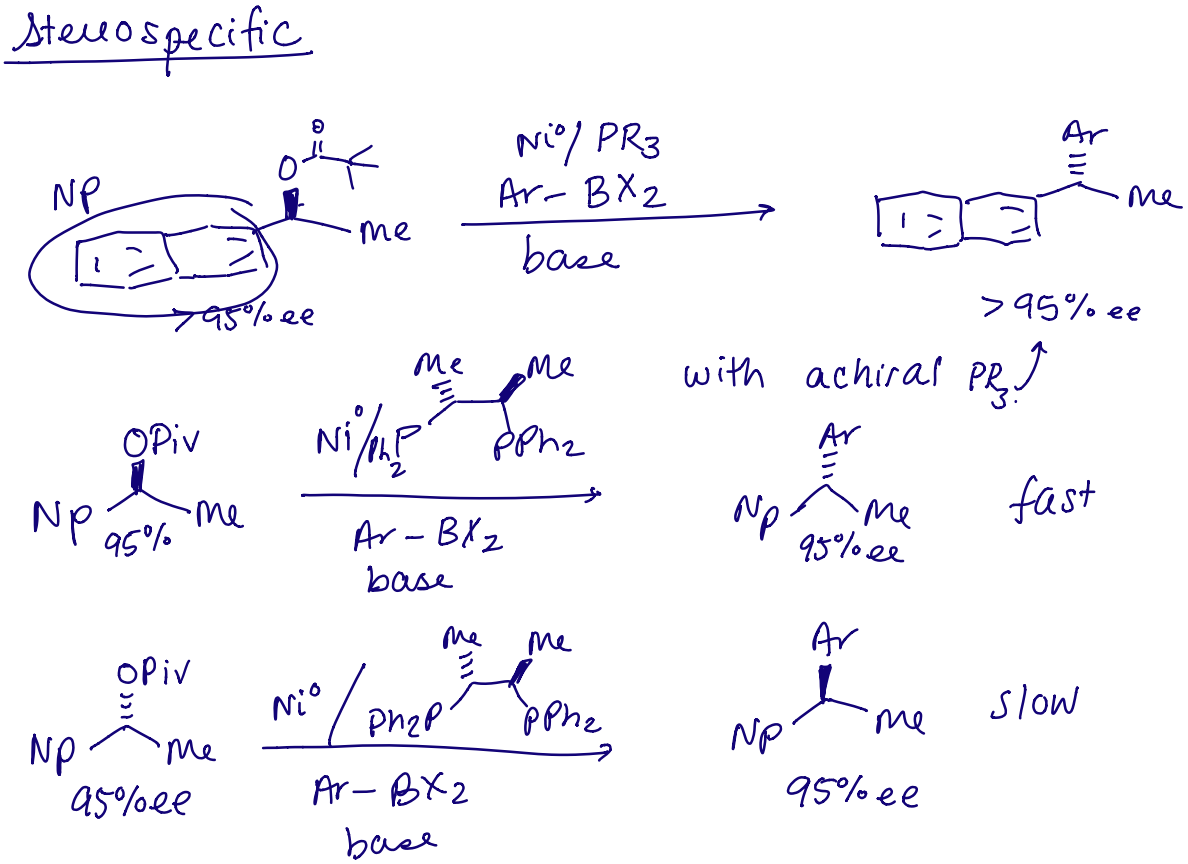
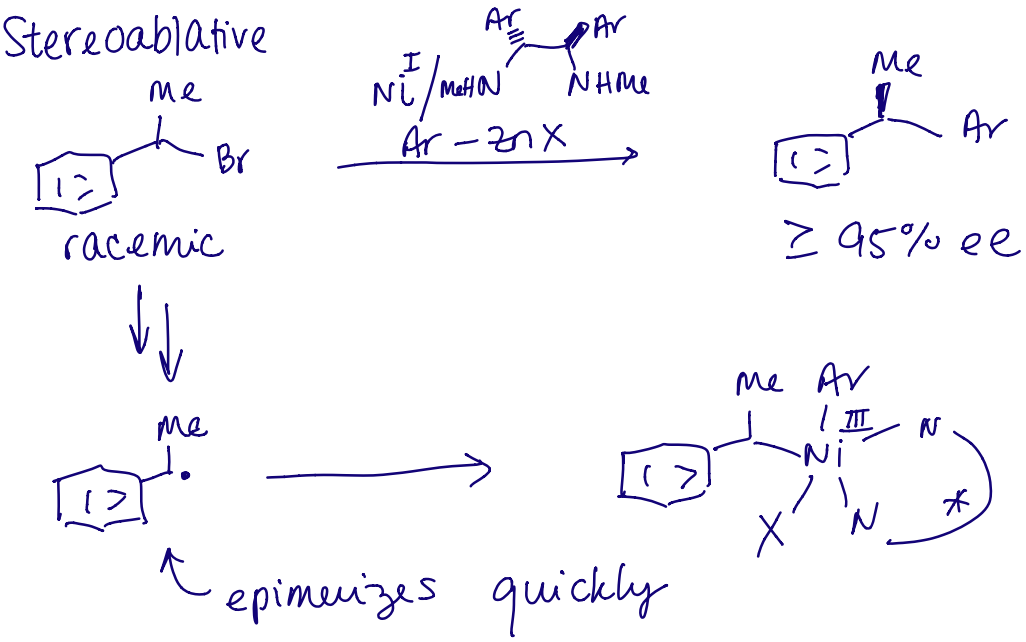
Lecture 19: Kinetics (continued)

Announcements:
- Problem Set 5 due now
- Midterm 2 on Thurs, 11/17

Today:
- Asymmetric Catalysis (continued)
- Other Mechanistic Tools
  - Linear Free Energy Relationships
  - Isotope Effects
  - Nonlinear Effects
  - Radical Clock Experiments



Stereoablative



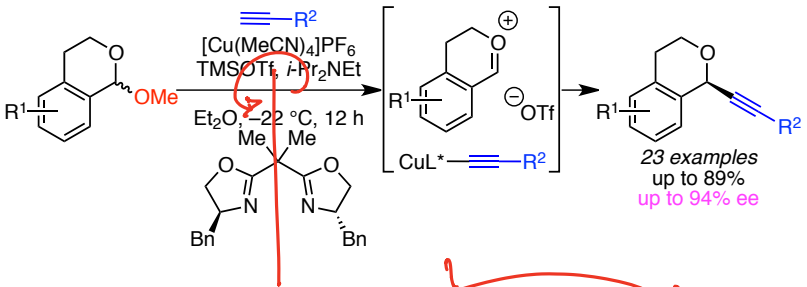
Catalyst / Ligand Design

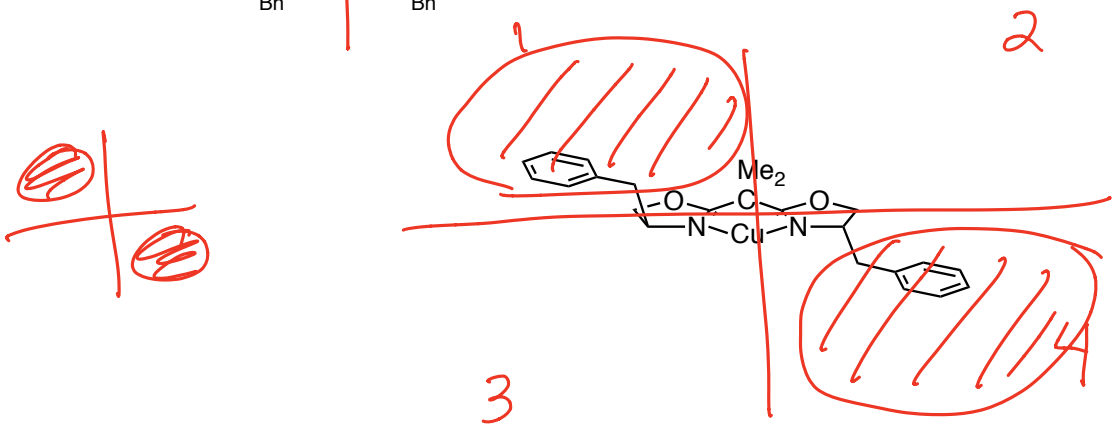
L*—M or cat*

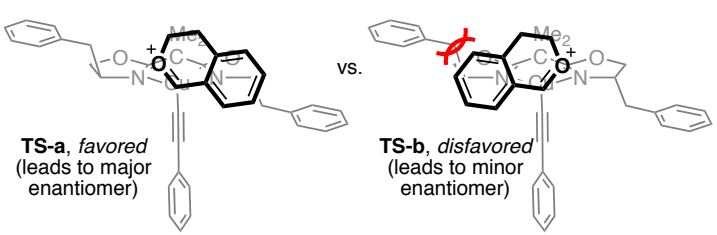
Design Principles:

1) Symmetry
   - often C2

Quadrant Formalism



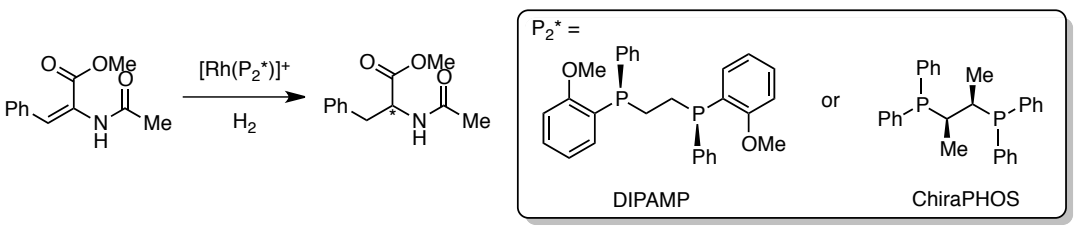




Maity, Srinivas, Watson. *JACS* 2011, 17142

2nd Design Principle: It's hard to depict TS's, so people often think about intermediates. This can be completely WRONG.

Asymmetric Hydrogenation & Curtin-Hammett Situations



Halpern, J. *Science* **1982**, *217*, 401

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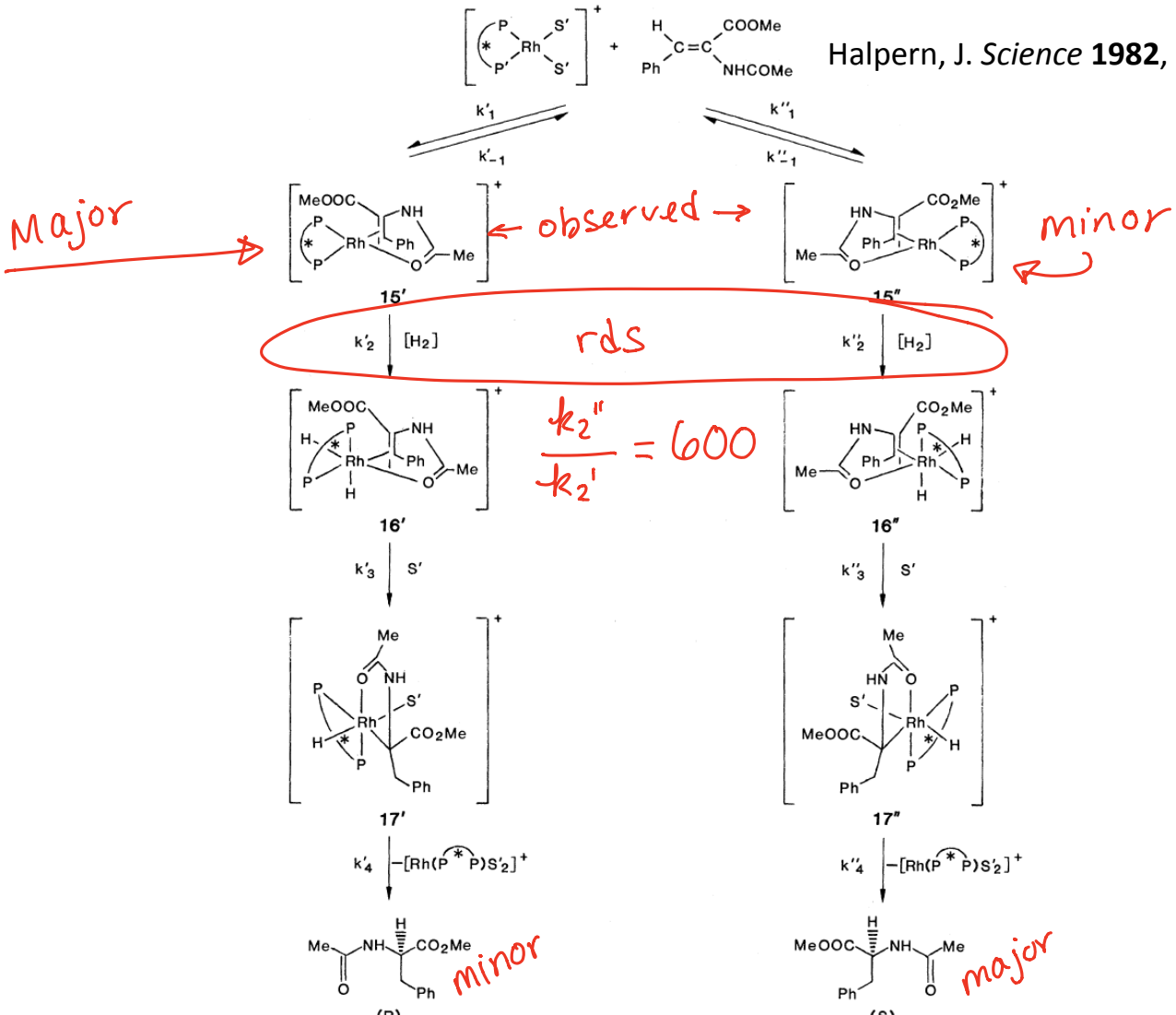
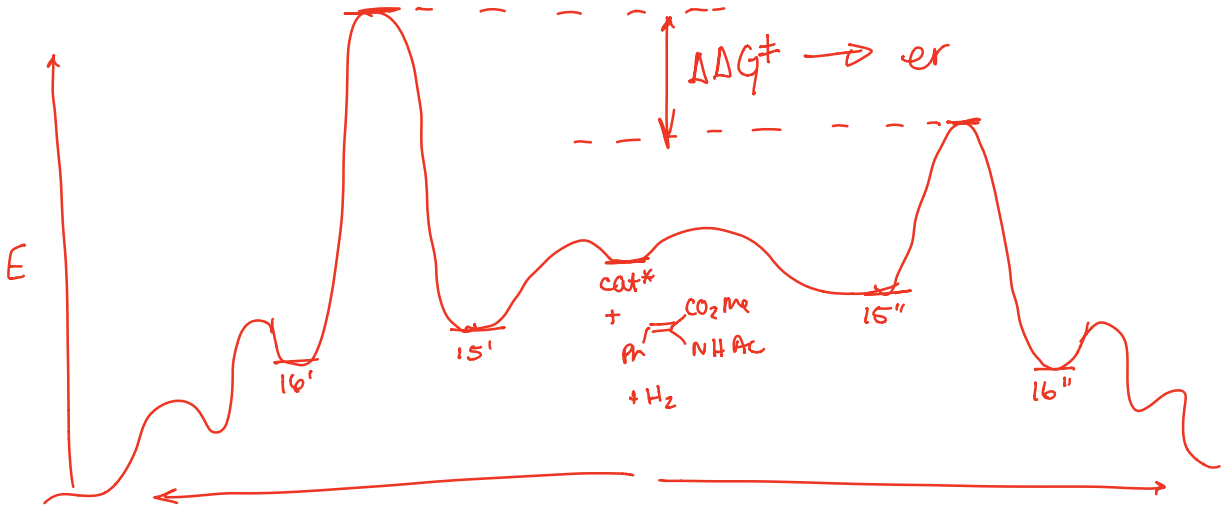
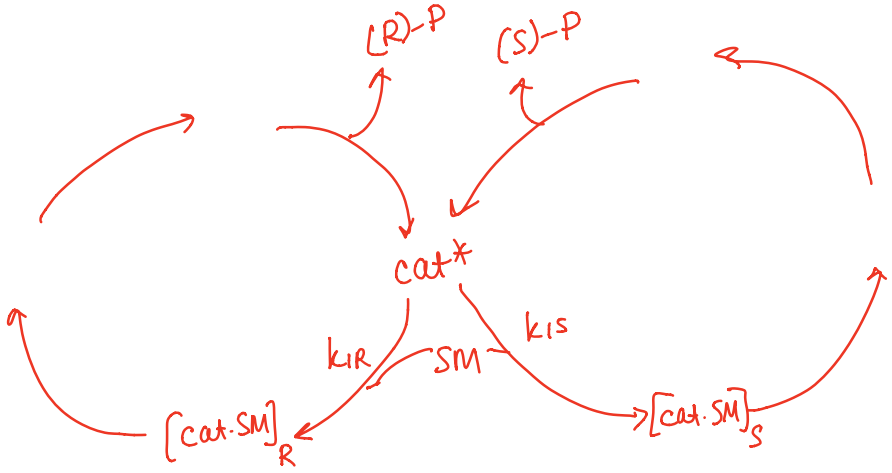




Curtin-Hammett Situation:

- Rapid equilibration of intermediates before rds/ enantiodetermining step.

Asym Catalysis : Kinetics



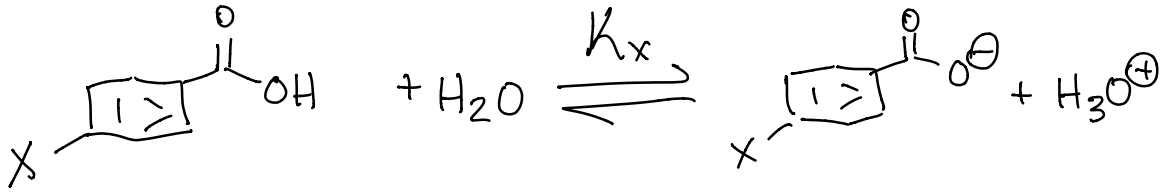
$k_{1R} \neq k_{1S}$

Other Mechanistic Tools

Linear Free Energy Relationships (LFER's)

- probes substituent effects on kinetics or thermodynamics of a reaction.

Hammett Plot



K_X vs. K_H

$$\sigma = \log \frac{K_X}{K_H} = pK_{a_H} - pK_{a_X}$$

↑ measure of substituent's ability to donate or withdraw e- density by induction

$\sigma > \emptyset \Rightarrow$ X is better at stabilizing ⊖ than H $\Rightarrow$ X = inductively EWG

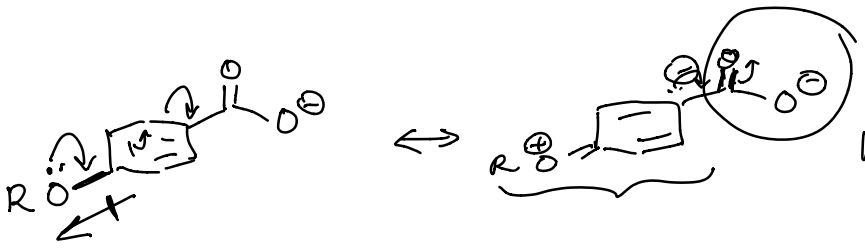
$\sigma < \emptyset \Rightarrow$ X = inductively EDG

See Table 8.2 for common substituents.

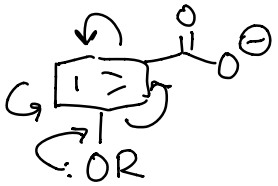
σ_p for OCH_3

Substituent's position matters:

X	σ_{para}	σ_{meta}
H_3CO-	−0.27	+0.10
HO−	−0.38	+0.13



para: resonance wins.



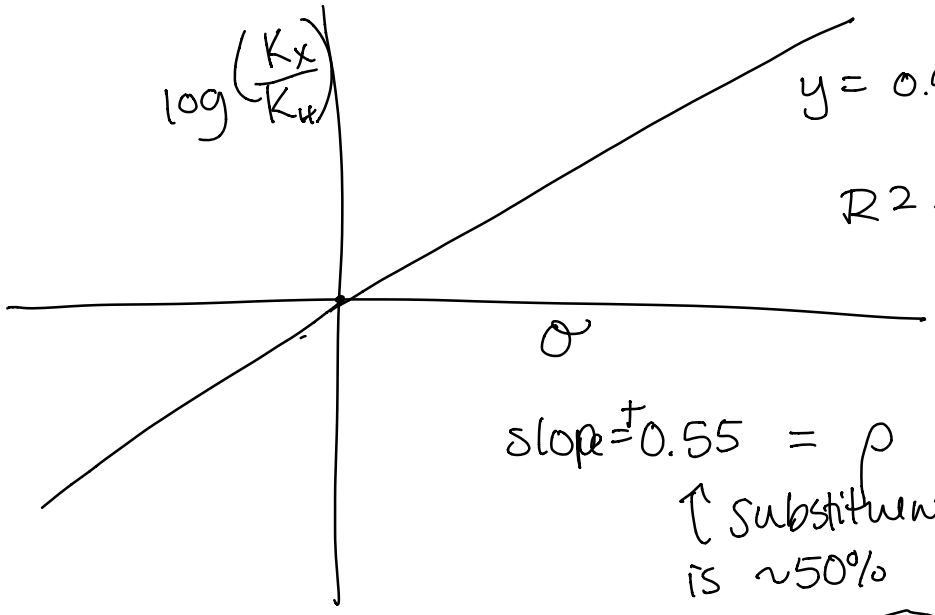
meta: purely inductive

Why is this useful?

X	σ_p	$\frac{K_{sub}}{K_{unsubstituted}}$	$\log\left(\frac{K_{sub}}{K_{unsub}}\right)$
Me	−0.14	0.87	−0.060
OMe	−0.27 ← −0.12?	0.89	−0.051
H	0	1	0
Cl	0.24	1.32	0.1257
NO_2	0.81	2.89	0.4609

J Chem Soc 1938, 357

Hammett Plot:



$y = 0.5498\,x + 0.0072$

$R^2 = 0.9967$

slope $= \pm 0.55 = \rho$

↑ substituent effect is ~50% as that of X-C$_6$H$_4$-CO$_2$H

ρ : ⊕ ⇒ Build-up of ⊖ charge in pdt.

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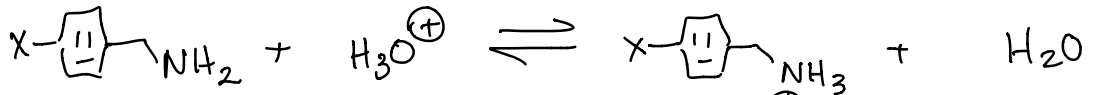
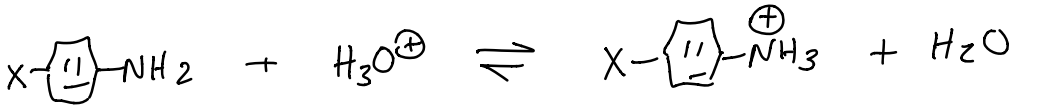
$\rho = 2.26$



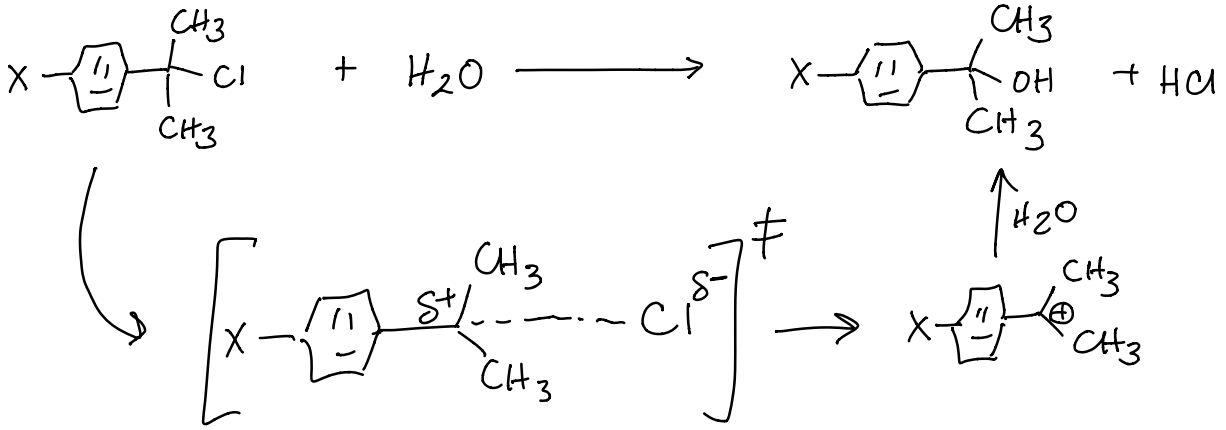
$\rho = -1.05$



$\rho = -3.19$

Also applies to TS's!

→ measure k_x/k_H. Plot σ vs. $\log\left(\frac{k_x}{k_H}\right)$



$\rho = -4.48$ ← late TS.

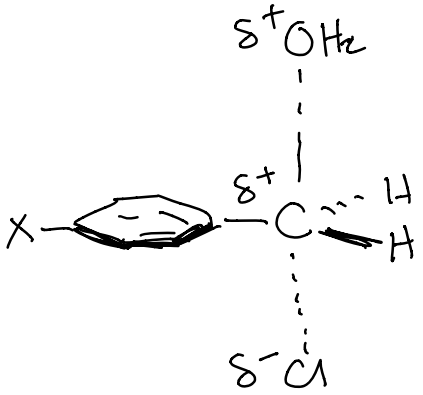
↑ Build-up ⊕ in TS

prototypical ρ for S_N1.

ex: S_N2

$\rho = -1.31$

↑ prototypical for S_N2.



Other LFER's ⟹ Steric
Charton values

Matt Sigman

material for Midterm 2 stops here.