$\eta^3$-Allyl Palladium Chemistry
On the Polarization of Allyl-Complexes

Unless in the presence of special bulky ligands (see later the “memory effect” section) palladium usually prefers \( \eta^3 \)-allyl structures, whereas other transition metals (i.e. Rh) prefer \( \eta^1,\eta^2 \)-olefin type structures.
During the syn-anti equilibration switch of the face coordinated to the metal takes place. The process does not bring about switch between the allylic C1 and C3 carbons with respect to the ancillary ligands A and B, but it involves inversion of the C2 orientation with respect to the palladium atom.

\( \eta^3 \)-Allyl-Pd Complexes are Fluxional Compounds

Apparent allyl rotation via \( \eta^3\rightarrow \eta^1\rightarrow \eta^3 \) rearrangement / Pd-C rotation

The process involves \( \eta^3 \rightarrow \eta^1 \) rearrangement, rotation about the C-Pd bond, geometry change around the metal, \( \eta^1 \rightarrow \eta^3 \) rearrangement. Addition of chloride anions can accelerate the apparent allyl rotation via pentacoordination and pseudorotation. Alternatively, ligand dissociation is another possible pathway for apparent allyl rotation.
Generation of $\eta^3$-Allyl Palladium Complexes

Via Pd(0)

$\text{ArX} \xrightarrow{\text{[Pd(0)]}} \text{Ar[Pd]X} \xrightarrow{\text{[Pd(0)]}} \text{ArC} \xrightarrow{\text{[Pd(0)]}} \text{Ar[Pd]X}$

$\xrightarrow{\text{Nu, PdX}_2}$

$\xrightarrow{\text{Nu}^{\ominus}}$

$\xrightarrow{\text{[Pd]X}}$

$\xrightarrow{\text{[Pd]X}}$

Via Pd(II)

$\xrightarrow{\text{Base, PdX}_2}$

$\xrightarrow{\text{Base}}$

$\xrightarrow{\text{Base XH}}$

G. Poli
Oxidative Addition of Allyl Acetates to Pd(0)

Generation of π-allyl-Pd complexes from allylic acetates is reversible and thermodynamically disfavored.

Many allylic systems undergo oxidative addition in the presence of Pd(0) to generate a $\eta^3$-allyl-Pd complex. This reaction is usually reversible and the extent of its equilibrium depends on the nature of the leaving group.
Facial Exchange in the $\pi$-Allyl Complex

Displacement of palladium from the $\pi$-allyl complex by Pd(0)

Rapid isomerization to a 45 : 55 equilibrium mixture is observed even at -15°C starting from either complex

Inversion mechanism: Pd(0) approaches anti with respect to the acetate moiety.

\[
\text{Me} = \text{Ph} = \text{Pd(dppe)} + \text{NaBF}_4 \rightarrow [\text{Pd} + \text{Ph} \text{Ph} \text{Ph} \text{Ph} + \text{BF}_4^-] ^+ \\
\text{58% ee} \rightarrow \text{47% ee}
\]
Oxidative Addition of Pd(0) on Allyl Systems

Stereoelectronic effects are important.
In conformationally locked cyclohexanes: the equatorial isomer is unreactive

Reactions of $\eta^3$-Allyl Palladium Complexes

In all these cases Pd(0) is regenerated and transformation can be catalytic in Pd
Non-stabilized Nucleophiles (pKa > 25)

ionization (formation of the \(\pi\)-allyl complex) and nucleophilic attack are not similar processes. Pd(0)Ln approaches the alkene anti to the leaving group, to generate the \(\pi\)-allyl complex. Subsequently, the nucleophile first attacks palladium (inner sphere, transmetalation), then it undergoes reductive elimination The two latter steps proceed with retention mechanism. Thus, starting from a sterogenic substrate overall inversion is observed.

Global inversion of configuration is observed.

Stabilized Nucleophiles (pKa < 25)

When Nu is an active methylene the reaction is named allylic alkylation or Tsuji-Trost reaction.

Ionization and nucleophilic attack are similar processes. However, the former step is usually reversible (as metal-alkene coordination), whereas the latter is normally irreversible. Pd(0)L \_n\_ approaches the alkene anti to the leaving group, to generate the \( \pi \)-allyl complex. Then, the nucleophile approaches the \( \pi \)-allyl moiety anti to Pd(II)L\_n\_, (outer sphere). Thus, starting from a sterogenic substrate overall retention (via double inversion) is observed.

\( \eta^3 \)-allyl-Pd complexes are generated from acetates only in very small amounts. However, the irreversible reaction with the nucleophile gradually drives the reaction to completion.
The Seminal Paper

Organic Syntheses by Means of Noble Metal Compounds

XVII. Reaction of \( \pi \)-Allylpalladium Chloride with Nucleophiles

Jiro Tsuji, Hidetaka Takahashi and Masanobu Morikawa

Basic Research Laboratories, Toyo Rayon Company, Ltd.

Kamakura, Japan

(Received 24 August 1965)
Active Methylenes: Typical Soft Nucleophiles

Double inversion mechanism (with or without anti-syn equilibration)

\[
\text{Me} - \text{C} = \text{Me} \quad \text{Ph} \\
\text{OAc} \quad \text{Pd(0) dppe (inversion)} \\
\text{Me} - \text{C} = \text{Me} \quad \text{Ph} \\
\text{OAc} \quad \text{Pd(0) dppe (inversion)}
\]

\[
\begin{align*}
\text{Me} & \quad \text{Me} - \text{Ph} \quad \text{Ph} \\
\text{OAc} & \quad \text{Me} \quad \text{Pd(0) dppe (inversion)} \\
\text{Me} & \quad \text{Me} - \text{Ph} \quad \text{Ph}
\end{align*}
\]

\[
\begin{align*}
\text{Me} & \quad \text{Me} - \text{Ph} \\
\text{OAc} & \quad \text{Me} \quad \text{Pd(0) dppe (inversion)} \\
\text{Me} & \quad \text{Me} - \text{Ph}
\end{align*}
\]


G. Poli
Ionization of the Allylic System to the $\eta^3$-Allyl Complex

Proof of the mechanism with this particular allylic acetate

Complete Transfer of the Stereoinformation

Starting from a stereogenic acetate


G. Poli
Complete transfer of the stereochemical information can be obtained if the transiently formed π-allyl-Pd complex can be trapped before it can equilibrate. The degree of transfer of the stereochemical information depends, inter alia, on the concentration of the Pd catalyst: the higher the Pd concentration the lower the transfer of the stereochemical information.

G. Poli
Allylic Alkylation via Titanated Nucleophiles

Poli, G.; Giambastiani, G.; Mordini, A.

J. Org. Chem. 1999, 64, 2962-2965

Ph\(\text{CO}_2\text{Et}\) + CO\(\text{Et}_2\text{CO}\) → Ph\(\text{CO}_2\text{Et}\)

\[\text{Ph-CHCH}_2\text{CO}_2\text{Et} \xrightarrow{\text{Pd}(\text{dba})_3 (0.05 \text{ eq}), \text{PPh}_3 (0.05 \text{ eq.}), \text{Ti(OPr-i)}_4 (1.3 \text{ eq.)}} \xrightarrow{\text{CH}_2\text{Cl}_2 \text{ reflux 9h}} \text{Ph-CHCH}_2\text{CO}_2\text{Et}\]

R' = OAc or i-PrO

Poli, G.; Giambastiani, G.; Mordini, A. J. Org. Chem. 1999, 64, 2962-2965

G. Poli
Direct Use of Allylic Alcohols


It is proposed that water activates the allyl alcohol via hydration of the hydroxy group and stabilizes the resulting hydroxide ion by strong solvation.

Generation of the $\eta^3$-Allyl Pd Complex after a Carbopalladation

484 discrete mechanistic steps !!!

\[
\begin{align*}
\text{E} + \text{CO}_2\text{Et} + \text{PhI} & \rightarrow \text{Ph} + \text{PdI} \\
\text{E} = \text{CO}_2\text{Et} & \\
\text{PhI} & \rightarrow \text{Ph} + \text{H[Pd]I} \\
\text{Pd} & \rightarrow \text{PdH} \text{ migration} \\
\text{H[Pd]I} & \rightarrow \text{H}[\text{Pd}]I
\end{align*}
\]

\[\text{i : Pd(dba)}_2, \text{NaHCO}_3, \text{NBu}_4\text{Cl}, \text{DMSO}, 80^\circ\text{C}\]


G. Poli
In Situ Generation of Base

With allylic oxiranes, carbonates, and phenates (see next sheet) as substrates use of a base can be avoided since the anion generated during ionization can deprotonate the pronucleophile.

\[
\begin{align*}
\text{OAc} & \quad + \quad \text{CO}_2\text{Me} \\
\text{Pd}_2(\text{dba})_3, \text{TMPP} & \quad \text{rt, 72\%} \\
\text{rt, 72\%} & \quad \text{89 : 11}
\end{align*}
\]


G. Poli
In Situ Generation of Base

With allylic acetates use of the base can be also avoided if the pro-nucleophile is sufficiently acidic ($pK_a \text{ DMSO} \leq 12$).


pK$_a$ Scale of Pro-nucleophiles


G. Poli
The Memory Effect

Isomerization of the \( \pi \)-allyl intermediates is slow when bulky ligands are used such as MeO-MOP or \( \text{t-Bu}_3\text{P} \)

\[
\begin{align*}
\text{D-OAc} & + \text{NaCMe(CO}_2\text{Me)}_2 \quad \xrightarrow{\text{cat}} \quad \text{D} \quad \xrightarrow{\text{(R)-MeO-MOP}} \quad \text{83} : \quad \text{17}
\end{align*}
\]

\[
\begin{align*}
\text{D-OAc} & + \text{NaCMe(CO}_2\text{Me)}_2 \quad \xrightarrow{\text{cat}} \quad \text{D} \quad \xrightarrow{\text{(R)-MeO-MOP}} \quad \text{17} : \quad \text{83}
\end{align*}
\]


G. Poli
Regioselectivity of Addition and the Memory Effect

Normally, Pd-catalyzed allylation of nucleophiles with substituted $\pi$-allyl systems occurs with preference at the less substituted allylic terminus to give the linear product as the major compound. The bulkier the nucleophile, the higher the preference for the linear product. In line with the fact that a common $\pi$-allyl-Pd intermediate is involved, the final product ratio is independent of the regiochemistry of the chosen starting substrate.

However, in the presence of special bulky monophosphine ligands, allylation takes place preferentially on the C atom originally occupied by the leaving group. Such a behavior, which is more pronounced with the branched substrate, is named “memory effect”, and indicates that, in contrast to the previous case, different $\pi$-allyl-Pd intermediates are implicated as a function of the starting regioisomeric substrate used.
Regioselectivity of Addition and the Memory Effect

No memory effect (no bulky monophosphines as ligands)

Memory effect (special bulky monophosphines as ligands)

G. Poli
Regioselectivity of Addition and the Memory Effect

\[
\text{Ph} = \text{MeO} + \text{NaCMe(CO}_2\text{Me)}_2 \xrightarrow{\text{L, THF, rt}} \text{Ph} = \text{MeO} + \text{MeO}_2\text{C} = \text{CO}_2\text{Me}
\]

\[
\text{Ph} = \text{MeO} + \text{NaCMe(CO}_2\text{Me)}_2 \xrightarrow{\text{L, THF, rt}} \text{Ph} = \text{MeO} + \text{MeO}_2\text{C} = \text{CO}_2\text{Me}
\]

\[
L = \text{PPh}_3, \quad 91 \quad 9
\]

\[
L = (R)-\text{MeO-MOP}, \quad 79 \quad 21
\]

\[
L = \text{PPh}_3, \quad 92 \quad 8
\]

\[
L = (R)-\text{MeO-MOP}, \quad 23 \quad 77
\]

Rationale for the Memory Effect

When \( L \) is a bulky monophosphine the generated \( \pi \)-allyl complex features \( L \) and \( R \) in anti positions. Furthermore, apparent allyl rotation is slow compared to the addition of the nucleophile.

Poli, G. Scolastico C. Chemtracts - Org.Chem. 1999, 12, 822-836
Poli, G. Scolastico C. Chemtracts - Org.Chem. 1999, 12, 837-845
Pd-catalyzed allylation of oxygen-based nucleophiles is also possible. However, good results in intermolecular O-allylations can be obtained only by enhancing the nucleophilicity of these coupling partners via their transformation into metal (i.e. Zn or Sn) alkoxides.

\[
\text{CO}_2\text{Me} + \text{PhOH} \xrightarrow{\text{ZnEt}_2 \text{(0.5 eq.) THF}} \text{CO}_2\text{Me} + \text{CO}_2\text{Me} \\
\text{L} = \begin{array}{c}
\text{Ph} \\
\text{Ph}
\end{array}
\]

\[
Pd(OAc)_2 / L > 40 : 1 \quad (70\%)
\]

\[
Pd(PPh_3)_4 \quad 1 : 2 \quad (20\%)
\]

Several nitrogen-based nucleophiles attack $\eta^3$-allylpalladium complexes thereby generating allylic amines or amine derivatives. These nucleophiles include primary (but not ammonia) and secondary amines, carboxamides, sulfonamides, and azides. The reaction proceeds under conditions similar to the Pd-catalyzed allylic alkylation (Tsuji-Trost reaction). The allylic amination reaction may be a reversible step. In other words, the resulting allylic amine may, in the presence of Pd(0), give back the parent $\eta^3$-allylpalladium complex.

Primary and secondary amines can add as such, whereas the less nucleophilic carboxamides or sulfonamides usually need prior deprotonation.

Allylation of Nitrogen Nucleophiles

\[
\begin{align*}
\text{N} & \quad \text{O} \\
\text{s-Bu} & \quad \text{Ts} \\
\text{Ph} & \quad \text{N} \\
\text{OAc} & \quad \text{O} \\
\text{s-Bu} & \quad \text{Ts} \\
\text{Ph} & \quad \text{N} \\
\text{OAc} & \quad \text{O} \\
\text{cis : trans} & \quad 95 : 5 \\
\text{less stable} & \quad \text{more stable}
\end{align*}
\]

\[\text{Pd(0)} \quad \text{Pd(0)}\]

Allylation of Nitrogen Nucleophiles (Allylic Amination)

\[ \text{OAc} + \text{H}_{2}\text{O, K}_2\text{CO}_3 \rightarrow \text{H}_2\text{O, K}_2\text{CO}_3 \]


The latter example shows that even allylic alkylation, in special cases, can be a reversible process.

G. Poli
Indirect Preparation of Primary Allylic Amines

The direct Pd-cat allylation of ammonia is not a clean reaction. However, indirect preparation of primary allylic amines via Pd-catalysis is possible using ammonia “surrogates”.


Wang, Y.; Ding, K. J. Org. Chem. 2001, 66, 3238
σ-donor ligands raise the antisymmetrical MO and slightly lower the symmetrical one, while π-acceptor ligands, owing to back-donation, lower the antisymmetrical MO. Thus, under frontier orbital control, σ-donor ligands favor central carbon atom addition, while π-acceptor ligands direct the addition to the terminal position.

Low-lying unoccupied MO's in \((\eta^3\text{-allyl})\text{PdL}_2\) complex

Antisymmetrical
Lower with π-acceptor ligands

Symmetrical
Lower with σ-donor ligands
However, competition between terminal and central addition may be present only with rather hard nucleophiles. If the energy level of the nucleophile is too low (i.e. if the nucleophile is too stabilized) charge control may override frontier orbital control, and terminal attack is restored.
Enantiodiscrimination in the Allylic Alkylation
Types of Enantiodiscrimination

$\eta^3$-Allyl complex formation (ionization)

- [Pd(0)]$_n$*, $\sigma$ $\sigma$ $\sigma$
  - enantiotopic faces of the starting alkene

- [Pd(0)]$_n$*, $\sigma$
  - enantiotopic allylic leaving groups in the starting meso substrates

- [Pd(0)]$_n$*, $\sigma$
  - enantiotopic geminal allylic leaving groups

Product formation

- [Pd(II)]$_n$*, $\sigma$
  - enantiotopic allylic sites of the meso $\pi$-allyl-moiety in the Pd allyl complexes

- [Pd(II)]$_n$*, $\sigma$
  - enantiotopic faces of the $\pi$-allyl moiety in the Pd allyl complexes

- [Pd(II)]$_n$*, $\sigma$
  - forming stereogenic center
  - enantiotopic faces of the nucleophile

G. Poli
Which is the Best Chiral Catalyst?

**Phosphines:** good $\sigma$-donors and $\pi$-acceptors. They stabilize the monomeric species while providing control over the steric and electronic properties of the system. The different properties of the donor atoms are transmitted to the $\pi$-system through the metal, thus allowing the fine tuning of the reactivity of the substrate.

**Phosphites:** strong back bonding

**Amines:** pure $\sigma$-donors

Bonds trans to $P$ are expected to be longer than bonds trans to $N$.

Predictions are very difficult because: 1) information on the olefinic complexes is not available 2) In palladium catalyzed allylic alkylations, allyl-palladium complexes are often in dynamic equilibrium. On the time scale of the catalytic cycle ligands can dissociate, reassociate, and change their conformations and geometry. When a stabilized nucleophile attacks a $\pi$-allyl-Pd-complex, bond reorganization is also occurring between the ligands and the allylic moiety as the substrate undergoes a change in hapticity. Interactions between the chiral ligands and the allyl fragment during the $\eta_3$-$\eta_2$ reorganization may be just as important as interactions between the allyl fragment and the incoming nucleophile.
Some Chiral Ligands for Pd-cat Allylic Alkylation

Two different concepts:
- Envelopment of the π-allyl moiety by creating a chiral pocket.
- Interaction with the incoming nucleophile.
X-ray Structures of Some $\eta^3$-Allyl Complexes

T. Hayashi et al.

H. Yang et al.
*Organometallics*, 1993, 12, 3485

G. Helmchen et al.

M. Yamaguchi et al.

A. Pfaltz et al.

G. Poli
The reaction is dependent on solvent and counterion. For example, yields and enantioselectivities dropped with toluene as the solvent or in the presence of crown ethers. The enantioselectivity correlates roughly with the leaving group ability: better leaving groups gave poorer enantioselectivities.

Enantioface exchange is not occurring during the reaction. Enantiomeric purity is preserved.

Discrimination of Enantiotopic Faces

\[
\text{Ph} \quad \text{OAc} \quad \text{Ph} \quad \text{R} \quad \xrightarrow{2.5 \% [\text{Pd(allyl)}\text{Cl}]_2, \quad \text{NaCH(CO}_2\text{Me)}_2, \quad \text{Ligand 10 \%}} \quad \text{MeO}_2\text{C} \quad \text{CO}_2\text{Me} \quad \text{Ph} \quad \text{R} \quad \text{Ph} \quad \text{R}
\]

<table>
<thead>
<tr>
<th>R</th>
<th>Yield %</th>
<th>ee %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>95</td>
<td>95</td>
</tr>
<tr>
<td>Ph</td>
<td>88</td>
<td>99</td>
</tr>
<tr>
<td>ClC\text{6H}_4^-</td>
<td>91</td>
<td>&gt;95</td>
</tr>
<tr>
<td>2-Py</td>
<td>89</td>
<td>92</td>
</tr>
<tr>
<td>1-Naphth</td>
<td>96</td>
<td>&gt;96</td>
</tr>
<tr>
<td>Mesityl</td>
<td>91</td>
<td>98</td>
</tr>
</tbody>
</table>

Discrimination of Enantirotopic Faces

\[ \pi-\sigma-\pi \text{ Pd/C rotation may bring about } \text{apparent allyl rotation.} \]

In contrast to what happens with symmetrical allyl fragments (see later), only complex A has the less substituted allyl terminus trans to P atom of the ligand. This may explain the lower reactivity of these non symmetrical complexes with respect to the symmetrical ones. The nucleophile has to “wait” for the allyl group to arrange itself in the more sterically crowded isomer.

Brown, J. Oxford
Discrimination of Enantiotopic Faces

\[ \pi-\sigma-\pi \text{ C/C rot. accounts for generation of the same reactive intermediate from the two enantiomeric acetates (enantioface exchange).} \]
Desymmetrization of Meso $\eta^3$-Allyl Complexes

This substrate is often taken as a model to test new chiral ligands in asymmetric allylic alkylation. With this substrate the ionization step produces a meso form, and the nucleophile is directly involved in the enantiodiscriminating step. A wide variety of bidentate ligands are capable of inducing high ee’s.
The Oxaxoline P/N Ligand

H2C(CO2Me)2 3 equiv.
1/2 [C3H5PdCl]2 cat.
BSA 3 equiv.
AcOK 0.01 equiv.
THF / rt

yield 98% e.e.: 98%

ligand / Pd ratio: 1.2

Major and more reactive complex
Attack trans to P atom
i-Pr is pseudo-axial

Oxazoline Ligands do not Exchange Enantiofaces during Rxn

\[
\begin{align*}
\text{L} = \text{PPh}_3 & \quad 58 : 42 \\
\text{L} = \text{A} & \quad 99 : 1 \\
\text{L} = \text{B} & \quad 1 : 99 \\
\text{L} = \text{C} & \quad 93 : 7
\end{align*}
\]

Enantiofaces are not exchanged during the reaction

Facial Exchange in $\pi$-Allyl Complexes ($\eta^3$-$\eta^1$-$\eta^3$)

<table>
<thead>
<tr>
<th>The complexed allyl face is exchanged</th>
<th>P/N Oxazoline ligands</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Chemical Structure" /></td>
<td><img src="image2" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>d.r.: 1</td>
<td>d.r.: 1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>The complexed allyl face is not exchanged</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image3" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>d.r.: 8</td>
</tr>
</tbody>
</table>

Via NOESY ROESY cross peaks: A: 1-$H^b$/1$H^a$; 1-$H^a$/1$H^c$; 3-$H^g$/3$H^s$. B: 3-$H^g$/3$H^a$

Under the conditions of the allylic alkylation the two conformations interconvert at least 50 times faster than nucleophilic attack.

Attack trans to the weaker (and longer) Pd-P bond is easier than trans to the Pd-N bond. The major conformer turns out to be also the more reactive one.


G. Poli
Rationalization of the Enantioselectivity

The enantioselectivity is determined by the regioselectivity of the nucleophilic attack.

According to $^1$H-NOESY the allyl complex exists in at least two rapidly interconverting conformations.

The coordination at Pd is pseudo-square planar and the central chelated 6-membered ring system is in a boat-like conformation. The C-Pd distance of the two allylic termini is different. The nucleophile attacks preferentially the allylic terminus associated to the longer, and thus more reactive, C-Pd bond.
Rationalization of the Enantioselectivity

The different energies of the two possible diastereomeric Pd(0) complexes resulting from the nucleophilic attack, or of the corresponding transition states leading to them, may be the factors dictating the selectivity (a pseudo square planar geometry is assumed for Pd).
1,3-syn-disubstituted Pd π-allyl complexes may interconvert only via π−σ−π (C-Pd rot) mechanism (apparent allyl rotation), as shown above. An alternative π−σ−π (C-C rot) mechanism, which would bring about syn/anti interconversion, is usually at work only with terminal π-allyl complexes, where the syn/anti interconversion is hidden.

If $R_1 = R_2$, the π-allyl fragment has $C_{2h}$ symmetry, and the two allylic termini become enantiotopic. Now, if the chiral bischelating ligand has $C_1$ symmetry, complexes A and B are different diastereoisomers. The two isomers, usually referred to as *endo* and *exo*, can be distinguished spectroscopically, in fact, their interconversion in solution is slow with respect to NMR time scale.

If, on the other hand, the ligand has $C_2$ symmetry ($L_1 = L_2$), the above interconversion becomes hidden, since it would re-generate the same diastereoisomer ($A = B$).
**C₂ vs C₁ Symmetric Ligands**

Apparent allyl rotation

C₂

\[
\text{Ph} - \begin{array}{c}
\text{O} \\
\text{N} \\
\text{Pd} \\
\text{R} \\
\text{R} \\
\text{Ph} \\
\text{R} \\
\text{Ph} \\
\end{array}
\]

\[
\text{R} - \begin{array}{c}
\text{O} \\
\text{N} \\
\text{Pd} \\
\text{R} \\
\text{R} \\
\text{Ph} \\
\text{R} \\
\text{Ph} \\
\end{array}
\]

C₁

\[
\text{Ph} - \begin{array}{c}
\text{O} \\
\text{N} \\
\text{Pd} \\
\text{Ph} \\
\text{R} \\
\text{R} \\
\text{Ph} \\
\text{R} \\
\end{array}
\]

\[
\text{R} - \begin{array}{c}
\text{O} \\
\text{N} \\
\text{Pd} \\
\text{Ph} \\
\text{R} \\
\text{R} \\
\text{Ph} \\
\text{R} \\
\end{array}
\]

G. Poli
The Syn/Anti Exchange may be Selective

With Josiphos the allylic carbon attached to the $\text{Cy}_2\text{P}$ group always remains trans to this group. Only the bond trans to $\text{Ph}_2\text{P}$ group is broken during the syn/anti exchange process.

The Trost Ligands


The $\pi$-allyl unit sits in a chiral pocket defined by the propeller arrangements of the aryl rings which orient in edge-face relationships.

The P-Pd-P bite angle is 110.5°, considerably larger than the normal (~90°) bite angle of square planar complexes.
The Trost Ligands: Concept

For both series opening of the bite angle (P-Pd-P) is believed to enhance the depth of the chiral pocket in which the substrate must reside. This is expected to create a chiral space that controls enantioselectivity.

Discrimination of Enantiotopic Leaving Groups

intramolecular

\[
\text{TsHN} \quad \text{O} \quad \text{O} \quad \text{NHTs}
\]

\[
\text{Ts} \quad \text{Ts}
\]

Clockwise

2.5 mol\% \text{(Pd}_2\text{dba)}_3

7.5 mol\% Ligand THF rt

Counterclockwise

G. Poli
A Mnemonic Device...  

Enantioselective ionization of enantiotopic leaving groups

...to correlate absolute stereochemistry with the chirality of the ligand

Clockwise ligand induces a clockwise motion of the catalyst with respect to the substrate, thereby preferentially ionizing the pro-R leaving group.

G. Poli
Discrimination of Enantiotopic Leaving Groups

intermolecular

<table>
<thead>
<tr>
<th>Nu</th>
<th>ligand</th>
<th>A:B</th>
<th>yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCH(CO$_2$Me)$_2$</td>
<td>L3</td>
<td>96.5 : 3.5</td>
<td>80</td>
</tr>
<tr>
<td>NaCH(CO$_2$Me)$_2$</td>
<td>L4</td>
<td>4 : 96</td>
<td>68</td>
</tr>
<tr>
<td>PhCH$_2$NHMe</td>
<td>L3</td>
<td>89 : 11</td>
<td>75</td>
</tr>
<tr>
<td>PhCH$_2$NHMe</td>
<td>L4</td>
<td>&lt;1 : &gt;99</td>
<td>77</td>
</tr>
</tbody>
</table>


G. Poli
The epimerization (deracemization) has to occur faster than alkylation so that one of the two complexes reacts faster than the other. In the ligand, rotation of the carboxylate bond is restricted owing to the peri interactions. The nature of the chiral cavity is different with respect to the parent phenyl-type ligand.

Interaction Between $\eta^3$-Allyl Pd-Complexes and Allenes

Allenes can intramolecularly syn carbopalladate with a $\pi$-allyl Pd complex to generate a new $\pi$-allyl Pd complex, which can in turn be trapped to give a cyclized allylic ester.

![Chemical structure diagram]


However, allenes are also able to act as $\pi$-nucleophiles, giving trans attack on a ($\pi$-allyl)Pd complex instead of cis insertion.

![Chemical structure diagram]

Pd(0)-Catalyzed Cyclization of 1,3-Dienyl Allenes

Possible Mechanisms of the Cyclization

1st hypothesis

A palladacycle is formed by oxidative cycloaddition to Pd(0). This species rearranges to a bis-(η3,η1-allyl)Pd complex, which in turn can be protonated by the protic nucleophile at the γ-position of the σ-allyl ligand, to give a new (η3-allyl)Pd complex. An external nucleophilic attack on this (η3-allyl)Pd complex would give the products and regenerate Pd(0).

2nd hypothesis

The Pd-hydride species, generated by oxidative addition of NuH to Pd(0), hydropalladates the distal allenic double bond thereby forming a vinyl-Pd species. The latter intermediate would then undergo intramolecular carbo palladation to give an (η3-allyl)Pd complex. Subsequent external nucleophilic attack would give the products.