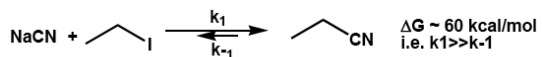


There are only two important things in chemistry, kinetics and thermodynamics. And,  $\exp(-\Delta G/RT) = k_1/k_{-1}$ , so there's really only one thing.

Kinetics provides information about the transition state of a reaction.

We'll use a simple example to learn the basic tools, then look at more applications to catalysis.

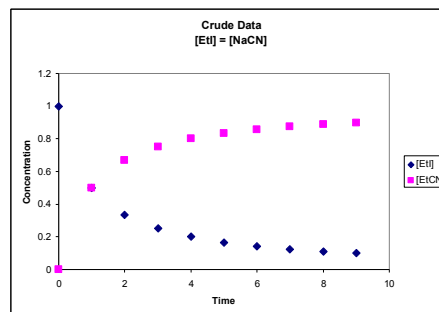


$$\text{rate} = \frac{d[\text{EtCN}]}{dt} = -\frac{d[\text{NaCN}]}{dt} = -\frac{d[\text{EtI}]}{dt} = k[\text{NaCN}][\text{EtI}]$$

1<sup>st</sup> step: measure change in concentration over time under known conditions.

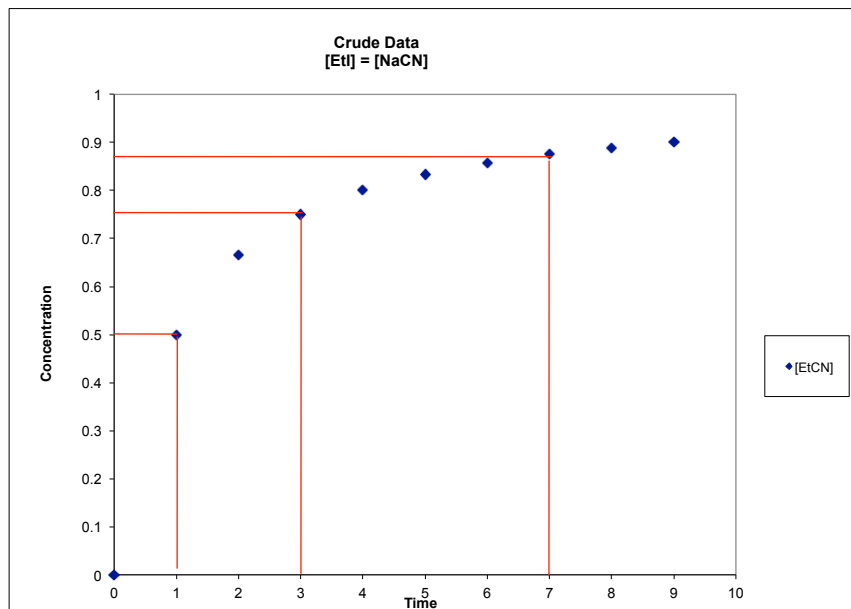
Common techniques:

GC  
UV/Vis  
NMR  
IR  
HPLC

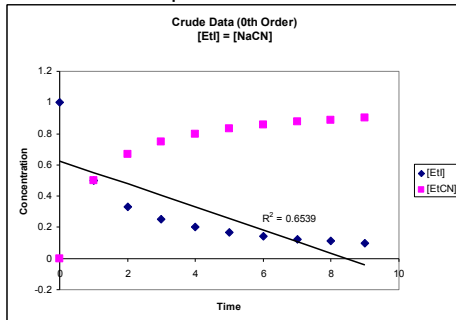


Note: data for EtCN are hypothetical

#### An aside on reaction deceleration



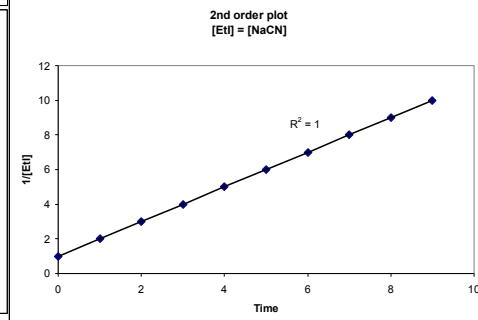
Data can be plotted to determine reaction's overall order:



0<sup>th</sup>:  $-d[A]/dt = k \rightarrow [A] = kt$

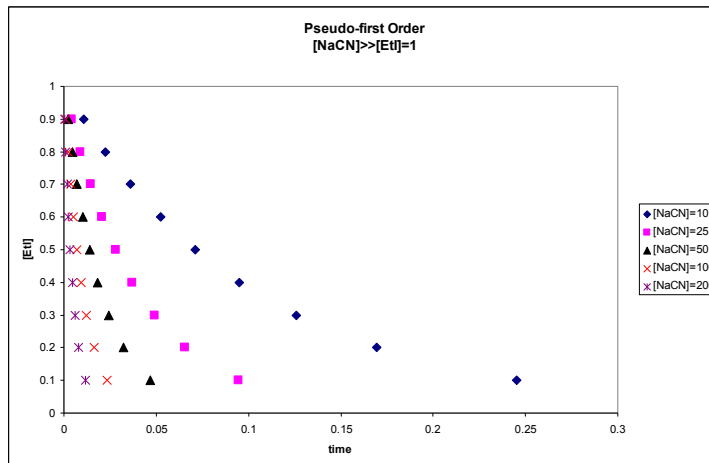
1<sup>st</sup>:  $-d[A]/dt = k[A] \rightarrow [A] = \exp(kt)$   
 $\ln[A] = kt$

2<sup>nd</sup>:  $-d[A]/dt = k[A]^2 \rightarrow 1/[A] = kt$   
(also for  $k[A][B]$  if  $[A] = [B]$ )

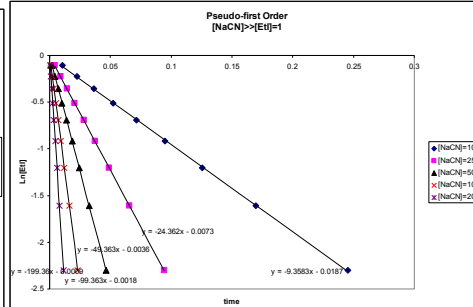
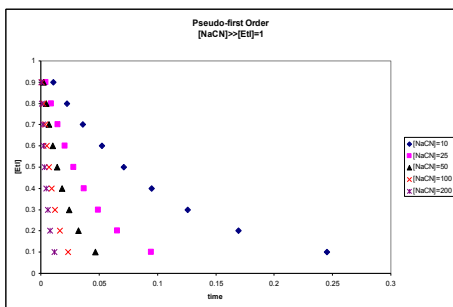


2 common methods to determine order in individual components.

**Pseudo 1<sup>st</sup>-order:** one component in huge excess (its concentration ~ constant)  
Collect data at various excessive concentrations



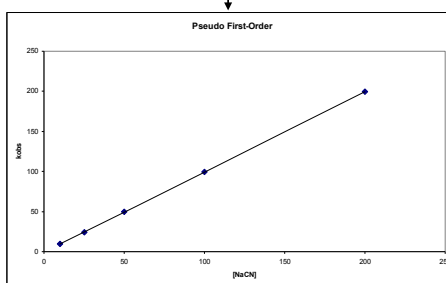
Note  $[EtI] = 1 \rightarrow 0$ , but  $[NaCN] = 10 \rightarrow 9$  up to  $200 \rightarrow 199$   
Rate =  $k[NaCN][EtI] \sim k[NaCN]_0[EtI] = k_{obs}[EtI]$



Replot data in 1<sup>st</sup> order coordinates  
Slope of line =  $k_{obs}$

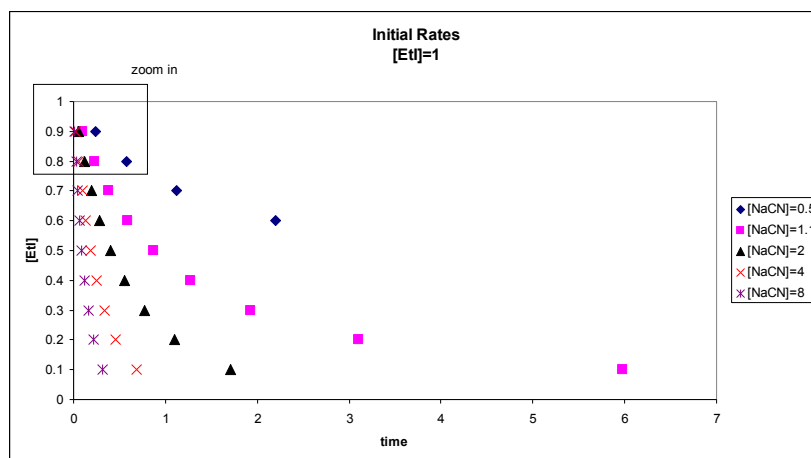
Plot slope v [NaCN]

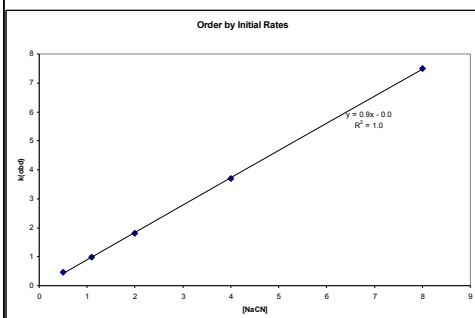
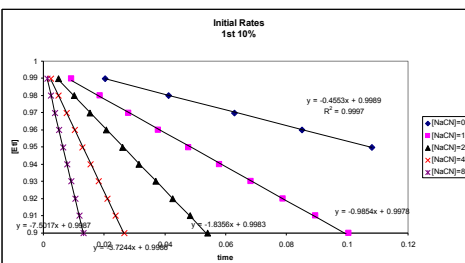
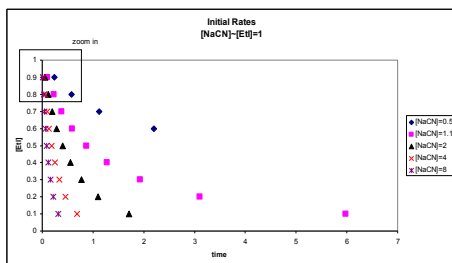
Rxn is 1<sup>st</sup> order in NaCN!!  
But...is 10-200 equiv NaCN really representative??



An alternative is the method of 'initial rates'  
Keep one component constant (EtI) and vary the other (NaCN), but keep close to synthetic conditions

Look at the first 10% of the reaction. Assume concentrations don't change much at low conversion. i.e.  $v = k[EtI][NaCN] \sim k[EtI]_0[NaCN]_{0(c=0 \rightarrow 10\%)}$





## Notes

Need more data points/time for initial rate

Data looks pretty linear for first 10%

Slope of best-fit line is  $k_{obs}$

$k_{obs} = k[NaCN][EtI]$  and  $[EtI]$  was constant

Again, the rxn is first order in  $[NaCN]$   
But... we ignored 90% of the reaction.

## Case Study 1: Bergman, JACS, 1981, 7028

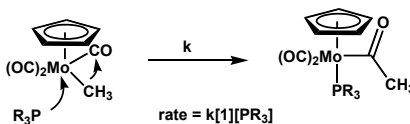
## Migratory insertion



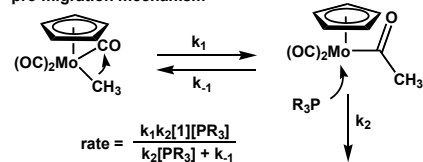
Confusion: Huge solvent effects on rate and (in related systems) stereochemistry

What's the mechanism??

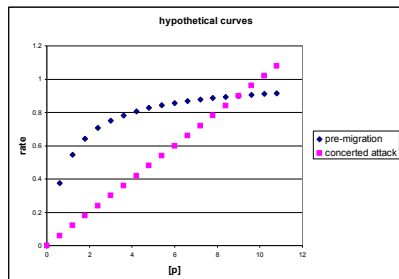
concerted attack/migration mechanism:



pre-migration mechanism



notes: you should be able to derive these equations.  
Why not consider an associative mechanism?



## Case Study 1: Bergman, JACS, 1981, 7028

## Actual data

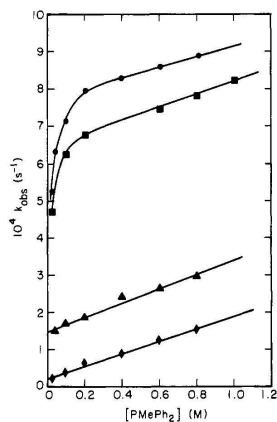
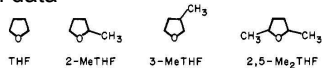
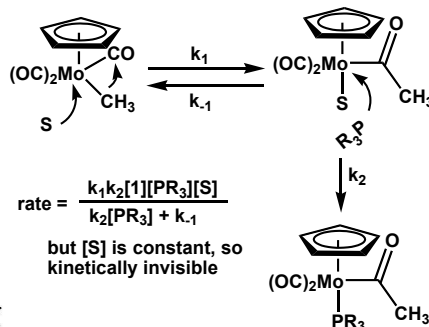


Figure 1. Dependence of the pseudo-first-order rate constant  $k_{\text{obs}}$  for conversion of 1 to 2 in excess  $\text{PMePh}_2$ , upon phosphine concentration in the following solvents: (●) THF; (■) 3-MeTHF; (▲) 2-MeTHF; (◆) 2,5-Me<sub>2</sub>THF.

Rxn in THF and 3-MeTHF look like superposition of concerted attack and pre-migration

$$\text{rate} = \frac{k_1 k_2 [1][\text{PR}_3]}{k_2 [\text{PR}_3] + k_{-1}} + k_3 [1][\text{PR}_3]$$

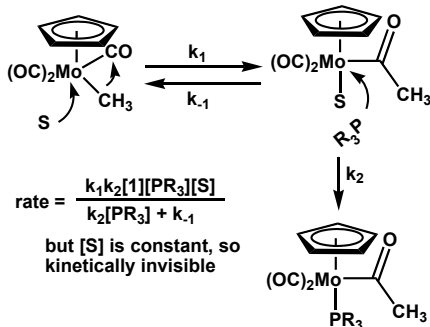
Rxn in 2,5-Me<sub>2</sub>THF only shows concerted attack. How to explain? Solvent assistance.



$$\text{rate} = \frac{k_1 k_2 [1][\text{PR}_3][\text{S}]}{k_2 [\text{PR}_3] + k_{-1}}$$

but [S] is constant, so kinetically invisible

## Case Study 1: Bergman, JACS, 1981, 7028



$$\text{rate} = \frac{k_1 k_2 [1][\text{PR}_3][\text{S}]}{k_2 [\text{PR}_3] + k_{-1}}$$

but [S] is constant, so kinetically invisible

Mechanism predicts 1<sup>st</sup> order dependence on THF. Do expt in 2,5-Me<sub>2</sub>THF, add THF (note only minor change in dipole)

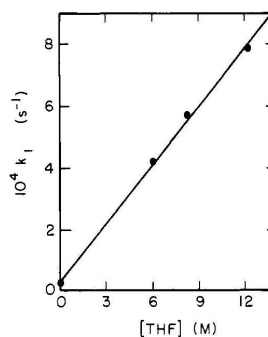
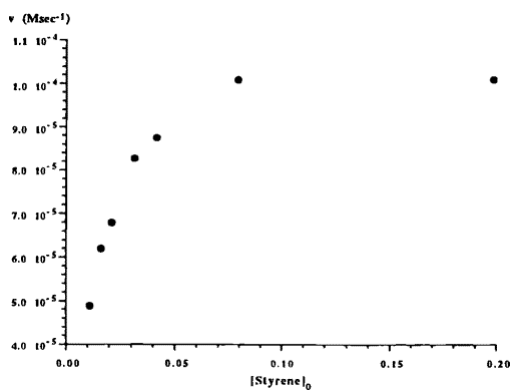
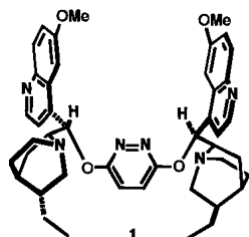
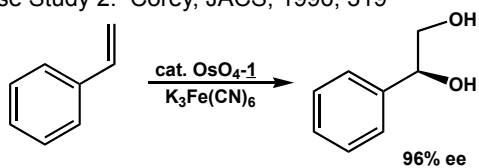


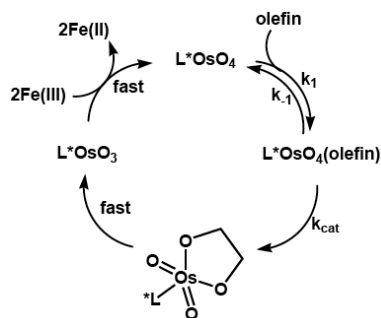
Figure 2. Dependence upon [THF] of  $k_1$  for reaction of 1 with  $\text{PMePh}_2$ , determined in studies using 0.01 M 1 and varying excess concentrations of phosphine in THF/2,5-Me<sub>2</sub>THF mixtures.

## Case Study 2: Corey, JACS, 1996, 319

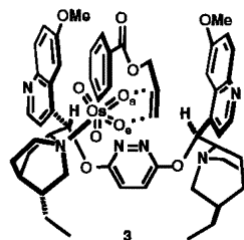


Previous work (JACS 1993, 12226) had shown 1<sup>st</sup> order in OsO<sub>4</sub>-L, zero order in Fe(III)

## Case Study 2: Corey, JACS, 1996, 319



Proposed structure of L\*OsO<sub>4</sub> (olefin) for allyl benzoate












$$V = \frac{k_{\text{cat}}K[\text{Os}]_T[\text{olefin}]}{1 + K[\text{olefin}]} \approx \frac{k_{\text{cat}}[\text{Os}]_T[\text{olefin}]}{K_m + [\text{olefin}]}$$

These are saturation kinetics!! Same as many enzymes and Lewis-Acid cat Rxns

## Case Study 2: Corey, JACS, 1996, 319

Binding appears correlated to selectivity in asymmetric dihydroxylation  
 Poor correlation between rate and selectivity

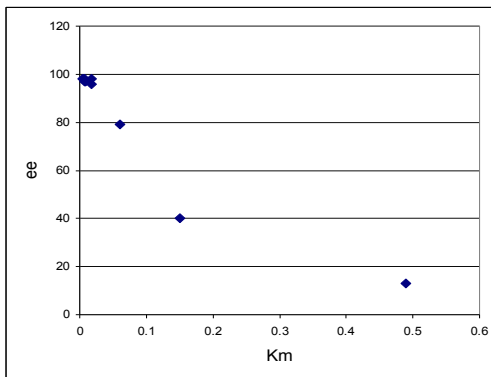
Table 1. Comparison of the Michaelis-Menten parameters  $K_m$  and  $V_{max}$  and Observed Enantioselectivity in the Catalytic Asymmetric Dihydroxylation of Olefins<sup>a</sup>

Entry	Olefin (formula no.)	$K_m$	$V_{max}$	% ee
1	 (2)	0.017M	$1.1 \times 10^{-6}$	98 <sup>b</sup>
2	 (6)	0.49M	$8.6 \times 10^{-6}$	13 <sup>b</sup>
3	 (7)	0.017M	$1.3 \times 10^{-6}$	96 <sup>b,c</sup>
4	 (8)	0.0088M	$6.6 \times 10^{-6}$	97 <sup>c</sup>
5	 (4)	0.0088M	$1.0 \times 10^{-6}$	97 <sup>c</sup>
6	 (10)	0.081M	$3.8 \times 10^{-6}$	19 <sup>b,c</sup>
7	 (11)	0.0076M	$1.7 \times 10^{-6}$	98 <sup>c</sup>
8	 (12)	0.0046M	$1.4 \times 10^{-6}$	98 <sup>c</sup>
9	 (7)	0.18M	$4.0 \times 10^{-6}$	60 <sup>b</sup>

<sup>a</sup> This reaction was performed using 0.8 mM (DHQD)<sub>2</sub>PHAL ligand and 0.26 mM K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>.

<sup>b</sup> This work.

<sup>c</sup> Unless otherwise indicated, all reactions were performed at 0 °C in 1:1 *tert*-butyl alcohol-water using the (DHQD)<sub>2</sub>PHAL ligand (1 mM) and K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>·2H<sub>2</sub>O (0.5 mM).



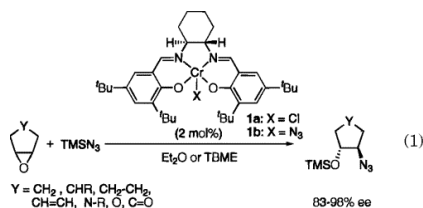
J. Am. Chem. Soc. 1996, 118, 319-329

Kinetic Investigations Provide Additional Evidence That an Enzyme-like Binding Pocket Is Crucial for High Enantioselectivity in the Bis-Cinchona Alkaloid Catalyzed Asymmetric Dihydroxylation of Olefins

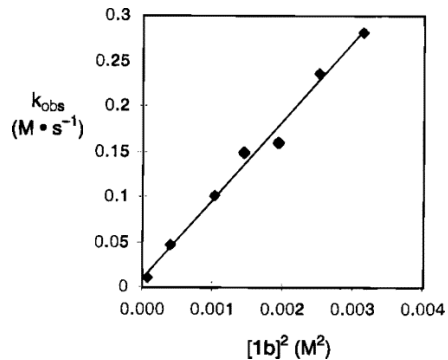
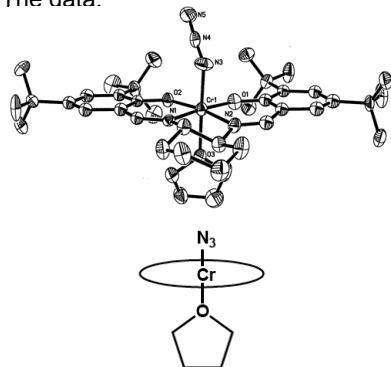
E. J. Corey\* and Mark C. Nee

## Case Study 3: Jacobsen, JACS, 1996, 10924

The reaction



The data:



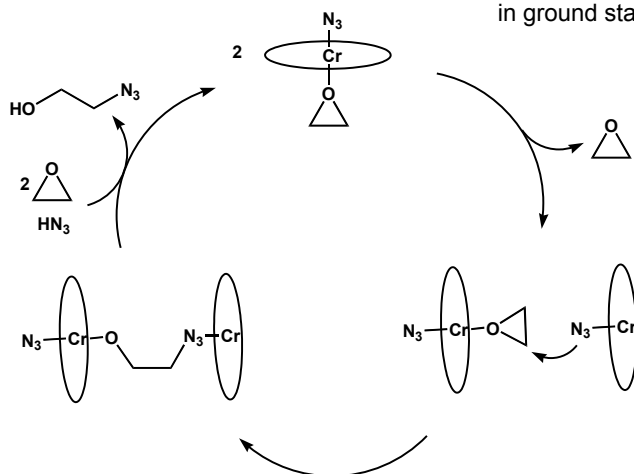
## Case Study 3: Jacobsen, JACS, 1996, 10924

$$\text{Rate} = k[(\text{salen})\text{Cr}]^2[\text{epoxide}]^{-1}[\text{Azide}]^0$$

2 Cr's involved in RDS

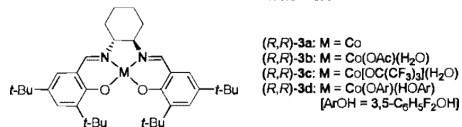
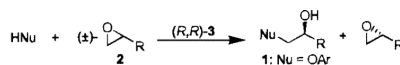
Epoxide inhibits rxn!!

Azide either (a) involved after RDS or (b) present in ground state

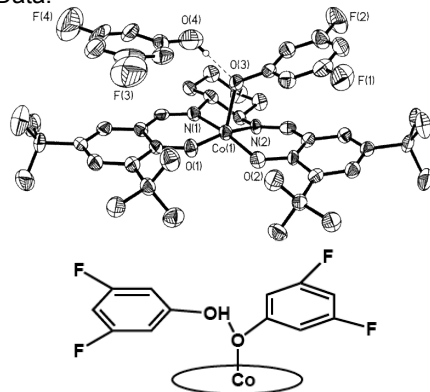


## Case Study 4: Jacobsen, JACS 1999, 6086 and unpublished work

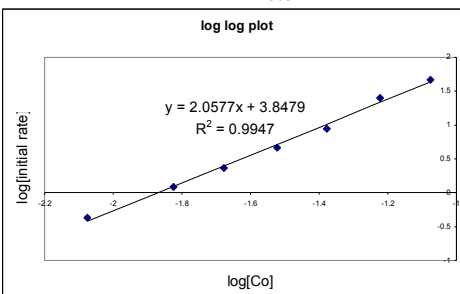
The rxn:



Data:



$$\text{Rate} = k_{\text{obs}}[\text{Co}]^2$$

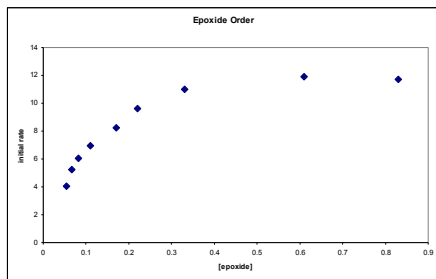


$$V = k[A]^n$$

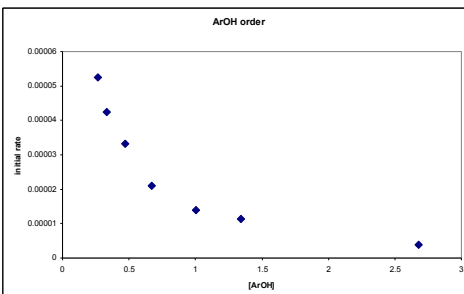
$$\log(V) = \log(k[A]^n) = n \cdot \log(k[A])$$



## Case Study 4: Jacobsen, JACS 1999, 6086 and unpublished work

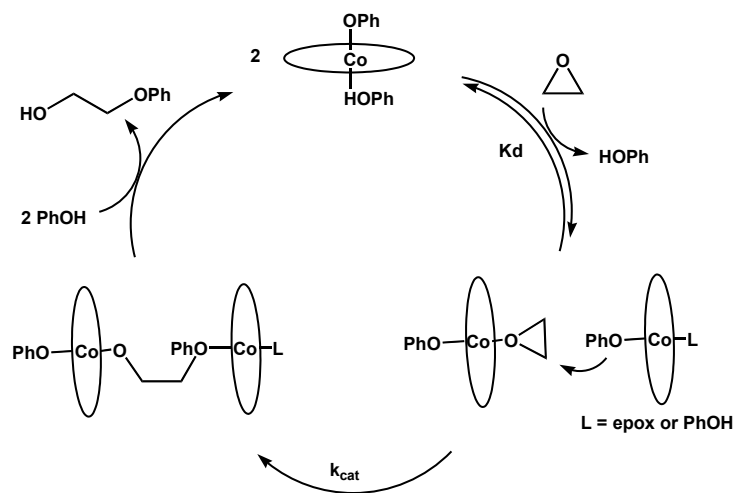


Saturation kinetics with epoxide



Inhibition by PhOH

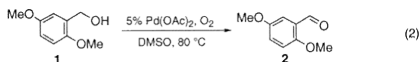
## Case Study 4: Jacobsen, JACS 1999, 6086 and unpublished work



$$\text{rate} = \frac{k_{\text{cat}}[\text{Co}]_T^2[\text{Epo}]}{K_d[\text{ArOH}] + [\text{Epo}]}$$

## Case Study 5: Stahl, JACS 2002, 766

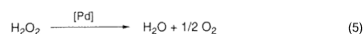
The rxn



The data: DMSO critical, but is not reduced (O<sub>2</sub> required) or oxidized (no dimethyl sulfone is formed)

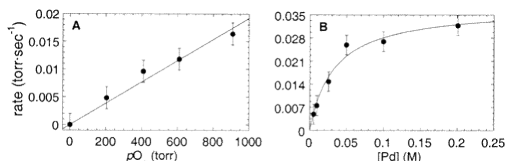
2 formed:O<sub>2</sub> consumed = 2 (O<sub>2</sub> is a 4 e- oxidant here)

Under the rxn conditions, disproportionation observed (sometimes referred to as 'catalase activity')



Pd black (precipitated Pd metal) observed during course of reaction

## Case Study 5: Stahl, JACS 2002, 766



Also: Pd black correlates with rate decrease  
Rate independent of [ROH]

Conclude oxidation of Pd is rate limiting

Predicts rate =  $k[\text{O}_2][\text{Pd}]$  (i.e. linear increase in rate with [Pd])

Propose catalyst decomposition is time-dependent. Decomposition is bimolecular; more pronounced at higher [Pd]

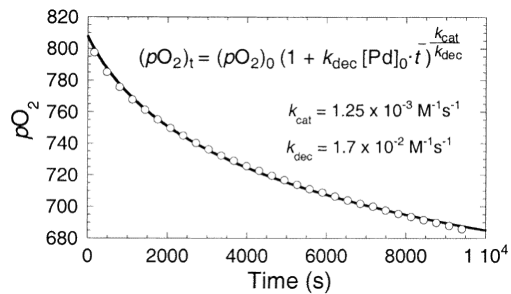
Described by  $k_{\text{dec}}$  competitive with  $k_{\text{cat}}$

Eq 7 models data in trace B

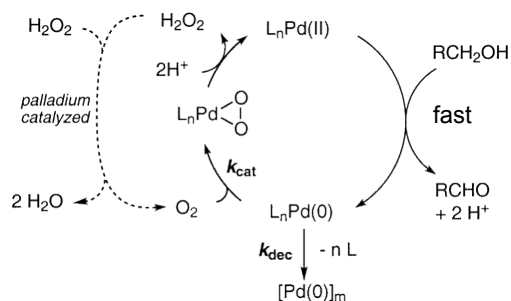
$$\frac{d(p\text{O}_2)}{dt} = k_{\text{cat}}[\text{Pd}]_t \cdot p\text{O}_2; \quad [\text{Pd}]_t = \frac{[\text{Pd}]_0}{1 + [\text{Pd}]_0(k_{\text{dec}} \cdot t)} \quad (7)$$

## Case Study 5: Stahl, JACS 2002, 766

Integrated form models  
experimental data

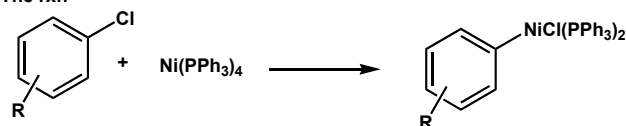


## Proposed mechanism

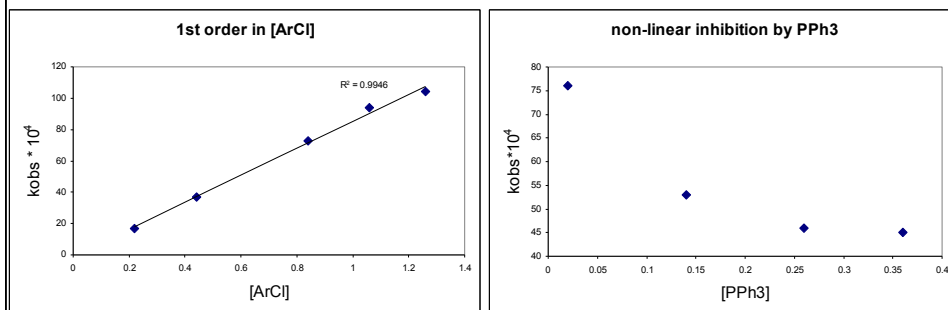


## Case Study 6: Foa et al., J. Chem Soc. Dalton, 1975, 2572.

## The rxn

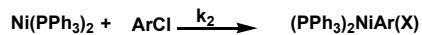
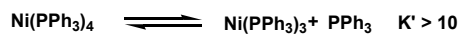


## The data



## Case Study 6: Foa et al., J. Chem. Soc. Dalton, 1975, 2572.

## Proposed mechanism



$$\text{Rate} = \frac{k_1[\text{PPh}_3] + k_2K}{[\text{PPh}_3]} [\text{Ni}]_T [\text{ArCl}] = k_{\text{obs}}[\text{Ni}]_T$$

$$k' = \frac{k_{\text{obs}}}{[\text{ArCl}]} = \frac{k_1[\text{PPh}_3] + k_2K}{[\text{PPh}_3]}$$

$$k'[\text{PPh}_3] = k_1[\text{PPh}_3] + k_2K$$

plot  $k'[\text{PPh}_3]$  vs.  $[\text{PPh}_3]$

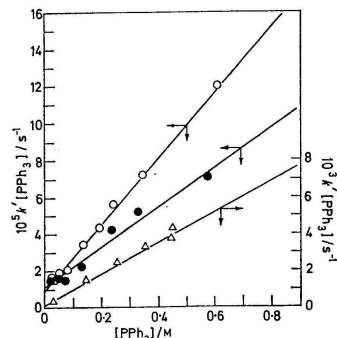


FIGURE 2 Plot of  $k'$  against  $[\text{PPh}_3]$  in benzene at 15 °C for *p*-dichlorobenzene (O), *p*-chloroanisole (●), and *m*-dichlorobenzene (Δ)

For *p*-Cl<sub>2</sub>Ph:

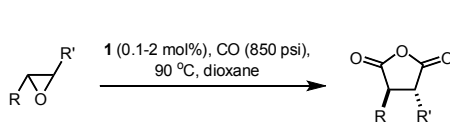
$$k_1 = 1 \times 10^{-4}$$

$$Kk_2 = 1.1 \times 10^{-5}$$

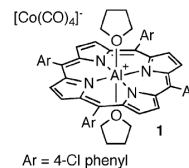
$$k_2 \sim 10$$

So  $\text{Ni}[\text{PPh}_3]_2$  10<sup>5</sup>x more reactive than  $\text{Ni}[\text{PPh}_3]_3$ , but much less prevalent

Coates, JACS, 2007, 4948



High yields for terminal and internal epoxides; stereospecific:

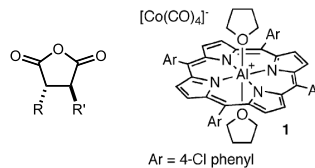
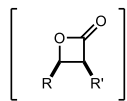
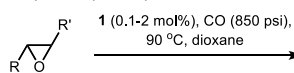


anhydride	yield (%) <sup>b</sup>	ee (%) <sup>c</sup>	entry	epoxide	epoxide/1	anhydride	yield (%) <sup>b</sup>	trans:cis <sup>b</sup>
(S)-7	97	97	1 <sup>c</sup>		100		95	1 : 20
(S)-7	99	>99	2		200		99	> 100 : 1
(R)-11	99	>99	3		75		99	> 100 : 1
(S)-21	96	97 (>99) <sup>c</sup>	4		100		99	> 100 : 1

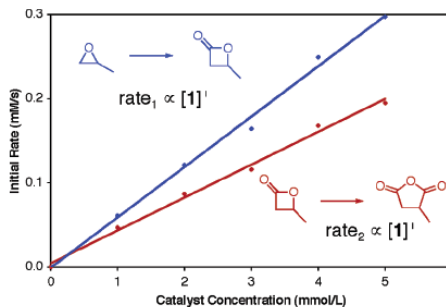
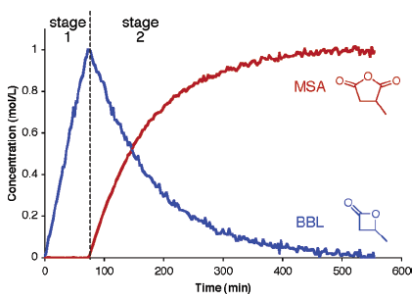
Ready; Catalysis

Kinetics-case study 7

Coates, JACS, 2007, 4948



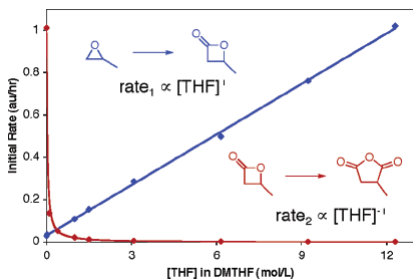
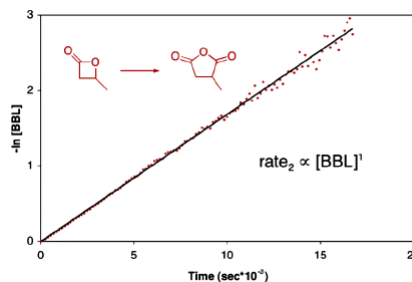
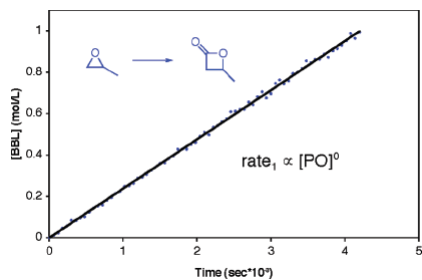
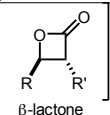
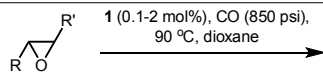
Unusual kinetics observed:



Anhydride formation displays induction period; no anhydride formed until epoxide consumed. Independent rxns similar in rate; show first order dependence on catalyst.

Ready; Catalysis

Kinetics-case study 7

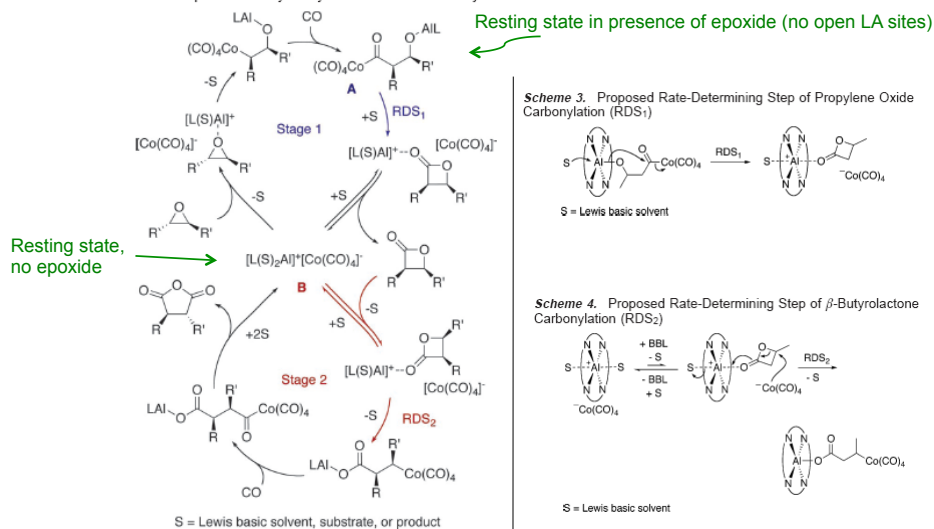
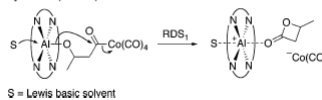


Rate (lactone) =  $k[\text{epox}]^0[\text{CO}]^0[\text{catalyst}]^1[\text{Solvent}]^1$   
 Rate (anhydride) =  $k[\text{lactone}]^1[\text{CO}]^0[\text{catalyst}]^1[\text{Solvent}]^{-1}$

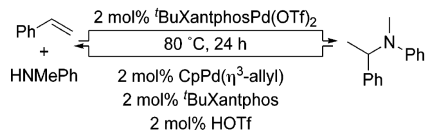
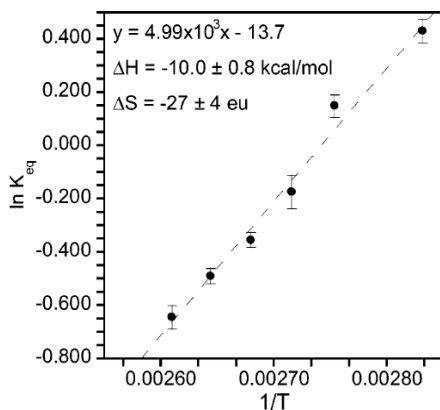
Epoxide (and solvent) inhibit lactone  $\rightarrow$  anhydride

Coates, JACS, 2007, 4948

Scheme 2. Proposed Catalytic Cycle of Double Carbonylation

Scheme 3. Proposed Rate-Determining Step of Propylene Oxide Carbonylation (RDS<sub>1</sub>)Scheme 4. Proposed Rate-Determining Step of  $\beta$ -Butyrolactone Carbonylation (RDS<sub>2</sub>)

Coates, JACS, 2007, 4948

Recall:  $\Delta G = -RT \ln(K)$  and  $\Delta G = \Delta H - T\Delta S$ Merging and rearranging gives the **Van't Hoff Equation**:  $\ln(K) = (-\Delta H/R)(1/T) + (\Delta S/R)$   
 $\rightarrow \ln(K)$  vs.  $1/T$  gives  $\Delta H$  and  $\Delta S$ n.b. *increasing temperature decreases contribution of  $\Delta H$* 

Hartwig, JACS, 2006, 9306

Ready; Catalysis

Kinetics-Eyring Equation

The Eyring equation: determination of  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$ :

$$\ln \frac{k}{T} = -\frac{\Delta H^\ddagger}{R} \cdot \frac{1}{T} + \ln \frac{k_B}{h} + \frac{\Delta S^\ddagger}{R}$$

$$y = m \cdot x + b$$

Self exchange reaction

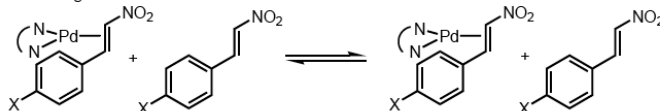
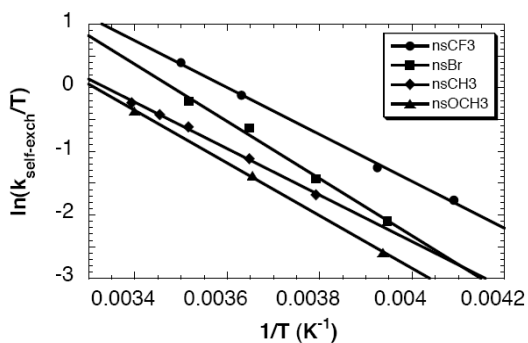


Table 2. Activation Parameters for Degenerate Olefin Exchange between (bc)Pd(ns<sup>2</sup>) and ns<sup>2</sup>.<sup>a</sup>

entry	olefin	temp range (K)	k (M <sup>-1</sup> s <sup>-1</sup> ), 25 °C	$\Delta H^\ddagger$ (kcal/mol) <sup>b</sup>	$\Delta S^\ddagger$ (eu) <sup>b</sup>
1	ns <sup>CF3</sup>	224–286	749	7.3	-24
2	ns <sup>Br</sup>	253–284	492	8.8	-30
3	ns <sup>CH3</sup>	264–295	284	7.2	-24
4	ns <sup>OCH3</sup>	254–294	257	8.2	-27

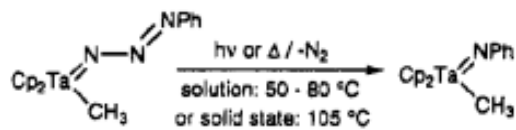
Supports associative mechanism  
(usually associative approx -30eu  
Dissociative +10-20eu)

Stahl, JACS, 2004, 14832

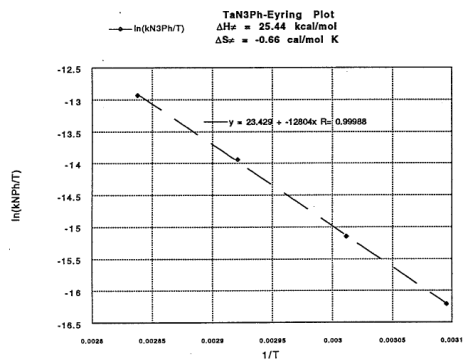
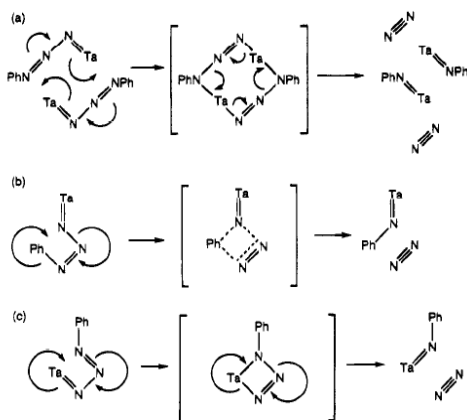


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Kinetics-Eyring Equation



Potential mechanisms:



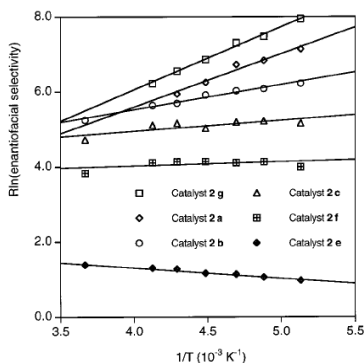
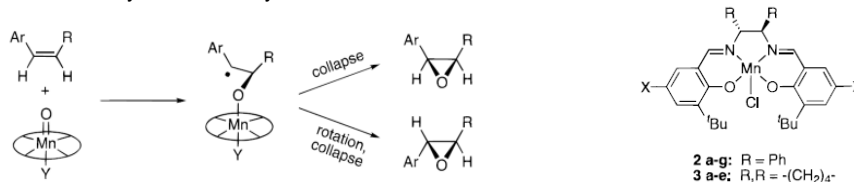
Small entropy of activation inconsistent with mechanism a. (Labeling studies ruled out mechanism b).

Bergman, 1995, 6382

Ready; Catalysis

Kinetics-Eyring Equation

Use in asymmetric catalysis



$$\ln(e.r.) = (\Delta\Delta H^\ddagger/R)(1/T) - \Delta\Delta S^\ddagger/R$$

$$\Delta\Delta H^\ddagger = \Delta H^\ddagger_{\text{minor}} - \Delta H^\ddagger_{\text{major}}$$

$$\Delta\Delta S^\ddagger = \Delta S^\ddagger_{\text{minor}} - \Delta S^\ddagger_{\text{major}}$$

Table 2. Relative Activation Parameters for the Formation of Indene Oxide Enantiomers Catalyzed by Complexes 2a-c, e-g

entry	catalyst	substituent	$\Delta\Delta H^\ddagger$ (kcal mol <sup>-1</sup> )	$\Delta\Delta S^\ddagger$ (cal mol <sup>-1</sup> K <sup>-1</sup> )
1	2g	OSi(tPr) <sub>3</sub>	1.70 ± 0.08	-0.69 ± 0.35
2	2a	OCH <sub>3</sub>	1.40 ± 0.16	-0.07 ± 0.76
3	2b	CH <sub>3</sub>	0.66 ± 0.05	2.90 ± 0.21
4	2c	H	0.29 ± 0.10	3.80 ± 0.44
5	2f	Br	0.11 ± 0.09	3.60 ± 0.40
6	2e	NO <sub>2</sub>	-0.28 ± 0.02	2.50 ± 0.10

Biggest change in selectivity with temperature when  $\Delta\Delta H^\ddagger$  dominates.

Note with 2e, ee decrease with decreasing T  
Jacobsen, JACS, 1998, 948.

Figure 8. Eyring plots for the epoxidation of indene with catalysts 2a-c and 2e-g

Ready; Catalysis

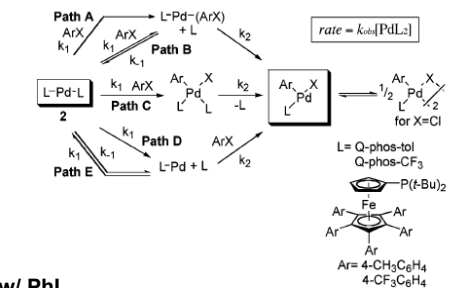
Kinetics

Practice problem: oxidative addition of ArX to Pd(0). Hartwig, JACS, 2005, 6944

Kinetics studied for ArCl, ArBr and ArI

Your job: derive rate laws for each path; determine which one(s) is(are) consistent with data.

Scheme 1. Possible Mechanisms and Rate Expressions for the Oxidative Addition of ArX to 2



w/ PhI

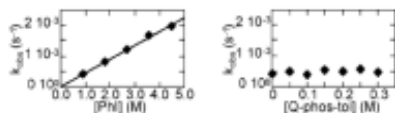


Figure 1. Plots of  $k_{\text{obs}}$  vs [PhI] and  $k_{\text{obs}}$  vs [Q-phos-tol] ([PhI] = 0.95 M) for the oxidative addition of PhI to 2 at 30 °C in THF.

w/ PhBr: rate = [ArBr]<sup>0</sup>[L]<sup>0</sup>  
Small  $\Delta S^\ddagger$ ; same rate with sub. ArBr's

'Lineweaver-Burk Plot'

w/ ArCl

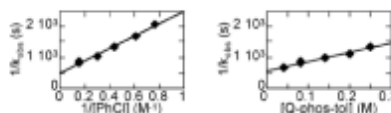
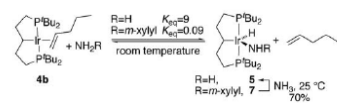


Figure 2. Plots of  $1/k_{\text{obs}}$  vs  $1/[\text{PhCl}]$  ([Q-phos-tol] = 0.08 M) and  $1/k_{\text{obs}}$  vs [Q-phos-tol] ([PhCl] = 6.56 M) for the oxidative addition of PhCl to 2 at 60 °C in THF.

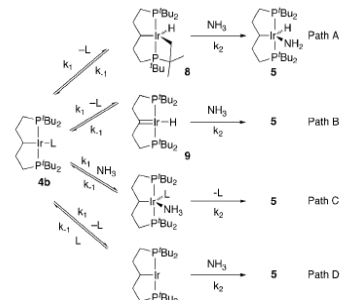


Hartwig, Science, 307, 2005, 1082

Determine the mechanism for oxidative addition of ammonia to Ir(I) olefin complex



Scheme 4.



Data:  
Rxn with  $\text{ND}_3$  showed no D  
incorporation into ligand

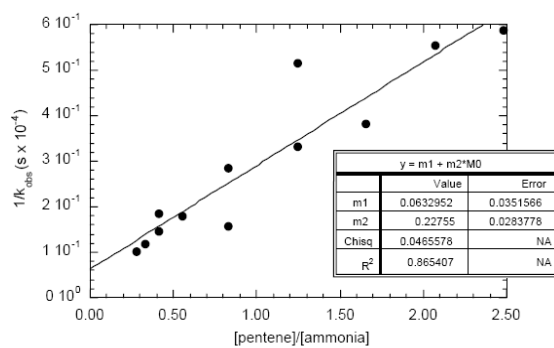


Figure S2. Plot of  $k_{obs}$  for the oxidative addition of ammonia and the ratio of the concentrations of pentene and ammonia that includes all data points.