Lecture 21: More Mechanistic Experiments

Announcements:
- Midterm 2 is not yet graded (sorry).
- Problem Set 6 due on Thurs, 12/8. Will be posted online by tomorrow.
- Please fill out online course evaluation. I'll email a link tomorrow.
- Only 3 lectures left!
    - Today: More mechanistic experiments (the last ones)
    - Tues, 12/6: Pericyclic Reactions: The Physical Organic Side
    - Thurs: 12/8: Noncovalent Interactions

Today: More Mechanistic Experiments
- Secondary Kinetic Isotope Effects
    - Singleton Experiment
- Isotopic Labelling
- Nonlinear Effects (handout)
- Radical Clock Experiments
- If we have time, we'll start on Pericyclic Reactions.

Kinetic Isotope Effects

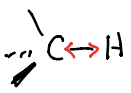
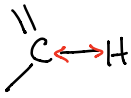
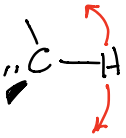
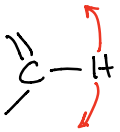
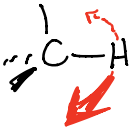
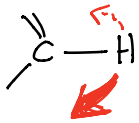
1° KIE : X–H bond breaking in (before) the rds.

Intermolecular KIE: before or during rds.

$\frac{k_H}{k_D}$: 2–7 Intramolecular KIE: see beyond rds to the product-determining step.

Secondary KIE

- due to rehybridization ⇒ change in relative ZPE's.
- See A & D, 8.1.3

	sp^3	sp^2
C–H stretch	 $\nu \sim 2900\ cm^{-1}$	 $\nu = 2800\ cm^{-1}$
Bending (up/down)	 $\nu = 1350\ cm^{-1}$	 $\nu = 1350\ cm^{-1}$
Bending (forward/backward)	 $\nu = 1350\ cm^{-1}$	 $\nu = 800\ cm^{-1}$ "Stiffer"

$sp^3 \rightarrow sp^2$ $\quad 1.4 > \frac{k_H}{k_D} > 1.0$

$sp^2 \rightarrow sp^3$ $\quad 0.7 < \frac{k_H}{k_D} < 1.0$

Inverse 2° KIE

Singleton Experiment (JACS 1995, 117, 9357)

→ use natural abundance

SM ⟶ P

↑ becomes enriched in slower-reacting isotopes. (high conversion)

↖ starts out enriched in faster-reacting isotopes (low yield)

→ Stop Rxn before complete conversion

$$\frac{R}{R_0} = (1 - F)^{(1/KIE) - 1}$$

R: isotopic enrichment in RSM

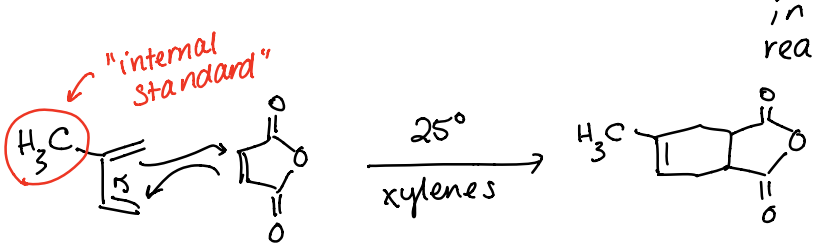
R_0: isotopic enrichment @ $t = 0$

F: fractional conversion of reactants

Towards completion of Rxn, $\frac{R}{R_0} \to \infty$

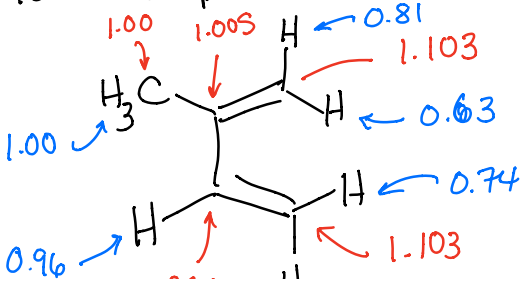
ex: KIE = 1.05. @ 99% conversion → ~25% enrichment in RSM of slower reacting isotope!

ex:



How symmetric is TS?

98.9% completion → measured relative ^2H & ^{13}C-enrichment of RSM

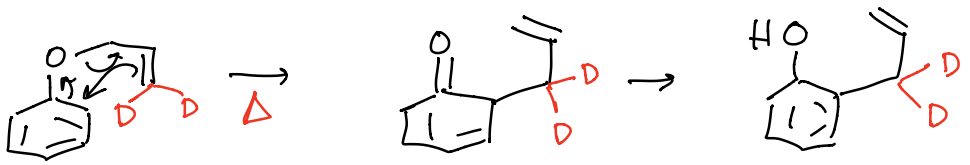


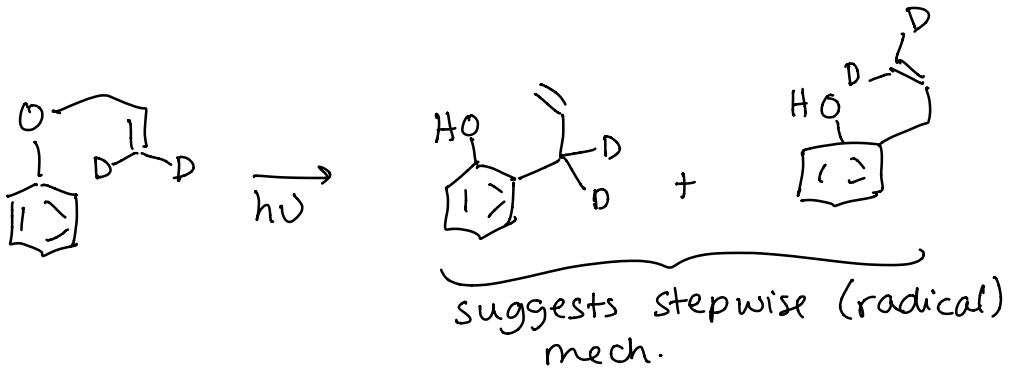
⇒ KIE's.

0.999 H ↖ 0.86

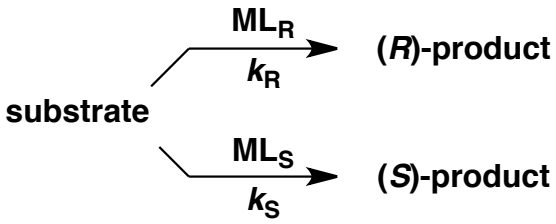
Isotopic Labelling to Probe Mechanism

ex: Claisen Rearrangement



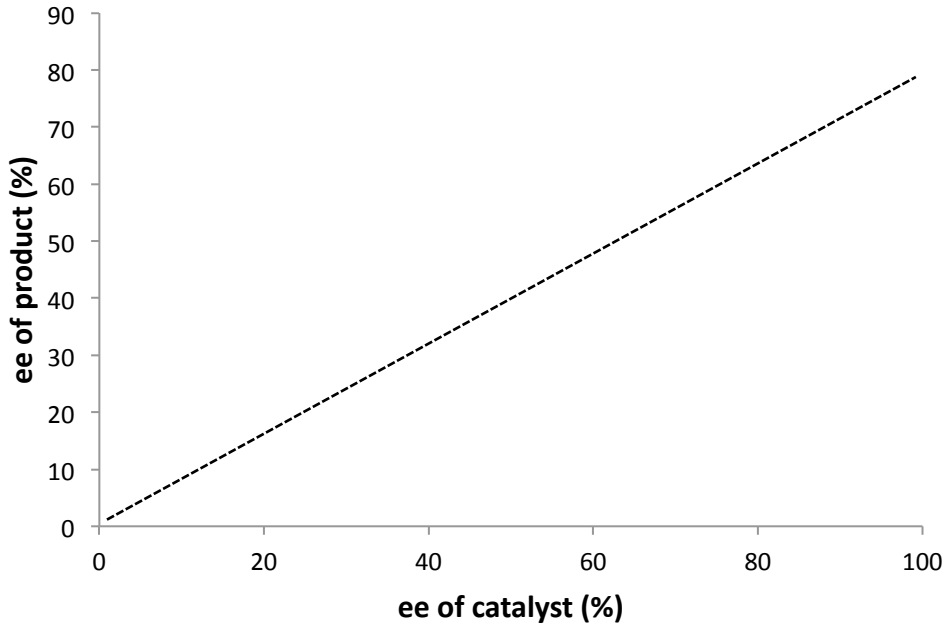


Nonlinear Effect Experiment



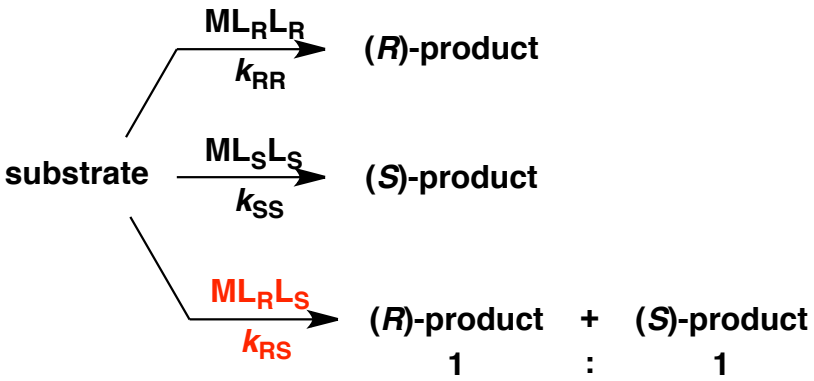
ML_R and ML_S are *enantiomers*.

$k_R = k_S$



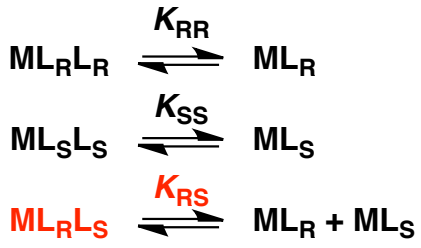
Girard, C.; Kagan, H. *Angew. Chem. Int. Ed.* **1998**, *37*, 2922.

Nonlinear Effect Experiment

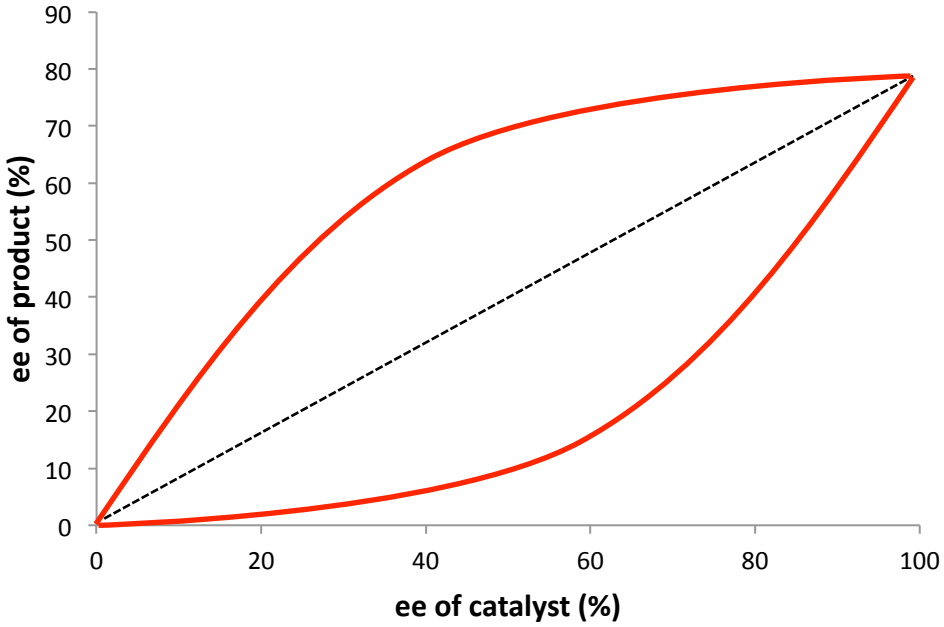


ML_RL_R and ML_SL_S are *enantiomers*, but ML_RL_S is their *diastereomer*.

$k_{RS} \neq k_{RR}$ or k_{SS}



$K_{RR} = K_{SS} \neq K_{RS}$



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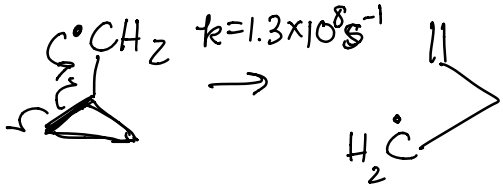
Radical Clock Experiments

Does your reaction involve radical intermediate?

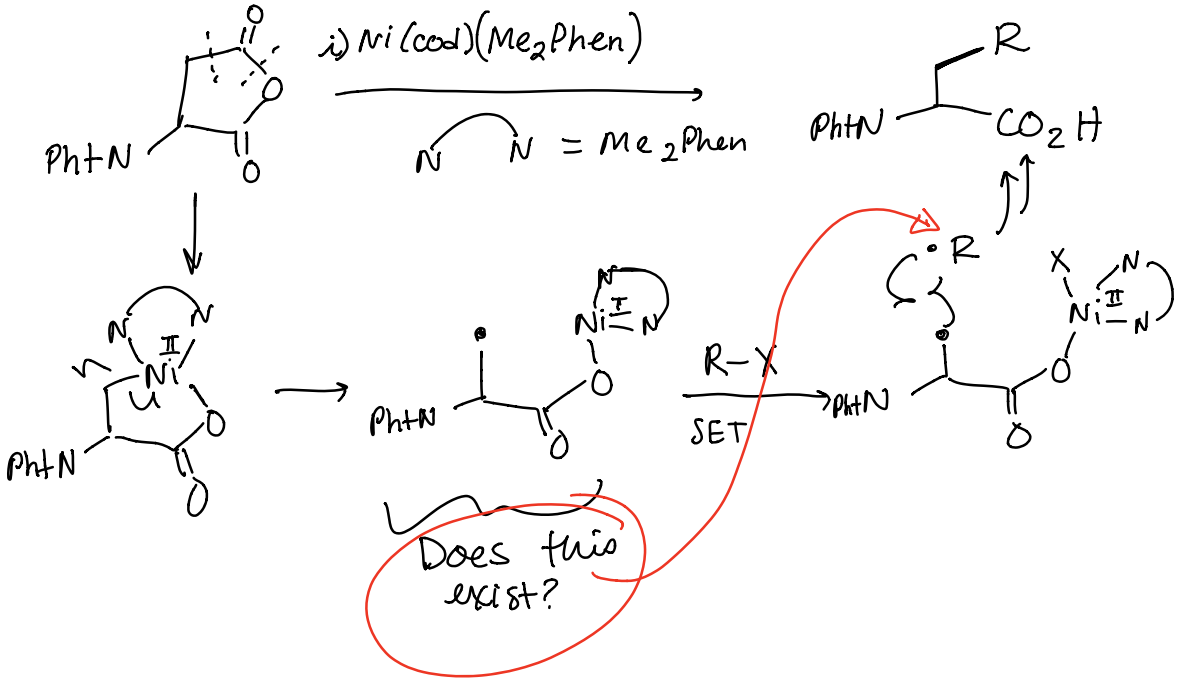
Options: ① Spin trapping → Add a reagent that will trap / quench radical.

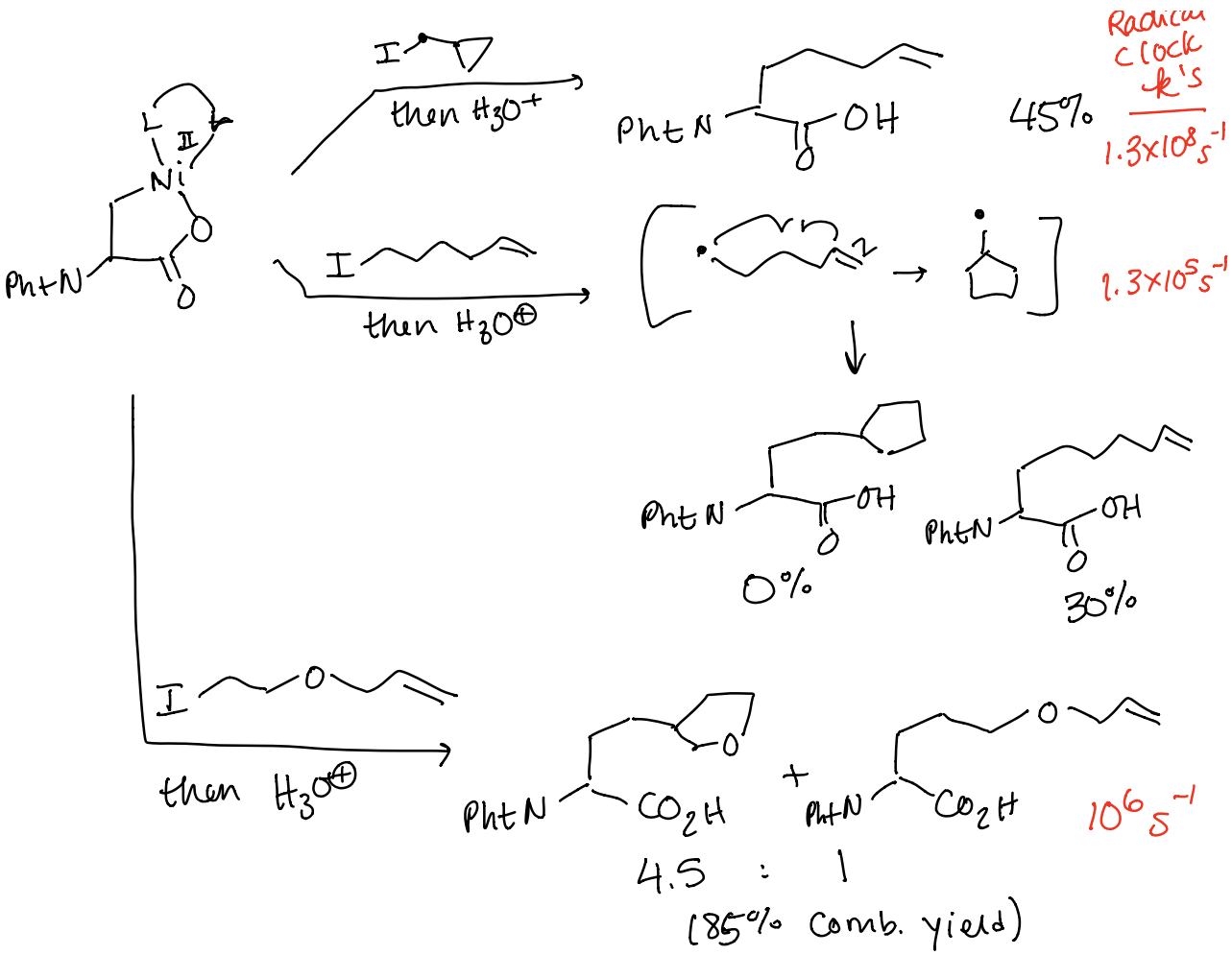
② Radical Clock (A&D, p. 479, Table 8.7)
Design your substrate to "detect" radical intermediate.

Most famous:



OM 1994, 13, 2262:





Rate for radical trapping = $2 \times 10^6\ M^{-1} s^{-1}$

Consistent w/ •R

Summary of Mech Experiments

(Just 1 option of possible steps)

1) Have a reaction
2) Propose a mechanism (≥ 1)
3) Make predictions about what you should see. → What expt differentiates mech's?
4) Collect data
   - kinetic rate law
   - substituent effects
   - KIE's
   - computational
   - etc.
5) Revise mech as necessary.
6) Run the next experiment.