 18).[34] Such metal-organic complexes comprising electron donor, π-bridge, and acceptor (D-π-A) subunits are believed to be of potential interest for their nonlinear optical properties.

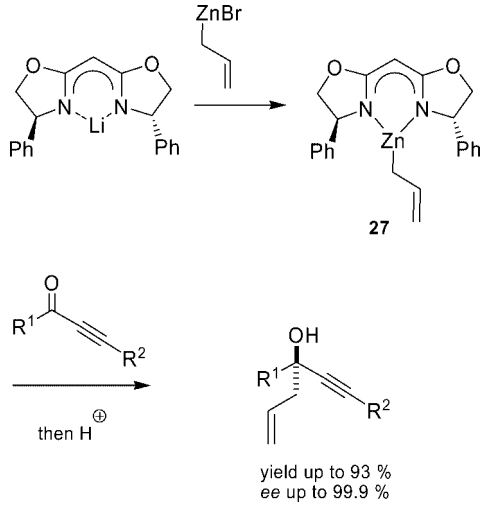
Apart from the above work, it is noteworthy that the chiral bisoxazolinate(allyl)zinc(II) complex **27**, which is readily accessible by reaction of an allylzinc bromide derivative with the corresponding bisoxazolinatolithium salt, has been shown to add in an enantioselective manner to various substrates such as olefins,[35] imines,[36] or ketones.[37] For example, addition of the allyl complex **27** to alkynyl ketones proceeds with excellent yields and *ee* values of up to 99.9% when the reaction is carried out at –100 °C (Scheme 19). This enantioselective allylic addition represents a rare example of a highly enantioselective addition to alkyl alkenyl ketones; in general, addition to ketone substrates other than alkyl aryl ketones occurs with a lower selectivity than that observed here.



Scheme 17. Asymmetric allylic amination using self-assembled chiral bidentate P,P-ligands **25**.

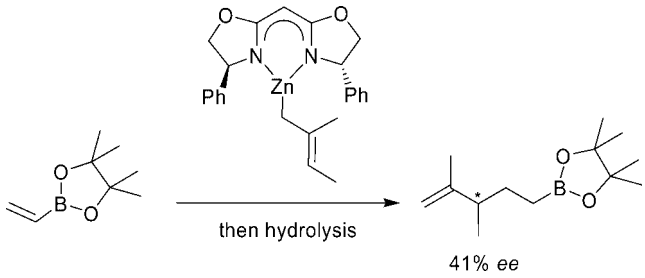


Scheme 18. Chiral self-assembly of bisoxazolinates containing an electron donor and acceptor.



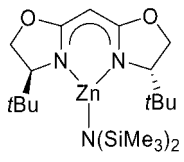
Scheme 19. Stoichiometric allylation of alkynyl ketones with **27**.

Nakamura further extended his studies on zinc complexes similar to **27** and briefly reported their use in the regioselective allylzincation of alkenyboronate; however, poor asymmetric inductions (up to 41% *ee*) as well as low yields were observed (Scheme 20).[38]



Scheme 20. Stoichiometric allylation of vinylboronate.

Coates et al. have probed the potential of the chiral bisoxazolinato(amido)zinc complex **28** (Scheme 22) as a catalyst for the copolymerization of CO_2 and cyclohexene oxide.[39] Surprisingly, complex **28** was found to be inactive in the aforementioned catalysis even though the structurally similar β-diketiminato(amido)zinc analogs exhibit an excellent activity. Finally, the chiral bis(bisoxazolinato)zinc(II) complex **29** (Scheme 21) has also been structurally characterized by Halcrow, Kee et al. and tested in for phospho-aldol catalysis, albeit with no success.[40]



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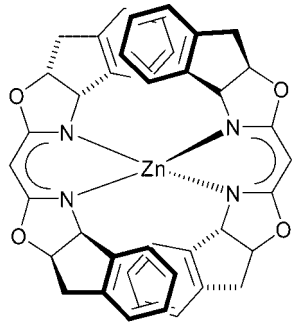

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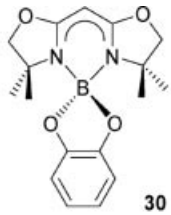
Scheme 21.

Group 13 Metal Complexes

Boron bisoxazolinate complexes have also been structurally characterized and employed as chiral catalysts for the asymmetric reduction of various prochiral ketones. Thus, in 2001, Cozzi, Umani-Ronchi et al. reported that catecholborane readily reacts with neutral bisoxazolines to afford the corresponding four-coordinate bisoxazolinate boron complexes **30**, whose molecular structure was determined by X-ray crystallography, thereby confirming the formation of a four-coordinate coordinatively saturated boron complex and the effective chelation of one bisoxazolinate ligand to the boron center (Figure 8).[41]

Chiral versions of **30** were found to be effective catalysts in the enantioselective reduction of various ketones in the presence of catecholborane. This catalysis proceeds with *ee* values up to 86% and good yields when the bisoxazoline **31** is used as the supporting chiral ligand (Scheme 22).[42]



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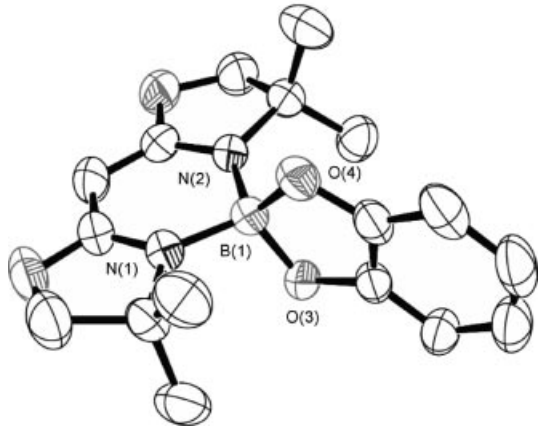
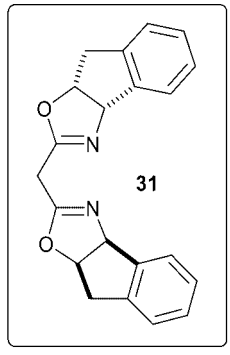


Figure 8. Molecular structure of **30**. Selected distances [Å] and angles [°]: B(1)–N(1) 1.541(2), B(1)–N(2) 1.548(2), B(1)–O(3) 1.481(2), B(1)–O(4) 1.479(2); N(1)–B(1)–N(2) 105.8(1), O(3)–B(1)–O(4) 104.5(1).



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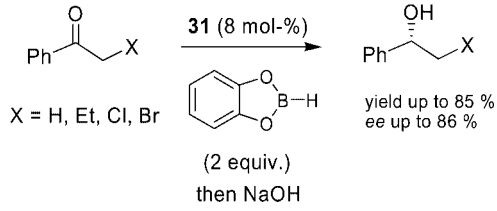
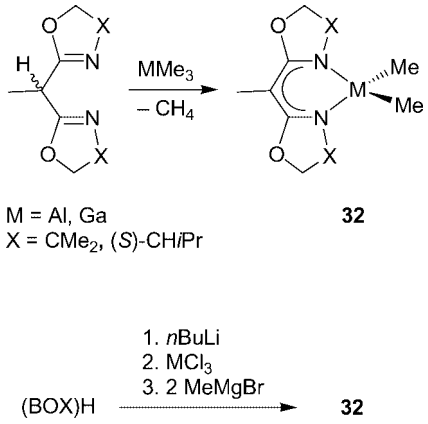


Scheme 22. Enantioselective reduction of ketones in the presence of **31**.

On the basis of detailed DFT calculations, the authors managed to gain insight into the mechanism of this reduction reaction and proposed that the transfer of the hydride ion from the boron atom of the catecholborane to the carbonyl of the prochiral ketone is the rate-determining step of the catalytic process. They also concluded that the origin of the enantioselectivity arises from a complex interplay involving, for the most part, steric repulsions between the ketone substituents and the boron-bisoxazolinate ring.

Monoanionic bisoxazolinate ligands are also suitable for coordination to aluminum and gallium, thus allowing the synthesis of the corresponding dimethyl and dichlorido mono-bisoxazolinate complexes **32** by either salt metathesis or an alkane elimination (Scheme 23).[43,44]



Scheme 23. Synthesis of aluminum and gallium bisoxazolinates **32**.

As illustrated in Figure 9, the molecular structure of the chiral bisoxazolinate aluminum derivative [{BOX-*i*Pr}-$AlMe_2$] exhibits a nearly perfectly planar six-membered Al metallacycle, with the Al metal center adopting a distorted tetrahedral geometry and being chelated by a π-delocalized bisoxazolinate ligand.

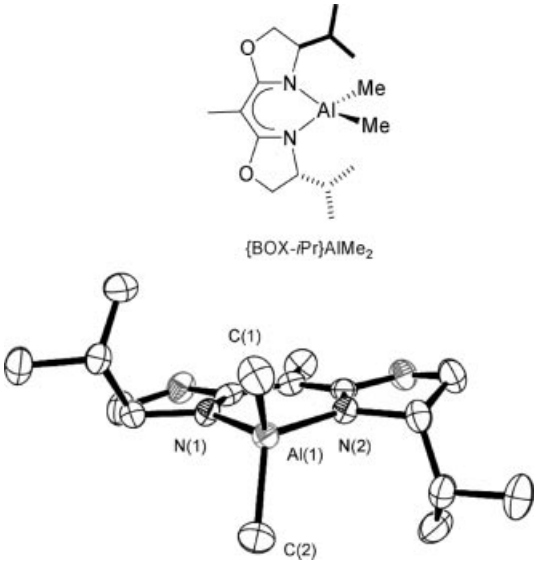
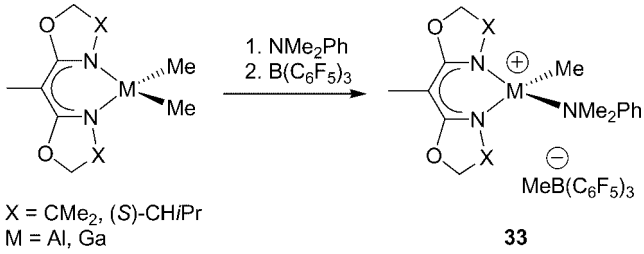


Figure 9. Molecular structure of **32** [M = Al]. Selected distances [Å] and angles [°]: Al(1)–N(1) 1.906(2), Al(1)–N(2) 1.899(2), Al(1)–C(1) 1.967(2), Al(1)–C(2) 1.968(3); N(1)–Al(1)–N(2) 93.13(7), C(1)–Al(1)–C(2) 111.8(1).

More importantly, the dimethylaluminum and -gallium mono-bisoxazolinato derivatives can be readily converted into four-coordinate metal cations **33** by a Me^- abstraction reaction with $B(C_6F_5)_3$ in the presence of an external Lewis base such as an amine (Scheme 24). The excellent stability of the highly Lewis acidic cations **33** illustrates the suitability of the bisoxazolinate ligand for the generation of cationic chiral group 13 alkyl derivatives. The molecular structures of these complexes were unambiguously confirmed by X-ray crystallographic studies. The molecular structure of the aniline-stabilized, four-coordinate bisoxazolinate Al cation $[\{BOX\text{-}Me_2\}Al(Me)(NMe_2Ph)]^+$ is illustrated in Figure 10 as an example. Unlike [{BOX-*i*Pr}$AlMe_2$], the Al chelated six-membered ring is significantly distorted from planarity, with the Al center lying out of the plane of the bisoxazolinate backbone. In fact, the bidentate chelating ligand appears to be pushed away from the Al-NMe_2Ph group, which may be to avoid significant steric interactions between the aniline and the bidentate ligand. Preliminary reactivity studies suggest that these cationic Lewis acids may be of interest as catalysts of hetero-Diels–Alder reactions and propylene oxide polymerizations.



Scheme 24. Synthesis of the cationic species **33**.

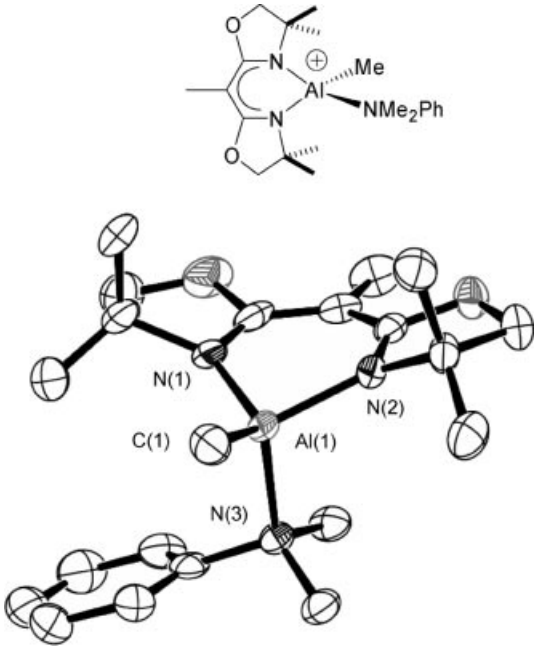
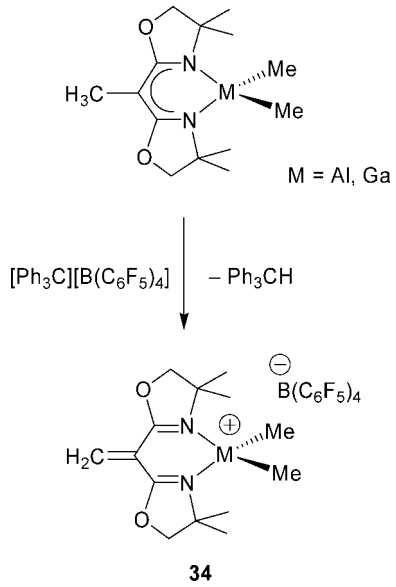


Figure 10. Molecular structure of **33** (M = Al; X = CMe_2). Selected distances [Å] and angles [°]: Al(1)–N(1) 1.852(5), Al(1)–N(2) 1.857(4), Al(1)–N(3) 2.018(4), Al(1)–C(1) 1.942(6); N(1)–Al(1)–N(2) 95.8(2), C(1)–Al(1)–N(3) 111.3(2).

Finally, from a reactivity point of view, it is interesting to note that, unlike $B(C_6F_5)_3$, $[Ph_3C][B(C_6F_5)_4]$ does not abstract a Me^- from the Al or Ga metal center when treated with the dimethyl bisoxazolinate derivatives **32**; rather, it abstracts a hydride from the back of the bisoxazolinate ligand to afford the unexpected bisoxazoline metal complex

34 (Scheme 25). This observed reactivity illustrates an unusual Lewis base character for a bisoxazolinate ligand incorporated in a metal complex.



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Scheme 25. Hydride abstraction reaction by $[Ph_3C]^+$ on **32**.

Conclusions

Over the past few years, bisoxazolinate ligands have established themselves as a versatile class of monoanionic bidentate N,N-ligands that are able to effectively chelate various metal centers, with a coordination chemistry, for the most part, reminiscent of that of the β-diketiminate ligand. It is thus not surprising to find chiral C_2-symmetric bisoxazolinate ligands involved as supporting ligands in numerous metal-complex-catalyzed enantioselective reactions, as summarized in the present contribution. Overall, the excellent stability and robustness of this class of ligands, their good level of asymmetric induction in various enantioselective catalyses, and their frequent commercial availability at a moderate cost in an enantiomerically pure form are three major advantages that should promote the use of bisoxazolinato–metal complexes in the near future so as to extent their scope of applications.

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