Midterm Exam 3

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 8 pages, including this one. Please check to make sure that your packet contains 8 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
	$c = 2.99 \times 10^{8}$ m/sec	
	$e = 2.718$	

1. Ricin, a protein present in castor beans, is poisonous because is catalyzes the hydrolytic depurination of nucleic acids. However, the specific mechanism of ricin catalysis is not known. In an attempt to help develop antidotes to ricin poisoning, Vern Schramm and coworkers at Einstein College of Medicine have studied the kinetic isotope effect of DNA depurination in the presence of ricin.[1] In particular, Schramm was interested in determining whether ricin assists S_N2 attack of H_2O on the ribose ring, or whether the enzyme encourages S_N1 dissociation of the purine before H_2O adds.

k_{H_1}/k_{D_1}	1.14
$k_{H_{2S}}/k_{D_{2S}}$	1.07
$k_{H_{2R}}/k_{D_{2R}}$	1.11
$k^{14}N_1/k^{15}N_1$	1.023
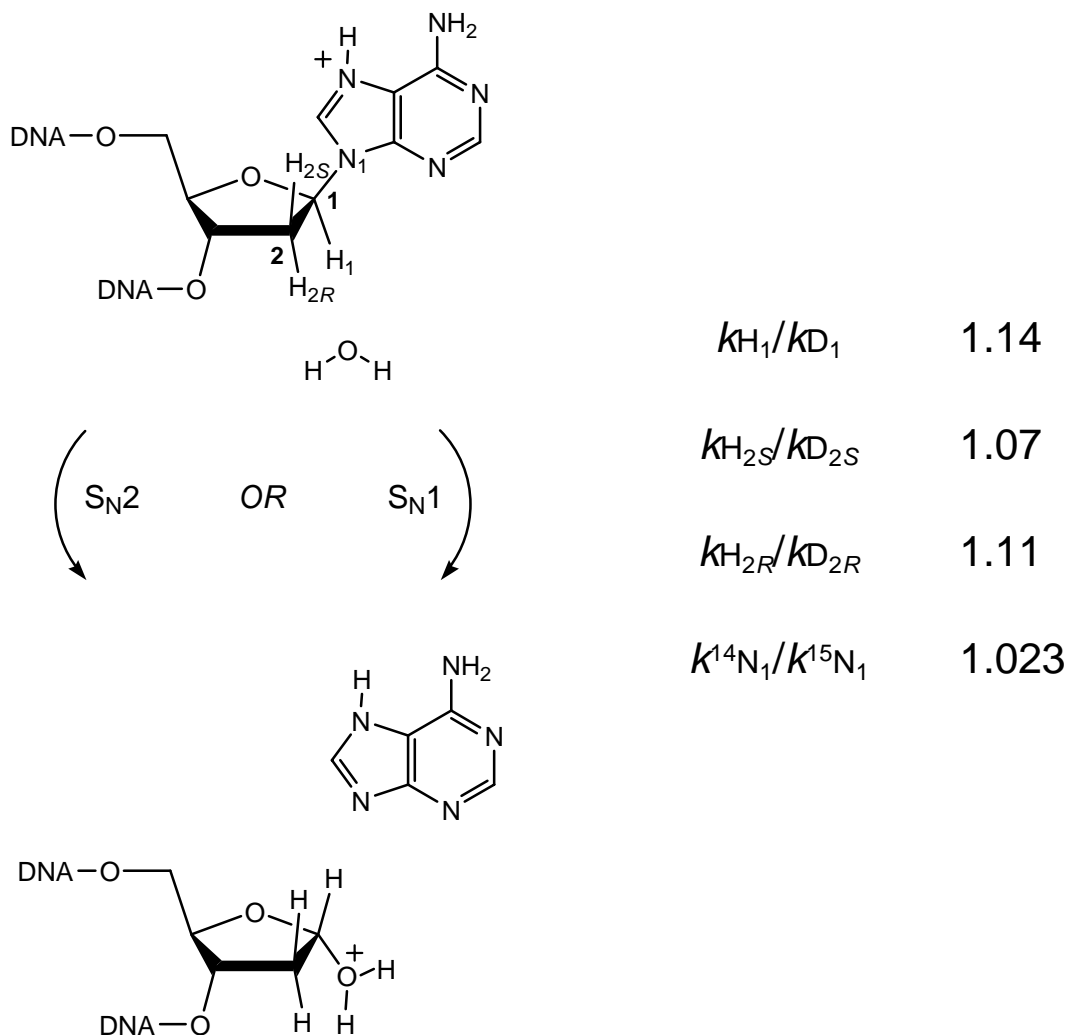
[1] Chen, X.-Y.; Berti, P. J.; Schramm, V. L. *J. Am. Chem. Soc.* **2000**, *122*, 6527-6534.

a. (10 pts) **Draw the transition states** for the rate determining steps of the S_N2 and S_N1 mechanisms for this transformation.

S_N2	S_N1
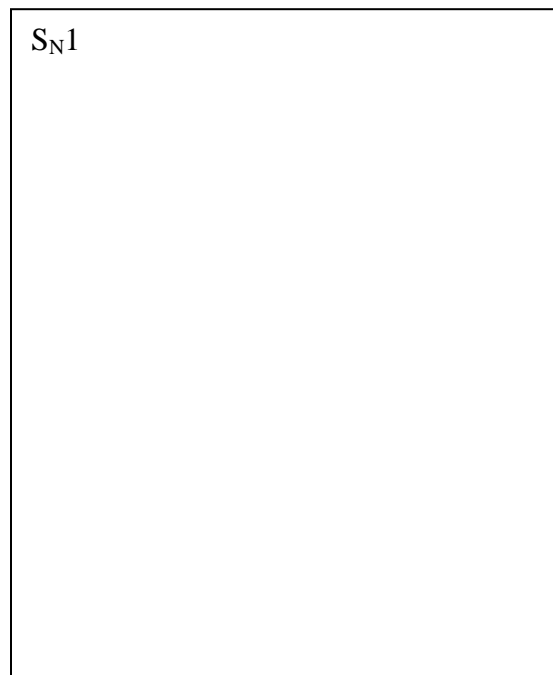
b. (10 pts) Regardless of the mechanism, the C_1-N_1 bond is partly broken in the rate-determining transition state. **Draw a generic potential energy diagram that illustrates the rate-determining step** for either mechanism, in which the reaction coordinate includes C-N bond breaking. On this diagram, **also illustrate the energetic basis of the k_{14N}/k_{15N} kinetic isotope effect**, including energy levels for C-^{14}N and C-^{15}N zero-point energies.

E

reaction coordinate
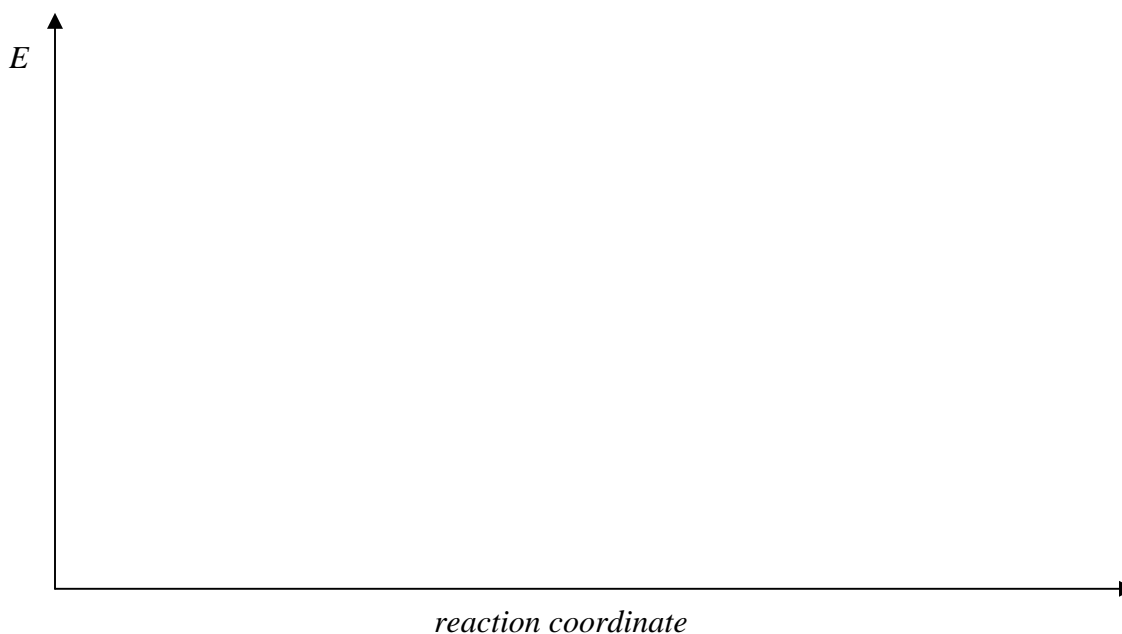
c. (10 pts) If we assume that $v(C\text{-}^{14}N) = 1080 \text{ cm}^{-1}$, **what is the maximum value for k_{14N}/k_{15N}** you would expect for either mechanism at room temperature?

<div style="border:1px solid black; padding:10px;">
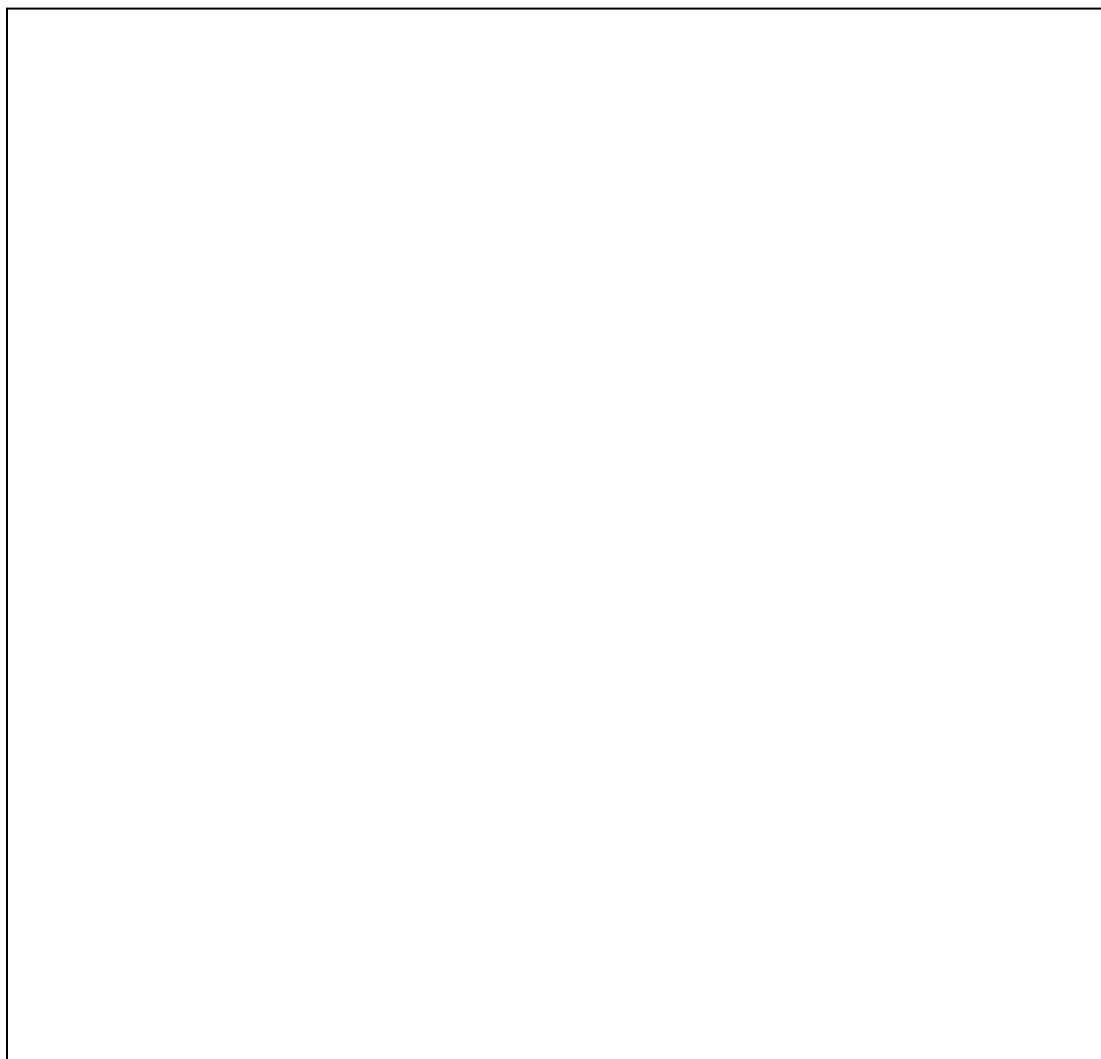
$(k_{14N}/k_{15N})_{max} =$

</div>

Calculations (will be graded for partial credit if answer above is incorrect):

d. Explain the observed kinetic isotope data in terms of either the S_N1 or S_N2 mechanism for depurination. (Note: Choosing the wrong mechanism will only lose you only a fraction of the total points for this problem. Consistent but incorrect answers will receive credit.) In your explanation, you will need to address these questions:

i. (5 pts) **Which mechanism is correct?**

S_N2 or S_N1 (circle one)

ii. (15 pts) Re-draw the transition state structure you drew in part (a) for the mechanism you've chosen, and use it to **explain how the C-H$_{2R}$ and C-H$_{2S}$ bonds would interact with the transition state differently** (as a basis for explaining the different isotope effects in the next question).

iii. (20 pts) **Draw potential energy diagrams that illustrate the difference between k_{H2R}/k_{D2R} and k_{H2S}/k_{D2S}.** As much as possible, align these diagrams against the same vertical (energy) scale. (Exaggerate energy differences, though, as we have in lecture.)

k_{H2R}/k_{D2R}

k_{H2S}/k_{D2S}

E

reaction coordinate

reaction coordinate
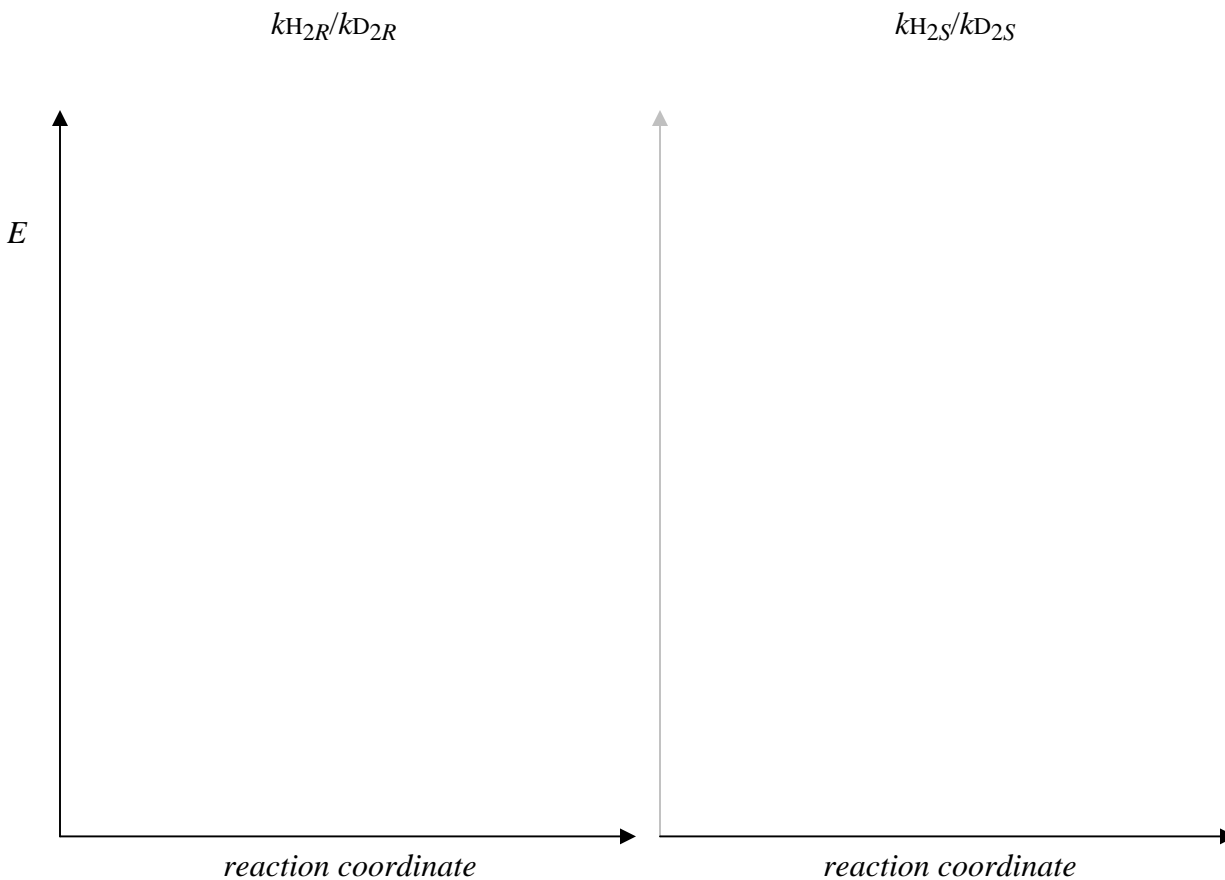
2. Cationic rhodium(I) complexes catalyze the hydrogenation of enamide **1** to the amino acid derivative **2**. A mechanistic catalytic cycle for this hydrogenation is shown below:
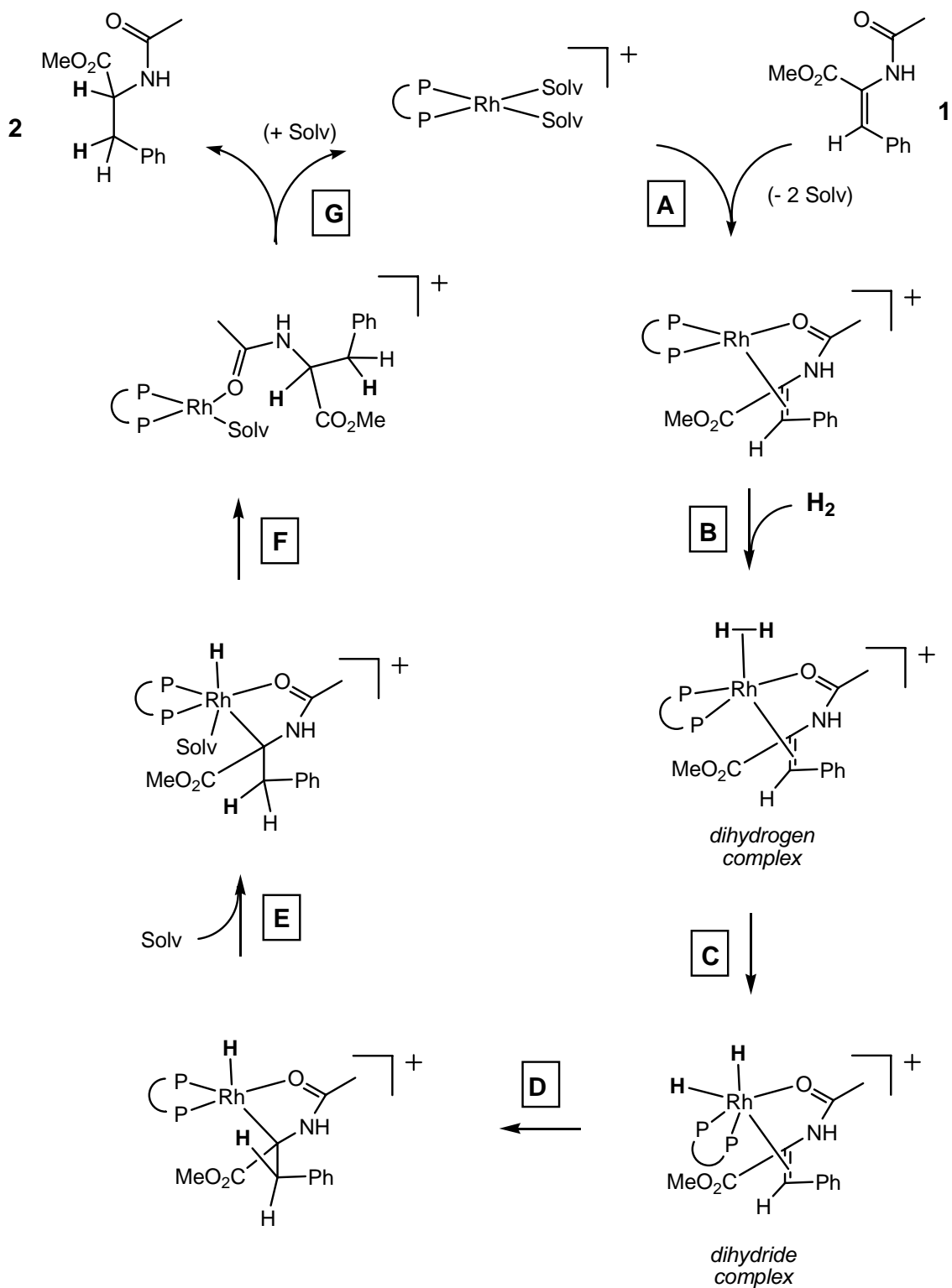
The conversion of **1** to deuterated **2** ("**2**-d_2") with D_2 gas occurs at a different rate than the conversion of **1** to **2** with H_2. Although the large kinetic isotope effect k_{H2}/k_{D2} could be explained by zero-point energy differences, theoretical studies on this cycle suggest that quantum tunneling may also play an important role.

a. (10 pts) For which steps is tunneling most likely? In the boxes below, **circle the letters of two steps** which might exhibit tunneling. (Do not make any judgements about which step is rate-determining—base your answer solely on whether there should be tunneling in the individual steps you circle.)

<p style="text-align:center">A B C D E F G</p>

b. (8 pts) *For this part only*, assume that each of the steps you circled above might be rate determining. If this were true, **would you expect k_{H2}/k_{D2} to be greater than, equal to, or less than one?**

<p style="text-align:right">>, < or =</p>

If step [   ] exhibited tunneling and was rate-determining, then $\dfrac{k_{H2}}{k_{D2}}$ [   ] 1

<p style="text-align:right">>, < or =</p>

If step [   ] exhibited tunneling and was rate-determining, then $\dfrac{k_{H2}}{k_{D2}}$ [   ] 1

c. (12 pts) Substituting D_2 for H_2 would lead to an anomalously large k_{H2}/k_{D2} only if tunneling were important in the rate-determining step; if tunneling occurred in a fast step, it might not effect the overall reaction rate. Using HD gas as the source of deuterium instead of D_2, on the other hand, might illustrate whether a non-rate-determining step exhibited tunneling by not only affecting the reaction rate, but also affecting the ratio of products **2a** and **2b** that were formed. In each of the boxes below, assume that tunneling occurs in one of the steps you circled in part (a), and not in the other step. **If HD gas were used, would you expect the product ratio 2a/2b would be greater than, equal to, or less than one?**

MeO$_2$C NH
D
H   Ph
2b

2a

MeO$_2$C NH
H
D   Ph
H

2b
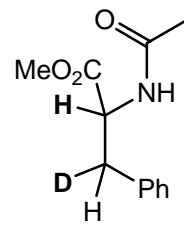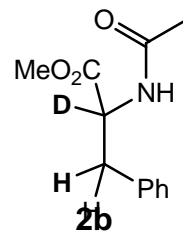
If step [ ] exhibited tunneling (and the other step did not), then $\dfrac{2a}{2b}$ [**>, < or =**] 1

If step [ ] exhibited tunneling (and the other step did not), then $\dfrac{2a}{2b}$ [**>, < or =**] 1

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