Chemistry 5011/8011 Friday, November 12, 2004

Midterm Exam 2

Please do not open or sign this packet until you are instructed to do so.

Please write all of your answers for this exam in this exam packet. Although you may use as many blue books for scratch work as you would like, the blue books will not be collected at the end of the exam or graded. Answer each question in the space provided if you can, but feel free to continue your answer on the back of the page if you need more room. (Please write a note by your answer pointing us to the continuation if you do this.) You will be given 50 minutes total to finish the exam.

This exam contains two problems, which are split into parts. *Do not get stuck* on one part and then assume that you will be unable to answer the rest of the question—move on. In addition, partial credit will be given for incorrect but plausible or consistent answers, so *guess* on problems you cannot answer perfectly.

At the end of the 50-minute exam period you will be asked to return your exam to the proctor. (You may, of course, also turn the packet in earlier if you choose.) This exam is *open-resource*—you may use any books, notes, calculator, etc. you have brought with you to the exam. However, you are not allowed to communicate with anyone during the exam, or to bring any materials in or out of the room while you are taking the exam. You are also not allowed to use any devices that could be used to communicate with anyone (laptop computers, cellphones, etc.). Please do not take any part of the exam packet with you when you are done; everything will be returned to you after the exams are graded.

This packet should contain 10 pages, including this one. Please check to make sure that your packet contains 10 pages before beginning your exam.

Name: _____

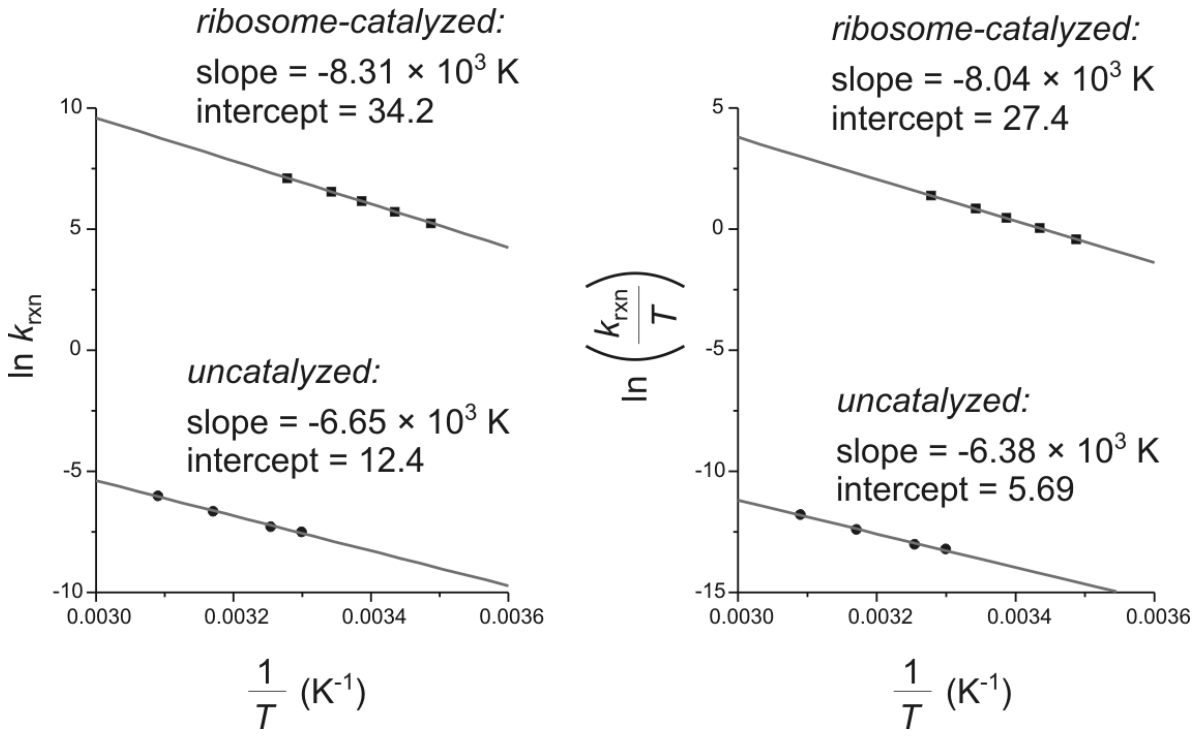
Signature: _____

Helpful constants to know for this exam:

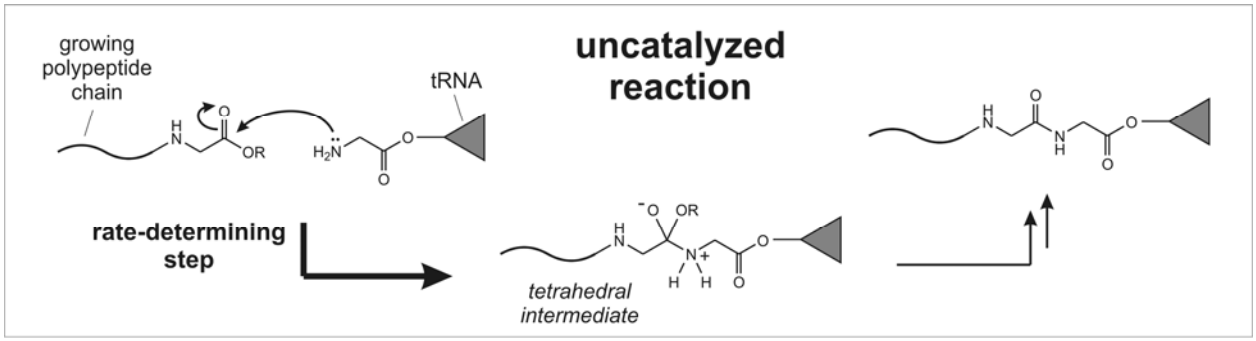
Boltzmann's constant:	$k = 2.94 \times 10^{-24}$ cal K^{-1}	$= 1.38 \times 10^{-23}$ J K^{-1}
Gas constant:	$R = 1.99$ cal K^{-1} mol^{-1}	$= 8.314$ J K^{-1} mol^{-1}
Planck's constant:	$h = 1.58 \times 10^{-34}$ cal sec	$= 6.626 \times 10^{-34}$ J sec
	$e = 2.718$	

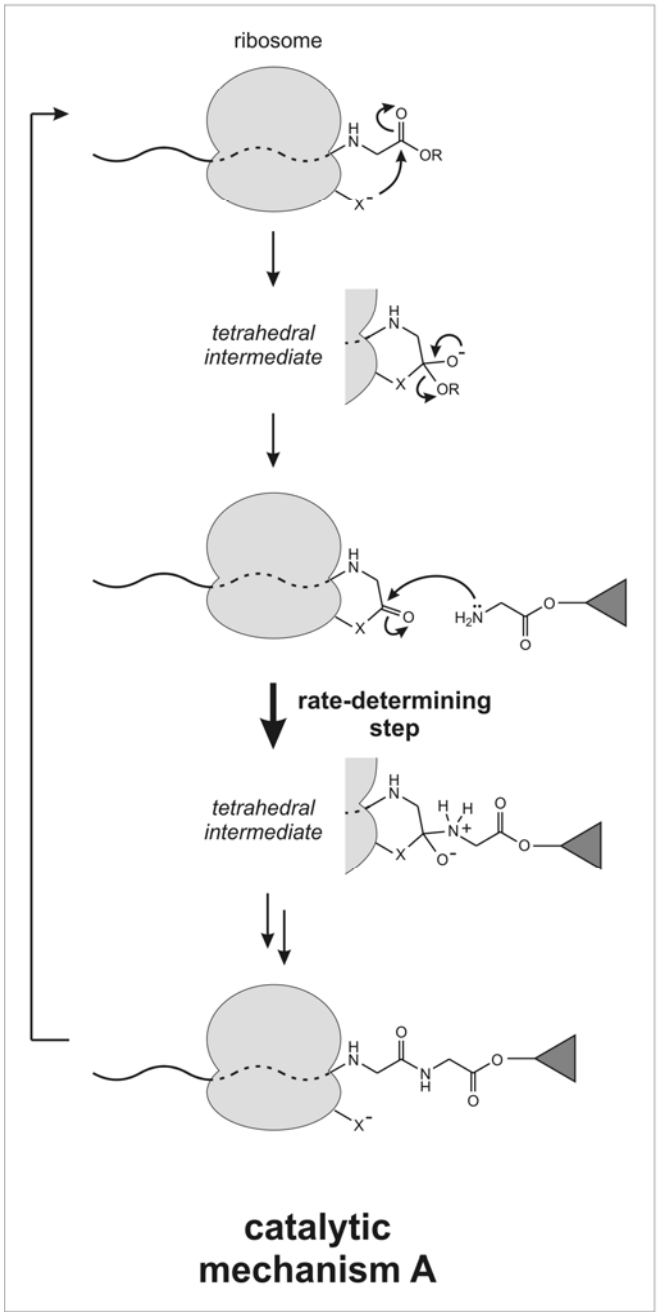
1. The ribosome is a biomolecular complex that is responsible for synthesizing virtually all of the proteins (polypeptides) in your body from amino acid building blocks. Ribosomes act by catalyzing the reaction between an ester at the end of the growing peptide chain and the amine of the next amino acid to be added to the chain. The result is a new amide bond. (See figure on next page.) While the ribosome increases the reaction rate between an ester and an amine by roughly eight orders of magnitude, esters and amines actually react spontaneously, even in the absence of catalyst. As a result, researchers have wondered whether the ribosome catalyst plays a chemical role in activating the formation of the amide bond, or whether the ribosome merely brings the two reactants together so that they can react normally. These two catalyst mechanisms are shown on the next page as "A" and "B", respectively.

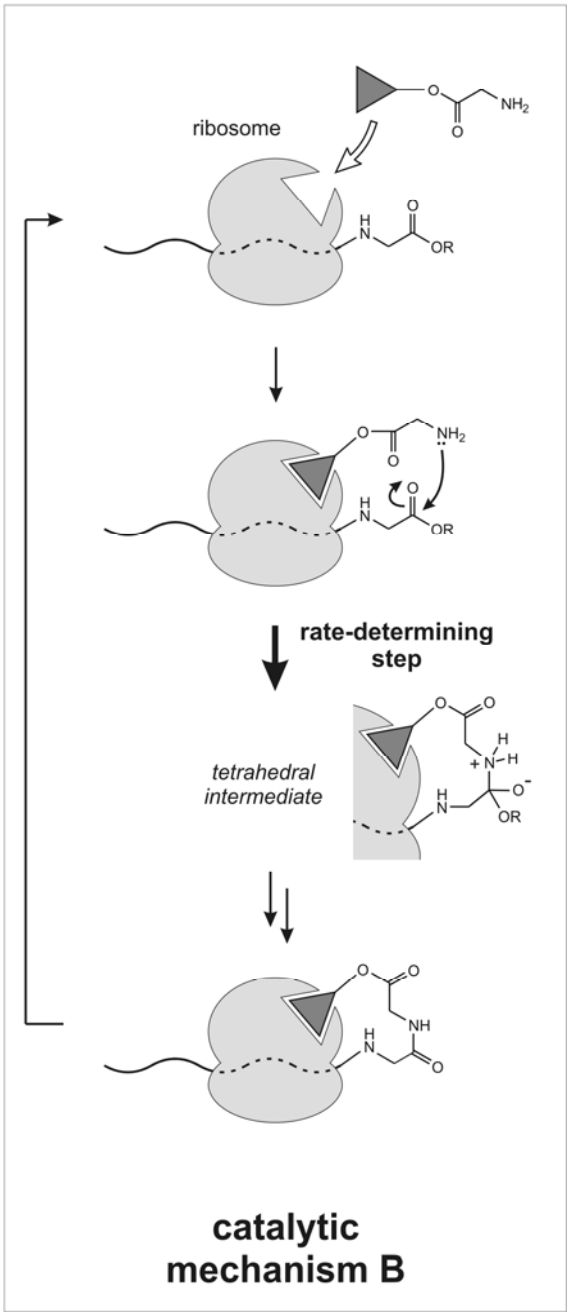
Sievers et al.[1] recently evaluated the $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for amide formation, both in the absence and presence of ribosome, in an effort to determine whether mechanism A or B more accurately describes ribosome catalysis. They did this by measuring second-order rate constants k_{rxn} (M^{-1}•sec^{-1}) for the uncatalyzed and ribosome-catalyzed reactions with varying temperature.[2] This data that they used to do this is graphed two different ways below. (*Hint: You will only need one of these graphs to answer this problem.*) Linear fits to this data are also given for each graph.



[1] Sievers, A.; Beringer, M.; Rodnina, M. V.; Wolfenden, R. *Proc. Natl. Acad. Sci. USA*, **2004**, *101*, 7897-7901.
[2] In the catalyzed case, Sievers technically measured k_{cat}/K_m (M^{-1}•sec^{-1}).This is comparable to k_{rxn} for the uncatalyzed case.


growing
polypeptide
chain
tRNA
uncatalyzed
reaction
rate-determining
step
tetrahedral
intermediate


ribosome
tetrahedral
intermediate
rate-determining
step
tetrahedral
intermediate
catalytic
mechanism A


ribosome
rate-determining
step
tetrahedral
intermediate
catalytic
mechanism B

a. (18 pts) Based on the proposed mechanisms alone (and not on Sievers' experimental data), **compare the $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ that you would expect for the uncatalyzed reaction and the reactions catalyzed by mechanisms A and B.** Which would you expect to be greater than, less than or about equal to which?

<, >, or ≈

$\Delta H^{\ddagger}$(uncatalyzed)		$\Delta H^{\ddagger}$(mechanism A)
$\Delta H^{\ddagger}$(uncatalyzed)		$\Delta H^{\ddagger}$(mechanism B)
$\Delta H^{\ddagger}$(mechanism A)		$\Delta H^{\ddagger}$(mechanism B)
$\Delta S^{\ddagger}$(uncatalyzed)		$\Delta S^{\ddagger}$(mechanism A)
$\Delta S^{\ddagger}$(uncatalyzed)		$\Delta S^{\ddagger}$(mechanism B)
$\Delta S^{\ddagger}$(mechanism A)		$\Delta S^{\ddagger}$(mechanism B)

b. (12 pts) **Calculate experimental activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for both the uncatalyzed and catalyzed reactions**, using the data on page 2. Include units in your answer. (There is space for your work on the next page.)

$\Delta H^{\ddagger}$(uncatalyzed)	$\Delta H^{\ddagger}$(ribosome-catalyzed)
$\Delta S^{\ddagger}$(uncatalyzed)	$\Delta S^{\ddagger}$(ribosome-catalyzed)

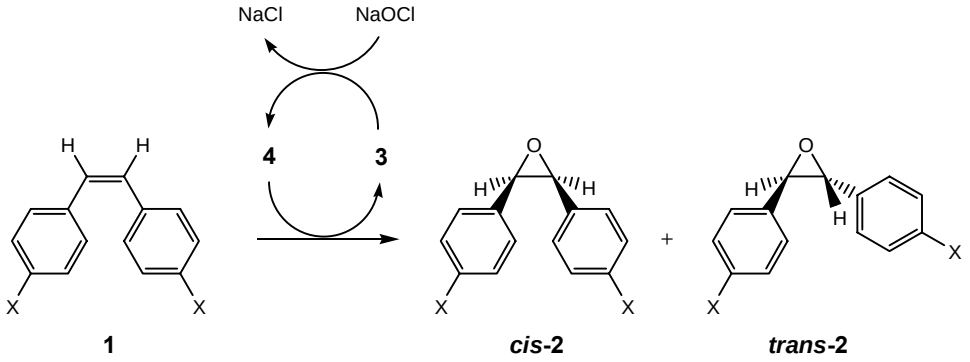
(*scratch space*)

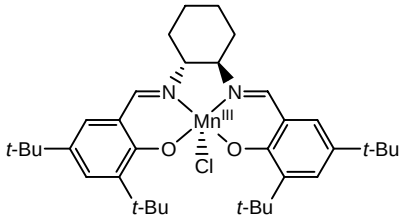
c. (15 pts) **Which catalytic mechanism (A or B) is most consistent with your calculated $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values? Explain your choice** in terms of the characteristics of each mechanism.

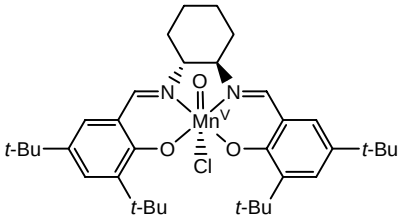
Which mechanism?

Why?

2. Certain organometallic manganese(salen) complexes can catalyze the epoxidation of olefins, using aqueous NaOCl (household bleach) as the stoichiometric oxidizer. The catalytic species in this case is a Mn(V)-oxo species that transfers an oxygen atom to the olefin. While this catalyst normally retains the stereochemistry of the olefin in the product epoxide, epoxidation of sterically strained *cis*-olefins can yield some *trans*-epoxide products. For example, substituted *cis*-stilbenes **1** are transformed into a mixture of *cis*- and *trans*-diphenylepoxides **2** by bleach and Mn(salen) complex **3**.



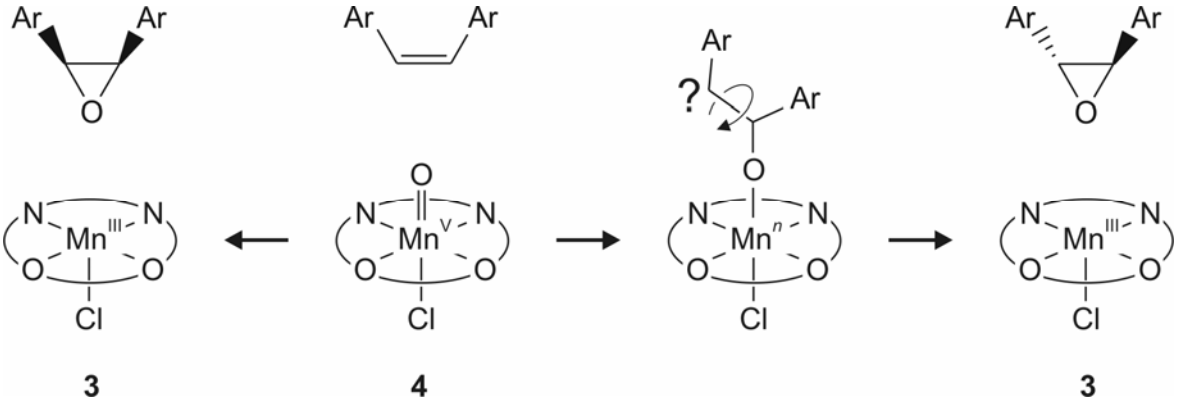




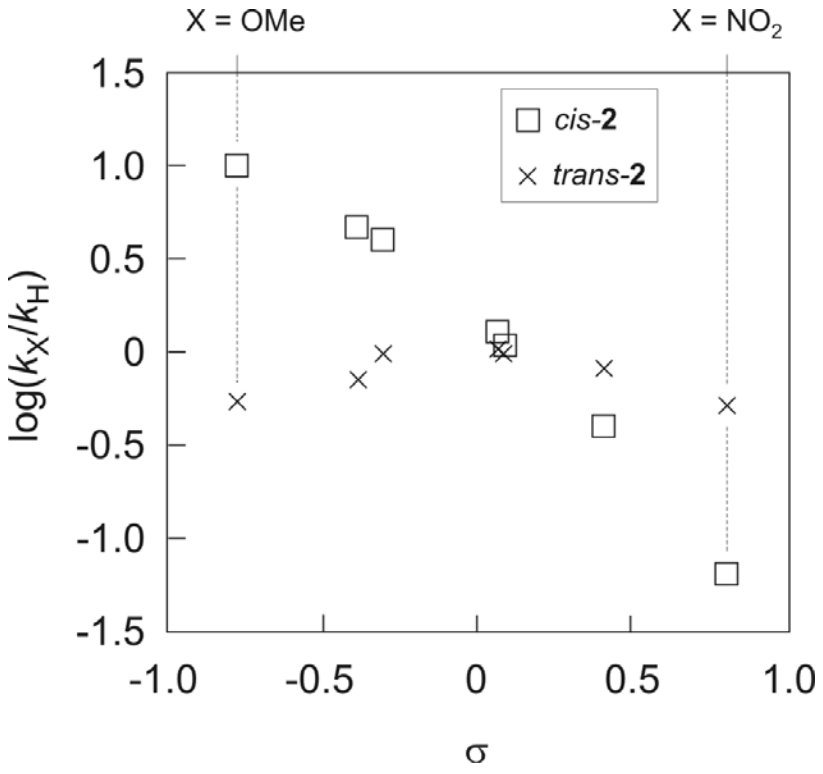
X	ratio of *cis*-2:*trans*-2
NO_2	4:96
H	25:75
OMe	86:14

As shown above, the ratio of *cis*- to *trans*-product depends upon the electronic character of the stilbene substrate.

Researchers have proposed that *cis*-**2** and *trans*-**2** are actually formed by two different mechanisms: *cis*-**2** by concerted transfer of the oxygen atom from Mn(V)-oxo to stilbene, and *trans*-**2** by stepwise addition of the Mn(V)-oxo complex to the alkene followed by loss of **3**.



In this diagram, the question mark could represent an anion, cation, or radical, depending on the redox character of the reaction. To test this mechanism, Linde et al.[3] have constructed a linear free-energy relationship plot in which the rates of formation of *cis*- and *trans*-**2** were independently measured in the same reaction mixtures for different substituents X. In principle, if different mechanisms were responsible for generating *cis*- and *trans*-products, the rates should show different substituent dependencies (and thus different ρ values). The data is shown below.



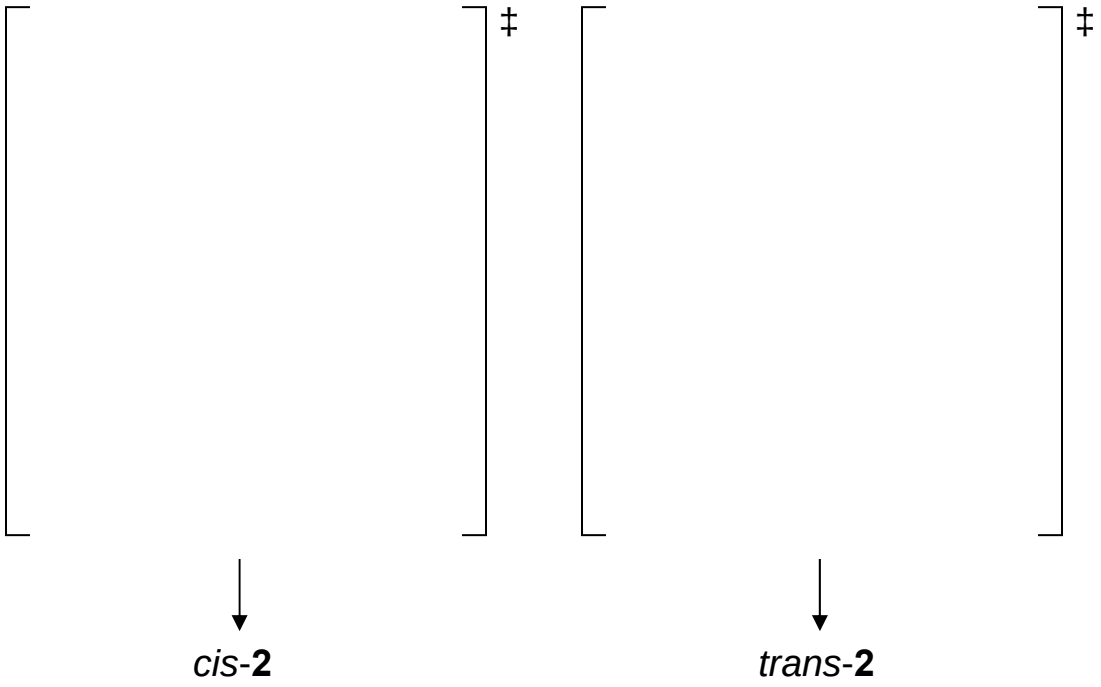
a) (10 pts) **Estimate ρ_{cis} and ρ_{trans} from this graph**.

ρ_{cis} = ☐ ρ_{trans} = ☐

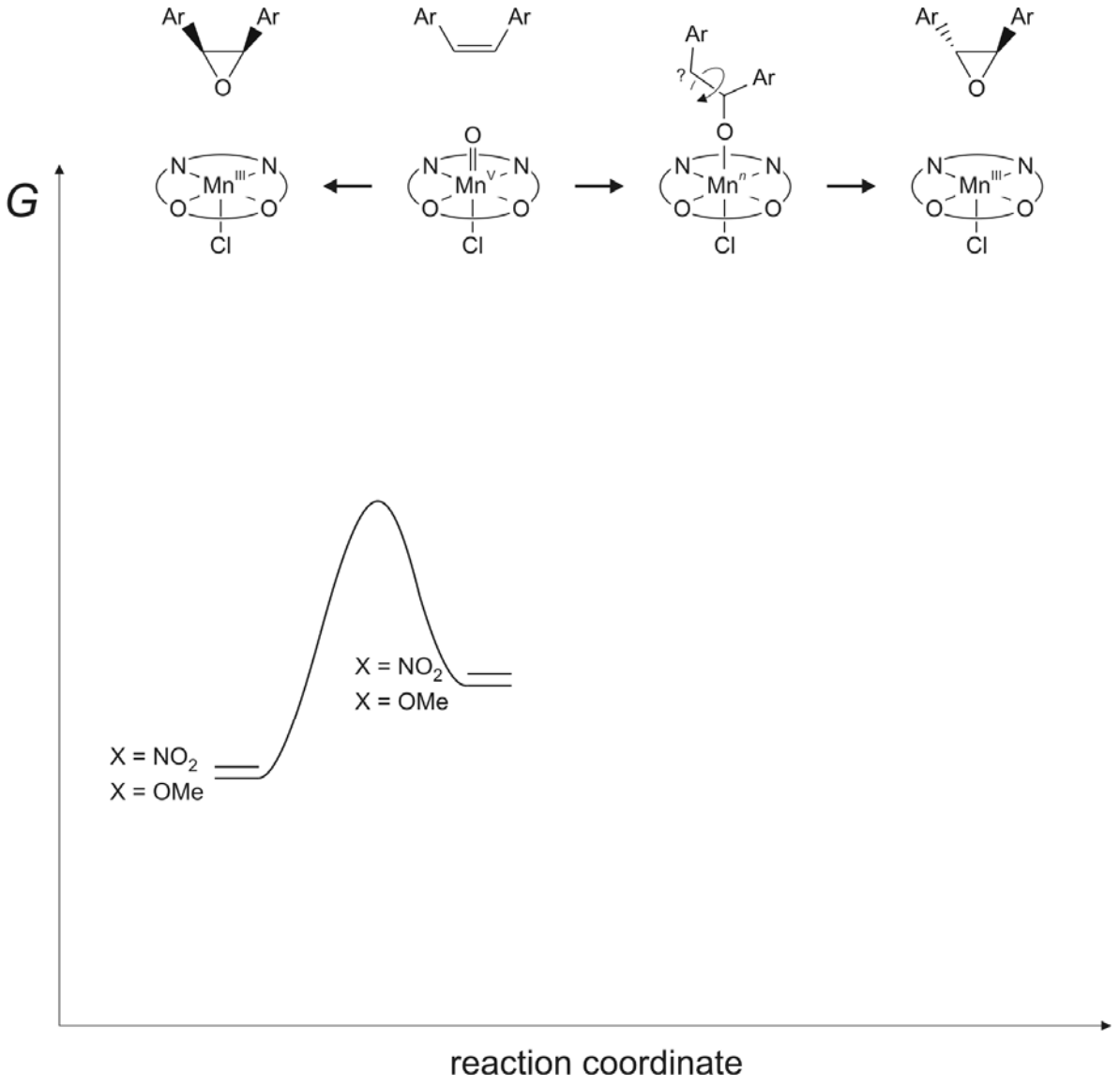
[3] Linde, C.; Koliaï, N.; Norrby, P.-O.; Åkermark, B. *Chem. Eur. J.* **2002**, *8*, 2568-2573.

b) (15 pts) **Draw transition states for the rate-determining step for each reaction pathway**. Feel free to use cartoons rather than full chemical structures. Make sure you illustrate

(i) which bonds are being made and broken at the transition state, and
(ii) any partial positive or negative charges (δ+ or δ-) that develop at the transition state.



c) (20 pts) Assuming that the product distribution (between *cis*- and *trans*-) is determined entirely by kinetics, **complete the potential energy diagram on the following page** for X = OMe and X = NO_2. The curve for conversion of **1** (X = OMe) to *cis*-**2** (X = OMe) has already been drawn for you; make sure you draw in the curve on the left for X = NO_2. For this problem, assume that the ground-state energies of the substituted stilbenes and the epoxides are the same, regardless of substituent. (This is a pretty reasonable assumption.)



Checklist: Did you

(i) Draw four more ground-state energy levels, and label each one NO_2 or OMe?
(ii) Draw five more reaction coordinate curves—one on the left, two in the middle, and two on the right?
(iii) Make sure that ground-state and transition-state energies are consistent with what you know about the reaction?

d) (10 pts) Although the previous section made you assume that product distribution was determined entirely by kinetics, reactions that generated primarily the more stable *trans*-epoxide (e.g., X = NO_2) might also be thermodynamically controlled. What experiment might Linde et al. run to determine whether the epoxidation of **1** (X = NO_2) operated under kinetic or thermodynamic control?