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PERSPECTIVE

Recent advances in the use of chiral metal complexes with achiral ligands for application in asymmetric catalysis

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This perspective describes recent progress in asymmetric catalysis with chiral only-at-metal complexes displaying Λ / Δ enantiomorphs in the absence of central chirality within the ligands, with an emphasis on Ir(III) and Rh(III) systems. The good selectivity achieved when using these complexes in asymmetric catalysis has been demonstrated in asymmetric transformations through various mechanisms, including hydrogen-bond donor-acceptor, secondary amine or Brønsted base hydrogen-bond donor bifunctional catalysis, Lewis acid and photoredox catalysis under mild reaction conditions. This perspective highlights the widening field of chiral-at-metal catalysis and presents a selection of asymmetric transformations which have been successfully carried out using them.

Introduction

The ability to form new chiral metal complexes for use in asymmetric catalysis is an important task in modern synthetic chemistry.[1] Chiral metal-containing catalysts allow for a host of chemical transformations to be carried out with high selectivity and efficiency.[2] Indeed a number of industrially important asymmetric processes are carried out under control of chiral metal-containing catalysts.[3] There are many ways to impart chirality about a metal centre. The use of chiral ligands to surround the metal centre with chiral information and relay this to the forming product is a mainstay of the field.[4] Such ligands can contain, central chirality of stereogenic carbon atoms. Kobayashi and co-workers used centrally chiral nickel diamine complexes (Fig. 1, **I**) for enecarbamate additions to butane-2,3-dione.[5] The use of atropisomeric ligands has been elegantly demonstrated by Noyori and co-workers in many reactions including ruthenium BINAP (**II**) catalysed hydrogenation of aldehydes and ketones.[6] Planar chirality (**III**) has been pioneered as a chiral information transformation format by Fu and co-workers exemplified by their transformative reports in kinetic resolution of racemic secondary alcohols.[7]

A less well studied form of chirality in catalytically active complexes is where the metal centre itself is chiral, by dissymmetric ligand coordination. In these cases the ligands associated to the metal do not have any inherent chiral information. But the arrangement of non-chiral ligands around a metal can form enantiomeric complexes, as first predicted and witnessed by Werner over a century ago.[8] Centrally chiral at metal complexes result in both tetrahedral (**IV**) and octahedral (**V**) complex geometries, are possible. Using non-chiral polydentate ligands can also give rise to chiral at metal complexes where bidentate (**VI**) and tridentate (**VII**) ligands impart a sense of twist in the complex. This type of "propeller" chirality assigned as Λ for left and Δ for right handed twist.[9]

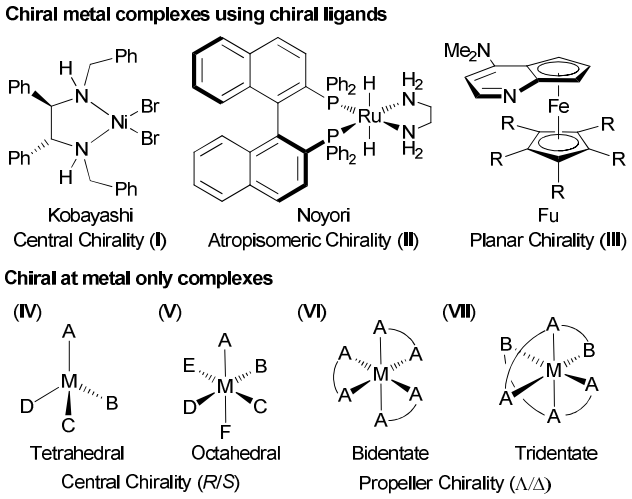


Fig. 1 Chiral metal catalysts with different aspects of stereogenicity.

Chiral at metal complexes have several advantageous features over their chiral ligand containing counterparts.[10] As non-chiral ligands are used, this means that ligand scope is massively increased. Chiral ligands are often more synthetically challenging to access compared to their non-chiral counterparts. Due to this increased ligand scope, multiple functional groups can be more readily installed around the metal centre. Therefore, it can be envisaged that multifunctional chiral at metal complexes could be formed and used in catalysis.

One limitation in the use chiral only at metal complexes is in their asymmetric synthesis, in high e.e., or the requirement for resolution to deliver catalysts themselves in high e.e.. The ability to selectively form single stereoisomers of these complexes is challenging, not least because of the huge number of possible stereoisomers possible in some cases. But within the field a number of approaches, including the use of multidentate ligands, can address some of the otherwise daunting selectivity issues.

In this perspective, recent developments in the field of chiral only-at-metal complexes and their use as asymmetric catalysts, with an emphasis on Ir(III) and Rh(III) based systems, are presented. In most cases, the catalysts discussed provide asymmetric induction through their coordinated ligand sphere[11] or through the central metal directly.

Complexes with direct metal carbon bonds and the use of CN ligands

The ability to form complexes where the catalytically active metal centre is directly bonded to a carbon atom is an important synthetic procedure in allowing for the formation of chiral metallocycles, a class of important catalysts.[12] Carbon-nitrogen (CN) ligands are among the most commonly employed bidentate ligands.[13]

For ruthenium, non-chiral, metallocyclic complexes find many applications, such as the NCN tridentate ligands, employed by Beley *et al.* (Fig. 2), forming a bimetallic complex **1**,[14a] or the similar complexes of Gagliardo and coworkers[14b] used a hexadentate pincer ligand to form diorganoruthenium complex **2**. Pincer complexes have been successfully employed as asymmetric catalysts, Medici *et al*. used a ruthenium pincer system for asymmetric hydrogen transfer to acetophenone.[15]

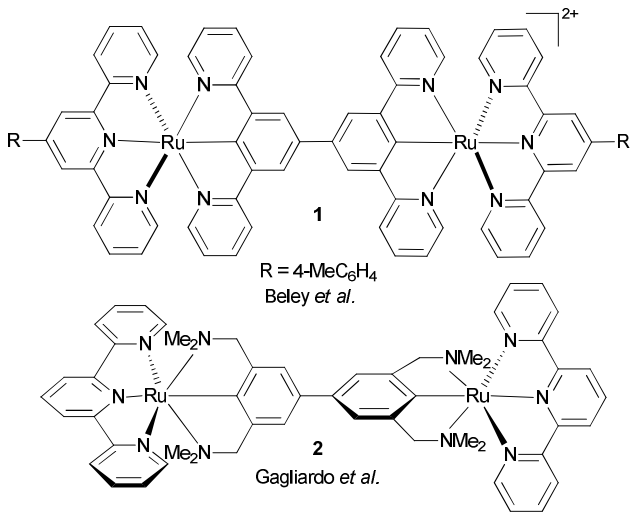


Fig. 2 Non-chiral ruthenium metallocyclic complexes with NCN ligand.

Iridium is another metal with demonstrated high catalytic activity and application in asymmetric synthesis.[16] The formation of dichloro-bridged metallocyclic iridium dimers was first demonstrated in 1984 by Sprouse *et al*.. They showed that CN ligands in combination with bridging chlorine atoms could lead to a synthetically useful dimer **3**.[17,18] This dimer has been used to synthesise many important iridium containing, chiral at metal complexes (e.g. Scheme 2). Such iridium based complexes have found many applications outside of the asymmetric catalysis arena, based on their absorption and emission characteristics.[19]

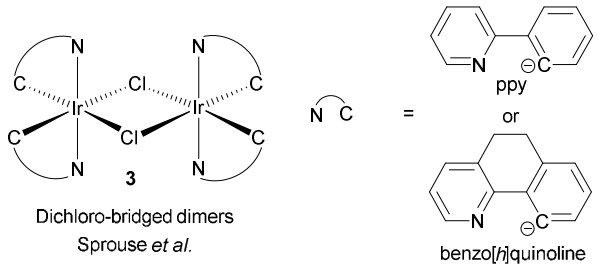
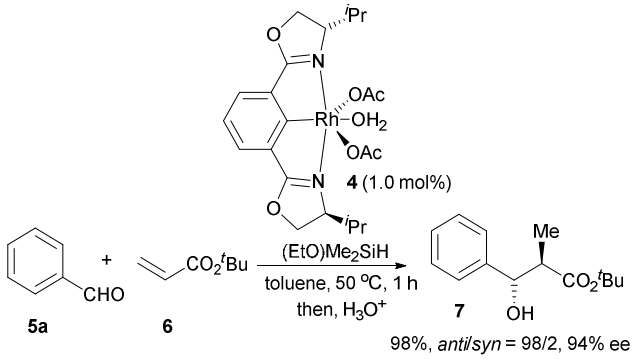


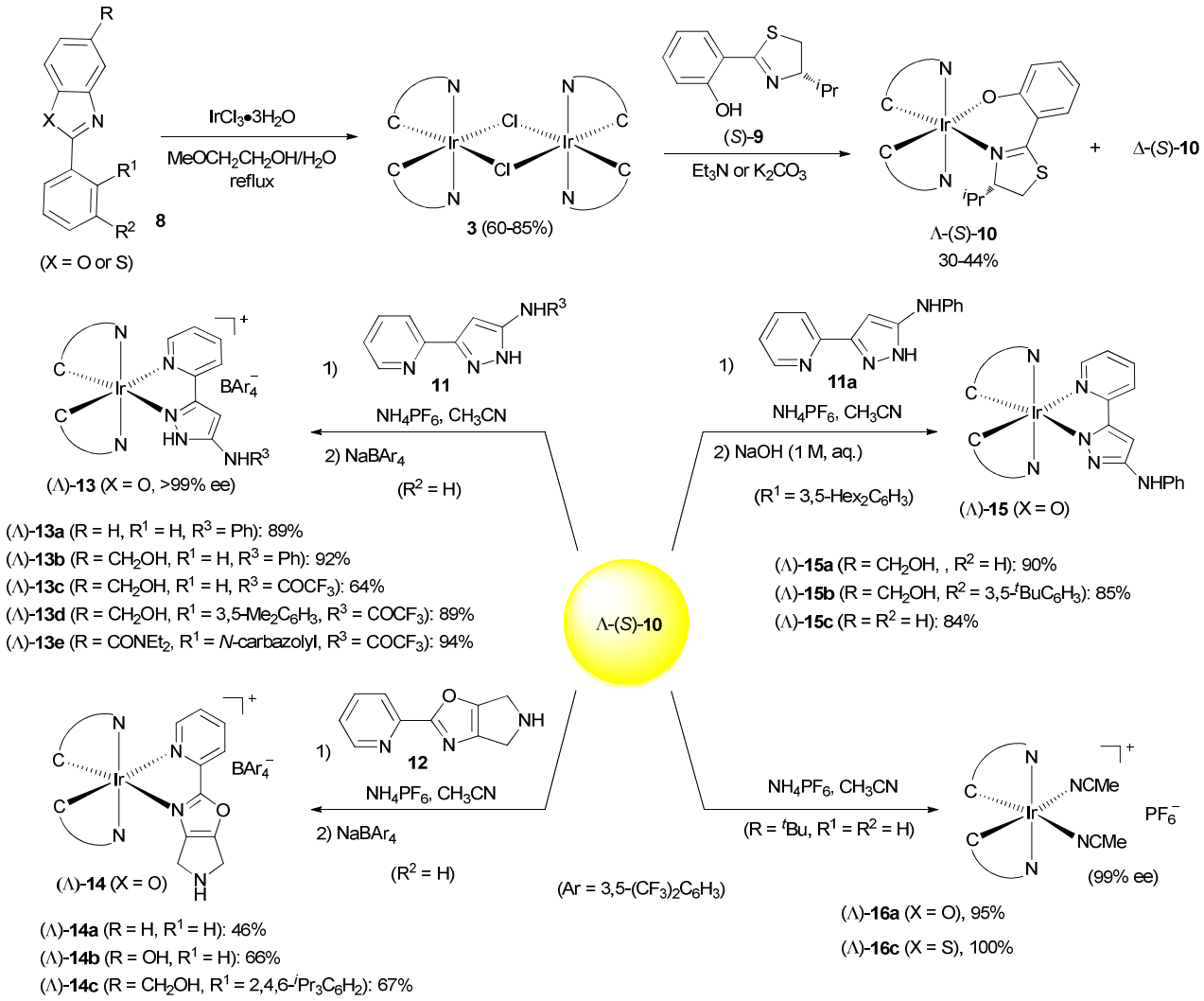
Fig. 3 Ir-based complexes with metal carbon bonds.

Rhodium is another metal which has been used in several chiral at metal complexes.[20] The use of bisoxazoline ligands which coordinate in an NCN arrangement have been successfully used as asymmetric catalysts. Nishiyama *et al.* who showed the use of rhodium bisoxazoline complexes (RhPheBOX) for asymmetric reductive aldol reactions. They found that in the presence of catalyst **4** a high level of *anti*-selectivity was obtained in the alcohol product **7** (Scheme 1).[21] In addition, Ito *et al*. successfully used RhPheBOX in enantioselective hydrogenation and transfer hydrogenation of ketones.[22] As demonstrated later in this perspective, these types of ligands can play a vital part in the formation of chiral at metal complexes.



Scheme 1 Rh catalysis for asymmetric reductive aldol reaction.

Strategies for the preparation of chiral only-at-metal Co(III), Cr(III), Ru(II) complexes used in asymmetric catalysis originally relied on resolution methods, either chiral resolving agents or preparative chiral HPLC were used.[10,23] A practical strategy for the generation of enantiomerically pure chiral only-at-metal Ir(III) or Rh(III) complexes, initially developed for asymmetric synthesis of chiral-at-metal Ru complexes,[24a] which contain direct metal carbon bonds was developed by Meggers and co-workers.[24b] As shown in Scheme 2, the reaction of $IrCl_3 \cdot 3H_2O$ with benzoxazole/benzothiazole **8** gave the mesomeric Ir(III) dimer **3** with high diastereoselectivity. Subsequent reaction with chiral auxiliary (*S*)-thiazoline **9** provided the two key diastereomeric intermediates Λ-(*S*)-**10** and Δ-(*S*)-**10**, which could be separated by simple silica gel chromatography, and isolated in good yields. Replacing the auxiliary under different conditions delivered the corresponding enantiopure chiral at-metal Ir(III) complex (Λ)-**13**, (Λ)-**14**, (Λ)-**15**, (Λ)-**16a** and (Λ)-**16c** containing versatile functional groups.[25] Simply switching the chiral auxiliary to L- or D-proline enabled the preparation of both enantiomers of the more coordinatively labile Rh(III)-based complex **16b**, a congener of **16a** (the synthetic details are not shown in Scheme 2).[25f]



Scheme 2 Synthesis of chiral only-at-metal complexes *via* chiral auxiliary strategy.

Through this protocol, a series of Ir(III) and Rh(III) complexes with different functional groups substituted within the ligands were easily synthesised. Interestingly, the absolute configuration of the central metal was retained during these transformations, which might be attributed to the stabilising bis-cyclometalated chelate effect.[25b] The installation of hydroxyl or amide groups is desirable since they might be important for hydrogen bonding activation, while the existence of secondary amines may have implications for enamine or imine catalysis. On the other hand, by coordination, the acidity of N-H bond in pyrazole ligand was enhanced and treatment with base gave rise to the neutral pyrazolato Ir(III) complex **15**, which might serve as chiral Brønsted base catalyst; the presence of secondary amino group in the 3-position of coordinated pyrazolato ligand enables to raise the basicity of catalyst and provide a hydrogen bond acceptor. Noticeably, these synthesised chiral only-at-metal multifunctional catalysts are different from analogous organocatalysts[26] that engender asymmetry by similar mechanisms. Fig 4 depicts some representative amine-containing organocatalysts to allow comparison with (Λ)-**14c**, bearing similar functional groups.

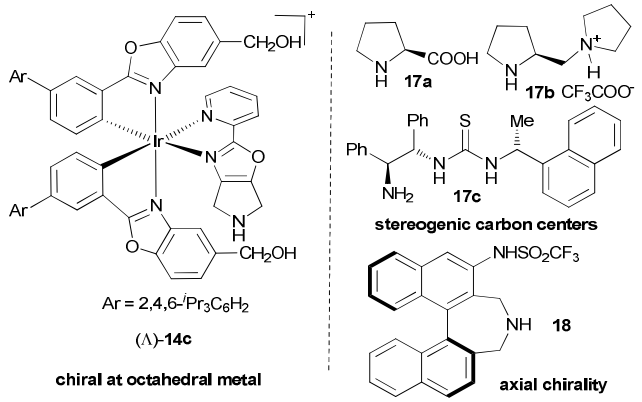
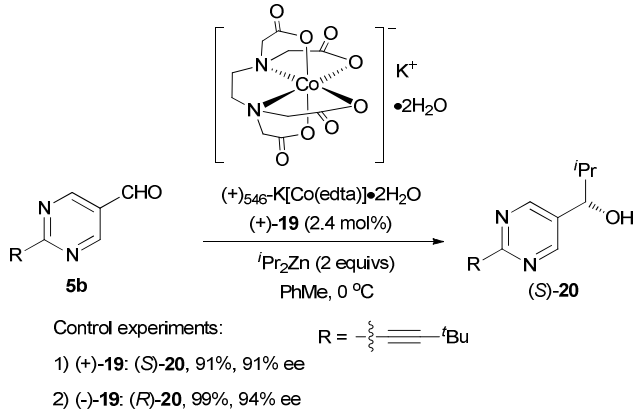


Fig. 4 Comparing chiral only-at-metal Ir(III) complex with traditional organocatalysts.

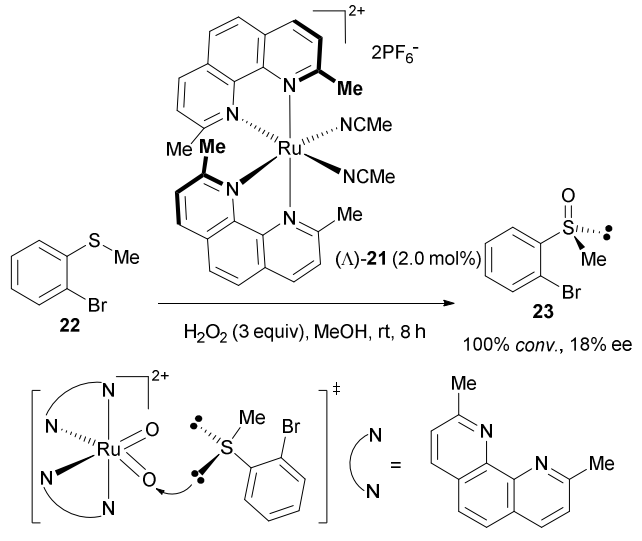
Early examples using chiral only-at-metal complexes for asymmetric catalysis

Attempts to use chiral only-at-metal Co(III) complex ($[Co(en)_2NH_3Cl]Br_2$) for oxidative kinetic resolution of *rac*-3,4-dihydroxyphenylalanine had been reported by Shibata and Tsuchida in their pioneering work as early as 1929.[27] However, the chemistry of this area had been largely ignored until 2001. In their continuing study on asymmetric autocatalysis,[28] Soai and co-workers found that the asymmetric addition of $^{i}Pr_2Zn$ to pyrimidine-5-carbaldehyde **5b** was affected by octahedral Co(III) salt $K[Co(edta)]\cdot 2H_2O$ **19** with excellent e.e., the absolute configuration of the product **20** was controlled by the chirality of the Co(III) complex (Scheme 3).[29]



Scheme 3 Co(III) complex initiated asymmetric autocatalysis.

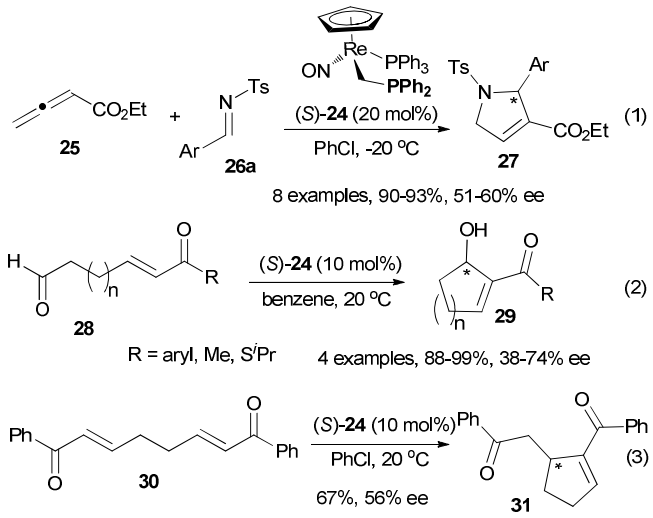
Due to the poor solubility of cobalt complex **19** in toluene, the asymmetric induction appears to happen at the interface between the crystal of metal salt and the solvent. It is postulated that the potassium ion within the Co(III) salt might act as a Lewis acid to promote the asymmetric addition of $^{i}Pr_2Zn$ to aldehyde **5b** first, forming the alkoxide of **20** with low e.e.. *Chirality amplification* takes place in the subsequent asymmetric autocatalysis process.[30] Strictly speaking, even though the selectivity is high (up to 94% e.e.), Co(III) complex **19** is not a true catalyst but acts as the initiator in the process. Subsequently another chiral only-at-Cr(III) complex has also been used for this purpose by the same group with high enantioselectivity.[31]



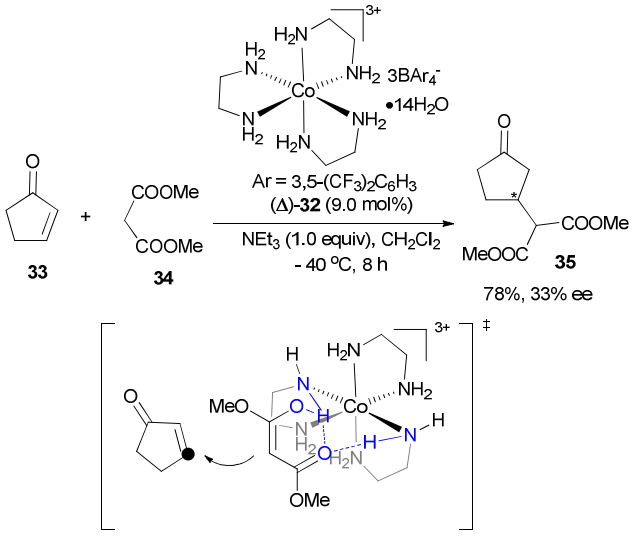
Scheme 4 Ru(II)-catalysed asymmetric oxidation.

In 2003, Fontecave and co-workers reported that chiral only-at-metal Ru(II) complex (Λ)-**21** was able to catalyse the asymmetric oxidation of sulfide **22** to sulfoxide **23** in up to 18% e.e. (Scheme 4).[32] This result demonstrated, for the first time, that chiral only-at-metal complexes can be used for asymmetric catalysis. As shown in the suggested transition state, a Ru(VI)-oxo intermediate was proposed as the true oxidant.[33]

As depicted, the catalytic activity of chiral only-at-metal Co(III) (Scheme 3) and Ru(II) (Scheme 4) complexes is dependent on the metal ion. Additionally, chiral only-at-metal complex could also provide asymmetric induction through their coordinated ligand sphere. In 2006, an asymmetric version was developed by Gladysz and colleagues (Eq 1, Scheme 5) using rhenium-containing (*S*)-phosphine **24** as a chiral catalyst.[34a] Although the enantioselectivity was moderate (51-60% e.e.), this metal-templated Lewis base represents a promising new direction for the development of nucleophilic catalysis. Applications of the same catalyst to asymmetric intramolecular Morita-Baylis-Hillman (Eq 2) and Rauhut-Currier reactions (Eq 3) were also disclosed in 2007.[34b, 35]



Scheme 5 Rhenium-containing phosphine catalysed asymmetric reactions.



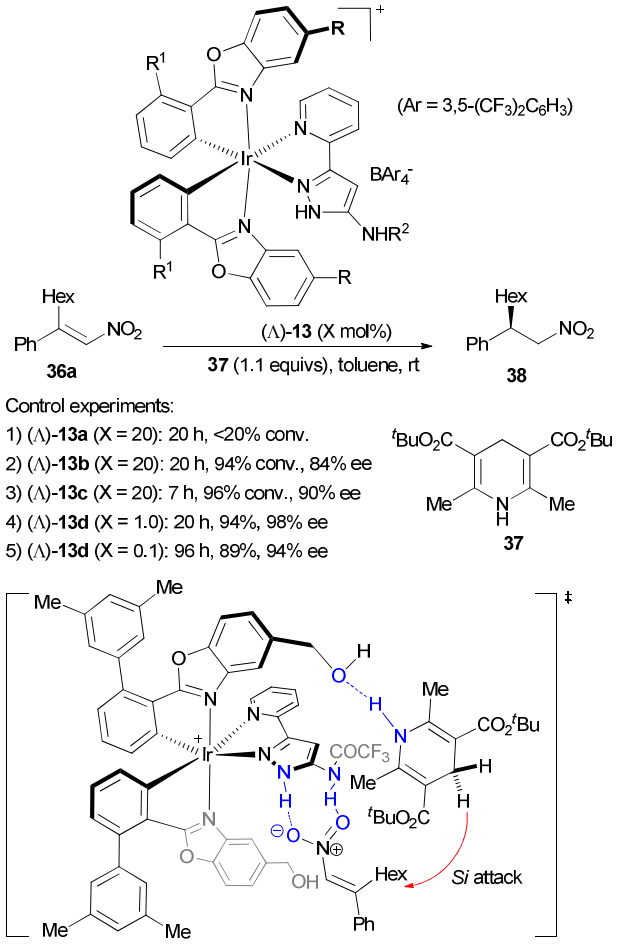
Scheme 6 Cobalt(III)-catalysed asymmetric addition reactions.

In 2008, Ganzmann and Gladysz noted that chiral only-at-metal Co(III) Werner salt (Δ)-**32** could catalyse the Michael addition of dimethyl malonate to cyclopentenone **33**, albeit with only 78% yield and 33% e.e. (Scheme 6).[36] The bulky BAr_4^- (Ar = 3,5-$(CF_3)_2C_6H_3$) anion was used to enhance the solubility of the Werner cation in CH_2Cl_2. Since the catalyst is substitutionally inert and due to the strong binding capability of the bidentate ethylenediamine ligand, asymmetric induction is hypothesised to take place through the abundance of N-H bonds as hydrogen-bond donors around the metal centre. This sometimes overlooked, novel, family of chiral hydrogen bond donor catalysts will likely find more applications in the near future.

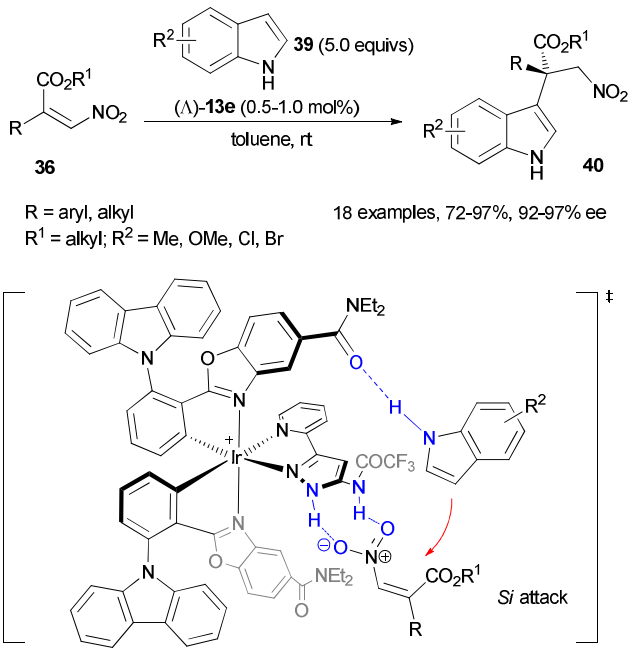
Highly enantioselective asymmetric reactions catalysed by chiral only-at-metal Ir(III) and Rh(III) complexes

Owing to their high catalytic activities, as well as the convenient preparation methods developed by Meggers *et al.* (Scheme 2), chiral only-at-metal Ir (III) and Rh (III) promoted enantioselective asymmetric reactions have become more well developed in recent years. For example, chiral Ir(III) complex **13** catalysed asymmetric transfer hydrogenation of β, β-disubstituted nitroalkene **36a** with Hantzsh ester **37** was first tested by Gong and Meggers in 2013.[25a] As evidenced by control experiments shown in Scheme 7, the outcome was very poor (20 h, <20% conv.) when 20 mol% of (Λ)-**13a** was employed. In sharp contrast, introduction of a CH_2OH group to the benzoxazole ligand significantly accelerated the conversion to 94% within 22 hours, implying the importance of the hydroxyl group in this transformation. Increasing the acidity of the amide NH group and the steric constraint at the two R^1 positions gave a jump in efficiency in the asymmetric induction. With only 1.0 mol% of catalyst (Λ)-**13d**, 94% isolated yield and 98% e.e. was obtained, this matches or even surpasses the best result using equivalent metal, bio, or organocatalysts.[37] The result was deemed satisfying (89%, 94% e.e.) even when decreasing the catalyst loading of (Λ)-**13d** to 0.1 mol%, removing the concern that a considerable amount of catalyst would be required due to its large molecular weight.

Since the catalyst (Λ)-**13** is substitutionally inert, functional groups in the ligand sphere should be responsible for catalytic performance. Based on these observations, a proposed transition state was outlined. The electrophility of nitroalkene **36a** was increased by a double hydrogen bonding effect with the amidopyrazole moiety. The hydroxyl group was thought to serve as a hydrogen bond acceptor, activating the Hantzsch ester **37** *via* the formation of a further hydrogen bond, and thus shortening the distance between the two substrates as well as guiding the transfer hydrogenation from the *si* face. The presence of bulky 3,5-dimethylphenyl substituents might facilitate the formation of these hydrogen bonds, due to them stabilising the major transition state. It is not hard to envisage, the Ir(III) complex acting as a novel hydrogen bond donor-acceptor bifunctional catalyst in this reaction, while the iridium centre itself acts as an unreactive spectator fulfilling a purely structural role. Distinguished from typical (thio)urea-based hydrogen-bonding donor catalysts with a flexible conformation,[38] the three-dimensional and rigid chiral only-at-metal Ir(III) complexes resulting from the chelate effect could provide new advantageous routes for designing a family of metal-templated catalysts for other asymmetric reactions. This seminal work represented the first example of highly enantioselective asymmetric reactions being carried out using chiral only-at-metal catalysts, despite the metal not being intimately involved.



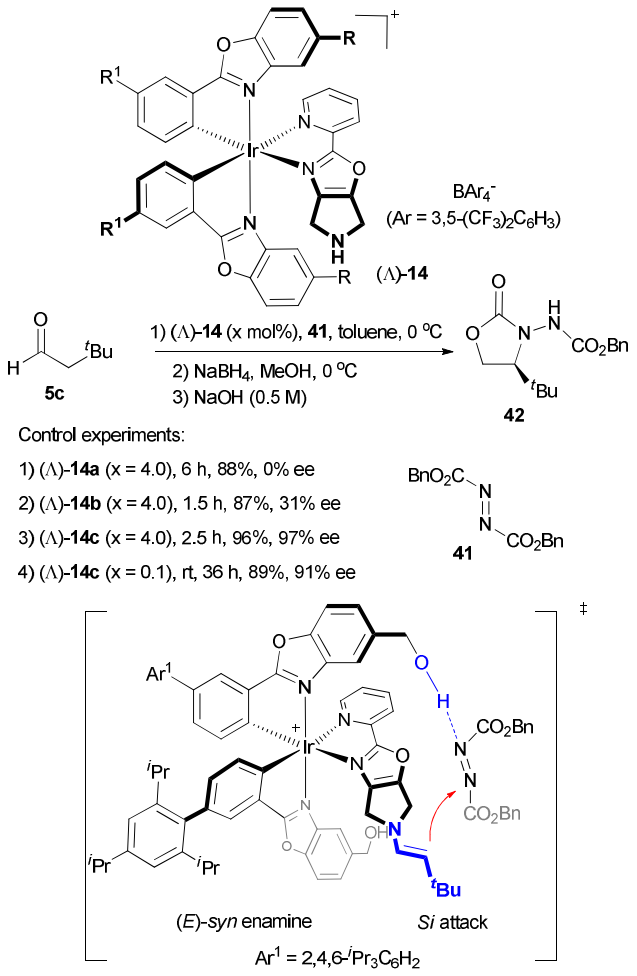
Scheme 7 Ir(III)-catalysed asymmetric reduction reaction.



Scheme 8 Ir(III)-catalysed asymmetric Michael addition reaction.

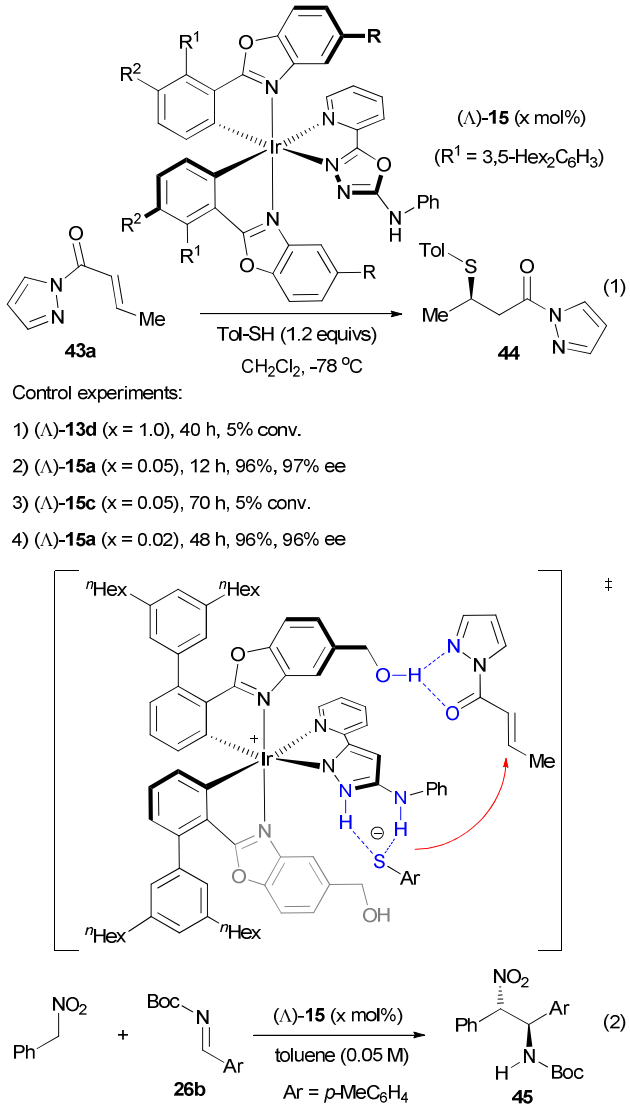
The unique nature of these Ir(III)-based hydrogen bond donor-acceptor bifunctional catalysts was applied in

promoting other, more challenging transformations such as the asymmetric addition of indoles **39** to β,β-disubstituted nitroalkenes **36** (Scheme 8), for the construction of all-carbon quaternary stereogenic centres with high yields and enantioselectivities.[25b] The performance of the catalyst (Λ)-**13e** was dramatically improved by replacing the hydroxyl group with carboxamide, a stronger hydrogen-bond acceptor, as well as changing the 3,5-dimethylphenyl to a carbazolyl moiety. Moreover, the practicality of the catalyst has been improved by its recyclable utilisation of at least three applications without any significant loss in catalytic activity. Interestingly, the same reaction had also been accomplished by Akiyama[39] and co-workers *via* Brønsted acid catalysis, the advantage of this chiral only-at-metal Ir(III) complex lies in its low catalyst loading with high enantioselectivities, in combination with its recyclability.



Scheme 9 Asymmetric α-amination of aldehydes.

Besides these two applications, this substitutionally inert metal complex has been utilised as a powerful template for designing other multifunctional catalysts. For instance, by adopting a similar chiral auxiliary strategy, iridium (III) complex **14** containing a secondary amine for performing enamine catalysis alongside an hydroxyl were readily prepared by Meggers and co-workers (Scheme 2).[25c] It was found that this novel bifunctional catalyst enabled the asymmetric α-amination of aldehyde **5c** with dibenzyl azodicarboxylate **41** as a nitrogen source.[40] As shown in the control experiments (Scheme 9), the pre-assembled hydroxymethyl and the bulky 2,4,6-$^{i}Pr_3C_6H_2$ groups in the organic ligand sphere of the catalyst were required for achieving high enantioselectivity (91% e.e.) with catalyst loadings as low as 0.1 mol%. A possible reaction model was also proposed, it was suggested that the reaction proceeds through a bifunctional dual activation mode which converts the aldehyde into the enamine intermediate. At the same time, the hydroxyl group is thought to activate the electrophile **41** through a single hydrogen bond. The sterically bulky 2,4,6-$^{i}Pr_3C_6H_2$ group is used in enforcing the (*E*)-*syn* enamine conformation, favouring the *si* face attack. In view of the high catalyst loading in asymmetric organocatalysis, the Ir(III) complex (Λ)-**14c** proved to be relatively efficient for asymmetric α-amination of aldehydes.[41] Once again, the success of this reaction not only exhibits the potential of chiral only-at-metal complexes for developing new "organocatalysts", but also expands the scope of secondary amine-hydrogen bonding donor catalysts.



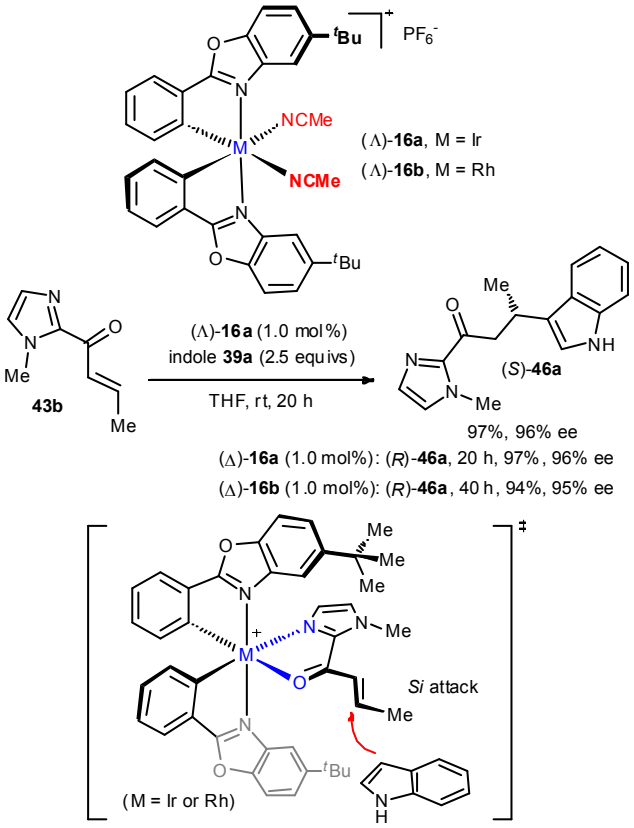
Scheme 10 Asymmetric Brønsted base catalysis.

As we discussed in Scheme 2, the aforementioned neutral aminopyrazolato complex **15** has the potential to be Brønsted base catalysis and recently, this concept had also been realized by Gong and Meggers (Eq 1, Scheme 10).[25d] It's found that direct asymmetric sulfa-Michael addition of thiol to *N*-pyrazolylcrotonate **43a** was able to be nicely controlled by using only 0.05 mol% of (Λ)-**15a** to form product **44** with 96% yield and 97% e.e., whereas, in sharp contrast, very low conversion was observed using even 1.0 mol% of bifunctional catalyst (Λ)-**13d**. Control experiment indicated the hydroxymethyl group of the ligand was necessary since almost no reaction took place without it. Even dropping the catalyst loading to 0.02 mol%, the excellent result can still be seen with high TON (4800). Mechanistically, due to the pKa of protonated (Λ)-**15a** is about 16, higher than that of thiol (pKa ~ 10), it can be effectively activate thiol *via* deprotonation. Subsequently, assemble of thiolate and cationic Ir complex aggregated to form ion pair through a double hydrogen bond. The role of hydroxymethyl in catalyst was thought to arrange a ternary complex with Michael acceptor, allowing the reaction to proceed with high-rate acceleration while keeping high enantioselectivity. Undoubtedly, the chiral only-at-metal templated Brønsted base organocatalysts broadened the traditional basic functional groups[42a] such as amines, amidines, guanidines, cyclopropenimines,[42b] iminophosphoranes[42c] and some chiral metal complex with weak-coordinated anions,[42d] which should find more application. Indeed, their merit had been demonstrated by applying for highly stereoselective aza-Henry reaction of (nitromethyl)benzene with *N*-Boc-Schiff base **26b** (Eq 2) to construct two continuous stereogenic carbon centres with down to 0.25 mol% catalyst loading.

In the above examples chiral only-at-metal Ir(III) complexes promoted asymmetric reactions, the catalysis is mediated through the ligand sphere, the installation of functionalised ligands bearing hydroxyl, amide or aromatic groups help make the metal centre relatively inert during the catalytic process, due to their strongly coordinating nature. In other words, such chiral-at-metal complexes have limited potential as chiral Lewis acid catalysts, due to their high stability and the absence of exchangeable coordination sites, in which substrates could bind for activation.

In order to broaden these conceptually new chiral only-at-metal complexes for asymmetric catalysis, another class of Ir(III) and Rh(III) complexes, such as **16**, were developed (Scheme 2). Due to the presence of two substitutionally labile CH_3CN ligands in catalyst **16**, the metal atom is able to interact through coordinated substrates *via* ligand exchange; at the same time, the remaining two bidentate ligands were chosen to keep the metal-centred chirality intact throughout the reaction.

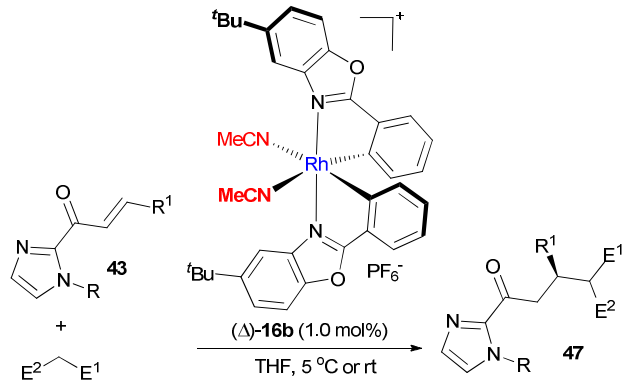
Meggers reported that, only 1.0 mol% of catalyst (Λ)-**16a** was able to efficiently catalyse the enantioselective Friedel-Crafts addition of indoles **39a** to α,β-unsaturated 2-acyl imidazoles **43b** with 97% yield and 96% e.e. (Scheme 11).[25e] The Rh(III)-based catalyst (Δ)-**16b** was also able to realise 94% yield and 95% e.e., but the reaction time, yield and enantioselectivity did not quite match the performance of the homologous (Δ)-**16a**.[25f] Even though these catalysts contain two substitutionally liable monodentate CH_3CN ligands, excellent enantioselectivities were observed in these reactions, indicating good stability of the catalyst's core during the whole process. The NMR spectra recorded demonstrate rapid coordination of the *N*,*O*-bidentate substrate **43b** to the catalytic Ir(III)-centre along with the release of the CH_3CN ligand when 20 mol% of catalyst (Λ)-**16a** was mixed with **43a** without any other detectable by-product. Upon mixing of the racemic **16b** with α,β-unsaturated 2-acyl imidazole, a crystal structure was obtained, confirming the anticipated coordination of the substrate to the Rh(III) centre by replacing the two labile acetonitrile ligands.[25f] Based on these phenomenon, a possible mechanism was proposed where the chiral only-at-metal Ir(III) or Rh(III) complex served as a powerful Lewis acid precursor to activate the substrate. The tight interaction between metal centre and substrate brings the reaction site *close* to the chirality of catalyst, which induces the high enantioselectivity, even using structurally-simple catalysts, highlighting one of the advantages of using the metal centre of a chiral only-at-metal complex for asymmetric catalysis.



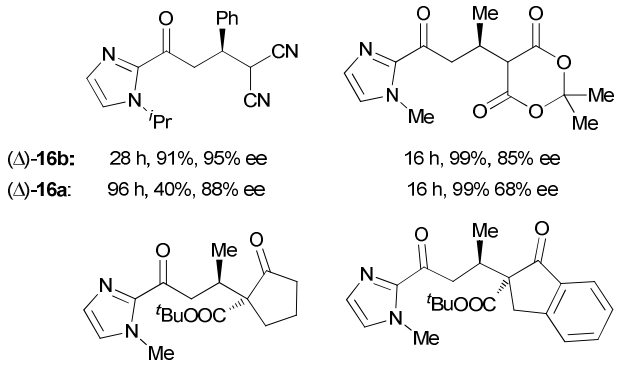
Scheme 11 Ir(III) and Rh (III)-catalysed asymmetric Friedel-Crafts reaction.

Besides indole, other CH-acidic carbonyl-containing groups such as malodinitrile, Meldrum's acid, β-carbonyl esters were also suitable nucleophiles for asymmetric addition to α,β-unsaturated 2-acyl imidazoles (Scheme 12).[25f] In this case, 1.0 mol% of Rh(III)-based (Δ)-**16b** catalyst gave rise to excellent results (83-97% yield, 92-99% e.e.), better than that of the Ir(III) complex (Δ)-**16a**. This might be because the substrate coordination and/or release step is rate determining in this reaction. Due to the longer coordinative bond lengths of the acetonitrile ligands in Rh catalyst (Δ)-**16b** compared to Ir catalyst (Δ)-**16a**, its higher turnover frequency could suppress the undesired background reaction, and thus give rise to improved enantioselectivity. This hypothesis was evidenced by the fact that the ligand exchange rate of (Δ)-**16b** with **43** is about an order of magnitude faster than that of (Δ)-**16a** in NMR experiments.

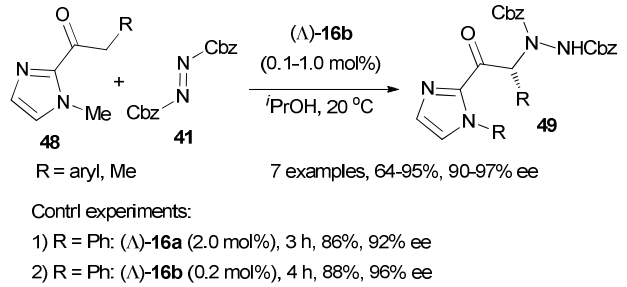
In addition to acting as powerful Lewis acids for activating electrophiles, the generality of these Rh(III) and Ir(III) catalysts has been demonstrated by the activation of nucleophiles, such as 2-acyl imidazoles for asymmetric amination reactions.[25f] As shown in Scheme 13, using only 0.1-1.0 mol% of catalyst (Λ)-**16b**, the reaction of **48** with dibenzyl azodicarboxylate **41** proceeded smoothly in 64-95% yield and 90-97% e.e. at room temperature.



Selected examples:

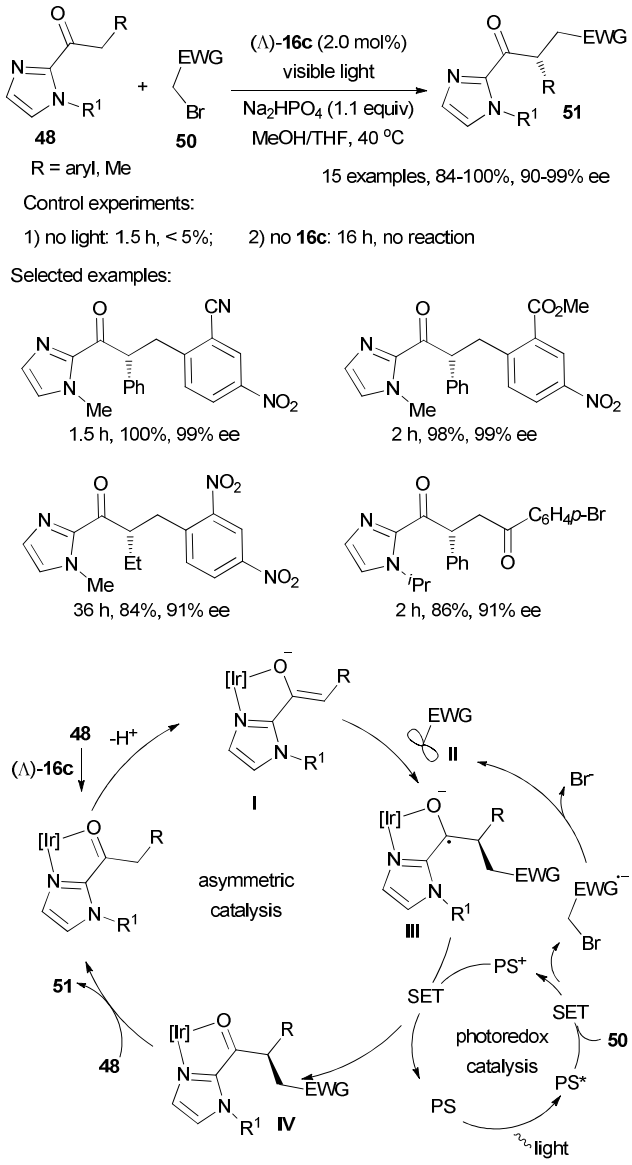


Scheme 12 Asymmetric Michael additions.



Scheme 13 Asymmetric α-amination of ketones.

Given that Ir(III) complexes have widespread applications in photochemistry,[43] there is possibility to apply Meggers' chiral only-at-metal Ir(III) catalysts for asymmetric photocatalysis. If possible, the chiral-at-Ir(III) complexes not only would act as a photoredox sensitiser to activate the substrate, but also serves as a chiral Lewis acid to combine with the substrate and induce chirality. Recently, this idea was successfully realised by the group of Meggers.[44] It was reported that the presence of 2.0 mol% of (Δ)-**16c** enabled the highly enantioselective (90-99% ee) asymmetric α-alkylation of 2-acyl imidazoles **48** with acceptor substituted primary bromides **50** (Scheme 14). As seen in the control experiments, both the catalyst and visible light were required for this transformation. The catalyst was thought to initially react with **48** to form the key intermediate Ir(III) enolate complex **I**, as evidenced by an X-ray crystal structure. The geometry of the catalyst shields one face of the planar enolate which can be enantioselectively captured by the photo-reductively generated electrophilic radical **II** to afford ketyl radical **III**. Oxidation of **III** *via* single electron transfer regenerates the catalyst and forms the Ir(III) complex **IV**. Exchange with the unreacted substrate finishes the cycle. It's no doubt that this reaction will provide new avenues for other asymmetric photoreactions.



Scheme 14 Asymmetric photoredox reactions.

Conclusions

Recent exploration in using chiral only-at-metal complexes as catalysts, although in its infancy, shows the possibility of their utilisation in highly stereoselective transformations. Complementary to traditional catalysts, these chiral only-at-metal complexes exhibit even better reaction selectivity in some reactions owing to their particular structural properties. Without question, the success of Meggers and Gong will further promote development and prosperity in this area. As discussed above, the prerequisite for future development is to synthesise a variety of chiral only-at-metal catalysts with versatile functional groups, the first hurdle to achieving this is to develop highly effective methods for preparing these catalysts with more metal scaffolds. Secondly, successful examples using chiral only-at-metal complexes as catalysts are

restricted to a narrow range of substrates, expanding the scope to other more challenging transformations is yet to be achieved. Detailed mechanistic studies are also required to understand the nature of these metal-centred chiral catalysts. However, overall the field of chiral at metal complexes shows many avenues for future development and the widening of the asymmetric catalytic field as a whole.

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Notes and references

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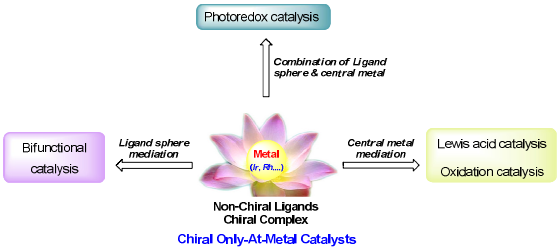

This perspective describes recent progress in asymmetric catalysis with chiral only-at-metal complexes displaying Λ / Δ enantiomorphs in the absence of central chirality within the ligands, with an emphasis on Ir(III) and Rh(III) systems. The good selectivity achieved when using these complexes in asymmetric catalysis has been demonstrated in asymmetric transformations through various mechanisms, including hydrogen-bond donor-acceptor, secondary amine or Brønsted base hydrogen-bond donor bifunctional catalysis, Lewis acid and photoredox catalysis under mild reaction conditions. This perspective highlights the widening field of chiral-at-metal catalysis and presents a selection of asymmetric transformations which have been successfully carried out using them.