There are only two important things in chemistry, kinetics and thermodynamics. And, exp(-ΔG/RT) = k_f/k_r, 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.

1st 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:

0th: \[-d[A]/dt = k \rightarrow [A] = kt\]

1st: \[-d[A]/dt = k[A] \rightarrow \ln[A] = kt\]

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

2 common methods to determine order in individual components.

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

Note \([EtI] = 0\), but \([NaCN] = 10 \rightarrow 9\) up to 200 \(\rightarrow 199\)
Rate = \(k[NaCN][EtI] \sim k[NaCN][EtI] = k_{obs}[EtI]\)
Pseudo-first Order \([\text{NaCN}] \gg [\text{EtI}] = 1\)

\[
y = -199.36x - 0.0009 \\
y = -99.363x - 0.0018 \\
y = -49.363x - 0.0036 \\
y = -24.362x - 0.0073 \\
y = -9.3583x - 0.0187 
\]

Rxn is 1st order in NaCN!!
But…is 10-200 equiv NaCN really representative??

Replot data in 1st order coordinates
Slope of line = \(k_{\text{obs}}\)

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. \(v = k_{\text{obs}}[\text{EtI}][\text{NaCN}] \sim k_{\text{obs}}[\text{EtI}][\text{NaCN}]_{0 \rightarrow 10\%}\)
Case Study 1: Bergman, JACS, 1981, 7028

Kinetics-6

Notes
Need more data points/time for initial rate
Data looks pretty linear for first 10%
Slope of best-fit line is k<br>
Kobs = k[NaCN][EtI] and [EtI] was constant
Again, the rxn is first order in [NaCN]
But...we ignored 90% of the reaction.

Kinetics-7

Case Study 1: Bergman, JACS, 1981, 7028

Migratory insertion

Confusion: Huge solvent effects on rate and (in related systems) stereochemistry
What's the mechanism??

congealed 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

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

$$\text{rate} = \frac{k_1k_2[1][PR_3]}{k_0[PR_3] + k_1}$$

Rxn in 2.5 Me_2THF only shows concerted attack. How to explain? Solvent assistance.

Mechanism predicts 1st order dependence on THF. Do exp in 2.5-Me_2THF, add THF (note only minor change in dipole)

Figure 1. Dependence of the pseudo-first-order rate constant $k_{\text{exp}}$ for conversion of 1 to 2 in excess PMePh_3 upon phosphine concentration in the following solvents: (●) THF; (●) 3-MeTHF; (●) 2-MeTHF; (●) 2.5-Me_2THF.

Figure 2. Dependence upon [THF] of $k_1$ for reaction of 1 with PMePh_3, determined in studies using 0.01 M 1 and varying excess concentrations of phosphine in THF/2.5-Me_2THF mixtures.
Previous work (JACS 1993, 12226) had shown 1st order in OsO4-L, zero order in Fe(III)

Proposed structure of L*OsO₄(olefin) for allyl benzoate

These are saturation kinetics!!. Same as many enzymes and Lewis-Acid cat Rxns
Ready: Catalysis

Case Study 2: Corey, JACS, 1996, 319

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

| Table 1: Correlation of the Michaelis–Menten parameters (K, and kcat) and Enzymatic Activity in the Corey
| Reaction System
<table>
<thead>
<tr>
<th>Reaction System</th>
<th>K</th>
<th>kcat</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.2</td>
<td>0.5</td>
<td>80%</td>
</tr>
<tr>
<td>2</td>
<td>2.4</td>
<td>1.0</td>
<td>70%</td>
</tr>
<tr>
<td>3</td>
<td>3.6</td>
<td>1.5</td>
<td>60%</td>
</tr>
<tr>
<td>4</td>
<td>4.8</td>
<td>2.0</td>
<td>50%</td>
</tr>
</tbody>
</table>


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

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Case Study 3: Jacobsen, JACS, 1996, 10924

The reaction

The data:
Case Study 3: Jacobsen, JACS, 1996, 10924

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

Data:

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

The rxn:

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

Data:

$V = k[A]^n$
$log(V) = log(k[A]^n) = n*\log(k[A])$
Saturation kinetics with epoxide

Inhibition by PhOH

rate = \frac{k_{\text{cat}}[\text{Co}][\text{Epox}]}{K_d[\text{ArOH}][\text{Epox}]}

L = \text{epox or PhOH}
Case Study 5: Stahl, JACS 2002, 766

The reaction (rxn)

The data: DMSO critical, but is not reduced (O₂ required) or oxidized (no dimethyl sulfone is formed)

2 formed: O₂ consumed = 2 (O₂ is a 4 e- oxidant here)

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

\[ \text{H}_2\text{O}_2 \xrightarrow{\text{Pd}} \text{H}_2 + \frac{1}{2} \text{O}_2 \]  

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

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

Conclude oxidation of Pd is rate limiting

Predicts rate = k[O₂][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

\[
\frac{d\left[\text{O}_2\right]}{dt} = k_{\text{cat}}[\text{Pd}]\cdot[\text{O}_2]; \quad [\text{Pd}]_t = \frac{[\text{Pd}]_0}{1 + [\text{Pd}]_0/k_{\text{dec}}} \quad (7)
\]
Case Study 5: Stahl, JACS 2002, 766

Integrated form models
experimental data

Proposed mechanism

\[
\begin{align*}
\text{H}_2\text{O}_2 & \rightarrow \text{H}_2\text{O}_2 + 2\text{H}^+ \\
\text{L}_x\text{Pd}(I) & \rightarrow \text{RCH}_2\text{OH} \\
\text{O}_2 & \rightarrow \text{RCHO} + 2\text{H}^+ \\
2\text{H}_2\text{O} & \rightarrow \text{non-linear inhibition by PPh}_3
\end{align*}
\]

\[k_{\text{fast}} = 1.25 \times 10^9 \text{ M}^{-1}\text{s}^{-1}\]

\[k_{\text{sec}} = 1.7 \times 10^8 \text{ M}^{-1}\text{s}^{-1}\]


\[
\text{R} \begin{array}{c}
\text{Cl} \\
\text{Ni(PPh)}_3 \text{C} \\
\text{O}
\end{array}
\rightarrow \text{R} \begin{array}{c}
\text{NiCl(PPh)}_3 \\
\text{O}
\end{array}
\]

The data

1st order in [ArCl]

\[k_{\text{obs}} \times 10^4 \text{ s}^{-1}
\]

\[0 \quad 20 \quad 40 \quad 60 \quad 80 \quad 100 \]

\[0 \quad 0.2 \quad 0.4 \quad 0.6 \quad 0.8 \quad 1 \quad 1.2 \quad 1.4 \]

non-linear inhibition by PPh3

\[k_{\text{obs}} \times 10^4 \text{ s}^{-1}
\]

\[0 \quad 50 \quad 60 \quad 70 \quad 80 \]

\[0 \quad 0.05 \quad 0.1 \quad 0.15 \quad 0.2 \quad 0.25 \quad 0.3 \quad 0.35 \quad 0.4 \]

\[0 \quad 0.05 \quad 0.1 \quad 0.15 \quad 0.2 \quad 0.25 \quad 0.3 \quad 0.35 \quad 0.4 \]

Proposed mechanism

\[
\begin{align*}
\text{Ni(PPh\textsubscript{3})}_4 & \rightarrow \text{Ni(PPh\textsubscript{3})}_3 + \text{PPh}_3 & K' > 10 \\
\text{Ni(PPh\textsubscript{3})}_3 & \rightarrow \text{Ni(PPh\textsubscript{3})}_2 + \text{PPh}_3 & K < 10^6 \\
\text{Ni(PPh\textsubscript{3})}_2 + \text{ArCl} \quad & k_1 \rightarrow (\text{PPh\textsubscript{3}})_2\text{Ar}(X) + \text{PPh}_3 \\
\text{Ni(PPh\textsubscript{3})}_2 + \text{ArCl} \quad & k_2 \rightarrow (\text{PPh\textsubscript{3}})_2\text{Ar}(X)
\end{align*}
\]

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

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

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

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

For p-Cl\textsubscript{2}Ph:

\( k_1 = 1 \times 10^{-3} \)

\( k_2 = 1.1 \times 10^{-5} \)

\( k_2 \sim 10 \)

So Ni(PPh\textsubscript{3})\textsubscript{2} is 10\textsuperscript{6} times more reactive than Ni [PPh\textsubscript{3}]\textsubscript{3}, but much less prevalent.

Ready; Catalysis, Kinetics-case study 7

Coates, JACS, 2007, 4948

High yields for terminal and internal epoxides; stereospecific:

<table>
<thead>
<tr>
<th>anhydride</th>
<th>yield (%)(^a)</th>
<th>ee (%)(^b)</th>
<th>entry</th>
<th>epoxide</th>
<th>epoxide/(\text{R}^1)</th>
<th>anhydride</th>
<th>yield (%)(^a)</th>
<th>trans/cis(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(S)-7</td>
<td>97</td>
<td>97</td>
<td>1</td>
<td>100</td>
<td>O</td>
<td>(S)-7</td>
<td>99</td>
<td>&gt;99</td>
</tr>
<tr>
<td>(S)-7</td>
<td>99</td>
<td>&gt;99</td>
<td>2</td>
<td>200</td>
<td>O</td>
<td>(R)-11</td>
<td>99</td>
<td>&gt;99</td>
</tr>
<tr>
<td>(R)-11</td>
<td>99</td>
<td>&gt;99</td>
<td>3</td>
<td>75</td>
<td>O</td>
<td>(S)-21</td>
<td>96</td>
<td>97 (99%)</td>
</tr>
<tr>
<td>(S)-21</td>
<td>97</td>
<td>&gt;99</td>
<td>4</td>
<td>100</td>
<td>O</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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.

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

Epoxide (and solvent) inhibit lactone $\rightarrow$ anhydride
Recall: \( \Delta G = -RT \ln(K) \) and \( \Delta G = \Delta H - T \Delta S \)

Merging and rearranging gives the Van’t Hoff Equation: \( \ln(K) = \left( \frac{-\Delta H}{R} \right) \left( \frac{1}{T} \right) + \left( \frac{\Delta S}{R} \right) \)

\( \ln(K) \) vs. \( 1/T \) gives \( \Delta H \) and \( \Delta S \)

n.b. increasing temperature decreases contribution of \( \Delta H \)
The Eyring equation: determination of $\Delta H^\ddagger$ and $\Delta S^\ddagger$.

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

Self exchange reaction

Table 2. Activation Parameters for Degenerate Olefin Exchange between (so/PdIm)²⁺ and so²⁺

<table>
<thead>
<tr>
<th>entry</th>
<th>olefin</th>
<th>lang-range</th>
<th>kM (M⁻¹s⁻¹)</th>
<th>25 °C</th>
<th>$\Delta H^\ddagger$</th>
<th>$\Delta S^\ddagger$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>αPd</td>
<td>224 – 286</td>
<td>109</td>
<td>7.3</td>
<td>-23</td>
<td>6.4</td>
</tr>
<tr>
<td>2</td>
<td>αPd</td>
<td>231 – 238</td>
<td>105</td>
<td>7.6</td>
<td>-26</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>αPd</td>
<td>234 – 298</td>
<td>264</td>
<td>7.9</td>
<td>-24</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>αPd</td>
<td>234 – 298</td>
<td>297</td>
<td>8.2</td>
<td>-21</td>
<td></td>
</tr>
</tbody>
</table>

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

Stahl, JACS, 2004, 14832

Potential mechanisms:

Potential mechanisms:

Stahl, JACS, 2004, 14832

Stahl, JACS, 2004, 14832
Use in asymmetric catalysis

\[
\ln(e.r) = \left(\frac{\Delta\Delta H^\ddagger}{R}\right) \left(\frac{1}{T}\right) - \left(\frac{\Delta\Delta S^\ddagger}{R}\right)
\]

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

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

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

Note with 2e, ee decrease with decreasing T


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

\[
\text{w/ PhI: } \text{rate} = \left[\text{ArBr}\right]_{0} [L]_{0}
\]

Small \(\Delta S^\ddagger\); same rate with sub. ArBr's

'Lineweaver-Burk Plot'

w/ ArCl
Determine the mechanism for oxidative addition of ammonia to Ir(I) olefin complex.

Data:
Rxn with 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.