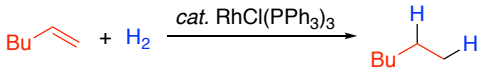
3. Stereocontrol in Catalytic Reactions

(1) Hydrogenation of alkenes

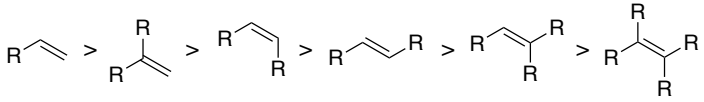


G. Wilkinson, *Chem. Commun.*, 131 (1965); *Nature*, **208**, 1203 (1965).

- As with metal-particle catalysts such as palladium on charcoal, Wilkinson complex, $RhCl(PPh_3)_3$, catalyzes the hydrogenation of alkenes.
- Some other metal complexes also work as catalysts for the hydrogenation.
- The homogeneous metal-complex catalysts are as useful for organic synthesis as the heterogeneous metal-particle catalysts, because the former exhibits setreo- and/or site-selectivity different from the latter.

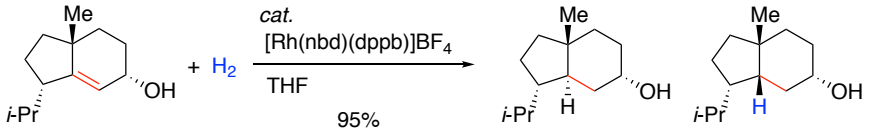
(a) Reactivity of C–C double bond

- Reaction rate of the rhodium-catalyzed hydrogenation is sensitive to the steric effect of the substituents on the C–C double bond.
- The reactivity depends on the binding constant of olefin to the metal atom.

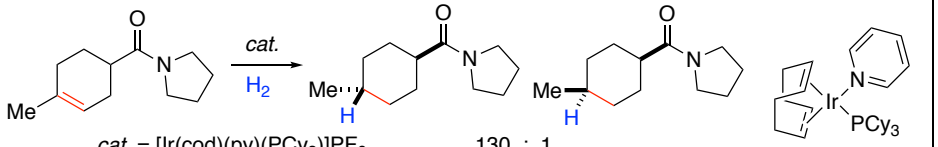


for $RhCl(PPh_3)_3$

- An electron-withdrawing group enhance the reactivity.
- Lewis basic functional group neighboring on the alkene often works as the directing group to facilitate the hydrogenation.



D. A. Evans, *J. Am. Chem. Soc.*, **106**, 3866 (1984).

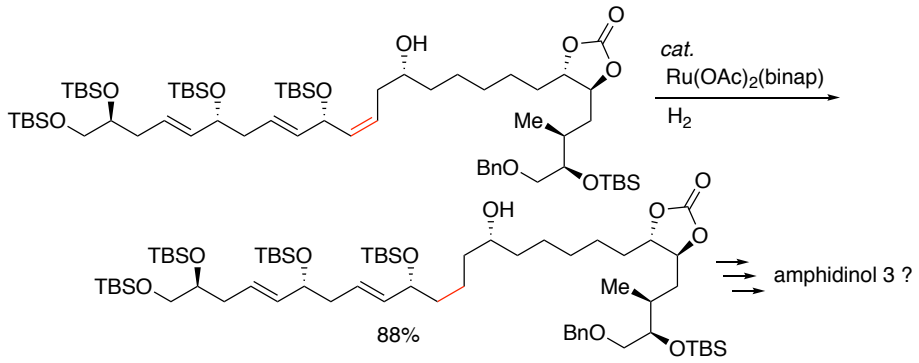


cat. = $[Ir(cod)(py)(PCy_3)]PF_6$ 130 : 1

cat. = 5% Pd/C 1.6 : 1

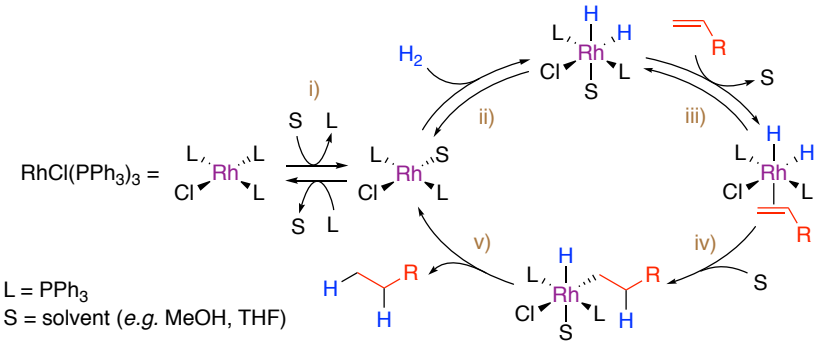
$[Ir(cod)(py)(PCy_3)]$

A. G. Schultz, *J. Org. Chem.*, **50**, 5905 (1985).



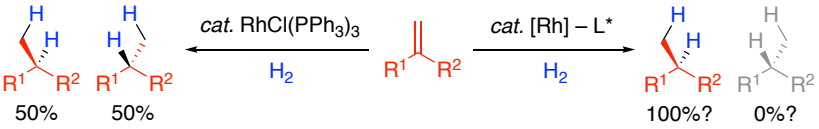
W. R. Roush, *Org. Lett.*, **7**, 1411 (2005).

(b) Mechanism of the hydrogenation with Wilkinson catalyst



- A typical catalytic cycle of the hydrogenation of alkenes with Wilkinson complex is as follows:
  - i) Dissociation of L: One of phosphine ligands on Rh is replaced by a solvent molecule.
  - ii) Oxidative addition of H_2: The rhodium(I) species is inserted into the H–H bond.
  - iii) Coordination of alkene: The solvent on rhodium is replaced by the alkene substrate.
  - iv) Migratory insertion of alkene: One of the Rh–H bond adds to the C–C double bond.
  - v) Reductive elimination: The resulting alkyl group and hydride are eliminated from the Rh to form the C–H bond.
- The mechanism is affected by the substrate, catalyst, and reaction conditions. For example, the C–C double bond will interact with the rhodium(I) prior to the oxidative addition of H_2 when the substrate has an appropriate directing group. In some cases, monohydridometal species participates in the catalytic cycle.

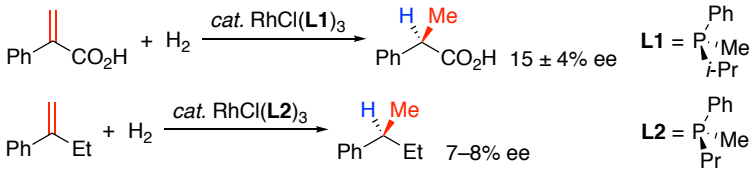
(c) Enantioselective hydrogenation of alkenes with asymmetric catalysis



L* = optically active phosphine

- The hydrogenation of prochiral alkenes must yield the racemic products when an achiral or racemic metal complex is employed as the catalyst, because the frontside attack of H2 equally takes place to the backside attack.
- The frontside (or backside) attack may be restricted when the metal complex has a well-designed phosphine ligand in place of PPh_3.

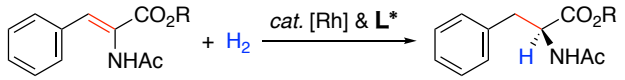
(i) Initial attempt



W. S. Knowles, *Chem. Commun.*, 1443 (1968); L. Horner, *Angew. Chem. Int. Ed.*, **7**, 942 (1968).

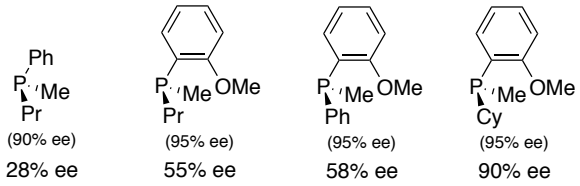
- To achieve the asymmetric catalysis, the PPh3 ligands in Wilkinson complex were replaced by the optically active phosphine bearing three different substituents.
- The chiral ligand possesses its stereogenic center on its phosphorus atom.
- These reports proved the chiral spectator ligand possible to control the stereochemistry in catalytic reactions. However, the enantioselectivities are very low and insufficient for organic synthesis.

(ii) Progress of asymmetric hydrogenation of 2-(*N*-acylamino)cinnamates



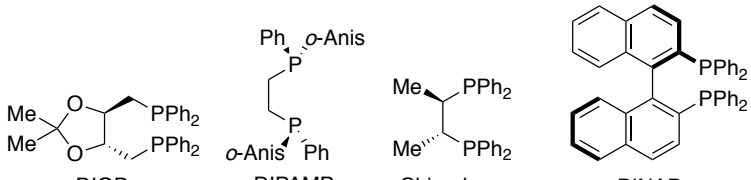
- The asymmetric hydrogenation transforms the substrate, 2-(*N*-acylamono)cinnamate or related compound, into the optically active protected phenylalanine.
- The C–C double bond and amide carbonyl oxygen in the substrate chelate the rhodium atom. The chelation restricts the conformation of the substrate–catalyst complex.

i) Optimization of *P*-chiral monophosphine (–1972)



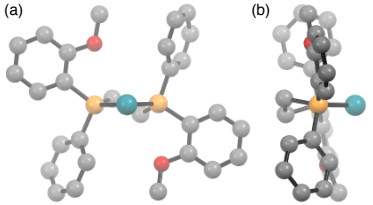
W. S. Knowles, *J. Chem. Soc., Chem. Commun.*, 10 (1972).

ii) Application and improvement of bidentate bisphosphine (1971–1980)

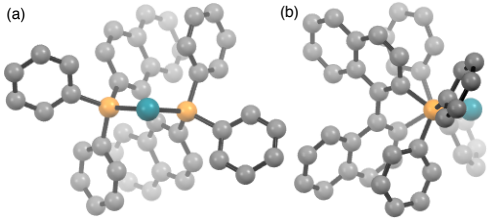


Review: W. S. Knowles, *Acc. Chem. Res.*, **16**, 106 (1983). 1) H. Kagan, *J. Chem. Soc., Chem. Commun.*, 481 (1971); *J. Am. Chem. Soc.*, **94**, 6429 (1972). 2) W. S. Knowles, *J. Am. Chem. Soc.*, **97**, 2567 (1975); *J. Am. Chem. Soc.*, **99**, 5946 (1977). 3) B. Bosnich, *J. Am. Chem. Soc.*, **99**, 6262 (1977). 4) R. Noyori, *J. Am. Chem. Soc.*, **102**, 2567 (1980).

- The bidentate ligands form the chelate complex with various metal atom. The chelation restricts the position and arrangement of the *P*-substituents, which create rigid steric hindrance (chiral reaction field) around the rhodium atom.



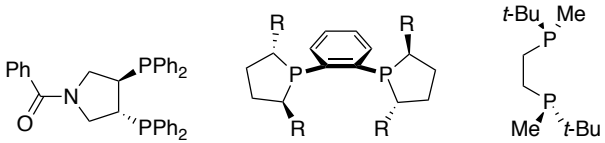
Crystal structure of {Rh(cod)[(*R*,*R*)-dipamp]}BF_4 (All H atoms, COD, and BF_4 are omitted for simplification). (a) Front view. (b) Side view.



Crystal structure of {Rh(nbd)[(*R*)-binap]}ClO_4 (All H atoms, NBD, and ClO_4 are omitted for simplification). (a) Front view. (b) Side view.

D. Heller, *Tetrahedron: Asymmetry*, **15**, 2139 (2004); R. Noyori, *J. Am. Chem. Soc.*, **102**, 2567 (1980).

iii) Further improvement of chiral bisphosphine ligand

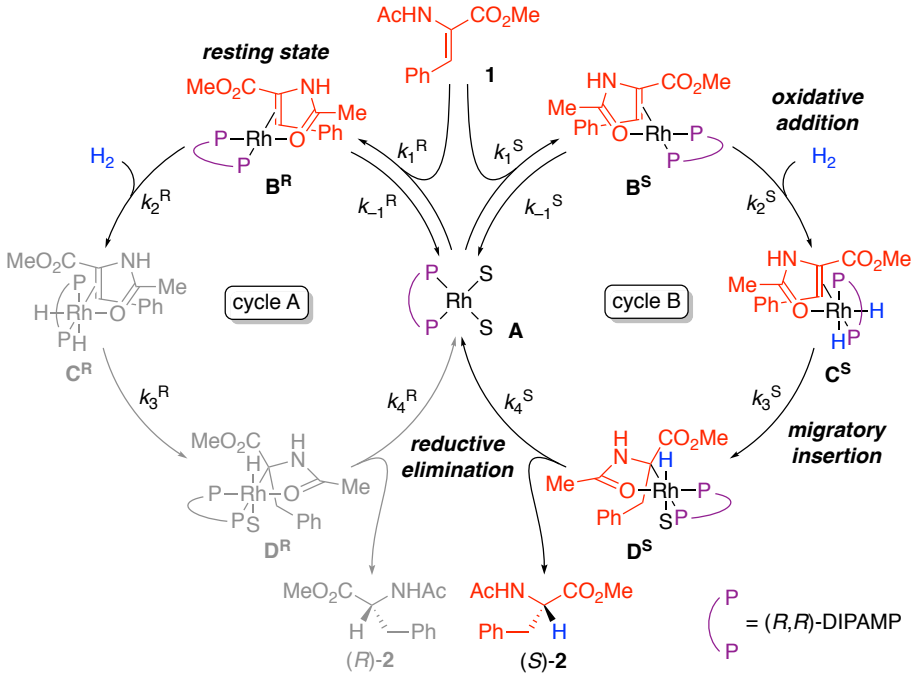


Deguphos 99% ee[1)] Duphos 99% ee[2)] BisP* 99% ee[3)]

1) U. Nagel, *Chem. Ber.*, 119, 3326 (1986). 2) M. J. Burk, *J. Am. Chem. Soc.*, **113**, 8518 (1991); **115**, 10125 (1993). 3) T. Imamoto, *J. Am. Chem. Soc.*, **120**, 1635 (1998).

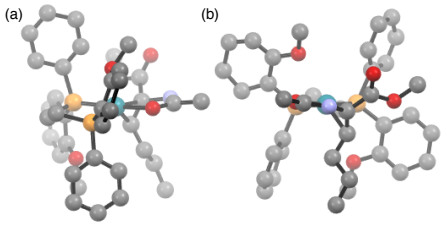
- Commonly, 5-membered chelation is favorable to the asymmetric hydrogenation of α-(*N*-acylamino)acrylates.
- Alkyl substituent, which is electron-donating, is preferable for enhancing the catalytic activity to aryl one, because the rate-determining oxidative addition is accelerated by the resulting electron-rich phosphorus. However, the alkyl group is disadvantageous to create the rigid chiral reaction field, because it is flexible.
- Nowadays, a broad range of chiral ligand, including monophosphine, amino-phosphine, phosphoramidite ones.

(iii) Reaction mechanism of the asymmetric hydrogenation with Rh–DIPAMP catalyst

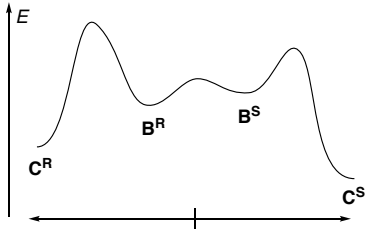


J. Halpern, *J. Am, Chem. Soc.*, **109**, 1746 (1987).

- The hydrogenation of **1** with (*R*,*R*)-DIPAMP–rhodium catalyst yields (*S*)-**2** as the major enantiomeric product.
- The hydrogenation starts from the coordination of substrate **1** on the solvated rhodium(I) cation **A**. Then, the **1**–rhodium(I) **B** undergoes the oxidative addition of H_2 to give dihydridorhodium(III) **C**. The C–C double bond on rhodium inserts into one of the Rh–H bonds. The remaining hydride and alkyl ligand are eliminated from intermediate **D** to form another C–H bond.
- The diastereoisomeric intermediates $\mathbf{B^R}$ and $\mathbf{B^S}$ are in equilibrium. The alkene–rhodium(I) $\mathbf{B^S}$ is less thermodynamically stable than $\mathbf{B^R}$, which leads to the formation of the minor enantiomer (*R*)-**2**.



Crystal structure of {Rh(substrate)[(*R*,*R*)-dipamp]}BF_4 $\mathbf{B^R}$ (All H atoms and BF_4 are omitted for simplification). (a) View adjusted to $\mathbf{B^R}$ in the above scheme. (b) Front view.



Energy diagram for the oxidative addtions of diastereoisomeric intermmediates $\mathbf{B^R}$ and $\mathbf{B^S}$.

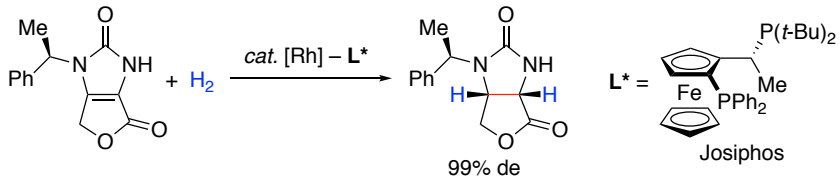
J. Halpern, C. R. Landis, *Organometallics*., **9**, 1392 (1990).

- However, $\mathbf{B^R}$ is too inert to undergo the oxidative addition of H_2. Therefore, molecular hydrogen preferentially reacts with $\mathbf{B^S}$, leading to the selective formation of (*S*)-**2**.
- When $\mathbf{B^S}$ is consumed, the remaining $\mathbf{B^R}$ isomerizes to the more reactive $\mathbf{B^S}$ to keep the equilibrium between $\mathbf{B^R}$ and $\mathbf{B^S}$.
- **Caution! Don't generalize the above mechanism for asymmetric hydrogenation.** Profile of the asymmetric hydrogenation strongly depends on chiral ligand and reaction conditions.

T. Imamoto, *J. Am. Chem. Soc.*, **122**, 7183 (2000); **130**, 2560 (2008); *ACS Catal.*, **5** 2911 (2015).

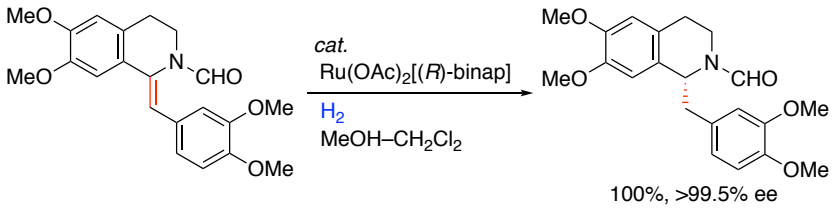
(iv) Asymmetric hydrogenation of other alkenes

- Nowadays, a broad range of prochiral alkenes can be hydrogenated with high enantioselectivities through asymmetric catalysis. The highly enantioselective catalysts have been applied to the synthesis of various useful compounds.

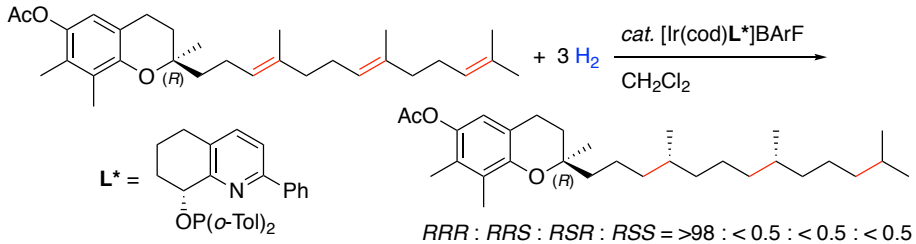


99% de Josiphos

R. Imwinkelried, *Chimia*, **51**, 300 (1997); EP 602653 (1994).



R. Noyori, H. Takaya, *J. Am. Chem. Soc.*, **108**, 7117 (1986); *J. Org. Chem.*, **59**, 297 (1994).



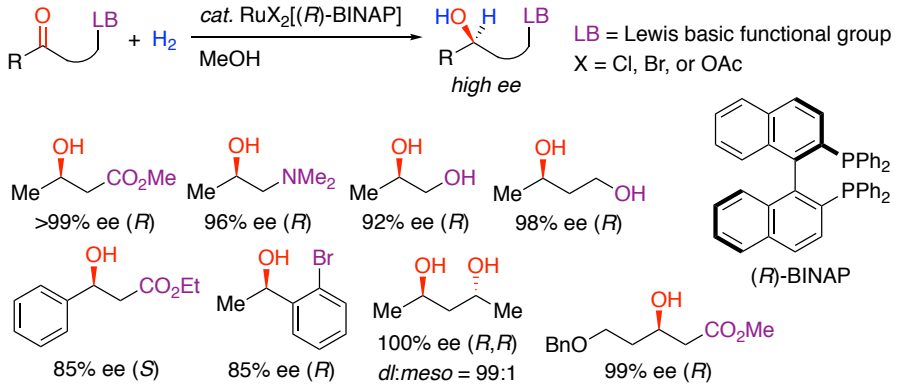
A. Pfaltz, *Science*, **311**, 642 (2006).

(2) Catalytic asymmetric hydrogenation of ketones

- Ketone carbonyl groups can be reduced with molecular hydrogen by transition-metal complex catalysts, such as $RhCl(PPh_3)_3$ and $RuCl_2(PPh_3)_3$.
- The reaction pathway depends on the catalyst or conditions. In most cases, the monohydridometal species seems to participate in the catalytic cycle.

(a) Asymmetric hydrogenation of functionalized ketones

(i) General

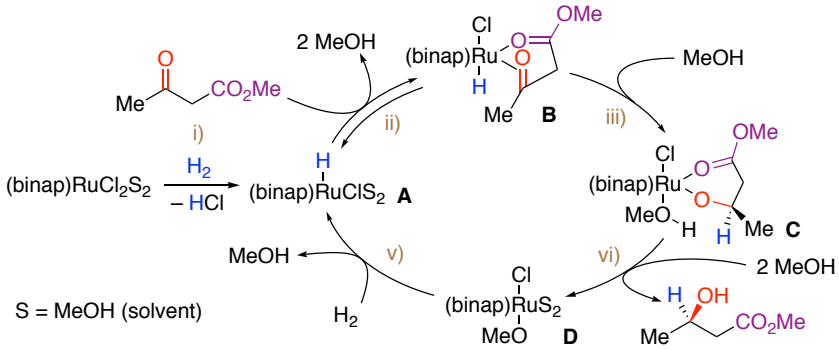


R. Noyori, H. Takaya, S. Akutagawa, *J. Am, Chem. Soc.*, **109**, 5856 (1987); **110**, 629 (1988).

- Various ketones bearing a Lewis basic functional group at α-, β-, or γ-position are converted the corresponding chiral secondary alcohols with high enantiomeric excesses through the chiral BINAP–ruthenium catalysis.

(ii) Mechanism

- The following catalytic cycle was proposed for the ruthenium-catalyzed asymmetric hydrogenation of functionalized ketones.



R. Noyori, *Angew. Chem. Int. Ed.*, **40**, 40 (2001); *Proc. Nat. Acad. Sci.*, **101**, 5356 (2004).

i) Generation of monohydridoruthenium(II) species **A** from the catalyst precursor

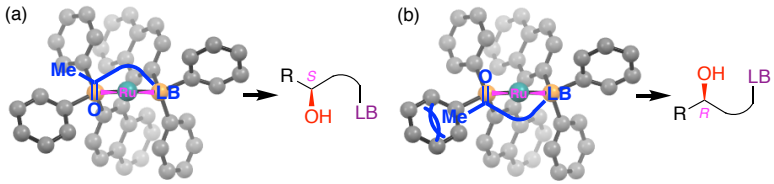
ii) Coordination of the substrate: The ketone carbonyl coordinates to the ruthenium through its π-bond in η^2 manner because of the following migratory insertion.

iii) Migratory insertion of ketone: The stereoselectivity is determined in this process.

iv) Methanolysis of the ruthenium alkoxide **C**: The product is eliminated from Ru.

v) Regeneration of **A**: The ruthenium methoxide **D** induces the heterolysis of molecular hydrogen.

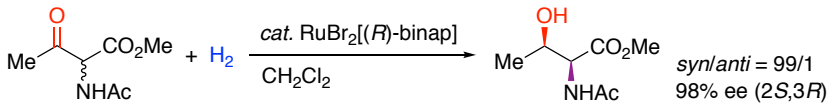
- In the intermediate **B**, the ester carbonyl oxygen, which is Lewis basic, coordinates to the ruthenium and works as the directing group. The coordination results in restricting the conformation of the substrate in the TS of the following migratory insertion.



3D models of the interaction between (*S*)-BINAP–Ru and the substrate. (a) The model leading to (*S*)-alcohol (major product). (b) The model leading to (*R*)-alcohol (minor product).

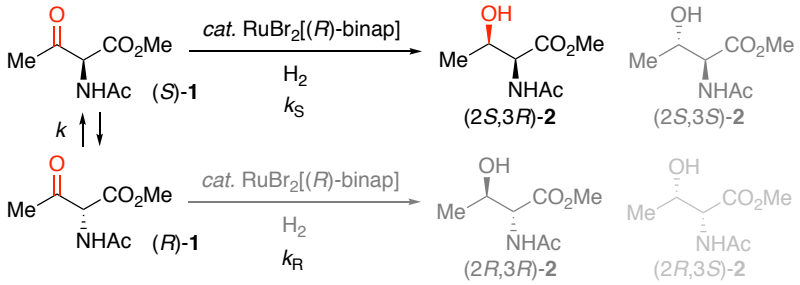
- In the model (b) leading to the minor enantiomer, the methyl group on the carbonyl carbon undergoes the steric repulsion from one of *P*-phenyl groups of BINAP. Therefore, the model (a) is preferable to the model (b).

(iii) Dynamic kinetic resolution in asymmetric hydrogenation



R. Noyori, S. Akutagawa, *J. Am. Chem. Soc.*, **111**, 9134 (1989); **115**, 144 (1993).

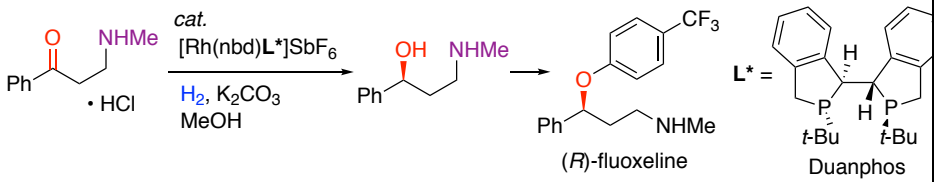
- Racemic α-substituted β-keto esters are converted to α-substituted β-hydroxy ester in high diastereoselectivities as well as high enantioselectivities.
- Commonly, the β-keto ester is possible to racemize through their enol during the hydrogenation.



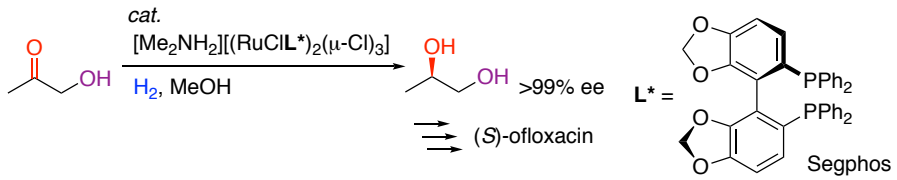
- The hydrogenation of **1** proceeds in similar manner to that of b-keto esters to give the product bearing *S* configuration at its α-carbon ($k_S >> k_R$).
- The major stereoisomer (2*S*,3*R*)-**2** will be selectively obtained from the asymmetric hydrogenation of racemic **1**, when its racemization is much faster than the hydrogenation of (*R*)-**1** with the chiral catalyst ($k >> k_R$).

(iv) Applications

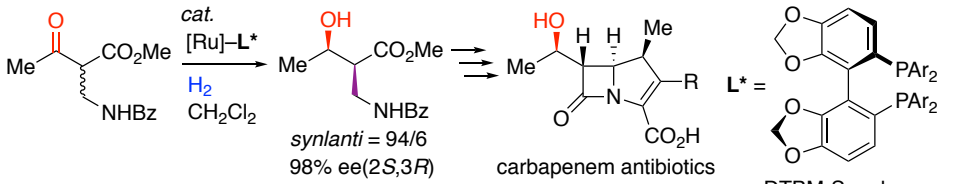
- The highly enantioselective hydrogenation of functionalized ketones has been applied to the synthesis of various useful biologically active compounds, including medicines.



X. Zhang, *Angew. Chem. Int. Ed.*, **44**, 1687 (2005).



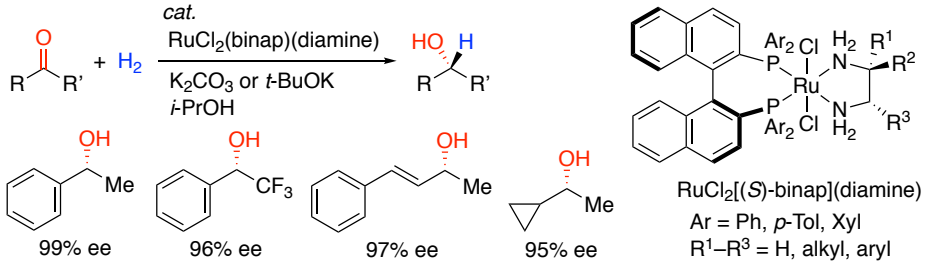
T. Saito, *Adv. Synth. Catal.*, **343**, 264 (2001).



T. Saito, *Adv. Synth. Catal.*, **343**, 264 (2001).

(b) Asymmetric hydrogenation of simple ketones

(i) General

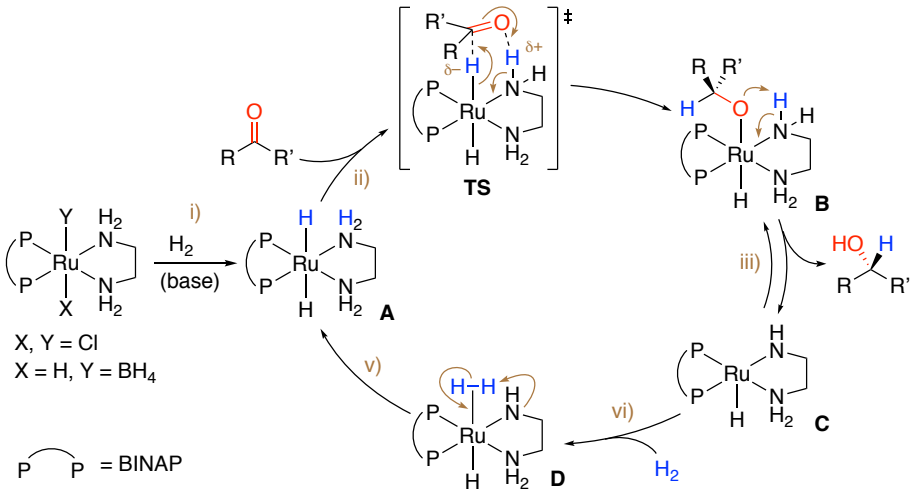


R. Noyori, *J. Am. Chem. Soc.*, **117**, 2675 (1995); **120**, 13529 (1998);.**124**, 6508 (2002).

- Simple ketones, which has no directing group, had been formidable substrates for the catalytic asymmetric hydrogenation as compared to the functionalized ketones.
- RuX2(bisphosphine)(1,2-diamine)-type catalyst allows the chemoselective hydrogenation of ketones. This catalyst is compatible with various functional groups, including nitro, olefin, and cyclopropane.

(ii) Mechanism

- The hydrogenation through the RuX_2(bisphosphine)(1,2-diamine)-type catalyst proceeds through an outer-sphere mechanism.



R. Noyori, *J. Am. Chem. Soc.*, **125**, 13490 (2003); S. H. Bergens, *J. Am. Chem. Soc.*, **130**, 11979 (2008).

i) Generation of dihydridoruthenium(II) species **A** (or **B**) from the catalyst precursor

ii) Transfer of hydride (on Ru) and proton (on N) to ketone: The nucleophilic attack of the hydride to the carbonyl carbon takes place simultaneously with the protonation of carbonyl oxygen through 6-membered transition state **TS**. The resulting alcoholic product is immediately converted to ruthenium alkoxide **B**.

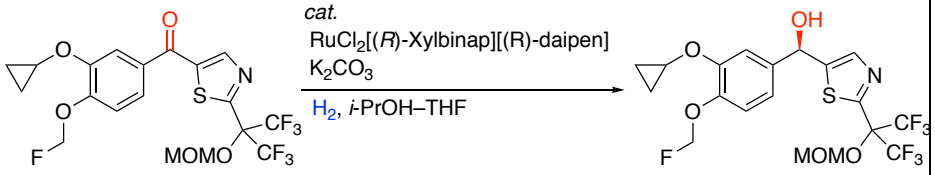
iii) Protonation of alkoxide on ruthenium: One of the protons on N reacts with the alkoxo ligand to release the desired product.

iv) Formation of molecular hydrogen complex: The coordination of H_2 on Ru leads to the decrease in its pK_a.

v) Regeneration of **A**: The H–H bond in D

(iii) Applications

- $RuCl_2$(binap)(diamine)-type catalysts are often used for the preparation of various biologically active compounds and drug candidates.



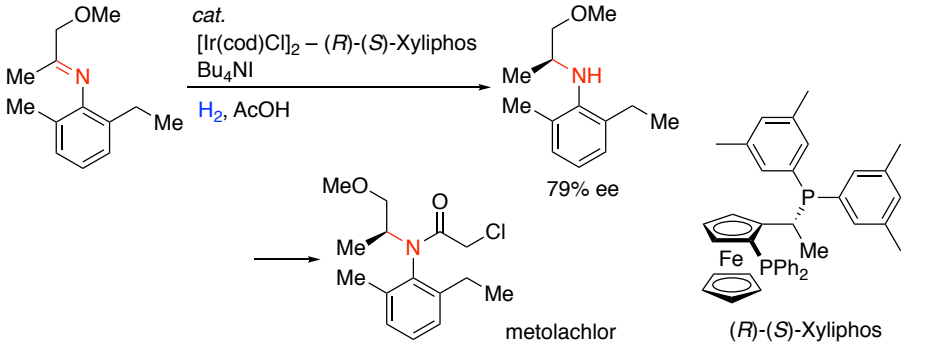
⇌ an FDE-IV inhibitor

C.-y. Chen, *Org. Lett.*, **5**, 5039 (2003).

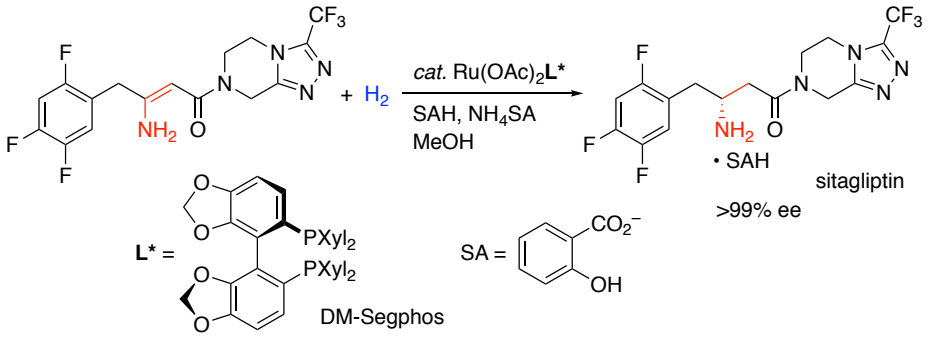
(3) Catalytic asymmetric hydrogenation of imines

- As with ketones, imines are also reduced with molecular hydrogen through transition-metal catalysis.
- Enantioselective hydrogenation of imines is useful for preparing optically active amines, which are often seen in many useful compounds.
- However, the hydrogenation of imines is more formidable than those of alkenes and ketones. The amine product commonly poisons the metal catalyst, because the lone pair on its N strongly interacts with the metal atom.
- Many excellent chiral catalysts have been developed for the asymmetric hydrogenation of specific imines, which can be converted into useful chiral compounds.

Examples



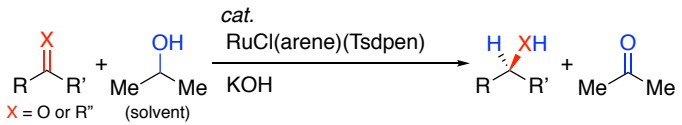
H.-U. Blaser, *Adv. Synth. Catal.*, **344**, 17 (2002).

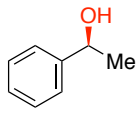


D. Steinhuebel, K. Matsumura, *J. Am. Chem. Soc.*, **131**, 11316 (2009).

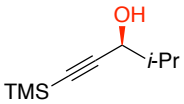
(4) Asymmetric reduction other than hydrogenation

(a) Transfer hydrogenation of ketones and imines

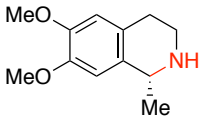




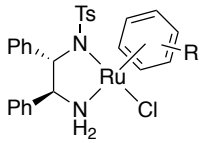
97% ee



99% ee



95% ee (with HCO_2H/Et_3N)

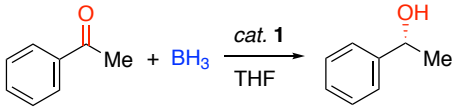


RuCl(arene)[(S,S)-Tsdpen]

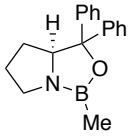
R. Noyori, *J. Am. Chem. Soc.*, **117**, 7562 (1995); **118**, 4916 (1996); **119**, 8738 (1997).

- The transfer of hydrogen from secondary alcohols to ketones, Meerwein–Ponndolf–Varley-type reduction, is known to proceed in the presence of not only Lewis acid but also transition-metal complex catalyst.
- Optically active Ru(η^6-arene)(*N*-Ts-diamine) complexes work as useful catalysts for the enantioselective transfer hydrogenation of various ketones and imines with 2-propanol.
- The transfer hydrogenation with 2-propanol is an equilibrated reaction. Therefore, the prolonged reaction time and/or high concentration of substrate are disadvantageous for high enantioselectivity.
- A mixture of formic acid and triethylamine is also usable for the asymmetric transfer hydrogenation with Ru(η^6-arene)(*N*-Ts-diamine) catalyst. In this case, the reaction is irreversible.

(b) CBS (Corey–Bakshi–Shibata) reduction



96.5% ee



oxazoborolidine **1**

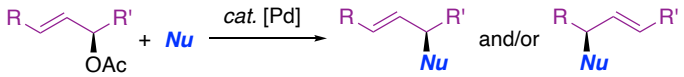
E. J. Corey, *J. Am. Chem. Soc.*, **109**, 5551 (1987); **109**, 7925 (1987); *Angew. Chem. Int. Ed.* **37**, 1986 (1998).

- Various ketones are reduced to the chiral secondary alcohols with high enantiomeric excesses through CBS reduction.
- In the CBS reduction, oxazaborolidine **1** works as the Lewis acid catalyst for the borane reduction of the carbonyl.

(5) Stereochemistry in Tsuji–Trost reaction

(a) Tsuji–Trost reaction

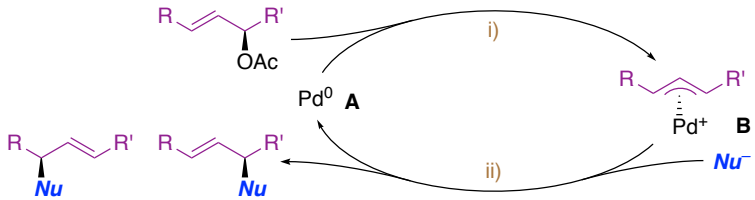
Overview



G. Hata, *J. Chem. Soc., Chem. Commun.* **1970**, 1392; K. E. Atkins, *Tetrahedron Lett.* **1970**, 3821.

- Palladium complexes catalyze the nucleophilic substitution of allylic carboxylates (or ethers, alcohols), which are regarded as inert substrates for nucleophilic substitution under mild conditions.
- Transition metals other than palladium, *e.g.* iridium, molybdenum, are also known to work as the catalyst for the allylic substitution.
- Various Lewis basic compounds, *e.g.* stabilized carbanions, primary and secondary amines, phenoxides, can react as nucleophiles in the catalytic allylic substitution to yield the corresponding allylated products.
- The nucleophiles can react with the allylic electrophiles in S_N2 and/or S_N2' manner. The site-selectivity of the nucleophilic attack is strongly affected by the substituents on allylic group, choice of catalyst, and reaction conditions
- When the allylic substrate is chiral, the stereochemistry looks to be retained during the palladium-catalyzed reaction.

Mechanism



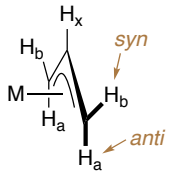
i) Oxidative addition of the allylic C–O bond to palladium(0) **A** to form the (π-allyl)palladium(II) intermediate **B**

ii) Attack of a nucleophile on a terminus of the π-allyl ligand in **B** to give the substitution products.

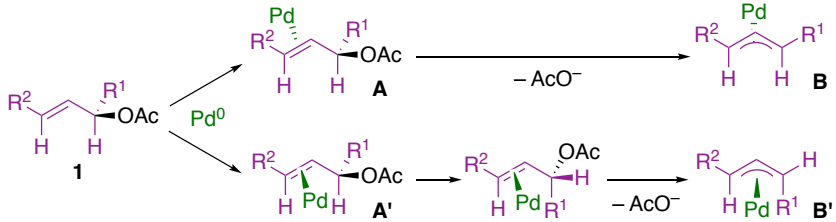
(b) Stereochemistry in the Tsuji–Trost reaction of chiral allylic electrophiles

1) Structure of (π-allyl)metal intermediate

- In the intermediate, delocalized allyl anion binds to a metal atom through its three carbon atoms. The metal is positioned on the C–C–C plane of the allyl ligand.
- Two hydrogen atoms on each allylic terminus is non-equivalent. Their positions are defined *syn* or *anti* based on the substituent (or atom) on the central carbon.

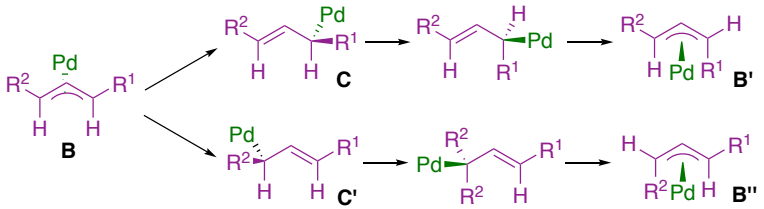


2) Oxidative addition of allylic electrophiles: formation of (π-allyl)palladium

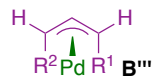


- The C–C double bond of the allylic ester **1** interacts with the palladium(0) atom.
- The palladium(0) attacks on the backside of the allylic C–O bond in **A** when the metal is located at the antiperiplaner of the bond through the bond rotation.
- Virtually, the process proceeds through S_N2-like (or S_N2'-like) pathway to form (π-allyl)palladium **B**.
- When **1** is optically active (R^1, $R^2 \neq H$) and $R^1 \neq R^2$, its oxidative addition is possible to yield two diastereomeric (π-allyl)palladiums **B** and **B'**. However, steric repulsion between R^1 and Pd is ordinarily unfavorable for the formation of **B'**.

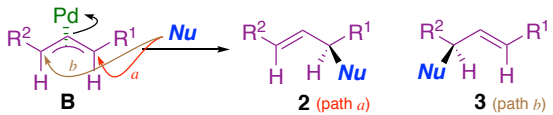
3) Isomerization of (π-allyl)palladium



- π-Allyl complex **B** is possible to reversibly isomerize to (σ-allyl)palladium **C** although **B** is generally much more thermodynamically stable than **C**.
- Complex **B** is possible to isomerize to its diastereomeric **B'** and **B"** through the π-σ-π interconversion and related bond rotations in **C** (or **C'**). **B'** or **B"** further isomerize to **B'"**.
- In principle, no racemization of **B** should be observed during the π-σ-π isomerization, when **B** is optically active.



4) Nucleophilic attack on (π-allyl)palladium

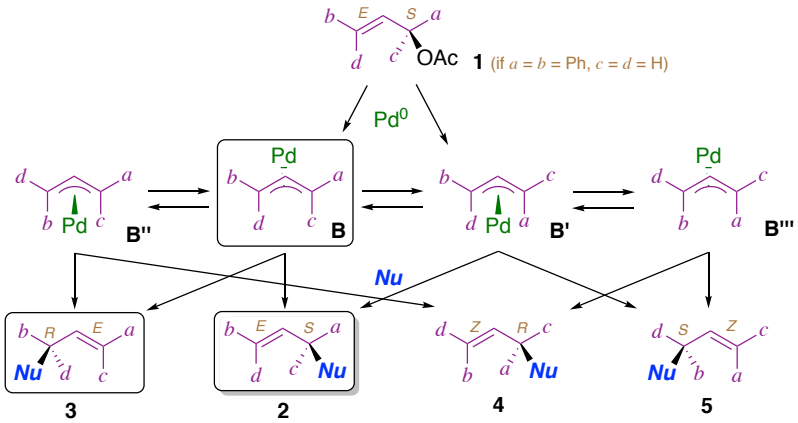


- A nucleophile attacks one of the allylic termini in **B** to form the allylic substitution product **2** or **3**. The site-selectivity is normally affected by the steric demand of substituents R^1 and R^2.
- The nucleophile accesses the allyl ligand from the opposite side of the palladium.

This process virtually proceeds through S_N2-like pathway.

- The stereochemistry of this process should be inversion when complex **B** is optically active ($R^1 \neq R^2$).
- When $R^1 = R^2 \neq H$, the products **2** and **3** are enantiomeric each other.
- The stereochemistry of non-reacting terminus is reflected in the *E*/*Z* isomerism of the allylation product.

4) Stereochemical overview of Tsuji-Trost reaction

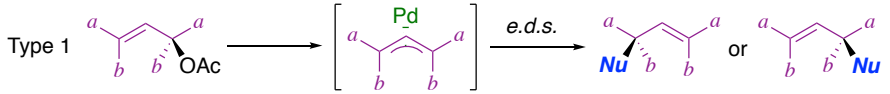


- Four products, **2**–**5**, can be obtained from the Tsuji-Trost reaction of **1**, when the substrate is optically active, $a \neq c$, $b \neq d$, and $a \neq b$ (or $c \neq d$). No formation of the enantiomers of **2**–**5** should be observed during the reaction.
- When $b = d$ (= H), the achiral product **3** will be obtained as the sole product from the reaction of optically active **1**, because the nucleophile attacks on the less hindered allylic terminus of **B**. Furthermore, intermediate **B** is racemized (isomerized to **B''**) through the π-σ-π interconversion. In this case, **B''** is the enantiomer of **B**.
- When $a = b$ and $c = d$, racemic **2** will be obtained from the reaction of **1**, because **3** is the enantiomer of **2**. Furthermore, the chirality of **1** is lost in the oxidative addition process, because intermediate **B** is achiral.
- When $a > c$, $b > d$ (sterically), formation of **4** and **5** would be less preferable to those of **2** and **3**, because steric repulsion between the palladium and substituent a or b hamper the π-σ-π isomerization of **B**.

(c) Enantioselective Tsuji–Trost reactions with asymmetric catalysis.

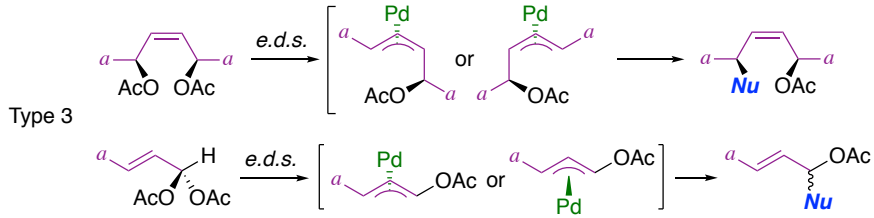
Overview

- Although many asymmetric catalyses had been developed for Tsuji–Trost reactions, they can be loosely classified under three categories.
- One creates a new stereogenic center on the allylic substrates (Type 1). In this case, the allylpalladium intermediate possesses C_S-symmetric π-allyl ligand, although the allylic substrate is chiral (but racemic). Therefore, the allylic substrate loses its own chirality through the formation of (π-allyl)palladium intermediate.



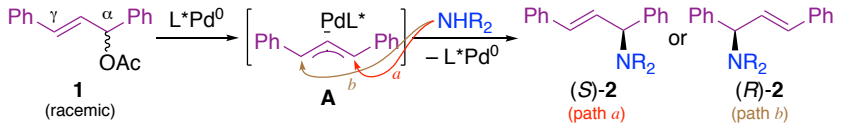
- Another type is the reaction creating a setereogenic center on the nucleophilic substrates (Type 2).

- The third type is the Tsuji–Trost reaction of achiral allylic electrophiles bearing two enantiotopic acetate leaving groups (Type 3). Chiral catalyst distinguishes the two enantiotopic leaving groups to lead enantioselective formation of one of enantiomeric (π-allyl)palladium intermediates. The nucleophile stereospecifically attacks on the allylic terminus to give the desired product with high enantiopurity.

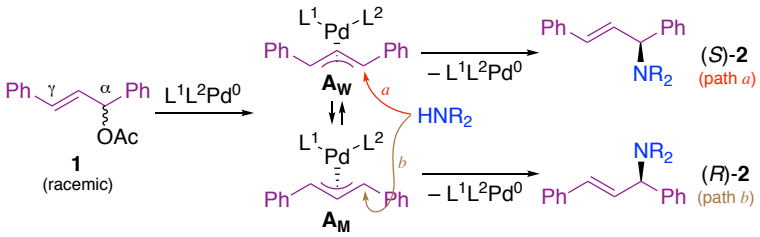


1) Type 1: Enantioselective allylic substitution

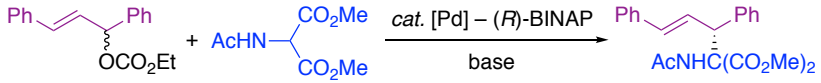
- This type of enantioselective Tsuji–Trost reaction employs the allyl esters **1**, which have the identical substituents at the α and γ carbons.
- A new stereogenic center is generated in the attack of a nucleophile on an allylic terminus. Therefore, the chiral catalyst should control the nucleophilic attack as well as the stereochemical behavior of (π-allyl)metal intermediate **A**.
- Nucleophiles can attack on both α- and γ-allylic termini of **A**. If the α-attack (path a) lead to the formation of (*S*)-**2**, (*R*)-**2** is specifically formed through the γ-attack (path b).
- To achieve high enantioselectivity, the chiral catalyst must control the site selectivity of the nucleophilic attack, when its ligand is C_2-symmetric.

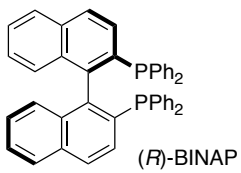


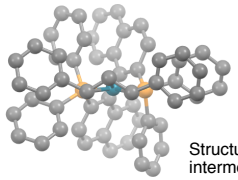
- When the catalyst has a non-symmetric ligand, the diastereoisomerism of **A** (M- vs W-shape) must be controlled in order to achieve high stereoselectivity. For example, the M- and W-shaped intermediate, $\mathbf{A_W}$ and $\mathbf{A_M}$, will provide (*S*)- and (*R*)-**2** respectively, if the chiral catalyst restricts the nucleophilic γ-attack.



Examples

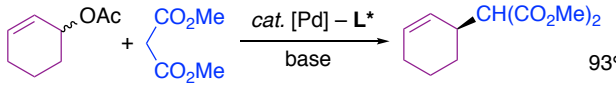


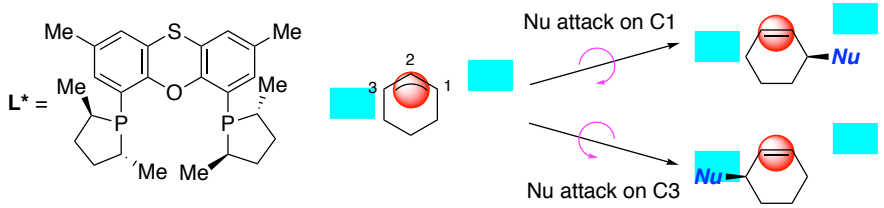




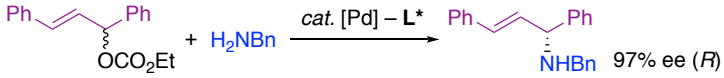
Structure of (π-allyl)palladium intermediate bearing (*S*)-BINAP

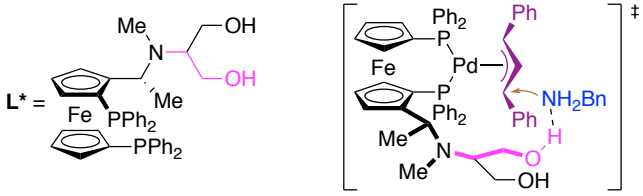
M. Yamaguchi, T. Yamagishi, *Tetrahedron Lett.* **1990**, *31*, 5049.



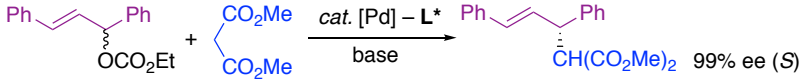


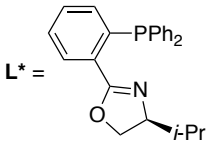
J. A. Osborn, *Angew. Chem. Int. Ed.* **1998**, *37*, 3116.

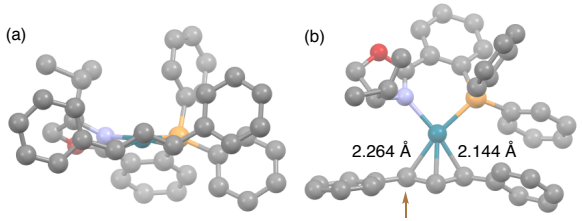




T. Hayashi, *Tetrahedron Lett.* **1986**, *27*, 191; *J. Am. Chem. Soc.* **1989**, *111*, 6301.







Structure of (π-allyl)palladium intermediate bearing L*; (a) front view, (b) top view.

A. Pfaltz, *Angew. Chem. Int. Ed.* **1993**, *32*, 567;
G. Helmchen *Tetrahedron Lett.* **1993**, *34*, 1769; J. M. J. Williams, *Tetrahedron Lett.* **1993**, *34*, 3149.

2) Type 2: Enantioselective allylation of prochiral nucleophiles