

Award Accounts

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Rhodium-Catalyzed Asymmetric Addition of Organo-Boron and -Titanium Reagents to Electron-Deficient Olefins

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Asymmetric 1,4-arylation and -alkenylation was achieved by use of organoboronic acids or their derivatives in the presence of a rhodium catalyst coordinated with binap or its related ligands. The scope of this asymmetric addition is very broad, α,β-unsaturated ketones, esters, amides, 1-alkenylphosphonates, and 1-nitroalkenes being efficiently converted into the corresponding 1,4-addition products with over 95% enantioselectivity. The catalytic cycle of the reaction in water is proposed to involve three intermediates (aryl- or alkenyl-rhodium, (oxa-π-allyl)rhodium, and hydroxo-rhodium), as suggested by NMR studies on the rhodium intermediates. The asymmetric addition of *B*-aryl-9BBN and $ArTi(OPr\text{-}i)_3$ in aprotic solvents proceeded with high enantioselectivity under mild conditions to give the corresponding metal enolates as the 1,4-addition products.

Recently, the catalytic asymmetric reduction and oxidation have been developed so well that some of the processes are used for industrial production of enantiomerically enriched compounds.[1] On the other hand, the examples of high efficiency in terms of catalytic activity and enantioselectivity are still rare in the catalytic asymmetric carbon–carbon bond forming reactions. Among the asymmetric carbon–carbon bond forming reactions catalyzed by chiral transition metal complexes, the asymmetric 1,4-addition is one of the most promising reactions. This is because its non-asymmetric version is a basic synthetic reaction often used for the carbon–carbon bond formation; such a reaction allows us to introduce carbon nucleophiles to the β-position of electron-deficient olefins such as α,β-unsaturated ketones and esters.[2] Recently two types of 1,4-addition reactions where high enantioselectivity is achieved have been reported.[3] One is the copper(I)-catalyzed addition of organozinc reagents by use of copper(I) catalysts coordinated with chiral phosphorous ligands, represented by phosphoramidite ligand based on the axially chiral 1,1′-bi-2-naphthol.[4] The other is the Michael addition to α,β-unsaturated ketones catalyzed by Shibasaki's heterobimetallic catalysts consisting of chiral 1,1′-bi-2-naphthol and two kinds of metals.[5] In these two types of reactions, sp^3-alkyl groups and soft carbon nucleophiles, respectively, are introduced at the stereogenic carbon center at the β-position of α,β-unsaturated ketones.

Miyaura's report in 1997 describing the first example of rhodium-catalyzed 1,4-addition of aryl- and alkenyl-boronic acids to α,β-unsaturated ketones[6] stimulated us to modify the reaction conditions of the rhodium-catalyzed reaction for catalytic asymmetric 1,4-addition reactions. We succeeded in obtaining high catalytic activity and high enantioselectivity by carrying out the reaction in dioxane and water at 100 °C in the presence of a rhodium catalyst coordinated with (*S*)-binap ligand, as was reported in 1998.[7] As a typical example, the reaction of 2-cyclohexenone with phenylboronic acid gave (*S*)-3-phenylcyclohexanone of 97% ee. After this publication, several reports appeared on the use of some other chiral phosphorus ligands for this type of rhodium-catalyzed 1,4-addition of organoboronic acids to α,β-unsaturated ketones under conditions similar to ours.[8] We have successfully applied the rhodium-catalyzed asymmetric reaction to some other organometallic reagents and electron-deficient olefins. In this account I describe the recent developments of the rhodium-catalyzed asymmetric 1,4-addition reactions recently studied in our research group.[9] Key points include the mechanistic studies on the rhodium-catalyzed 1,4-addition and the successful use of organotitanium reagents in place of organoboron reagents.

1. Rhodium-Catalyzed Asymmetric 1,4-Addition of Organoboronic Acids and Organoboroxines to Electron-Deficient Olefins

In the first report, the rhodium-catalyzed asymmetric 1,4-addition of aryl- and alkenylboronic acids proceeded with high enantioselectivity for both cyclic and linear α,β-unsaturated ketones (Scheme 1).[7] Important points for the high catalytic activity and the high enantioselectivity at this stage are (1) the use of $Rh(acac)(C_2H_4)_2$ as a rhodium catalyst precursor, (2) binap as a chiral bisphosphine ligand, (3) high reaction temperature (100 °C), and (4) the use of a mixture of dioxane and water in a ratio of 10 to 1 as a solvent. The high reaction temperature is essential, because almost no reaction takes place at 60 °C or lower. With $Rh(acac)(CO)_2$ as a catalyst precursor, the reaction

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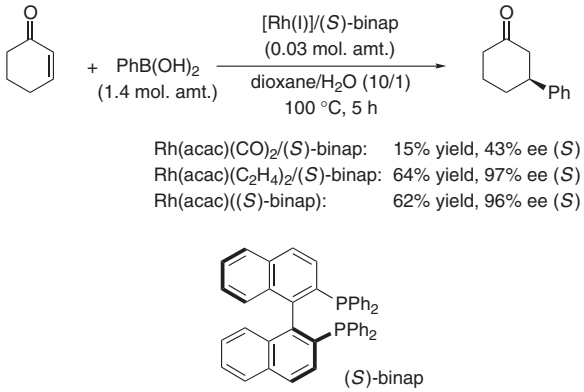
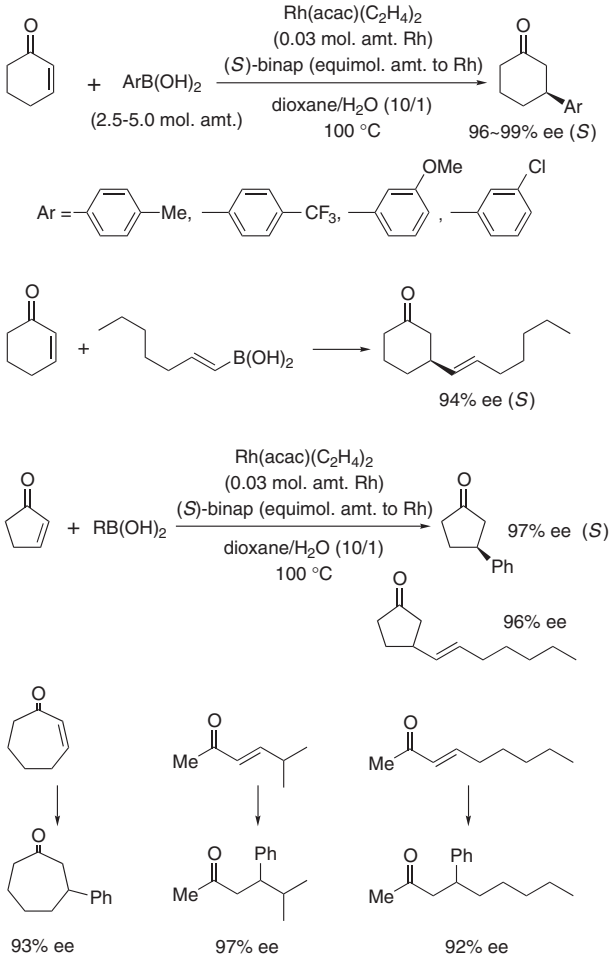


Scheme 1. Rhodium-catalyzed asymmetric 1,4-addition of phenylboronic acid to 2-cyclohexenone.

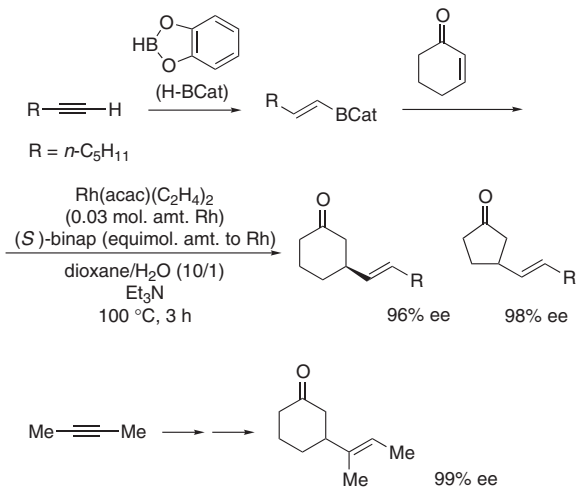
is slower and the enantioselectivity is much lower. NMR studies showed that the addition of equimolar amount of binap ligand to Rh(acac)$(C_2H_4)_2$ immediately generates Rh(acac)(binap) quantitatively, while Rh(acac)$(CO)_2$ generates two kinds of unidentified rhodium complexes together with a small amount of the Rh(acac)(binap) complex.

The scope of this rhodium-catalyzed asymmetric 1,4-addition of organoboronic acids is very broad.[7] Some of the results obtained for the addition to α,β-unsaturated ketones are summarized in Scheme 2. Under standard conditions, that is, 0.03 molar amount of Rh(acac)$(C_2H_4)_2$ and binap in dioxane/H_2O (10/1) at 100 °C, aryl groups substituted with either electron-donating or -withdrawing groups, 4-MeC_6H_4, 4-$CF_3C_6H_4$, 3-MeOC_6H_4, and 3-ClC_6H_4, were introduced onto 2-cyclohexenone with high enantioselectivity by the reaction with the corresponding boronic acids. Asymmetric addition of 1-alkenylboronic acids was as successful as that of arylboronic acids, the alkenylation product with 1-heptenylboronic acid being obtained with 94% enantioselectivity. Cyclopentenone underwent the asymmetric addition of phenyl- and 1-heptenylboronic acids with high enantioselectivity under the same reaction conditions to give 3-substituted cyclopentanones with over 96% ee in high yields. High enantioselectivity was also observed in the reaction of linear enones, 5-methyl-3-hexen-2-one and 3-nonen-2-one, which have *trans* olefin geometry. Thus, the rhodium-catalyzed asymmetric 1,4-addition proceeds with high enantioselectivity for both cyclic and linear α,β-unsaturated ketones with a variety of aryl- and alkenylboronic acids. The procedures for the preparation of (*S*)-3-phenylcyclohexanone on a scale of several grams have been published in *Organic Synthesis*.[10] High enantioselectivity has been recently reported by use of other chiral ligands than binap under reaction conditions similar to those we reported.[8]

(1-Alkenyl)catecholboranes obtained by the hydroboration of alkynes with catecholborane were found to be good alkenylating reagents for the asymmetric 1,4-addition[11] (Scheme 3). For a high chemical yield in this reaction, triethylamine must be added, which probably neutralizes the catechol generated under the reactions conditions. The reaction of (*E*)-1-heptenylborane, which is obtained by the hydroboration of 1-heptyne, with 2-cyclohexenone gave 92% yield of 1,4-addition product, which is an (*S*) isomer of 96% ee. High enantioselectivity (99% ee) was observed in the reaction starting from 2-butyne, which



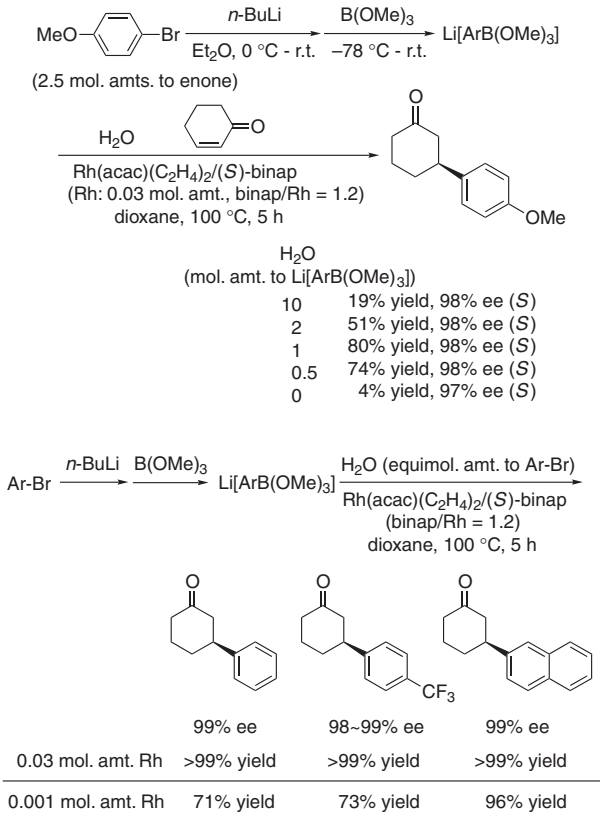
Scheme 2. Asymmetric 1,4-addition of organoboronic acids to α,β-unsaturated ketones.



Scheme 3. Rhodium-catalyzed asymmetric 1,4-addition of alkenylcatecholboranes.

is an internal acetylene. One-pot synthesis of the optically active β-alkenyl ketones is possible from alkynes and catecholborane without isolation of the alkenylcatecholboranes.

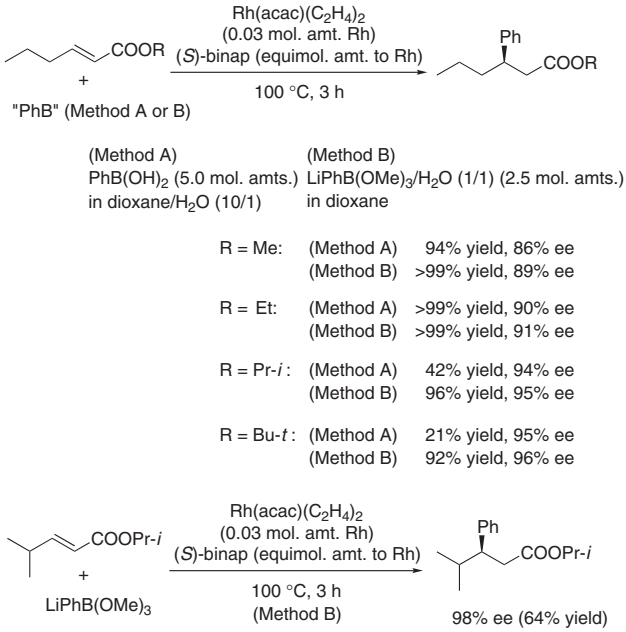
Lithium aryltrimethoxoborates, readily generated in situ by treatment of aryllithiums with trimethoxyborane, can also be



Scheme 4. Rhodium-catalyzed asymmetric 1,4-addition of lithium arylborates.

used for the asymmetric 1,4-addition[12] (Scheme 4). This is another one-pot reaction. In general, this reaction provides higher yields than those obtained with arylboronic acids. Studies of the reaction conditions indicated that the amount of water has an effect on the yields, while the enantioselectivity remains unaffected. The highest yield was obtained in the reaction carried out in the presence of equimolar amount (to arylborate) of water. The enantioselectivity was high for the addition of any of several arylborate reagents. Using these in situ generated arylborate reagents, we could reduce the amount of the catalyst without loss of enantioselectivity. As a typical example, in the reaction of 2-cyclohexenone with borate generated from 2-bromonaphthalene, 0.001 molar amount of the catalyst gave 96% yield of the 3-(2-naphthyl)cyclohexanone that is 99% enantiomerically pure. In the addition to α,β-unsaturated ketones, this one-pot reaction is superior to the reaction of arylboronic acids both in higher catalytic activity, resulting in higher chemical yield, and in easier manipulation, avoiding the isolation of arylboronic acids.

α,β-Unsaturated esters are also good substrates for the rhodium-catalyzed asymmetric addition.[13] The results obtained for the phenylation of (*E*)-hexenoic esters are shown in Scheme 5, where phenylboronic acid in dioxane/H_2O (10/1) (Method A) or phenylborate generated from phenyllithium and trimethoxyborane (Method B) was used as the phenylation reagent. In the reaction of methyl ester and ethyl ester, Method A gave high yields of the phenylation products, but in the reaction of isopropyl ester and *tert*-butyl ester the yields were much lower (<42% yield). These yields were greatly improved by



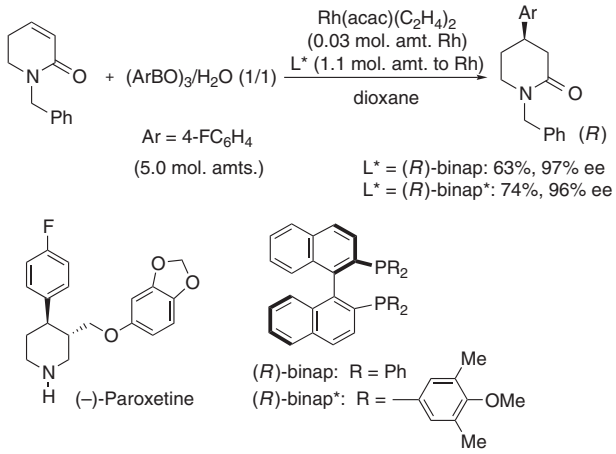
Scheme 5. Rhodium-catalyzed asymmetric 1,4-addition to α,β-unsaturated esters.

use of Method B, which gave the phenylation products in 96% and 92% yield, respectively. Interestingly, the enantioselectivity increases as the steric bulkiness of the ester moiety increases. The enantiomeric purities of the phenylation products are 89%, 91%, 95%, and 96% ee for methyl, ethyl, isopropyl, and *tert*-butyl esters, respectively, in the reactions using Method B. The sterically more bulky ester shows the higher enantioselectivity. Aryl groups: 4-ClC_6H_4, 4-MeC_6H_4, 4-$CF_3C_6H_4$, 3-$MeOC_6H_4$, and 2-naphthyl, were also introduced at the β-position of isopropyl ester with enantioselectivity ranging between 93% and 97% ee in high yields in the reactions with the corresponding lithium arylborates. The highest enantioselectivity (98% ee) was observed in the phenylation of isopropyl 4-methyl-2-pentenoate under Method B conditions, though the yield was not high enough.

Similar results for the asymmetric 1,4-addition of arylboronic acids to α,β-unsaturated esters have been independently reported by Miyaura.[14] The asymmetric addition to α,β-unsaturated amides under similar conditions has also been reported by Miyaura.[15] The enantioselectivity is comparable to that in the addition to the corresponding esters.

Asymmetric 1,4-addition to cyclic α,β-unsaturated amides provides a new and efficient route to enantiomerically enriched 4-aryl-2-piperidones[16] (Scheme 6). For the 1,4-addition of 4-$FC_6H_4B(OH)_2$, which is related to asymmetric synthesis of (−)-Paroxetine, slightly modified conditions were required to obtain a high yield of the arylation product. The main side reaction, that is, hydrolysis of the boronic acid to give fluorobenzene, was suppressed by use of a minimum amount of the water. Thus, the reaction with 4-fluorophenylboroxine and equimolar amount (to boron) of water in the presence of Rh(acac)$(C_2H_4)_2$/(*R*)-binap catalyst in dioxane at 40 °C gave 63% yield of (*R*)-lactam with 97% enantioselectivity.

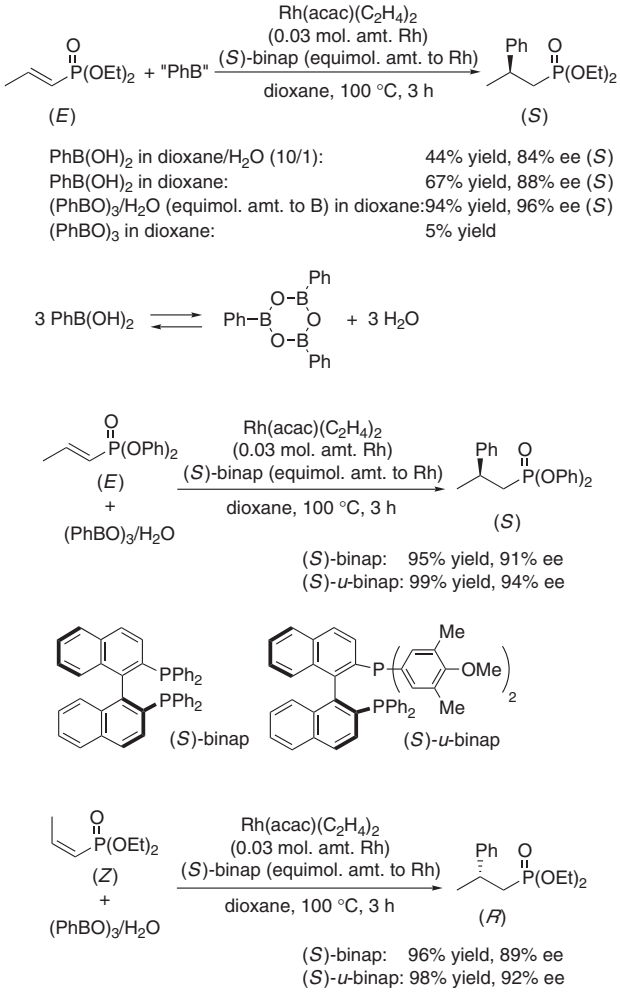
Alkenylphosphonates are less reactive toward 1,4-addition than α,β-unsaturated carbonyl compounds are. Under the reac-



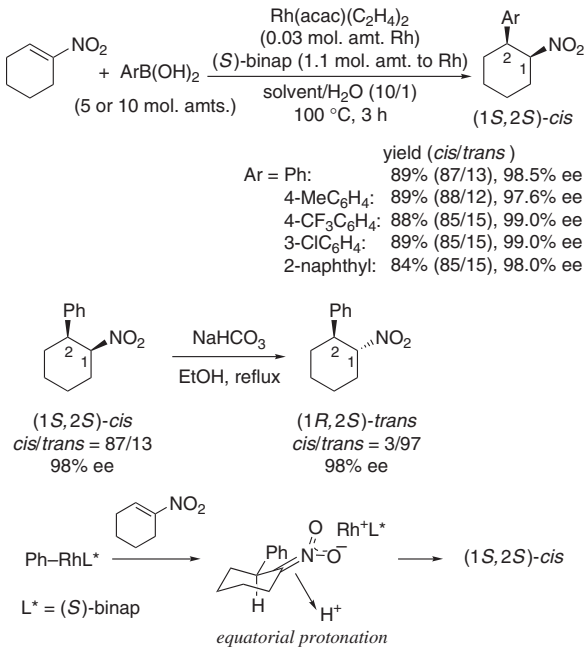
Scheme 6. Rhodium-catalyzed asymmetric 1,4-addition to cyclic α,β-unsaturated amide.

tion conditions used for α,β-unsaturated ketones (phenylboronic acid in dioxane/H_2O (10/1)), the yield of 1,4-addition was very low (44%) for diethyl (*E*)-1-propenylphosphonate. The asymmetric 1,4-addition was greatly improved (94% yield with 96% ee) by carrying out the reaction using phenylboroxine $(PhBO)_3$ and equimolar amount of water (Scheme 7).[17] The addition of equimolar amount of water is essential for the high yield, almost no reaction taking place in the absence of water. Boroxine and water should be in equilibration with boronic acid under the reaction conditions,[18] and hence the use of arylboroxine in combination with equimolar amount of water for the asymmetric 1,4-addition should result in the same outcome as using the corresponding arylboronic acid with no water added. Nevertheless, the results of the catalytic reactions are better with the combination of boroxine and water. The enantioselectivities and chemical yields were slightly higher with the rhodium catalyst coordinated with unsymmetrically substituted binap ligand, (*S*)-*u*-binap, which has diphenylphosphino and bis(4-methoxy-3,5-dimethylphenyl)phosphino groups at the 2 and 2′ positions on the 1,1′-binaphthyl skeleton. In the reaction of diphenyl (*E*)-1-propenylphosphonate with phenylboroxine, (*S*)-*u*-binap ligand gave 99% yield of the 1,4-addition product with 94% ee, while the standard (*S*)-binap gave 95% yield with 91% ee. It is remarkable that the asymmetric phenylation of (*Z*) isomer of diethyl 1-propenylphosphonate with phenylboroxine gave *R* isomer. The optically active alkylphosphonates containing the stereogenic carbon center at β-position can be used as chiral building blocks for the synthesis of optically active alkenes by the Horner–Emmons-type reaction.

Nitroalkenes are good substrates for the rhodium-catalyzed asymmetric 1,4-addition of organoboronic acids.[19] The reaction of 1-nitrocyclohexene with phenylboronic acid in the presence of the rhodium/(*S*)-binap catalyst at 100 °C for 3 h gave 89% yield of 1-nitro-2-phenylcyclohexane (Scheme 8). The main phenylation product is a *cis* isomer (*cis*/*trans* = 87/13) and both the *cis* and the *trans* isomers are 98% enantiomerically pure. Treatment of the *cis*-rich mixture with sodium hydrogencarbonate in refluxing ethanol caused *cis*–*trans* equilibration, giving the thermodynamically more stable *trans* isomer (*trans*/*cis* = 97/3). It should be noted that this rhodium-catalyzed asymmetric phenylation produced the thermodynamical-



Scheme 7. Rhodium-catalyzed asymmetric 1,4-addition to alkenylphosphonates.

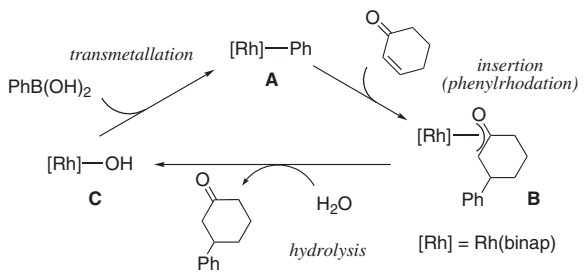


Scheme 8. Rhodium-catalyzed asymmetric 1,4-addition to a nitroalkene.

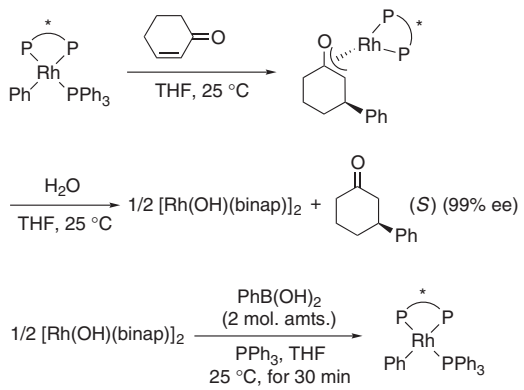
ly less stable *cis* isomer of high enantiomeric purity; it can be isomerized, if one wishes, into *trans* isomer without loss of its enantiomeric purity. The preferential formation of *cis*-isomer in the catalytic phenylation may indicate the protonation of a rhodium nitronate intermediate in the catalytic cycle. Under similar reaction conditions, 1-nitrocyclohexene could experience asymmetric addition of some other arylboronic acids in good yields with high enantioselectivity. The corresponding *cis*-2-aryl-1-nitrocyclohexanes were produced with over 85% *cis* selectivity and with the enantioselectivity ranging between 97.6% and 99.0% ee. The optically active nitroalkanes obtained here are useful chiral building blocks that can be readily converted into a wide variety of optically active compounds by taking advantages of the versatile reactivity of nitro compounds.

2. Catalytic Cycle of the Rhodium-Catalyzed 1,4-Addition of Organoboron Reagents

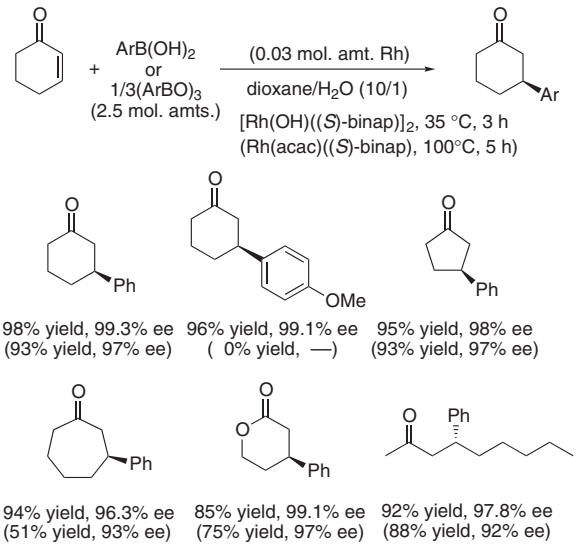
We succeeded in characterizing the important intermediate involved in the catalytic cycle of the rhodium-catalyzed 1,4-addition by use of $RhPh(PPh_3)(binap)$ as a key intermediate.[20] The catalytic cycle for the reaction of phenylboronic acid with 2-cyclohexenone is shown in Scheme 9. The reaction proceeds by way of three intermediates: phenylrhodium **A**, oxa-π-allylrhodium **B**, and hydroxorhodium **C** complexes. All of the intermediates and transformations among the three complexes were observed in NMR spectroscopic studies (Scheme 10). The reaction of phenylrhodium complex $RhPh(PPh_3)(binap)$ with 2-cyclohexenone gave oxa-π-allylrhodium; this is formed by insertion of the carbon–carbon double bond of enone into the phenyl–rhodium bond, followed by isomerization into the thermo-



Scheme 9. Catalytic cycle for the rhodium-catalyzed 1,4-addition.



Scheme 10. Supporting experiments for the catalytic cycle.

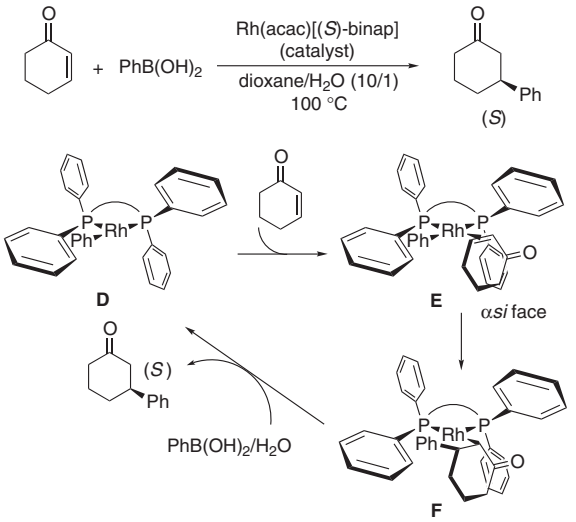


Scheme 11. Asymmetric 1,4-addition catalyzed by [Rh(OH)((*S*)-binap)]$_2$.

dynamically stable complex. The oxa-π-allylrhodium complex was converted immediately into hydroxorhodium complex $[Rh(OH)(binap)]_2$ on addition of water, liberating the phenylation product. Transmetallation of phenyl group from boron to rhodium takes place by addition of phenylboronic acid in the presence of triphenylphosphine to regenerate the phenylrhodium $RhPh(PPh_3)(binap)$.

All the three transformations in Scheme 10 was found to proceed at 25 °C, but the catalytic reaction in the presence of a rhodium catalyst generated from $Rh(acac)(C_2H_4)_2$ does not proceed at 60 °C or lower. It turned out that the acetylacetonato ligand retards the transmetallation step because of the high stability of the rhodium–acac moiety. Use of the hydroxo complex $[Rh(OH)(binap)]_2$ as a catalyst made it possible to run the reaction at lower temperature[20] (Scheme 11). Thus, the addition of phenylboronic acid or phenylboroxine to 2-cyclohexenone is catalyzed by $[Rh(OH)(binap)]_2$ at 35 °C to give a quantitative yield of 3-phenylcyclohexanone, which is over 99% enantiomerically pure. This catalyst system is also applicable to the reaction of other enones and organoboron reagents. The enantioselectivity is always higher than that in the reaction catalyzed by the rhodium–acac complex at 100 °C because the reaction temperature is lower. The chemical yields are higher and less boron reagent is used because the hydrolysis of the boronic acids, which is the main side reaction, is suppressed at the lower temperature.

Scheme 12 shows the stereochemical pathway in the reaction catalyzed by the rhodium complex coordinated with (*S*)-binap.[7] According to the highly skewed structure known for transition metal complexes coordinated with a binap ligand,[21] (*S*)-binap–rhodium intermediate **D** should have an open space at the lower part of the vacant coordination site, the upper part being blocked by one of the phenyl rings of the binap ligand. The olefinic double bond of 2-cyclohexenone coordinates to rhodium with its αsi face forming **E** rather than with its αre face. Migratory insertion forms a stereogenic carbon center in **F** whose absolute configuration is *S*. The absolute configurations of all the 1,4-addition products can be predicted by this type of stereo-



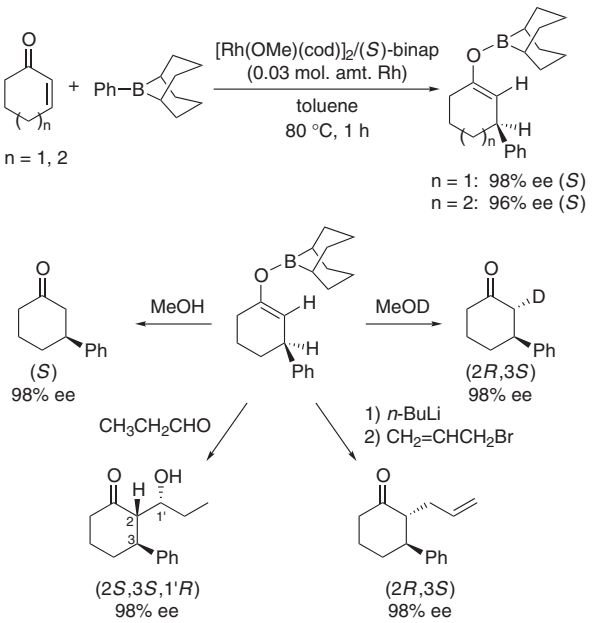
Scheme 12. Stereochemical pathway in the rhodium-catalyzed asymmetric 1,4-addition.

control model: (*S*)-binap–rhodium intermediate attacking the αsi face of α,β-unsaturated ketones, both cyclic and linear ones, and of other electron-deficient olefins including α,β-unsaturated esters and 1-alkenylphosphonates.

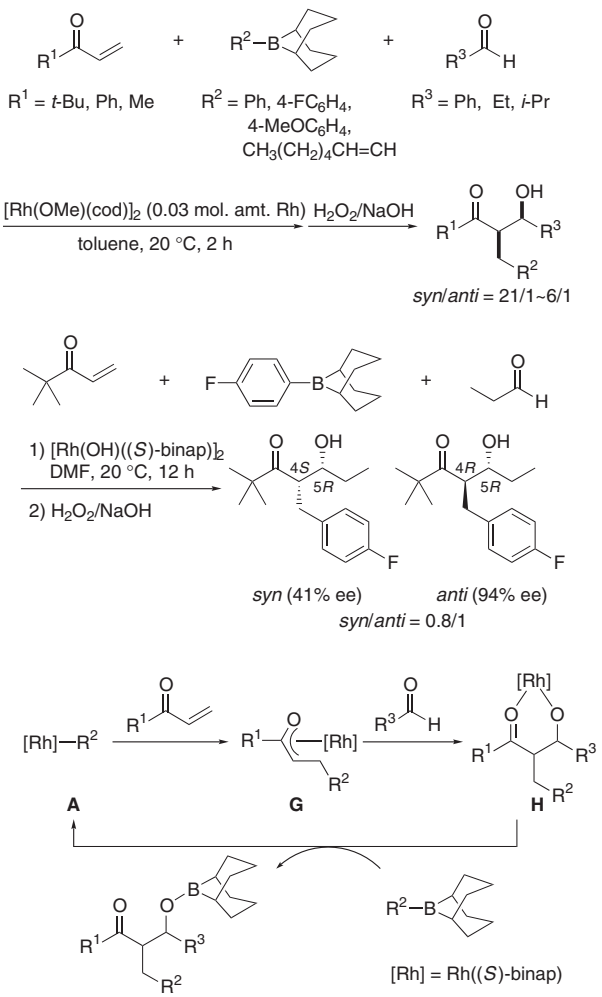
3. Asymmetric 1,4-Addition of *B*-Aryl-9BBN to α,β-unsaturated Ketones Forming Boron Enolates

In the rhodium-catalyzed 1,4-addition of organoboron reagents to electron-deficient alkenes described above, protic solvents represented by water play a key role in the catalytic cycle. This cycle involves hydrolysis of oxo-π-allylrhodium, giving hydroxorhodium species and the hydrolyzed 1,4-addition product (cf. Scheme 9). The use of water as a cosolvent is one of the advantages of this reaction over other 1,4-addition reactions, but one major drawback is that the 1,4-addition product is obtained as the hydrolyzed product. A catalytic asymmetric 1,4-addition giving boron enolates as the products would be more useful. Recently, it was found that the use of *B*-Ar-9BBN allows the catalytic asymmetric 1,4-addition, forming chiral boron enolates (Scheme 13).[22] As a typical example, the reaction of 2-cyclohexenone with 1.1 molar amount of *B*-Ph-9BBN in the presence of 0.03 molar amount of a rhodium catalyst generated from $[Rh(OMe)(cod)]_2$ and (*S*)-binap in toluene at 80 °C for 1 h gave a high yield of the boron enolate, which is an *S* isomer of 98% ee. Unfortunately, this reaction forming chiral boron enolate is observed only for 2-cyclohexenone and 2-cycloheptenone. The reaction of boron enolate with electrophiles provides us with chances for the further transformation, as expected.

A new type of catalytic tandem 1,4-addition–aldol reaction has also been found by use of *B*-Ar-9BBN.[23] The reaction of *B*-Ar-9BBN, vinyl ketone, and aldehyde catalyzed by $[Rh(OMe)(cod)]_2$ proceeded in toluene at 20 °C to give a high yield of the aldol-type product with high syn selectivity (Scheme 14). Asymmetric reaction using $[Rh(OH)((S)\text{-binap})]_2$ as a catalyst gave optically active products: *syn*-(4*S*,5*R*)-aldol of 41% ee and *anti*-(4*R*,5*R*)-aldol of 94% ee, though the *syn*/*anti* selectivity is low. The formation of the enantiomerically enriched products demonstrates that the reaction proceeds



Scheme 13. Rhodium-catalyzed asymmetric 1,4-addition of *B*-Ar-9BBN.

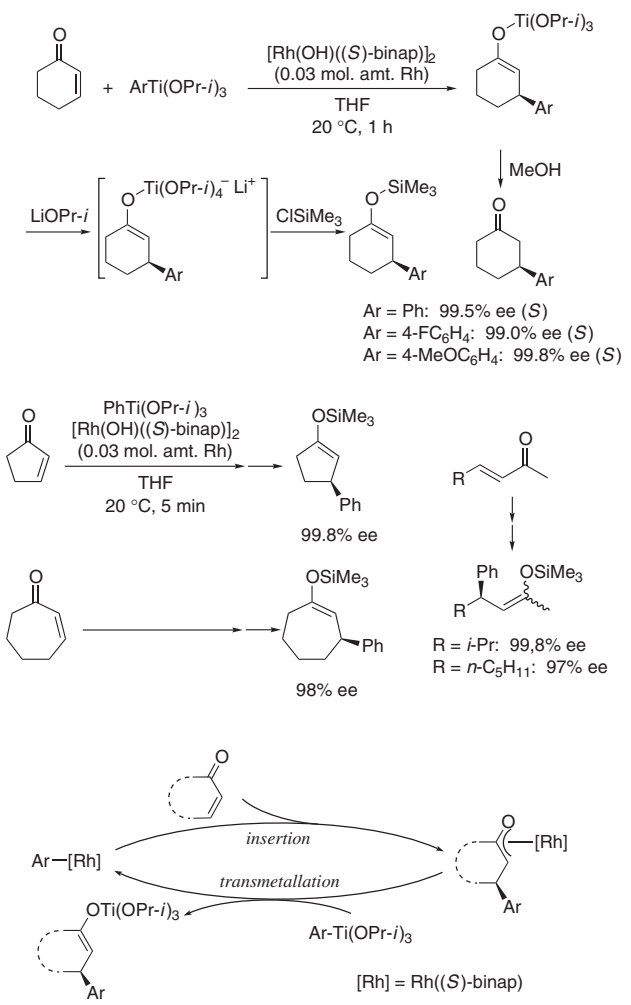


Scheme 14. Rhodium-catalyzed tandem 1,4-addition–aldol reaction.

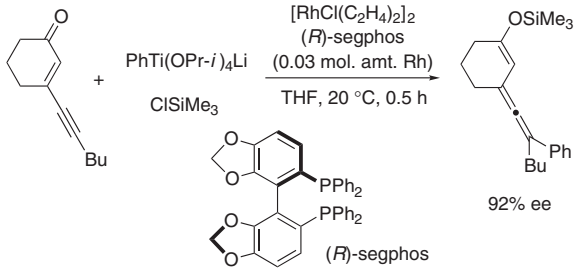
through (oxa-π-allyl)rhodium complex **G** coordinated with (*S*)-binap ligand, which is formed by the carbo-rhodation of the vinyl ketone and undergoes aldol-type reaction with aldehyde, forming rhodium aldolate **H**. The boron enolate as an intermediate is ruled out, since it would lead to a racemic aldol product.

4. Catalytic Asymmetric 1,4-Addition of Organotitanium Reagents to α,β-unsaturated Ketones and Other Electron-Deficient Olefins

Recently we found that a rhodium catalyst and aryltitanium triisopropoxide (ArTi(OPr-*i*)$_3$) is a good combination for the asymmetric 1,4-addition to α,β-unsaturated ketones in an aprotic solvent (Scheme 15).[24] The addition of ArTi(OPr-*i*)$_3$ to 2-cyclohexenone was completed within 1 h in the presence of 0.03 molar amount of [Rh(OH)((*S*)-binap)]$_2$ in THF at 20 °C to give high yields of the titanium enolates as 1,4-addition products. The enantioselectivity is very high: 99.5%, 99.0%, and 99.8% ee, for Ar = Ph, 4-FC$_6$H$_4$, and 4-MeOC$_6$H$_4$, respectively. The titanium enolates were converted into silyl enol ethers by treatment with chlorotrimethylsilane and lithium isopropoxide. Other cyclic enones, 2-cyclopentenone and 2-cycloheptenone, and some linear enones are also good substrates for



Scheme 15. Rhodium-catalyzed asymmetric 1,4-addition of aryltitanium reagents.



Scheme 16. Rhodium-catalyzed asymmetric 1,6-addition forming axially chiral allene.

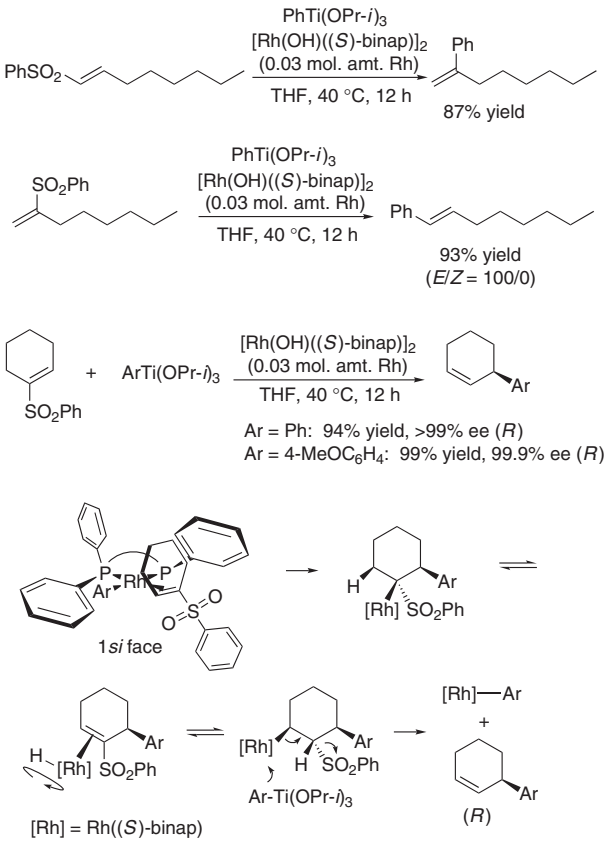
the asymmetric 1,4-addition of phenyltitanium triisopropoxide, giving the corresponding arylation products with over 97% enantioselectivity. The catalytic cycle was demonstrated by NMR studies to involve the transmetalation of the aryl group from titanium to rhodium of the (oxa-π-allyl)rhodium intermediate, leaving an arylrhodium species and the titanium enolate.

The addition of aryltitanate reagents ArTi(OPr-*i*)$_4$Li to 3-alkynyl-2-en-1-ones in the presence of chlorotrimethylsilane and rhodium–(*R*)-segphos as a catalyst proceeded in a 1,6-fashion to give a high yield of axially chiral allenylalkenyl silyl enol ethers with up to 93% ee (Scheme 16).[25] For example, the 1,6-addition of PhTi(OPr-*i*)$_4$Li to 3-(1-hexynyl)-2-cyclohexenone in the presence of chlorotrimethylsilane, [RhCl(C$_2$H$_4$)$_2$]$_2$ (0.03 molar amount Rh), and (*R*)-segphos in THF at 20 °C for 0.5 h gave an axially chiral allene, 3-(2-phenyl-1-hexen-1-ylidene)-1-trimethylsiloxy-1-cyclohexene of 92% ee, in a high yield.

The use of 1-alkenyl sulfones for the rhodium-catalyzed addition of aryltitanium reagents (ArTi(OPr-*i*)$_3$) was found to give us an interesting result (Scheme 17).[26] The addition to linear 1-alkenyl sulfones, 1-phenylsulfonyl-1-octene and 2-phenylsulfonyl-1-octene, resulted in a *cine* substitution reaction, where the sulfonyl group is substituted with the phenyl group on the next carbon of the double bond, took place regioselectively. The catalytic cycle was established by deuterium labeling studies to proceed through *anti*-elimination of rhodium and sulfonyl group from an alkylrhodium intermediate. In the addition reaction to cyclic 1-alkenyl sulfone, 1-phenylsulfonylcyclohexene, the asymmetric carbon center created at the carbo–rhodation step is retained in the substitution product. Thus, the reaction of with aryltitanium triisopropoxides (ArTi(OPr-*i*)$_3$) in the presence of 0.03 molar amount of [Rh(OH)((*S*)-binap)]$_2$ in THF at 40 °C gave a quantitative yield of 3-aryl-1-cyclohexenes with over 99% enantioselectivity.

5. Conclusion

The rhodium-catalyzed asymmetric 1,4-addition reaction of organoboron reagents, which provides a highly efficient method of enantioselective transfer of aryl and alkenyl groups onto the β-position of electron-deficient olefins, is complementary to the copper-catalyzed reactions where alkyl organometallic reagents are incorporated with high enantioselectivity.[4] The rhodium-catalyzed reaction involves a rhodium–aryl or –alkenyl species as an intermediate in the catalytic cycle. Considering the reactivity of the transition metal–carbon bond toward car-



Scheme 17. Rhodium-catalyzed asymmetric arylation of alkenylsulfones with aryltitaniums.

bon–carbon or carbon–hetero atom multiple bonds, the rhodium intermediate is expected to add to unsaturated bonds other than the electron-deficient olefins. Actually, the addition of organoboron reagents to aldehydes[27] and imines[28] has been reported to be catalyzed by a rhodium complex. The addition to aldehydes is applied to asymmetric synthesis of diarylmethanols, though the enantioselectivity is not high enough.[27a] Some interesting reactions of arylboronic acids with norbornene and oxanorbornene derivatives have been reported by Miura[29] and Lautens,[30] respectively; these involve the addition of rhodium–aryl bond to the norbornene double bond. In the reaction of oxanorbornene derivatives forming chiral functionalized cyclohexenes as ring-opening products, over 90% enantioselectivity has been achieved.[27] The arylrhodium species can be also generated by transmetallation from some other organometallic reagents. The addition of aryltin,[31] -silicon,[32] and -bismuth[33] reagents to α,β-unsaturated carbonyl compounds catalyzed by a rhodium complex is thought to proceed through a similar catalytic cycle. The addition of arylsilanes has recently been applied to the catalytic asymmetric synthesis.[34] High enantioselectivity has been achieved in the arylation of imines with arylstannanes; the reaction is catalyzed by a rhodium complex coordinated with an axially chiral monodentate phosphine ligand (MOP).[35] Many new catalytic reactions of synthetic value will be developed by combinations of various types of organometallic reagents and unsaturated molecules, and some of them will be extended to catalytic asymmetric reactions of high enantioselectivity by proper tuning of the chiral catalyst.

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