The Trans Effect. Implications in Enantioselective Catalyst Design

Kevin Campos
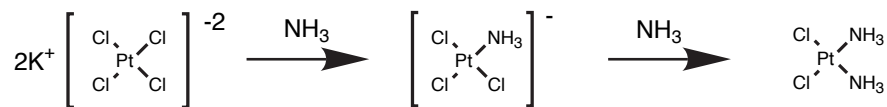
October 4, 1996

Reviews:
- ❏ Appleton, T., Manzer, L., *Coord. Chem. Rev.*, **1973**, *10*, 335
- ❏ Quagliano, J., Schubert, L., *Chem. Rev.*, **1952**, *50*, 201
- ❏ Kukushkin, Y., *Russ. Chem. Rev.,* **1974**, *43*, 805.

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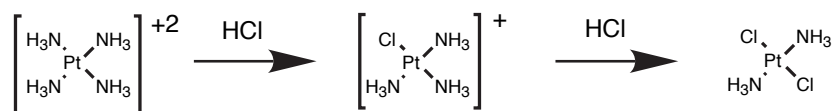
The Experimental Observation

❏ Peyrone's Reaction (1845)

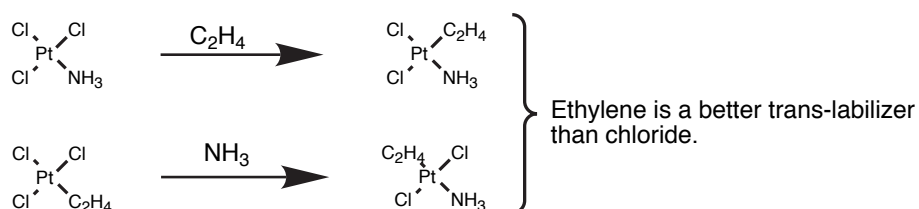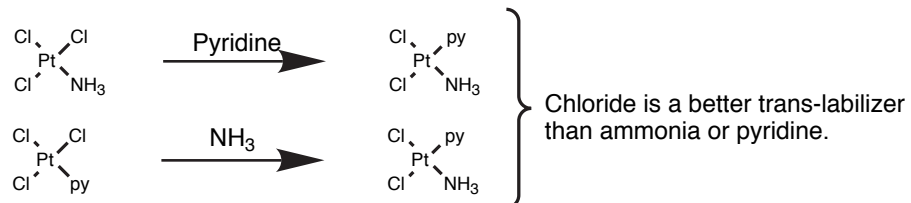❏ Peyrone, M., *Ann.* **1845**, *51*, 1.

❏ Jorgensen's Reaction (1886)

❏ Jorgensen, S.M., *J. prakt. Chem.* **1886**, *33,* 489.

The trans Effect

❑ The trans effect states that the bond holding a group *trans* to an electronegative group is weakened. This *trans* group is the first to be removed in a substitution reaction. Cheryaev (1926)

Chloride is a better trans-labilizer than ammonia or pyridine.

Ethylene is a better trans-labilizer than chloride.

❑ Quagliano, J., Schubert, L., *Chem. Rev.* **1952**, *50*, 201.

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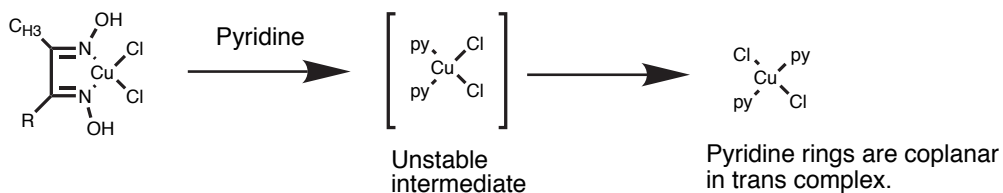
Applications of theTrans Effect

❑ Kurnakov's test
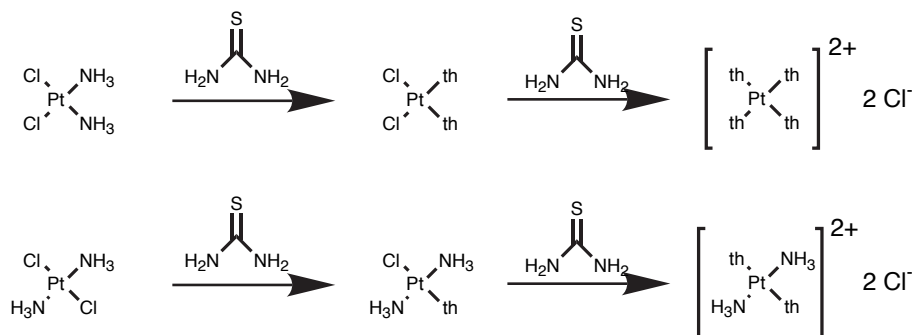
❑ Kurnakov, N., *J. prakt. Chem.,* **1894**, *50*, 483, 498.

❑ Use in copper coordination chemistry.

Unstable intermediate

Pyridine rings are coplanar in trans complex.

❑ Cox and coworkers, *J. Chem Soc.,* **1936**, 129.

Kinetic Studies to Determine trans-Effect of Ligands
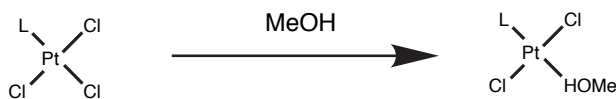
L	$k \ (s^{-1})$
C_2H_4, CO	too fast
$P(OMe)_3$	10.3
PEt_3	6.6
PPh_3	3.1
Me_2SO	0.0082
Et_2S	0.0024
Me_2S	0.0015
NH_3	6.3×10^{-6}
H_2O	8.0×10^{-8}

❑ Tobe, M., *Inorg. Chem.,* **1983**, *22*, 1235.
❑ Tobe, M., *J. Chem. Soc. Dalt. Trans.,* **1985**, 27.

Trans Effect vs. Trans Influence

❑ The trans effect is the effect of a ligand (L) on the rate of substitution of the ligand trans to it (X).
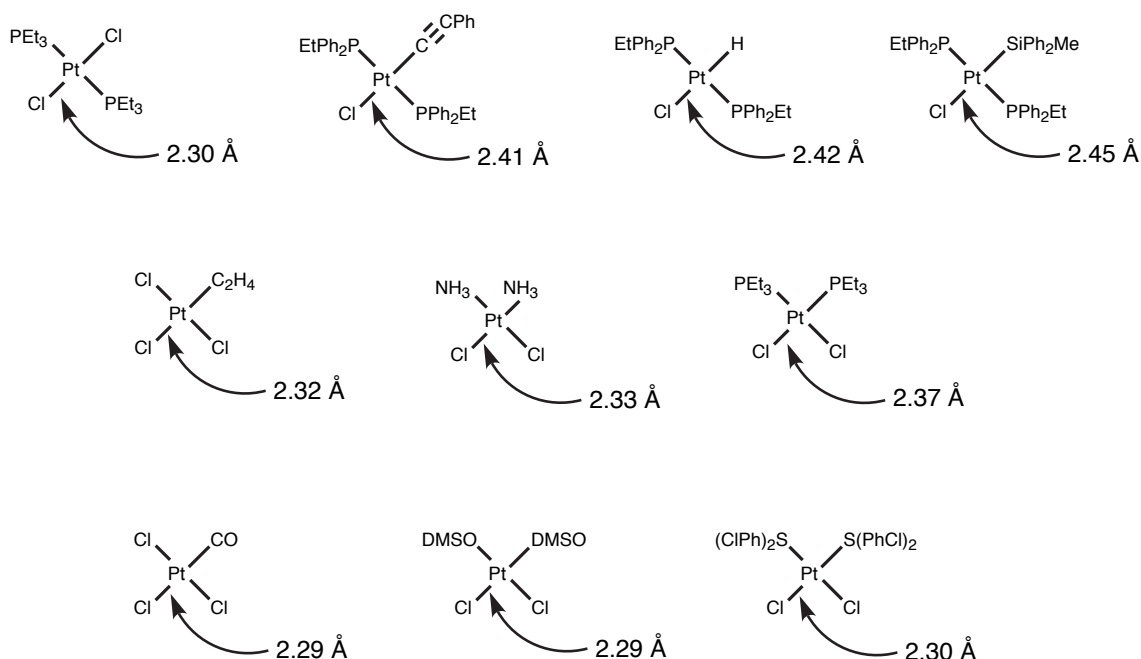Kinetic effect (ground and transition states).

$H^- = CH_3^- = CN^- = C_2H_4 = CO \gg PR_3 = SR_2 > NO_2 = SCN^- = I^- > Br^- > Cl^- > py > RNH_2 = NH_3 > OH^- > H_2O$
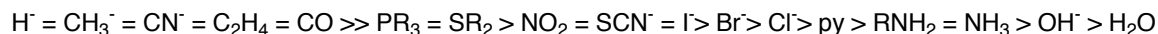
❑ The trans influence is the extent to which a ligand (L) weakens the bond that is trans to itself.
Thermodynamic effect (ground state).

$R_3Si^- = R^- = H^- > PEt_3 > PMe_2Ph > PPh_3 > P(OPh)_3 = CN^- > SEt_2 > Et_2NH > py > OSMe_2 = C_2H_4 = CO > Cl^-$
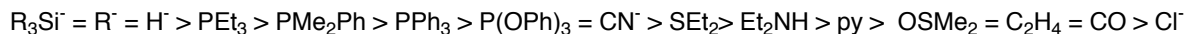
❑ The trans effect is often the manifestation of the trans influence although there are some ligands (DMSO, CO, C_2H_4) which do not show significant trans-influences yet show strong effects.
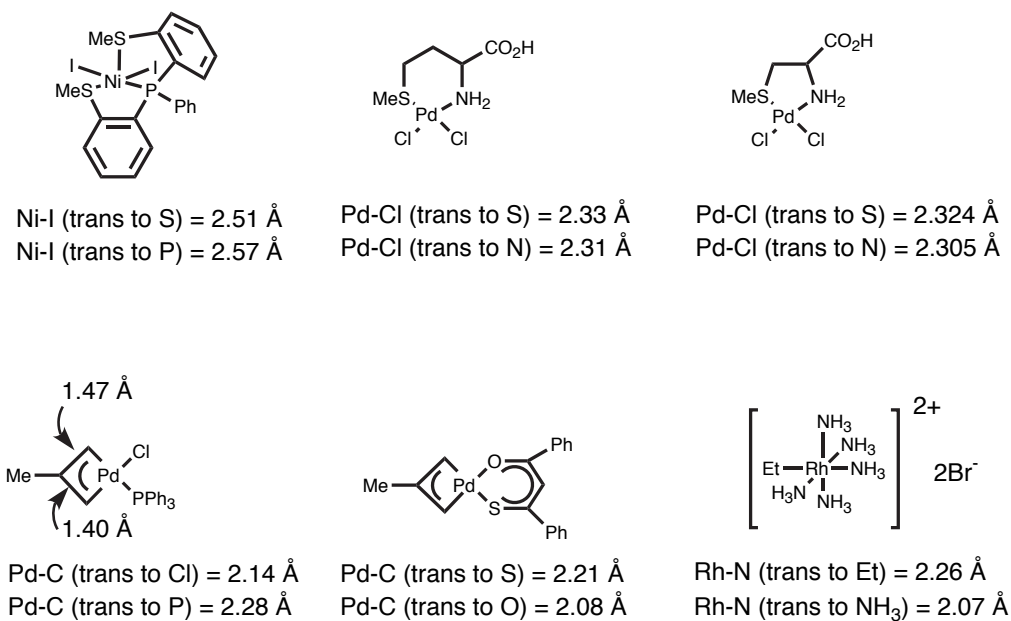
❑ *Comp. Coord. Chem. vol 1,* 315.

X-Ray Crystallography to Measure trans-Influence

PEt₃ / Cl — Pt — Cl / PEt₃ — 2.30 Å

EtPh₂P / C≡CPh — Pt — Cl / PPh₂Et — 2.41 Å

EtPh₂P / H — Pt — Cl / PPh₂Et — 2.42 Å

EtPh₂P / SiPh₂Me — Pt — Cl / PPh₂Et — 2.45 Å

Cl / C₂H₄ — Pt — Cl / Cl — 2.32 Å

NH₃ / NH₃ — Pt — Cl / Cl — 2.33 Å

PEt₃ / PEt₃ — Pt — Cl / Cl — 2.37 Å

Cl / CO — Pt — Cl / Cl — 2.29 Å

DMSO / DMSO — Pt — Cl / Cl — 2.29 Å

(ClPh)₂S / S(PhCl)₂ — Pt — Cl / Cl — 2.30 Å

❑ Kukushkin, Y., *Russ. Chem. Rev.,* **1974**, *43*, 805.
❑ Jacobson, R., *Inorg. Chem.,* **1971**, *10*, 1795.
❑ Muir, K., *Inorg. Chim. Acta.,* **1974**, *10*, 47.

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Some More Complex Crystal Structures

Ni-I (trans to S) = 2.51 Å
Ni-I (trans to P) = 2.57 Å

Pd-Cl (trans to S) = 2.33 Å
Pd-Cl (trans to N) = 2.31 Å

Pd-Cl (trans to S) = 2.324 Å
Pd-Cl (trans to N) = 2.305 Å

1.47 Å
1.40 Å
Pd-C (trans to Cl) = 2.14 Å
Pd-C (trans to P) = 2.28 Å

Pd-C (trans to S) = 2.21 Å
Pd-C (trans to O) = 2.08 Å

Rh-N (trans to Et) = 2.26 Å
Rh-N (trans to NH₃) = 2.07 Å

❑ Murray, S., Hartley, F., *Chem. Rev.,* **1981**, *81*, 365.

Vibrational Spectroscopy to Determine trans-Influence

L	υ Pt-Cl (cm^{-1})
CO	322
SMe$_2$	310
C$_2$H$_4$	309
SEt$_2$	307
PPh$_3$	279
PEt$_3$	271

L	υ Pt-Cl (cm^{-1})
py	336
SMe$_2$	336
COD	327
SEt$_2$	324
NH$_3$	321
PPh$_3$	305
PEt$_3$	294

L	υ Pd-Cl (cm^{-1})
py	342
Cl	330
NH$_3$	327
EtSCH$_2$CH$_2$SEt	323
H$_2$NCH$_2$CH$_2$NH$_2$	307
PCH$_3$	297

❑ Ligands with high trans-influence have high trans-effect.
❑ Exceptions to this rule include CO, C$_2$H$_4$, and DMSO.
❑ Frequency order for Rh(III)-Cl: H$^-$ > PR$_3$ > Me$^-$ > CO > I$^-$ > Br$^-$ > Cl$^-$.
❑ For octahedral complexes, trans-influence parallels trans-effect.

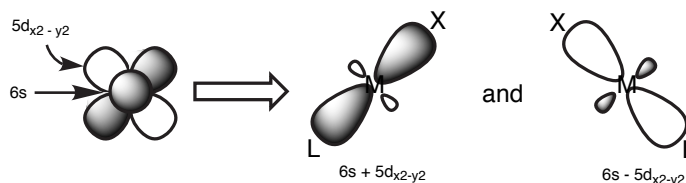❑ Kukushkin, Y., *Russ. Chem. Rev.,* **1974**, *43*, 805.
❑ Park, P., Hendra, P., *Spectochim. Acta.,* **1969**, *25*, 227.

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Early Theory on Trans Influence
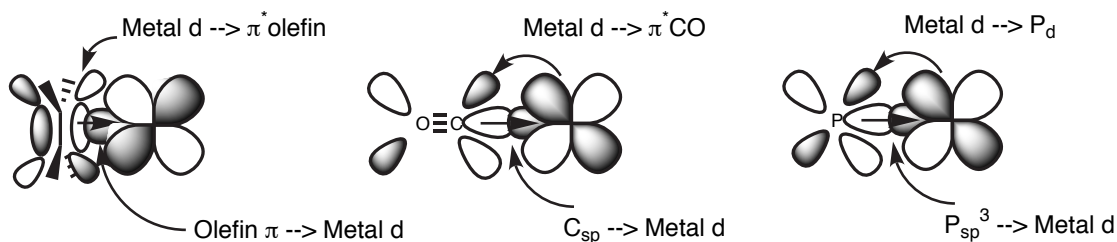
❑ Grinsberg Polarization Theory (1935)

❑ Syrkins' s/d hybrid orbital theory

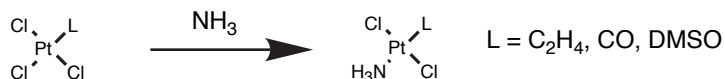❑ Appleton, T., Manzer, L., *Coord. Chem. Rev.* **1973**, *10*, 335.

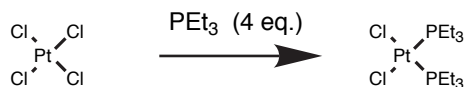❑ Chatt / Orgel Theory (Metal-Ligand Double Bond aka Back-bonding).

Metal d --> π^*olefin
Metal d --> π^*CO
Metal d --> P$_d$

Olefin π --> Metal d
C$_{sp}$ --> Metal d
P$_{sp}^3$ --> Metal d

❑ Chatt, J., Duncanson, L., *J. Chem. Soc.,* **1955**, 4456, 4461.

Stronger Trans Effect Due to Back-bonding?

❑ The trend holds for olefins, CO, and DMSO...

$$\text{Cl}\underset{\text{Cl}}{\overset{\text{L}}{\diagdown}}\text{Pt}\diagup \text{Cl} \quad \xrightarrow{\text{NH}_3} \quad \text{Cl}\overset{\text{L}}{\underset{\text{Cl}}{\diagdown}}\text{Pt}\underset{\text{Cl}}{\overset{\text{H}_3\text{N}}{}} \qquad \text{L} = \text{C}_2\text{H}_4, \text{CO}, \text{DMSO}$$

❑ Phosphorus donors...

$$\text{Cl}\overset{\text{Cl}}{\underset{\text{Cl}}{\diagdown}}\text{Pt}\overset{\text{Cl}}{\underset{\text{Cl}}{\diagup}} \quad \xrightarrow{\text{PEt}_3 \ (4 \ \text{eq.})} \quad \text{Cl}\overset{\text{PEt}_3}{\underset{\text{Cl}}{\diagdown}}\text{Pt}\overset{\text{PEt}_3}{\underset{\text{PEt}_3}{\diagup}}$$

❑ Quagliano, J., Schubert, L., *Chem. Rev.* **1952**, *50,* 201.

❑ And sulfur donors to a lesser extent...

$$\text{Cl}\overset{\text{SEt}_2}{\underset{\text{Cl}}{\diagdown}}\text{Pt}\overset{\text{SEt}_2}{\underset{\text{SEt}_2}{\diagup}} \quad \xrightarrow[\text{H}_2\text{N} \quad \text{NH}_2]{} \quad \text{Et}_2\text{S}\overset{\text{N}}{\underset{\text{Et}_2\text{S}}{}}\text{Pt}\overset{\text{H}_2}{\underset{\text{N}}{}}\quad \xrightarrow{\text{HCl}} \quad \text{Cl}\overset{\text{SEt}_2}{\underset{\text{Cl}}{\diagdown}}\text{Pt}\overset{\text{SEt}_2}{\underset{\text{SEt}_2}{\diagup}}$$
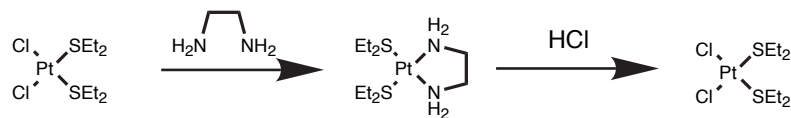
❑ Cox and coworkers, *J. Chem Soc.,* **1934**, 182.

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No

❑ But, metal akyl and metal hydrides have large trans effects and no back-bonding.

$$\text{H}\overset{\text{PEt}_2\text{Ph}}{\underset{\text{Cl}}{\diagdown}}\text{Pt}\overset{}{\underset{\text{Cl}}{\diagup}} \quad \xrightarrow{\text{NaI}} \quad \text{H}\overset{\text{PEt}_2\text{Ph}}{\underset{\text{H}}{\diagdown}}\text{Pt}\overset{}{\underset{\text{I}}{\diagup}}$$
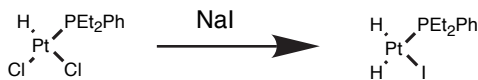
❑ Crabtree, R., *J. Organomet. Chem.,* **1977**, *141*, 205.

$$\left[\begin{array}{c} \text{NH}_3 \\ \text{NH}_3 \\ \text{L}-\text{Rh}-\text{NH}_3 \\ \text{H}_3\text{N} \quad \text{NH}_3 \end{array} \right]^{2+} \quad \xrightarrow{\text{H}_2\text{O}} \quad \left[\begin{array}{c} \text{NH}_3 \\ \text{NH}_3 \\ \text{L}-\text{Rh}-\text{OH}_2 \\ \text{H}_3\text{N} \quad \text{NH}_3 \end{array} \right]^{2+} \qquad \text{Rates of aquation: } \text{H} > \text{Et} > \text{CF}_2\text{CF}_2\text{H} \gg \text{Cl}$$
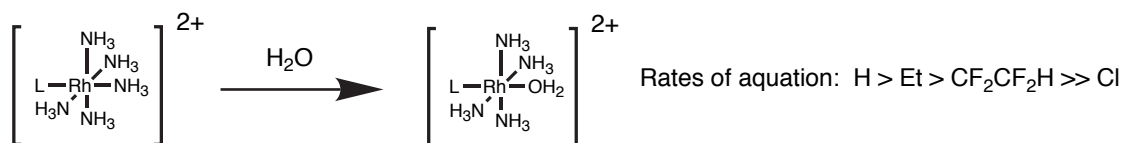
❑ Wilkinson, G., *J. Chem Soc. (A),* **1968**, 1801.

## Calculations of trans-PtCl$_2$(L)(NH$_3$)
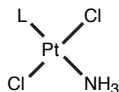
L	Pt-L bond length A	Overlap Population Pt-L	Overlap Population Pt-N	Overlap Population Pt(6s)-N	Overlap Population Pt(5dx2-y2)-N	Overlap Population Pt(6py)-L	Overlap Population Pt(6py)-N
H$_2$O	2.00	0.2406	0.3370	0.1205	0.1275	0.1114	0.1235
NH$_3$	2.00	0.3221	0.3221	0.1139	0.1145	0.1313	0.1313
Cl$^-$	2.53	0.3822	0.3240	0.1181	0.1225	0.1759	0.1212
H$_2$S	2.30	0.4295	0.3244	0.1158	0.1154	0.2070	0.1320
CH$_3^-$	2.15	0.4637	0.3009	0.1036	0.0949	0.1945	0.1431
PH$_3$	2.25	0.5685	0.3092	0.1054	0.0966	0.2435	0.1490
H$^-$	1.06	0.6069	0.3074	0.1046	0.1009	0.2603	0.1415

❏ From L=H$_2$O to L = H$^-$, the bond to trans-ligand is weakend by only 10%.
❏ Large changes in bonding with 6py observed for stronger trans-effect ligands.
❏ Conclusion is that differing rates of substitution arise from differing stabilization of transition state.

❏ Zumdahl, S., Drago, R., *J. Am. Chem. Soc..* **1968**, *90*, 6669.

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Calculations of trans-PtCl$_2$(L)(NH$_3$)
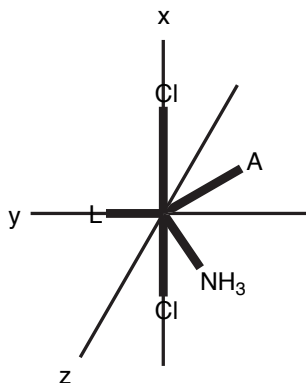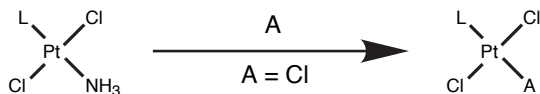
Complex	Pt(6p$_y$)-L	Pt-L	Pt-N	Pt-A
Pt(H$_2$O)(NH$_3$)Cl$_3^-$	0.1602	0.1895	0.2920	0.3117
P(H)(NH$_3$)Cl$_3^-$	0.3356	0.5868	0.2674	0.2859

❏ Groups A and NH$_3$ both occupy part of the 6p$_y$ and 6p$_z$ orbitals.
❏ L is orthogonal to the 6p$_z$ orbital, but it overlaps well with the 6p$_y$ orbital.
❏ Stabilization of the transition state is achieved by increased donation ligand (L) into 6p$_y$ orbital in ≠.
❏ Calculations for trigonal bipyamidal complex show strengthening of Pt-L and weakening of Pt-N, Pt-A.

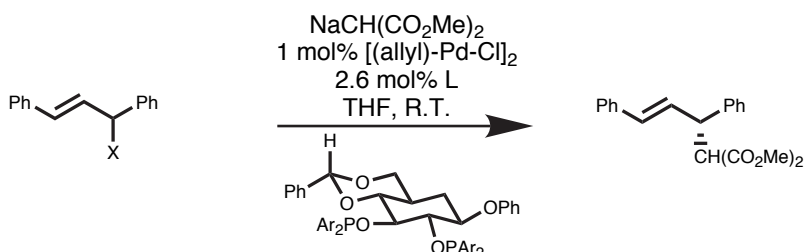❏ Zumdahl, S., Drago, R., *J. Am. Chem. Soc..* **1968**, *90*, 6669.

Electronics Play an Important Role in Catalysis

HCN, Ni-L, Hexane
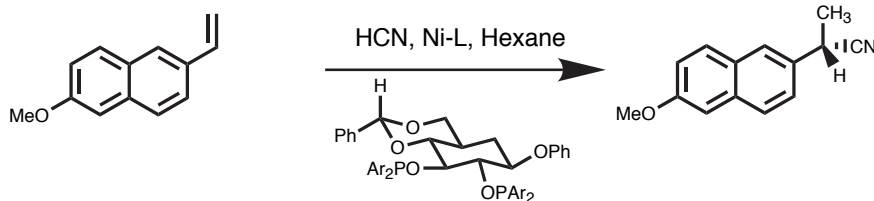
Ar	% e.e.
Ph	40
3,5-Me$_2$Ph	16
3,5-(CF$_3$)$_2$Ph	85
3,5-F$_2$Ph	78

H$_2$ (30-40 psi), Rh-L(COD)-X
THF, RT
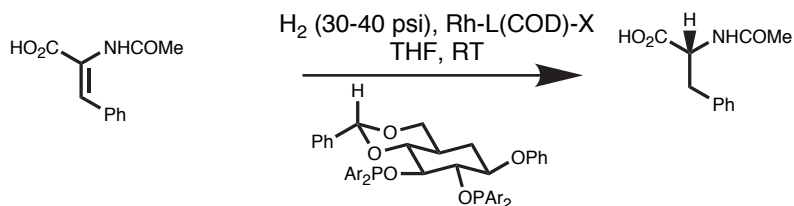
Ar	% e.e.
Ph	99
3,5-Me$_2$Ph	94
3,5-(CF$_3$)$_2$Ph	71
3,5-F$_2$Ph	60

NaCH(CO$_2$Me)$_2$
1 mol% [(allyl)-Pd-Cl]$_2$
2.6 mol% L
THF, R.T.

Ar	% e.e.
3,5-Me$_2$Ph	0
Cy	59 (R)
3,5-(CF$_3$)$_2$Ph	39 (R)
3,5-F$_2$Ph	41 (S)

❏ RajanBabu, T., *P. Appl. Chem.,* **1994**, *66*, 1535.
❏ RajanBabu, T., *J. Am. Chem. Soc.,* **1994**, *116*, 9869.
❏ RajanBabu, T., *Synlett.,* **1996**, 745.

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Palladium Allylation:
The Mechanism
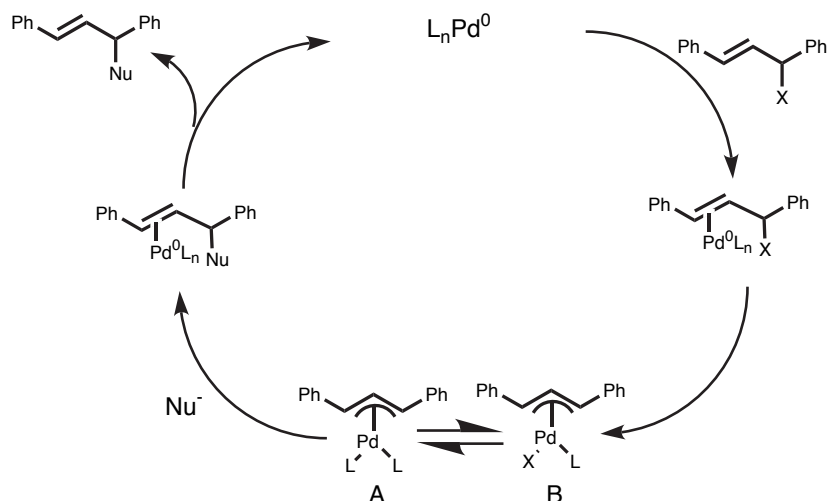
❏ X = OAc, Cl, OCO$_2$R, OPO(OR)$_3$
❏ Complex A is favored over complex B for bidentate ligands.
❏ *syn, syn* allyl complex favored, but *syn, anti* allyl complex has been made.

❏ Williams, J., *Tet. Asymm.,* **1992**, *3*, 1089.

Stereochemical Aspects of Pd Allylation
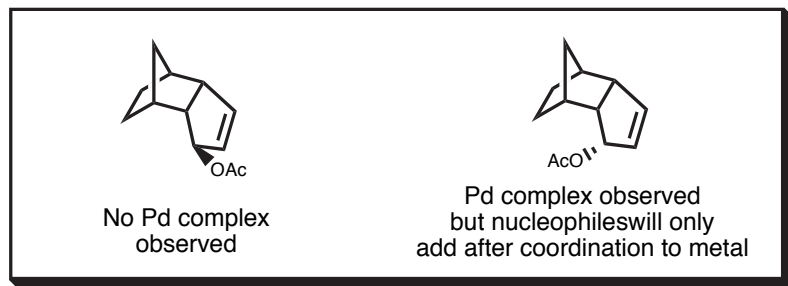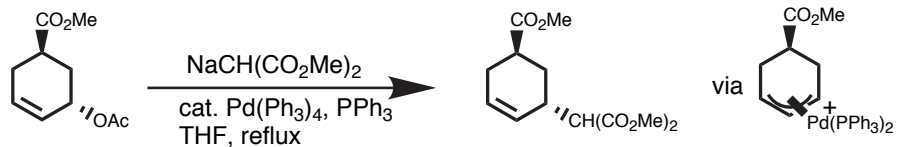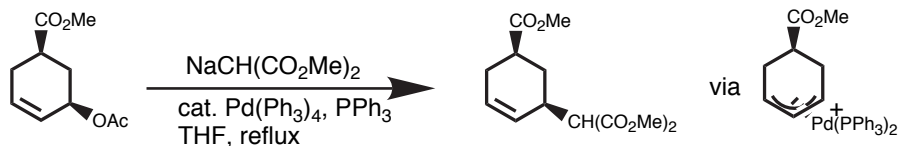
❑ Net retention is observed for allylations via 2 inversions (1. Pd addition, 2. Nu displacement).
❑ Nucleophiles with pKa > 20 will attack through metal complex.
❑ Nucleophiles with pKa < 20 will attack the allyl directly.
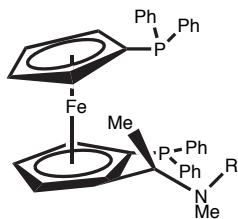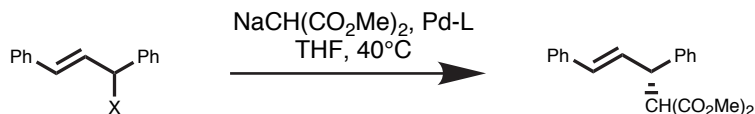
❑ Williams, J., *Tet. Asymm.,* **1992**, *3*, 1089.

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Enantiocontrol via meso ∏-allyl complexes

Product from (a)

Product from (b)

| 18% e.e. | 31% e.e. | 38% e.e. | 69% e.e. |

Ar = 3,5-bisTMSPh
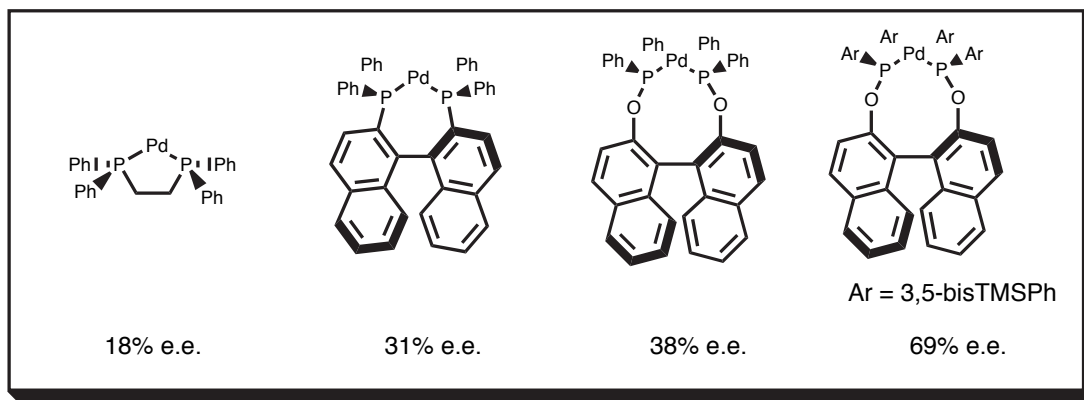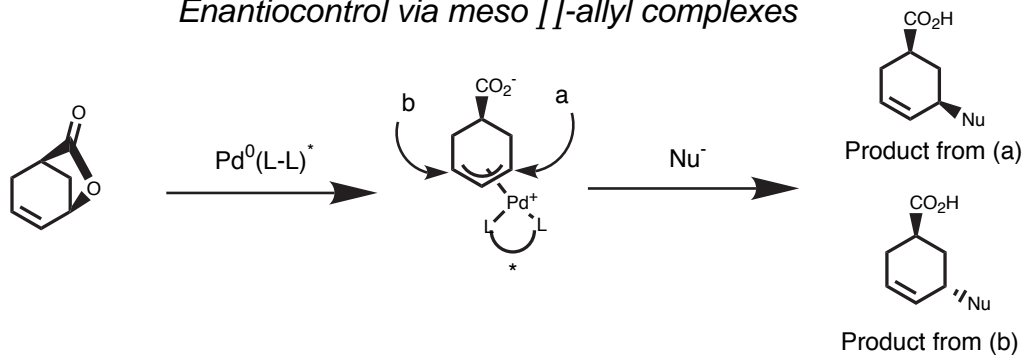
❑ Asymmetry of ligand is on the opposite face of the ∏-allyl than the incoming nucleophile.
❑ Increasing bite angle of ligands gives moderate success.

❑ Williams, J., *Tet. Asymm.,* **1992**, *3*, 1089.

Palladium Allylation:
The Reacharound

Ph⧸＝⧹Ph / X → [NaCH(CO₂Me)₂, Pd-L / THF, 40°C] → Ph⧸＝⧹Ph / CH(CO₂Me)₂

$$NaCH(CO_2Me)_2, Pd\text{-}L$$
$$THF, 40°C$$

R	% e.e.
CH_2CH_2OH	71
$CH(CH_2OH)_2$	90
$C(CH_2OH)_3$	96
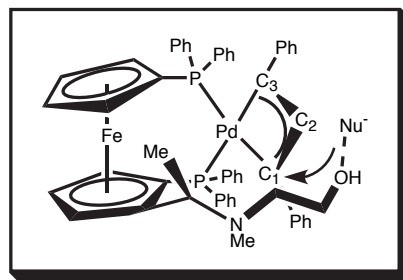
Proposed Model

- ❑ When no coordinating group is attached to the linker, e.e.'s are <10%.
- ❑ X-ray structure of Pd-allyl shows that the linker extends around the allyl group.
- ❑ $O\text{-}C_1 = 3.36$ Å, $O\text{-}C_3 = 5.24$ Å, and product arises from attack at C_1.

❑ Hayashi, T., *Tet. Lett.,* **1986**, *27*, 191.

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Palladium Allylation:
Unsymmetrical Bidentate Ligands

Ph⧸＝⧹Ph / X → [$CH_2(CO_2Me)_2$, BSA / 2.5 mol% [(allyl)-Pd-Cl]₂ / CH_2Cl_2, R.T.] → Ph⧸＝⧹Ph / CH(CO₂Me)₂

$$CH_2(CO_2Me)_2, BSA$$
$$2.5\ mol\%\ [(allyl)\text{-}Pd\text{-}Cl]_2$$
$$CH_2Cl_2, R.T.$$
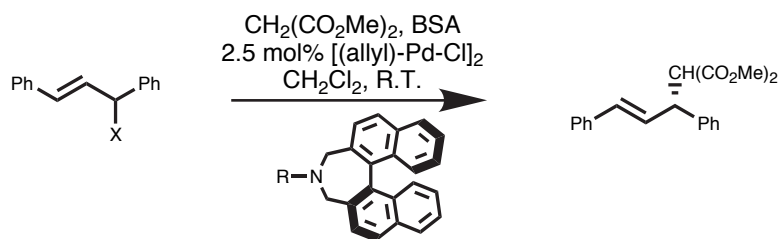
R	mol% L	Time (min)	% e.e.
$Ph_2PCH_2CH_2$	2.5	100	93
$Ph_2PCH_2CH_2$	4.0	60	90
$Ph_2PCH_2CH_2$	6.0	3	3
$Ph_2PCH_2CH_2CH_2$	2.5	150	96

- ❑ Phosphorus has stronger trans-influence than nitrogen.
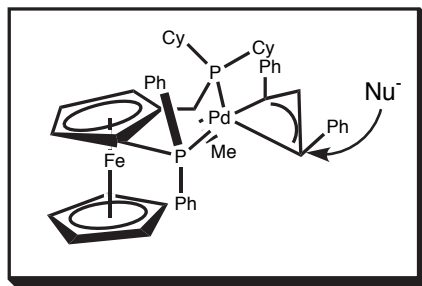- ❑ Substituion on allyl presumed to occur trans to phosphorus.
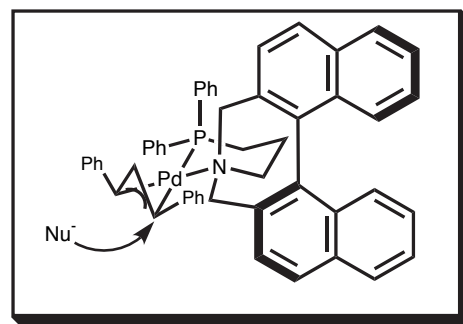
Proposed Model For Induction.

❑ Koga, K., *Tet. Lett.,* **1994**, *35*, 6689.

Palladium Allylation:
Electronic Differentiation of Phosphines

$$CH_2(CO_2Me)_2, BSA$$
$$0.5 \text{ mol\% Pd-L}$$
$$CH_2Cl_2, RT, 2\text{-}30 \text{ hr.}$$

Ph〜CH(Ph)X → Ph〜CH(Ph)CH(CO_2Me)_2
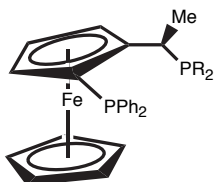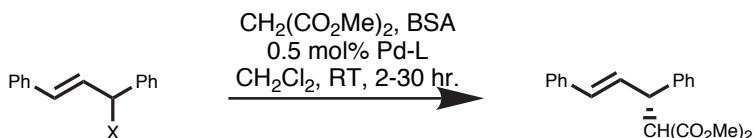
| R	% e.e.
Ph	66
tBu	81
Cy	93

Proposed Model

❏ Varying substituents on one of the phosphines has dramatic effects on the e.e.
❏ Excellent e.e.'s in hydrogenations, hydroborations, and β-ketoester reductions with Rh.
❏ NMR experiments show a preference for the shown Pd-allyl species.
❏ Nucleophile attacks trans to phosphine with stronger trans-influence.

❏ Togni, A., *J. Am. Chem. Soc.*, **1994**, *116*, 4062.

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Palladium Allylation:
Mixed P,N ligands

$$3 \text{ mol\% Pd-L}$$
$$THF, 40°C, PhCH_2NH_2.$$

Ph〜CH(Ph)OCO_2Et → Ph〜CH(Ph)NHCH_2Ph
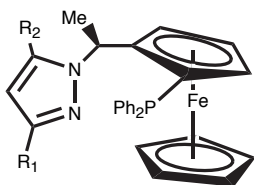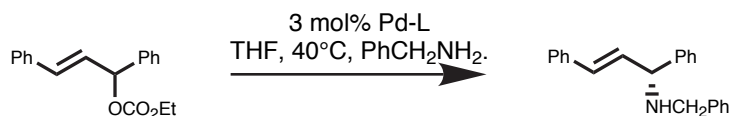
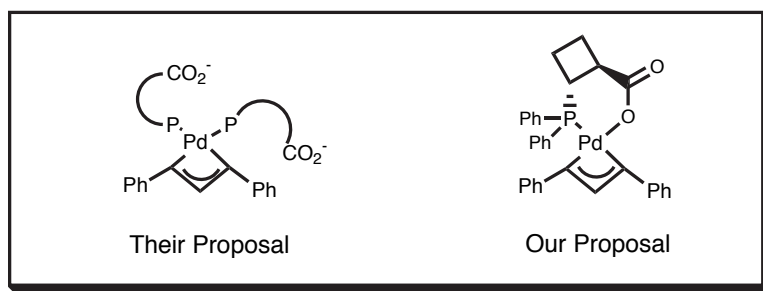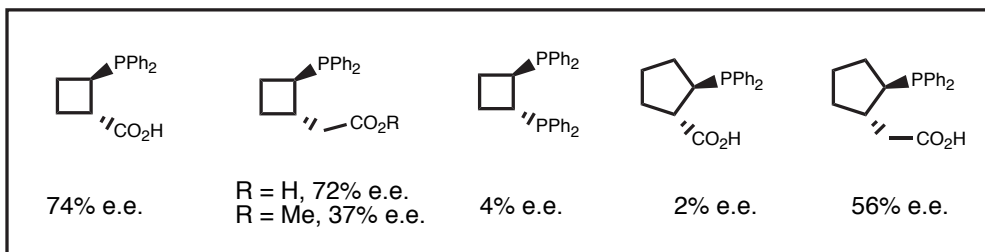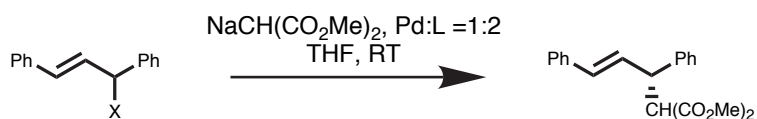| R_1	R_2	% e.e.
Me	Me	90 (R)
Ph	Me	96 (R)
Ph	H	95 (R)
Cy	Me	95 (R)
1-adamantyl	H	99 (R)
9-anthryl	Me	40 (S)
9-triptycyl	H	n.r.
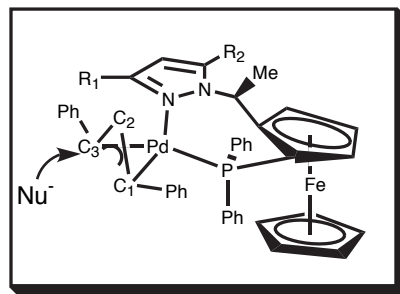
Proposed Model

❏ X-ray structure for Pd-allyl (R_1=Ph, R_2=Me) shows Pd-C_1 = 2.138 Å, Pd-C_3 = 2.268 Å.

❏ X-ray structure for Pd-allyl (R_1=Ph, R_2=Me) shows syn/syn arrangement of Pd-allyl.

❏ X-ray structure for Pd-allyl (R_1=9-triptycyl, R_2=Me) shows anti/syn arrangement of

Pd-allyl.

❏ Togni, A., *J. Am. Chem. Soc.*, **1996**, *118*, 1031.

$$NaCH(CO_2Me)_2, \ Pd:L = 1:2$$
$$THF, \ RT$$

Ph⟶Ph
X

Ph⟶Ph
$\underline{CH(CO_2Me)_2}$

PPh₂ / ""CO₂H	PPh₂ / "―CO₂R	PPh₂ / ""PPh₂	PPh₂ / ""CO₂H	PPh₂ / "―CO₂H
74% e.e.	R = H, 72% e.e. \ R = Me, 37% e.e.	4% e.e.	2% e.e.	56% e.e.

Their Proposal

Our Proposal

❑ Minami, T., *Tet. Asymm.,* **1991**, *2*, 667.

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Palladium Allylation:
More Phosphinocarboxylic Acids

OAc

$$MCH(CO_2R)_2, \ Pd:L = 1:3$$
$$THF$$

CH(CO₂R)₂

HO₂C⟶ / PPh₂
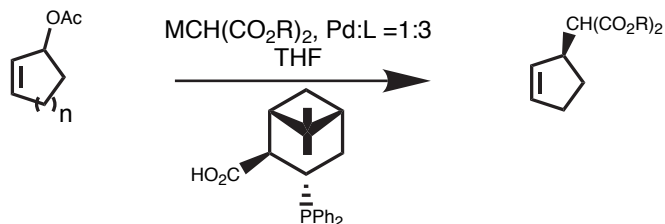
| R	n	M	T (°C)	% e.e.
Me	1	Na	25	75
tBu	1	Na	0	81
Me	1	Li	25	83
tBu	1	Li	25	85
Me	2	Na	25	91
tBu	2	Na	25	96
Me	2	Li	25	98
tBu	2	Li	25	98
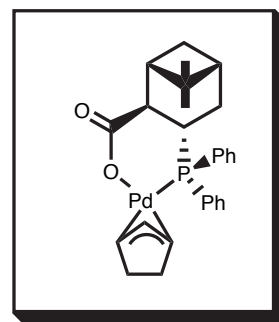
Proposed Intermediate

❑ Helmchen, G., *J. Chem. Soc. Chem. Comm.,* **1995**, 1845.
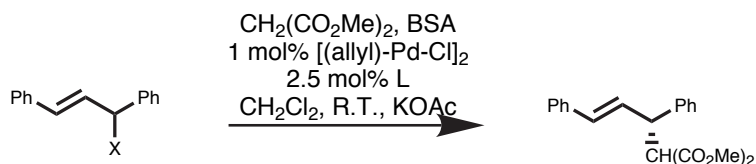
Palladium Allylation:
More Phosphinocarboxylic Acids

CH$_2$(CO$_2$Me)$_2$, BSA
2.0 mol% [(allyl)-Pd-Cl]$_2$
CH$_2$Cl$_2$, R.T.

Ph ⟶ Ph

X

Ph — Ph
CH(CO$_2$Me)$_2$

PPh$_2$
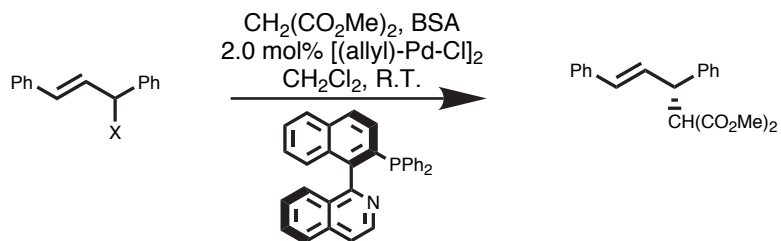
Solvent	% e.e.
CD$_2$Cl$_2$	76
CD$_3$CN	78
CD$_2$Cl$_2$/NaCH(CO$_2$Me)$_2$	75
CD$_2$Cl$_2$/NaCH(CO$_2$Me)$_2$ and 1 eq. 15-crown-5	90
CD$_3$CN/NaCH(CO$_2$Me)$_2$ and 1 eq. 15-crown-5	98

Proposed Model
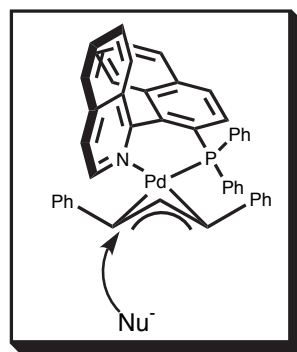
❏ Brown, J., *Tetrahedron,* **1994**, *50*, 4493.

Palladium Allylation:
## Phosphinoxazolines

CH$_2$(CO$_2$Me)$_2$, BSA
1 mol% [(allyl)-Pd-Cl]$_2$
2.5 mol% L
CH$_2$Cl$_2$, R.T., KOAc

Ph ⟶ Ph

X

Ph — Ph
CH(CO$_2$Me)$_2$

PPh$_2$

R

R	% e.e.
Me	89
PhCH$_2$	97
iPr	98
Ph	99
tBu	95
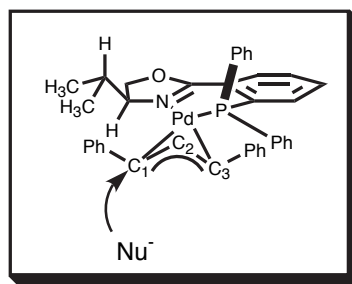
❏ Other nucleophiles have also been used (CH$_2$(COMe)$_2$, HC(NHAc)(CO$_2$Et)$_2$, PhCH$_2$NH$_2$

❏ Diakyl propenyl substrates can also be used with these ligands.

❏ Xray structure shows Pd-C$_1$ = 2.263 Å, Pd-C$_3$ = 2.143 Å

❏ Modest success has also been acheived with cyclic substrates. (Up to 85% e.e.)

❏ Helmchen, G., *Tet. Letters.,* **1993**, *34*, 1769.
❏ Williams, J., *Tet. Letters.,* **1993**, *34*, 3150.
❏ Pfaltz, A., *ACIEE,* **1993**, *32*, 566.
❏ Pfaltz, A., *Tet. Asymm.,* **1994**, *5*, 573.
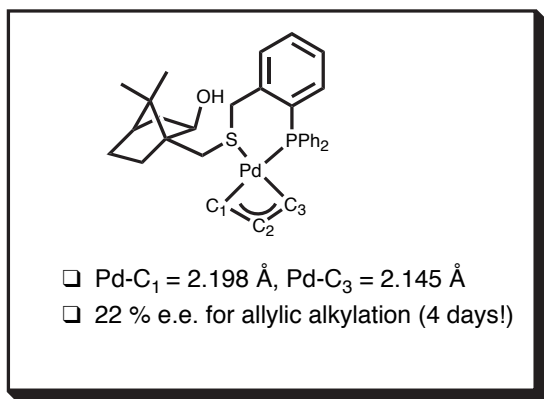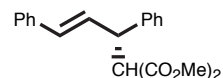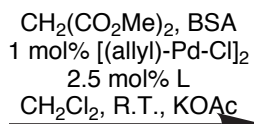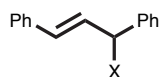
Palladium Allylation: Mixed S,N Ligands

$CH_2(CO_2Me)_2$, BSA
1 mol% [(allyl)-Pd-Cl]$_2$
2.5 mol% L
CH_2Cl_2, R.T., KOAc
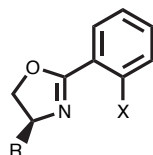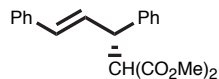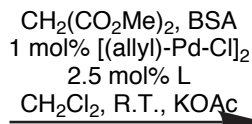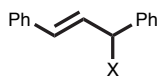
R	X	% e.e.
iPr	PPh$_2$	98
iPr	SPh	92
iPr	(S)-S(O)Tol	88
H	(S)-S(O)Tol	56
iPr	(R)-S(O)Tol	55
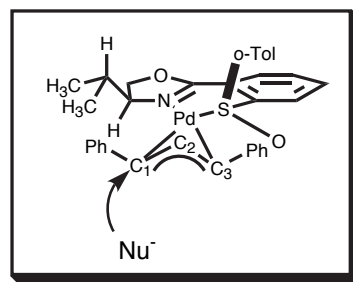
It's not so easy to see here...

❑ Helmchen, G., *Tet. Letters.,* **1994**, *35*, 1523.
❑ Williams, J., *Tet. Asymm.,* **1994**, *5*, 1895.

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Palladium Allylation: Mixed P/S Ligands

$CH_2(CO_2Me)_2$, BSA
1 mol% [(allyl)-Pd-Cl]$_2$
2.5 mol% L
CH_2Cl_2, R.T., KOAc

❑ Pd-C$_1$ = 2.198 Å, Pd-C$_3$ = 2.145 Å
❑ 22 % e.e. for allylic alkylation (4 days!)

❑ Pregosin, P., *Organomet.,* **1995**, *14*, 3311.

92% e.e
Rh catalyzed
hydrosilylation.
- M. Gagne

88% e.e.
Pd-catalyzed
allylic alkylation.
- K. Campos

64% e.e.
Rh-catalyzed
hydrogenation.
- K. Campos / F. Michael