



# CATALYSIS

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## 4.1 HISTORY

### **Berzelius (1836)**

Introduces the word “catalysis”

*Ich werde sie daher [...] die **katalytische** Kraft der Körper und die Zersetzung durch dieselbe **Katalyse** nennen, gleichwie wir mit dem Wort Analyse [...] verstehen.*

### **Ostwald (1901)**

*A catalyst is a substance that changes the rate of a chemical reaction without itself appearing into the products*

*Ein Katalysator ist jeder Stoff, der, ohne im Endprodukt einer chemischen Reaktion zu erscheinen, ihre Geschwindigkeit verändert*

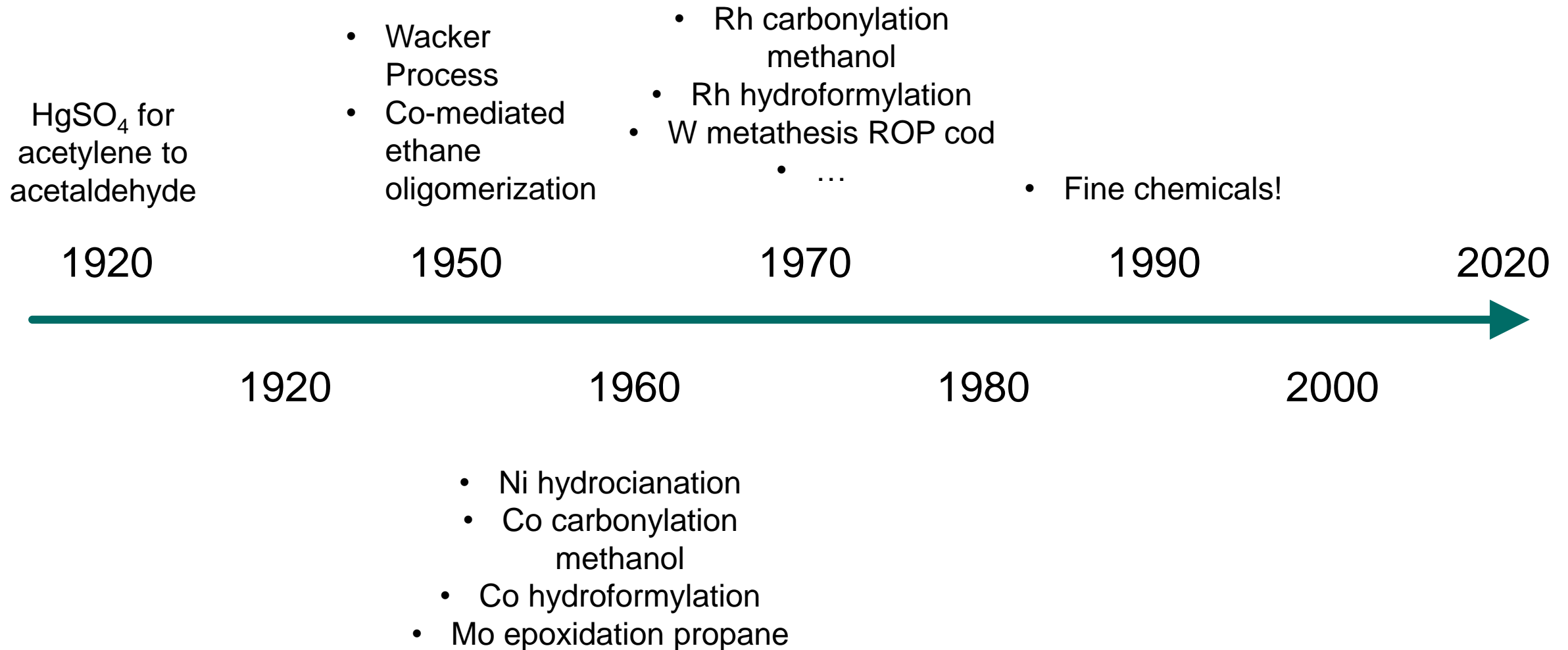
### **Modern-version**

A catalyst is a substance which increases the rate at which a chemical reaction approaches equilibrium without becoming itself permanently involved

Berzelius, *Jahresberichte Chemie* **1836**, 15, 237-245 [relevant portion at p. 243]. [LINK](#)  
Ostwald, *Zeitschrift für Elektrochemie*, **1901**, 7, 72, 995. DOI: [10.1002/bbpc.19010077203](https://doi.org/10.1002/bbpc.19010077203)

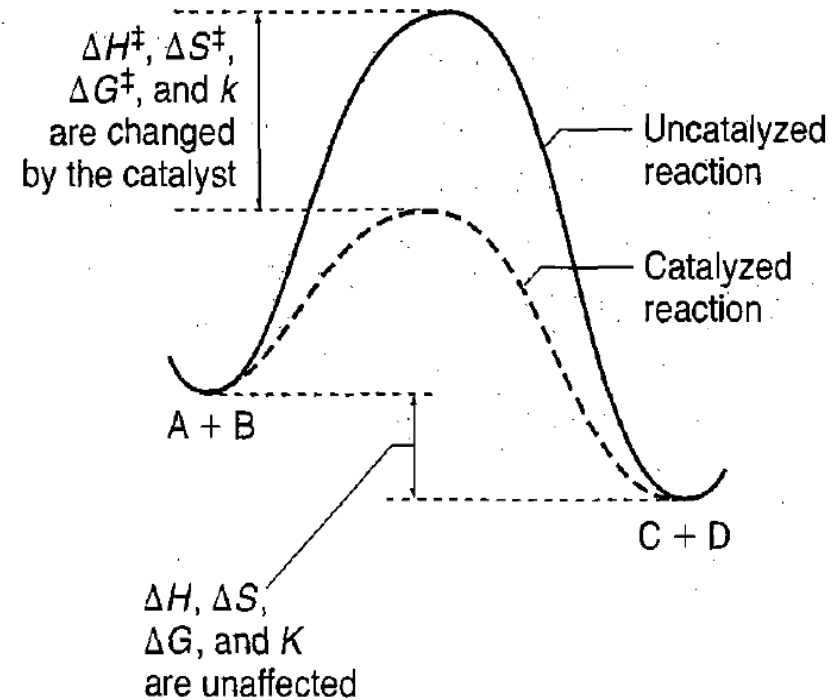


## 4.1 HISTORY





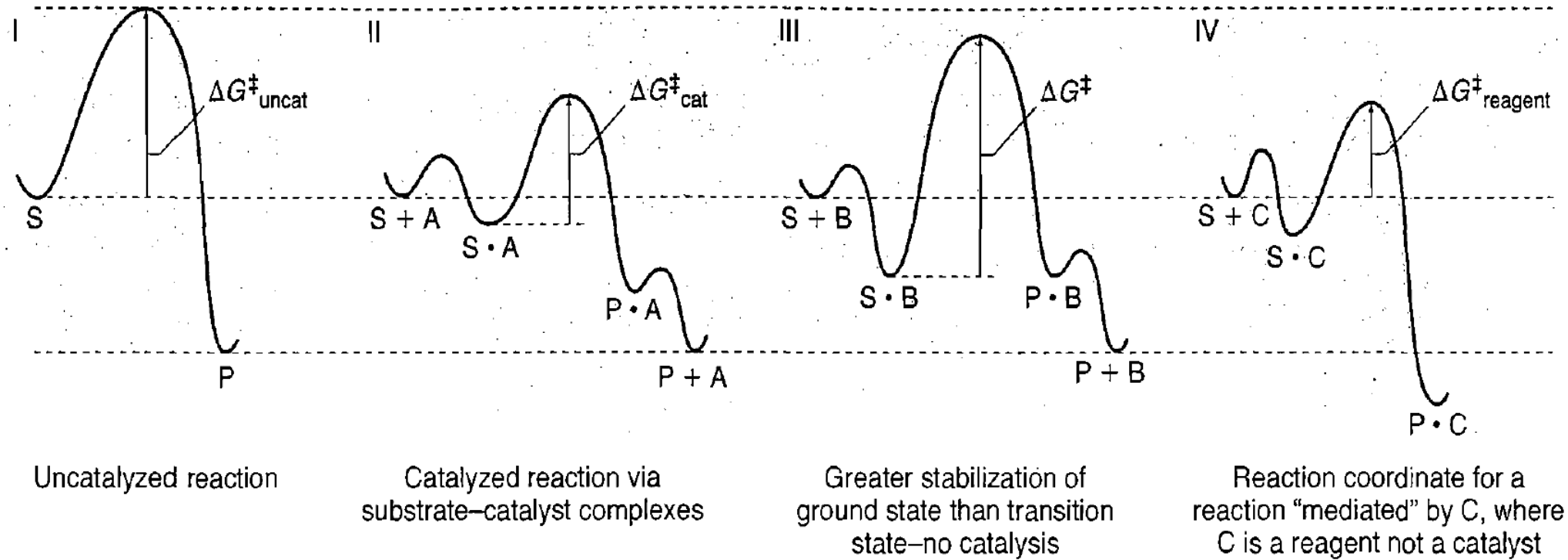
## 4.2.1 PRINCIPLES OF CATALYSIS – THERMODYNAMICS



Hartwig, 14.1



## 4.2.2 PRINCIPLES OF CATALYSIS – REACTION COORDINATE



Hartwig, 14.2



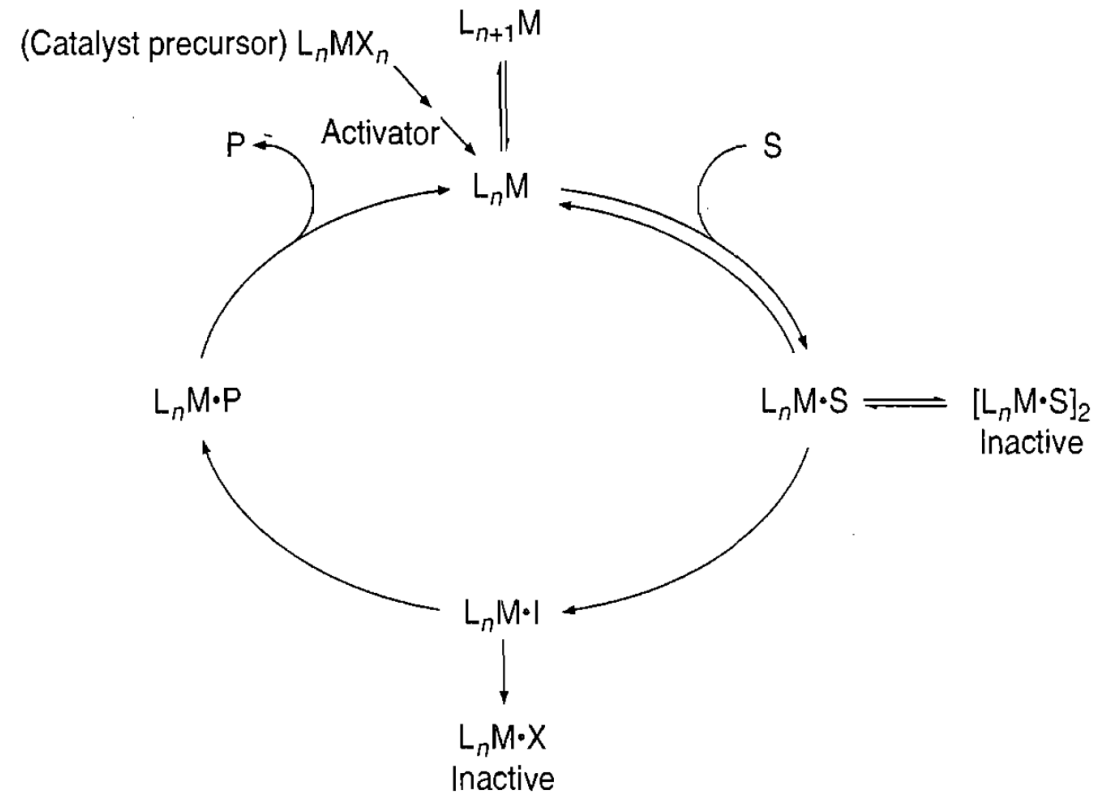


## 4.2.4 PRINCIPLES OF CATALYSIS – CATALYTIC CYCLE

### Catalytic cycle

combination of steps for:

- Reagent consumption
- Product formation
- Catalyst regeneration



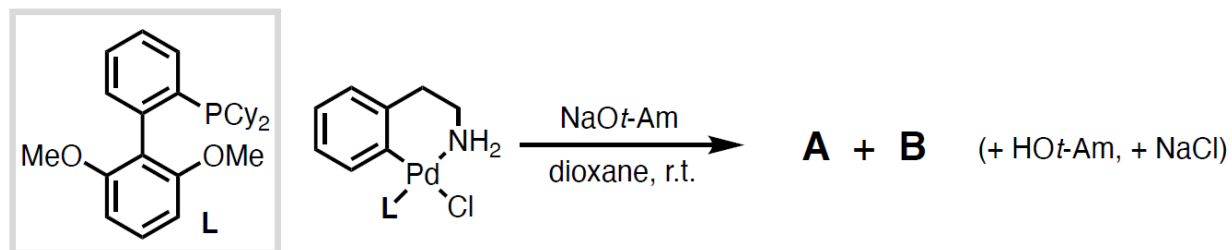
### Active catalyst

sum of the concentrations of all catalytic species on-cycle

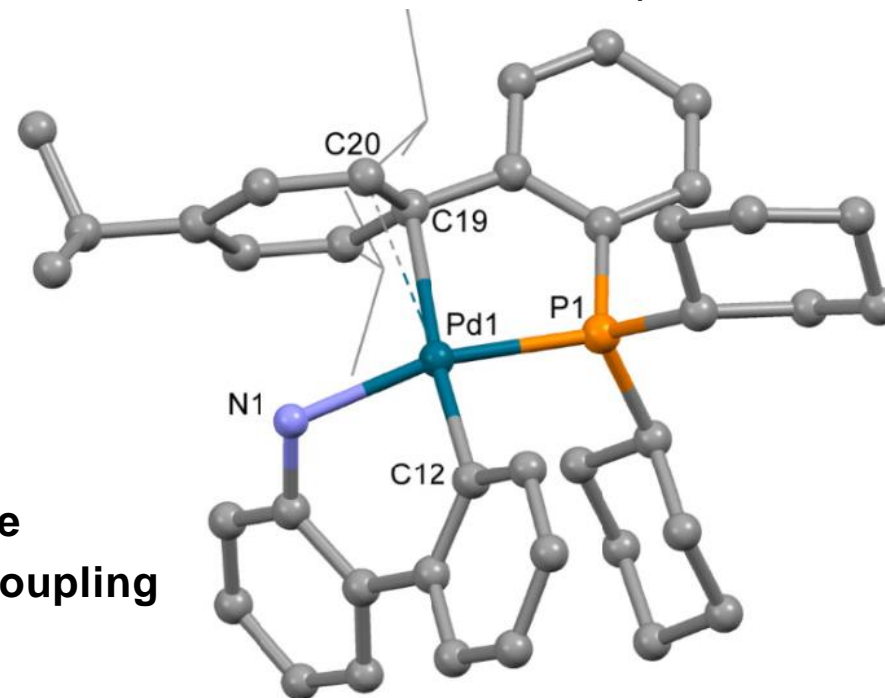


## POD #2 – CATALYST PRECURSORS (PRECATALYSTS)

The following complex reacts to give two products, A and B, upon treatment with base at room temperature.



- Draw the structures for A and B
- Propose a synthetic route to the starting complex
- Describe one or more potential advantages and one or more potential disadvantages of using this complex as a cross-coupling precatalyst.



Buchwald and co-workers, *JACS* **2008** 130, 21, 6686. DOI: [10.1021/ja801137k](https://doi.org/10.1021/ja801137k)





## 4.3 COMMON METRICS

$$TON = \frac{\text{number of substrate molecule converted into product molecules}}{\text{number of catalyst molecule}} \quad \text{stability}$$

$$TOF = \frac{TON}{\text{time}} \quad \text{kinetic reactivity}$$

- Turnover limiting step vs. rate limiting step
- Catalyst resting state (may be off-cycle/dormant state)



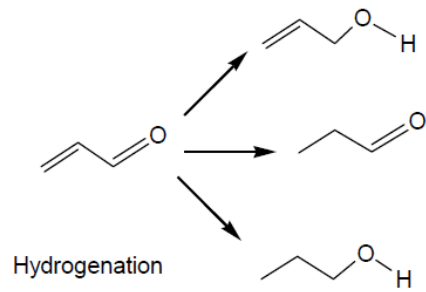
## 4.4.1 HOMOGENEOUS VS. HETEROGENEOUS

- **HOMOGENEOUS** catalyst in the same phase as reactants (usually liquid phase). Generally discrete, molecular.
- **HETEROGENEOUS** catalyst in a different phase (usually solid phase).

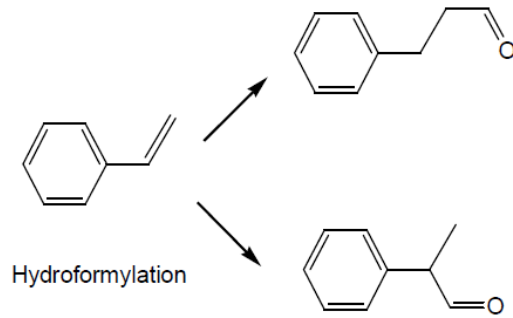
	homogeneous	heterogeneous
✓	Rapid diffusion/heat rate in solution Mechanism (cat. Characterization) Tunability (ligand design) Selectivity (chemo-, regio-, diastereo-, enantio-)	Low-cost Ease of separation and recyclability Stability (e.g. high T) Catalyst regeneration
✗	Difficult catalyst regeneration Catalyst separation	Slow-rate Low-selectivity Non-uniformity



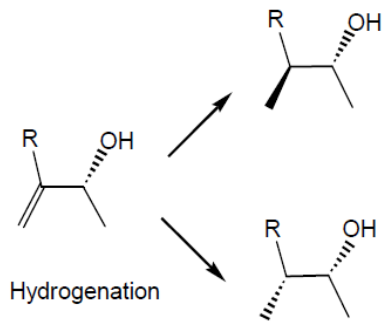
# 4.4.1 HOMOGENEOUS CATALYSIS



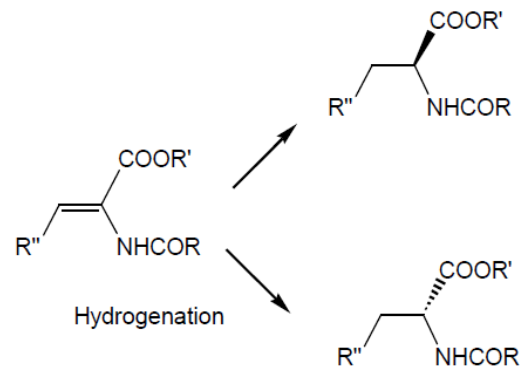
Chemoselectivity



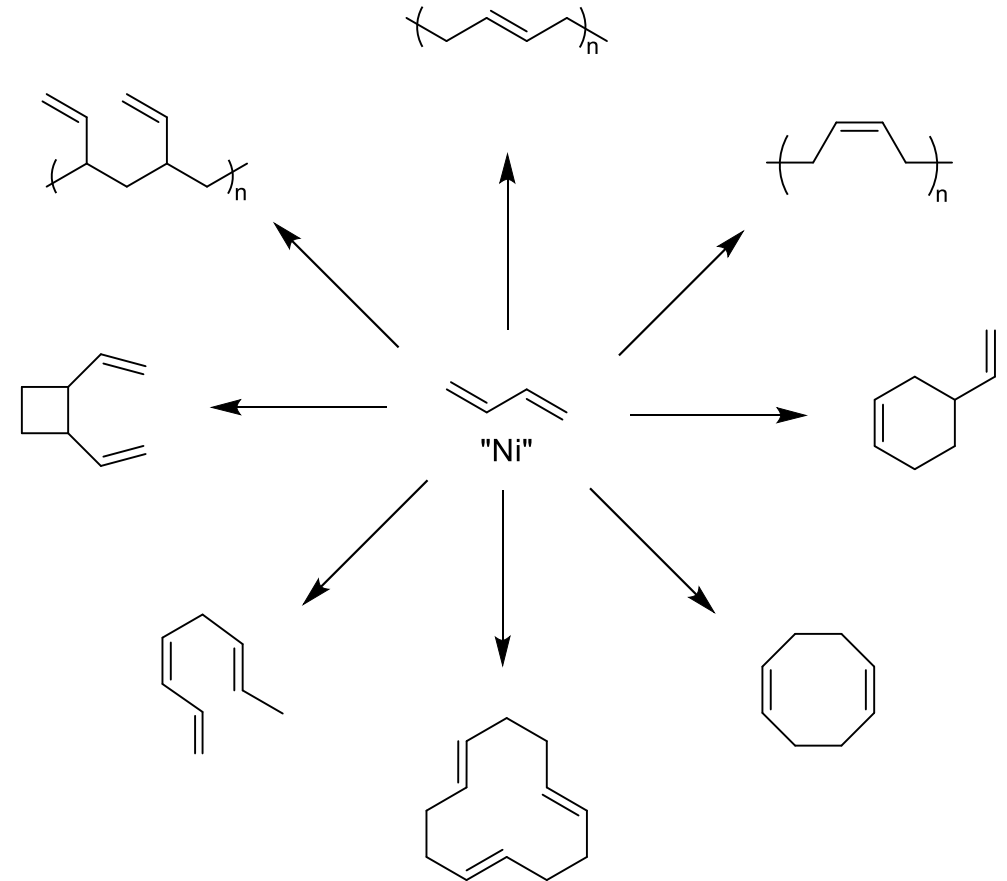
Regioselectivity



Diastereoselectivity



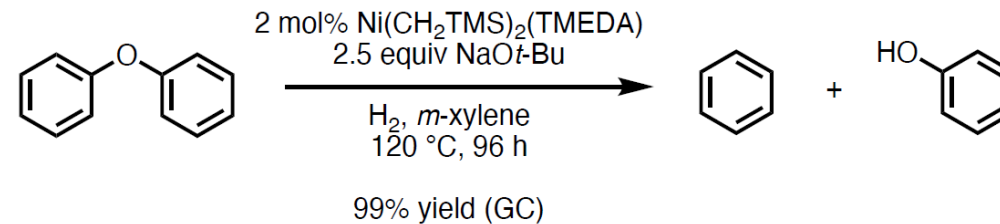
Enantioselectivity





## POD #3

Consider the following diaryl ether hydrogenation method. **Propose one or more experiment(s) to elucidate whether the reaction is homogenous or heterogeneous.**



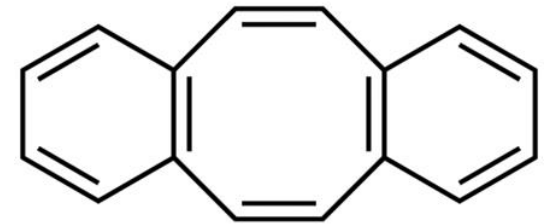
Hartwig and co-workers *JACS* **2012**, 134, 50, 20226. DOI: [10.1021/ja3085912](https://doi.org/10.1021/ja3085912)



## 4.4.2 HOMOGENEOUS VS. HETEROGENEOUS

**Q:** *Homogeneous reaction or nanoparticulate / colloidal metal particles?*

- TEM / DLS
- Kinetic analysis
- “Three phase test”
- Additives (Hg and dibenzo[a,e]cyclooctatetraene)



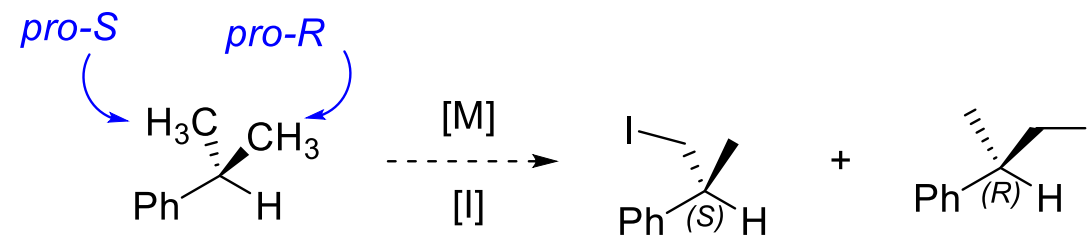
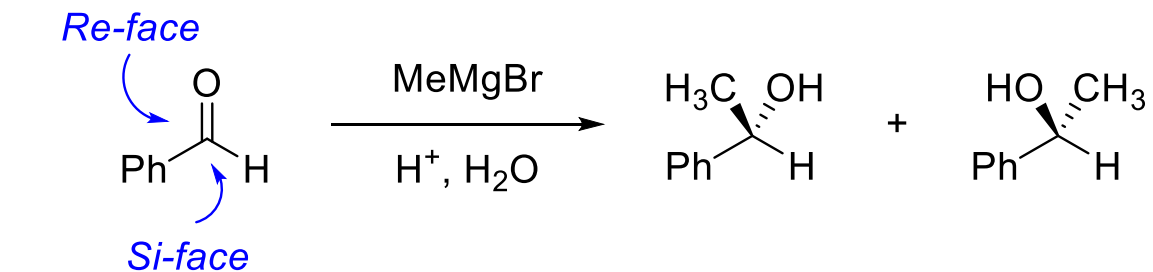


## 4.5.1 FUNDAMENTALS OF ASYMMETRIC CATALYSIS – INTRO

Most commonly: chiral catalyst + prochiral substrate

**Prochiral** a position on an achiral molecule that becomes a chiral center upon addition of an achiral group to one face or replacement of one group by a new group

**Nomenclature (CIP)**



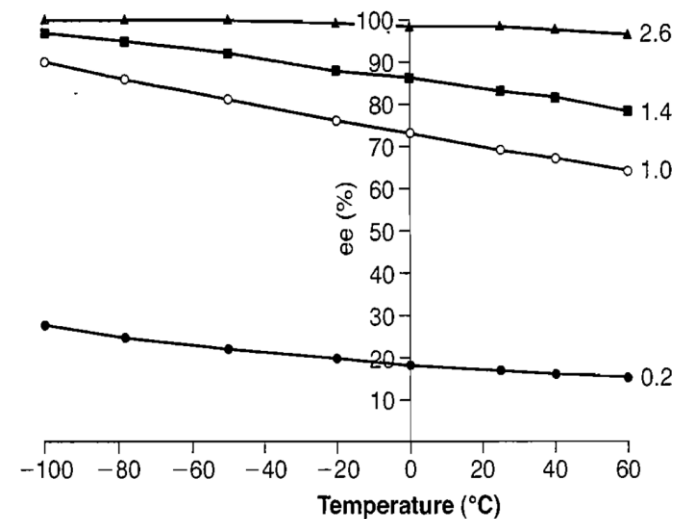
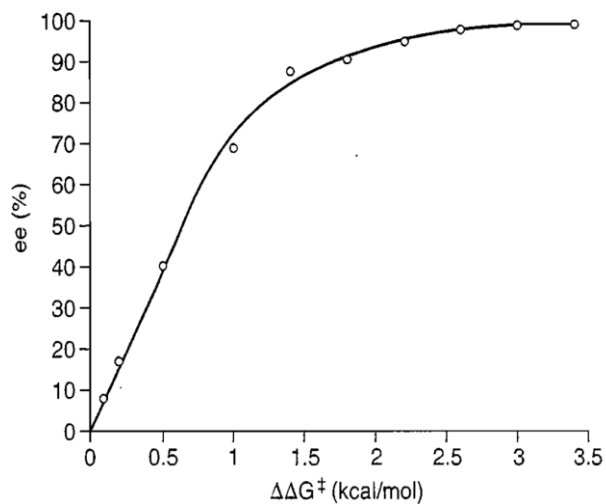


## 4.5.1 ASYMMETRIC CATALYSIS – DESCRIPTORS

**Optical purity** = optical rotation mixture / optical rotation single enantiomer \* 100 = ee (%)

**Enantiomeric excess (%)** = ([maj] – [min]) / ([maj]+[min]) \* 100 = ee (%)

**Enantiomeric ratio** = [maj] / [min] =  $e^{-(\Delta\Delta G^\ddagger/RT)}$





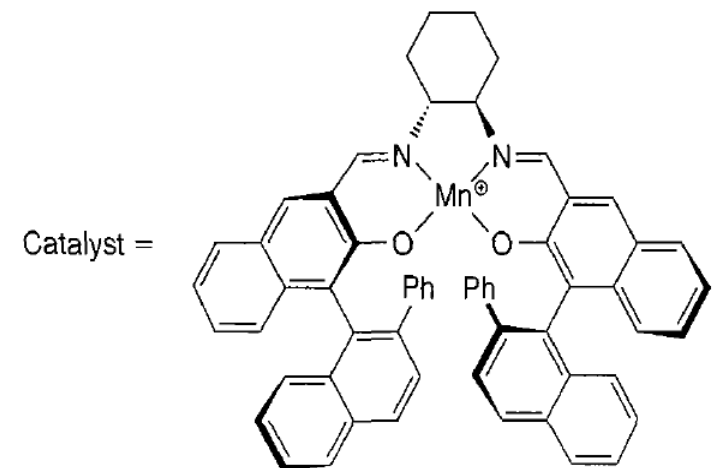
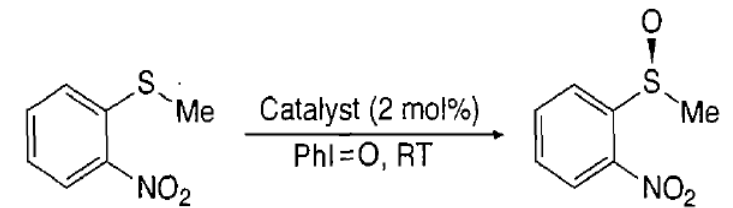
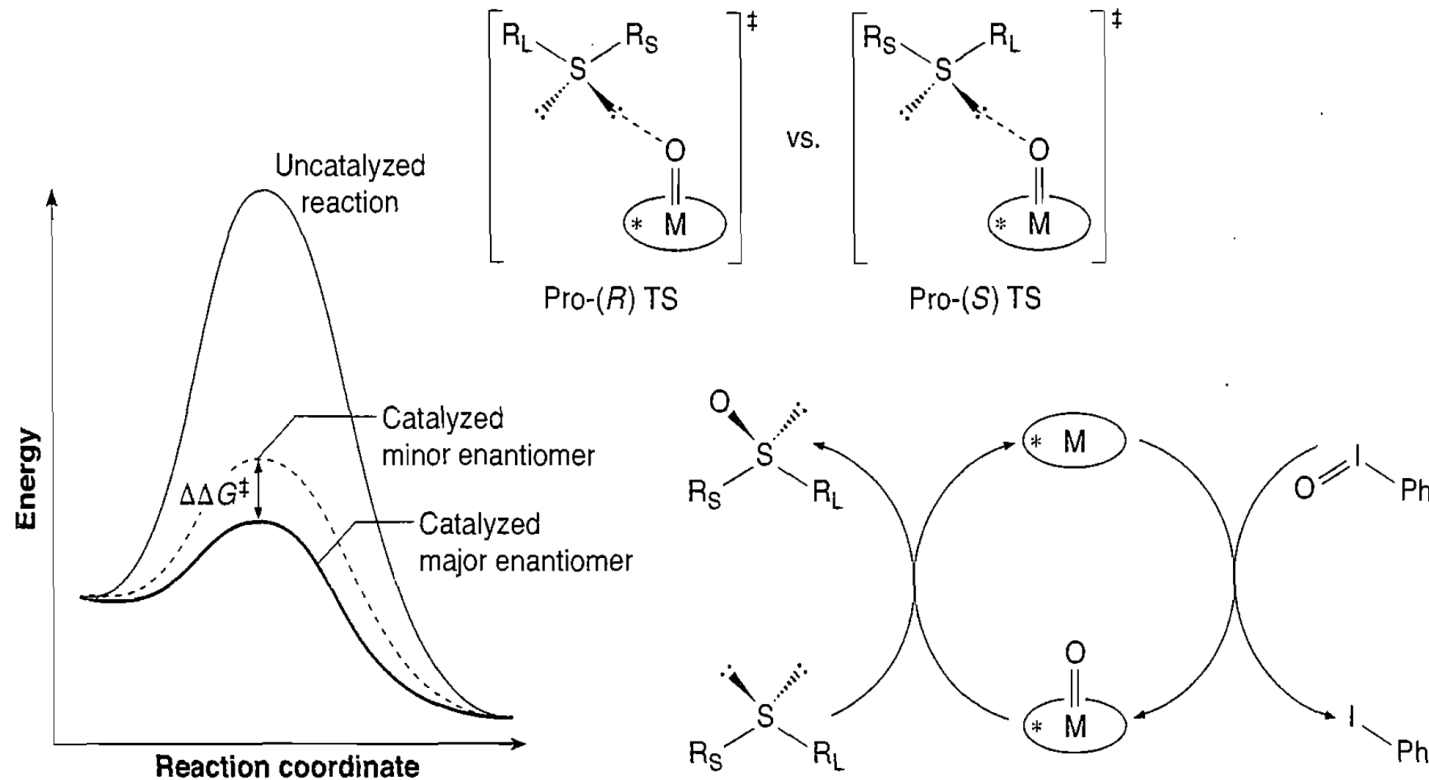
## 4.5.2 TYPES OF CATALYTIC ASYMMETRIC REACTIONS

1. Reactions with a single enantioselectivity-determining step
2. Reactions with reversibility prior to the enantioselectivity-determining step





## 4.5.2.1 SINGLE ENANTIOSELECTIVITY-DETERMINING STEP





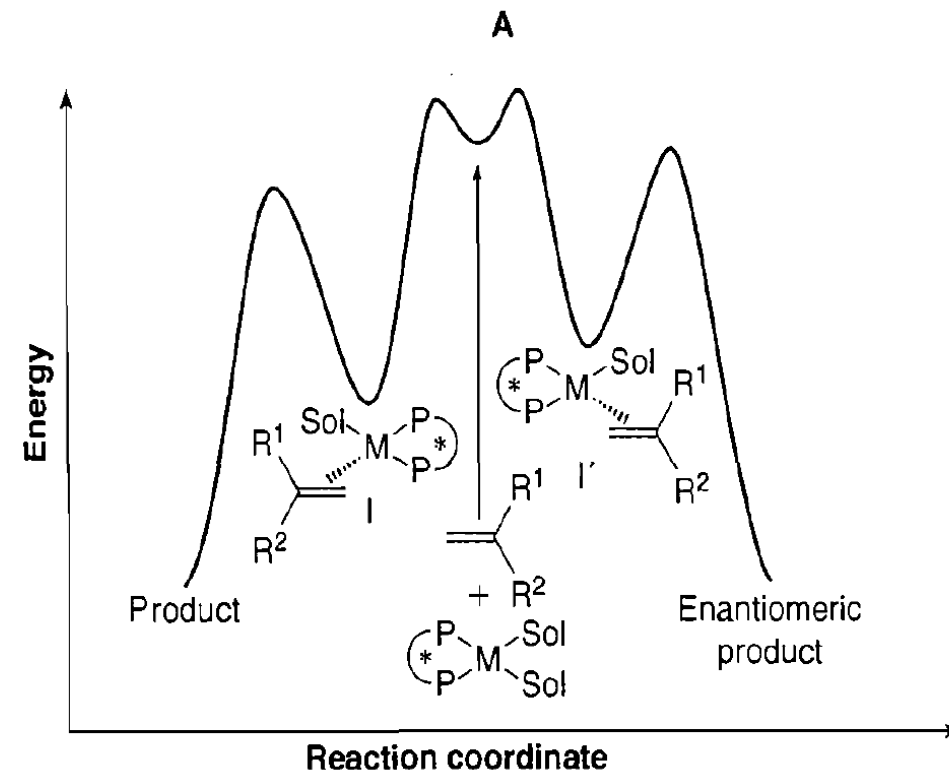
## 4.5.2.2 REACTIONS WITH REVERSIBILITY PRIOR TO THE ENANTIOSELECTIVITY-DETERMINING STEP

### Two possible scenarios:

1. Interconversion of diastereoisomeric M-olefin complex is slow compared relative to the rate of conversion into products
2. Interconversion of the two diastereoisomeric M-olefin complexes is faster than the reaction to form the products (i.e. meets Curtin—Hammet conditions)



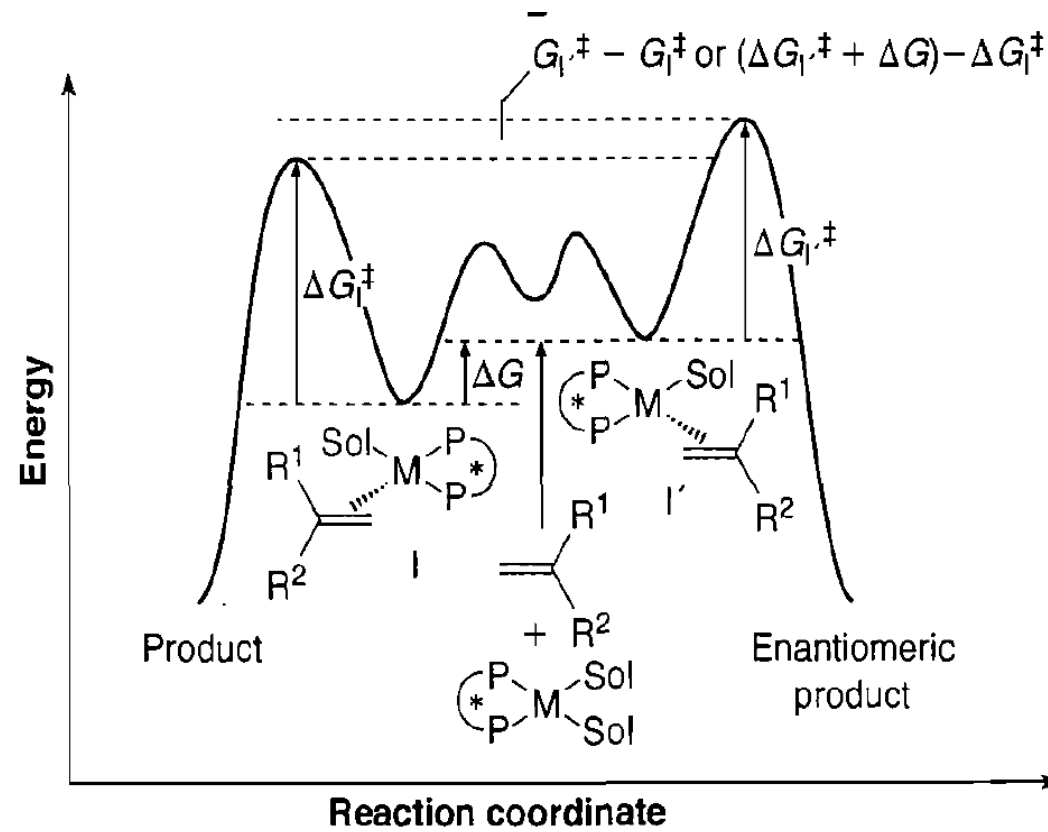
## 4.5.2.2 SCENARIO 1





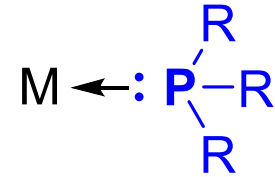
## 4.5.2.2 SCENARIO 2 – CURTIN—HAMMET

$$\frac{[R]}{[S]} = k_{eq} \frac{k_I}{k_{I'}}$$





## 4.6 PHOSPHINES



- Among the most important family of ligands
- Soft-soft match (e.g. w/ late TM)
- Can dramatically affect property of M-center



## 4.6.1 PHOSPHINES – BITE ANGLE

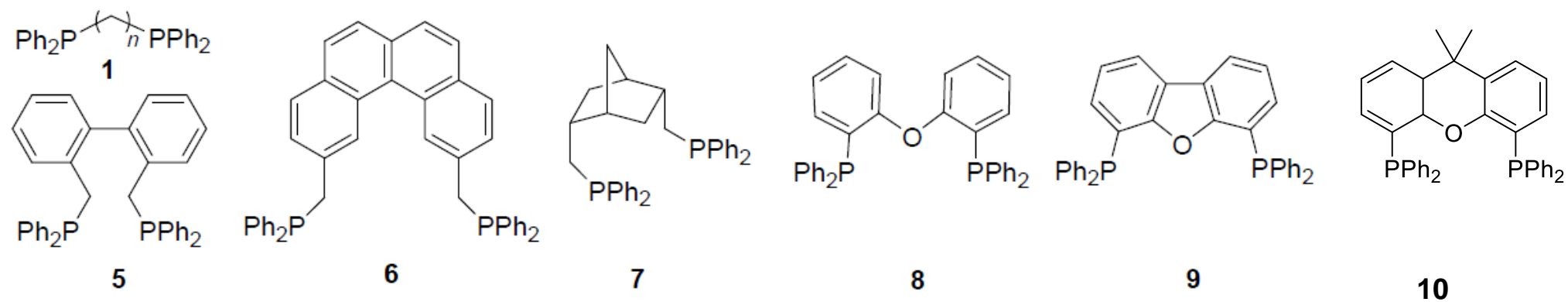
### Bite angle

- Crystal structures, depends on M

### “Natural bite angle”

- Only ligand-based, from comp. chem. calculations

Ligand	$\beta_n^a$ (in $^\circ$ )	Ligand	$\beta_n^a$ (in $^\circ$ )
<b>1</b> , $n = 1$ (dppm)	72	<b>5</b> (BISBI)	113 (92–155)
<b>1</b> , $n = 2$ (dppe)	84 (70–95)	<b>6</b> (TRANSPHOS)	111
<b>1</b> , $n = 3$ (dppp)	91	<b>7</b> (NORPHOS)	123 (110–145)
<b>1</b> , $n = 4$ (dppb)	98	<b>8</b> (DPEphos)	102 (86–120)
<b>2</b> (DIOP) <sup>b</sup>	102 (90–120)	<b>9</b> (DBFphos)	131 (117–145)
<b>3</b> (BINAP) <sup>b</sup>	92	<b>10</b> (Xantphos) <sup>c</sup>	112 (97–135)
<b>4</b> (Me-DuPHOS) <sup>b</sup>	83	<b>11</b> (DPPF) <sup>c</sup>	96



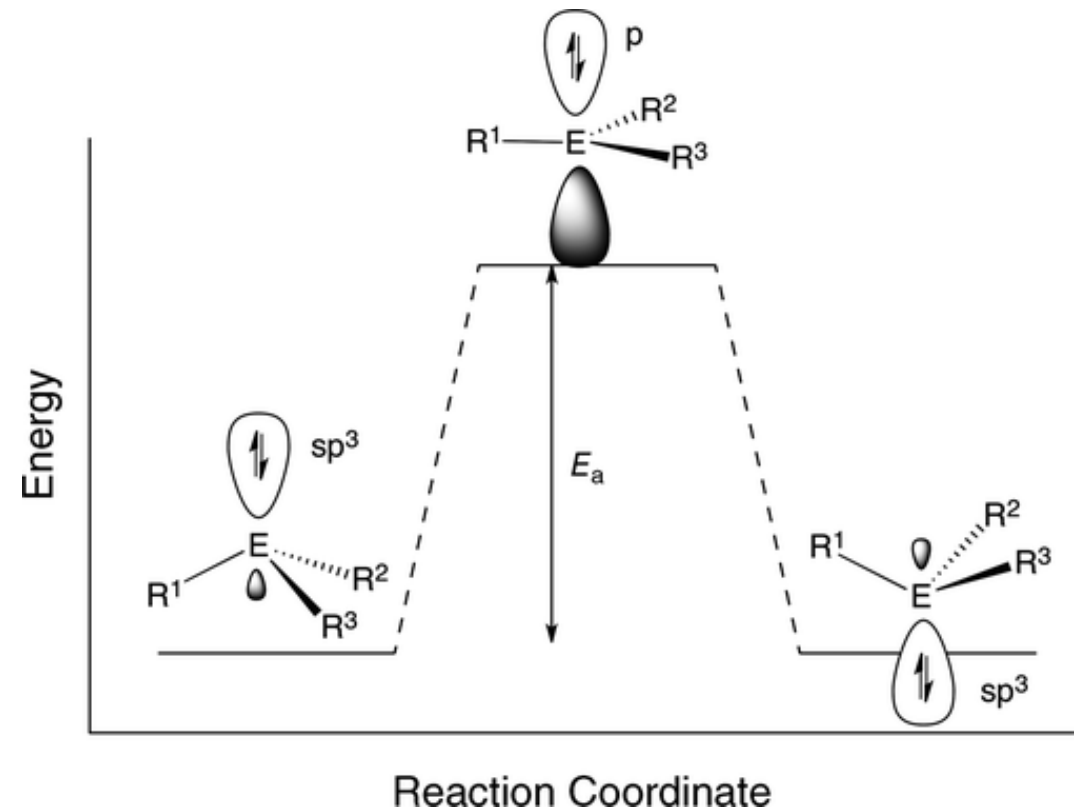
van Leeuwen, *Chem Rev* **2000** 100, 8, 2741. DOI: [10.1021/cr9902704](https://doi.org/10.1021/cr9902704)



## 4.6.2 PHOSPHINES – BARRIER TO INVERSION

- **1971**: barrier 29-35 kcal/mol
- Relative insensitive to substituents  
(1960's homogeneous hydrogenation)

Ligands chiral at P?

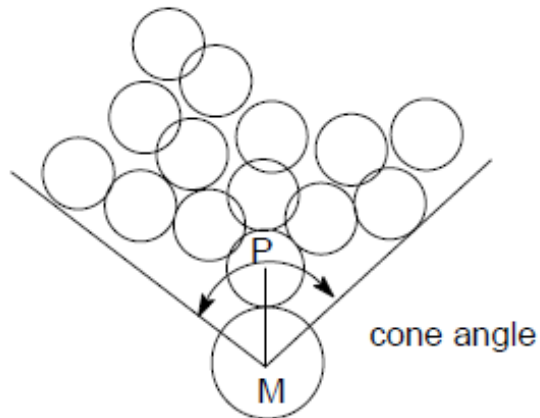


Mislow, *JACS* **1971** 93, 3, 773. DOI: [10.1021/ja00732a036](https://doi.org/10.1021/ja00732a036)



## 4.6.3 PHOSPHINES – CONE ANGLE

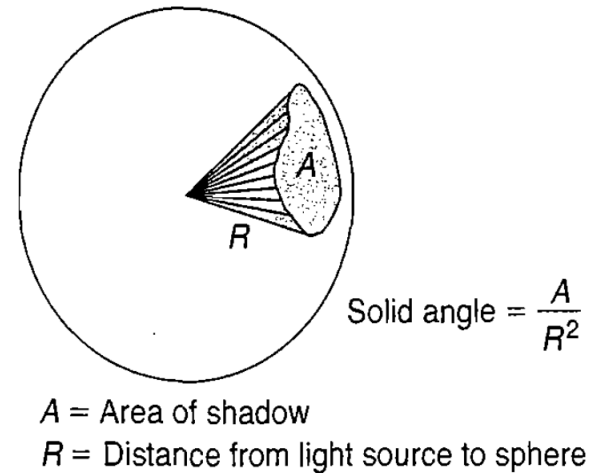
### Tolman's cone angle



### Limits:

- Conformations
- Unsymmetrical phosphines

### Solid angle



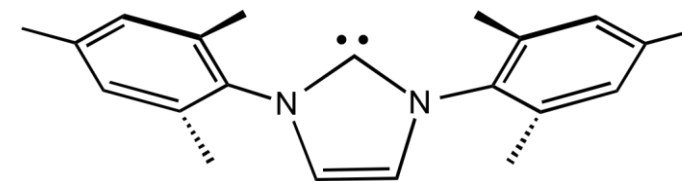
Tolman, *Chem Rev* **1977** 77, 3, 313. DOI: [10.1021/cr60307a002](https://doi.org/10.1021/cr60307a002)





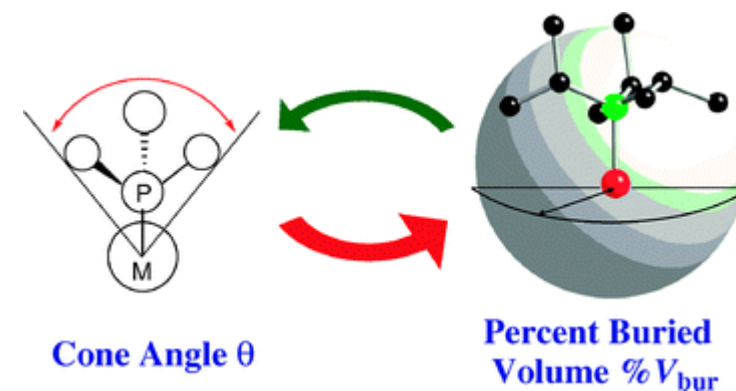
## 4.7 NHC VS. PHOSPHINES

- Stronger  $\sigma$ -donor than phosphines
- NHC-M does not dissociate
- If N-Ar they create a more sterically hindered metal-center than phosphines



% **buried volume** (originally for NHC now for phosphines as well)

Online tool at <https://www.molnac.unisa.it/OMtools/sambvca.php>



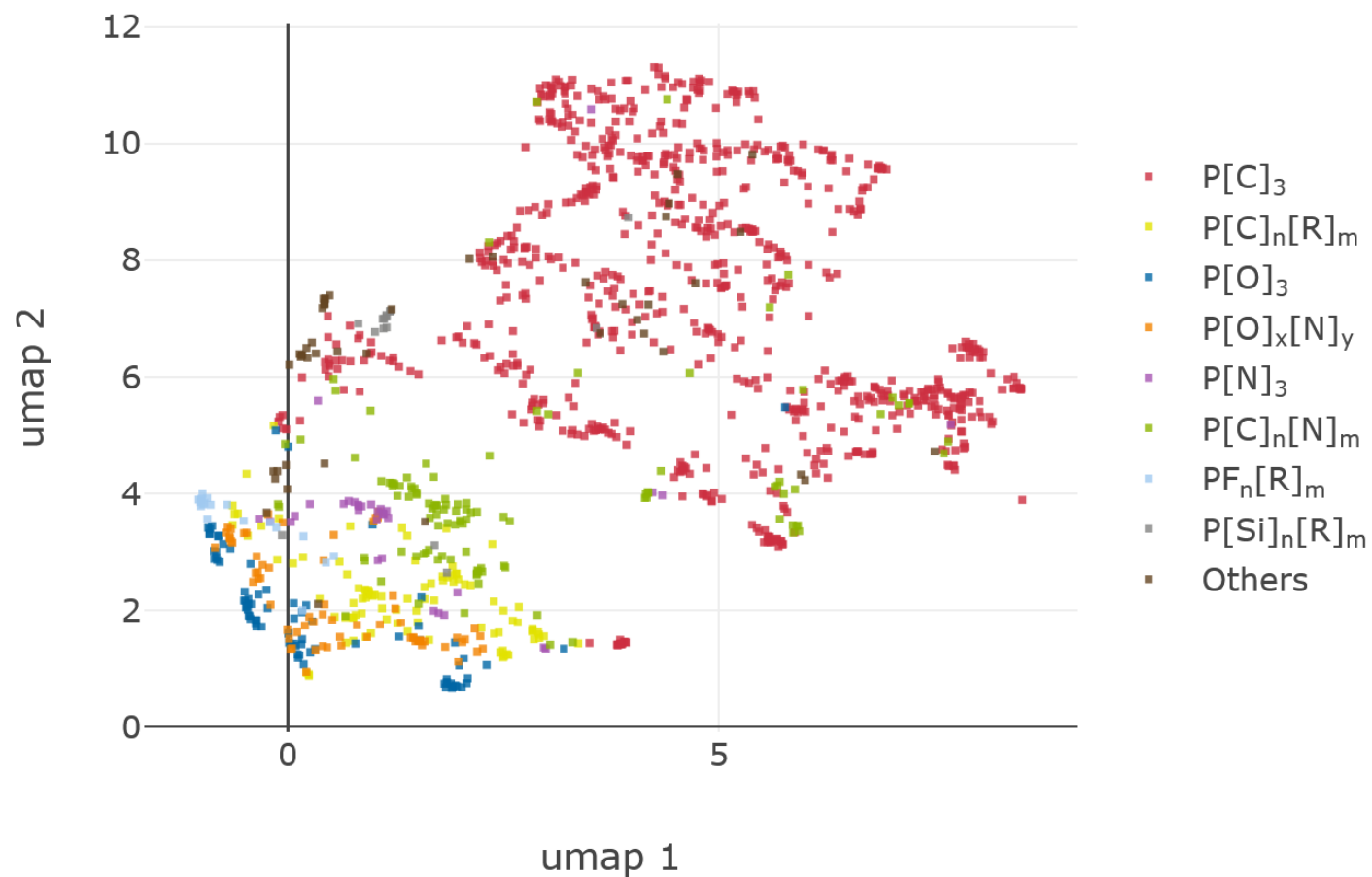


## 4.8 PHOSPHINES PARAMETRIZATION – KRAKEN

### Kraken

<https://kraken.cs.toronto.edu/>

*“calculated descriptors for 1558 ligands, including commercially available examples, and trained machine learning models to predict properties of over 300000 new ligands”*

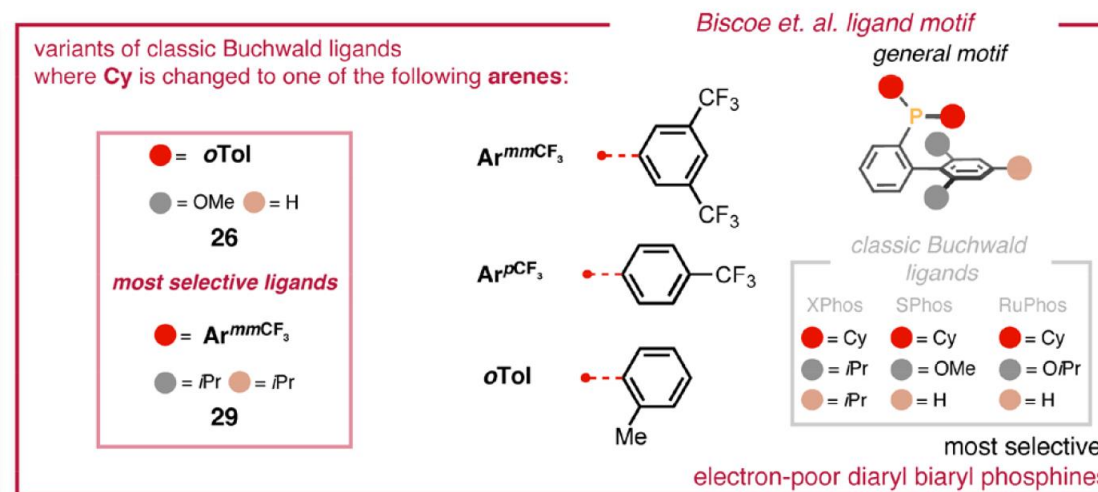
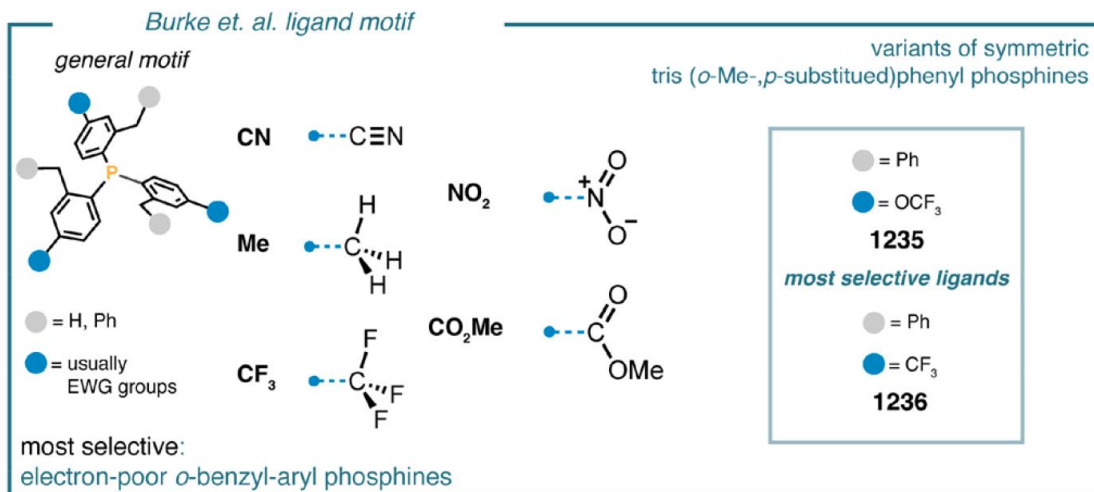
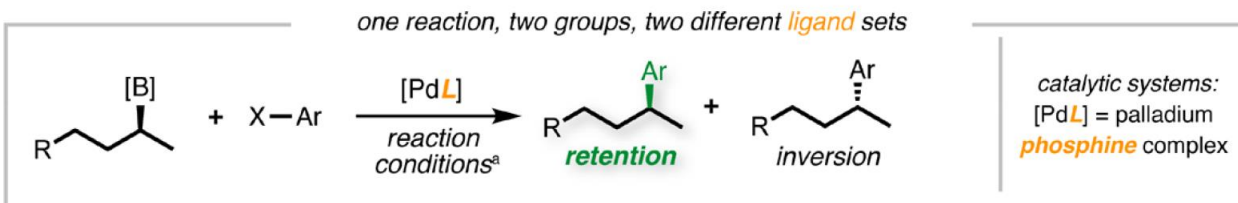


Gensch et al., *JACS* **2022** 144, 3, 1205. DOI: [10.1021/jacs.1c09718](https://doi.org/10.1021/jacs.1c09718)



## 4.8 PHOSPHINES PARAMETRIZATION – KRAKEN

### the role of organophosphorus ligands on stereospecific Suzuki couplings



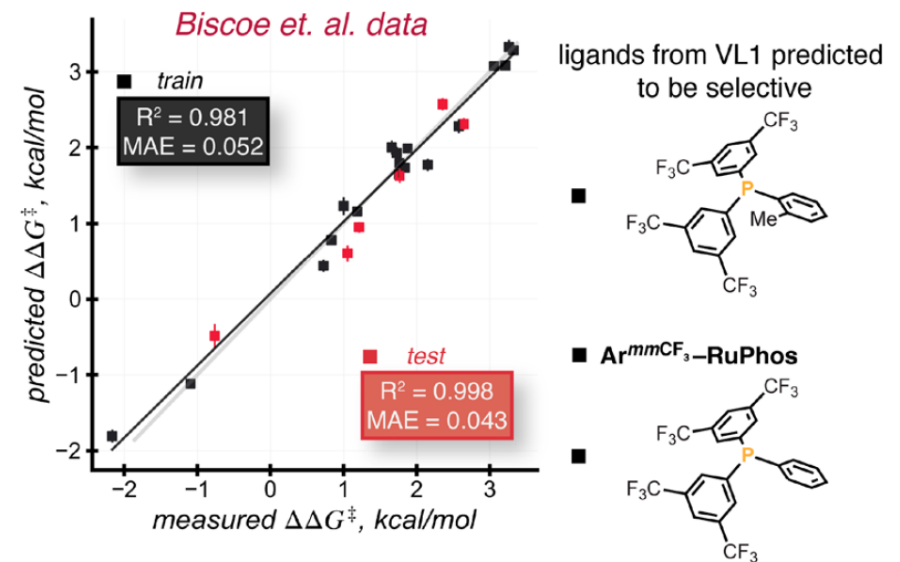
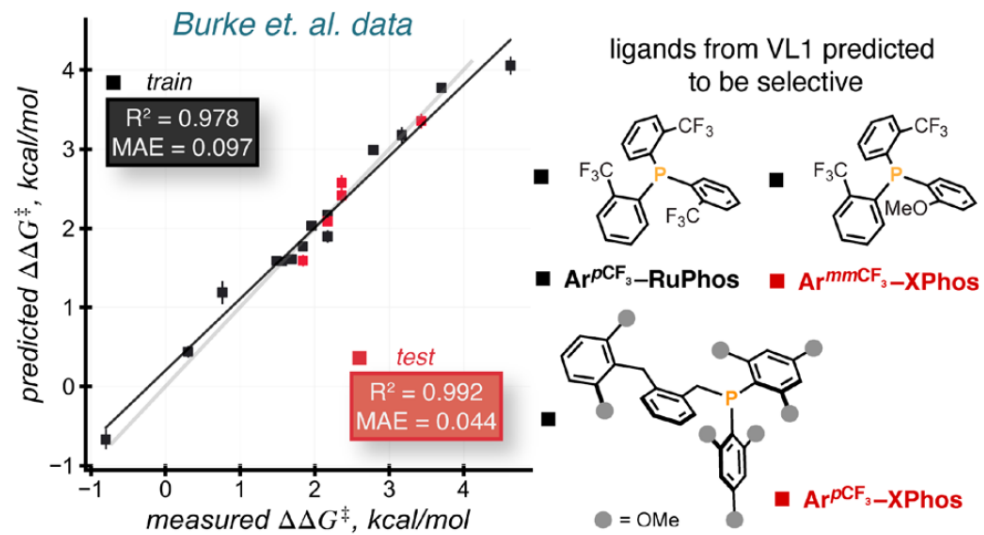
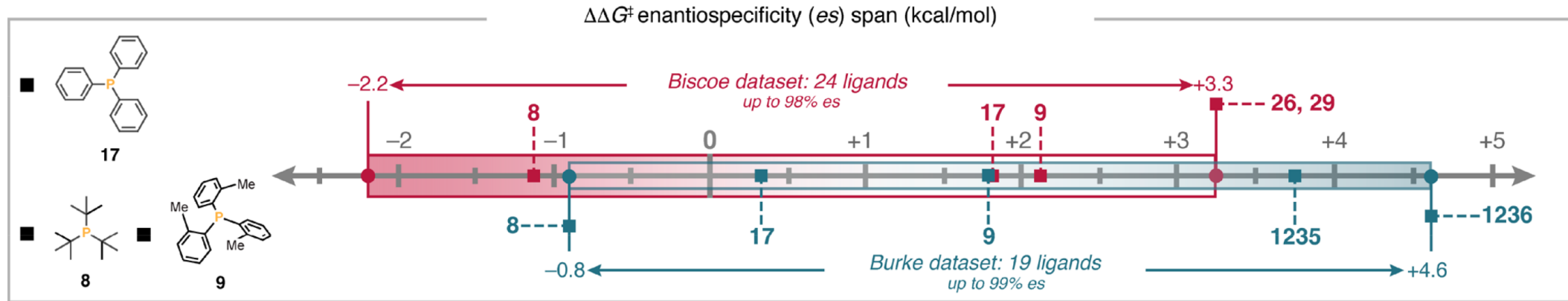
[B] = BF<sub>3</sub>K (R), R = Ph, X-Ar = 1-Cl-4-CO<sub>2</sub>Et-C<sub>6</sub>H<sub>4</sub>,  
[PdL] = G3 Buchwald precatalyst (10 mol %),  
base = K<sub>2</sub>CO<sub>3</sub> (3 equiv), solvent = toluene:H<sub>2</sub>O (2:1), T = 100 °C, t = 24 h

[B] = B(OH)<sub>2</sub> (S), R = H, X-Ar = 1-Br-4-Ph-C<sub>6</sub>H<sub>4</sub>,  
[PdL] = Pd<sub>2</sub>dba<sub>3</sub> (5 mol %) + 10 mol % L,  
base = Ag<sub>2</sub>O (3 equiv), solvent = dioxane, T = 85 °C, t = 24 h.

Gensch et al., *JACS* **2022** 144, 3, 1205. DOI: [10.1021/jacs.1c09718](https://doi.org/10.1021/jacs.1c09718)



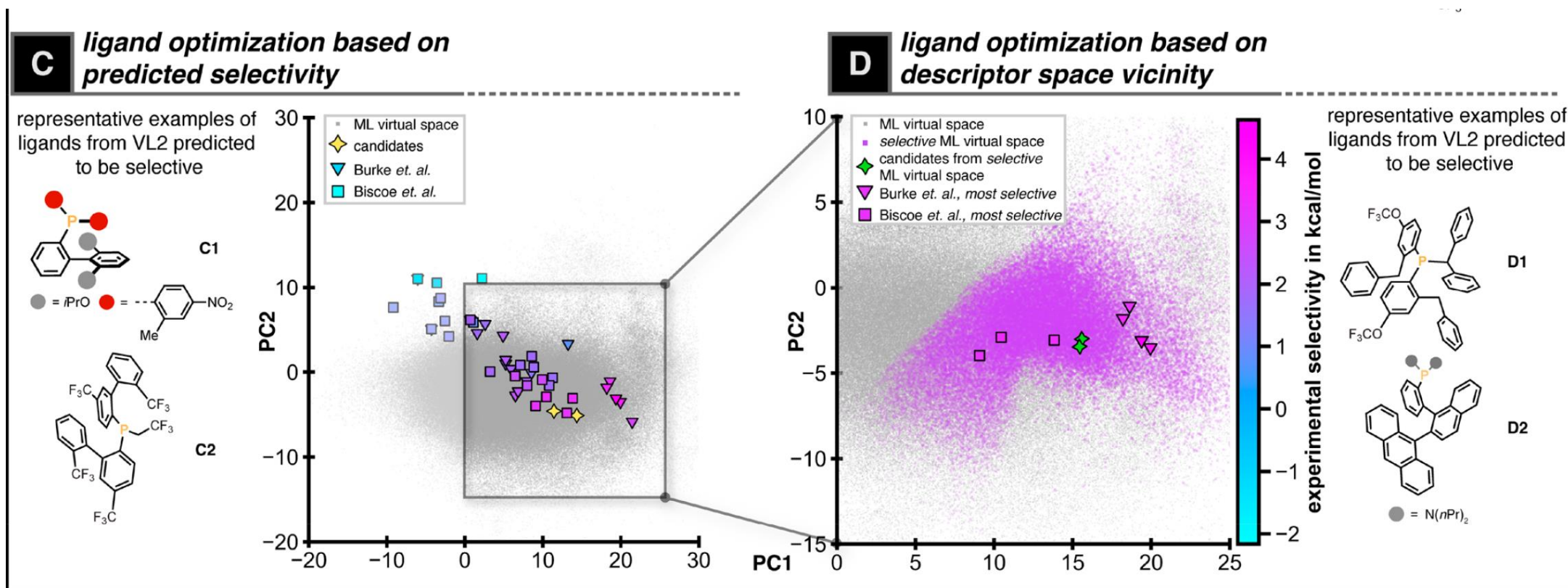
## 4.8 PHOSPHINES PARAMETRIZATION – KRAKEN



Gensch et al., *JACS* **2022** 144, 3, 1205. DOI: [10.1021/jacs.1c09718](https://doi.org/10.1021/jacs.1c09718)



## 4.8 PHOSPHINES PARAMETRIZATION – KRAKEN



Gensch *et al.*, *JACS* **2022** 144, 3, 1205. DOI: [10.1021/jacs.1c09718](https://doi.org/10.1021/jacs.1c09718)



## POD #4

Consider a generic mono-phosphine complex of the form  $(\text{CO})_3\text{Ni}(\text{PR}_3)$ .

- **Predict how the CO stretching frequency would compare to that of  $\text{Ni}(\text{CO})_4$ .**
- **Consider a series of  $(\text{CO})_3\text{Ni}(\text{PR}_3)$  complexes where  $\text{R} = t\text{-Bu, Ph, OPh}$ . Predict how the CO stretching frequency would vary across this series.**



## 4.6.3 PHOSPHINES – SUBSTITUENTS EFFECT

