Lit Seminar

H. Kakei (D3)
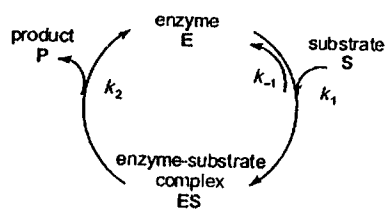
Reaction Progress Kinetic Analysis toward Mechanic Studies of Complex Catalytic Reactions

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1. Efficient Method for kinetic Analysis (Blackmond)

2. Detailed Kinetic Modeling (1) - Hydrolytic Kinetic Resolution of Terminal Epoxide (Jacobsen)

3. Detailed Kinetic Modeling (2) Rhodium - Catalyzed Asymmetric 1.4-addition (Hayashi)

1. Efficient Method for kinetic Analysis (Ref. Angew Chem Int Ed. 2005. 44, 4302)

(1) Introduction

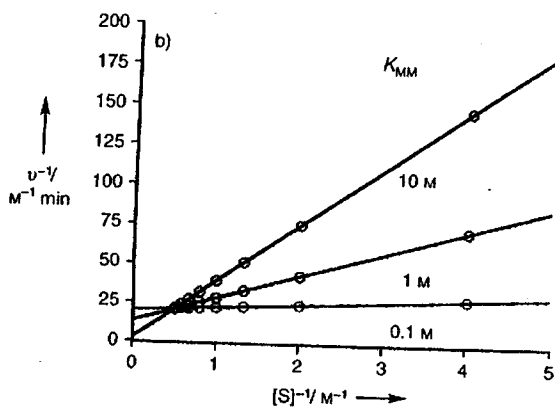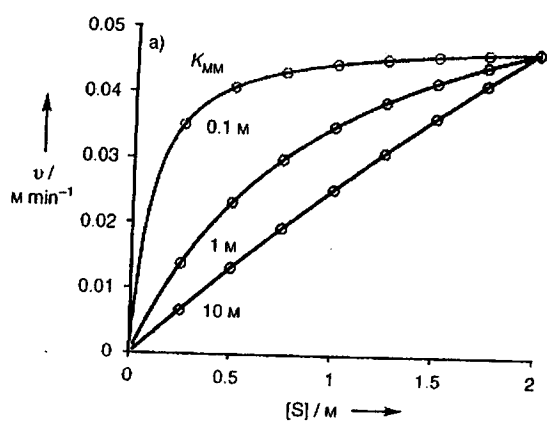Scheme 1. Catalytic reaction cycle for a simple enzyme-catalyzed reaction.

Figure 1. Plots of a) the Michaelis–Menten Equation [Eq. (1)] and b) the Lineweaver–Burk Equation [Eq. (2)] to describe the reaction mechanism shown in Scheme 1 for different values of v_{max} and K_{MM}.

$$[ES] = \frac{k_1[E][S]}{k_{-1}+k_2} \quad \text{①} \qquad [E_0] = [ES] + [E] \quad \text{②}$$

$$[ES] = \frac{k_1([E_0]-[ES])[S]}{k_{-1}+k_2} \quad \text{③} \qquad [ES] = \frac{k_1[E_0][S]}{k_{-1}+k_2+k_1[S]} \quad \text{④}$$

$$v = \frac{d[P]}{dt} = k_2[ES] = \frac{k_1 k_2[E_0][S]}{k_{-1}+k_2+k_1[S]} = \frac{k_2[E_0][S]}{\frac{k_{-1}+k_2}{k_1}+[S]} \quad \text{⑤}$$

$$k_M = \frac{k_{-1}+k_2}{k_1} \quad (\text{Michaelis constant}) \quad \text{⑥}$$

At the initial stage of reaction $[S] \gg k_M$

$$v_{max} = \frac{k_2[E_0][S]}{k_M+[S]} \cong \frac{k_2[E_0][S]}{[S]} = k_2[E_0] \quad \text{⑦}$$

$$v = \frac{d[P]}{dt} = \frac{v_{max}[S]}{k_M+[S]} \quad \text{⑦} \ (\text{Michaelis-Menten Equation})$$

$$\frac{1}{v} = \frac{1}{v_{max}} + \frac{k_M}{v_{max}}\frac{1}{[S]} \quad \text{⑧} \ (\text{Lineweaver-Burk Equation})$$

(2) Measurements methodology
  ① Integral Measurements
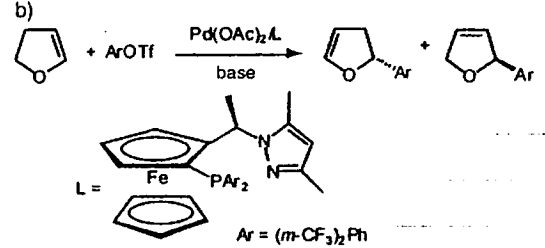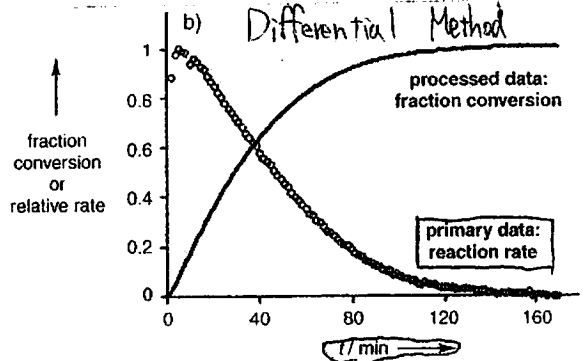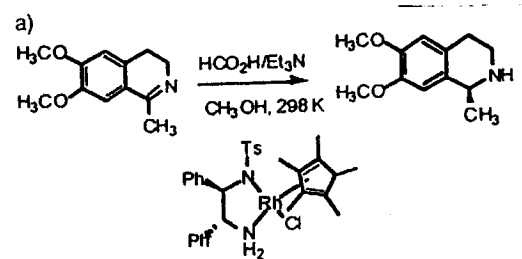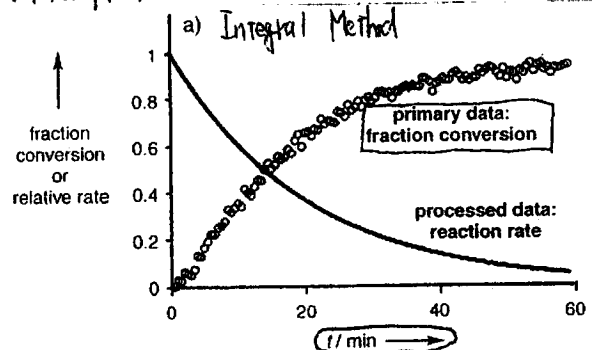   Relationship between the measurable parameter and species concentration

  ② Differential Measurements
    Measure reaction rate directly

Table 1: Integral and differential measurements of reaction progress.

FTIR spectroscopy as an example of an integral measurement[a]	Reaction calorimetry as an example of a differential measurement[b]
$A = \varepsilon b c$ rate $= \frac{dc}{dt}$ conversion $= 1 - \frac{A}{A_0}$	$\dot{q} = \Delta H_{rxn} \times$ volume $\times$ rate conversion $= \int_{t=0}^{t=t} q(t)dt / \int_{t=0}^{t=t(end)} q(t)dt$
measured parameter: conversion processed parameter: reaction rate	measured parameter: reaction rate processed parameter: conversion

[a] A = absorbance, c = concentration, ε = extinction coefficient, b = cell path length. [b] $\dot{q}$ = reactant heat flow, ΔH_{rxn} = heat of reaction.

< Examples >

a) Integral Method

fraction conversion or relative rate

primary data: fraction conversion

processed data: reaction rate

t / min

b) Differential Method

fraction conversion or relative rate

processed data: fraction conversion

primary data: reaction rate

t / min

a)

HCO$_2$H/Et$_3$N
CH$_3$OH, 298 K

b)

+ ArOTf
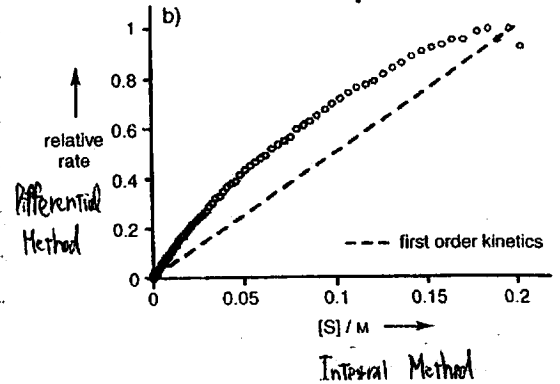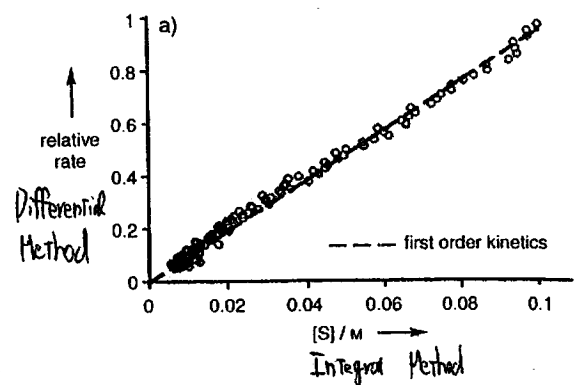
Pd(OAc)$_2$·L
base

Ar = (m-CF$_3$)$_2$Ph

(3) Graphical Rate Equation

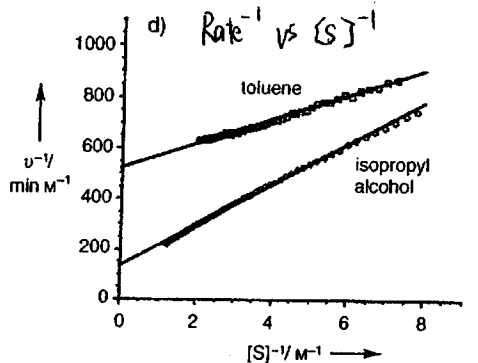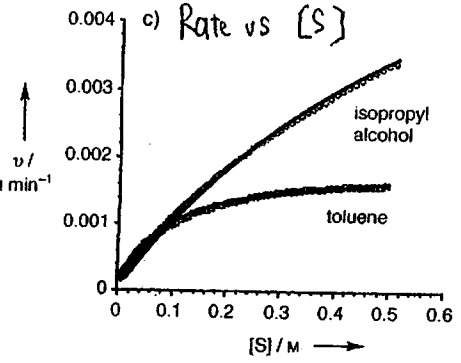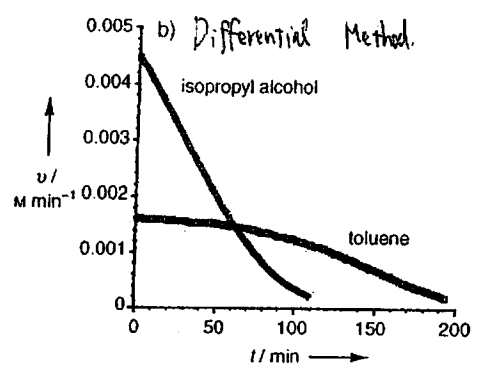Viewing reaction progress as a function of time is not the best way to extract kinetic information
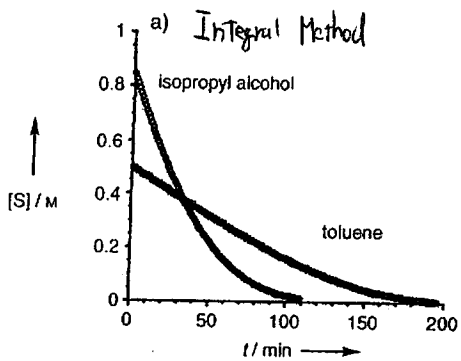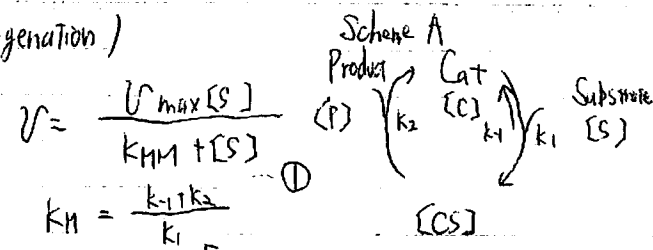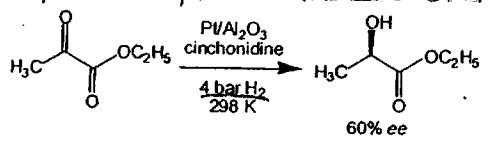
Combine the two ways in which reaction progress data
    x-axis → Integral Measurement
    y-axis — Differential Measurement
          ↓
    leaving time out of the picture

a)
relative rate
Differential Method

first order kinetics

[S] / M

Integral Method

b)
relative rate
Differential Method

first order kinetics

[S] / M

Integral Method

(4) Simple example of kinetic Studies   (hydrogenation)

$$V = \frac{V_{max}[S]}{k_{MM} + [S]} \quad (1)$$

$$k_M = \frac{k_{-1} + k_2}{k_1}$$

Scheme A

$$[CS]$$

From
a) and b)

The reaction is slower in toluene and appears to exhibit a greater degree of flatness.

A-constant-pressure hydrogenation is shown in Scheme (A) with rate constant k_2 replaced by a pseudo-first-order constant that incorporates the constant hydrogen concentration.

C) shows that excellent fit to (1) (Michaelis-Menten Equation)

in Toluene $V_{max} = 0.002 \pm 0.07\%$ M
            $k_{MM} = 0.083 \pm 0.23\%$ M
in IPA $V_{max} = 0.008 \pm 0.33\%$ M
            $k_{MM} = 0.684 \pm 0.56\%$ M

a) Integral Method

b) Differential Method.

c) Rate vs [S]

### d) $Rate^{-1}$ vs $[S]^{-1}$

$k_M \left(\frac{k_{-1} + k_2}{k_1} \right)$ inverse of the binding constant, this result suggests that much stronger catalyst-substrate binding occurs in toluene   (k_{MM} [Tol] << k_{MM} (IPA)) and confirm the pseudo-zero-order form of (1)

In IPA, the Michaelis-Menten Equation cannot be simplified to an integer order resulting in a reaction order that lies between 0 and 1, with its value changing with [S]

D) showed Lineweaver-Burk double reciprocal plot

Merits: Slopes and intercepts can be easily extracted. (V_{max} k_M)
Drawback: Less easy to visualize the relative value of k_M

(5) Reaction with two substrates : beyond the Lineweaver-Burk Plot.
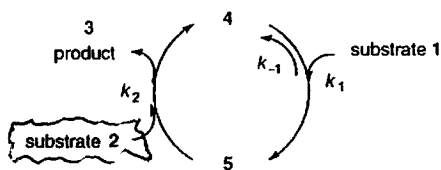
Scheme 2. Mechanism for a simple reaction with two substrates and one intermediate species.

$$\nu = \frac{V_{max}[1]}{k_M + [1]} \quad -- ①$$

$$V_{max} = k_2[2][4]_{total} \quad [1] \gg k_M$$
$$\qquad\qquad -② \qquad [5] = [4]_{total}$$

$$k_M = \frac{k_{-1} + k_2[2]}{k_1} \quad ③$$

① written out instead in terms of the elementary step rate constants

$$\nu = \frac{k_1 k_2 [1][2][4]_{total}}{k_{-1} + k_1[1] + k_2[2]} \quad -④ \qquad \nu = \frac{a[1][2][4]_{total}}{1 + b[1] + c[2]} \quad ⑤ \ (④ \times k_1^{-1})$$

$$a = \frac{k_1}{k_{-1}}k_2, \quad b = \frac{k_1}{k_{-1}}, \quad c = \frac{k_2}{k_{-1}}$$

For the reaction shown in scheme 2, the stoichiometric rule says that each time one molecule of 1 is converted into one molecule of product 3, one molecule of 2 is necessary also converted.

$$[2] = [2]_0 - [1]_0 + [1] \Rightarrow [2] = ["excess"] + [1] \quad -- ⑥$$

Ⓐ Difference in the initial concentrations of the two substrates,

Ⓑ does not change as the reaction progresses

→ One of the key feature of reaction progress kinetic analysis is that reactions can be carried out using synthetically relevant conditions. A synthetically reasonable value for the excess of one substrate over the other is employed, thus avoiding the synthetically unreasonable tenfold concentration differences typical of the pseudo-zero-order" classical kinetic approach.
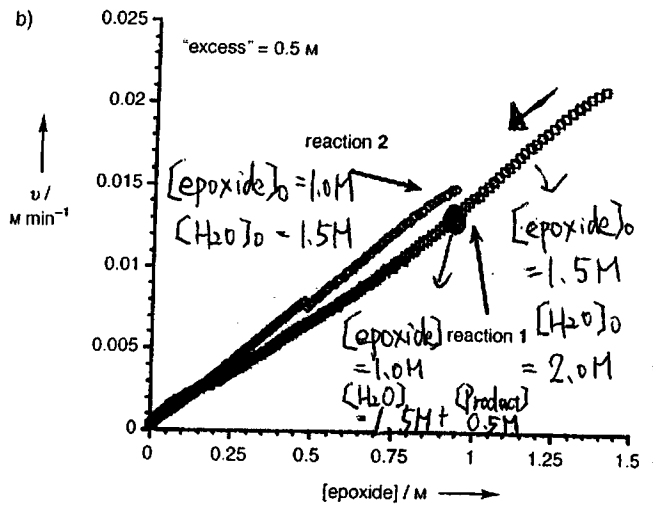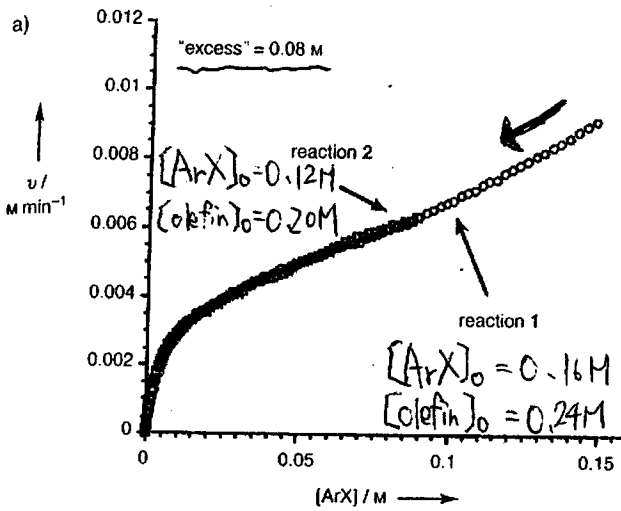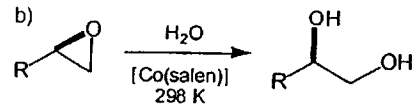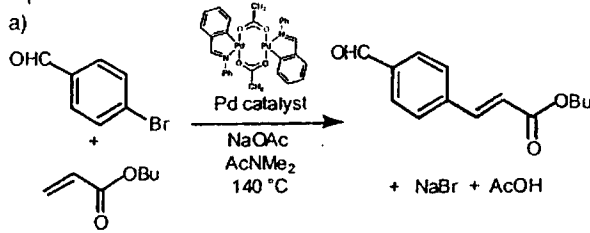
If the stoichiometric relationship of ⑥ is substituted into ⑤, Equation ⑦ is given

$$\boxed{\nu = a' \frac{["excess"][1] + [1]^2}{1 + b'[1]} [4]_{total} \ ⑦} \quad a' = \frac{k_1 k_2}{k_{-1} + k_2["excess"]} \qquad b' = \frac{k_1 + k_2}{k_{-1} + k_2["excess"]}$$

→ [4]_{total}, ["excess"], k_1, k_{-1}, k_2 are constant
   the leaving [1] as the only variable.

Two different ["excess"] value gives an extra equation and allow a solution obtained for all three rate constants (k_1, k_2, k_{-1})

Ⅲ Experiment employing the same "excess" → Determine Catalyst deactivation and product inhibition

a)

OHC—⟨benzene ring⟩—Br + ⟨acrylate⟩OBu →[Pd catalyst / NaOAc / AcNMe₂ / 140 °C]→ OHC—⟨benzene ring⟩—CH=CH—C(=O)—OBu + NaBr + AcOH

b)

R—⟨epoxide⟩ →[H_2O / [Co(salen)] / 298 K]→ R—CH(OH)—CH₂—OH

a)

"excess" = 0.08 M

$v / M\,min^{-1}$

reaction 2
$[ArX]_0 = 0.12 M$
$[olefin]_0 = 0.20 M$

reaction 1
$[ArX]_0 = 0.16 M$
$[olefin]_0 = 0.24 M$

[ArX] / M ⟶

b)

"excess" = 0.5 M

$v / M\,min^{-1}$

reaction 2
$[epoxide]_0 = 1.0 M$
$[H_2O]_0 = 1.5 M$

$[epoxide]_0 = 1.5 M$
$[H_2O]_0 = 2.0 M$

$[epoxide]$ reaction 1
$= 1.0 M$
$[H_2O]_0 = 1.5 M + [Product] 0.5 M$

[epoxide] / M ⟶

Two curves fall exactly on top of one another
↓
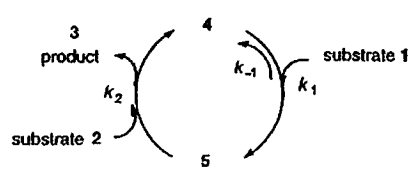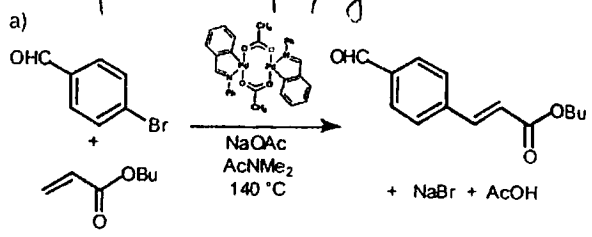neither catalyst deactivation nor product inhibition is occured

Reaction 2 showed higher rate than 1
↓
Either product inhibition or Catalyst deactivation
↓
The curve with addition product [reaction3]
($[epoxide]_0 = 1.0 M$, $[H_2O]_0 = 1.5 M$, $[Product] = 0.5 M$)
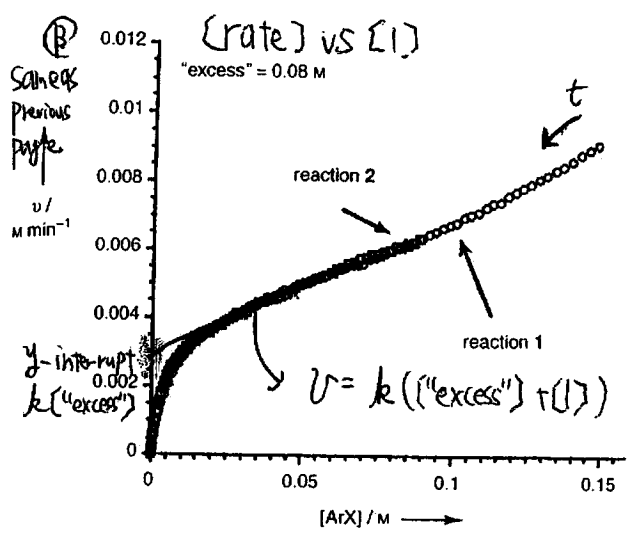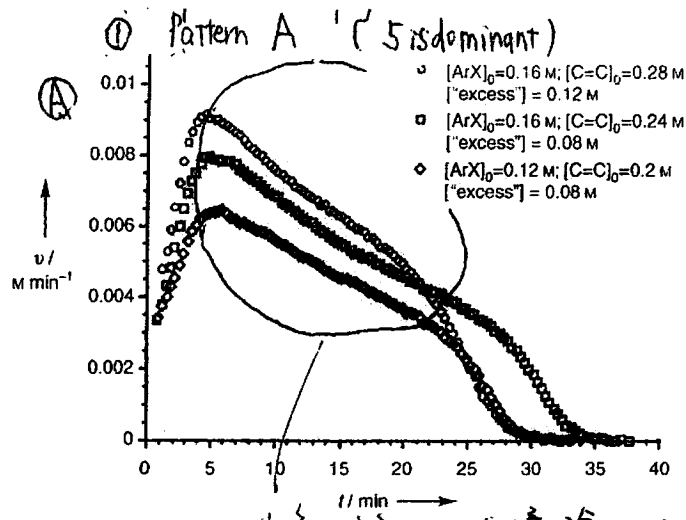overlays the curve of reaction 2
↓
Catalyst deactivation is occured

[2] experiment employing the different excess

a)

OHC—⟨benzene⟩—Br + ⟨acrylate⟩ OBu
$\xrightarrow[\text{140 °C}]{\text{NaOAc} \atop \text{AcNMe}_2}$
OHC—⟨benzene⟩—CH=CH—C(=O)OBu + NaBr + AcOH

$$v = \frac{a[1][2][4]_{cat}}{1 + b[1] + c[2]}$$

$$a = \frac{k_1}{k_{-1}} k_2$$

$$b = \frac{k_1}{k_{-1}}, \quad c = \frac{k_2}{k_{-1}}$$

Catalytic cycle:
3 product — 4 — substrate 1
k_2 ... k_{-1} ... k_1
substrate 2 — 5

① Pattern A ('5 is dominant)

Ⓐ

- ○ $[ArX]_0 = 0.16$ M; $[C=C]_0 = 0.28$ M ["excess"] = 0.12 M
- □ $[ArX]_0 = 0.16$ M; $[C=C]_0 = 0.24$ M ["excess"] = 0.08 M
- ◇ $[ArX]_0 = 0.12$ M; $[C=C]_0 = 0.2$ M ["excess"] = 0.08 M

v / M min^{-1} vs t / min

Ⓑ (rate) vs [1] Same as Previous page

"excess" = 0.08 M

v / M min^{-1} vs [ArX] / M

reaction 2, reaction 1, t

y-interupt k ("excess")

$$v = k(["excess"] + [1])$$

快的从慢 ∴源搞子

$$v = k[2] = k(["excess"] + [1])$$

slope = k
y-intercept = k ("excess")

(3) product ~ (4) cat ~ ArX (1)
k_{-1} ... k_{+1} ... k_1
(2) olefin ~ (5)
(ArCat-X) → major

$[Cat]_{Total} = [Cat] + [ArCat-X]$

$$v = \frac{a[ArX][olefin][Cat]_{Total}}{1 + b[ArX] + c[olefin]} \quad —①$$
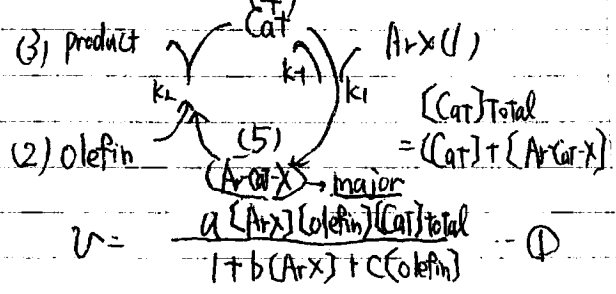
- $b = \frac{k_1}{k_{-1}} \gg \frac{k_2}{k_{-1}} = c \quad (a = \frac{k_1}{k_{-1}} k_2)$
- $b[ArX] \gg 1$

$$v = k_2[olefin][Cat]_{Total} \quad —②$$

$$\frac{v}{[olefin]} = k_2[Cat]_{Total} \quad —③ \quad \text{accord with } ©$$
= Constant

Ⓒ $\frac{v[M]}{[2]}$ vs [1]

$v[olefin]^{-1}$ / min^{-1} vs [ArX] / M [1]

$\frac{v}{[2]}$ olefin

- ○ ["excess"] = 0.12 M
- □ ["excess"] = 0.08 M
- ◇ ["excess"] = 0.08 M

[ArX] pseudo zero order
[olefin] first-order

基于②化简

② Pattern B (4 is dominant)

(4)

OHC–⟨ ⟩–Br(1) $\xrightarrow{Pd(P(Ph)_3)_2}$ OHC–⟨ ⟩–CH=CH–C(=O)–O^{t}Bu

(3)

CH$_2$=CH–C(=O)–O^{t}Bu (2)
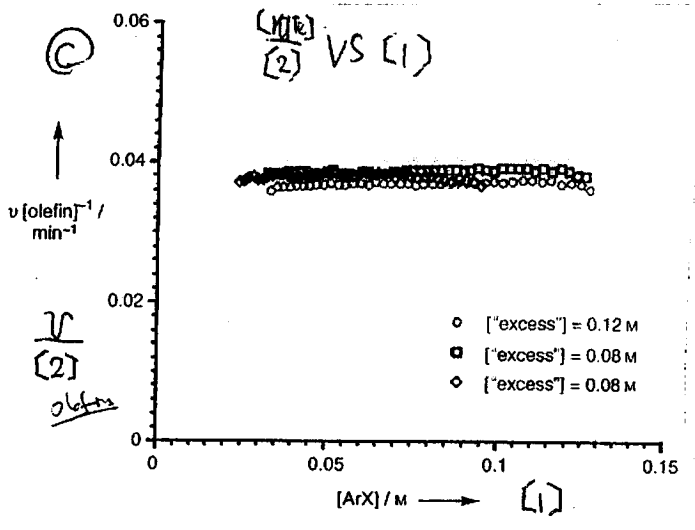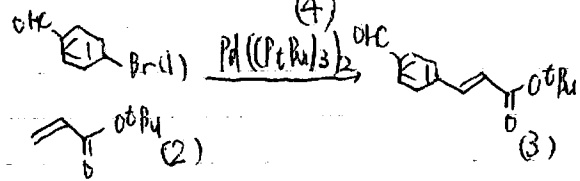
$$v = \frac{a\,[ArX][olefin][Cat]_{Total}}{1 + b\,[ArX] + c\,[Olefin]} \quad — ①$$

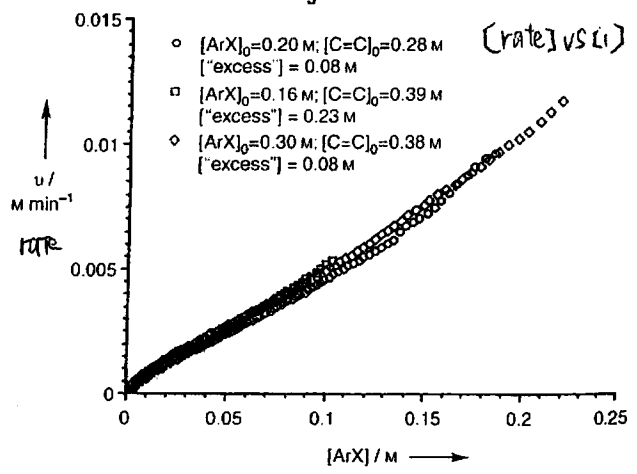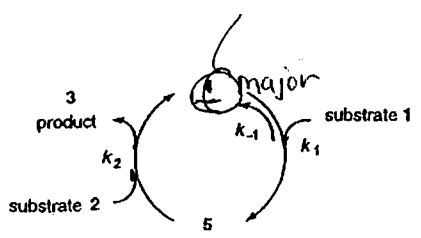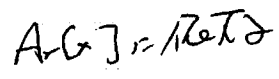$$\frac{k_2}{k_{-1}} = c \gg b = \frac{k_1}{k_{-1}} \quad \left(a = \frac{k_1}{k_2}\right)$$

$$v = a\,[ArX][Cat]_{Total} \quad — ②$$

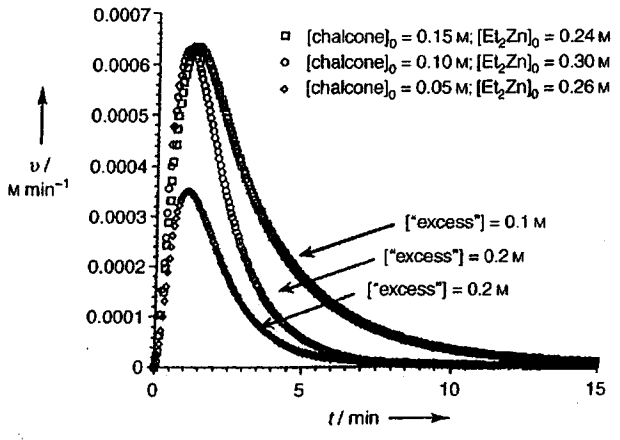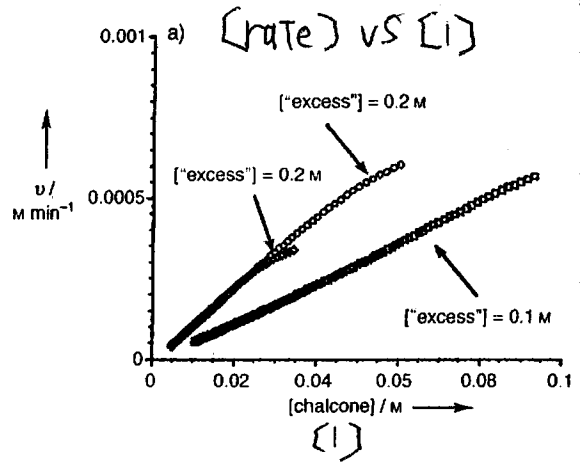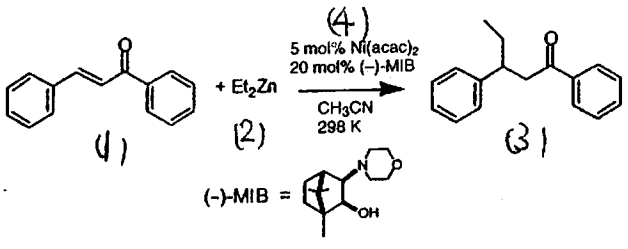At the different "excess" give first order relationship for rate vs [ArX] with y-intercept at zero

→ unbound catalyst (4) is the resting state, rate determining step is oxidative addition

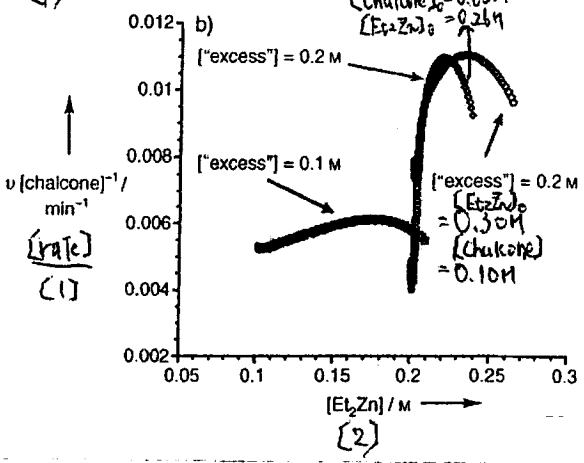$$\frac{v}{[1]} = \frac{v}{[ArX]} = const \qquad → \text{First order in } [ArX]$$

ArG = 1/2 RTd

③ Pattern C (Ambiguous case of resting state)

rate vs [1]

The two curves at same ["excess"] showed no catalyst deactivation

4 Flow chart for carrying out kinetic analysis of a reaction with two substrates
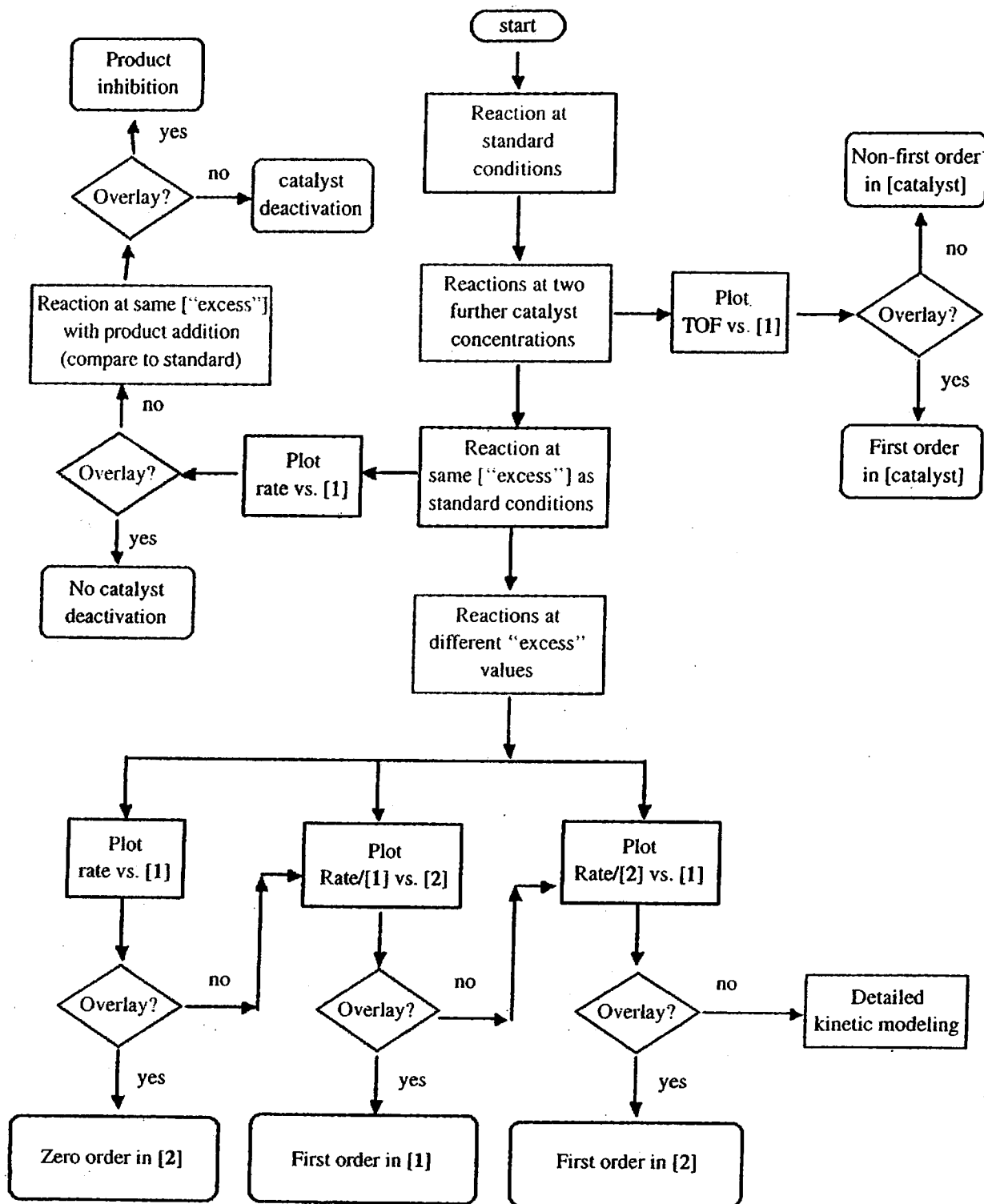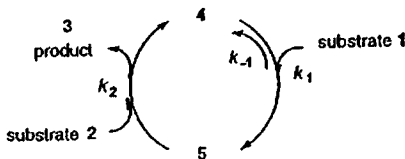
2. Detailed kinetic Modeling (1) Hydrolytic kinetic Resolution of Terminal Epoxide

Mechanistic Investigation Leads to a Synthetic Improvement in the Hydrolytic Kinetic Resolution of Terminal Epoxides

Lars P. C. Nielsen,[†] Christian P. Stevenson,[†] Donna G. Blackmond,[*,‡] and Eric N. Jacobsen[*,†]

1a X=OAc
1b X=OH
1c X=Cl
1d X=OBz
1e X=OPh
1f X=OTs
1g X=SbF$_6$

$\longrightarrow$ beneficial effect of counter ion.

(Ref)

ring-opened products   (2)

epoxide opening of azide phenolic kinetic resolution

(Second order dependence on cat Metal-Nu generated)

(1)

From 1a (OAc) or 1c (Cl)

(3)

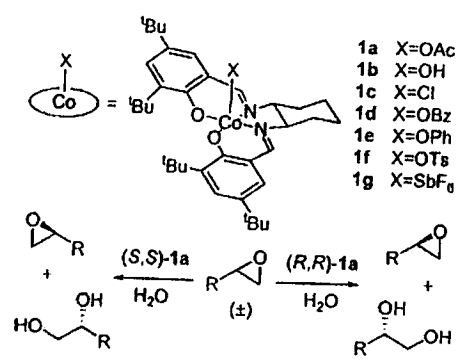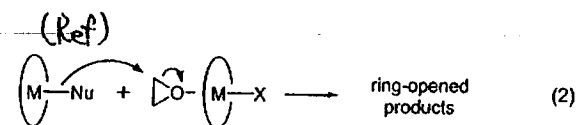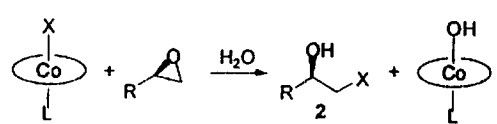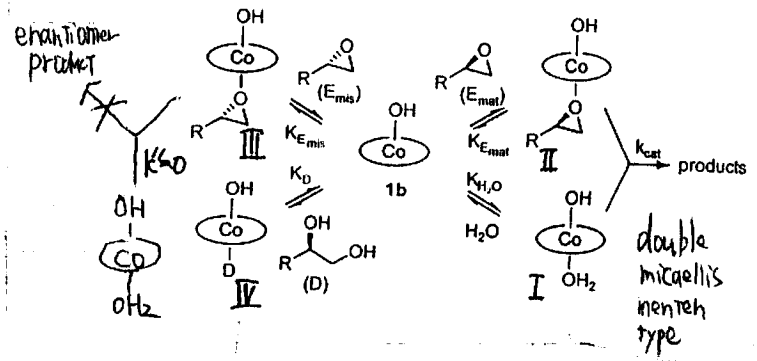Scheme 1. Kinetic Parameters for the HKR of 1-Hexene Oxide Catalyzed by 1b

enantiomer product

double michaellis menten type

$$rate = \frac{d[P]}{dt} = k_{cat} \left[\overset{OH}{\underset{OH_2}{Co}}\right]_{(I)} \left[\overset{OH}{\underset{E_{mat}}{Co}}\right]_{(II)}$$

$$K_{H_2O} = \frac{\left[\overset{OH}{\underset{OH}{Co}}\right] (I)}{[Co][H_2O]} \qquad K_{mat} = \frac{\left[\overset{OH}{\underset{OH}{Co}}\right] (II)}{[Co][H_2O]}$$

$$K_{mis} = \frac{\left[\overset{OH}{\underset{E_{mis}}{Co}}\right] (III)}{[Co][E_{mis}]} \qquad K_D = \frac{\left[\overset{OH}{\underset{OH}{Co}}\right] (IV)}{[Co][D]}$$

$$[Co-OH]_{TOT} = \underset{1b}{[Co]} + \underset{(I)}{\left[\overset{OH}{\underset{OH_2}{Co}}\right]} + \underset{(II)}{\left[\overset{OH}{\underset{E_{mat}}{Co}}\right]} + \underset{(III)}{\left[\overset{OH}{\underset{E_{mis}}{Co}}\right]} + \underset{(IV)}{\left[\overset{OH}{\underset{D}{Co}}\right]} = (1 + K_{H_2O}[H_2O] + K_{mat}([E_{mat}]) + K_{mis}([E_{mis}]) + K_D[D])[Co]^0$$

rate =

$$\frac{k_{cat}K_{H_2O}K_{E_{mat}}[H_2O][E_{mat}][Co-OH]_{tot}^2}{(1 + K_{H_2O}[H_2O] + K_{E_{mat}}[E_{mat}] + K_{E_{mis}}[E_{mis}] + K_D[D])^2} \quad (4)$$

$k_{cat} = 17.88 \pm 0.03 \ M^{-1} s^{-1}$

$K_{H_2O} = 0.1800 \pm 0.0002 \ M^{-1}$

$K_{E_{mat}} = 0.1178 \pm 0.0003 \ M^{-1}$

$\dfrac{K_{E_{mat}}}{K_{E_{mis}}} = 1.0 \pm 0.2 \ M^{-1}$
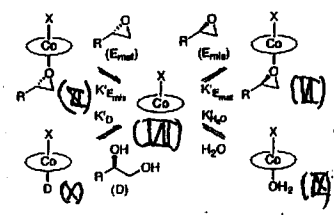
$K_D = 0$ (fixed)

As compared to the pure Co-OH system (1a or 1c X= Cl or OAc)
HKR reaction carried out under conditions in which both Co-OH and Co-X are present
display dramatic increase in activity. (up to 30-fold with X=OTs)

Scheme 1. Kinetic Parameters for the HKR of 1-Hexene **Scheme 2.** Dominant Catalytic Cycle in HKR Reactions Catalyzed by Co−X (X ≠ OH)
Oxide Catalyzed by **1b**   Where Addition of X to Epoxide Is Incomplete
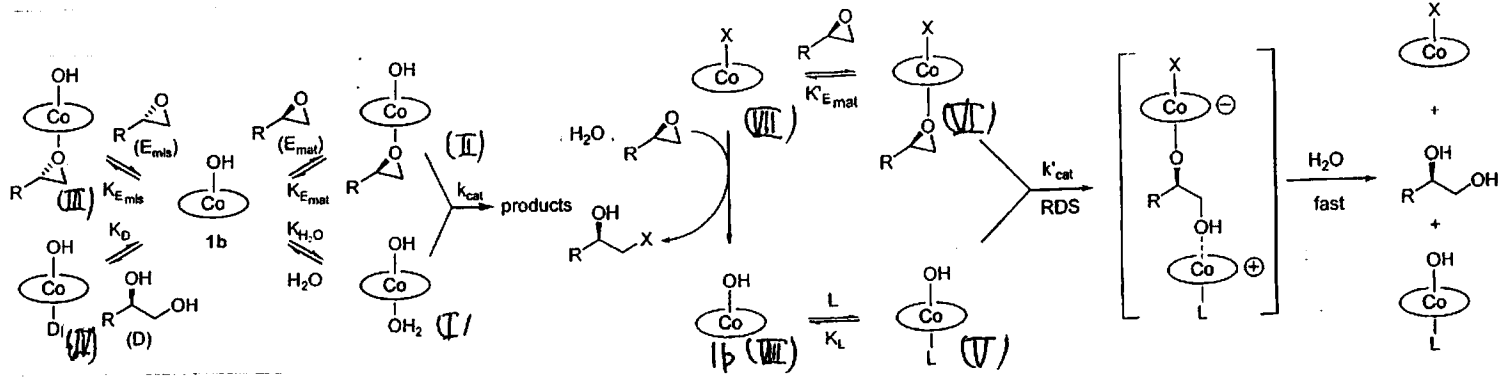
$$\text{rate} = k_{cat}[1b \cdot H_2O][1b \cdot E] + k_{cat}'[1b \cdot L][(Co-X) \cdot E] \quad (5)$$

$$\begin{matrix}(I) & (II) & (V) & (VI)\end{matrix}$$

$$= k_{cat}' \; [1b \cdot L] \cdot [(Co-X) \cdot E] \qquad -(5)' \qquad (k_{cat}' \gg k_{cat}) \qquad Co-X - (strong\ lewis\ acid)$$

$$(V) = \{Co\}_L^{OH} \qquad (VI) = \{Co\}_{Emat}^X$$

$$[Co-X]_{tot} = \{Co\}^X + \{Co\}_{OH_2}^X + \{Co\}_{Emat}^X + \{Co\}_{Emis}^X + \{Co\}_P^X$$

$$\qquad\qquad\qquad (VII) \qquad (IX) \qquad (VI) \qquad (XI) \qquad (X)$$

$$[Co-X]_{tot} = (1 + K'_{H_2O}(H_2O) + K'_{Emat}(Emat) + K'_{Emis}(Emis) + K'_P(D)) \{Co\}^X$$

$$\{Co\}_L^{OH} = \frac{K_L[L][Co-OH]_{tot}}{(1 + K_{H_2O}(H_2O) + K_{Emat}(Emat) + K_{Emis}(Emis) + K_P(D))}$$

$$\{Co\}_{Emat}^X = \frac{K'_{Emat}(Emat)[Co-X]_{tot}}{(1 + K'_{H_2O}(H_2O) + K'_{Emat}(Emat) + K'_{Emis}(Emis) + K'_P(P))}$$

$$\text{rate} = k_{cat}' \frac{K_L[L][Co-OH]_{tot}}{(1 + K_{H_2O}(H_2O) + K_{Emat}(Emat) + K_{Emis}(Emis) + K_P(D))} \cdot \frac{K'_{Emat}(Emat)[Co-X]_{tot}}{(1 + K'_{H_2O}(H_2O) + K'_{Emat}(Emat) + K'_{Emis}(Emis) + K'_P(P))} \quad -(5)''$$

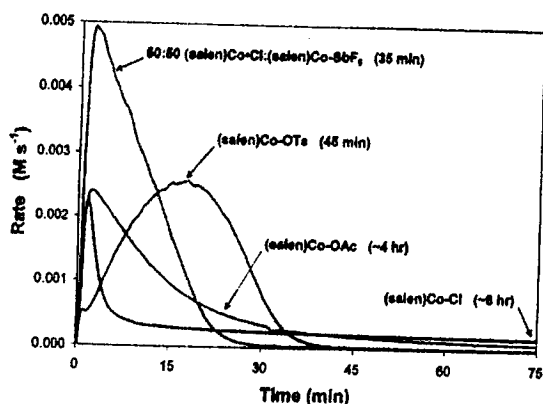$$\text{rate} = k_{cat}' f[Co-OH]_{tot}[Co-X]_{tot} \qquad (6)$$

f accounts for the order dependence on water, matched epoxide, mismatched epoxide
and diol the reaction proceeds

$$\text{rate} = k_{cat}' f\ ([Co\text{-}OH]_{tot})\ [Co\text{-}X]_{tot}$$

Figure 1. Parabolic dependence of rate on partitioning between Co–OH (1b) and Co–SbF$_6$ (1g).
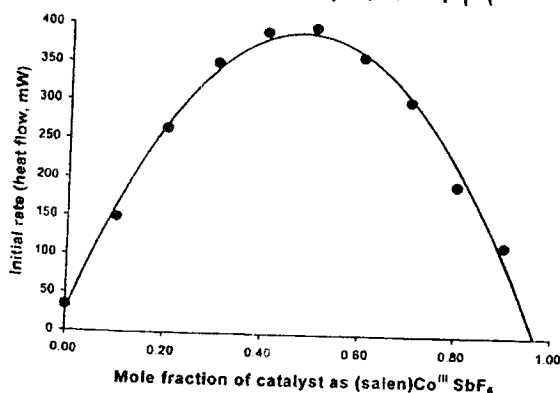
$$\text{maximum rate arises when } [Co\text{-}OH]_{tot} = [Co\text{-}X]_{tot}$$
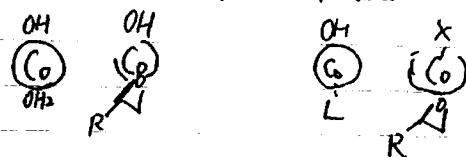
Figure 2. Hydrolysis of 1-hexene oxide catalyzed by different Co–X complexes as monitored by reaction calorimetry (completion times in parentheses). All runs were carried out at the same total catalyst concentration.

$$\text{rate} = k_{cat}\ \{1b\text{-}H_2O\}\ [1b\text{-}E] + k_{cat}'\ [1b\text{-}L]\ [(Co\text{-}X)\text{-}E]$$

Figure 3. Representation of the HKR using three-dimensional kinetic surfaces. The lines track the progress of the reactions with different catalysts as a function of rate and catalyst partitioning.

3. Detailed Kinetic Modeling &) Rhodium - Catalyzed Asymmetric 1,4-addition

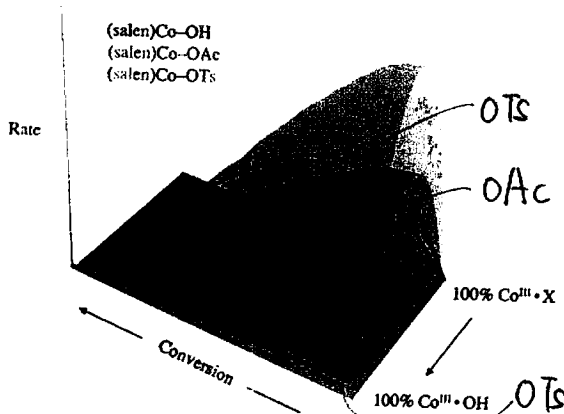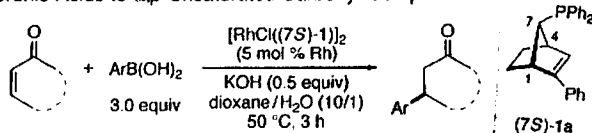# Chiral Phosphine–Olefin Ligands in the Rhodium-Catalyzed Asymmetric 1,4-Addition Reactions

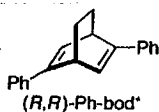Wei-Liang Duan,[†] Hiroshi Iwamura,[‡] Ryo Shintani,*,[†] and Tamio Hayashi*,[†]

(Results)

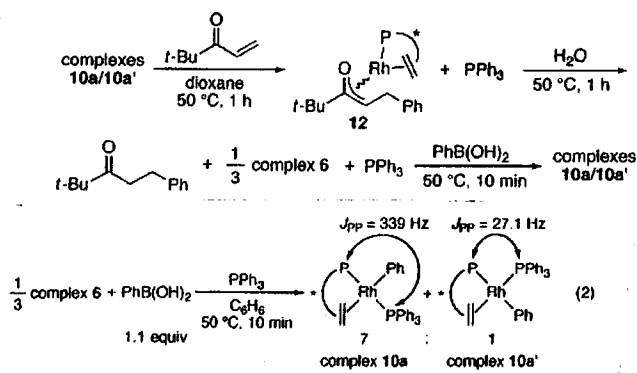**Table 1.** Rh/(7S)-1-Catalyzed Asymmetric 1,4-Addition of Arylboronic Acids to α,β-Unsaturated Carbonyl Compounds

entry	substrate	Ar	ligand	yield (%)	ee (%)*	config.
1		Ph	1a	91	98 (99)	(R)
2		4-MeOC₆H₄	1a	94	98 (98)	(R)
3		4-CF₃C₆H₄	1a	92	95 (96)	(R)
4		2-MeC₆H₄	1a	99	98 (96)	(R)
5		Ph	1a	94	93 (96)	(R)
6		Ph	1a	91	72 (83)	(S)
7		Ph	1a	89	97 (95)	(R)

(R,R)-Ph-bod*

Rh/(7S)-1 cat proceed earlier than bicyclic diene ligand.

(X-ray of pre-catalyst)

$$\frac{3}{2}\,[Rh(OH)(cod)]_2 + 3\,(7S)\text{-}1a \xrightarrow[\text{50 °C, 5 h}]{C_6H_6}$$

$$[Rh_3(\mu\text{-}O)(\mu\text{-}OH)((7S)\text{-}1a)_3] + H_2O$$

6: 70% yield   (1)

Figure 3. X-ray structure of [Rh₃(μ-O)(μ-OH)((7S)-1a)₃] (6).

(NMR Study)

Scheme 2

$$\frac{1}{3}\text{ complex 6} + \text{PhB(OH)}_2 \xrightarrow[\text{50 °C, 10 min}]{\text{PPh}_3}{C_6H_6} \quad (2)$$

1.1 equiv

J_{PP} = 339 Hz J_{PP} = 27.1 Hz

complex 10a : complex 10a'

7 : 1

NMR Study Suggests
① Phenylrhodium
② oxa-π-allylrhodium
③ hydrorhodium trimer
were generated in catalytic cycle.

(Proposed Catalytic System)
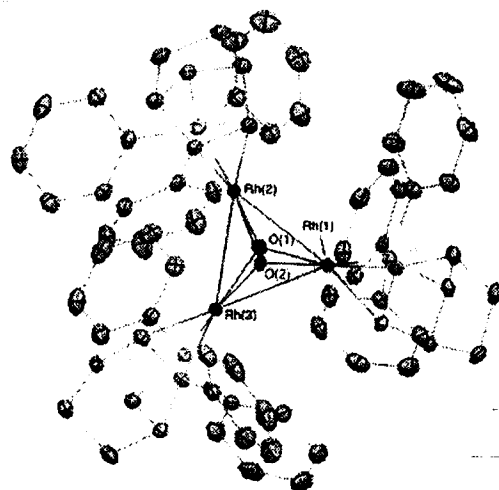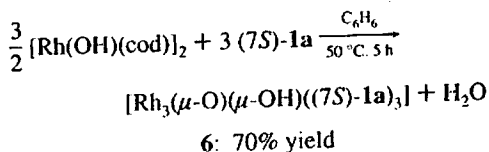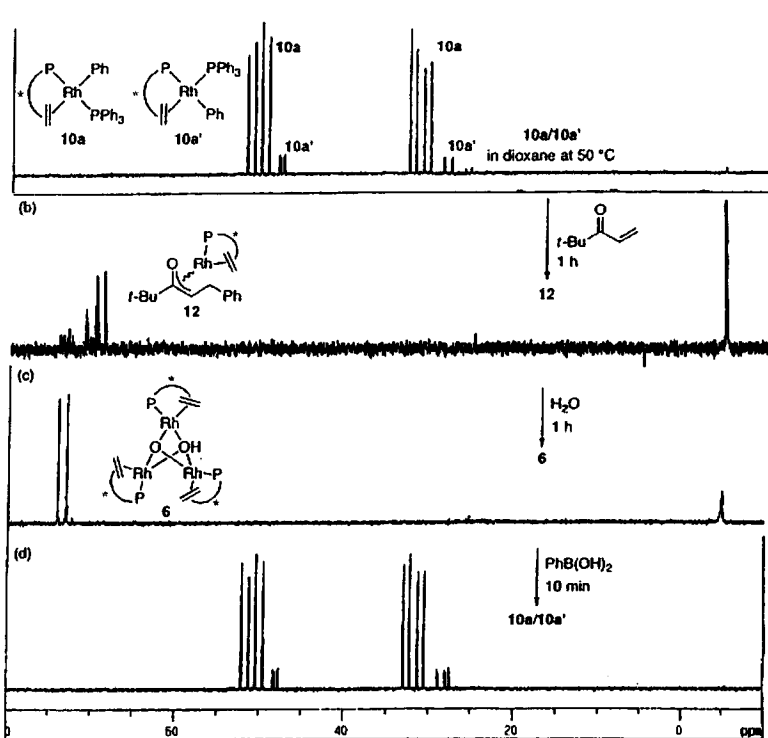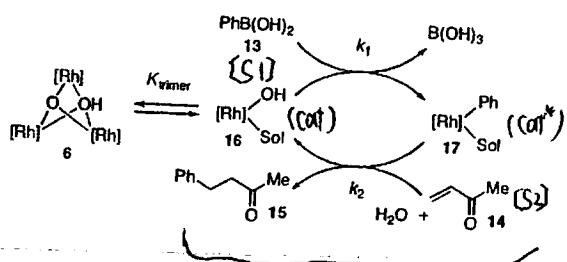

Reaction with two substrates
and one intermediate

(Kinetic Study — follow flow chart of Blackmond)

(1) Same ["excess"]

Figure S1. Reaction conditions: 1,4-dioxane = 3.0 mL, H_2O = 0.30 mL, $[6]_0$ = 2.7 mM Rh at 30 °C.

a, –: $[13]_0$ = 67 mM, $[14]_0$ = 201 mM (["excess"] = 134 mM).
b, –: $[13]_0$ = 80 mM, $[14]_0$ = 214 mM (["excess"] = 134 mM).

The two curves overlay exactly
→ no catalyst deactivation
   no product inhibition
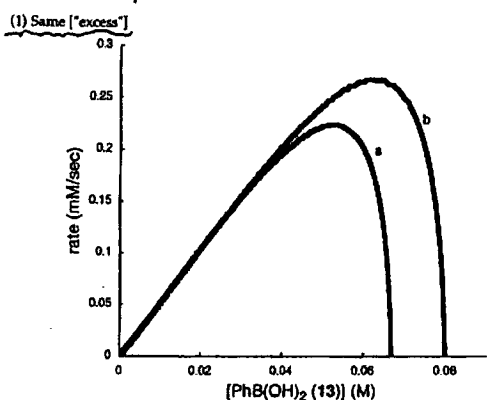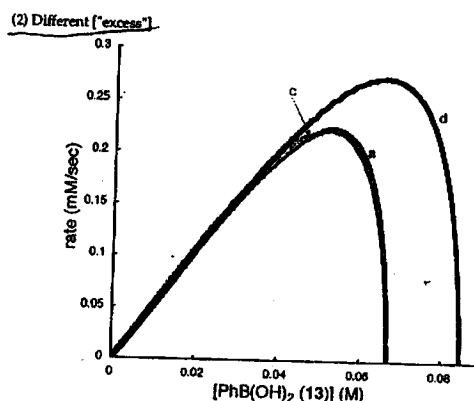
(2) Different ["excess"]

Figure S2. Reaction conditions: 1,4-dioxane = 3.0 mL, H_2O = 0.30 mL, $[6]_0$ = 2.7 mM Rh at 30 °C.

a, –: $[13]_0$ = 67 mM, $[14]_0$ = 201 mM, (["excess"] = 134 mM).
c, –: $[13]_0$ = 67 mM, $[14]_0$ = 101 mM, (["excess"] = 34 mM).
d, –: $[13]_0$ = 85 mM, $[14]_0$ = 201 mM, (["excess"] = 116 mM).

At different excess, the curves overlay
which indicates that the reaction follows
Zero-order kinetics in [14]

$\dfrac{rate}{[13]}$ = const   First-order in [13]
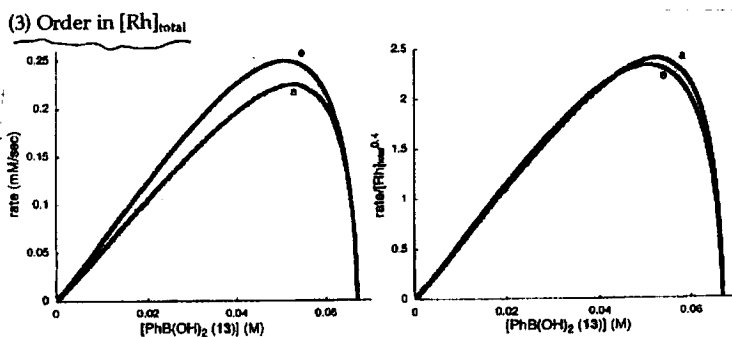
(3) Order in $[Rh]_{total}$

Figure S3. Reaction conditions: 1,4-dioxane = 3.0 mL, H_2O = 0.30 mL at 30 °C.

a, –: $[13]_0$ = 67 mM, $[14]_0$ = 201 mM, $[6]_0$ = 2.7 mM Rh.
e, –: $[13]_0$ = 67 mM, $[14]_0$ = 201 mM, $[6]_0$ = 3.8 mM Rh.

The right graph, which is plotted rate
divided by $[Rh]_{total}^{0.4}$ vs [13]
show overlay

0.4-order kinetics in $[Rh]_{total}$

14

(Determination of Reaction Rate)

Scheme 3. Proposed Catalytic Cycle for the Rh/1a-Catalyzed 1,4-Addition of Phenylboronic Acid (13) to Methyl Vinyl Ketone (14) ([Rh] = Rh/1a)
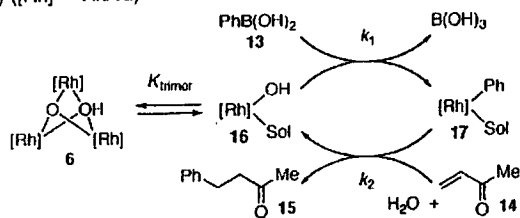
Reaction from 14 to 15 proceed very first

$$v = k_1 [13][16] \quad \text{—} \textcircled{1}$$

$$[Rh]_{total} = 3[6] + [16] \quad \text{—} \textcircled{2}$$

$$k_{trimer} = \frac{[6]}{[16]^3} \quad \text{—} \textcircled{3} \qquad [6] = k_{trimer}[16]^3 \quad \textcircled{4}$$

$$[Rh]_{total} = 3k_{trimer}[16]^3 + [16] \quad \text{—} \textcircled{5}$$
$$\searrow \text{ Substituted for } [6] \text{ in } \textcircled{2}$$

$$[16] = \frac{[Rh_{total}]^{1/3}}{(6k_{trimer})^{1/3}} \left\{ (1+A)^{1/6} + (1-A)^{1/6} \right\} \quad \textcircled{6}$$

$$A = \left(1 + \frac{4}{81 k_{trimer}[Rh]_{total}} \right)^{1/2} \quad \text{—} \textcircled{7}$$

in this system $\quad A \doteq 1$

$$[16] = \frac{[Rh]_{total}^{1/3}}{(3k_{trimer})^{1/3}} \quad \text{—} \textcircled{8}$$

$$v = \frac{k_1 [13][Rh]_{total}^{1/3}}{(3k_{trimer})^{1/3}}$$

accord with 0.4-order kinetics of $[Rh]_{total}^{1/3}$

(Nonlinear Effect analysis)
→ determine k_{trimer} and k_1
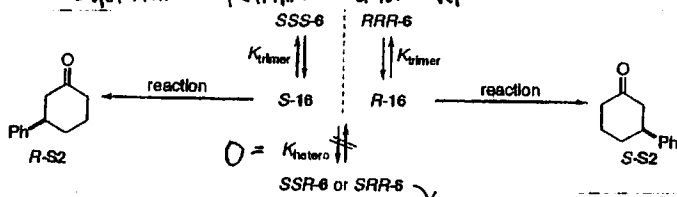
not observed in ^{31}P NMR

$$ee \; prod = ee_{100\%} \cdot \frac{[S-16] - [R-16]}{[S-16] + [R-16]} \quad \textcircled{1}$$

$$[S]_{total} = 3[SSS-6] + [S-16] \quad \text{—} \textcircled{2}$$
$$[R]_{total} = 3[RRR-6] + [R-16] \quad \text{—} \textcircled{3}$$

$$k_{trimer} = \frac{[SSS-6]}{[S-16]^3} = \frac{[RRR-6]}{[R-16]^3} \quad \text{—} \textcircled{4}$$

from $\textcircled{2}$ and $\textcircled{4}$ [S-16] and [R-16] can be derived

$$[S-16] = \left\{ \frac{[S]_{total}}{6k_{trimer}} + \left\{ \left(\frac{[S]_{total}}{6k_{trimer}} \right)^2 + \left(\frac{1}{9k_{trimer}} \right)^3 \right\}^{1/2} \right\}^{1/3} + \left[\frac{[S]_{total}}{6k_{trimer}} - \left\{ \left(\frac{[S]_{total}}{6k_{trimer}} \right)^2 + \left(\frac{1}{9k_{trimer}} \right)^3 \right\}^{1/2} \right]^{1/3} \quad \textcircled{5}$$

$$[R-16] = \left\{ \frac{[R]_{total}}{6k_{trimer}} + \left\{ \left(\frac{[R]_{total}}{6k_{trimer}} \right)^2 + \left(\frac{1}{9k_{trimer}} \right)^3 \right\}^{1/2} \right\}^{1/3} + \left[\frac{[R]_{total}}{6k_{trimer}} - \left\{ \left(\frac{[R]_{total}}{6k_{trimer}} \right)^2 + \left(\frac{1}{9k_{trimer}} \right)^3 \right\}^{1/2} \right]^{1/3} \quad \textcircled{6}$$

$[13]_0 = 67 \text{mM}$

$[14]_0 = 201 \text{mM}$
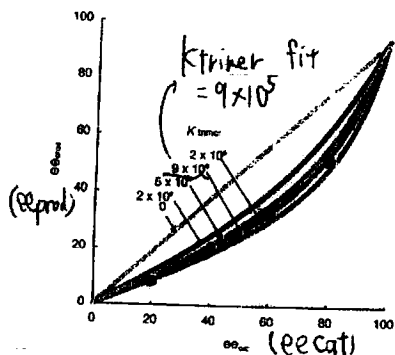
$[6]_0 = 2.7 \text{mM Rh}$

1,4-dioxane = 3.0 ml

$H_2O = 0.3 \text{ml}$

at 30°C

$$ee_{prod} = ee_{100\%} \cdot \frac{[S-16] - [R-16]}{[S-16] + [R-16]} \quad - \textcircled{1}$$

$\searrow K_{trimer}$ $\underline{9 \times 10^5}$

$$v = \frac{k_1 [13] [Rh]_{total}^{1/3}}{(3 k_{trimer})^{1/3}}$$

$$k_1 = \frac{v (3 k_{trimer})^{1/3}}{[13] [Rh]_{total}^{1/3}}$$

$$= \frac{0.2 \times (27 \times 10^5)^{1/3}}{40 \times (2.7)^{1/3}}$$

$$= 5.0 \ M^{-1} S^{-1} > 1.3 M^{-1} \ (k_1 \text{ of } Rh(cod) \ cat)$$