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Electronic and Steric Tuning of an Atropisomeric Disulfoxide Ligand Motif and its Use in the Rh(I)-Catalyzed Addition Reactions of Boronic Acids to a Wide Range of Acceptors

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Abstract. A novel chiral disulfoxide ligand pair bearing fluorine atoms at the 6 and 6' position of its atropisomeric backbone, (*M*,*S*,*S*)- and (*P*,*S*,*S*)-*p*-Tol-6F-BIPHESO, was synthesized. Complexation to a rhodium(I) precursor gave rise to μ-Cl- and μ-OH-bridged rhodium dimer complexes incorporating the new (*M*,*S*,*S*)-*p*-Tol-6F-BIPHESO ligand, while its sibling (*P*,*S*,*S*)-*p*-Tol-6F-BIPHESO was not complexed efficiently to the rhodium precursor. The performance of this disulfoxide ligand [(*M*,*S*,*S*)-*p*-Tol-6F-BIPHESO] in catalysis was tested in both 1,4- and 1,2-addition reactions of arylboronic acids. We show that addition to both cyclic and acyclic enones as well as *N*-tosylarylimines proceeds with high yields and high enantioselectivities to give the corresponding products. The synthesis of enantiomerically pure *p*-Tol-6F-BIPHESO is straightforward and inexpensive, which together with the high catalytic performance and wide substrate scope for these addition reactions makes it a very attractive alternative to more classical chiral ligand entities.

Keywords: chiral sulfoxide; atropisomers; rhodium; asymmetric catalysis; addition reactions

1. Introduction

Enantioselective transition metal catalysis, which offers a very elegant and atom-economical way to the production of all-important enantiomerically pure compounds, has attracted extensive attention from the chemistry community over the decades. What has clearly been established is the fact that reliable and versatile catalysts with good reactivities and selectivities are highly dependent on the chiral ligands coordinated to the central metals. Therefore, the correct design as well as the facile synthesis of novel ligands has always been and continues to represent a major task in asymmetric catalysis. [1] Phosphorous, nitrogen and oxygen are frequently embedded as donor atoms in such ligand architectures. Sulfoxides, due to their inherent chirality at sulfur, have a well-known coordination chemistry and have played a very important role in asymmetric catalysis as chiral auxiliaries initially.[2] However, for a long time, the utilizations of sulfoxides as ligands for transition metal catalysis,[3] whether bound through oxygen or sulfur, did not enjoy much success. Seemingly, their questionable binding ability and possibly unfortunate ligand design choices did not offer efficient chiral environments for asymmetric metal catalysis.

In 2008, our group introduced the disulfoxide *p*-Tol-BINASO [1,1'-binaphthalene-2,2'-diyl-bis(p-tolylsulfoxide)] (**Figure 1**, bottom left),[4a] as a highly efficient ligand for the rhodium catalyzed 1,4-addition of arylboronic acid to cyclic α,β-unsaturated ketones and esters.[5,6,7] This first report on utilizing this

ligand class in the Hayashi-Miyaura reaction has led to a renewed interest in the development of chiral sulfoxide ligands.[8] Later on, with the adoption of other C_2-symmetric atropisomeric backbone units,[9] new ligand analogues were synthesized and tested in our group. For example, *p*-Tol-Me-BIPHESO, a sulfoxide analogue of BIPHEMP,[4b] was obtained similarly easily to *p*-Tol-BINASO and showed even better catalytic results at lower catalyst loading for this addition reaction (**Figure 1**, bottom center). By comparing the X-ray crystal structures of Rh complexes of disulfoxide ligands *p*-Tol-BINASO and *p*-Tol-Me-BIPHESO,[4c] it can be seen that this subtle modification of the backbone was beneficial for the rhodium-catalyzed conjugate addition reactions, as the particular geometry of the backbone and its associated characteristics (dihedral angle and bite angle) were slightly modified.[10] In these first studies, a few problems though arose: First of all, even the most active ligand/metal combination incorporating *p*-Tol-Me-BIPHESO as the ligand was not able to asymmetrically add arylboronic acids to open-chain type chalcone substrates. Indeed, what we saw was that the addition of an arylboronic acid to the parent *trans*-1,3-diphenyl-2-propenone would give the addition product in low yield and negligible enantioselectivity (20% *ee*).[4b] Secondly, all of the ligands with these atropisomeric backbones have so far been particular in the sense that only one of the diastereoisomers of the atropisomeric ligand pair was able to bind to the rhodium precursor to give the precatalyst. And as a third point, modifications done on the axially chiral backbones in these disulfoxide ligands until now pertained to the synthesis of more electron-rich variations of *p*-Tol-BINASO, whereas recently, electron-poor versions of the more widely studied chiral diphosphine and diene ligands achieved significant success in various addition

reactions.[6j,11] For example, Sakai *et al.*,[6j] described the synthesis of MeO-F_{12}-BIPHEP, an atropisomeric diphosphine ligand with electron-poor, fluorinated phenyl groups on phosphorous, which was very efficient in the Rh-catalyzed 1,4-additions of arylboronic acids, clearly outperforming its non-fluorinated congeners (**Figure 1**, top left). Ratovelomanana-Vidal *et al.*,[11f] employed (*R*)-3,5-diCF_3-SYNPHOS, again an electron-deficient diphosphine ligand with atropisomeric backbone, in the same Rh-catalyzed asymmetric 1,4-addition of arylboronic acids to *α,β*-unsaturated ketones and nonsubstituted maleimide with equally high success (**Figure 1**, top middle). A group of chiral diene ligands with an electron-poor tetrafluorobenzobarrelene backbone was developed by Hayashi *et al.*,[11c,d] and shown to behave exceedingly well in similar rhodium-catalyzed addition reactions (**Figure 1**, top right).[11h,i]

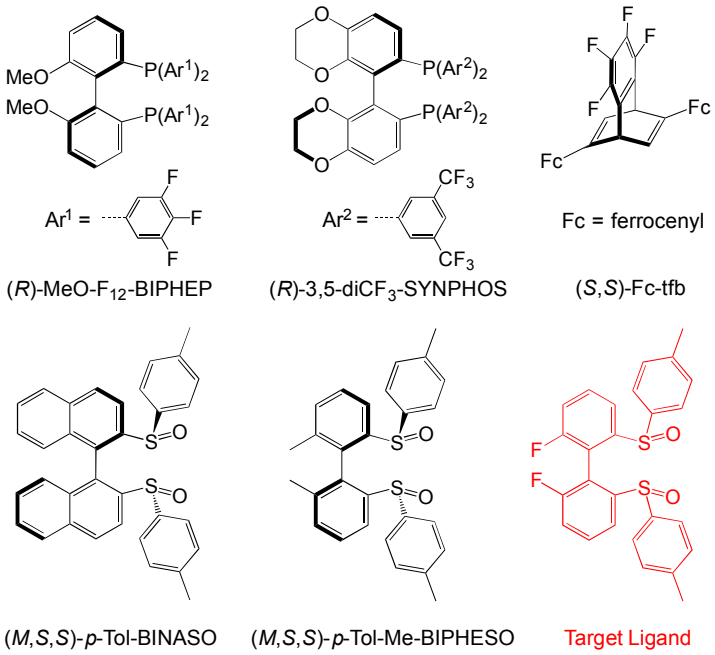


Figure 1. Sakai's and Ratovelomanana-Vidal's fluorous BINAP-type phosphorus ligands, Hayashi's fluorous diene ligand, atropisomeric disulfoxide ligands and the target ligand (from top left to bottom right).

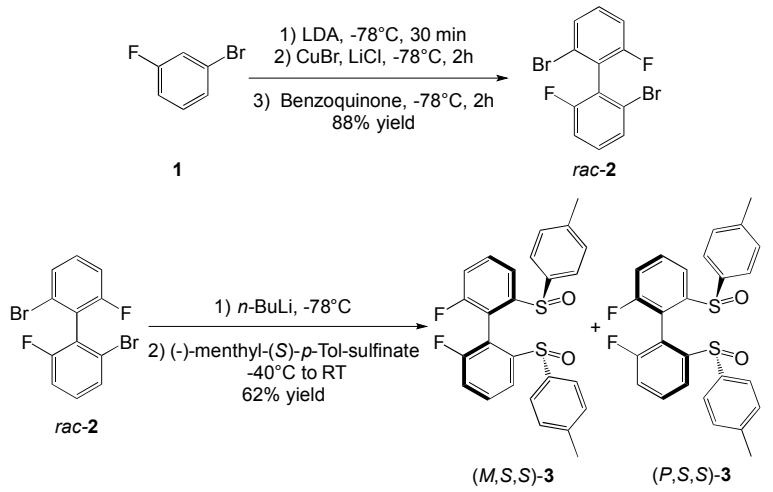
While these developments already gave us an incentive to see how such incorporations of fluorine atoms would affect the reactivity of our disulfoxide ligands, we also wanted to simultaneously come up with a ligand design that might hopefully be able to address the shortcomings mentioned above in terms of reactivity (no reactivity with open chain substrates) and diastereomer binding [no binding of *P*,*S*,*S* (or *M*,*R*,*R*) diastereomers]. To this end, we chose the target ligand shown in **Figure 1** (bottom right). It incorporates a very small 6,6'-difluorobiphenyl backbone that should hopefully enhance flexibility of its dihedral angle, all the while reaching a new electronic situation in these ligands (electron-poor *vs* electron-rich BINASO and derivatives).

We herein report the facile and straightforward synthesis of this electron-deficient disulfoxide ligand, report on its binding ability to rhodium and its use in arylboronic acid additions to various acceptors. In particular, we show how open-chain chalcone type substrates can be used successfully with this new catalyst system. The fact that the same ligand/catalyst combination can be used for the addition reaction of arylboronic acids to both cyclic/acyclic enones (1,4-addition) and *N*-tosylarylimines (1,2-addition) makes this new catalyst system rather unique, as high selectivity of a catalyst often precludes broadness of the scope of substrates. Indeed, in the context of these addition reactions, very few single ligand systems exist that successfully promote both the 1,4-addition to α,β-unsaturated compounds and the 1,2-addition to imines,[12] meaning that steric or electronic tuning of the ligand is usually necessary to reach good results in one or the other reaction scheme.

2. Results and Discussion

Compared with other chiral ligand designs, the synthesis of enantiopure sulfoxides is often significantly more straightforward, making them appealingly practical and green. The new ligand that we describe here is no exception and its synthesis involves a mere two steps to access in optically pure form (**Scheme 1**). As a comparison, its diphosphine analogue 6,6'-difluorobiphenyl-2,2'-diyl-bis(diphenylphosphine),[13] needed four synthetic steps to access in racemic form and a subsequent, tedious and expensive enantiomer resolution with a chiral palladium complex to reach its optically pure version.

The first synthetic step involved a copper-catalyzed Ullman coupling of commercially available and reasonably priced 1-bromo-3-fluorobenzene **1** (ca. 40$ for 100 g). Here, various procedures were tested before establishing a modified reaction process that gave the coupled, racemic dibromo derivative 2,2'-dibromo-6,6'-difluorobiphenyl (*rac*-**2**) in excellent yield (88%) after column chromatography and crystallization.[14] Subsequently, careful treatment with *n*-butyllithium and reaction with commercially available (-)-menthyl-(*S*)-*p*-tolyl-sulfinate led to the isolation of the desired disulfoxide 6,6'-difluorobiphenyl-2,2'-diyl-bis(*p*-tolylsulfoxide (*p*-Tol-6F-BIPHESO, **3**) as a pair of diastereoisomers. The respective diastereomers were separated by simple column chromatography to give the pure (*M*,*S*,*S*)-**3** and (*P*,*S*,*S*)-**3** ligands in equal amounts (31% yield each) and in 62 % overall yield. The two diastereomeric ligands were fully characterized by NMR spectroscopy (^{1}H, ^{13}C and ^{19}F NMR) as well as elemental analyses and their absolute configuration was determined and attributed via X-ray diffraction studies (see discussion below).



Scheme 1. Synthetic procedure for obtaining disulfoxide *p*-Tol-6F-BIPHESO (**1**).

Because the Van der Waals radius of fluorine is the smallest next to hydrogen, we had to make sure that these diastereomers [(*M*,*S*,*S*)-**3** and (*P*,*S*,*S*)-**3** respectively] would not interconvert via backbone rotation. While it is known in the literature that the corresponding diphosphine ligand is resistant to thermally induced racemization of its atropisomeric backbone,[13] we nevertheless needed to ascertain that it would not happen in our case. This because of the fact that the *p*-tolyl sulfoxide unit is clearly less sterically demanding than the diphenylphosphine moiety in its phosphine congener, translating into a possibly rather facile rotation of the atropisomeric unit. **Figure 2** [(*M*,*S*,*S*)-**3**] and **Figure 3** [(*P*,*S*,*S*)-**3**] show the VT ^{1}H NMR spectra (DMSO-d_6) of our diastereomers and these experiments clearly prove that racemization of the atropisomeric backbone does not occur within the temperature range studied (up to 150° C).

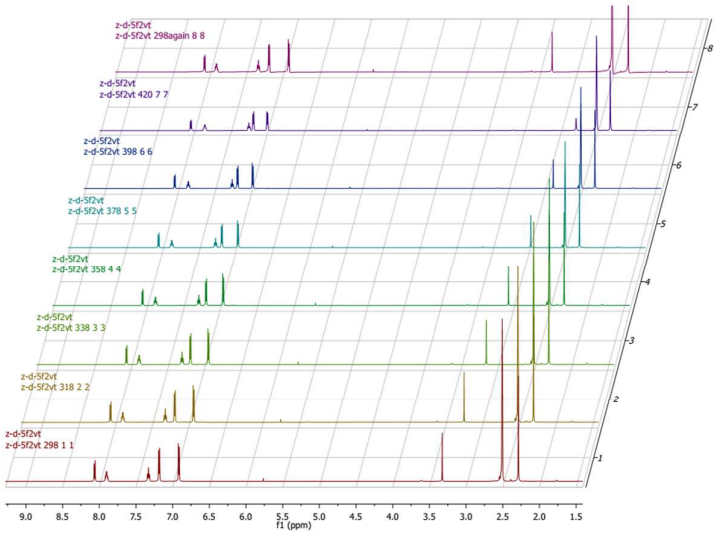


Figure 2. VT ^{1}H NMR analysis of possible backbone racemization in (*M*,*S*,*S*)-*p*-Tol-6F-BIPHESO [(*M*,*S*,*S*)-**3**]. Top spectrum in purple shows the ^{1}H NMR spectrum at 298 K after heating (signal at ca. 3.3 ppm is residual water in DMSO).

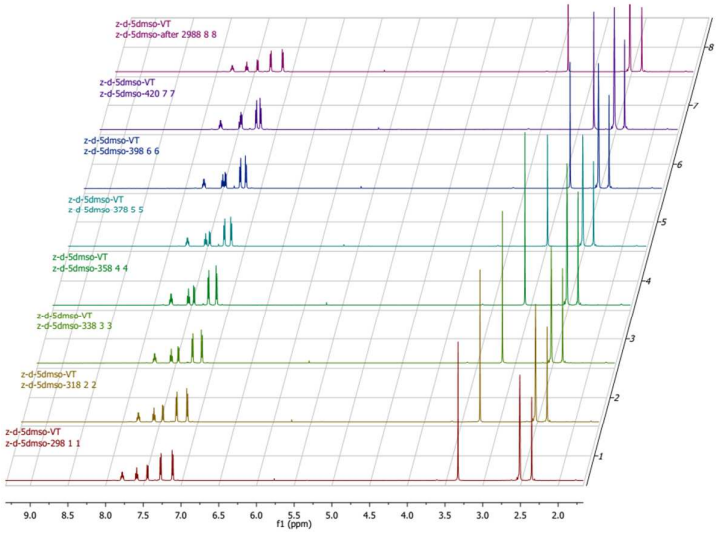


Figure 3. VT ^{1}H NMR (DMSO-d_6) analysis of possible backbone racemization in (*P*,*S*,*S*)-*p*-Tol-6F-BIPHESO [(*P*,*S*,*S*)-**3**]. Top spectrum in purple shows the ^{1}H NMR spectrum at 298 K after heating (signal at ca. 3.3 ppm is residual water in DMSO).

As mentioned above, unambiguous assignment of the absolute stereochemistry of the new ligands was possible by means of X-ray diffraction studies from appropriately grown crystals of both diastereomers [(*M*,*S*,*S*)-**3** and (*P*,*S*,*S*)-**3**]. Representations are shown in **Figure 4** with figure captions that include selected

bond lengths and angles. Not surprisingly, (*M*,*S*,*S*)-**3** and (*P*,*S*,*S*)-**3** show very similar structures, with differing axial chirality of the backbone. The average S=O bond lengths reveal a near identical value {1.494 Å (av.) [(*M*,*S*,*S*)-**3**] and 1.492Å (av.) [(*P*,*S*,*S*)-**3**]}, which incidentally is very close to the average S=O bond distances recorded for the parent *p*-Tol-BINASO [1.4922(16)Å] and *p*-Tol-Me-BIPHESO [1.4988(16)Å] ligands.[4a,b] This indicates that the electronic situation in **3** is not sufficiently different to translate into significant changes in S=O bond length values in the solid state.

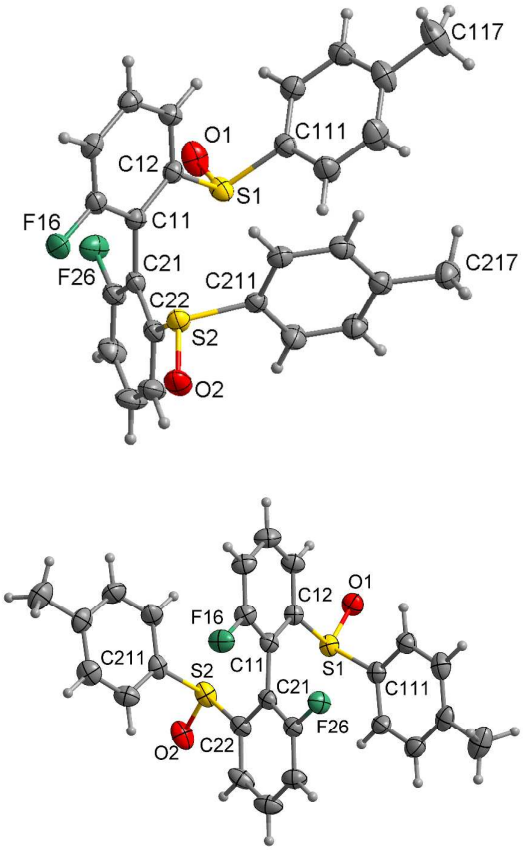
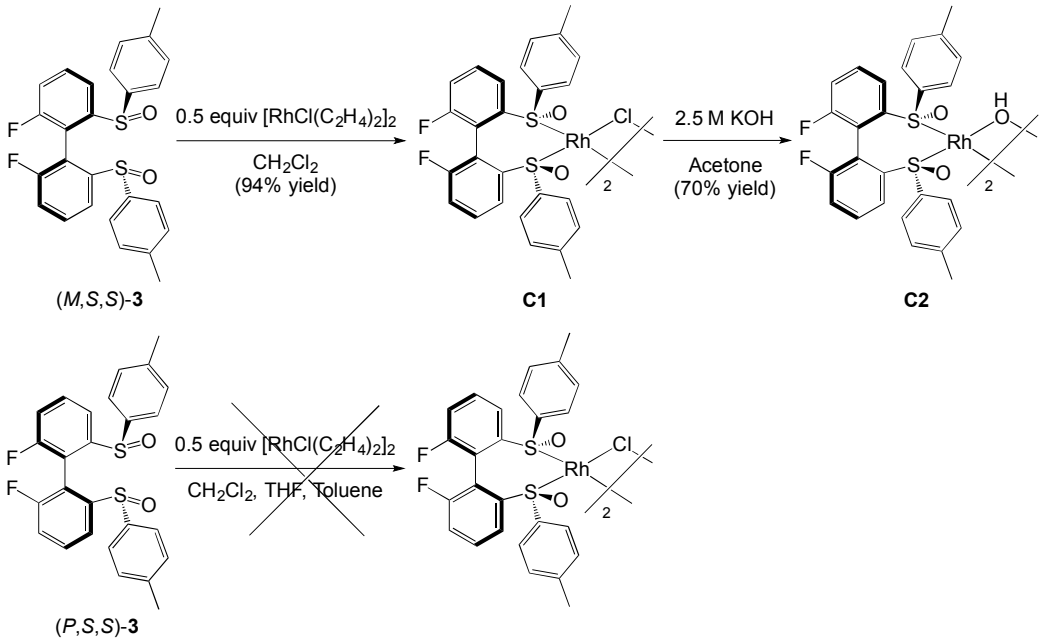


Figure 4. Top: Molecular structure of (*P*,*S*,*S*)-*p*-Tol-6F-BIPHESO (**3**) (50% probability ellipsoids). Selected bond lengths (Å) and angles (deg): S1-O1, 1.4830(18); S2-O2, 1.5011(16); F16-C16, 1.354(2); F26-C26, 1.354(3); S1-C12, 1.811(2); S2-C22, 1.804(2); C111-S1-C12, 98.42(10); C211-S2-C22, 99.87(10). Bottom: Molecular structure of (*M*,*S*,*S*)-*p*-Tol-6F-BIPHESO (**3**) (50% probability ellipsoids). Selected bond lengths (Å) and angles (deg): S1-O1, 1.4933(18); S2-O2, 1.4953(19); F16-C16, 1.356(3); F26-C26, 1.352(3); S1-C12, 1.823(2); S2-C22, 1.809(2); C111-S1-C12, 96.30(10); C211-S2-C22, 98.12(10).

The next step in our investigation was to see how this new ligand, with its smaller and more flexible backbone, would behave when binding it to the rhodium precursor $[RhCl(C_2H_4)_2]_2$. Synthesis of the chloro-bridged rhodium precatalyst $[RhCl\{(M,S,S)$-*p*-Tol-6F-BIPHESO$\}]_2$ (**C1**) by reacting (*M*,*S*,*S*)-*p*-Tol-6F-BIPHESO (**3**) at room temperature with the ethylene-bridged dimer $[RhCl(C_2H_4)_2]_2$ in CH_2Cl_2 was straightforward and gave, after appropriate workup, complex **C1** as an orange powder in 94% yield (**Scheme 2**, top). Our hope that the second diastereomer (*P*,*S*,*S*)-*p*-Tol-6F-BIPHESO (**3**) would also undergo straightforward ligation to the metal was unfortunately not met with success. Repeated attempts invariably led to complicated mixtures of products that were difficult to interpret by NMR spectroscopy. Following the ligation event by running the complexation in various deuterated solvents (CD_2Cl_2, THF-d_8, C_6D_6) indicated that a clean complex was not generated during the time course of the reaction, in contrast to an identical run recorded for (*M*,*S*,*S*)-*p*-Tol-6F-BIPHESO (**3**) with dimer $[Rh(C_2H_4)_2Cl]_2$ (see Supporting Information for spectra).

The corresponding OH-bridged dimer $[Rh(OH)\{(M,S,S)$-*p*-Tol-6F-BIPHESO$\}]_2$ (**C2**) was successfully synthesized by treating complex **C1** with KOH in acetone and was obtained in a 70% yield after workup. The synthetic pathway to these new disulfoxide complexes is shown in **Scheme 2**.



Scheme 2. Synthesis of rhodium precatalysts **C1** and **C2**.

Crystals suitable for an X-ray diffraction study of the chloro-bridged rhodium complex **C1**,[15] were grown by slow diffusion of diethyl ether into a concentrated CH_2Cl_2 solution containing the compound and representations of [RhCl{(*M*,*S*,*S*)-*p*-Tol-6F-BIPHESO}]$_2$ (**C1**), together with selected bond lengths and angles, are shown in **Figure 5**. When comparing the S-Rh-S bond angles, the bond lengths for Rh-Cl, Rh-S and $C_{backbone}$-S in complex **C1** with corresponding values measured for the previously reported Rh complex analogues formed with ligands *p*-Tol-Me-BIPHESO and *p*-Tol-BINASO (**Table 1**), we note that the value for the S-Rh-S bond angle is slightly bigger in complex **C1**. There is an apparent and rather significant difference between the new complex and the former two with respect to the dihedral angles of the two planes of backbone units. The value for **C1** is 68.3°, while the one for the *p*-Tol-BINASO analogue measures 74.1° and the one for the *p*-Tol-Me-BIPHESO is highest at 75.6°. This trend is to be expected based on the fact that lower values for the dihedral angle can only be

accommodated in ligand structures where the two halves of the atropisomeric backbone can appropriately approach each other given their lower steric pressure (see introduction part). Not surprisingly, the different backbone orientation that we see in **C1** is translated onto the overall structure of the dimer. In fact, the dihedral angle between the two coordination planes defined by two groups of Cl—Rh—Cl of the four-membered 'RhClRhCl' ring is 173.9(4)°, which is the maximum value among the three μ-chloro-bridged rhodium(I) dimers that we compare. As a consequence, [RhCl{(*M*,*S*,*S*)-*p*-Tol-6F-BIPHESO}]$_2$ (**C1**) possesses the largest intermetallic separation [3.5577(7) Å]. Finally, another expected outcome of the sulfoxide moiety binding to the metal through its lone electron pair at sulfur is the fact that the S=O / S-O bond length is shortened [going from 1.494(2) (av) Å in ligand **3** to 1.476(4) (av) Å in **C1**].

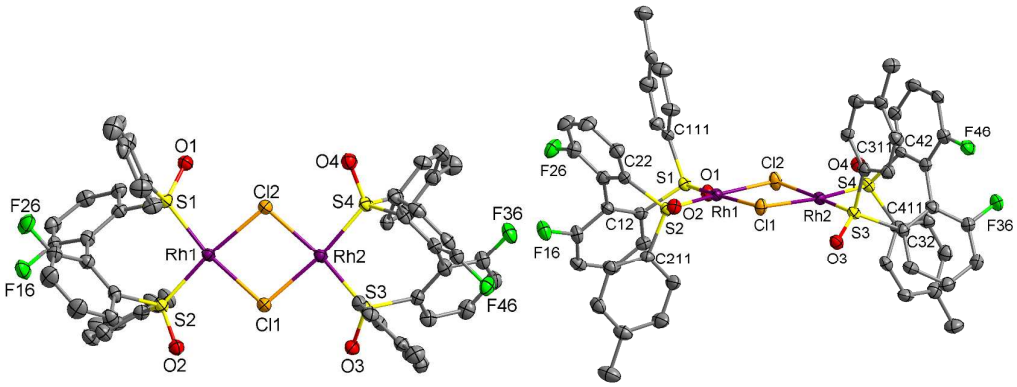


Figure 5. Two views of the molecular structure of [RhCl{(*M*,*S*,*S*)-*p*-Tol-6F-BIPHESO}]$_2$ (**C1**) (50% probability ellipsoids; hydrogen atoms omitted for clarity). Selected bond lengths (Å) and angles (deg): Rh1-Cl1, 2.3757(13), Rh1-Cl2, 2.3625(14); Rh1-S1, 2.1833(13), Rh1-S2, 2.1926(14); S1-O1, 1.481(4), S2-O2, 1.471(4); S1-Rh1-S2, 99.15(5); Cl1-Rh1-S2, 90.58(5); Cl2-Rh1-S2, 172.83(5); Cl1-Rh1-S1, 169.87(5); Cl2-Rh1-S1, 88.00(5); Cl1-Rh1- Cl2, 82.25(5). Rh(2)-S(4) 2.1822(14); Rh(2)-S(3) 2.1928(13); Rh(2)-Cl(2) 2.3505(13); Rh(2)-Cl(1) 2.3782(14); S(4)-Rh(2)-S(3) 98.43(5); S(4)-Rh(2)-Cl(2) 89.22(5); S(3)-Rh(2)Cl(2)171.81(5);S(4)-Rh(2)-Cl(1)171.23(5); S(3)-Rh(2)-Cl(1); 89.77(5); Cl(2)Rh(2)Cl(1) 82.45(5)

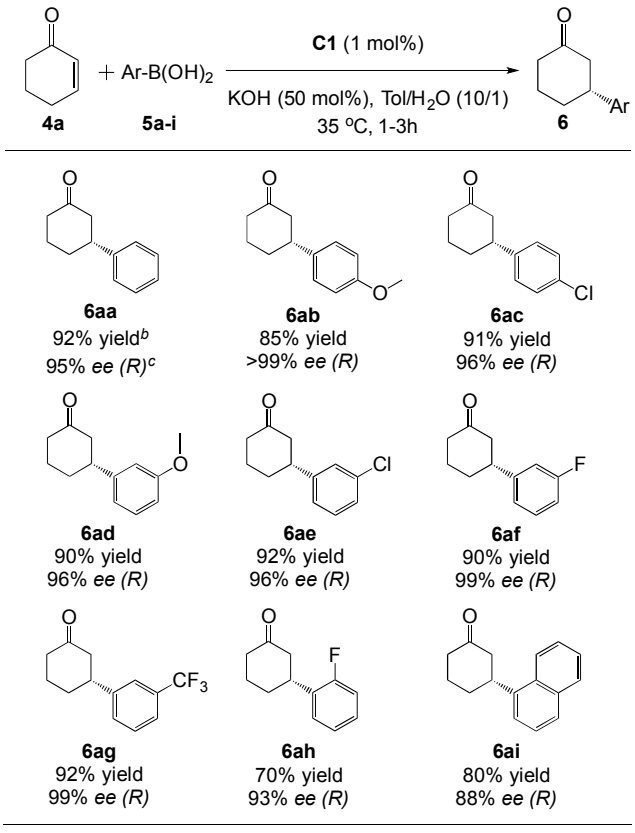
Bond lengths/angles	**C1**	[RhCl(*p*-Tol-BINASO)]$_2$[4a]	[RhCl(*p*-Tol-Me-BIPHESO)]$_2$[4b]	[RhCl(BIPHEMP)]$_2$[4b]
Rh-S/P	2.188(1) Å(av)	2.192(1) Å(av)	2.196(1) Å(av)	2.198(1) Å(av)
Rh-Cl	2.366(1) Å(av)	2.370(1) Å(av)	2.384(1) Å(av)	2.406(1) Å(av)
$C_{backbone}$-S/P [#]	1.807(6) Å(av)	1.804(7) Å(av)	1.801(4) Å(av)	1.854(6) Å(av)
Rh.....Rh	3.5577(7) Å	3.0193(5) Å	3.1993(3) Å	3.3526(7) Å
S/P-Rh-S/P	98.79(5)°	98.14(4)°	98.00(3)°	91.61(6)°
Dihedral angle (backbone)	68.3(7)°	74.1(2)°	75.6(1)°	73.9(1)°

[#] $C_{backbone}$ = C_{12} / C_{22} and C_{32}/C_{42}

Table 1. Structural comparison of **C1** with μ^2-Cl bridged dimeric disulfoxide- and diphosphine-rhodium complexes.

With the two Rh complexes **C1** and **C2** at hand, we proceeded to evaluating their enantioinduction abilities as catalyst precursors in the rhodium-catalyzed carbon-carbon bond-forming addition reactions. We first turned our attention to the 1,4-addition of arylboronic acids to the α,β-unsaturated cyclic enone 2-cyclohexen-1-one. As is shown in **Table 2**, experiments were carried out in a mixture of toluene/water/KOH using our chloro-bridged precatalyst **C1**, following the procedure established by our group in 2008,[4a] but with using a slightly lower reaction temperature of 35 °C. To our delight, all catalytic runs showed excellent reactivity and gave high isolated yields of product with typical reaction runs lasting 1.5 h. Moreover, the enantioselectivities were excellent throughout, underlining the usefulness of the new chiral disulfoxide ligand (*M*,*S*,*S*)-**3** in this reaction. The brief survey employing electron-donating and electron-withdrawing boronic acids highlighted the fact that the catalytic system is relatively insensitive to the electronic nature of the nucleophile. Furthermore, *para*-, *meta*- as well as *ortho*-substituted arylboronic acids are tolerated and give similarly high yields and enantioselectivities. Overall, the catalytic results recorded in this first assessment of (*M*,*S*,*S*)-(**3**) were very encouraging and are

comparable to those obtained with the 'classical' disulfoxide ligand *p*-Tol-BINASO.[4a]

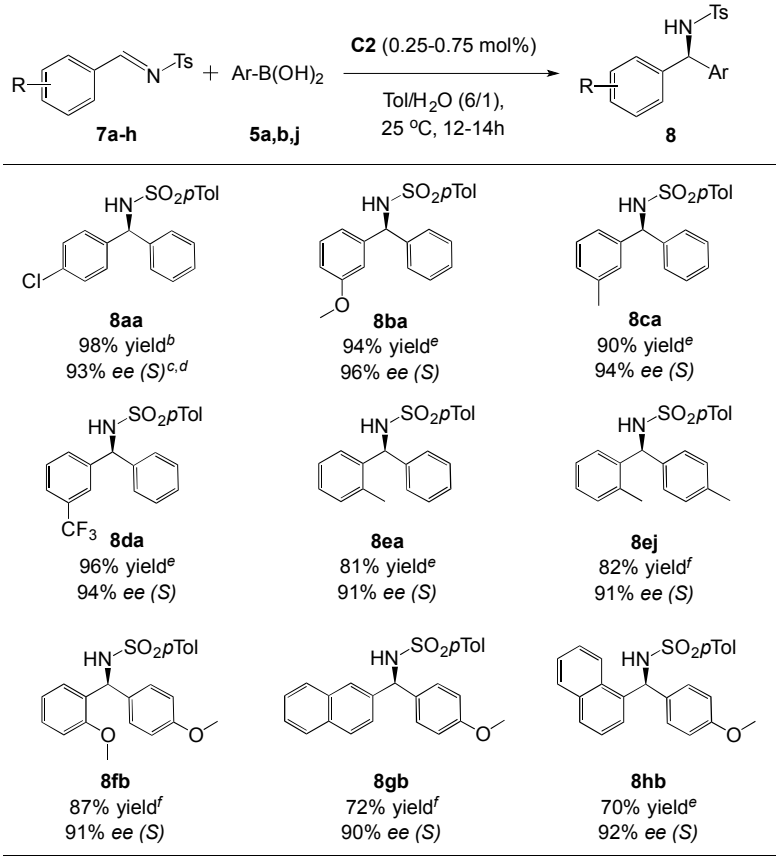


[a] Reaction conditions: A mixture of enone (0.80 mmol), boronic acid (0.88 mmol), KOH (0.4 mmol) and **C1** (1 mol%) was stirred in toluene (1.6 mL) and H_2O (0.2 mL) at 35 °C for 1-3 h. [b] Isolated yields after column chromatography. [c] Determined by HPLC analysis; absolute stereochemistry assigned by comparing with reported results.

Table 2. Precatalyst **C1** for the 1,4-additon reactions to 2-cyclohexen-1-one.[a]

With these first positive results on the catalytic assessment of (*M*,*S*,*S*)-(**3**) in hand, we moved on to study the rhodium-catalyzed arylation of *N*-tosylarylimines with aryl boronic acids.[16] Here, the development of chiral disulfoxide ligands is still in its infancy with the only report containing such a ligand system having been recently published by our group.[16d] The OH-bridged rhodium complex **C2** was therefore tested in this reaction with results shown in **Table 3**. Here again and using extremely simple reaction conditions with low catalyst loadings of **C2**, high

reactivity at room temperature gave excellent yields (up to 98%) and high optical purities (> 90% *ee*) of the products. While the list of tested substrates is not exhaustive, the substitution pattern of the imine electrophile was rather systematically varied, pointing towards a catalyst system that can accommodate a wide range of both different electrophiles and nucleophiles.



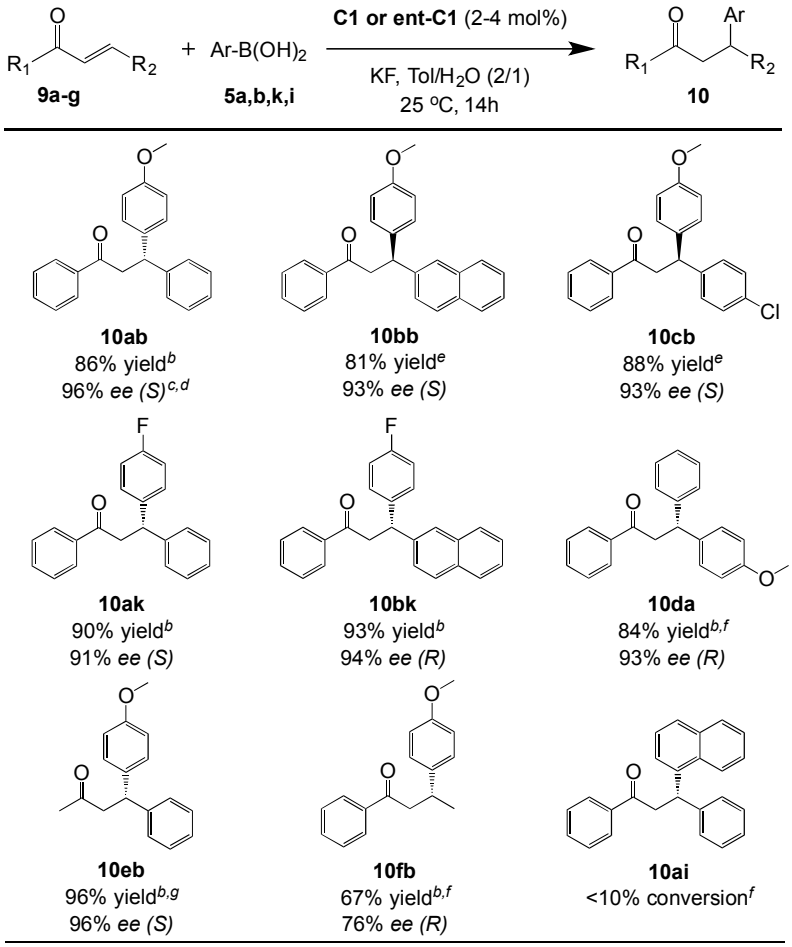
[a] Reaction conditions: A mixture of imine (0.45 mmol), boronic acid (0.90 mmol), and **C2** was stirred in toluene (6.0 mL) and H_2O (1.0 mL) at 25 °C for 12-14 h. [b] Isolated yields after column chromatography. [c] Determined by HPLC analysis; absolute stereochemistry assigned by comparison with reported results. [d] 0.75 mol% **C2** was used. [e] 0.5 mol% **C2** was used. [f] 0.25 mol% **C2** was used.

Table 3. 1,2-addition reactions of arylboronic acids to imines catalyzed by precatalyst **C2**.[a]

As a last application of this new catalyst/chiral ligand system, we finally tackled the problem that we had encountered earlier with our atropisomeric backbone-type chiral disulfoxides. This pertains to their apparent inability to be used

efficiently in the rhodium-catalyzed 1,4-addition of arylboronic acids to chalcone-type, open chain α,β-unsaturated carbonyl substrates.[4b] It should be pointed out that such asymmetric additions of arylboronic acids to chalcones are overall far less developed than normal 1,4-addition reactions and reported methods generally provide lower enantioselectivities,[17] although creating stereocenters that incorporate the diarylmethine motif through this reaction would potentially provide an easy entry into this class of compounds, which occurs in many pharmaceuticals and natural products.[18] The results that we have now obtained using our new catalyst **C1** are shown in **Table 4**. While the reactivity was indeed lower than for the cyclic α,β-unsaturated carbonyl compound shown in **Table 2**, increasing the catalyst loading of **C1** to 2-4 mol% gave high yields and excellent enantioselectivities for the addition of arylboronic acids to these chalcone-type substrates at room temperature. It should be noted that for these substrates, we also needed to confirm the absolute stereochemistry, as there is some uncertainty over it in the literature.[19] We did so by crystallizing product **10ab** from a cold pentane solution and subjecting it to an X-ray crystallographic analysis that confirmed the proposed absolute stereochemistry (*S*). While the selectivities recorded with our catalyst are of the highest reported, there still seem to be limitations as to what catalyst **C1** can do. For example, there is a clear dependence on the conjugation pattern of the chalcone motif. When the R_1 group was changed to a methyl group instead of a phenyl, reactivity and enantioselectivity remained excellent, whereas when omitting the aryl group that is conjugated to the olefinic bond (R_2), both the yield as well as the optical purity of the product dropped rather significantly (**10fb**, 67% yield, 76% *ee*). Another limitation that remains in these conjugate addition

reactions to chalcone-type substrates is the inability of **C1** (or of any of the previously reported catalyst systems) to add sterically demanding aryl boronic acids to them (**10ai**, last entry in **Table 4**).[20] Overall though, the new disulfoxide ligand (*M*,*S*,*S*)-**3**, which combines both a less sterically hindered as well as a modified, electron-poor backbone, generates a catalyst system that expands the reactivity profile of this disulfoxide ligand family and as such further underlines the validity of the overall design of this type of chiral disulfoxide ligands.



[a] Reaction conditions: A mixture of enone (0.10 mmol), boronic acid (0.15 mmol), KF (0.40 mmol) and precatalyst (**C1** or **ent-C1**, 2 mol %) was stirred in toluene (1.0 mL) and H_2O (0.5 mL) at 25 °C for 14 h. [b] **ent-C1;** isolated yields after column chromatography. [c] Determined by HPLC analysis. [d] Absolute stereochemistry assigned by comparison with reported results. [e] **C1;** isolated yields after column chromatography. [f] 4 mol % **ent-C1** was used. [g] 3 mol % **ent-C1** was used.

Table 4. Representative examples of 1,4-addition reactions to chalcones using precatalyst **C1**/**ent-C1**.

3. Conclusion

In summary, we have reported the straightforward and inexpensive synthesis of a new type of C_2-symmetric chiral disulfoxide ligand bearing an electron-deficient atropisomeric backbone. One of the diastereomers of the ligand [(*M*,*S*,*S*)-**3**] was used to synthesize both chloro- and hydroxo-bridged dimeric rhodium catalyst precursors **C1** and **C2** and both the diastereomers of the ligand [(*M*,*S*,*S*)-**3** and (*P*,*S*,*S*)-**3**] and the dimeric, μ-chloro-bridged rhodium complex **C1** were analyzed by X-ray diffraction studies. Unfortunately, even the very flexible atropisomeric backbone of this new ligand did not permit efficient coordination of the (*P*,*S*,*S*)-**3** stereoisomer to the rhodium metal center.

The two well-defined rhodium complexes with the (*M*,*S*,*S*)-**3** ligand were then tested as catalysts in various addition reactions of arylboronic acids to different kinds of electrophilic acceptors. The μ-chloro-bridged rhodium complex **C1** was shown to be highly efficient for the 1,4-addition of a variety of representative arylboronic acids to the prototypical cyclic enone 2-cyclohexen-1-one, while the μ-hydroxo-bridged rhodium complex **C2** was successfully utilized in 1,2-addition to *N*-tosylarylimines under equally simple and mild reaction conditions. Results are overall very similar to using our previously reported atropisomeric disulfoxide ligands, meaning that they compare very favorably to other ligand classes that have been developed for these reactions.

Most importantly, the reactivity seen for precatalyst **C1** in the addition reaction of arylboronic acids to chalcone-type substrates expands the utility of these atropisomeric chiral disulfoxide ligands to a new class of reactions, that

incidentally represents one of the substrate types where this asymmetric addition reactions does not seem to perform well with other ligand families.[17a] Taken together with the fact that all of the reactions reported here can be run under very mild conditions, the new (*M*,*S*,*S*)-**3** ligand represents one of the most powerful single ligands for rhodium-catalyzed addition reactions. As outlined elsewhere,[4d,21] the versatility of this particular type of chiral disulfoxide ligands seems to originate from the appropriate synergy between classical steric and unique electrostatic effects, enforcing high differentiation between prochiral faces of a wide array of substrates. Overall, further studies on more electron-deficient and / or less sterically demanding variations of our disulfoxide ligand family seem warranted.

4. Experimental Section

4.1. General experimental methods

All reactions were carried out using standard Schlenk lines or gloveboxes (Innovative Technology) under a nitrogen (Schlenk lines) or argon (gloveboxes) atmosphere. $[RhCl(C_2H_4)_2]_2$,[22] chalcones,[17] and imines,[23] were prepared according to literature procedures. All other chemicals were purchased from commercial suppliers and used as received. Solvents were purged with argon and passed through alumina columns in a solvent purification system (Innovative Technology) or distilled under nitrogen from appropriate drying agents and kept in gloveboxes over activated molecular sieves of appropriate size. Solvents for NMR spectroscopy of metal complexes were degassed with nitrogen, dried over molecular sieves and stored in gloveboxes. TLC analysis was performed using Merck silica gel 60 F_{254} aluminum-backed silica plates. Column

chromatography was conducted using Silicycle or Davisil silica gel (40-63 μm). Optical rotations were determined using AUTOPOL I, KRÜSS P8000 or KRÜSS P1000 polarimeters. Enantiomeric excess values were obtained by HPLC analysis with a JASCO Chrompass system using the appropriate Daicel columns. NMR spectra were recorded on Bruker Avance IIIHD 500 MHz or 600 MHz NMR, Varian INOVA 300 MHz or Varian 400 MHz NMR spectrometers. Chemical shifts are given in ppm and the spectra were calibrated to the residual ^{1}H and ^{13}C signals of the solvent or 100% CF_3COOH (for ^{19}F NMR spectra). Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). High-resolution mass spectra (HRMS) were performed on a Waters LCT Premier XE mass spectrometer or a Waters GCT Premier mass spectrometer (TOF) or a Waters LCT Premier XE instrument (TOF). X-ray crystallography was performed on an Oxford Diffraction Gemini diffractometer fitted with Mo or Cu Kα radiation. Elemental analyses were performed by the Elemental Analysis Service at London Metropolitan University, UK. All catalytic reactions were carried out in duplicates.

4.2. Synthesis of ligand and metal complexes

*4.2.1. Synthesis of rac-2,2'-dibromo-6,6'-difluorobiphenyl (rac-**2**; CAS registry number: 1316276-94-4):*[14]

Diisopropylamine (14 mL, 0.098 mol) was added to a Schlenk flask containing a solution of *n*-butyllithium (38 mL, 0.098 mol, 2.54 M in hexane) in THF (150 mL) that was cooled to -78 °C with an acetone / dry ice bath. The solution was stirred for 1 hour reaching -20 °C. The solution was then cooled down again to -78 °C and 1-bromo-3-fluorobenzene (10 mL, 0.089 mol) in THF (90 mL) was added

slowly via a dropping funnel. The solution was left stirring at -78 °C for 2 hours. Keeping the temperature at -78 °C, anhydrous CuBr (6.42 g, 0.045 mol) and LiCl (2.28 g, 0.054 mol) were added to the solution which was stirred for another 2 hours at -78°C. Finally, benzoquinone (14.51 g, 0.134 mol) was added, the solution was stirred for another hour at -78°C before removing the acetone/dry ice bath and letting the solution warm slowly to room temperature. Subsequently, the reaction was quenched and filtered through a silica pad. The filtrate was dried with $MgSO_4$ and the solvent removed by rotary evaporation. The residue was chromatographed on silica gel with hexane / CH_2Cl_2 (8:1) to afford the final product as a white crystalline material after drying under vacuum (13.70 g, 0.039 mol, 88% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (d, *J* = 7.1 Hz, 2H), 7.32 (m, 2H), 7.16 (t, *J* = 8.5 Hz, 2H).

*4.2.2. Synthesis of p-Tol-6F-BIPHESO (**3**)*

In a 50 mL Schlenk flask was added *rac-2,2'-dibromo-6,6'-difluorobiphenyl* (**2**, 347.9 mg, 1.0 mmol) and THF (4.0 mL). The solution was cooled to -50 °C and *n*-BuLi (0.88 mL, 2.2 mmol, 2.5M in hexane) was added dropwise via syringe. The resulting green-yellow suspension was further stirred for 45 minutes at -50 °C and then cooled to -78 °C. Under stirring, (1*R*,2*S*,5*R*)-(-)-menthyl-(*S*)-*p*-Tol-sulfinate (647.8 mg, 2.2 mmol) in 10 mL THF was added dropwise (syringe). The dark-grey suspension was stirred and allowed to slowly warm to room temperature. The reaction was then quenched by addition of an aqueous NH_4Cl solution (10 mL, 1 M) and the water phase was extracted with Et_2O (3 times 10 mL) and THF (3 times 5 mL). The combined organic phase was dried with $MgSO_4$ and the solvent was then removed by rotary evaporation. The residue was

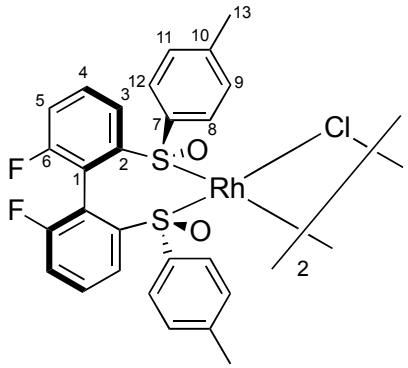
chromatographed on silica gel with CH_2Cl_2 / EtOAc (2:1) to afford the two diastereomers (*P,S,S*)- and (*M,S,S*)-*p*-Tol-6F-BIPHESO (**3**, 291.0 mg, 0.62 mmol, 62% combined yield) as white solids.[24]

(P,S,S)-p-Tol-6F-BIPHESO [(*P,S,S*)-**3**, 145.1 mg, 0.31 mmol, 31% yield, first diastereomer eluted from flash chromatography]: ^{1}H NMR (500 MHz, $CDCl_3$); δ 7.60–7.56 (td, *J* = 8.0, 5.0 Hz, 2H), 7.45 – 7.42 (m, 2H), 7.31 (t, *J* = 8.4 Hz, 2H), 7.14 (t, *J* = 2.0 Hz, 8H), 2.37 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$); δ 160.0 (d, *J* = 253.1 Hz), 146.8, 141.8, 139.5, 132.0 (d, *J* = 8.4 Hz), 130.0, 125.9, 122.7, 119.2 (d, *J* = 17.3 Hz), 119.0 (d, *J* = 22.4 Hz), 21.6. ^{19}F NMR (470 MHz, $CDCl_3$); δ -108.71. $[\alpha]_D^{20}$ = +232.75 (*c* 0.80, $CDCl_3$). M.p. 226-228 °C. Elemental analysis: Calcd for $C_{26}H_{20}F_2O_2S_2$: C, 66.93; H, 4.32; Found: 66.79; H, 4.26. A concentrated solution of (*P,S,S*)-**3** in CH_2Cl_2 layered with a mixture of hexane / EtOAc (3:1) afforded colorless crystals of (*P,S,S*)-**3** suitable for an X-ray structure analysis.

(M,S,S)-p-Tol-6F-BIPHESO [(*M,S,S*)-**3**, 146.0 mg, 0.31 mmol, 31% yield, second diastereomer eluted from flash chromatography]:, ^{1}H NMR (400 MHz, $CDCl_3$); δ 8.16 (d, *J* = 7.1 Hz, 2H), 7.69 (m, 2H), 7.04 (d, *J* = 8.3 Hz, 4H), 7.02 – 6.84 (m, 6H), 2.30 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$); δ 159.9 (d, *J* = 250.7 Hz), 146.8, 142.7, 140.7, 131.9 (d, *J* = 5.9 Hz), 129.9, 126.3, 119.9, 117.8 (d, *J* = 22.3 Hz), 115.9 (d, *J* = 20.1 Hz), 21.6. ^{19}F NMR (470 MHz, $CDCl_3$); δ -112.80. $[\alpha]_D^{20}$ = -238.62 (*c* 0.59, $CDCl_3$). M.p. 240-242 °C. Elemental analysis: Calcd for $C_{26}H_{20}F_2O_2S_2$: C, 66.93; H, 4.32; Found: 66.97; H, 4.40. A concentrated solution of (*M,S,S*)-**3** in CH_2Cl_2 layered with a mixture of hexane / EtOAc (3:1) afforded colorless crystals suitable for an X-ray structure analysis.

*4.2.3. Preparation of [RhCl{(M,S,S)-p-Tol-6F-BIPHESO}]$_2$ (**C1**)*

Inside the glovebox, a solution of of (*M,S,S*)-*p*-Tol-6F-BIPHESO [(*M,S,S*)-**3**, 368.2 mg, 0.79 mmol] in CH_2Cl_2 (50 mL) was added to a solution of $[Rh(C_2H_4)_2Cl]_2$ (149.0 mg, 0.38 mmol) in CH_2Cl_2 (48 mL). The mixture was stirred for 15 hours at room temperature, keeping the stopcock valve slightly open to release ethylene. The reddish solution was then filtered through Celite® and washed with additional CH_2Cl_2. The solution was concentrated to 1 mL. Pentane (15 mL) was added drop by drop to the stirred CH_2Cl_2 solution of **C1** in order to precipitate the product, which was then dried under vacuum to afford the corresponding complex as an orange-red, finely divided powder (437.7 mg, 0.36 mmol, 94% yield). ^{13}C DEPT-135, ^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC measurements were performed to assign all protons and carbons. X-ray quality crystals were obtained by using the following method: Inside the glovebox, complex **C1** (11 mg) was dissolved in CH_2Cl_2 (0.5 mL) and the solution was placed in an NMR tube. Diethyl ether was carefully layered on top of it (ca. 2 mL), the NMR tube was fitted with a cap and placed inside a freezer (-30 °C) for 2 days, affording platelike orange crystals of **C1**.[24]



^{1}H NMR (500 MHz, CD_2Cl_2); δ 8.07 (d, *J* = 7.9 Hz, 4H, 3-H), 7.98 (d, *J* = 7.9 Hz, 8H, 12,8-H), 7.51 (td, *J* = 8.1, 4.4 Hz, 4H, 4-H), 7.07 (d, *J* = 8.1 Hz, 8H, 11,9-H), 6.78 (t, *J* = 7.9 Hz, 4H, 5-H), 2.35 (s, 12H, 13-H). ^{13}C NMR (126 MHz, CD_2Cl_2); δ 158.8 (d, *J* = 128.5 Hz, C-6), 147.5 (C-2), 143.7 (C-7), 141.0 (C-10), 131.7 (C-4), 129.8 (C-9,11), 128.3 (C-8,12), 121.9 (C-3), 118.3 (d, *J* = 22.4 Hz, C-5), 114.6 (d, *J* = 19.4 Hz, C-1), 21.6 (C-13). ^{19}F

NMR (282 MHz, CD_2Cl_2); δ -110.90. $[\alpha]_D^{20}$ = -554.5 (*c* 0.33, CD_2Cl_2). Elemental analysis: Calcd for $C_{52}H_{40}Cl_2F_4O_4Rh_2S_4$: C, 51.62; H, 3.33; Found: C, 51.53; H, 3.28.

*4.2.4. Preparation of [Rh(OH){(M,S,S)-p-Tol-6F-BIPHESO}]$_2$ (**C2**)*

A solution of [RhCl{(*M*,*S*,*S*)-*p*-Tol-6F-BIPHESO}]$_2$ (**C1**) (120.9 mg, 0.1 mmol) in acetone (10 mL) was prepared in a Schlenk tube inside the glovebox. The Schlenk tube was taken outside, connected to a Schlenk line and aqueous KOH (0.5 mL, 2.5 M, degassed) was added under stirring. The solution was stirred at room temperature for 1.5 hours and then the solvent was removed under vacuum. Dichloromethane (10 mL) was added to the crude solid in the Schlenk flask, and the organic layer was washed with degassed water (3 x 5 mL) that was decanted off. Anhydrous Na_2SO_4 was added to the flask and the organic layer was then concentrated to a small volume (~1.0 mL). At this point, the Schlenk flask was reintroduced into the glove box and the content was filtered through Celite® and the cake was washed with an additional amount of CH_2Cl_2 (ca. 4 mL). All solvent was removed under vacuum. The residue was redissolved in a minimum amount of CH_2Cl_2 (0.5 mL) and pentane (10 mL) was added drop by drop to precipitate the product. The supernatant solution was subsequently decanted and the residual solid was dried under vacuum for 5 hours to afford the corresponding complex **C2** as an orange-yellow, finely divided powder (82.3 mg, 0.07 mmol, 70% yield). ^{1}H NMR (600 MHz, CD_2Cl_2); δ 8.09 (d, *J* = 5.6 Hz, 8H), 7.90 (d, *J* = 7.9 Hz, 4H), 7.50 – 7.47 (m, 4H), 7.07 (d, *J* = 8.0 Hz, 8H), 6.76 (t, *J* = 7.7 Hz, 4H), 2.39 (s, 12H), 0.36 (s, 2H). ^{13}C NMR (151 MHz, CD_2Cl_2); δ 159.0 (d, *J* = 253.3 Hz), 148.0, 143.5, 142.1, 131.3, 129.6, 128.2, 121.0, 117.8 (d, *J* = 22.2 Hz), 114.4

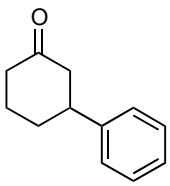
(d, *J* = 18.9 Hz), 21.6. ^{19}F NMR (564 MHz, CD_2Cl_2); δ -110.61. Elemental analysis: Calcd for $C_{52}H_{42}F_4O_6Rh_2S_4$: C, 53.25; H, 3.61; Found: C, 53.18; H, 3.51.

4.3. Typical procedure for the 1,4-addition to cyclic enones and characterization of products

In a 20 mL vial, inside a glove box, was added α,β-unsaturated substrate (0.80 mmol) and precatalyst **C1** (9.7 mg, 1.0 mol%) followed by the addition of toluene (1.6 mL) and arylboronic acid (0.88 mmol). The vial was fitted with a magnetic stirbar, closed with a teflon cap, and taken out of the glovebox. Degassed KOH (0.16 mL, 2.5 M in Milli-Q H_2O, 0.40 mmol) was then added via syringe. The reaction was stirred at 35°C for 1-3 hours. After this, the solvent was removed under vacuum. The residue was dissolved in a minimum amount of CH_2Cl_2 and charged on top of a silica gel column and purified by column chromatography (hexane/ethyl acetate or diethyl ether as eluents). Products were then dried under vacuum and analyzed.

All reactions were performed in duplicate. Racemic products were obtained in a similar way but using $[Rh(COD)Cl]_2$ (5 mol%) instead of precatalyst **C1**. All reactions were performed in duplicate.

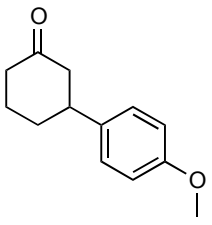
*4.3.1. (R)-3-phenylcyclohexan-1-one (**6aa** CAS registry number: 34993-51-6)*



Enone **4a** (76.9 mg, 0.8 mmol); boronic acid **5a** (107.3 mg, 0.88 mmol); **C1** (9.7 mg, 0.008 mmol, 1.0 mol%). Product **6aa** obtained as a transparent oil (128.8 mg, 0.74 mmol, 92%) yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.32 (m, 2H), 7.25 – 7.22 (m, 3H), 3.02 (t, *J* =

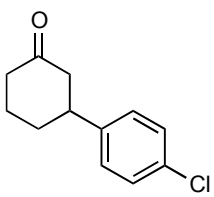
11.8 Hz, 1H), 2.61– 2.38 (m, 4H), 2.18 – 2.07 (m, 2H), 1.88 – 1.79 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.2, 144.5, 128.8, 126.84, 126.72, 49.1, 44.9, 41.3, 32.9, 25.7. HRMS (ESI-TOF) m/z: [M + Na]+ Calcd. for $C_{12}H_{14}ONa$: 197.0942; Found 197.0947. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (98:2); flow = 0.5 mL/min; detected at 220 nm; 95% *ee*. Retention times (first run): 23.7 min [(*S*) minor], 25.5 min [(*R*) major].[4,25]

*4.3.2. (R)-3-(4-methoxyphenyl)cyclohexan-1-one (**6ab** CAS registry number: 479586-33-9)*



Enone **4a** (76.9 mg, 0.8 mmol); boronic acid **5b** (133.7 mg, 0.88 mmol); **C1** (9.7 mg, 0.008 mmol, 1.0 mol%). Product **6ab** obtained as a white solid (138.1 mg, 0.68 mmol, 85% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), δ 3.80 (s, 3H), 2.97 (tt, *J* = 11.8, 3.9 Hz, 1H), 2.69 – 2.26 (m, 4H), 2.22 – 1.95 (m, 2H), 1.91 – 1.67 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.3, 158.4, 136.7, 127.6, 114.1, 55.4, 49.4, 44.1, 41.3, 33.2, 25.6. HPLC analysis: Daicel Chiralcel OJ-H column; hexane/2-propanol (99:1); flow = 1.0 mL/min; detected at 220 nm; >99.5% *ee*. Retention times: 37.9 min [(*S*) minor], 43.2 min [(*R*) major].[4]

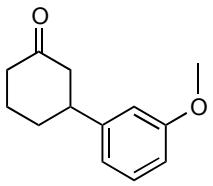
*4.3.3. (R)-3-(4-chlorophenyl)cyclohexan-1-one (**6ac** CAS registry number: 843674-22-6)*



Enone **4a** (76.9 mg, 0.8 mmol); boronic acid **5c** (137.6 mg, 0.88 mmol); **C1** (9.7 mg, 0.008 mmol, 1.0 mol%). Product **6ac**

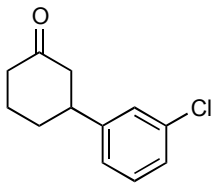
obtained as a white solid (152,2 mg, 0.73 mmol, 91% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.18 – 7.13 (m, 2H), 2.99 (dt, *J* = 11.7, 3.9 Hz, 1H), 2.57 (m, *J* = 1H), 2.53 – 2.42 (m, 2H), 2.37 (m, 1H), 2.22 – 1.99 (m, 2H), 1.91 – 1.70 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 210.6, 142.9, 132.5, 128.93, 128.06, 48.9, 44.2, 41.2, 32.8, 25.5. HPLC analysis: Daicel Chiralcel OJ-H column; hexane/2-propanol (99:1); flow = 1.0 mL/min; detected at 220 nm; 96% *ee*. Retention times: 23.9 min [(*S*) minor], 28.1 min [(*R*) major].[4]

4.3.4. (*R*)*-3-(3-methoxyphenyl)cyclohexan-1-one (**6ad** CAS registry number: 610273-85-3)*



Enone **4a** (76.9 mg, 0.8 mmol); boronic acid **5d** (133.7 mg, 0.88 mmol); **C1** (9.7 mg, 0.008 mmol, 1.0 mol%). Product **6ad** obtained as a light yellow oil (147.6 mg, 0.72 mmol, 90% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 – 7.22 (m, 2H), 6.87 – 6.70 (m, 3H), 3.81 (s, 3H), 2.98 (tt, *J* = 12.0, 3.9 Hz, 1H), 2.66 – 2.30 (m, 4H), 2.26 – 1.98 (m, 2H), 1.93 – 1.67 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.1, 160.0, 146.2, 129.8, 119.0, 112.8, 111.8, 55.3, 49.1, 44.9, 41.3, 32.8, 25.7. HPLC analysis: Daicel Chiralcel AD-H column; hexane/2-propanol (95:5); flow = 0.5 mL/min; detected at 220 nm; 96% *ee*. Retention times: 19.8 min [(*S*) minor], 21.2 min [(*R*) major].[4]

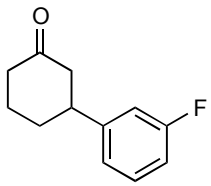
4.3.5. (*R*)*-3-(3-chlorophenyl)cyclohexan-1-one (**6ae** CAS registry number: 479639-20-8)*



Enone **4a** (76.9 mg, 0.8 mmol); boronic acid **5e** (137.6 mg, 0.88 mmol); **C1** (9.7 mg, 0.008 mmol, 1.0 mol%). Product **6ae**

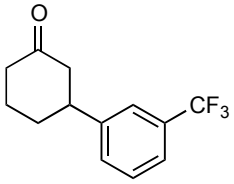
was obtained as a light yellow oil (151.7 mg, 0.73 mmol, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.18 (m, 3H), 7.09 (d, *J* = 7.5 Hz, 1H), 2.99 (tt, *J* = 11.8, 3.9 Hz, 1H), 2.58 (m, 1H), 2.54 – 2.43 (m, 2H), 2.37 (m, 1H), 2.24 – 1.99 (m, 2H), 1.93 – 1.66 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.4, 146.4, 134.6, 130.1, 127.04, 126.95, 125.0, 48.8, 44.5, 41.2, 32.7, 25.6. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (99.5:0.5); flow = 0.5 mL/min; detected at 220 nm; 96% *ee*. Retention times: 44.9 min [(*S*) minor], 50.4 min [(*R*) major].[4]

4.3.6. (*R*)*-3-(3-fluorophenyl)cyclohexan-1-one (**6af** CAS registry number: 1092695-24-3)*



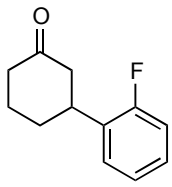
Enone **4a** (76.9 mg, 0.8 mmol); boronic acid **5f** (123.1 mg, 0.88 mmol); **C1** (9.7 mg, 0.008 mmol, 1.0 mol%). Product **6af** was obtained as a colorless oil (138.6 mg, 0.72 mmol, 90% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 1H), 6.99 (d, *J* = 7.7 Hz, 1H), 6.96 – 6.89 (m, 2H), 3.01 (tt, *J* = 11.8, 3.9 Hz, 1H), 2.59 (m, 1H), 2.55 – 2.43 (m, 2H), 2.37 (m, 1H), 2.23 – 2.01 (m, 2H), 1.91 – 1.69 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 210.6, 163.7 (d, *J* = 246.1 Hz), 147.0 (d, *J* = 7.6 Hz), 130.3 (d, *J* = 9.1 Hz), 122.4 (d, *J* = 1.5 Hz), 113.73 (d, *J* = 12.1 Hz), 113.59 (d, *J* = 12.1 Hz), 48.8, 44.5 (d, *J* = 1.5 Hz), 41.2, 32.7, 25.5. HPLC analysis: Daicel Chiralcel OJ-H column; hexane/2-propanol (99:1); flow = 0.5 mL/min; detected at 220 nm; 99% *ee*. Retention times: 31.4 min [(*R*) major], 35.1 min [(*S*) minor].[4,6k]

*4.3.7. (R)-3-(3-(trifluoromethyl)phenyl)cyclohexan-1-one (**6ag** CAS registry number: 1160606-10-9)*



Enone **4a** (76.9 mg, 0.8 mmol); boronic acid **5g** (167.1 mg, 0.88 mmol); **C1** (9.7 mg, 0.008 mmol, 1.0 mol%). Product **6ag** was obtained as a white solid (177.7 mg, 0.73 mmol, 92% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 – 7.38 (m, 4H), 3.07 (tt, *J* = 12.1, 3.9 Hz, 1H), 2.61 (m, 1H), 2.58 – 2.45 (m, 2H), 2.39 (m, 1H), 2.25 – 2.04 (m, 2H), 1.96 – 1.70 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 210.2, 145.3, 131.1 (q, *J* = 31.7 Hz), 130.20, 129.3, 125.1, 123.76 (q, *J* = 4.5 Hz), 123.45 (q, *J* = 4.5 Hz), 48.8, 44.6, 41.2, 32.7, 25.6. HRMS (ESI$^-$-TOF) m/z: [M - H]- Calcd. for $C_{13}H_{12}OF_3$: 241.0840; Found 241.0845. HPLC analysis: Daicel Chiralcel OJ-H column; hexane/2-propanol (99.5:0.5); flow = 1.0 mL/min; detected at 220 nm; 99% *ee*. Retention times: 20.1 min [(*R*) major], 23.4 min [(*S*)minor].[4,26]

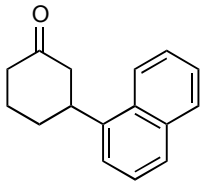
*4.3.8. (R)-3-(2-fluorophenyl)cyclohexan-1-one (**6ah** CAS registry number: 141632-32-8)*



Enone **4a** (76.9 mg, 0.8 mmol); boronic acid **5h** (167.9 mg, 1.2 mmol); **C1** (9.7, 0.008 mmol, 1.0 mol%). Product **6ah** was obtained as a colorless oil (108.1 mg, 0.56 mmol, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 7.8 Hz, 2H), 7.15 – 7.07 (m, 1H), 7.02 (d, *J* = 8.1 Hz, 1H), 3.31 (td, *J* = 8.4, 3.6 Hz, 1H), 2.57 (d, *J* = 8.6 Hz, 2H), 2.52 – 2.27 (m, 2H), 2.22 – 1.97 (m, 2H), 1.98 – 1.68 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.5, 160.6 (d, *J* = 245.7 Hz), 131.1 (d, *J* = 13.9 Hz), 128.2 (d, *J* = 8.8 Hz), 127.7 (d, *J* = 5.0 Hz), 124.4 (d, *J* = 3.8 Hz), 115.7 (d, *J* = 22.7 Hz), 47.3, 41.3, 38.2 (d, *J* = 1.3 Hz),

31.3, 25.5. HPLC analysis: Daicel Chiralcel AD-H column; hexane/2-propanol (99.5:0.5); flow = 0.5 mL/min; detected at 220 nm; 93% *ee* (only one run was performed). Retention times: 38.1 min [(*S*) minor], 44.7 min [(*R*) major].[4]

*4.3.9. (R)-3-(naphthalen-1-yl)cyclohexan-1-one (**6ai** CAS registry number: 479586-35-1)*



Enone **4a** (76.9 mg, 0.8 mmol); boronic acid **5i** (206.4 mg, 0.12 mmol); **C1** (0.008 mmol, 1.0 mol%). Product **6ai** was obtained as a white solid (143.7 mg, 0.64 mmol, 80% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.60 – 7.44 (m, 3H), 7.41 (d, *J* = 7.2 Hz, 1H), 3.86 (tt, *J* = 11.7, 3.7 Hz, 1H), 2.87 – 2.37 (m, 4H), 2.31 – 2.13 (m, 2H), 2.10 – 1.82 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.3, 140.2, 134.1, 131.0, 129.2, 127.4, 126.3, 125.75, 125.65, 122.82, 122.55, 48.7, 41.6, 39.5, 32.4, 25.7. HRMS (ESI-TOF) m/z: [M + Na]+ Calcd. for $C_{16}H_{16}ONa$: 247.1099; Found 247.1092. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (95:5); flow = 0.5 mL/min; detected at 220 nm; 88% *ee*. Retention times: 41.5 min [(*R*) major], 63.6 min [(*S*) minor].[4]

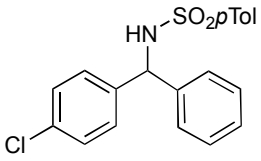
4.4. Typical procedure for the 1, 2-addition to imines and analytical data of products

A stock solution of **C2** (5.2 mg, 0.0045 mmol) was stirred in toluene (4.0 mL) inside the glovebox in a screwcap vial. During the mixing time, a septum-capped reaction vial was charged with imine substrate **7** (0.45 mmol) and the corresponding arylboronic acid **5** (0.90 mmol). To this vial was added the

required amount of the stock solution of **C2** [2.0 mL for 0.5 mol% runs]. Then more toluene was added to make up for a total volume of 6.0 mL. After this, a stirbar was added, the vial was sealed and was brought out from the glovebox. H_2O (1 mL, degassed, Milli-Q) was then added with a syringe and the mixture was stirred for 12 - 14 hours at room temperature. After this, the solvent was removed under vacuum. The residue was dissolved in a minimum amount of CH_2Cl_2, charged on top of a silica gel column and purified by column chromatography (hexane/EtOAc or diethyl ether as eluent). The products where then dried under vacuum and analyzed.

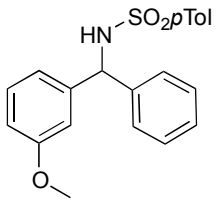
All reactions were performed in duplicate. Racemic products were obtained in a similar way but using $[Rh(COD)Cl]_2$ (5 mol%) instead of precatalyst **C2**.

*4.4.1. (S)-N-((4-chlorophenyl)(phenyl)methyl)-4-methylbenzenesulfonamide (**8aa** CAS registry number: 796966-17-7)*



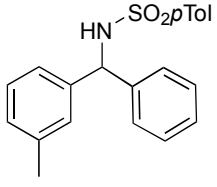
Imine **7a** (132.2 mg, 0.45 mmol); boronic acid **5a** (109.7 mg, 0.90 mmol); **C2** (3.9 mg, 0.0038 mmol, 0.75 mol%). Product **8aa** obtained as a white solid (164.1 mg, 0.44 mmol, 98% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.3 Hz, 2H), 7.22 – 7.20 (m, 3H), 7.19 – 7.10 (m, 4H), 7.05 (d, *J* = 9.3 Hz, 4H), 5.53 (d, *J* = 7.2 Hz, 1H), 5.25 (d, *J* = 7.2 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.6, 140.2, 139.1, 137.3, 133.6, 129.6, 128.9, 128.9, 128.8, 128.0, 127.39, 127.37, 127.30, 60.9, 21.6. HRMS (ESI$^-$-TOF) m/z: [M - H]- Calcd. for $C_{20}H_{17}NO_2S^{37}Cl$: 372.0639; Found 372.0654. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (70:30); flow = 0.7 mL/min; detected at 220 nm; 93% *ee*. Retention times: 8.2 min [(*S*) major], 9.8 min [(*R*) minor].[16,27]

*4.4.2. (S)-N-((3-methoxyphenyl)(phenyl)methyl)-4-methylbenzenesulfonamide (**8ba** CAS registry number: 898269-07-3)*



Imine **7b** (130.2 mg, 0.45 mmol); boronic acid **5a** (109.7 mg, 0.90 mmol); **C2** (2.6 mg, 0.0023 mmol, 0.5 mol%). Product **8ba** obtained as a white solid (155.3 mg, 0.42 mmol, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 2H), 7.24 – 7.17 (m, 3H), 7.17 – 7.07 (m, 5H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 6.61 (t, *J* = 2.1 Hz, 1H), 5.53 (d, *J* = 7.0 Hz, 1H), 5.08 (d, *J* = 7.0 Hz, 1H), 3.69 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.8, 143.3, 142.2, 140.5, 137.5, 129.74, 129.48, 128.7, 127.76, 127.46, 127.36, 119.8, 113.22, 113.13, 61.4, 55.3, 21.6. HRMS (ESI-TOF) m/z: [M + K]+ Calcd. for $C_{21}H_{21}NO_3SK$: 406.0879; Found 406.0879. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (90:10); flow = 0.5 mL/min; detected at 220 nm; 96% *ee*. Retention times: 26.4 min [(*R*) minor], 29.2 min [(*S*) major].[16]

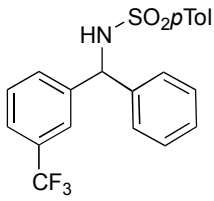
*4.4.3. (S)-4-methyl-N-(phenyl(m-tolyl)methyl)benzenesulfonamide (**8ca** CAS registry number: 765316-02-7)*



Imine **7c** (123.0 mg, 0.45 mmol); boronic acid **5a** (109.7 mg, 0.9 mmol); **C2** (2.6 mg, 0.0023 mmol, 0.5 mol%). Product **8ca** obtained as a white solid (141.9 mg, 0.41 mmol, 90% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.1 Hz, 2H), 7.22 – 7.19 (m, 3H), 7.16 – 7.10 (m, 5H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.92 – 6.79 (m, 2H), 5.53 (d, *J* = 7.0 Hz, 1H), 5.05 (d, *J* = 7.1 Hz, 1H), 2.38 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ

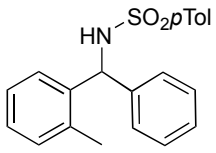
143.3, 140.73, 140.50, 138.3, 137.5, 129.4, 128.64, 128.59, 128.46, 128.17, 127.66, 127.48, 127.37, 124.6, 61.5, 21.6, 21.4. HRMS (ESI-TOF) m/z: [M + K]+ Calcd. for $C_{21}H_{21}NO_2SK$: 390.0930; Found 390.0935. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (90:10); flow = 0.5 mL/min; detected at 220 nm; 94% *ee*. Retention times: 18.6 min [(*R*) minor], 20.8 min [(*S*) major].[16,28]

*4.4.4. (S)-4-methyl-N-(phenyl(3-(trifluoromethyl)phenyl)methyl)benzenesulfonamide (**8da** CAS registry number: 1797442-85-3)*



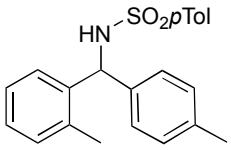
Imine **7d** (147.3 mg, 0.45 mmol); boronic acid **5a** (109.7 mg, 0.90 mmol); **C2** (2.6 mg, 0.0023 mmol, 0.5 mol%). Product **8da** obtained as a white solid (174.4 mg, 0.43 mmol, 96% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.3 Hz, 2H), 7.43 – 7.49 (m, 1H), 7.37 – 7.29 (m, 2H), 7.25 (m, 4H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.09 – 7.03 (m, 2H), 5.64 (d, *J* = 6.8 Hz, 1H), 5.09 (d, *J* = 6.8 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.8, 141.4, 139.9, 137.2, 131.02, 129.62, 129.20, 129.05, 128.3, 127.4 (d, *J* = 27.2 Hz), 124.60 (q, *J* = 4.5 Hz), 124.17 (q, *J* = 4.5 Hz), 61.1, 21.6. HRMS (ESI-TOF) m/z: [M + K]+ Calcd. for $C_{21}H_{18}NO_2SKF_3$: 444.0647; Found 444.0655. HPLC analysis: Daicel Chiralcel AS-H column; hexane/2-propanol (70:30); flow = 0.7 mL/min; detected at 220 nm; 94% *ee*. Retention times: 16.8 min [(*R*) minor], 26.6 min [(*S*) major].[16]

*4.4.5. (S)-4-methyl-N-(phenyl(o-tolyl)methyl)benzenesulfonamide (**8ea** CAS registry number: 738626-20-5)*



Imine **7e** (123.0 mg, 0.45 mmol); boronic acid **5a** (109.7 mg, 0.90 mmol); **C2** (2.6 mg, 0.0023 mmol, 0.5 mol%). Product **8ea** was obtained as a white solid (127.5 mg, 0.36 mmol, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 5.1 Hz, 3H), 7.15 – 7.00 (m, 8H), 5.81 (d, *J* = 7.2 Hz, 1H), 5.33 (d, *J* = 7.3 Hz, 1H), 2.37 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.2, 140.1, 138.4, 137.6, 135.5, 130.7, 129.4, 128.6, 127.62, 127.58, 127.57, 127.33, 127.18, 126.3, 58.2, 21.6, 19.5. HRMS (ESI-TOF) m/z: [M + K]+ Calcd. for $C_{21}H_{21}NO_2SK$: 390.0930; Found 390.0926. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (70:30); flow = 0.7 mL/min; detected at 220 nm; 91% *ee*. Retention times: 6.7 min [(*R*) minor], 7.8 min [(*S*) major].[16]

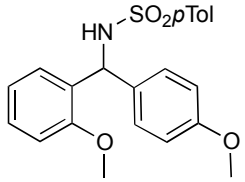
*4.4.6. (S)-4-methyl-N-(o-tolyl(p-tolyl)methyl)benzenesulfonamide (**8ej** CAS registry number: 1874150-46-5)*



Imine **7e** (123.0 mg, 0.45 mmol); boronic acid **5j** (122.3 mg, 0.90 mmol); **C2** (1.3 mg, 0.0011 mmol, 0.25 mol%). Product **8ej** obtained as a white solid (135.1 mg, 0.37 mmol, 82% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.17 – 7.08 (m, 4H), 7.05 (d, *J* = 7.5 Hz, 2H), 7.00 (d, *J* = 7.9 Hz, 2H), 6.93 (d, *J* = 8.1 Hz, 2H), 5.75 (d, *J* = 6.9 Hz, 1H), 5.05 (d, *J* = 7.0 Hz, 1H), 2.37 (s, 3H), 2.28 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.2, 138.5, 137.58, 137.44, 137.13, 135.5, 130.7, 129.39, 129.34, 127.58, 127.52, 127.24, 127.21, 126.2, 58.0, 21.6, 21.1, 19.5. HRMS (ESI-TOF) m/z: [M + K]+ Calcd. for $C_{22}H_{23}NO_2SK$: 404.1087; Found 404.1086. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol

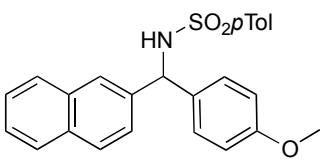
(70:30); flow = 0.7 mL/min; detected at 220 nm; 91% *ee*. Retention times: 6.5 min [(*R*) minor], 9.6 min [(*S*) major].[16]

*4.4.7. (S)-N-((2-methoxyphenyl)(4-methoxyphenyl)methyl)-4-methylbenzenesulfonamide (**8fb** CAS registry number: 940280-67-1)*



Imine **7f** (130.2 mg, 0.45 mmol); boronic acid **5b** (136.8 mg, 0.90 mmol); **C2** (1.3 mg, 0.0011 mmol, 0.25 mol%). Product **8fb** was obtained as a white solid (176.9 mg, 0.45 mmol, 99% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.18 – 7.11 (m, 1H), 7.07 (d, *J* = 8.2 Hz, 4H), 7.01 – 6.93 (m, 1H), 6.82 – 6.72 (m, 3H), 6.67 (d, *J* = 8.2 Hz, 1H), 5.71 (d, *J* = 9.0 Hz, 1H), 5.61 (d, *J* = 9.0 Hz, 1H), 3.75 (s, 3H), 3.60 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.8, 156.5, 142.8, 137.6, 132.8, 129.61, 129.14, 128.96, 128.18, 127.88, 127.1, 120.8, 113.6, 111.2, 58.7, 55.38, 55.36, 21.5. HRMS (ESI-TOF) m/z: [M + K]+ Calcd. for $C_{22}H_{23}NO_4SK$: 436.0985; Found 436.0984. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (70:30); flow = 0.7 mL/min; detected at 220 nm; 91% *ee*. Retention times: 9.4 min [(*R*) minor], 14.0 min [(*S*) major].[16]

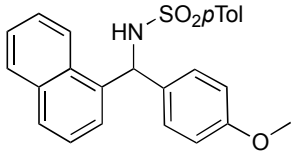
*4.4.8. (S)-N-((4-methoxyphenyl)(naphthalen-2-yl)methyl)-4-methylbenzenesulfonamide (**8gb** CAS registry number: 1874150-47-6)*



Imine **7g** (139.2 mg, 0.45 mmol); boronic acid **5b** (136.8 mg, 0.90 mmol); **C2** (1.3 mg, 0.0011 mmol, 0.25 mol%). Product **8gb** obtained as a white solid (142.4 mg, 0.32 mmol, 72% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 6.1 Hz,

1H), 7.71 – 7.61 (m, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.52 – 7.49 (m, 2H), 7.44 (d, *J* = 6.3 Hz, 1H), 7.20 – 7.02 (m, 5H), 6.74 (d, *J* = 8.7 Hz, 2H), 5.69 (d, *J* = 7.3 Hz, 1H), 5.29 (d, *J* = 7.3 Hz, 1H), 3.75 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.2, 143.3, 137.86, 137.50, 133.12, 132.74, 132.72, 129.38, 128.85, 128.51, 128.08, 127.64, 127.31, 126.33, 126.31, 126.20, 125.3, 114.1, 61.1, 55.4, 21.5. HRMS (ESI-TOF) m/z: [M + K]+ Calcd. for $C_{25}H_{23}NO_3SK$: 456.1036; Found 456.1035. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (70:30); flow = 0.7 mL/min; detected at 220 nm; 90% *ee*. Retention times: 13.4 min [(*R*) minor], 21.5 min [(*S*) major].[16,29]

*4.4.9. (S)-N-((4-methoxyphenyl)(naphthalen-1-yl)methyl)-4-methylbenzenesulfonamide (**8hb** CAS registry number: 940280-70-6)*



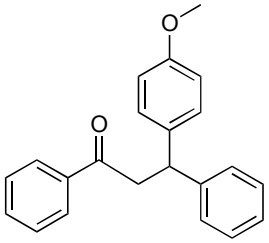
Imine **7h** (139.2 mg, 0.45 mmol); boronic acid **5b** (136.8 mg, 0.90 mmol); **C2** (2.6 mg, 0.0023 mmol, 0.5 mol%). Product **8hb** was obtained as a white foam in (138.7 mg, 0.32 mmol, 70% isolated yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 – 7.77 (m, 2H), 7.72 (m, 1H), 7.55– 7.27 (m, 6 H), 7.05 (d, *J* = 8.2 Hz, 4H), 6.72 (d, *J* = 8.8 Hz, 2H), 6.26 (d, *J* = 6.9 Hz, 1H), 5.10 (d, *J* = 6.9 Hz, 1H), 3.74 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 143.2, 137.4, 135.7, 134.1, 132.5, 130.5, 129.38, 128.96, 128.89, 128.62, 127.3, 126.6, 125.97, 125.81, 125.2, 123.6, 114.1, 58.2, 55.4, 21.6. HRMS (ESI-TOF) m/z: [M + K]+ Calcd. for $C_{25}H_{23}NO_3SK$: 456.1036; Found 456.1037. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (70:30); flow = 0.7 mL/min; detected at 220 nm; 92% *ee*. Retention times: 16.8 min [minor], 24.5 min [(*S)* major].[16,27]

4.5. Typical procedure for the 1,4-addition to open-chain enones and analytical data of products

In a 20 mL vial, inside a glove box, was added α,β-unsaturated substrate **9** (0.10 mmol) and precatalyst **C1** or **ent-C1** (2.4 mg, 2.0 mol%) followed by KF (23.2 mg, 0.40 mmol), toluene (1.0 mL) and arylboronic acid **5** (0.15 mmol). The vial was fitted with a magnetic stirbar, closed with a teflon cap, and taken out of the glovebox. H_2O (0.5 mL, degassed, Milli-Q) was then added with a syringe. The reaction was stirred at 25 °C for 14 hours. After this, the organic layer was extracted with EtOAc and then the solvent was removed under vacuum. The residue was dissolved in a minimum amount of CH_2Cl_2, charged on top of a silica gel column and purified by column chromatography (hexane/ethyl acetate or diethyl ether as eluent). Products **10** were then dried under vacuum and analyzed.

All reactions were performed in duplicate. Racemic products were obtained in a similar way but using $[Rh(COD)Cl]_2$ (5 mol%) instead of precatalyst **C1** / **ent-C1**.

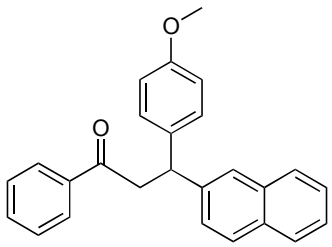
*4.5.1. (S)-3-(4-methoxyphenyl)-1,3-diphenylpropan-1-one (**10ab** CAS registry number:* 1338350-59-6*)*



Enone **9a** (20.8 mg, 0.1 mmol); boronic acid **5b** (22.8 mg, 0.15 mmol); **ent-C1** (2.4 mg, 0.002 mmol, 2 mol%). Product **10ab** was obtained as a light yellow solid in 86% yield (27.0 mg, 0.086 mmol). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.3 Hz, 2H), 7.54 (dd, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.32 – 7.12 (m, 7H), 6.81 (d, *J* = 9.0 Hz, 2H), 4.78 (t, *J* = 7.3 Hz, 1H), 3.75 (s, 3H), 3.71 (d, *J*

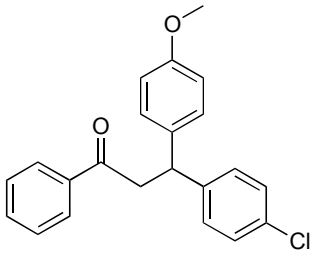
= 7.3, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.3, 158.2, 144.7, 137.2, 136.4, 133.18, 128.90, 128.72, 128.67, 128.19, 127.86, 126.4, 114.1, 55.3, 45.3, 45.1. HRMS (APCI-TOF) m/z: [M + H]+ Calcd. for $C_{22}H_{21}O$: 317.1542; Found 317.1549. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (98/2); flow = 1.0 mL/min; detected at 220 nm; 96% *ee*. Retention times: 19.5 min [(*S*) major], 22.2 min [(*R*) minor].[17,30] X-ray quality crystals were obtained from a pentane solution (ca. 0.8 mL) containing **10ab** (ca. 25 mg) left in the freezer (ca. -20°C) overnight.

*4.5.2. (S)-3-(4-methoxyphenyl)-3-(naphthalene-2-yl)-1-phenylpropan-1-one (**10bb**)*



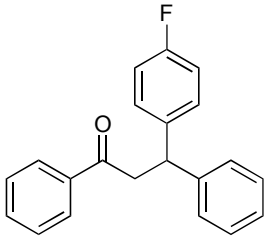
Enone **9b** (25.8 mg, 0.10 mmol); boronic acid **5b** (22.8 mg, 0.15 mmol); **C1** (2.4 mg, 0.002 mmol, 2 mol%). Product **10bb** was obtained as a light yellow oil (29.6 mg, 0.081 mmol, 81% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.2 Hz, 2H), 7.80 – 7.69 (m, 4H), 7.55 (dd, *J* = 7.4 Hz each, 1H), 7.48 – 7.36 (m, 5H), 7.23 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 4.96 (t, *J* = 7.3 Hz, 1H), 3.82 (dd, *J* = 7.1 Hz and 3.6 Hz, 2H), 3.76 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.2, 158.2, 142.1, 137.24, 136.24, 133.6, 133.2, 132.3, 129.05, 128.74, 128.38, 128.21, 127.89, 127.69, 126.88, 126.13, 125.73, 125.63, 114.1, 55.4, 45.4, 44.9. HRMS (APCI-TOF) m/z: [M + H]+ Calcd. for $C_{26}H_{23}O_2$: 367.1698; Found 367.1692. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (95:5); flow = 1.0 mL/min; detected at 220 nm; 93% *ee*. Retention times: 13.0 min [(*R*) minor], 17.4 min [(*S*) major].

*4.5.3. (S)-3-(4-chlorophenyl)-3-(4-methoxyphenyl)-1-phenylpropan-1-one (**10cb**)*



Enone **9c** (24.3 mg, 0.1 mmol); boronic acid **5b** (22.8 mg, 0.15 mmol); **C1** (2.4 mg, 0.002 mmol, 2 mol%). Product **10ab** was obtained as a white foam (30.9 mg, 0.088 mmol, 88% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93(d, *J* = 7.2 Hz, 2H), 7.56 (dd, *J* = 7.4 Hz each, 1H), 7.45 (dd, *J* = 8.0 Hz each, 2H), 7.25 – 7.13 (m, 6H), 6.83 (d, *J* = 11.8 Hz, 2H), 4.76 (t, *J* = 7.3 Hz, 1H), 3.76 (s, 3H), 3.68 (d, *J* = 7.3 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.9, 158.3, 143.1, 137.1, 135.9, 133.3, 132.2, 129.24, 128.81, 128.77, 128.16, 114.2, 55.4, 44.9, 44.6. HRMS (APCI-TOF) m/z: [M + H]+ Calcd. for $C_{22}H_{19}O_2Cl$: 351.1152; Found 351.1148. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol (98:2); flow = 0.5 mL/min; detected at 220 nm; 93% *ee*. Retention times: 33.5 min [(*R*) minor], 36.8 min [(*S*) major].

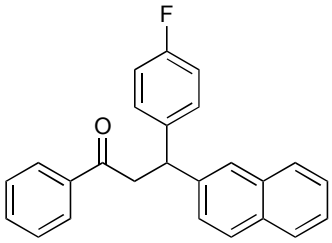
*4.5.4. (S)-3-(4-fluorophenyl)-3-(4-methoxyphenyl)-1-phenylpropan-1-one (**10ak** CAS registry number: 1663503-57-8)*



Enone **9a** (20.8 mg, 0.1 mmol); boronic acid **5k** (21 mg, 0.15 mmol); **ent-C1** (2.4 mg, 0.002 mmol, 2 mol%). Product **10ak** was obtained as a yellow solid (27.5 mg, 0.090 mmol, 90% isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ7.92 (d, *J* = 7.1Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.30-7.17 (m, 7H), 6.95 (t, *J* = 8.7 Hz, 2H), 4.81 (t, *J* = 8.7 Hz, 1H), 3.71 (dd, *J* = 3.1 and 2.6 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.0, 161.5 (d, *J* = 244.6 Hz), 144.1, 139.93, 139.91, 137.1, 133.3, 129.4 (d, *J* = 7.8 Hz), 128.75, 128.0 ((d, *J* = 48.5 Hz), 126.6, 115.4 (d, *J* = 21.2 Hz), 45.28, 44.91. HRMS (APCI-TOF) m/z: [M + H]+ Calcd. for $C_{21}H_{18}OF$: 305.1342; Found 305.1324. HPLC analysis: Daicel Chiralcel OD-H

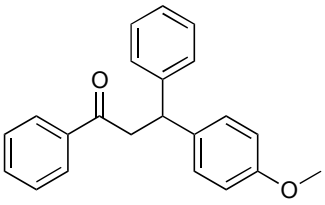
column; hexane/2-propanol (95:5); flow = 1.0 mL/min; detected at 220 nm; 91% *ee*. Retention times: 9.5 min [(*S*) major], 11.3 min [(*R*) minor].

*4.5.5. (R)-3-(4-fluorophenyl)-3-naphthalen-2-yl)-1-phenylpropan-1-one (**10bk**)*



Enone **9b** (25.8 mg, 0.1 mmol); boronic acid **5k** (21 mg, 0.15 mmol); **ent-C1** (3.6 mg, 0.003 mmol, 3 mol%). Product **10dk** was obtained as a yellow solid (32.8 mg, 0.093 mmol, 93% isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.3 Hz, 2H), 7.79-7.74 (m, 3H), 7.69 (s, 1H), 7.56 (dd, *J* = 7.4 Hz each, 1H), 7.48-7.41 (m, 4H), 7.35 (dd, *J* = 8.5 Hz and 1.7 Hz, 1H), 7.28-7.23 (m, 2H), 6.96 (dd, *J* = 7.3 Hz each, 2H), 4.89 (t, *J* = 6.1 Hz, 1H), 3.82 (dd, *J* = 5.9 Hz and 1.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.9, 161.6 (d, *J* = 245.4 Hz), 141.6, 139.8, 137.1, 133.59, 133.35, 132.36, 129.6 (d, *J* = 8.0 Hz), 128.80, 128.54, 128.20, 127.80 (d, *J* = 20.5 Hz), 126.72, 126.28, 125.81, 115.5 (d, *J* = 21.2 Hz), 45.4, 44.8. HRMS (APCI-TOF) m/z: [M + H]+ Calcd. for $C_{25}H_{20}OF$: 355.1498; Found 355.1487. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol = 95/5; flow = 1.0 mL/min; detected at 220 nm; 94% *ee*. Retention times: 13.8 min [(*R*) major], 18.3 min [(*S*) minor].

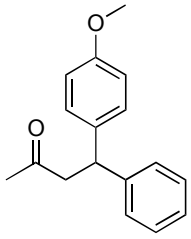
*4.5.6. (R)-3-(4-methoxyphenyl)-1,3-diphenylpropan-1-one (**10da** CAS registry number: 1020172-02-4)*



Enone **9d** (23.8 mg, 0.1 mmol); boronic acid **5a** (18.3 mg, 0.15 mmol); **ent-C1** (4.8 mg, 0.004 mmol, 4 mol%). Product **10da** was obtained as a yellow oily

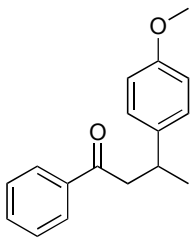
solid (26.6 mg, 0.084 mmol, 84% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.30-7.23 (m, 4H), 7.21-7.14 (m, 3H), 6.81 (d, *J* = 8.5 Hz, 2H), 4.78 (t, *J* = 7.3 Hz, 1H), 3.76 (s, 3H) 3.70 (d, *J* = 7.3 Hz 2H). ^{13}C NMR (600 MHz, $CDCl_3$) δ 198.3, 158.2, 144.7, 137.2, 136.4, 133.2, 128.90, 128.72, 128.67, 128.19, 127.87, 126.4, 114.1, 55.3, 45.29, 45.06. HRMS (APCI-TOF) m/z: [M + H]+ Calcd. for $C_{22}H_{21}O_2$: 317.1542; Found 317.1549. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol = 95/5; flow = 1.0 mL/min; detected at 220 nm; 93% *ee*. Retention times: 13.6 min [(*S*) minor], 15.2 min [(*R*) major].[30]

*4.5.7. (S)-4-(4-methoxyphenyl)-4-phenylbutan-2-one (**10eb** CAS registry number: 791854-83-6)*



Enone **9e** (14.6 mg, 0.1 mmol); boronic acid **5b** (22.8 mg, 0.15 mmol); **ent-C1** (3.6 mg, 0.003 mmol, 3 mol%). Product **10eb** was obtained as a yellow oil (24.3 mg, 0.096 mmol, 96% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26-7.13 (m, 7H), 6.82 (d, *J* = 9 Hz, 2H), 4.54 (t, *J* = 7.6 Hz, 1H), 3.76 (s, 3H), 3.15 (d, *J* = 9.6 Hz, 2H), 2.08 (s, 3H). ^{13}C NMR (600 MHz, $CDCl_3$) δ 207.2, 158.2, 144.3, 136.1, 128.77, 128.68, 127.7, 126.5, 114.1, 55.3, 50.0, 45.4, 30.8. HRMS (APCI-TOF) m/z: [M + H]+ Calcd. for $C_{17}H_{19}O_2$: 255.1385; Found 255.1366. HPLC analysis: Daicel Chiralcel OD-H column; hexane/2-propanol = 98/2; flow = 1.0 mL/min; detected at 220 nm; 96% *ee*. Retention times: 21.2 min [(*S*) major], 24.1 min [(*R*) minor].[17a]

*4.5.8. (R)-3-(4-methoxyphenyl)-1-phenylbutan-1-one (**10fb** CAS registry number: 87258-61-5)*



Enone **9f** (14.6 mg (0.1 mmol); boronic acid **5b** (22.8 mg, 0.15 mmol); **ent-C1** (4.8, 0.004 mmol, 4 mol%). Product **10fb** was obtained as a yellow oil (17 mg, 0.067 mmol, 67% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7 Hz, 2H), 7.54 (t, *J* = 7 Hz, 1H), 7.44 (t, *J* = 8 Hz, 2H), 7.19 (d, *J* = 9 Hz, 2H), 6.84 (d, *J* = 9 Hz, 2H), 3.78 (s, 3H), 3.46 (tq, *J* = 7.2 Hz each, 1H), 3.26 [dd, *J* = 16.3 Hz (gem), 5.9 Hz (vic), 1H], 3.15 [dd, *J* = 16.3 Hz (gem), 8,1 Hz (vic), 1H], 1.31 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (500 MHz, $CDCl_3$) δ 199.4, 158.1, 138.8, 137.4, 133.1, 128.69, 128.22, 127.88, 114.0, 55.4, 47.4, 35.0, 22.1. HPLC analysis: Daicel Chiralcel OJ-H column; hexane/2-propanol (95:5); flow = 1.0 mL/min; detected at 220 nm; 76% *ee*. Retention times: 20.6 min [(*R*) major], 24.0 min [(*S*) minor].

5. Author information

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# These authors have contributed equally to the present manuscript.

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7. Supporting Information

The supporting information is available free of charge on the ACS Publication website.

NMR spectra of all compounds, X-ray data and HPLC analysis of products.

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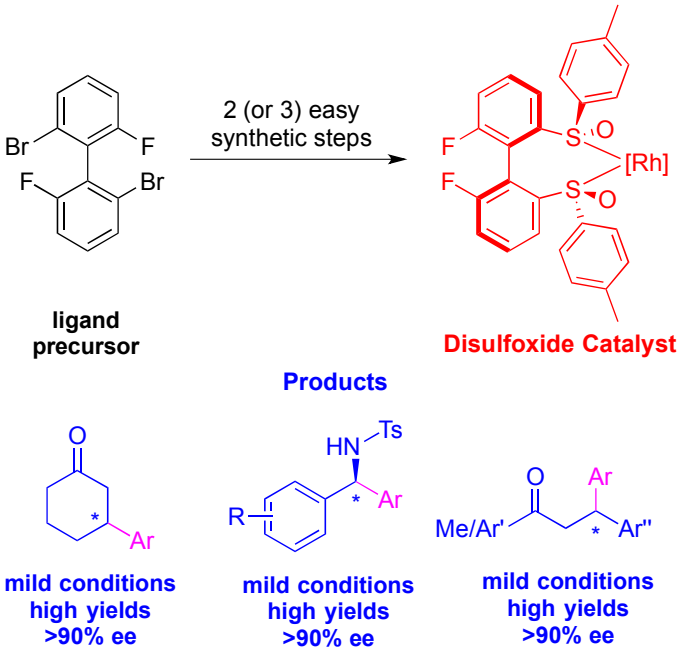
TOC graphic: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