Comparison of Reactivity and Enantioselectivity between Chiral Bimetallic Catalysts: Bismuth-Rhodium and Dirhodium Catalyzed Carbene Chemistry

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Supporting Information Placeholder

ABSTRACT: This paper describes the influence of replacement of one of the rhodium atoms by bismuth in a chiral dirhodium tetracarboxylate catalyst on asymmetric induction in the cyclopropanation and C–H functionalization chemistry of trichloroethyl aryldiazoacetates. The chiral ligand used in this study is *S*-*tert*-butylsulphonylprolinate (*S*-TBSP), which was used in the first highly enantioselective dirhodium tetracarboxylate catalyst. Even though the replacement of a Rh atom with Bi has changed electronic properties of the system, the RhBi complexes have several similarities to the corresponding Rh_2 catalysts in their reactions with donor/acceptor carbenes. The asymmetric induction with RhBi(*S*-TBSP)$_4$ is very similar to that achieved with Rh_2(*S*-TBSP)$_4$. The major differences between the two systems are the rates of reactions with the Rh_2 complexes reacting much faster, and the scope of the C–H functionalization with Rh_2 complexes capable of catalyzing reactions with a much wider range of substrates. An unexpected structural feature of the RhBi(*S*-TBSP)$_4$ catalyst is the arrangement of the arylsulfonyl groups in the periphery of the catalyst, leading to a C_4 symmetric structure.

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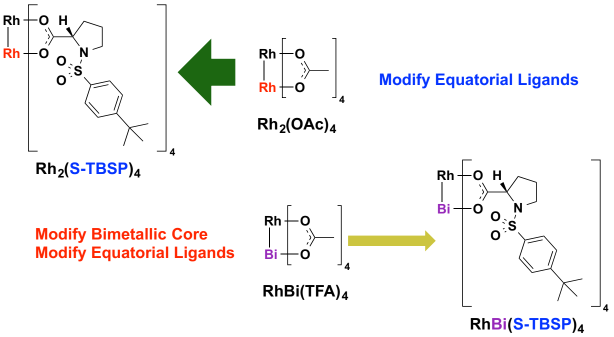
1. INTRODUCTION

Dirhodium(II) paddlewheel complexes have found widespread use in organic synthesis as catalysts for group transfer reactions[1,2] and as Lewis acid catalysts.[3] The dirhodium tetracarboxylate catalysts, in particular, are exceptional catalysts for carbene transfer reactions, capable of turnover numbers of greater than 10^6.[4] Considering the range of synthetic opportunities associated with these catalysts, considerable effort has been made to modify their characteristics. Several classes of chiral carboxylate ligands have been developed[5] and the resulting complexes are capable of a variety of enantioselective carbene reactions, such as cyclopropanation,[6] cyclopropenation,[7] C–H functionalization[8] and a range of ylide transformations.[9] The ligands can alter the electronics of the catalysts, with ligands such as trifluoroacetate leading to a more electrophilic carbene[10] and carboxamidates leading to a less reactive and more selective carbene.[11] The use of additives to coordinate to one of the axial sites of the dirhodium catalysts has also been shown to modulate the reactivity of the carbene.[12]

Relatively few investigations have been made to alter the electronic properties of the dirhodium catalyst core directly via metal atom substitution. A few studies have been reported on replacing the dirhodium core with other metals such as diruthenium[13] and molybdenum.[14] An intriguing system is the RhBi paddlewheel complexes which were synthesized and characterized in 2005,[15] At that time the mixed-ligand complexes were prepared via solid-state reactions, and catalyst synthesis was limited to achiral catalysts.[16] A series of these achiral RhBi complexes was applied to cyclopropanation and C–H functionalization reactions in the presence of diazo compounds in 2009.[17] From these studies, the selectivity of the RhBi catalyst was found to be quite similar to dirhodium catalysts, albeit with much slower rates of reaction. With the discovery of a new solution state preparation method for RhBi compounds described in 2012,[18] it has been possible to greatly expand the family of potential RhBi catalysts by equatorial ligand exchange with various carboxylate ligands,[19] oxypyridinate ligands,[20] and amidinate ligands.[21] Here, we report the synthesis of the first chiral RhBi catalyst and explore its ability to perform asymmetric cyclopropanation and C–H functionalization reactions (Scheme 1). We selected *S*-*tert*-butylsulphonylprolinate (*S*-TBSP) as the chiral ligand because this was the first highly enantioselective ligand for the dirhodium-catalyzed intermolecular reactions of donor/acceptor carbenes.[22]

Scheme 1. Development of Bimetallic Paddlewheel Catalysts.



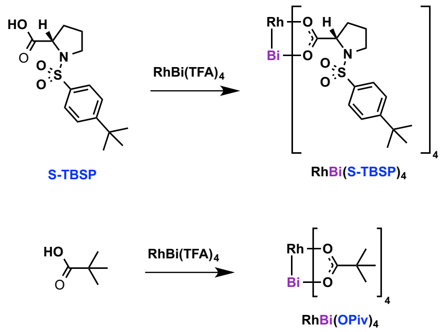
The report of highly enantioselective cyclopropanations with Rh_2(*S*-TBSP)$_4$ was an important stage in the development of chiral dirhodium tetracarboxylate catalysts because prior to then, their performance as enantioselective catalysts had been mixed and especially poor in intermolecular reactions.[23,24] When the prolinate catalysts were shown to give very high asymmetric induction, a hypothesis was made to explain why this was the case. It was proposed that the arylsulfonyl groups would be too large to exist in the periphery of the catalyst and instead would preferentially adopt an α,β,α,β orientation and the complex would have D_2-symmetry.[22] Since then, several high symmetry chiral dirhodium catalysts have been developed,[25] so the concept of generating high symmetry catalysts by using four identical ligands of lower symmetry has been established, but the validity of the Rh_2(*S*-TBSP)$_4$ D_2 model has not been confirmed. Therefore, the comparison of the enantioinduction between RhBi(*S*-TBSP)$_4$ and Rh_2(*S*-TBSP)$_4$ was considered to be particularly interesting because the RhBi complex would be unable to be D_2 symmetric.

2. EXPERIMENTAL RESULTS AND DISCUSSION

2.1 Catalyst Preparation

The chiral *S*-TBSP ligand was used for the preparation of the new chiral RhBi catalyst, RhBi(*S*-TBSP)$_4$ (Scheme 2). This complex was prepared via equatorial ligand exchange by refluxing a toluene solution of RhBi(TFA)$_4$ and a slight excess of ligand with a Soxhlet extractor containing K_2CO_3. The resulting yellow compound is bench stable and was purified by column chromatography. It was fully characterized by ^{1}H and ^{13}C NMR and IR spectroscopy along with ESI-MS and elemental analysis. The only well-resolved protons in the ^{1}H NMR spectrum of **1** in $CDCl_3$ are the doublets of the *para*-substituted aryl ring (J = 8.3 Hz) and the methyl protons of the ^{t}butyl group at 7.73, 7.48 and 1.29 ppm, respectively. The observation of only one set of aryl resonances suggests the equatorial ligands lie in a highly symmetric environment on the NMR timescale. The achiral catalyst, RhBi(OPiv)$_4$,[19] was also prepared in a similar way as a reference system for the structural analysis.

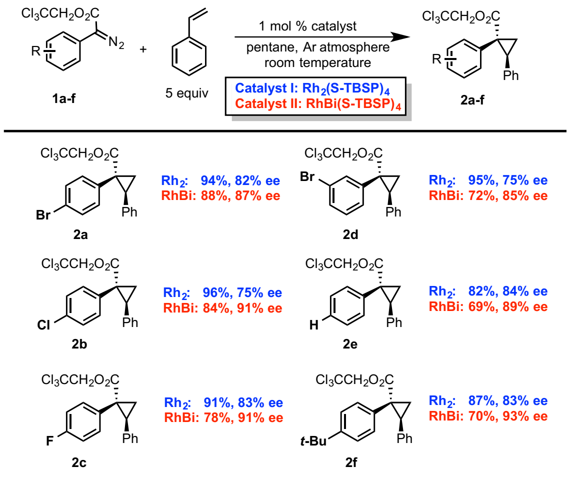
Scheme 2. Synthesis of RhBi Catalysts.



2.2 Catalytic Activity

Evaluation of the catalytic behavior of the newly prepared RhBi complexes began with the cyclopropanation of styrene with 2,2,2-trichloroethyl aryldiazoacetates **1**. The trichloroethyl esters of the carbene precursors have been shown to give superior carbene transformations. As shown in Scheme 3, the reactions were carried out with 1 mol % catalyst with the nonpolar solvent, pentane, at room temperature. Asymmetric induction with Rh_2(*S*-TBSP)$_4$ is very solvent dependent and hydrocarbon solvents are superior to dichloromethane, the standard solvent for carbene reactions. The diazo compound was rapidly added into the solution containing the catalyst and styrene. In general, the dirhodium catalyst is kinetically fast but the RhBi catalyst is much slower.[17] Hence, the Rh_2(*S*-TBSP)$_4$-catalyzed reaction to form the cyclopropanes **2** is complete in under 1 min, whereas the RhBi(*S*-TBSP)$_4$-catalyzed reaction takes 12 h. Even though the reaction rates are very different, the levels of enantioselectivity for both catalysts are similar with the RhBi catalyst giving slightly higher levels of enantioselectivity (85-93% ee) than the dirhodium catalyst (74-84% ee). As is typical for cyclopropanation with donor/acceptor carbenes, the diastereoselectivity is excellent (>95% de) for both catalysts.

Scheme 3. Asymmetric Cyclopropanation with Styrene[a]



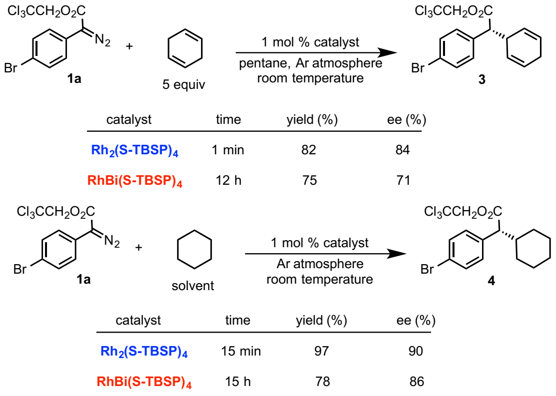
[a]Reaction conditions: A solution of diazo (0.1 mmol, 1 equiv) in 2 mL pentane was rapidly added to a solution of styrene (0.5 mmol, 5 equiv) and catalyst (1 mol %) in 1 mL pentane at room temperature. For Rh_2(S-TBSP)$_4$, the reaction was completed in 1 min. For RhBi(S-TBSP)$_4$, the reaction was completed in 12 h.

As shown in Scheme 4, the two catalysts were also evaluated in some standard C–H functionalization reactions. Rh_2(*S*-TBSP)$_4$ and its related n-dodecyl analog Rh_2(*S*-DOSP)$_4$ have shown broad utility in C–H functionalization reactions with donor/acceptor carbenes, and consequently, it would be of interest to determine how RhBi(*S*-TBSP)$_4$ would compare with them. Both Rh_2(*S*-

TBSP)$_4$ and RhBi(*S*-TBSP)$_4$ performed well in the reaction with cyclohexadiene, although once again the Rh$_2$(*S*-TBSP)$_4$-catalyzed reaction was much faster. Good yields of **3** were obtained with both catalysts but the enantioselectivity was slightly higher in the Rh$_2$(*S*-TBSP)$_4$ catalyzed reaction (84% ee vs 71% ee). Likewise, effective reactions were achieved with both catalysts when cyclohexane as solvent was used at the trapping agent and the enantioselectivity for the formation of **4** was quite similar (90% ee for Rh$_2$(*S*-TBSP)$_4$ and 86% ee for RhBi(*S*-TBSP)$_4$). Even though RhBi(*S*-TBSP)$_4$ performs comparably to Rh$_2$(*S*-TBSP)$_4$ in these reactions, when the C–H functionalization was attempted on less reactive substrates without using a vast excess of substrate, such as adamantane (3 equiv), the dirhodium catalyst gave much higher yields than the RhBi catalyst.

These benchmark reaction studies reveal that the chiral environments in Rh$_2$(*S*-TBSP)$_4$ and RhBi(*S*-TBSP)$_4$ are similar, with RhBi(*S*-TBSP)$_4$ doing slightly better in cyclopropanation and Rh$_2$(*S*-TBSP)$_4$ doing slightly better in C–H functionalization. As has been seen before for RhBi catalysts,[17] Rh$_2$(*S*-TBSP)$_4$ is kinetically a much more active catalyst than RhBi(*S*-TBSP)$_4$ and the dirhodium catalyst is far superior when the C–H functionalization reactions are conducted on challenging substrates.

Scheme 4. C–H Functionalization with Cyclohexadiene and Cyclohexane[a]



catalyst	time	yield (%)	ee (%)
Rh$_2$(S-TBSP)$_4$	1 min	82	84
RhBi(S-TBSP)$_4$	12 h	75	71

catalyst	time	yield (%)	ee (%)
Rh$_2$(S-TBSP)$_4$	15 min	97	90
RhBi(S-TBSP)$_4$	15 h	78	86

[a]Reaction conditions: A solution of diazo (0.1 mmol, 1 equiv) in 2 mL corresponding solvent was rapidly added to a solution of styrene (0.5 mmol, 5 equiv) and catalyst (1 mol %) in 1 mL solvent at room temperature. For Rh$_2$(S-TBSP)$_4$, the reaction was completed in 1 to 15 min. For RhBi(S-TBSP)$_4$, the reaction was completed in 12 to 15 h.

2.3 Catalyst Structural Information

Having established that the Rh$_2$(S-TBSP)$_4$, **5**, and RBi(S-TBSP)$_4$, **6**, catalysts give similar levels of asymmetric induction, structural studies were conducted to explore the similarities and differences between the two catalytic systems. Crystals of RhBi(*S*-TBSP)$_4$ were obtained by cooling a THF solution to –20 °C, and the structure was confirmed by X-ray diffraction. The asymmetric unit of the tetragonal *I*4 crystal of **6** contains one quarter molecule of RhBi(*S*-TBSP)$_4$, residing on a crystallographic four-fold axis of symmetry with a partially occupied molecule of THF coordinated to the Rh-atom at a distance of 2.291(7) Å, disordered over the four-fold symmetry axis (Figure 1). There are also two solvent accessible voids on opposite sides of the aryl ring of the equatorial ligand, which are both partially occupied by THF molecules. Crystallographic information and selected bond distances are shown in supporting information Table S1 and S2, respectively. The Rh–Bi bond distance is 2.5084(7) Å, consistent with a Rh–Bi single bond.[19] The M–O$_{eq}$ bond distances are 2.406(4) and 2.023(5) Å for Bi and Rh, respectively, having an ~ 0.4 Å longer M–O$_{eq}$ bond distance for Bi compared to Rh, consistent with all other RhBi crystal structures.[19-21] From a stereochemical perspective, the most interesting feature of the crystal structure is the positioning of the *tert*-butylphenylsulfonyl groups. The equatorial ligands adopt a pseudo-C_4 symmetry geometry with the *tert*-butylphenylsulfonyl groups splayed towards the periphery of the bimetallic core. Thus, contrary to the original hypothesis to explain the asymmetric induction with Rh$_2$(*S*-TBSP)$_4$, the *tert*-butylphenylsulfonyl-prolinate groups are not sufficiently large to be forced out of the periphery of the catalyst. The conformational preferences for the ligands in RhBi(*S*-TBSP)$_4$, were evaluated computationally and revealed that the prolinate ligands in several different conformations have similar energies, which suggest the ligands of this catalyst are flexible. The observed conformation in the crystalline form may simply represent the favored solid packing arrangement. These observations indicate that the ligands are most likely quite flexible and can change their conformation once the carbene is bound to the catalyst.[26]

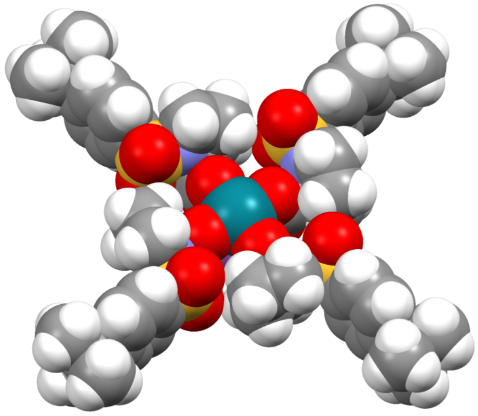


Figure 1. X-ray crystal structure of catalyst **6** end-on view. Eight partially occupied THF molecules, and the minor component of the disordered ^{t}butyl group have been removed for clarity.

Other important features of these catalysts necessary to understand their activity are the nature of the metal-metal bonds and the extent of π back-bonding. In principle, the Rh$_2$ and RhBi dimers have both covalent (**A**, Scheme 5) or ionic (**B**) resonance forms that contribute to their ground state wavefunctions. While **A** is expected to be the most important contributor for the homobimetallic Rh$_2$ complexes, resonance form **B** has been suggested to be important in the carbenoid reactivity of these compounds. In the heterobimetallic RhBi core, it is possible for **B** to have a greater contribution to the ground state due to the difference in electronegativity between Rh and Bi. Since **B** represents a species with two-electron mixed-valence, it is possible to gauge its importance to the ground state with a measure of the Rh oxidation state in Rh$_2$ and RhBi complexes. A particularly effective method for interrogating the Rh oxidation state is X-ray photoelectron spectroscopy (XPS), which measures the binding energies of electrons in the core orbitals of Rh. These element-specific energies are sensitive to the oxidation state, shifting to higher energy as the metal becomes more oxidized.[27]

Scheme 5 Covalent and ionic resonance structures of metal-metal bonded units.

$$\mathrm{M^{II}—M^{II}} \longleftrightarrow \mathrm{M^{I}—M^{III}}$$

covalent ionic

A **B**

The XPS spectra of **5** and **6** are shown in Figure 2, with full spectral details given in the supporting information (Figures S1.1 and S1.2, Tables S5 and S6). The Rh $3d_{5/2}$ and $3d_{3/2}$ binding energies of Rh_2(S-TBSP)$_4$ are 309 and 314 eV, respectively and those of RhBi(S-TBSP)4 are practically identical. Thus, according to these XPS results, there is no difference in the Rh oxidation state between the Rh_2 and RhBi complexes; both metal-metal bonds have a similar degree of covalency, in agreement with the small, 0.22, difference in electronegativities between Rh and Bi.

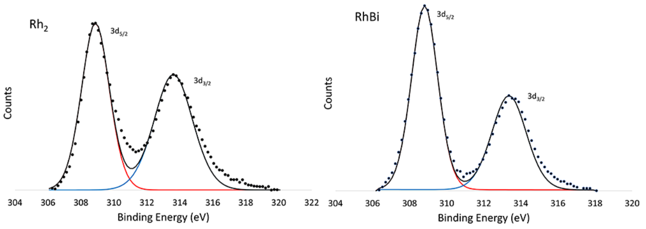


Figure 2. X-ray photoemission spectra of the Rh $3d_{5/2}$ and $3d_{3/2}$ region of Rh_2(S-TBSP)$_4$ (above) and RhBi(S-TBSP)$_4$ (below). Experimental and fit spectra are shown in red and blue, respectively.

To acquire a handle on how the Rh-for-Bi metal atom substitution affects ligands bound to the axial site of the catalyst, we have prepared PPh_3 adducts of RhBi(piv)$_4$ and Rh_2(piv)$_4$ and compared the ^{31}P NMR chemical shifts of their phosphorous atoms. The complex RhBi(piv)$_4$(PPh_3), **7**, was synthesized by heating RhBi(piv)$_4$ and 2 eq. of PPh_3 in pivalic acid. To confirm the structure, single crystals of **7** were grown by slow cooling a hexane solution of **7** to –20 °C. The molecular structure and crystallographic data are shown in Figure 3 and Supporting Information Tables S3 and S4. Complex **7** is indeed a Rh–PPh_3 adduct with a Rh–Bi bond distance of 2.5646(4) Å and an Rh–P bond distance of 2.511(1) Å (Rh–P bond distances of 2.494(2)[28] and 2.4771(5)[29] were found for $Rh_2(TFA)_4(PPh_3)_2$ and $Rh_2(OAc)_4(PPh_3)_2$, respectively).

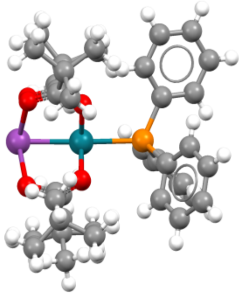


Figure 3. X-ray crystal structure of **7**. One disordered ^{t}Bu group has been removed for clarity.

The ^{31}P NMR spectrum of **7** reveals a single phosphorous signal with a chemical shift of 170.4 ppm, which is a doublet with a coupling constant, $J(^{31}P–^{103}Rh)$ of 82.3 Hz, indicative of an Rh–PPh_3 adduct (Figure 4, bottom). To compare the ^{31}P chemical shift, the analogous Rh_2(piv)$_4$$PPh_3$ complex **8** was synthesized by stirring a CH_2Cl_2 solution of Rh_2(piv)$_4$ and 1 eq. of PPh_3 together at room temperature. The ^{31}P NMR spectrum of **8** reveals a ^{31}P chemical shift of –38.4 ppm (dd, $^1J_{P–Rh}$ = 97.0, $^2J_{P–Rh}$ = 34.4 Hz) (Figure 4, top). Thus, we see a >200 ppm downfield shift in the ^{31}P signal simply by replacing the distal Rh-atom for a Bi-atom! This downfield shift suggests the phosphorous atom in **7** is much more electron poor compared to that **8**. The large change in chemical shift can be caused by changes in either the σ or π bonding framework within the complex. If the π backbonding ability plays a dominant role here, we might expect there to be important implications for the reactivity of the corresponding carbene complexes. However, in the previous evaluation of Rh-Bi complexes and the asymmetric inductions described here, except for the rate of reactions, the two catalysts systems behave very similarly, suggesting the charge distribution in the carbene complex is not changed significantly, and that the change in ^{31}P chemical shift is most likely due to changes in the nature of the Rh–P σ bonding.

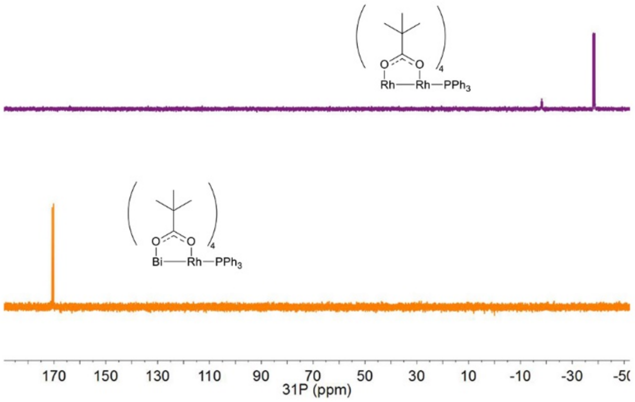
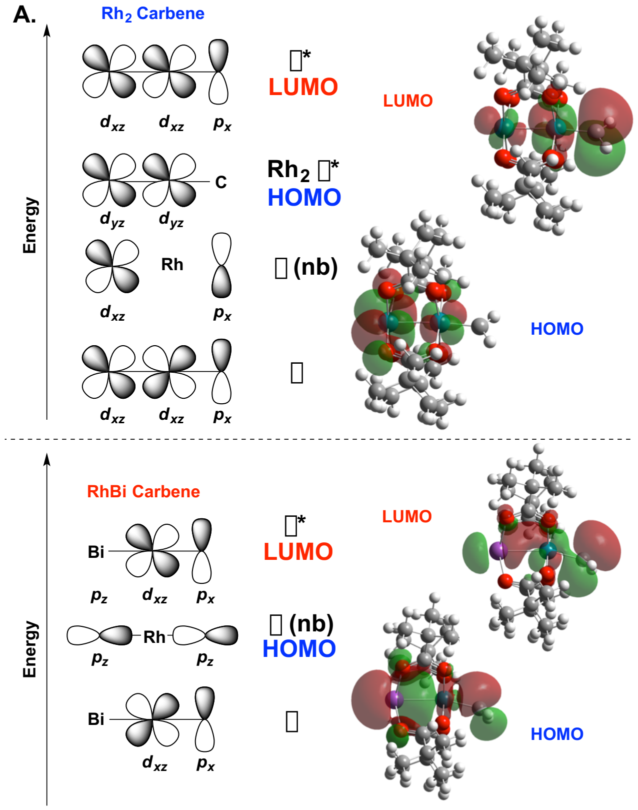


Figure 4. ^{31}P NMR spectra of **7** (bottom, orange) and **8** (top, purple) in $CDCl_3$

According to the previous achiral RhBi carbene studies, the RhBi catalyst demonstrates similar reactivity to the corresponding Rh_2 catalyst in reactions where the product distribution is dependent on the electron withdrawing ability of the catalyst. In the current study, the much slower RhBi catalyst shows similar enantioselectvity to the Rh_2 catalyst or C–H functionalization and cyclopropanation, whereas Rh_2 catalysts exhibit broader substrate scope for C–H functionalization. The previous calculations on the RhBi donor/acceptor carbenes revealed that the rate of the reaction is controlled by the rate of diazo decomposition and a Rh_2 complex is more effective than a RhBi complex at catalyzing this step. In order to gain further understanding of the selectivity issues, we considered Berry's three-center/four-electron (3c/4e) bonding model that has been used to explain the hyper-electrophilic character of Rh_2 carbenes.[30] An analysis of the molecular orbitals (MOs) of the carbene complexes of both catalysts was conducted (Figure 5). We examined the catalyst bound to both the methylene carbene (Figure 5A), as was originally done in the Berry analysis of the Rh_2 system, and a donor/acceptor carbene (Figure 5B). The electrophilic reactivity of the metal carbene depends on the nature of the LUMO (π^* MO) of the metal carbene complex. As seen in Figure 5A, the RhBi and Rh_2 methylene carbenes have a different π orbitals, and so one would expect different elelctrophilic characteristics for the methylene carbene bound to the two catalysts. However, methylene carbene is not a good model for donor-acceptor carbenes because it is well known that donor/acceptor carbenes have attenuated reactivity characteristics.[31] The analysis of the LUMO of the corresponding metal donor-acceptor carbenes leads to interesting findings. As seen in Figure 5B, the donor group is highly involved in the LUMO, which greatly delocalizes the positive charge of the carbene, and consequently, makes LUMO, mostly, a carbene-based orbital: so, the impact of the metal centers, both in RhBi and Rh_2, becomes a less important factor. As a result, the donor-acceptor carbene of both RhBi and Rh_2 is expected to act similarly, as an electrophile, in the addition reactions. However, it should be noted, that the Rh_2 complexes decompose diazo compounds faster than RhBi complexes and Rh_2 catalysts are more effective with a wider range of C–H functionalization substrates.

In contrast, as seen in the Figure 5B, the HOMOs of the RhBi and Rh_2 donor-acceptor carbenes are very different. Indeed, in case of the Rh_2 complex, it is a Rh-Rh π^* orbital with almost none carbene character. In contrary, HOMO of the RhBi donor-acceptor carbene is a non-bonding σ-orbital involving Bi and carbene carbon with insignificant Rh-character. Comparison of these HOMOs indicates that donor-acceptor carbene of RhBi catalyst can be expected to behave as a more effective nucleophile compared to the donor-acceptor carbene of Rh_2.



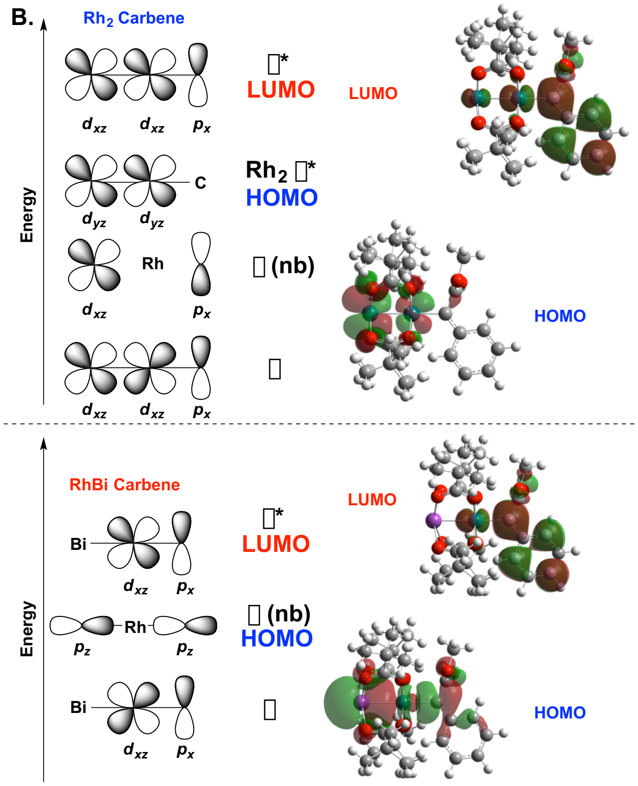


Figure 5. Illustrative molecular orbitals for Rh_2 and RhBi carbenes. A: with methylene as the carbene. B: with a donor/acceptor carbene

In conclusion, these studies reveal that the asymmetric induction with RhBi(*S*-TBSP)$_4$ is very similar to that achieved with Rh_2(*S*-TBSP)$_4$, Even though the replacement of a Rh with a Bi in these lantern complexes has a considerable influence on the electronics of these complexes, the RhBi complexes have several similarities to the corresponding Rh_2 catalysts in their reactions with donor/acceptor carbenes. The corresponding complexes behave with similar electron withdrawing capabilities and achieve similar levels of asymmetric induction. The major differences are between the rates of reactions with the Rh_2 complexes reacting much faster, and the Rh_2 complexes are capable of a much wider range of C–H functionalization reactions. An unexpected structural feature of RhBi(*S*-TBSP)$_4$ is the arrangement of the arylsulfonyl groups in the periphery of the catalyst, leading to a C_4 symmetric structure. These results suggest the original hypothesis proposed for the asymmetric induction for Rh_2(*S*-TBSP)$_4$ is not correct. A detailed computational study is currently ongoing to analyze why a conformationally mobile catalyst is capable of such high levels of asymmetric induction.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.
Experimental and computational details (PDF)
Crystallographic data for **6** and **7** (CIF)

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Notes

The authors declare no competing financial interests.

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