

## The Trans Effect. Implications in Enantioselective Catalyst Design

Kevin Campos

October 4, 1996

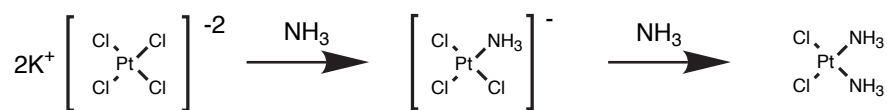
Reviews:

- 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.

---

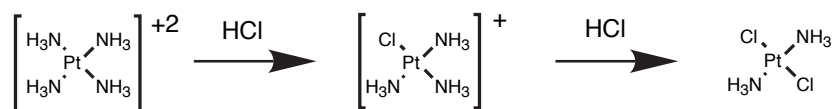
### The Experimental Observation

□ Peyrone's Reaction (1845)



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

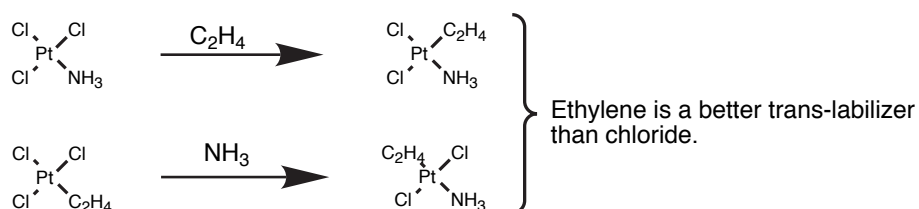
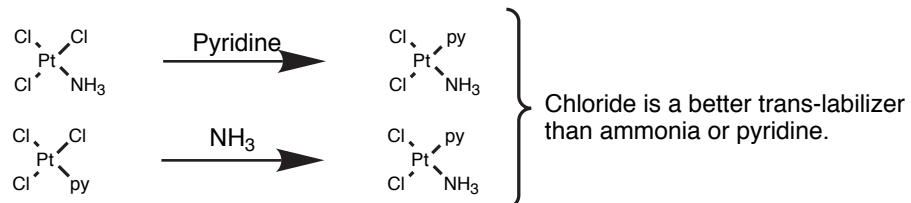
□ Jorgensen's Reaction (1886)



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

## The trans Effect

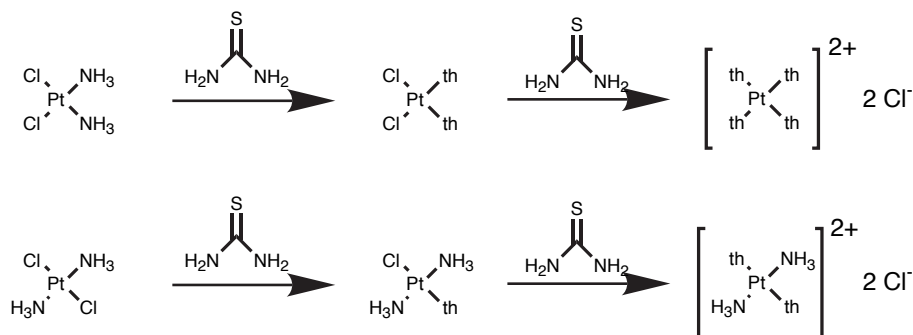
□ The trans effect states that the bond holding a group *trans* to an electronegative group is weakened. This *trans* group is the first to be removed in a substitution reaction. Cheryaev (1926)



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

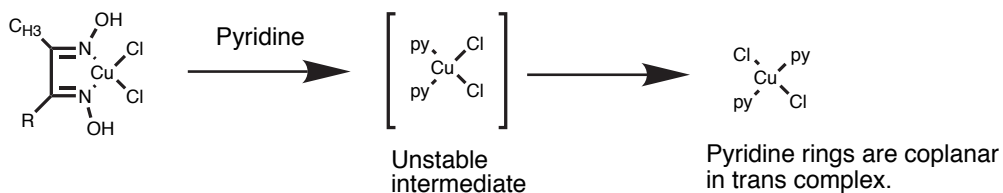
## Applications of the Trans Effect

□ Kurnakov's test



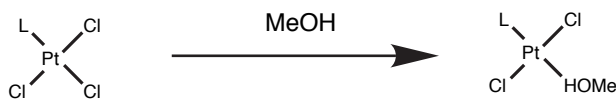
□ Kurnakov, N., *J. prakt. Chem.*, **1894**, 50, 483, 498.

□ Use in copper coordination chemistry.



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

## Kinetic Studies to Determine trans-Effect of Ligands

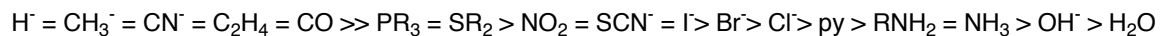


L	k (s <sup>-1</sup> )
C <sub>2</sub> H <sub>4</sub> , CO	too fast
P(OMe) <sub>3</sub>	10.3
PEt <sub>3</sub>	6.6
PPh <sub>3</sub>	3.1
Me <sub>2</sub> SO	0.0082
Et <sub>2</sub> S	0.0024
Me <sub>2</sub> S	0.0015
NH <sub>3</sub>	6.3x10 <sup>-6</sup>
H <sub>2</sub> O	8.0x10 <sup>-8</sup>

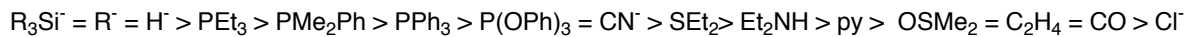
- Tobe, M., *Inorg. Chem.*, **1983**, 22, 1235.
- Tobe, M., *J. Chem. Soc. Dalt. Trans.*, **1985**, 27.

## 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).



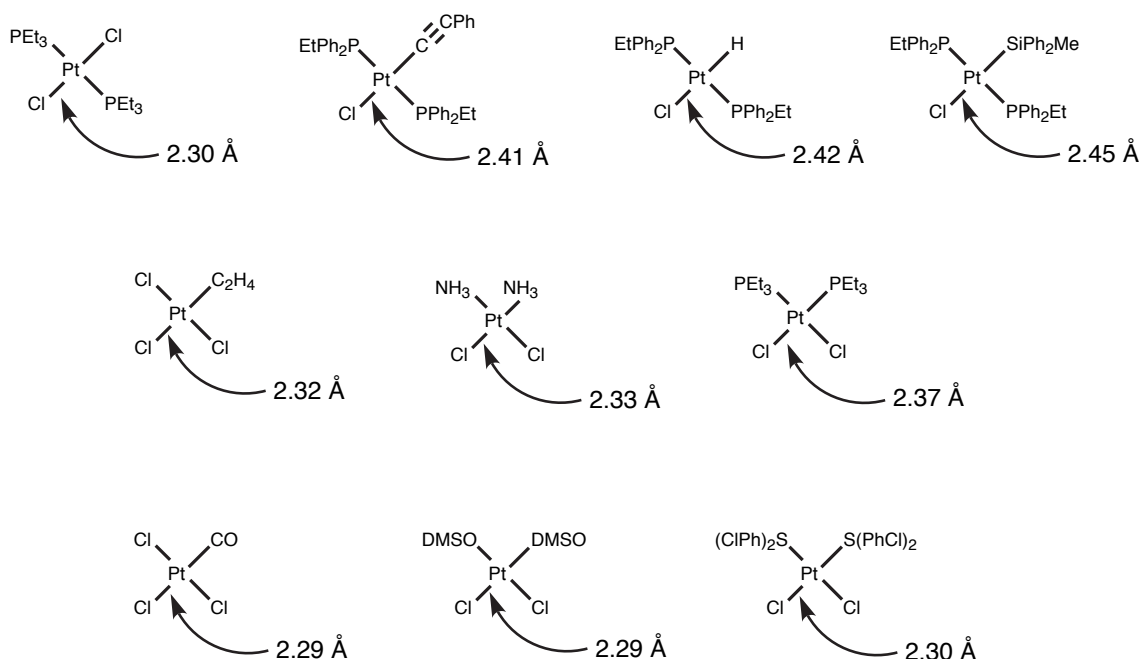
- The trans influence is the extent to which a ligand (L) weakens the bond that is trans to itself. Thermodynamic effect (ground state).



- The trans effect is often the manifestation of the trans influence although there are some ligands (DMSO, CO, C<sub>2</sub>H<sub>4</sub>) which do not show significant trans-influences yet show strong effects.

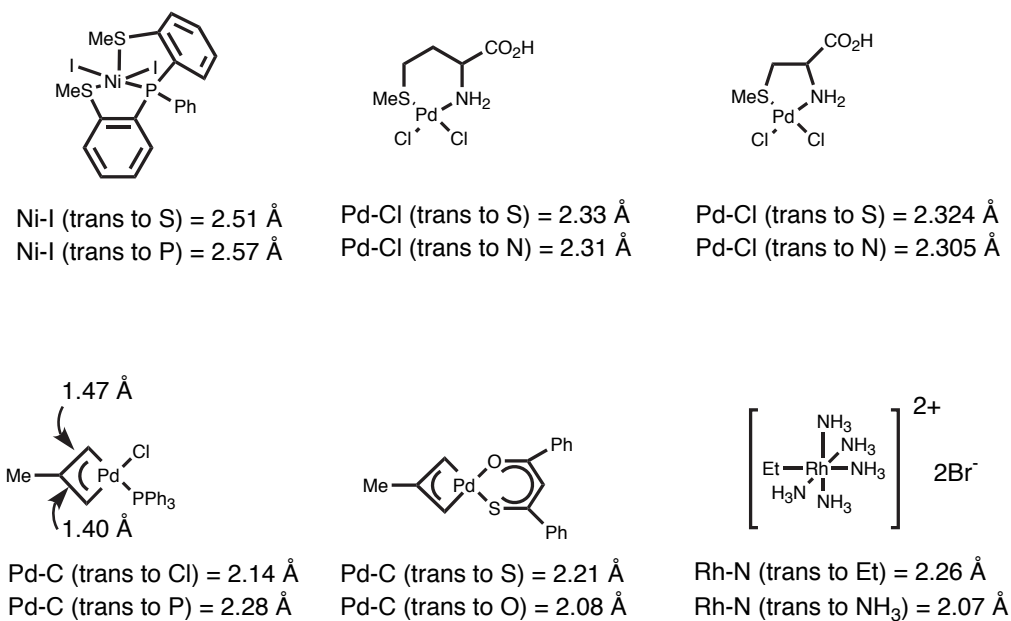
- *Comp. Coord. Chem. vol 1*, 315.

## X-Ray Crystallography to Measure trans-Influence



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

## Some More Complex Crystal Structures



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

## Vibrational Spectroscopy to Determine trans-Influence

L	$\nu$ Pt-Cl (cm <sup>-1</sup> )
CO	322
SMe <sub>2</sub>	310
C <sub>2</sub> H <sub>4</sub>	309
SEt <sub>2</sub>	307
PPh <sub>3</sub>	279
PEt <sub>3</sub>	271

L	$\nu$ Pt-Cl (cm <sup>-1</sup> )
py	336
SMe <sub>2</sub>	336
COD	327
SEt <sub>2</sub>	324
NH <sub>3</sub>	321
PPh <sub>3</sub>	305
PEt <sub>3</sub>	294

L	$\nu$ Pd-Cl (cm <sup>-1</sup> )
py	342
Cl	330
NH <sub>3</sub>	327
EtSCH <sub>2</sub> CH <sub>2</sub> SEt	323
H <sub>2</sub> NCH <sub>2</sub> CH <sub>2</sub> NH <sub>2</sub>	307
PCH <sub>3</sub>	297

- Ligands with high trans-influence have high trans-effect.
- Exceptions to this rule include CO, C<sub>2</sub>H<sub>4</sub>, and DMSO.
- Frequency order for Rh(III)-Cl: H<sup>-</sup> > PR<sub>3</sub> > Me<sup>-</sup> > CO > I<sup>-</sup> > Br<sup>-</sup> > Cl<sup>-</sup>.
- For octahedral complexes, trans-influence parallels trans-effect.

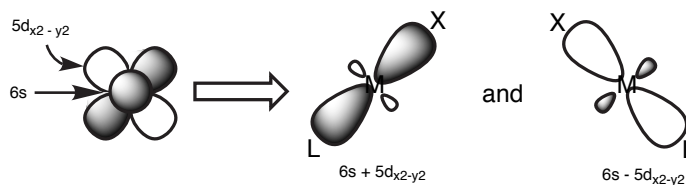
- Kukushkin, Y., *Russ. Chem. Rev.*, **1974**, 43, 805.
- Park, P., Hendra, P., *Spectrochim. Acta.*, **1969**, 25, 227.

## Early Theory on Trans Influence

- Grinsberg Polarization Theory (1935)

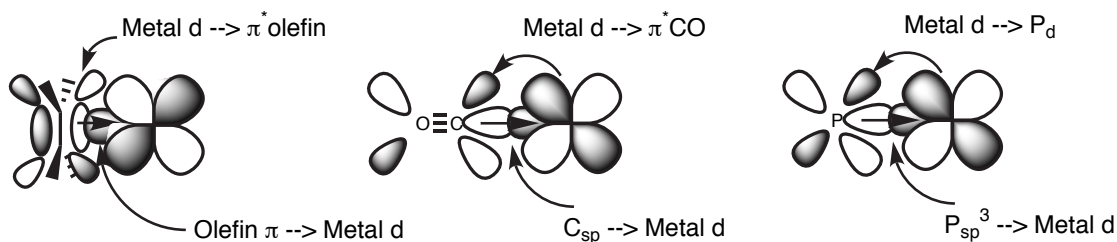


- Syrkins' s/d hybrid orbital theory



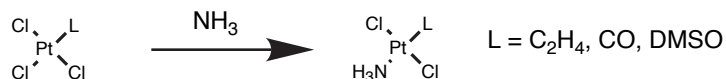
- Appleton, T., Manzer, L., *Coord. Chem. Rev.* **1973**, 10, 335.

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

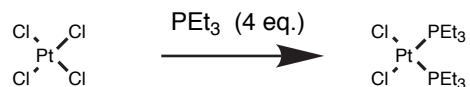


## Stronger Trans Effect Due to Back-bonding?

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

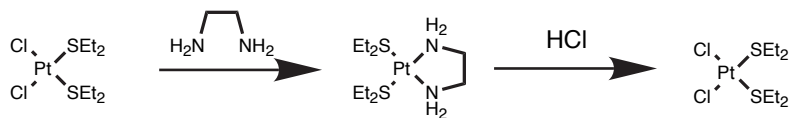


- Phosphorus donors...



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

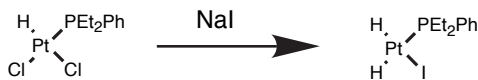
- And sulfur donors to a lesser extent...



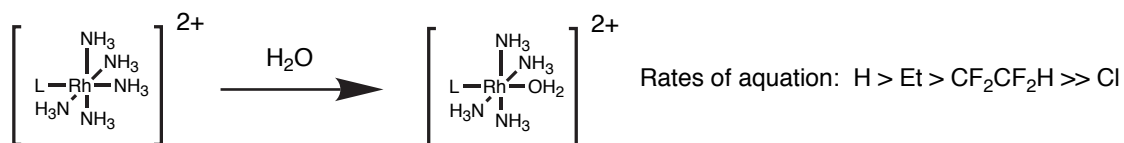
- Cox and coworkers, *J. Chem Soc.*, **1934**, 182.

No

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

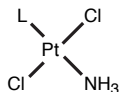


- Crabtree, R., *J. Organomet. Chem.*, **1977**, 141, 205.



- Wilkinson, G., *J. Chem Soc. (A)*, **1968**, 1801.

### Calculations of $trans\text{-PtCl}_2(L)(\text{NH}_3)$

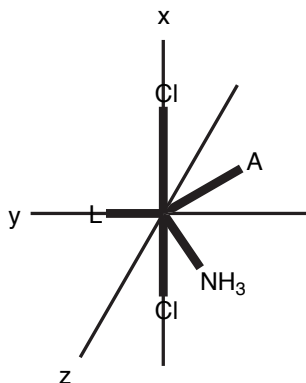
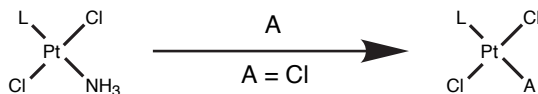


L	Pt-L bond length A	Overlap Population Pt-L	Overlap Population Pt-N	Overlap Population Pt(6s)-N	Overlap Population Pt(5dx2-y2)-N	Overlap Population Pt(6py)-L	Overlap Population Pt(6py)-N
H <sub>2</sub> O	2.00	0.2406	0.3370	0.1205	0.1275	0.1114	0.1235
NH <sub>3</sub>	2.00	0.3221	0.3221	0.1139	0.1145	0.1313	0.1313
Cl <sup>-</sup>	2.53	0.3822	0.3240	0.1181	0.1225	0.1759	0.1212
H <sub>2</sub> S	2.30	0.4295	0.3244	0.1158	0.1154	0.2070	0.1320
CH <sub>3</sub> <sup>-</sup>	2.15	0.4637	0.3009	0.1036	0.0949	0.1945	0.1431
PH <sub>3</sub>	2.25	0.5685	0.3092	0.1054	0.0966	0.2435	0.1490
H <sup>-</sup>	1.06	0.6069	0.3074	0.1046	0.1009	0.2603	0.1415

- From L=H<sub>2</sub>O to L = H<sup>-</sup>, the bond to trans-ligand is weakened 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.

### Calculations of $trans\text{-PtCl}_2(L)(\text{NH}_3)$

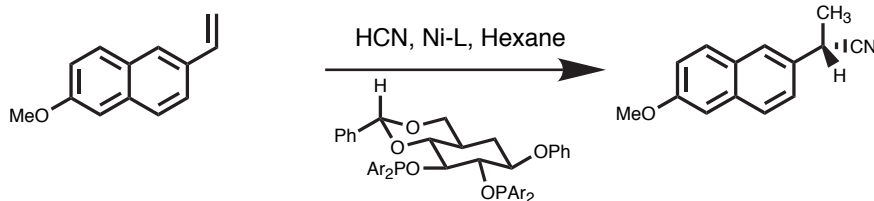


Complex	Pt(6py)-L	Pt-L	Pt-N	Pt-A
Pt(H <sub>2</sub> O)(NH <sub>3</sub> )Cl <sub>3</sub> <sup>-</sup>	0.1602	0.1895	0.2920	0.3117
P(H)(NH <sub>3</sub> )Cl <sub>3</sub> <sup>-</sup>	0.3356	0.5868	0.2674	0.2859

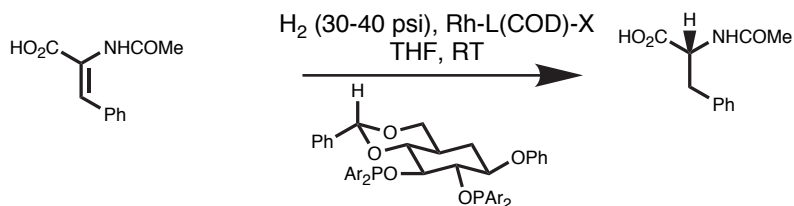
- Groups A and NH<sub>3</sub> both occupy part of the 6p<sub>y</sub> and 6p<sub>z</sub> orbitals.
- L is orthogonal to the 6p<sub>z</sub> orbital, but it overlaps well with the 6p<sub>y</sub> orbital.
- Stabilization of the transition state is achieved by increased donation ligand (L) into 6p<sub>y</sub> orbital in  $\pi$ .
- Calculations for trigonal bipyramidal complex show strengthening of Pt-L and weakening of Pt-N, Pt-A.

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

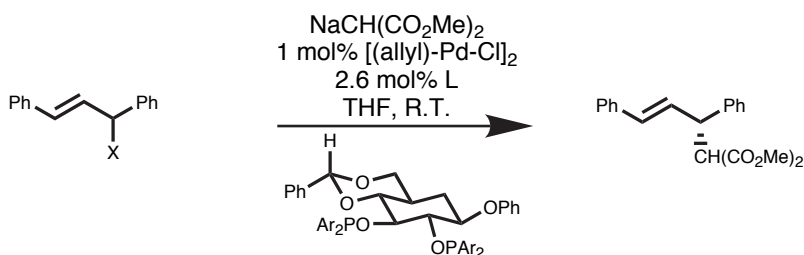
## Electronics Play an Important Role in Catalysis



Ar	% e.e.
Ph	40
3,5-Me <sub>2</sub> Ph	16
3,5-(CF <sub>3</sub> ) <sub>2</sub> Ph	85
3,5-F <sub>2</sub> Ph	78



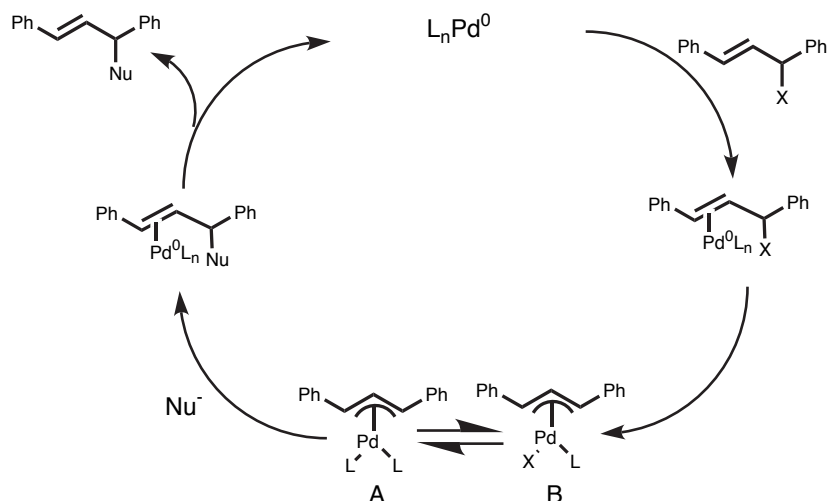
Ar	% e.e.
Ph	99
3,5-Me <sub>2</sub> Ph	94
3,5-(CF <sub>3</sub> ) <sub>2</sub> Ph	71
3,5-F <sub>2</sub> Ph	60



Ar	% e.e.
3,5-Me <sub>2</sub> Ph	0
Cy	59 (R)
3,5-(CF <sub>3</sub> ) <sub>2</sub> Ph	39 (R)
3,5-F <sub>2</sub> 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.

## Palladium Allylation: The Mechanism

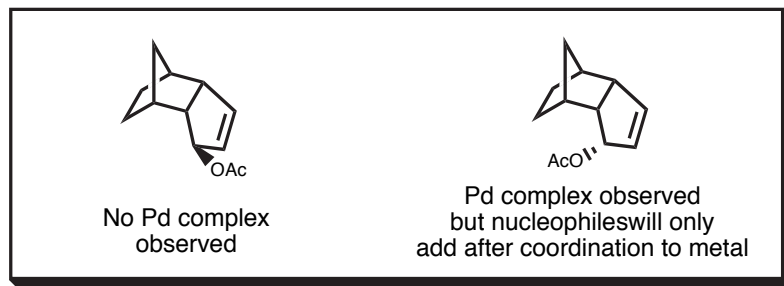
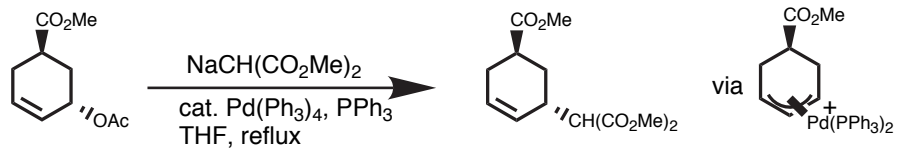
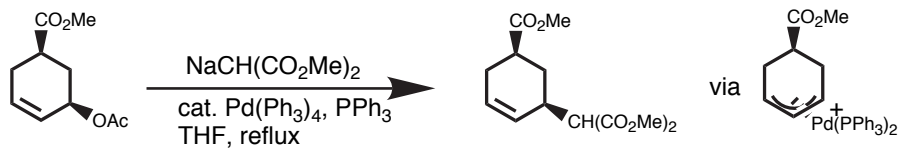


- X = OAc, Cl, OCO<sub>2</sub>R, OPO(OR)<sub>3</sub>
- Complex A is favored over complex B for bidentate ligands.
- *syn, syn* allyl complex favored, but *syn, anti* allyl complex has been made.

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



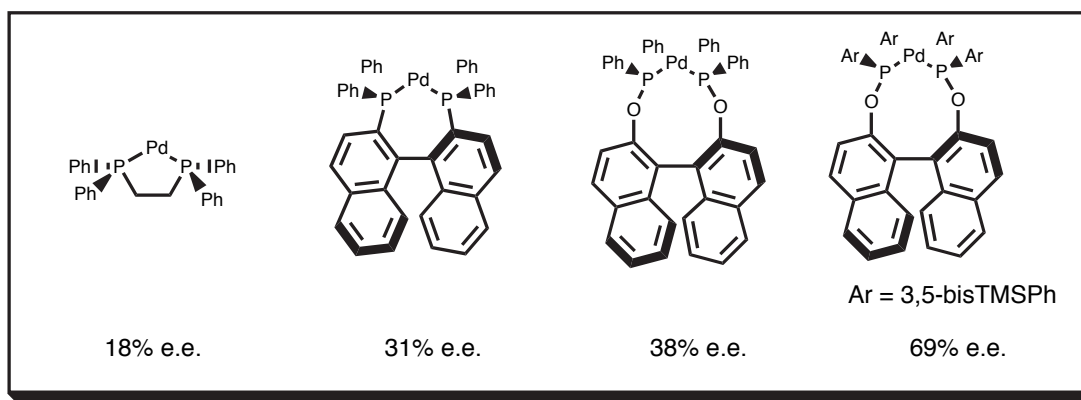
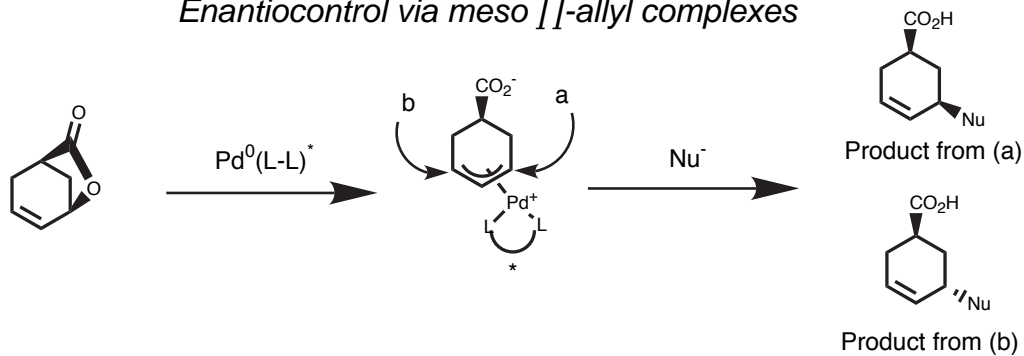
## Stereochemical Aspects of Pd Allylation



- Net retention is observed for allylations via 2 inversions (1. Pd addition, 2. Nu displacement).
- Nucleophiles with  $pK_a > 20$  will attack through metal complex.
- Nucleophiles with  $pK_a < 20$  will attack the allyl directly.

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

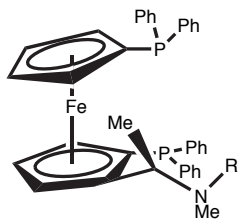
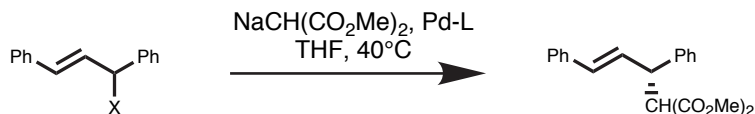
### Enantiocontrol via meso $\eta^3$ -allyl complexes



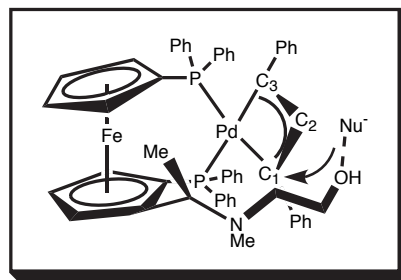
- Asymmetry of ligand is on the opposite face of the  $\eta^3$ -allyl than the incoming nucleophile.
- Increasing bite angle of ligands gives moderate success.

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

## Palladium Allylation: The Reacharound



R	% e.e.
CH <sub>2</sub> CH <sub>2</sub> OH	71
CH(CH <sub>2</sub> OH) <sub>2</sub>	90
C(CH <sub>2</sub> OH) <sub>3</sub>	96

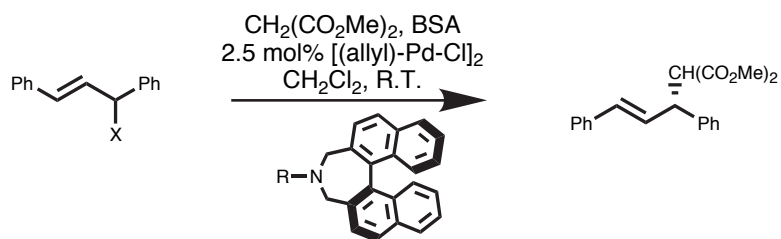


Proposed Model

- 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-C<sub>1</sub> = 3.36 Å, O-C<sub>3</sub> = 5.24 Å, and product arises from attack at C<sub>1</sub>.

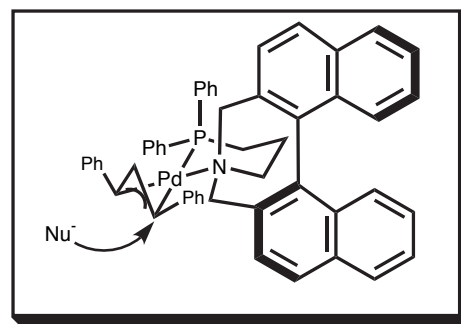
□ Hayashi, T., *Tet. Lett.*, **1986**, 27, 191.

## Palladium Allylation: Unsymmetrical Bidentate Ligands



R	mol% L	Time (min)	% e.e.
Ph <sub>2</sub> PCH <sub>2</sub> CH <sub>2</sub>	2.5	100	93
Ph <sub>2</sub> PCH <sub>2</sub> CH <sub>2</sub>	4.0	60	90
Ph <sub>2</sub> PCH <sub>2</sub> CH <sub>2</sub>	6.0	3	3
Ph <sub>2</sub> PCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	2.5	150	96

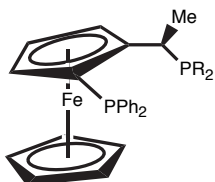
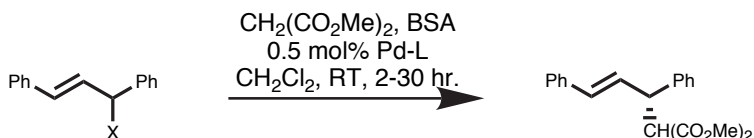
- Phosphorus has stronger trans-influence than nitrogen.
- Substitution on allyl presumed to occur trans to phosphorus.



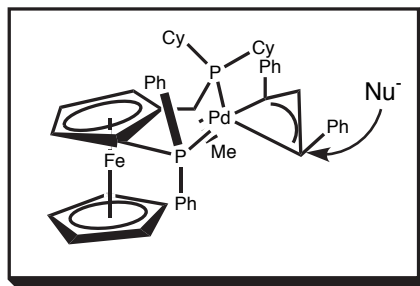
Proposed Model For Induction.

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

## Palladium Allylation: Electronic Differentiation of Phosphines



R	% e.e.
Ph	66
tBu	81
Cy	93

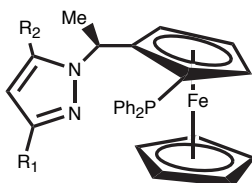
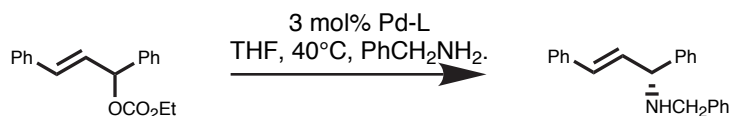


Proposed Model

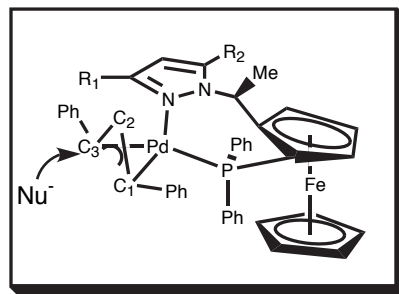
- Varying substituents on one of the phosphines has dramatic effects on the e.e.
- Excellent e.e.'s in hydrogenations, hydroborations, and  $\beta$ -ketoester reductions with Rh.
- NMR experiments show a preference for the shown Pd-allyl species.
- Nucleophile attacks trans to phosphine with stronger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

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

## Palladium Allylation: Mixed P,N ligands



R <sub>1</sub>	R <sub>2</sub>	% 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.

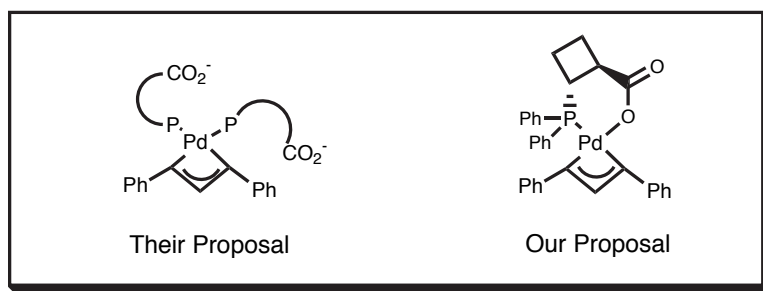
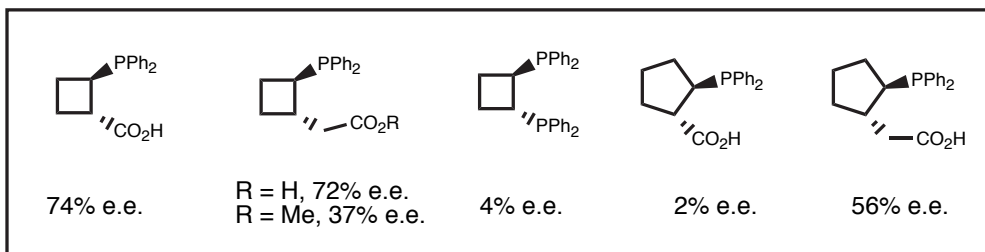
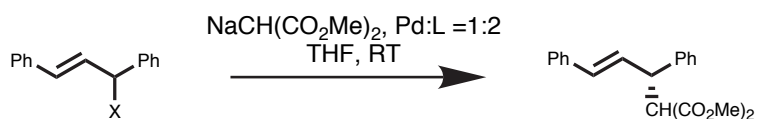


Proposed Model

- X-ray structure for Pd-allyl (R<sub>1</sub>=Ph, R<sub>2</sub>=Me) shows Pd-C<sub>1</sub> = 2.138 Å, Pd-C<sub>3</sub> = 2.268 Å.
- X-ray structure for Pd-allyl (R<sub>1</sub>=Ph, R<sub>2</sub>=Me) shows syn/syn arrangement of Pd-allyl.
- X-ray structure for Pd-allyl (R<sub>1</sub>=9-triptycyl, R<sub>2</sub>=Me) shows anti/syn arrangement of Pd-allyl.

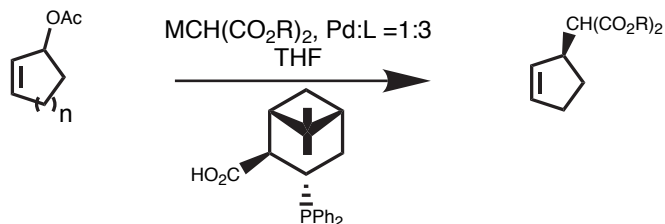
Togni, A., *J. Am. Chem. Soc.*, **1996**, 118, 1031.

**Palladium Allylation:  
Phosphinocarboxylic Acids**

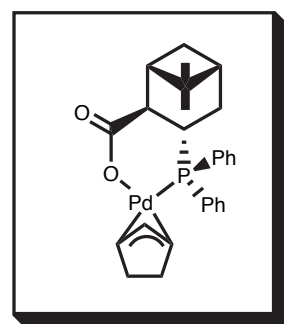


□ Minami, T., *Tet. Asymm.*, **1991**, 2, 667.

**Palladium Allylation:  
More Phosphinocarboxylic Acids**



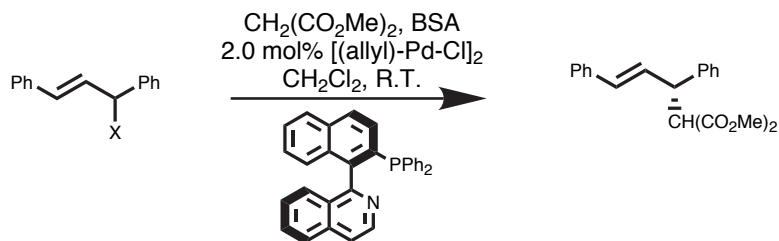
R	n	M	T (°C)	% e.e.
Me	1	Na	25	75
tBu	1	Na	0	81
Me	1	Li	25	83
tBu	1	Li	25	85
Me	2	Na	25	91
tBu	2	Na	25	96
Me	2	Li	25	98
tBu	2	Li	25	98



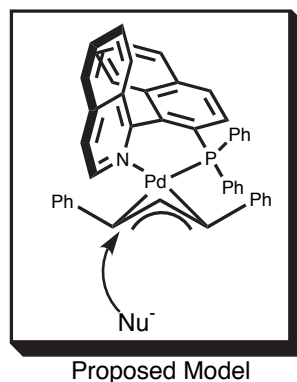
Proposed Intermediate

□ Helmchen, G., *J. Chem. Soc. Chem. Comm.*, **1995**, 1845.

**Palladium Allylation:  
More Phosphinocarboxylic Acids**

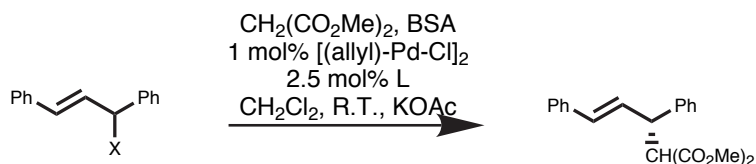


Solvent	% e.e.
$\text{CD}_2\text{Cl}_2$	76
$\text{CD}_3\text{CN}$	78
$\text{CD}_2\text{Cl}_2/\text{NaCH}(\text{CO}_2\text{Me})_2$	75
$\text{CD}_2\text{Cl}_2/\text{NaCH}(\text{CO}_2\text{Me})_2$ and 1 eq. 15-crown-5	90
$\text{CD}_3\text{CN}/\text{NaCH}(\text{CO}_2\text{Me})_2$ and 1 eq. 15-crown-5	98

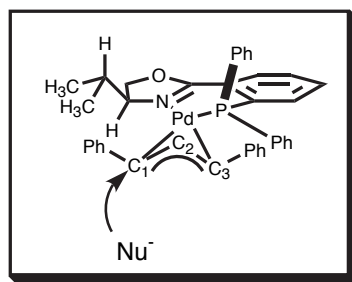


□ Brown, J., *Tetrahedron*, **1994**, 50, 4493.

**Palladium Allylation:  
Phosphinoxazolines**



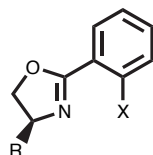
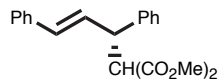
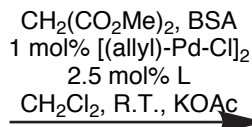
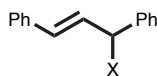
R	% e.e.
Me	89
PhCH <sub>2</sub>	97
iPr	98
Ph	99
tBu	95



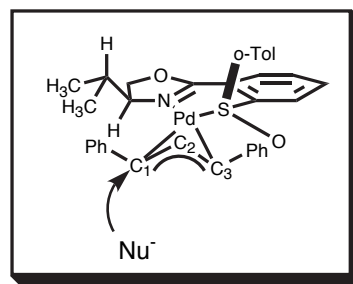
- Other nucleophiles have also been used ( $\text{CH}_2(\text{COMe})_2$ ,  $\text{HC}(\text{NHAc})(\text{CO}_2\text{Et})_2$ ,  $\text{PhCH}_2\text{NH}_2$ )
- Diakyl propenyl substrates can also be used with these ligands.
- Xray structure shows Pd-C<sub>1</sub> = 2.263 Å, Pd-C<sub>3</sub> = 2.143 Å
- Modest success has also been achieved 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



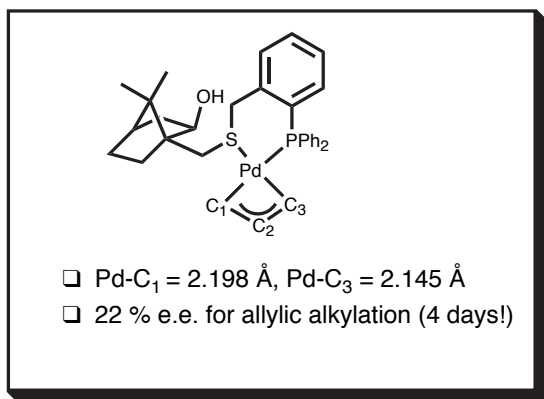
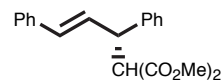
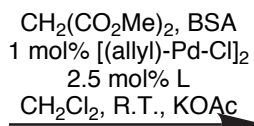
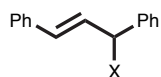
R	X	% e.e.
iPr	PPh <sub>2</sub>	98
iPr	SPh	92
iPr	(S)-S(O)Tol	88
H	(S)-S(O)Tol	56
iPr	(R)-S(O)Tol	55



It's not so easy to see here...

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

### Palladium Allylation: Mixed P/S Ligands



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

