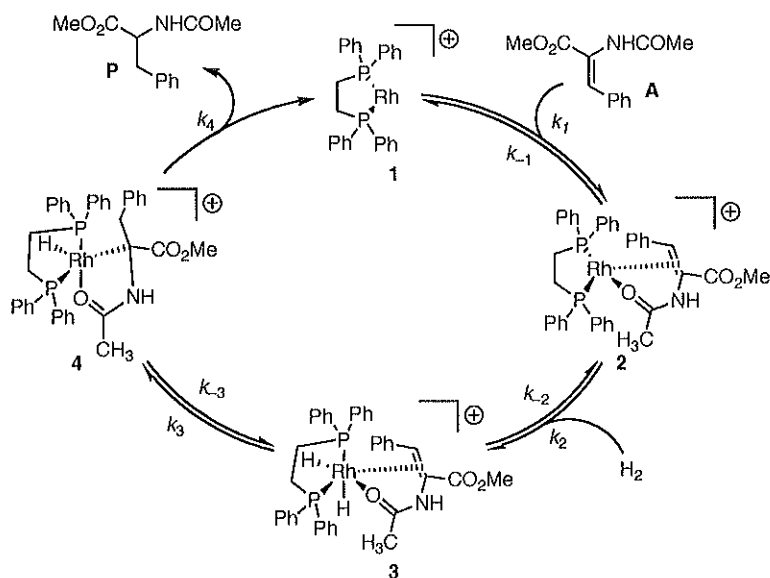
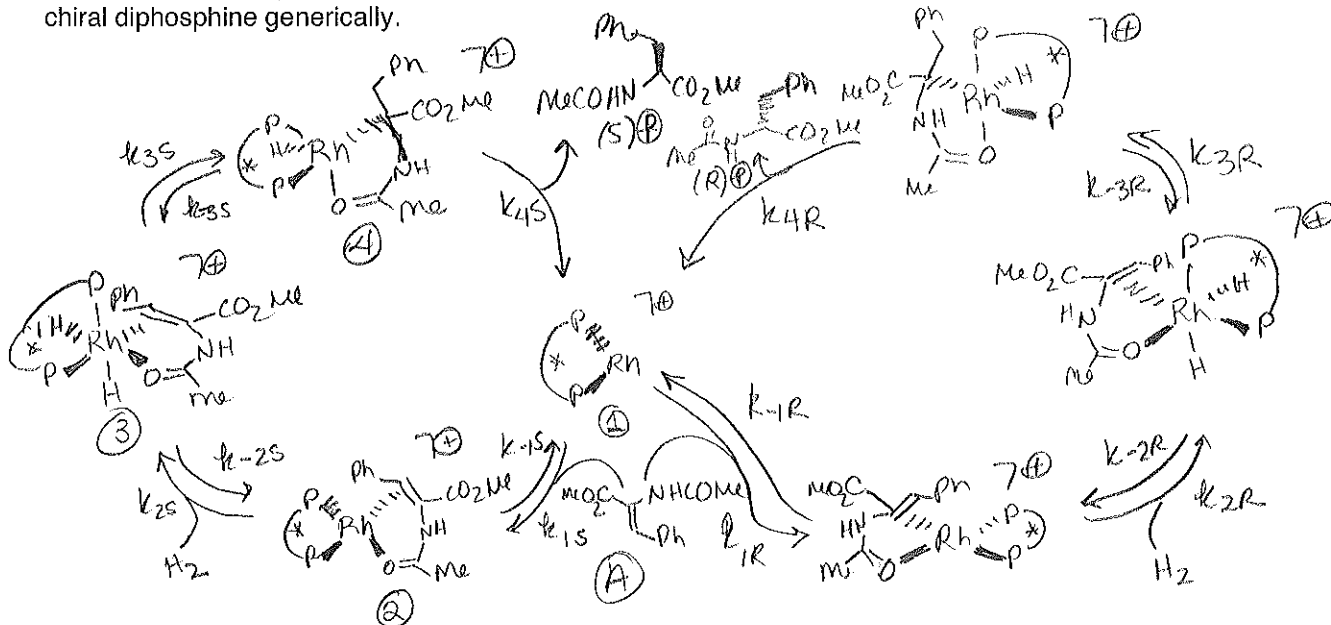


CHEM 633: Advanced Organic Chem: Physical
Problem Set 8
Due on THURS 11/12/09

1. On Problem Set 7, you considered the Rh(I)-catalyzed hydrogenation of cinnamate **A**. The following catalytic cycle has been proposed.



(a) The asymmetric hydrogenation of **A** using a chiral diphosphine ligand has an analogous mechanism. Draw a set of catalytic cycles that accounts for the formation of both enantiomers. You may depict the chiral diphosphine generically.



(b) Assuming that the second step (2 → 3) is rate-limiting and all subsequent steps to regenerate 1 are rapid and irreversible, write down a rate law for the total reaction rate using the steady-state approximation. (Hint: Use your "1+" rate law for the non-asymmetric reaction as a basis; it is not necessary to provide a new derivation for this rate law.)

$$\text{Now } [\text{RN}]_{\text{tot}} = [1] + [2-S] + [2-R]$$

$$\text{rate}_R = \frac{k_{1R} k_{2R} [\text{A}] [\text{RN}]_{\text{tot}} [\text{H}_2]}{(k_{-1R} + k_{2R} [\text{H}_2]) \left(1 + \frac{k_{1R} [\text{A}]}{k_{-1R} + k_{2R} [\text{H}_2]} + \frac{k_{1S} [\text{A}]}{k_{-1S} + k_{2S} [\text{H}_2]} \right)}$$

$$\text{rate}_S = \frac{k_{1S} k_{2S} [\text{A}] [\text{RN}]_{\text{tot}} [\text{H}_2]}{(k_{-1S} + k_{2S} [\text{H}_2]) \left(1 + \frac{k_{1R} [\text{A}]}{k_{-1R} + k_{2R} [\text{H}_2]} + \frac{k_{1S} [\text{A}]}{k_{-1S} + k_{2S} [\text{H}_2]} \right)}$$

$$\text{overall rate} = \text{rate}_R + \text{rate}_S$$

$$\text{rate} = \frac{[\text{A}] [\text{RN}]_{\text{tot}} [\text{H}_2]}{\left(1 + \frac{k_{1R} [\text{A}]}{k_{-1R} + k_{2R} [\text{H}_2]} + \frac{k_{1S} [\text{A}]}{k_{-1S} + k_{2S} [\text{H}_2]} \right)} \left(\frac{k_{1R} k_{2R}}{k_{-1R} + k_{2R} [\text{H}_2]} + \frac{k_{1S} k_{2S}}{k_{-1S} + k_{2S} [\text{H}_2]} \right)$$

(c) Show that the relative rates of formation of the two enantiomers depends only on $[H_2]$.

$$\frac{\text{rate}_R}{\text{rate}_S} = \frac{\frac{k_{1R} k_{2R} [A] [Rh]_{\text{tot}} [H_2]}{(k_{-1R} + k_{2R} [H_2])}}{1 + \frac{k_{1R} [A]}{k_{-1R} + k_{2R} [H_2]} + \frac{k_{1S} [A]}{k_{-1S} + k_{2S} [H_2]}}$$

$$\frac{k_{1S} k_{2S} [A] [Rh]_{\text{tot}} [H_2]}{(k_{-1S} + k_{2S} [H_2])}$$

$$1 + \frac{k_{1R} [A]}{k_{-1R} + k_{2R} [H_2]} + \frac{k_{1S} [A]}{k_{-1S} + k_{2S} [H_2]}$$

$$\frac{\text{rate}_R}{\text{rate}_S} = \frac{k_{1R} k_{2R}}{k_{1S} k_{2S}} \left(\frac{k_{-1S} + k_{2S} [H_2]}{k_{-1R} + k_{2R} [H_2]} \right)$$

(No dependence on $[A]$ or $[Rh]_{\text{tot}}$.)

(d) Use the boxed experimental data to determine the enantiomeric ratio expected from a reaction run at infinitely low $[H_2]$.

$$k_{-1S} \gg k_{2S}[H_2]$$

$$k_{-1R} \gg k_{2R}[H_2]$$

$$er = \frac{\text{rate}_R}{\text{rate}_S} = \frac{k_{1R} k_{2R}}{k_{1S} k_{2S}} \left(\frac{k_{-1S}}{k_{-1R}} \right)$$

$$er = \frac{(1.06 \times 10^4 \text{ M}^{-1}\text{s}^{-1})(630 \text{ M}^{-1}\text{s}^{-1})(0.15 \text{ s}^{-1})}{(5.3 \times 10^3 \text{ M}^{-1}\text{s}^{-1})(1.1 \text{ M}^{-1}\text{s}^{-1})(3.2 \text{ s}^{-1})}$$

5pts

$$er = 53.7$$

For R-enantiomer pathway:

$$k_1 = 1.06 \times 10^4 \text{ M}^{-1}\text{s}^{-1}$$

$$k_{-1} = 3.2 \text{ s}^{-1}$$

$$k_2 = 630 \text{ M}^{-1}\text{s}^{-1}$$

For S-enantiomer pathway:

$$k_1 = 5.3 \times 10^3 \text{ M}^{-1}\text{s}^{-1}$$

$$k_{-1} = 0.15 \text{ s}^{-1}$$

$$k_2 = 1.1 \text{ M}^{-1}\text{s}^{-1}$$

(e) Use the experimental data to determine the enantiomeric ratio expected from a reaction run at infinitely high $[H_2]$.

$$k_{-1S} \ll k_{2S}[H_2]$$

$$k_{-1R} \ll k_{2R}[H_2]$$

$$\frac{\text{rate}_R}{\text{rate}_S} = \frac{k_{1R} k_{2R}}{k_{1S} k_{2S}} \left(\frac{k_{2S}[H_2]}{k_{2R}[H_2]} \right)$$

$$er = \frac{(1.06 \times 10^4 \text{ M}^{-1}\text{s}^{-1})(630 \text{ M}^{-1}\text{s}^{-1})(1.1 \text{ M}^{-1}\text{s}^{-1})}{(5.3 \times 10^3 \text{ M}^{-1}\text{s}^{-1})(1.1 \text{ M}^{-1}\text{s}^{-1})(630 \text{ M}^{-1}\text{s}^{-1})}$$

5pts

$$er = 2$$

(f) Explain why it is necessary to use the steady-state approximation (rather than the pre-equilibrium approximation) to account for the kinetic profile of this reaction.

Pre-equilibrium neglects $k_2[H_2]$ term in denominator.

Relative rates are too close.

of step 1 (k_1 & k_{-1}) and step 2 (k_2)

2. In the recent literature, please find an example of asymmetric catalysis.

(a) Clearly draw the model the authors propose (or that you propose) to explain the observed enantioselectivity.

(b) Please label the 3 (or more) interactions that lead to different energies for the diastereotopic transition structures.

(c) Attach the first page of the article to your problem set.

You & your classmates chose:

JOC 2009, 74, 8403

JACS 2009, 131, 15608

JACS 2005, 127, 17012

JACS 2005, 127, 6964

Luo, Cheng, et al. "Asym Direct Aldol Rxns of Acetoacetals Catalyzed by a Simple Chiral Primary Amine" JOC 2009, ASAP.

JACS 2003, 125, 2208

JOC 2009, 74, 8392.

JACS 2009, 131, 14231

JACS 2009, 131, 7230

JACS 2009, 131, 10364

Org Lett 2007, 9, 3933

JACS 2008, 130, 2956 (Asym Autocatalysis)

JACS 2009, 131, 14990

ACIE 2009, 48, 8827

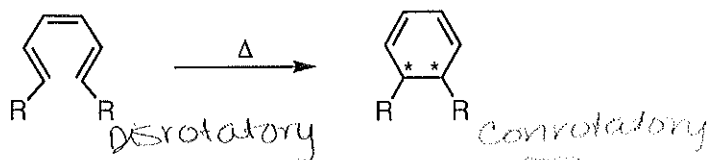
MacMillan et al. "Enantioselective α -Arylation of Aldehydes via Organo-SOMO Catalysis..." JACS 2009, ASAP.

Seidel et al. "Merging Nucleophilic \ddot{E} Hydrogen Bonding Catalysis..." JACS 2009, ASAP.

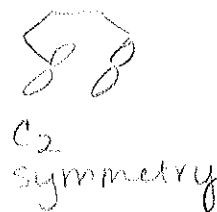
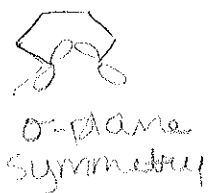
Org Lett 2009, 11, 4592.

JACS 2009, 131, 15118.

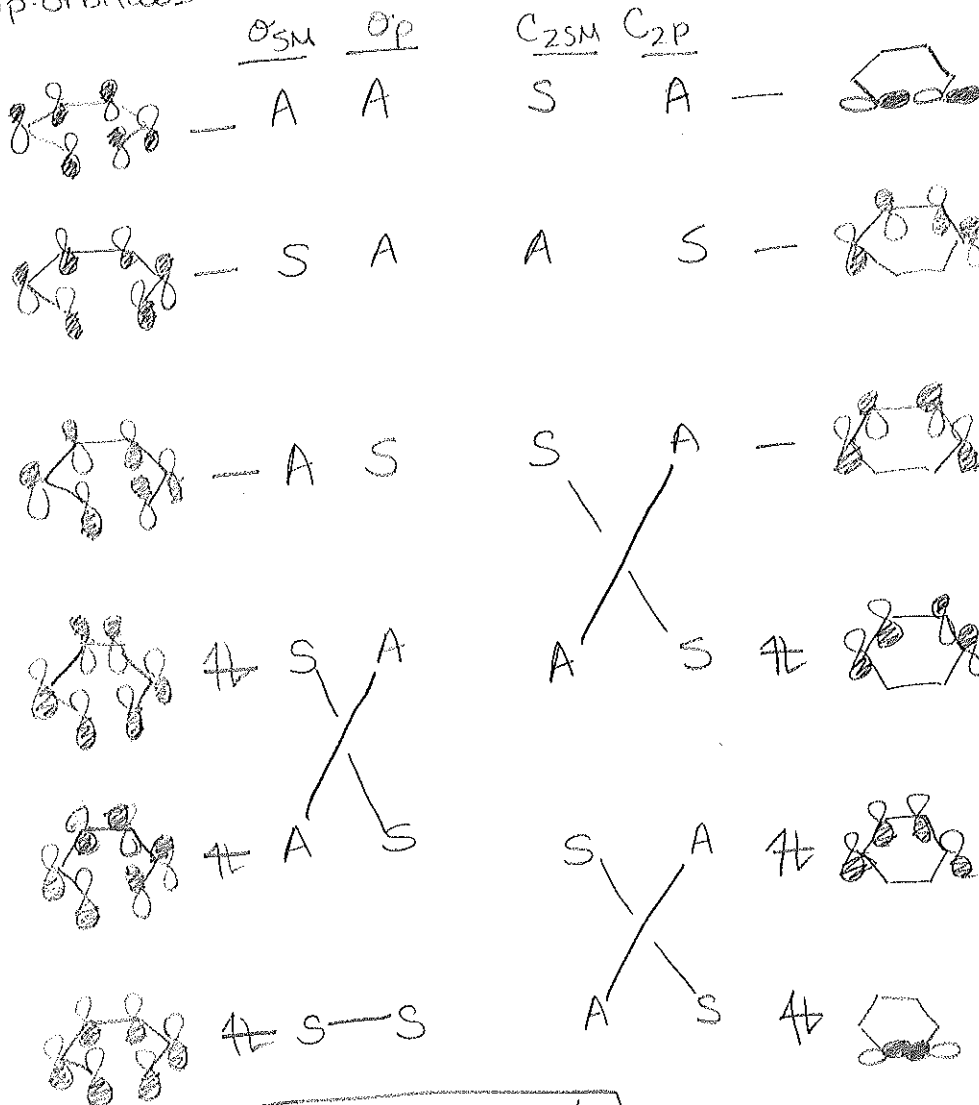
3. Please draw a Woodward-Hoffmann molecular orbital correlation diagram for the following reaction and use it to predict the stereochemistry of the product (stereocenters are starred).



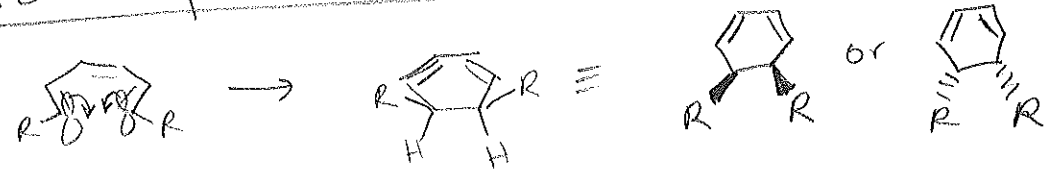
Transition States:



6p-orbitals → 6MO's

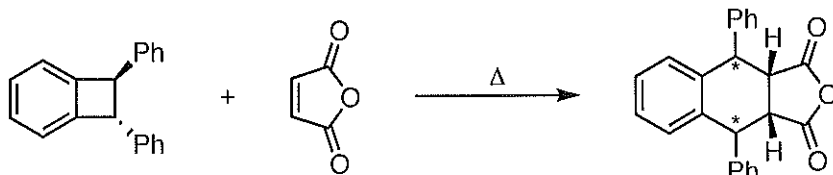


Disrotatory Allowed



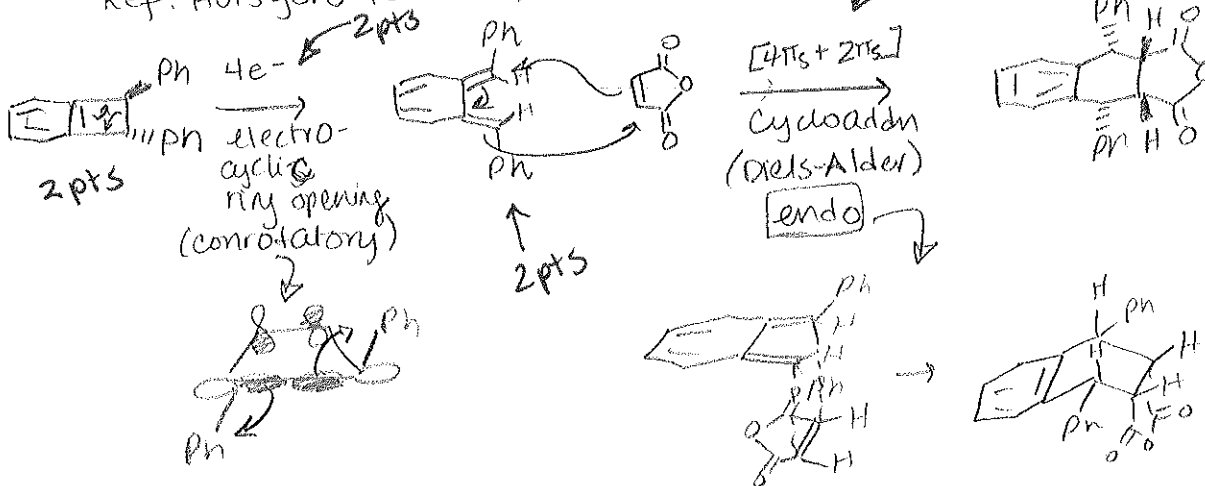
10 pts

4. Please propose an arrow-pushing mechanism for the following transformation. Name and classify each pericyclic reaction you propose and predict the stereochemical outcome.

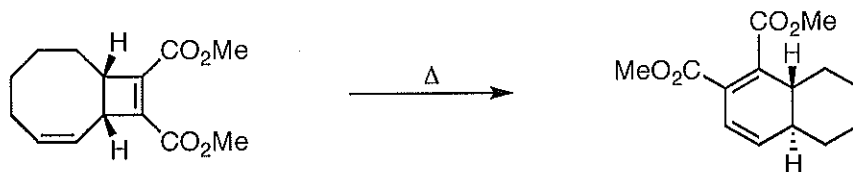


stereochem;
2pts

Ref: Huisgen TL 1964, 3381.



5. Please suggest of mechanism for the following transformation. Your mechanism should be consistent with the observed stereochemistry of the product. Please name and classify each pericyclic reaction of your mechanism.



Ref: Bloomfield TL 1969, 3719.

