

① Lecture 12: Kinetics, Practical Considerations

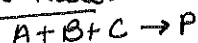
PS# 5 due now.

PS# 6 due 10/20/09

② Recall: If we determine kinetic rate law of a rxn, we know about what molecules are in t.s.

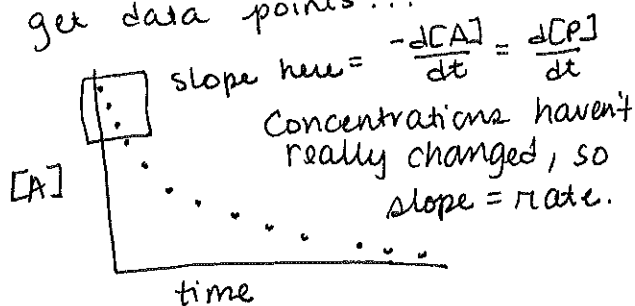
How do we determine rate laws?

③ Option 1: Initial Rates



What if...  
 $rate = \frac{d[P]}{dt} = k_{obs} [A]^m [B]^p [C]^w$   
 constant??

Then, vary [A], [B], [C] to get data points...



④ Is this accurate?

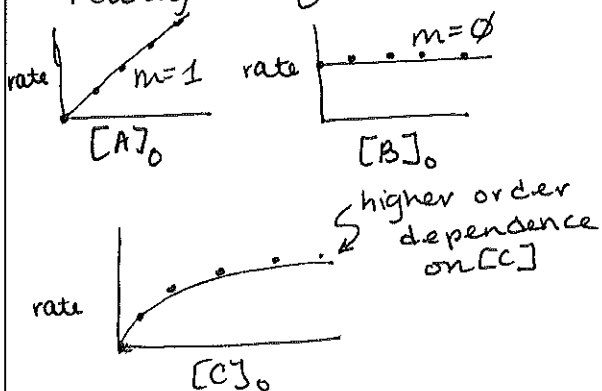
- Error is inherent.
- Cannot look beyond 1st 10% conversion (or you lose linearity).

Advantage: direct measurement of  $\frac{d[P]}{dt}$

Disadvantages:

- 1) Error in estimating slope.
- 2) Concentration are actually changing (if it might matter).
- 3) First 10% may not be representative. (Induction Period)

⑤ If "clean" behavior, can be really useful:



⑥ Option 2: Full Kinetic Profile  
 (Global Rxn Kinetics)

Warning: Rate constants may be coupled  $\rightarrow$  Particularly catalytic rxns...

"In view of the complexity of such systems, attempts to deduce "mechanisms" from kinetic studies on the overall catalytic reactions (although frequently attempted) generally lead to results that are incomplete & of questionable reliability."

Halpern, *Prog Chim Acta* 1981, 50, 11.

(Check his later papers, though!)

7  
 ⑦ But can give you information about the entire rxn course.

A) Nonlinear Fitting

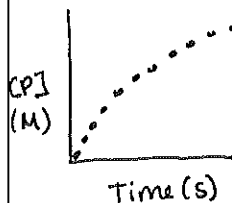
- Measure concentrations at various time points.
- Use Kaleidograph (or other graphing program) to fit data to appropriate equation.

ex: see handout.

\* Can get complicated w/ higher order rxns.

⑧ B) Extract rates (using math & Excel)

ex: Zand & Jacobsen. JACS 2007, 129, 15872.  $A \rightarrow P$

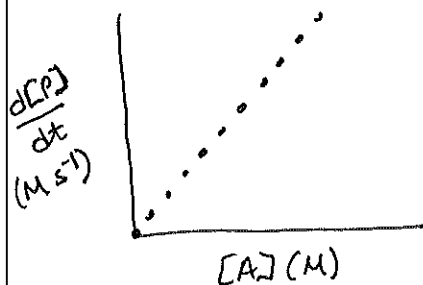


Fit data to  $[P] = f(t) = a + bt + ct^2 + dt^3 + et^4 + ft^5 + gt^6 + ht^7$  (7th order polynomial).

↑  
 Purely empirical!  
 No reflection of chemistry!

⑨ Extract rates using derivative:

$$\frac{d[P]}{dt} = \frac{df(x)}{dt}$$



↳ Rate dependence on [A].

⑩ Collecting Rate Data

Option 1: Sample Collection & Analysis (Aliquots)

Instruments used: GC, LC, NMR, etc.

Limitations: 1 rate data point for every 2 samples taken.

: Does removing aliquots affect rxn?

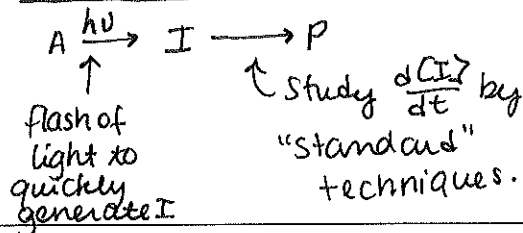
⑪ Option 2: In Situ Monitoring of Concentrations (or Rates) (Preferred Option).

Experimental Techniques:

See handout.

Mayr J Phys Org Chem 2008, 21, 584.

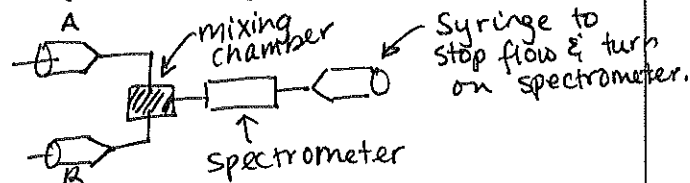
1) Laser Flash Photolysis



- ⑫
- Have been used to study  $TS \rightarrow P$  !!
  - Extremely powerful for elementary processes (1 step).

2) Stopped-flow

- faster than most org rxns (1 ms mixing time, so  $t_{1/2} \approx 1.5$  ok)



- Allows really fast mixing.

Difference in techniques is how you start the rxn.

③ More traditional rxn set-up

UV/Vis:  $t_{1/2} = 10s \rightarrow$  days.

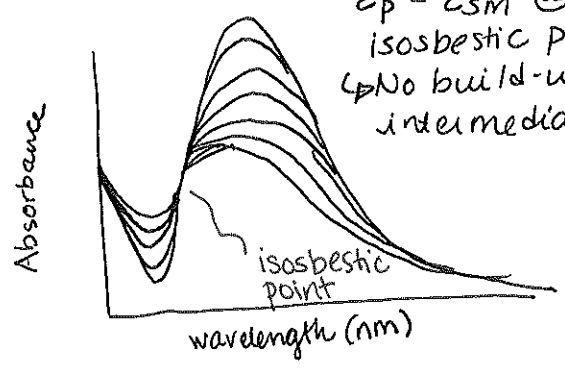
Use Beer's Law

$$A = \epsilon b c$$

$\epsilon$ : Extinction Coefficient  
 $b$ : Path Length  
 $c$ : Concentration extracted from Absorbance data.

Absorbance & Concentration must be linear (should be)  $\rightarrow$  Check!

⑭ Isosbestic Point: No change in absorbance at this wavelength over rxn course.



$E_p = E_{sm}$  @ isosbestic point  
 $\hookrightarrow$  No build-up of intermediates.

Each line = spectrum at a different time point.

⑮ Disadvantages: Limited concentration range.  
 Hard to control temp.

React IR (in situ IR)

- broader concentration range
- easier to control temp
- collect ~ every 15 s (lots of data points!)

Note: CBC is getting an awesome new React IR!!

⑯ NMR

- Useful data about intermediates
- Signal to noise / error bar is significant
- Requires lots of instrument (& your) time.

All these methods give you Concentrations at various time points (not rates).  
 You must extract the rates.  
 (see beginning of lecture).  
 Temperature is assumed to be constant.

⑰ Reaction Calorimetry (Donna Blackmond)

Direct rate measurement.  
 Measures rxn heat flow,  $q$   
 Each data point is a (rate, time) pair  $\approx$  "Initial rate" measurement at different substrate concentrations.

$$q_r = r_r \Delta H_{rxn} \cdot V_{rxn}$$

$q_r$  = rate of heat evolution  
 $r_r$  = rxn rate  
 $V_{rxn}$  = volume

$$r_r = \frac{dc_r}{dt} = -k_c c_r$$

Changes in concentrations are reflected in heat flow.

⑱ Easy to measure heat using calorimeter.  
 Must "correct" the data.

WARNING: Rxn calorimetry should be compared to a spectroscopic method to confirm you're not watching heat flow of the wrong process.

19) Other Mechanistic Tools:

Linear Free Energy Relationships (LFER's)

- Probes the affect of a substituent on kinetics or thermodynamics.

Recall: Substituent Effects:

- 1) Field effects (through space)
- 2) Inductive effects (withdraw or donate e<sup>-</sup>s through  $\sigma$  bonds)
- 3) Resonance (withdraw or donate e<sup>-</sup>s through  $\pi$  bonds)
- 4) Polarizability
- 5) steric
- 6) Solvation

20) HAMMETT PLOTS

Ex: substituent Effect on Acidity of Carboxylic Acids



X	pKa	$\sigma > 1$
H	4.18	$pK_{aX} < pK_{aH}$
OMe	4.47	X is better at stabilizing $\ominus$ than H.
Cl	3.98	X = inductively EWG.
NO <sub>2</sub>	3.43	

Defined for this rxn

$$\sigma = \log \frac{K_X}{K_H} = pK_{aH} - pK_{aX}$$

$\sigma < 1$   
 $pK_{aX} > pK_{aH}$   
X = inductively EDG.

= measure of substituent's ability to donate or withdraw e<sup>-</sup>s by induction.

21) See A & D, Table 8.2 for common substituents.

Substituent's position, p or m, affects whether it is EDG or EWG.

ex: X

X	$\sigma_{para}$	$\sigma_{meta}$
CH <sub>3</sub> O-	-0.12	+0.10
HO-	-0.38	+0.13

Note:  
 $\sigma^+$  &  $\sigma^-$   
used when there is also resonance effect.

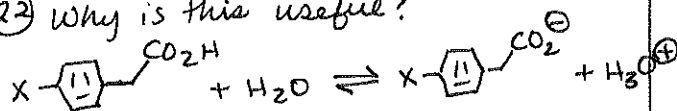
OR groups: EDG as para  
EWG as meta

Truly inductive effect:

X	$\sigma_{para}$
CH <sub>3</sub> O-	-0.12
CH <sub>3</sub> -	-0.14

Methyl is more electron-donating than OCH<sub>3</sub>!!

22) Why is this useful?

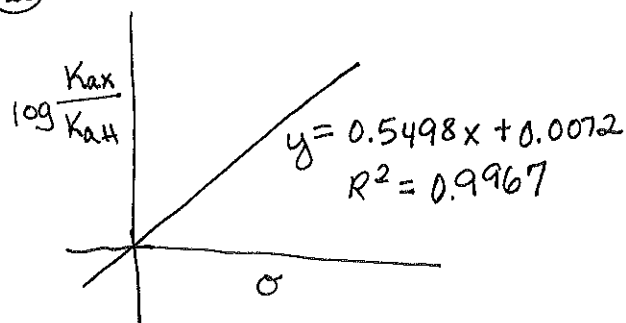


X	$\sigma_p$	$k/K_{unsub}$	$\log(k/K_{unsub})$
Me	-0.14	0.87	-0.060
OCH <sub>3</sub>	-0.12	0.89	-0.051
H	0	1	0
Cl	0.24	1.32	0.1257
NO <sub>2</sub>	0.81	2.89	0.4609

By definition

Data from Dippy & Page. J Chem Soc 1938, 357.

23)



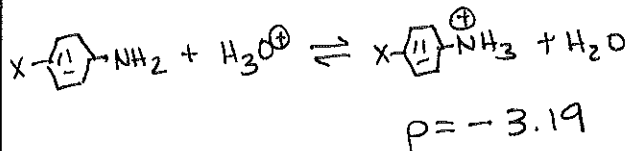
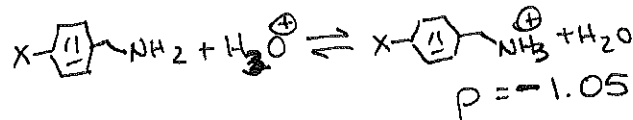
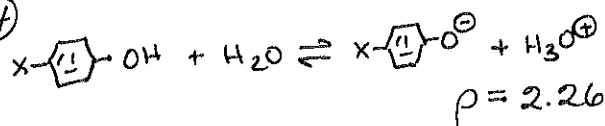
slope  $\approx 0.55$   $\leftarrow$  Substituent effect is  $\sim 50\%$  that of

$\rho$



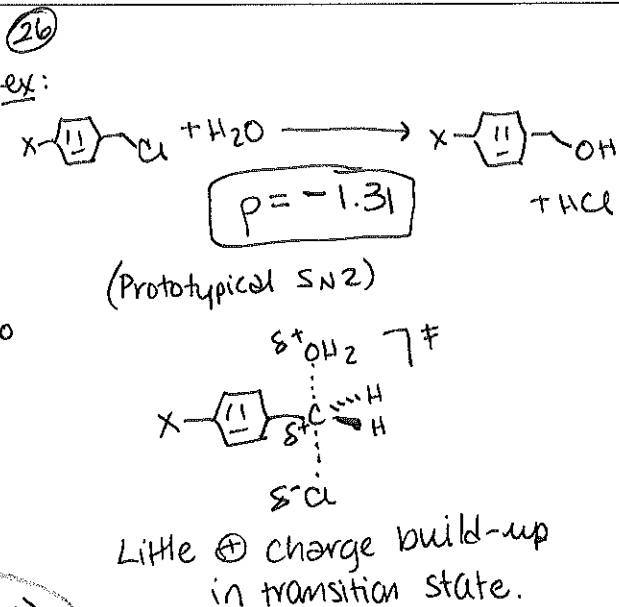
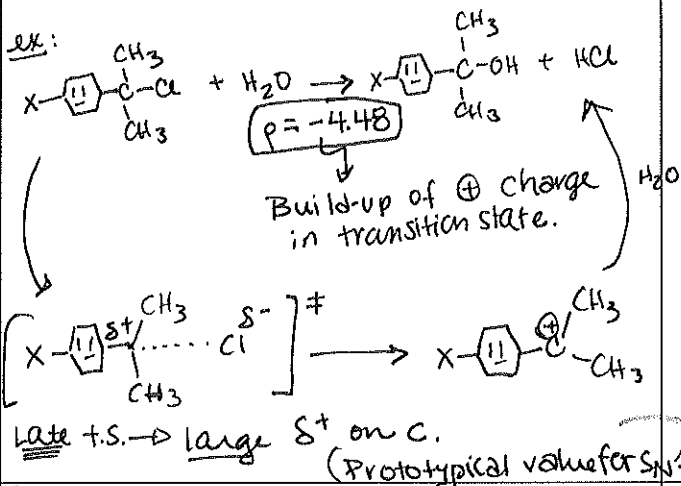
(This is a  $\rho$  plot.)

24)

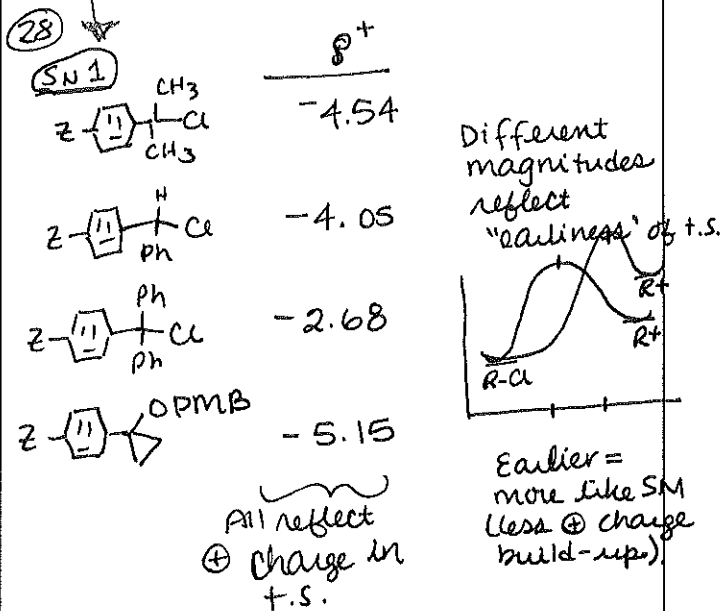
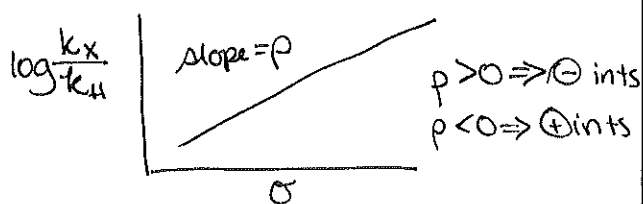


$\rho$ :  $\oplus$  means negative charge develops  
 $\ominus$  means  $\oplus$  charge develops  
Magnitude tells you amt of charge delocalization relative to standard.

25) The cool part...  
ALSO APPLIES TO TRANSITION STATES!!



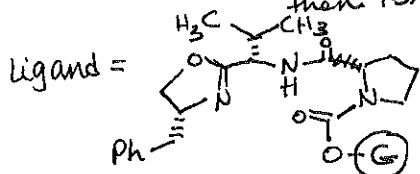
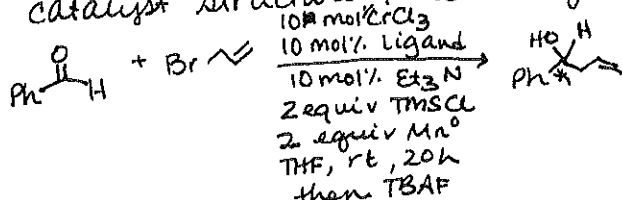
27) For transition states, use  $k$ 's instead of  $K$ 's...



29) Other Linear Free Energy Relationships:

Miller & Sigman ACIE 2008, 47, 771.  
To understand relationship between catalyst structure & selectivity.

Kozaki-Hiyama-Kishi RXN

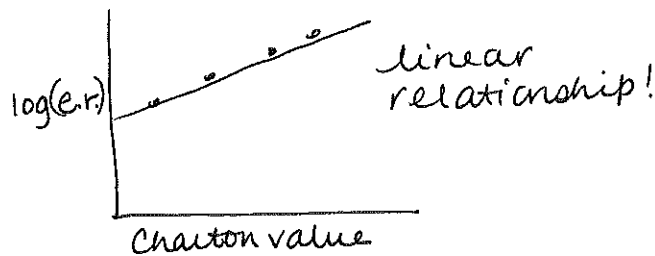


Linear Free Energy Relationship between size of  $G$  & enantioselectivity?

30)  $G$  e.r. (R/S) Chanton Value

$G$	e.r. (R/S)	Chanton Value
Me	1.5	0.52
Et	1.9	0.56
iPr	3.5	0.76
tBu	23	1.24
1-adamantyl	23	1.33

Measure of size.  
JACS 1975, 97, 1552  
JOC 1976, 41, 3205



NOTE: NOT true of all systems.

May become fool to determine if steric effects dominate selectivity.