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Review

High symmetry dirhodium(II) paddlewheel complexes as chiral catalysts

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Contents

Abstract

The design and use of chiral dirhodium(II) paddlewheel complexes as catalysts for asymmetric metal carbenoid and metal nitrenoid reactions, and as Lewis acids have become areas of considerable interest during the past two decades. The metal carbenoid chemistry is especially versatile, encompassing transformations such as C–H insertions, cyclopropanations and ylide formation. A number of different classes of dirhodium(II) catalysts have been found to be broadly effective in this chemistry. This review will highlight that many of these catalysts have higher symmetry than the individual chiral ligands themselves. An introduction of theoretical aspects concerning the structure and symmetry of chiral dirhodium(II) complexes will be given followed by an overview of the major classes of catalysts developed to date. Some representative examples of the synthetic potential of these catalysts will also be discussed.

Keywords: Dirhodium(II) complexes; Catalyst design; High symmetry chiral catalysts; Synthetic applications; Carbenoid chemistry

1. Introduction

Dirhodium(II) complexes are exceptional catalysts for a wide range of transformations. Even though most are extremely stable to heat, moisture and ambient atmosphere, they are exceptionally active catalysts for the decomposition of diazo compounds. The resulting rhodium carbenoids undergo a number of highly selective reactions such as cyclopropanation, C–H functionalization and ylide formation [1]. Recently, they have been recognized as effective catalysts in metal nitrene chemistry [2] and in Lewis acid-catalyzed cycloadditions [3]. Dirhodium(II) catalysis has experienced immense growth over the last few decades and

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since the early 1980s it has also been appreciated that the dinuclear scaffold can support chiral ligands [1j]. Consequently, these complexes would have the potential to catalyze asymmetric transformations. Both the design of new catalysts and the spectrum of applications have been developed in a number of directions [4]. This review will highlight the advances in this field, with particular emphasis on how the chiral catalysts can possess high symmetry even though the ligands themselves are of much lower symmetry.

Symmetry is an important concept that can play a major role in chiral catalyst design. The use of a high symmetry complex as catalyst will reduce the number of possible substrate trajectories in the catalytic steps of the reaction in question, which in turn can give more defined and predictable transition state structures. Consequently, the influencing elements for asymmetric induction can be more effectively controlled and manipulated. The traditional way to produce high symmetry catalysts has been to use ligands of high symmetry. One of the most important classes of high symmetry ligands has been bidentate C_2-symmetric ligands, and such complexes of copper(II) [5] and ruthenium(II) [6] have been very effective in metal carbenoid chemistry. Even higher symmetry catalysts for carbenoid chemistry have been prepared from D_2- and D_4-symmetric porphyrin ligands [7]. The practicality of these complexes, however, has been limited because the ligand synthesis and modification present significant challenges.

This review article will discuss theoretical concepts regarding the symmetry of dirhodium(II) complexes, survey the structures of catalysts that have been developed and highlight applications for each class. Emphasis will be placed on how the dirhodium paddlewheel framework is an excellent scaffold for the design of high symmetry chiral catalysts *via* a modular approach, in which several identical ligands of low symmetry surround the inherently high symmetry core.

2. Theoretical considerations

2.1. Structural features

The dirhodium(II) paddlewheel complexes consist of a dinuclear core surrounded by four equatorial μ_2-ligands and two axial ligands [8]. The core is held together by a rhodium–rhodium single bond and each rhodium is considered to have octahedral geometry [8]. $Rh_2(OAc)_4$, the parent compound of the dirhodium carboxylates (**1**) (Fig. 1), is D_{4h} symmetrical (**1**; R = CH_3), which is the highest obtainable symmetry for dirhodium paddlewheel complexes. *Chiral* rhodium carboxylates can possess up to D_4-symmetry. Another class of catalysts includes the dirhodium phosphonates (**2**) in which the dirhodium core is bridged by four phosphonate anions [1j]. Such complexes can also theoretically achieve D_{4h}-symmetry but those of *chiral* phosphonates are limited to D_4. Complexes of carboxamides (**3**) have a somewhat more complicated structure since this ligand type bridges the dirhodium core *via* both an oxygen and a nitrogen atom. The preferred geometry is the *cis*-(2,2) configuration, which defines that each rhodium is bound to two nitrogen atoms and two oxygen atoms in a *cis*-fashion [1j]. These complexes can only obtain C_2-symmetry due to this intrinsic ligand binding propensity.

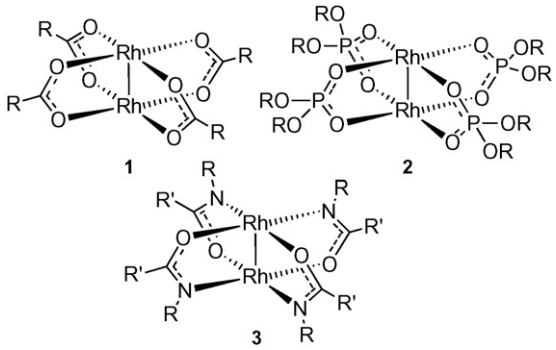


Fig. 1. General structures of dirhodium(II) complexes.

The axial ligands are labile and therefore occupy the catalytically active sites of the paddlewheel complex. The lantern structure is generally considered to remain intact during reactions at these sites although some alternative models have been proposed where the equatorial ligands dissociate. However, these have not yet gained general acceptance [9].

Let us now consider how chiral ligands (R and R′) influence the space around the axial active sites of the catalyst by introducing a simple model [10]. A dirhodium complex can be represented by a disk that corresponds with the O–Rh–O plane with the Rh active site in the center (Fig. 2). In order for ligands to exert a chiral influence on the course of reactions at the active site, they must necessarily possess geometrical features such that the space above the O–Rh–O plane is sterically restricted to favor only one enantiotopic substrate trajectory [4b]. This means that sterically blocking groups from the equatorial ligands must point towards the O–Rh–O plane. The two faces of the catalyst have arbitrarily been assigned as α (top face) and β (bottom face) so one can distinguish which face each ligand influences. With these definitions in hand, one can now consider the symmetries inherent in such systems [4b].

2.2. Ligand arrangements

2.2.1. Ligands of C_1-symmetry

The different possible arrangements of chiral C_1-ligands are first assessed. The sterically blocking groups creating the chiral pocket around the active sites are pictured as rods, where filled rods represent groups influencing the top (α) face, and unfilled rods the bottom (β) face of the catalyst [10]. In catalysts afford-

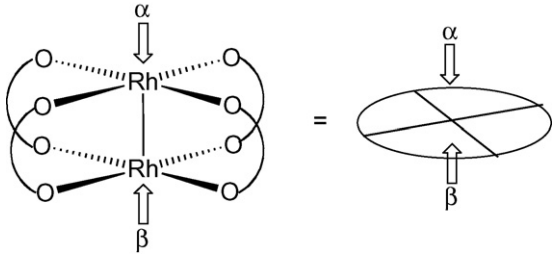


Fig. 2. Schematic representation of paddlewheel complexes.

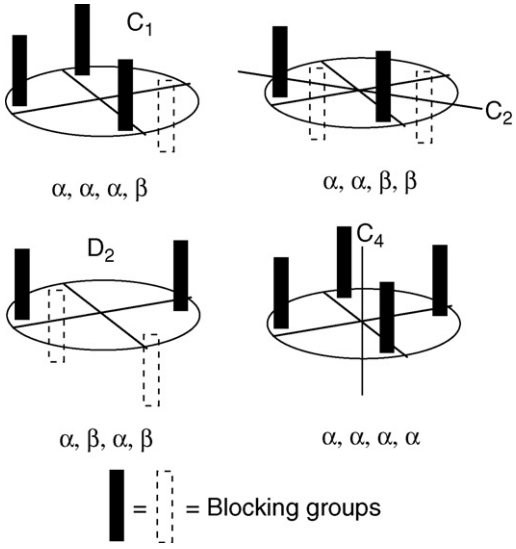


Fig. 3. Permutations of four C_1-ligands.

ing high enantiocontrol, the blocking groups cannot lie in the periphery of the catalyst. Because of this, the number of conformational permutations of the system can readily be derived. The groups can either orient themselves on the α-face or on the β-face of the catalyst. Four possibilities then arise: these are α, α, α, α (C_4-symmetry), α, α, α, β (C_1-symmetry), α, α, β, β (C_2-symmetry) and α, β, α, β (D_2-symmetry) (Fig. 3) [4b,10]. From these considerations, it is clear that only the C_2- or D_2-complexes possess two equivalent catalyst faces [10]. Indeed, the major effective catalyst classes based on the dirhodium scaffold belong to these point groups. The C_1 complex contains two faces affording different enantiocontrol, and it is likely that the single chiral influencing group on the β-face will give low or no enantioinduction. For the C_4-complex, the kinetically more active β-face is essentially achiral, so enantiocontrol will likely be overall low or absent [4b].

2.2.2. Ligands of C_2-symmetry

If the ligand itself possesses C_2-symmetry, even higher overall symmetry is accessible to the complex. A C_2-symmetric ligand will influence both faces of the catalyst and give the complex overall D_2- or D_4-symmetry depending on the geometry of the ligand. Four ligands of C_2-symmetry will give overall D_4-symmetry to the complex [4b]. This is in many regards the optimal symmetry of a *chiral* dirhodium paddlewheel catalyst, since not only are both faces equivalent, but all staggered binding orientations of the axial substituent involved in the asymmetric reaction are also identical with respect to the approaching substrate. D_2-symmetry is achieved with two *bridged* C_2-symmetric ligands, thereby affording a more rigidly defined version of the α, β, α, β-form of complexes with C_1-ligands (Fig. 4) [4b].

The advantages offered by the dirhodium scaffold in catalyst design are evident from considerations presented in this section. The catalysts can be assembled by a modular approach, in which coordination of several identical low symmetry chiral ligands around the inherently high symmetry core affords an overall high symmetry chiral catalyst [4b]. However, several factors are involved in determining the orientation of the individual ligands when coordinated to the dirhodium core, and it can be difficult to assess *a priori* whether a complex consisting of four C_1-ligands will preferentially adopt a high symmetry conformation or not. Controlling factors include solvent induced conformational preferences, flexibility of the blocking group and the polarity of the ligand [4b,10].

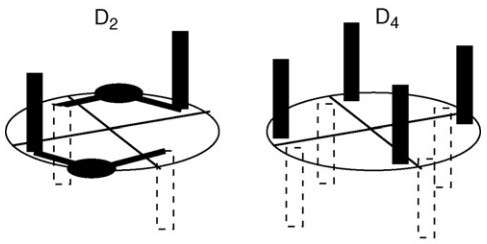


Fig. 4. Arrangements of C_2-ligands.

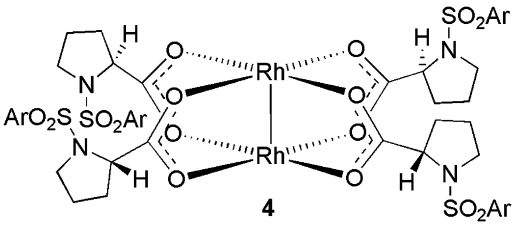
3. Catalyst structure and applications

3.1. Rhodium(II) carboxylates

3.1.1. Proline derived complexes

The dirhodium(II) carboxylates are attractive catalysts, particularly for carbenoid transformations, due to their electron deficient character. This class is therefore kinetically very active for decomposition of various carbene precursors [1j]. Chiral dirhodium(II) complexes based on optically active carboxylic acids were first systematically evaluated by Brunner in a test cyclopropanation between ethyl diazoacetate and styrene [11]. The results, however, were very poor (≤12% ee) and this led to the preliminary conclusion that dirhodium tetracarboxylates would not be effective catalysts for asymmetric transformations [12]. This impression began to change in the early 1990s as McKervey and Hashimoto demonstrated that chiral dirhodium tetracarboxylates were capable of inducing moderate levels of asymmetric induction in intramolecular C–H insertions [1a–e]. Dirhodium(II) tetraprolinates were shown to be capable of affording up to 82% ee in intramolecular C–H insertions [13], and their utilization was subsequently greatly expanded by the discovery by Davies that they are exceptional catalysts for reactions of donor/acceptor-substituted carbenoids [10]. The original catalyst, Rh_2(*S*-BSP)$_4$ (**4a**) (Fig. 5), developed by McKervey has been optimized by Davies to the more soluble catalysts Rh_2(*S*-TBSP)$_4$ (**4b**) and Rh_2(*S*-DOSP)$_4$ (**4d**).

The arylsulfonyl groups in these complexes can only be directed in an up (α) or down (β) fashion pointing out of the O–Rh–O plane on both faces of the catalyst. The conformation in which the arylsulfonyl group lies in the periphery of the catalyst is not favored since considerable steric conflict with the adjacent ligand prevents this orientation [4b]. The α, β, α, β-arrangement leads to a high-symmetry D_2-complex [10]. The high levels of asymmetric induction exhibited by these catalysts has been proposed to arise from their preferred D_2-symmetric orientation in solution [4b]. A molecular model of Rh_2(*S*-DOSP)$_4$ (**4d**) in a D_2-symmetric conformation, viewed

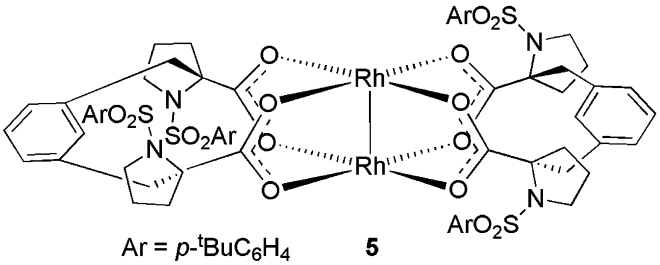


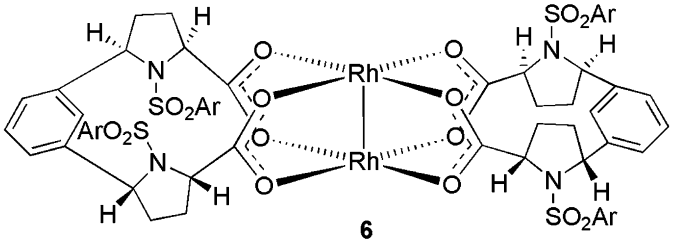
Ar			
C_6H_5	Rh_2(*S*-BSP)$_4$	**a**
4-*t*-BuC_6H_4	Rh_2(*S*-TBSP)$_4$	**b**
2,4,6-tri-^{i}PrC_6H_2	Rh_2(*S*-TISP)$_4$	**c**
4-($C_{12}H_{25}$)C_6H_4	Rh_2(*S*-DOSP)$_4$	**d**

Fig. 5. Representative prolinate-based complexes.

along the principal symmetry axis, is shown in Fig. 6. The *N*-dodecylarylsulfonyl groups are stretched out and arranged in an α, β, α, β-orientation affording two equivalent Rh active sites with sufficiently sterically encumbering groups to restrict nucleophile trajectories to the axial carbene ligand. Despite the expected free rotation of the prolinate ligands, and thereby the potential existence of many conformations, the D_2-symmetric form is the most reasonable for rationalizing the observed enantioselectivities in many reactions [4b,10]. The absolute stereochemistry of the products can be accurately predicted from this conformation of the catalyst [1d]. The model is furthermore consistent with observed solvent effects on enantiocontrol [4b]. The dirhodium(II) prolinates usually give high enantioselectivities in hydrocarbon solvents and significantly lower values even in slightly polar solvents such as dichloromethane [4b]. Studies by Jessop and co-workers on Rh_2(*S*-TBSP)$_4$ (**4b**) confirmed that enantioinduction decreases with increasing dielectric constant for asymmetric cyclopropanation in supercritical fluoroform [14].

Based on the D_2-symmetry hypothesis, Davies designed a second generation prolinate complexes in which the arylsulfonyl groups are conformationally locked in the α, β, α, β-arrangement [15]. This was achieved by synthesizing a C_2-symmetric dicarboxylate ligand with two arylsulfonylprolinates linked together. High temperature ligand exchange reactions with $Rh_2(OAc)_4$ afforded complexes **5** and **6** (Fig. 7). Complex **5** contains a bridging *meta*-xylene unit attached to C-2 of both proline rings, whereas complexes **6a**–**b** possess *meta*-benzene bridges at C-5 on both proline rings. Both complexes are locked in a D_2-symmetric arrangement due to restricted rotation of the ligands [10,4b,15].





Ar		
2,4,6-tri-^{i}PrC_6H_2	Rh_2(*S*-biTISP)$_2$	**a**
p-($C_{12}H_{25}$)C_6H_4	Rh_2(*S*-biDOSP)$_2$	**b**

Fig. 7. Second generation prolinate complexes.

Dirhodium(II) complexes can effectively catalyze cyclopropanation reactions *via* carbenoid intermediates [1j]. The choice of catalyst depends on what type of cyclopropanation is desired and the structure of the carbenoid precursor. For intermolecular cyclopropanation with aryl or vinyldiazoacetates the dirhodium(II) prolinates are superior catalysts and high enantiocontrol and chemoselectivity are readily achieved [1j]. For example, in the reaction of styrene with vinyldiazoacetate **7** (Scheme 1) the cyclopropane **8** can be obtained in 90% ee with Rh_2(*S*-DOSP)$_4$ (**4d**) and 98% ee with Rh_2(*S*-biTISP)$_4$ (**6a**) [10,16]. Highly enantioselective cyclopropanation reactions with Rh_2(*S*-DOSP)$_4$ have also been developed for aryldiazoacetates, heteroaryldiazoacetates [17] and alkynyldiazoacetates [18].

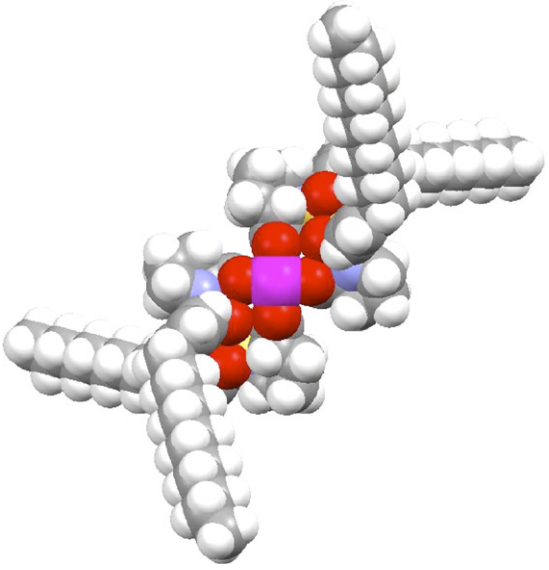
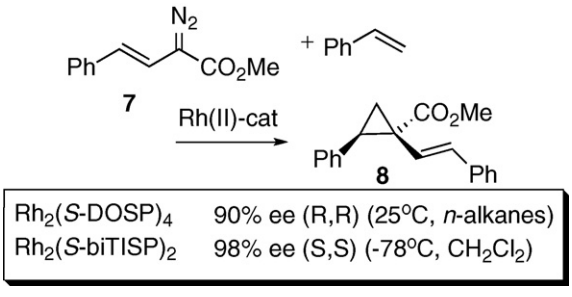
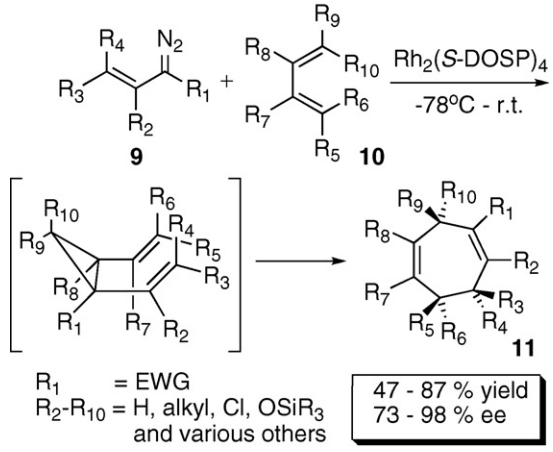


Fig. 6. Top view molecular model of Rh_2(*S*-DOSP)$_4$.



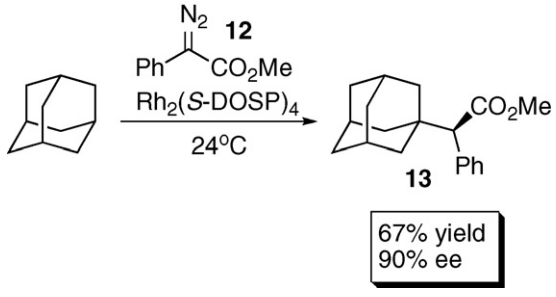
Scheme 1. Cyclopropanation.



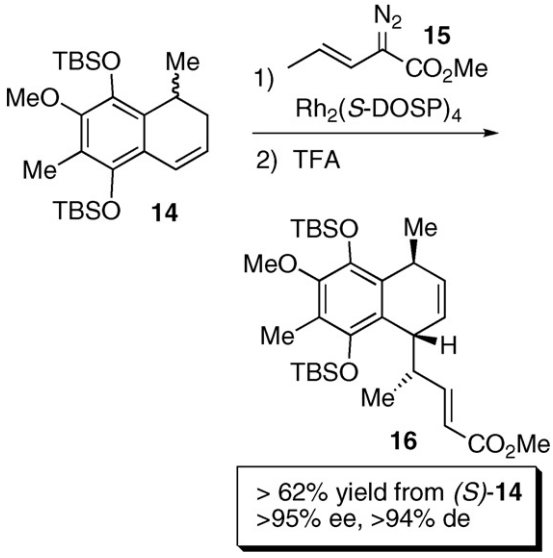
Scheme 2. Generalized [4 + 3] annulation.

The combination of Rh_2(*S*-DOSP)$_4$ (**4d**) as catalyst and vinyldiazoacetates (**9**) in the presence of conjugated dienes **10** affords powerful methodology for the formal, enantioselective [4 + 3] cycloaddition to form cycloheptadienes **11** *via* a tandem cyclopropanation/Cope rearrangement (Scheme 2). The method gives full control of the relative stereochemistry at up to three stereogenic centers [1c]. A variety of substitution patterns are tolerated and the cycloheptadienes are formed with high asymmetric induction (73–98% ee). An intramolecular version of this methodology has been used in the enantioselective synthesis of *epi*-tremulane [19].

Enantioselective intermolecular C–H functionalization mediated by metal carbenoids has become a powerful technique since the realization that dirhodium(II) complexes readily catalyze such processes [1d]. With donor/acceptor carbenes (derived from aryl or vinyldiazoacetates), the dirhodium prolinates have been shown to be the best catalysts for these transformations. These carbenes readily insert even into unactivated C–H bonds and are capable of achieving very high regio-, diastereo- and enantioselectivity [1d]. An example is the reaction of phenyldiazoacetate **12** with adamantane, which generates the C–H insertion product **13** in 90% ee and with full selectivity for the tertiary position (Scheme 3). Similarly, enantioselective C–H insertions in aliphatic systems have been achieved α to heteroatoms, such as in THF and *N*-Boc pyrrole [20]. The reaction has been utilized extensively in the synthesis of several pharmaceuticals and natural products, including Ritalin, Imperanene [21], Indatraline [22] Cetiedil and Venlafaxine [23]. The



Scheme 3. Aliphatic C–H insertion into adamantane.



Scheme 4. Combined C–H activation/Cope rearrangement.

methodology has also been expanded to provide surrogates for classical organic reactions such as the Aldol reaction [24,25], the Claisen condensation [26] and the Mannich reaction [27].

Another efficient transformation catalyzed by Rh_2(*S*-DOSP)$_4$ (**4d**) is the combined C–H activation/Cope rearrangement [28]. This powerful methodology has also been utilized in the synthesis of pharmaceutical targets [29] and natural products. One of the most impressive examples is a key step in the total syntheses of Colombiasin A and Elisapterosin B (Scheme 4) [30]. The Rh_2(*S*-DOSP)$_4$-catalyzed reaction of vinyldiazoacetate **15** with dihydronaphthalene **14** results in an enantiodivergent step in which only one enantiomer of **14** undergoes the combined C–H activation/Cope rearrangement to form **16** in >95% ee and >94% de. This reaction generally proceeds with higher enantioselectivity than the direct C–H insertion.

3.1.2. Phthalimide derived complexes

Ikegami, Hashimoto and co-workers developed a series of phthalimide protected amino acid derivatives as ligands for dirhodium(II) complexes (Fig. 8) [1j]. The optimum catalyst can vary depending on the specific reaction, but usually the *tert*-leucine derived catalyst Rh_2(*S*-PTPA)$_4$ (**17a**) gives the highest asymmetric induction [1j]. The crystal structure of Rh_2(*S*-PTPA)$_4$ (**17a**) shows the phthalimido groups aligned in an α, α, β, β-fashion around the dirhodium core, giving these complexes overall C_2-symmetry [31]. It has been assumed that this is the catalytically active conformation also in solution [31]. A perspective model of the phthalimide derived complexes is shown in Fig. 9 which shows the alignment of the phthalimide groups and the overall symmetry [31].

The Hashimoto group and others have prepared many derivatives by extending the length of the phthalimide moiety (**18a–e**), using halogenated phthalimides (**20a–b**) and by variation of the R-groups (**17a–f**, **19**) (Fig. 8) [32]. Müller used the same scaffold but changed the phthalimido-portion to give complexes **21a–c** [33]. Davies and co-workers recently synthesized the

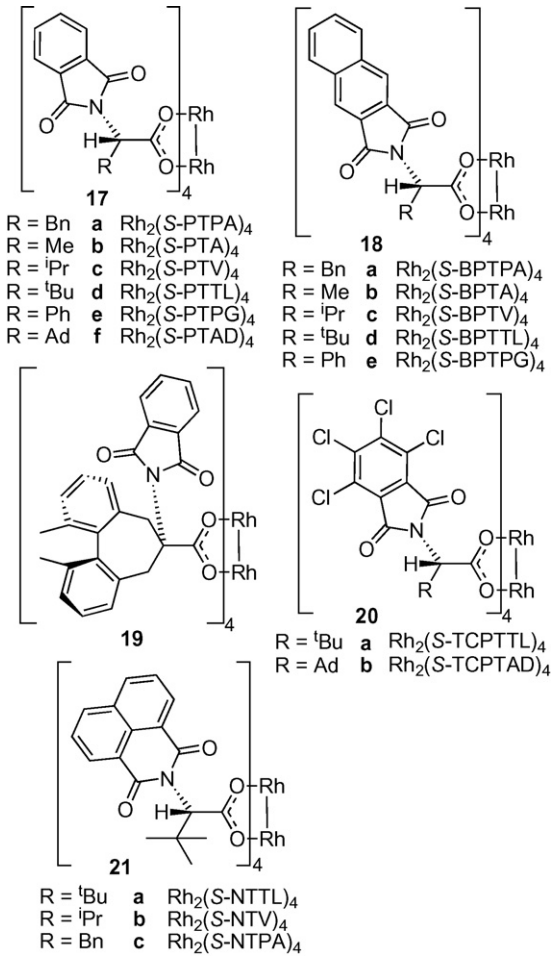


Fig. 8. Representative phthalimide derived dirhodium(II) complexes.

adamantyl glycine derived complexes Rh_2(*S*-PTAD)$_4$ (**17f**) and Rh_2(*S*-TCPTAD)$_4$ (**20b**). In several cases, **17f** and **20b** induce higher levels of enantioselectivity compared to their *tert*-leucine analogues **17d** and **20a** [34]. The phthalimide derived dirhodium complexes are generally kinetically very active, comparable to the dirhodium prolinates [1j].

The phthalimide derived dirhodium complexes have been successfully applied in intramolecular C–H insertions with excellent enantiocontrol, particularly in cyclopentanone formation [35] but also for β-lactam formation [36]. An impressive example is the formation of the spirobicyclic system **24** by double C–H insertion of **22** followed by thermal decarboxylation in 78% yield and 80% ee catalyzed by Rh_2(*S*-PTTL)$_4$ (**17d**) (Scheme 5) [37].

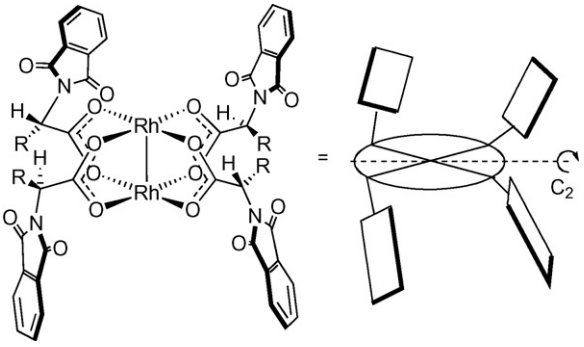
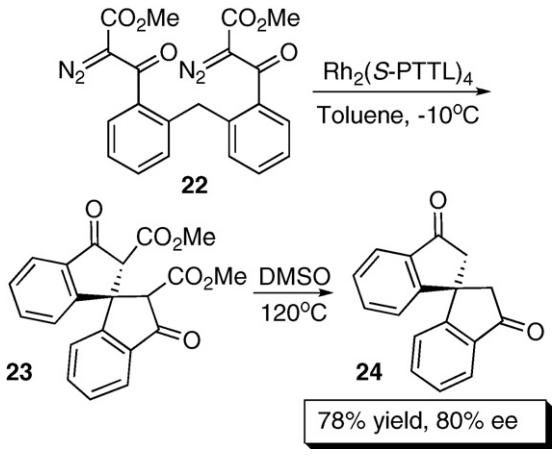


Fig. 9. Perspective model of phthalimide complexes.

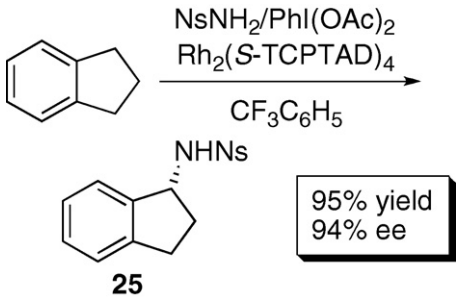


Scheme 5. Double C–H activation.

Functionalization of C–H bonds with amines has been a recent area of focus since the transformation can be mediated by dirhodium carboxylate-stabilized nitrenes [38]. Impressive diastereocontrol has been reported by Müller, Dodd, Dauban and co-workers in the enantioselective C–H amination of indene (>99% de) in 80% yield with Rh_2(*S*-NTTL)$_4$ (**21a**). High yield and enantiocontrol was also recently reported by Davies and co-workers in a similar reaction using the newly developed Rh_2(*S*-TCPTAD)$_4$ (**20b**) (Scheme 6) [39].

3.1.3. Other carboxylate complexes

A range of other chiral dirhodium(II) carboxylate complexes have been prepared, some of which are shown in Fig. 10 (**26**–**28a**–**d**) [40]. None of these have been extensively developed to date, although they do have some interesting design features. Complex **27** is D_4-symmetric because each carboxylate ligand has C_2-symmetry. Structural information is not available for **28a**–**d** but it is reasonable to speculate that the ligands in these complexes would have a fairly large group unable to align in the periphery of the catalysts. This leads to the possibility that these complexes would adopt a defined high symmetry conformation [4b]. Hashimoto and co-workers prepared atropisomeric biaryl dirhodium carboxylates of which one example is complex **26** [41]. The crystal structure of this complex shows that the ligands adopt the α, α, β, β-alignment giving overall



Scheme 6. C–H amination.

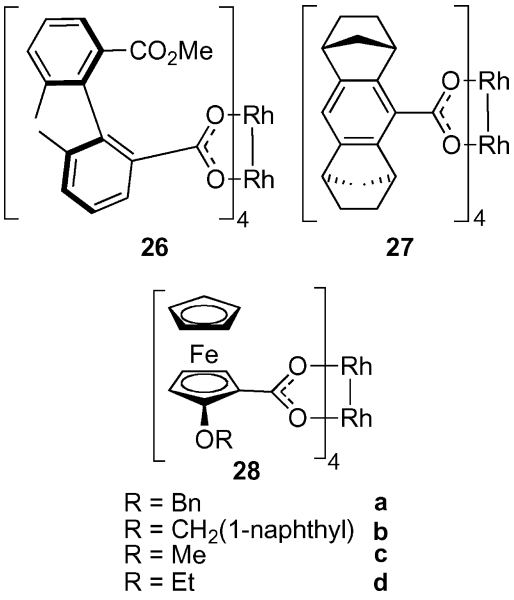


Fig. 10. Examples of other chiral dirhodium carboxylates.

C_2-symmetry. The complexes were tested in an intramolecular C–H insertion reaction and afforded moderate enantiocontrol (50–52% ee) [41].

3.2. Dirhodium(II) phosphonates

A great example of high symmetry catalysts is the dirhodium(II) binaphthylphosphonates developed by McKervey and co-workers [42]. Rh_2(*R*-BNP)$_4$ (**29a**) has four atropisomeric binaphthylphosphonate ligands around the dirhodium core (Fig. 11). Due to the C_2-symmetry of the chiral ligands, the overall complex has D_4-symmetry. McKervey prepared the mixed ligand system Rh_2(*R*-BNP)$_2$(HCO$_3$)$_2$ (**30**) [43]. In this

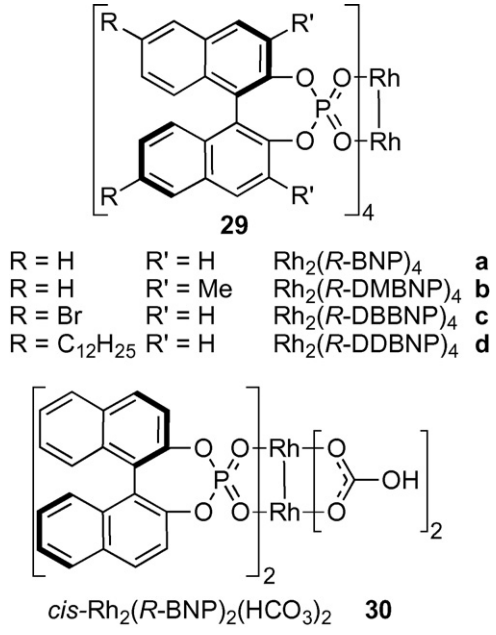


Fig. 11. Representative dirhodium(II) binaphthylphoshphonate complexes.

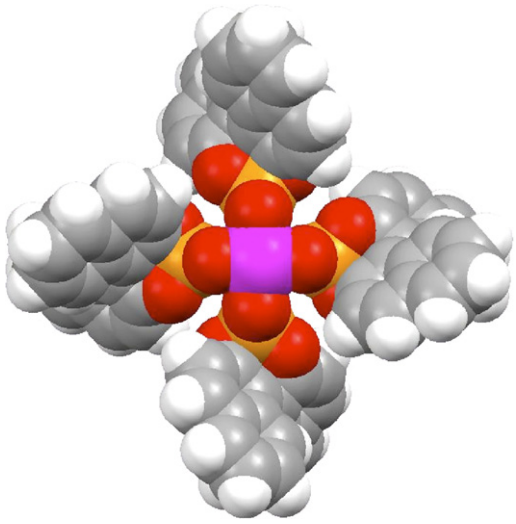


Fig. 12. Top view molecular model of Rh_2(*S*-BNP)$_4$.

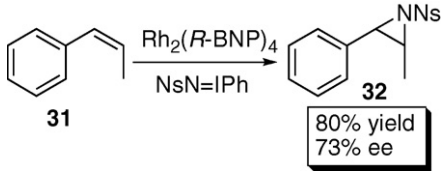
complex, two equivalent C_2-symmetric ligands are arranged in a *cis*-fashion, giving the complex overall C_2-symmetry.

The phosphonate complexes are typically very electron deficient due to the low basicity of the phosphonate ligands [1j]. This class of catalysts therefore has a somewhat different reactivity profile than the amino acid derived complexes. The tetraphosphonate complexes have shown considerable promise as chiral catalysts which has led to the generation of several new analogues (**29b–d**) [44]. The most significant is Rh_2(*R*-DDBNP)$_4$ (**29d**), which has much improved solubility because of the presence of the *n*-dodecyl groups. A molecular model of Rh_2(*S*-BNP)$_4$, viewed along the principal axis (Fig. 12) shows the propeller-like structure and the D_4-symmetry of this family of catalysts.

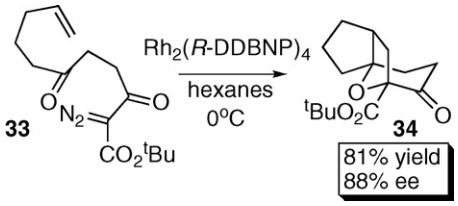
The most impressive applications of the binaphthylphosphonate catalysts have been in ylide reactions of carbenoids and in nitrene insertions [44]. Müller utilized Rh_2(*R*-BNP)$_4$ (**29a**) in the asymmetric aziridination of styrenes and achieved 73% ee with *cis*-β-methylstyrene **31** (Scheme 7) [45]. Hodgson successfully employed Rh_2(*R*-DDBNP)$_4$ (**34d**) in an ylide-mediated intramolecular cycloaddition of **33**, which afforded **34** in 81% yield and 88% ee (Scheme 8) [44].

3.3. Dirhodium(II) carboxamidates

The dirhodium carboxamidates are inherently limited to complexes with overall C_2-symmetry [1j]. This is due to the preferred alignment of the carboxamidate ligands in the *cis* (2,2) configuration in which two nitrogen and two oxygen atoms are attached



Scheme 7. Aziridination.



Scheme 8. Cycloaddition.

to each Rh in a *cis*-fashion [46]. Nevertheless, these catalysts have played a major role in the field, especially in the reactions of the highly reactive carbenoids derived from diazoacetate and diazoacetamide derivatives [1j].

Rhodium carboxamidates are very electron rich due to the relatively high basicity of the carboxamide ligands. This also leads to very rigid complexes with negligible ligand exchange occurring at room temperature. The high electron density increases the selectivity of the complexes in carbenoid reactions, but they are catalytically less active than the dirhodium carboxylates [1j].

Chiral dirhodium carboxamidates were initially developed by Doyle and co-workers using ligands that were derived from enantiomerically pure α-carboxamides [47]. The complexes have since been developed to great diversity with a variety of ligands and ligand substituents (Fig. 13). The most important catalysts are derived from 2-oxopyrrolidines [48], 2-oxazolidinones [49], *N*-acylimidazolidin-2-ones [50] and 2-acetidinones [51]. The nature and structure of the carboxamidate ligands have a large influence on reactivity and selectivity of these complexes. For example, the more strained acetidinones lead to elongation of the Rh–Rh bond and hence increase the reactivity of these complexes [52]. The perspective models in Fig. 13 show the C_2-symmetry and the alignment of the ligands in the α, α, β, β-arrangement.

Dirhodium(II) carboxamidates are the catalysts of choice for intramolecular allylic cyclopropanation [1j,k]. Intramolecular cyclopropanation of alkene tethered ester diazoacetates proceeds in high yields with moderate to excellent enantiocontrol with a variety of substituents on the olefin [4a]. In cases where Rh_2(5*S*-MEPY)$_4$ (**35a**) does not provide high enantiocontrol, Rh_2(4*S*-MPPIM)$_4$ (**35f**) usually performs better [4a]. The methodology also extends to the corresponding amides leading to γ-lactam formation in high yields and with excellent enantiocontrol. An example is the intramolecular cyclopropanation of **37** to form lactam **38** with a variety of groups R_1 and R_2 in up to 95% ee (Scheme 9) [1k]. Intermolecular cyclopropanation with this class of catalysts can be effected in high yields, but with only moderate enantiocontrol [53].

The dirhodium(II) carboxamidates are particularly suitable catalysts for intramolecular C–H insertions to form lactones or lactams [1d]. An example is the synthesis of **41** in which intermediate **40** was formed in 86% yield and 96% de from **39** catalyzed by **35e** (Scheme 10) [1d]. Chemoselectivity, yields and enantiocontrol are routinely very high (>90% ee) for suitable systems [54]. Enantioselective, intramolecular C–H insertion has been utilized in numerous syntheses, including the syntheses of (+)-isodeoxypodophyllotoxin [55], imperanene, (−)-enterolactone and (*R*)-(−)-baclofen [56].

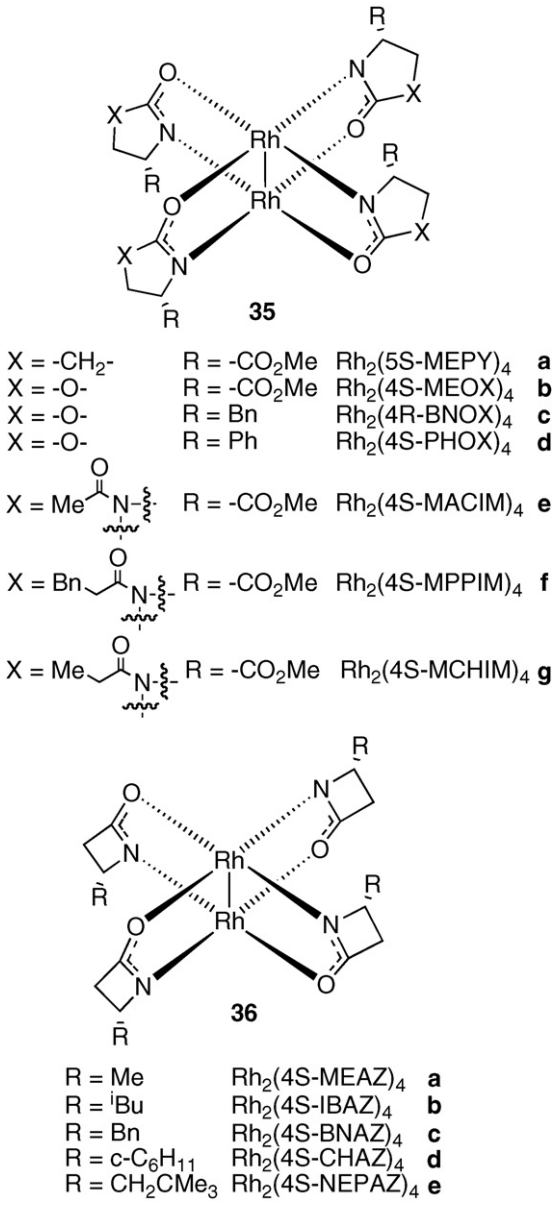
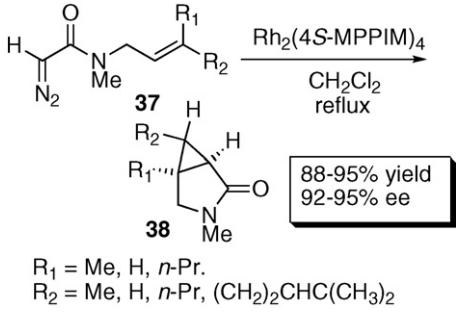
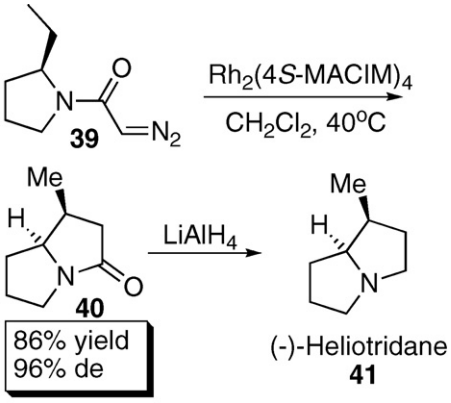


Fig. 13. Representative dirhodium(II) carboxamidate complexes.

The dirhodium carboxamidates have played an important role in advances made in ylide-mediated chemistry [1j]. Impressive levels of enantioinduction were achieved in the asymmetric oxonium ylide/[2,3]-sigmatropic rearrangement of **42** with ethyl



Scheme 9. Intramolecular cyclopropanation.



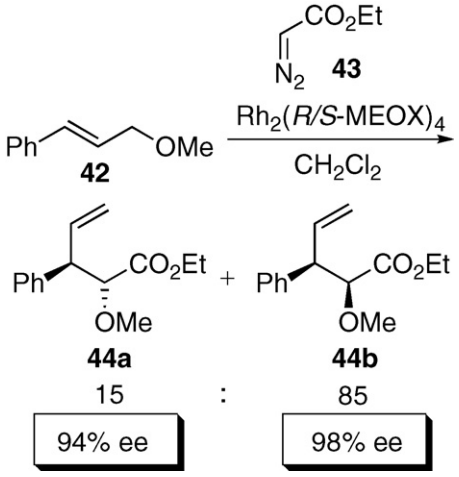
Scheme 10. Intramolecular C—H insertion.

diazoacetate (**43**) catalyzed by Rh_2(*R*/*S*-MEOX)$_4$ (**35b**) to form the two diastereomers **44a**–**b**, both in >94% ee (Scheme 11) [57]. Macrocyclization *via* ylide intermediates is a recently discovered transformation for the dirhodium(II) carboxamidates, but has not been fully developed to date [58].

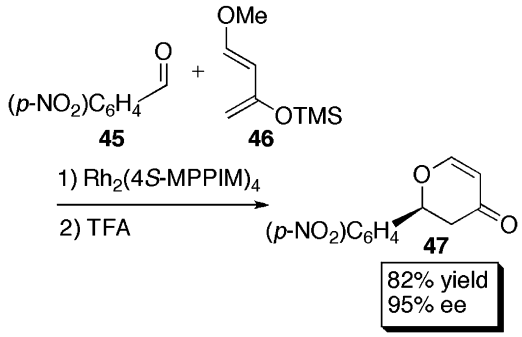
Asymmetric Lewis acid catalysis has been a field of great interest for the last two decades [59]. Many chiral Lewis acids have been applied successfully, but one of the major challenges is achieving high enantiocontrol accompanied by high turnover numbers. Traditionally, hetero-Diels Alder reactions usually demand relatively high catalyst loadings because of low turnover numbers [60]. Doyle and co-workers reported that the dirhodium(II) carboxamidates effectively catalyzed the hetero-Diels Alder reaction between aldehyde **45** and diene **46** to form **47** (Scheme 12) in 95% ee when catalyzed by Rh_2(4*S*-MPPIM)$_4$ (**35f**) [3]. Very low catalyst loadings were required and an impressive turnover number of 10,000 was achieved with reasonable yield and enantioselectivity.

3.4. Orthometallated phosphines

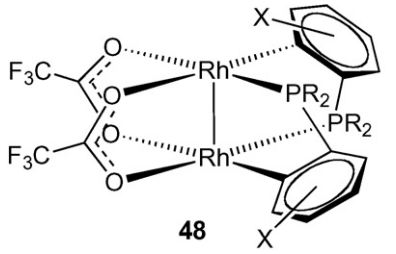
Lahuerta and co-workers introduced a new class of dirhodium catalyst containing two carboxylate ligands and two orthometallated phosphine ligands [61]. Several variations of these



Scheme 11. Oxonium ylide/[2,3] sigmatropic rearrangement.



Scheme 12. Lewis acid catalyzed hetero-Diels Alder reaction.



R = C_6H_5	X = H	**a**
R = *p*-MeC_6H_4	X = *p*-Me	**b**
R = *p*-MeC_6H_4	X = *m*-Me	**c**
R = *p*-3,5-$Me_2C_6H_4$	X = 3,5-Me	**d**
R = *p*-^{t}BuC_6H_4	X = *p*-^{t}Bu	**e**
R = *p*-FC_6H_4	X = *p*-F	**f**
R = CH_3	X = H	**g**

Fig. 14. Dirhodium(II) *ortho*-metallated phosphine complexes.

complexes have been prepared with different substituent patterns **48a**–**g** (Fig. 14). The phosphine ligands are in a *cis*-arrangement oriented opposite to each other giving the overall complex C_2-symmetry. This family of dirhodium(II) complexes has not been extensively tested, but up to 95% ee was obtained in intramolecular cyclopropanation of diazoketones [62]. Intramolecular C—H insertion to form cyclopentanones afforded up to 74% ee [61].

4. Conclusions

Although several classes of highly effective chiral dirhodium(II) complexes have been developed as catalysts in asymmetric metal carbene and Lewis acid processes, the importance of high symmetry as a design feature in these complexes has not yet been widely considered. High symmetry chiral complexes can readily be prepared by coordination of several identical lower symmetry ligands onto the dirhodium core. This modular approach for the rapid construction of high symmetry complexes makes this concept particularly attractive. The majority of the ligands that have been used to date have been C_1-symmetric, namely prolinates, phthalimide protected amino acids and carboxamidates, leading to catalysts that are considered to exist preferentially in C_2- or D_2-symmetric conformations. C_2-symmetric ligands, such as the binaphthylphosphonates or bridged prolinates, can be used to form rigid complexes of D_2- or D_4-symmetry. The design elements articulated in this review will hopefully lead to even more

superior high symmetric dirhodium catalysts for asymmetric synthesis.

Acknowledgements

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