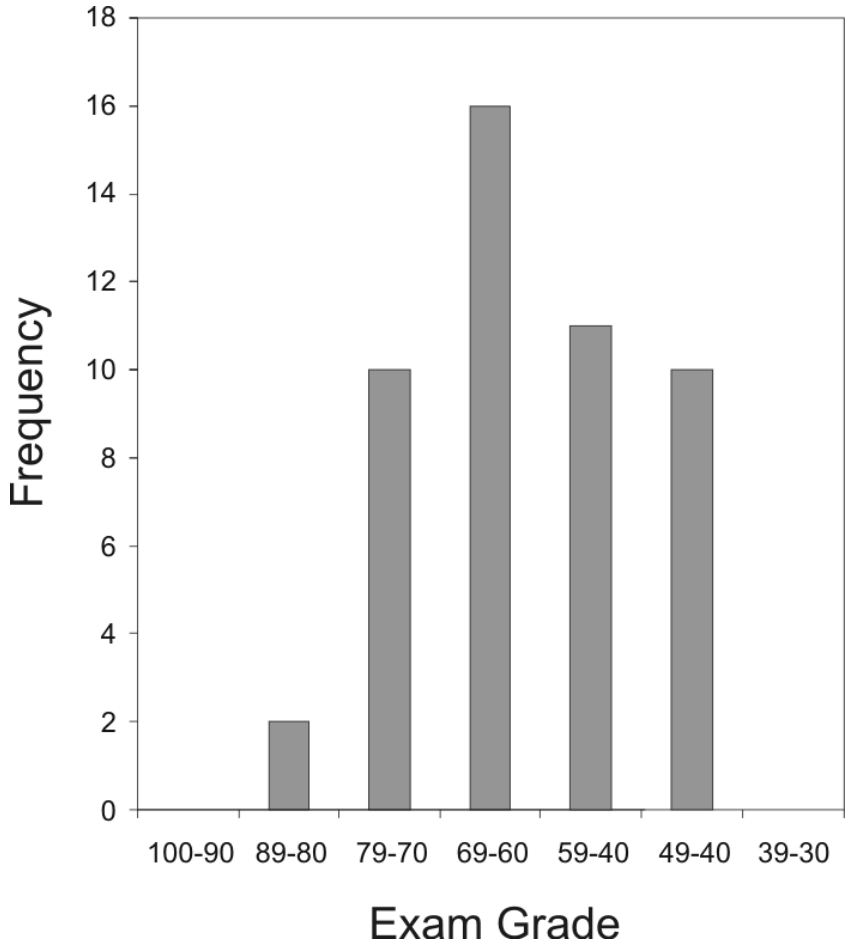
Chemistry 4011/8011 Monday, December 18, 2006

Exam 3
Answer Key

Exam 3 Mean:	61
Exam 3 Median:	60
Exam 3 St. Dev.:	12



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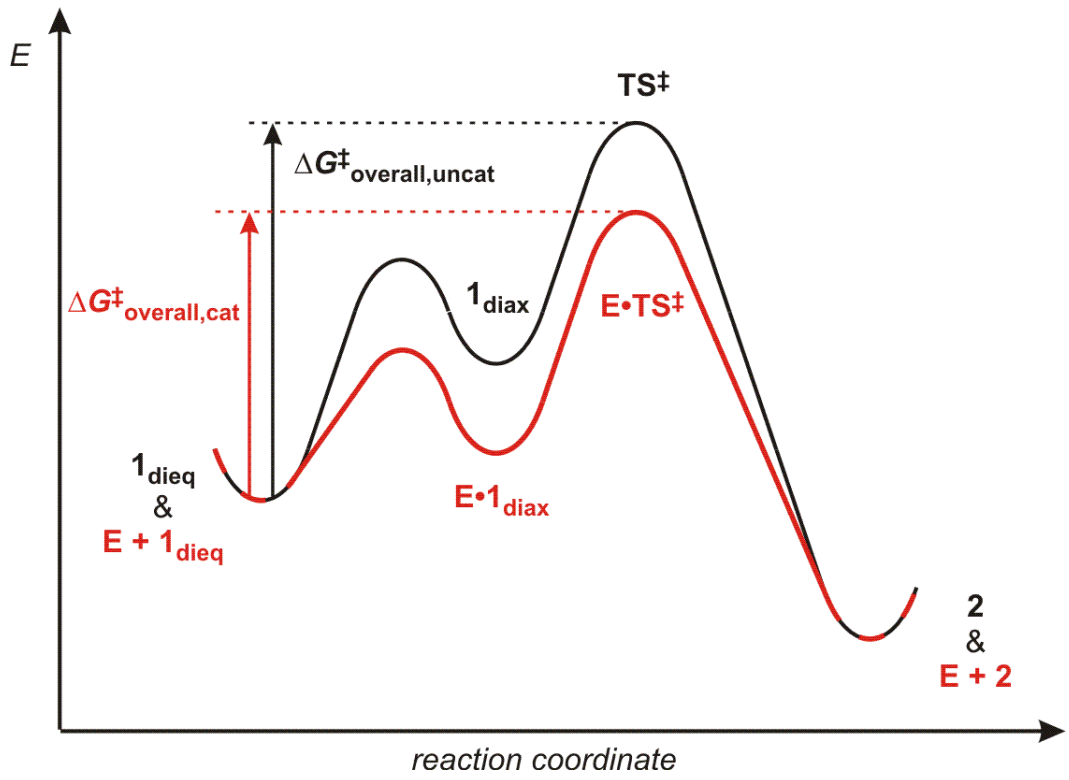
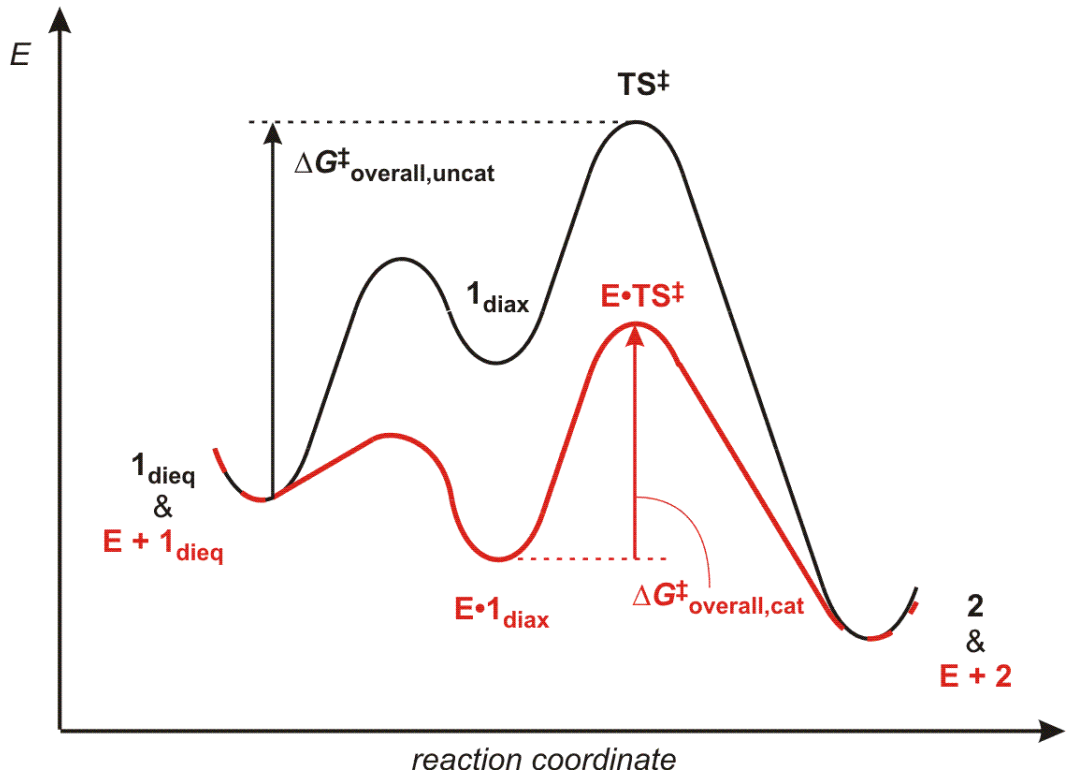
Exam 3 Solutions

1. a. The answer to this problem actually depends on whether you drew the enzyme stabilization of $\mathbf{1_{diax}}$ as more or less than 6 kcal/mol.

E•1$_{diax}$ stabilized by less than 6 kcal/mol:



E•1$_{diax}$ stabilized by more than 6 kcal/mol: (*next page*)



Either of these answers received full credit. I have shown, basically, the minimum number of items you could have drawn. There are a couple of items that I haven't shown my diagrams above that you could have included on yours, but that we didn't grade on:

E + 1_{diax}: It isn't clear whether the molecule has to flip into the diaxial conformation before it enters the enzyme pocket. Really, it doesn't matter to the kinetics, so you can include it or not.

E•2: It also isn't clear whether the enzyme forms a complex with the product. We have been assuming such a complex in all of the examples in class, but there are enzymes (and plenty of other catalysts) that don't have this step and that go straight to free product. Again, it doesn't matter to the kinetics.

Rubric:

3 points for uncatalyzed curve;

-1 point for each trivial mistake/omission (chemical state label omitted, things not lined up in energy, etc.)

3 points for catalyzed curve; (*same partial credit rules as above*)

3 points for drawing $\Delta G^{\ddagger}_{overall,uncat}$ appropriate to your diagram;

3 points for drawing $\Delta G^{\ddagger}_{overall,cat}$ appropriate to your diagram;

3 points for stabilizing **E•1_{diax}** and **E•TS‡** by the same energy.

b. The ratio of rates is determined by the difference in activation free energies:

$$\frac{k_{\text{overall,cat}}}{k_{\text{overall,uncat}}} = \frac{\frac{k_B T}{h} e^{-\Delta G^{\ddagger}_{\text{overall,cat}} / RT}}{\frac{k_B T}{h} e^{-\Delta G^{\ddagger}_{\text{overall,uncat}} / RT}}$$

$$= e^{\left(\Delta G^{\ddagger}_{\text{overall,uncat}} - \Delta G^{\ddagger}_{\text{overall,cat}}\right) / RT}$$

The uncatalyzed reaction takes place in two steps: ring flipping (step 1) and electrocyclization (step 2). Overall, $\Delta G^{\ddagger}_{\text{overall,uncat}}$ can be described as

$$\begin{aligned} \Delta G^{\ddagger}_{\text{overall,uncat}} &= \Delta G^{0}_{\text{step 1}} + \Delta G^{\ddagger}_{\text{step 2}} \\ &= 6 \text{ kcal/mol} + \Delta G^{\ddagger}_{\text{step 2}} \end{aligned}$$

If we assume that the catalyst doesn't stabilize **TS‡** any better than it stabilizes $\mathbf{1_{diax}}$, then $\Delta G^{\ddagger}_{\text{step 2}}$ shouldn't be any different for the catalyzed reaction; the only effect of the enzyme is to decrease $\Delta G^{0}_{\text{step 1}}$. But, if $\Delta G^{0}_{\text{step 1}}$ is decreased more than 6 kcal/mol (such that it's negative), the resting state of the catalytic cycle changes (such that the second of the two diagrams in part [a] above holds true). Under those circumstances,

$$\begin{aligned} \Delta G^{\ddagger}_{\text{overall,cat}} &= \Delta G^{\ddagger}_{\text{step 2}} \\ &= \Delta G^{\ddagger}_{\text{overall,uncat}} - 6 \text{ kcal/mol} \end{aligned}$$

$$\Delta G^{\ddagger}_{\text{overall,uncat}} - \Delta G^{\ddagger}_{\text{overall,cat}} = 6 \text{ kcal/mol}$$

$$\left(\frac{k_{\text{overall,cat}}}{k_{\text{overall,uncat}}}\right)_{\text{max}} = e^{(6 \text{ kcal/mol}) / RT} = e^{(10.1)} = \boxed{2.5 \times 10^{4}}$$

Rubric:

5 points for correct answer.

If answer is incorrect,

2 points for correctly expressing ratio of k's as ratio of $\Delta G^{\ddagger}$'s.

2 points for setting up difference as 6 kcal/mol.

(The other point is for the right answer.)

c. In both uncatalyzed and catalyzed reactions, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are determined by the difference between the true starting material and the rate-determining transition state.

In the uncatalyzed reaction, we are looking at the difference between $\mathbf{1_{dieq}}$ and $\mathbf{TS^{\ddagger}}$. $\Delta S^{\ddagger}$ will probably be slightly negative, but close to zero; the reaction does not create or consume molecules, so you might guess zero at first, but the transition state is very ordered (i.e., the positions of the six atoms undergoing reaction is strictly dictated by the mechanism), so some entropy will be lost constraining the molecule into this conformation. $\Delta H^{\ddagger}$ should predominate $\Delta G^{\ddagger}$, and should be large and positive.

How we treat the catalyzed reaction (and thus the correct answer to this problem) depends on what you drew in part (a).

<u>Case 1: $E(\mathbf{E{\bullet}1_{diax}}) > E(\mathbf{E} + \mathbf{1_{dieq}})$</u> [first answer I listed for (a)]

In this case, we are looking at the difference between $\mathbf{E} + \mathbf{1_{dieq}}$ and $\mathbf{E{\bullet}TS^{\ddagger}}$. $\Delta H^{\ddagger}$ for the reaction, like $\Delta G^{\ddagger}$, is decreased by stabilizing interactions between the enzyme and transition state (because these stabilizing interactions are not present in the starting material $\mathbf{E} + \mathbf{1_{dieq}}$). $\Delta S^{\ddagger}$ will be very negative; not only is the transition state constrained as in the uncatalyzed reaction, but the starting material has two molecules whereas the transition state has one complex. So, for this case,

>, < or =

$$\Delta H^{\ddagger}_{\text{overall,cat}} - \Delta H^{\ddagger}_{\text{overall,uncat}} \quad \boxed{<} \quad 0$$

>, < or =

$$\Delta S^{\ddagger}_{\text{overall,cat}} - \Delta S^{\ddagger}_{\text{overall,uncat}} \quad \boxed{<} \quad 0$$

<u>Case 2: $E(\mathbf{E{\bullet}1_{diax}}) < E(\mathbf{E} + \mathbf{1_{dieq}})$</u> [second answer I listed for (a)]

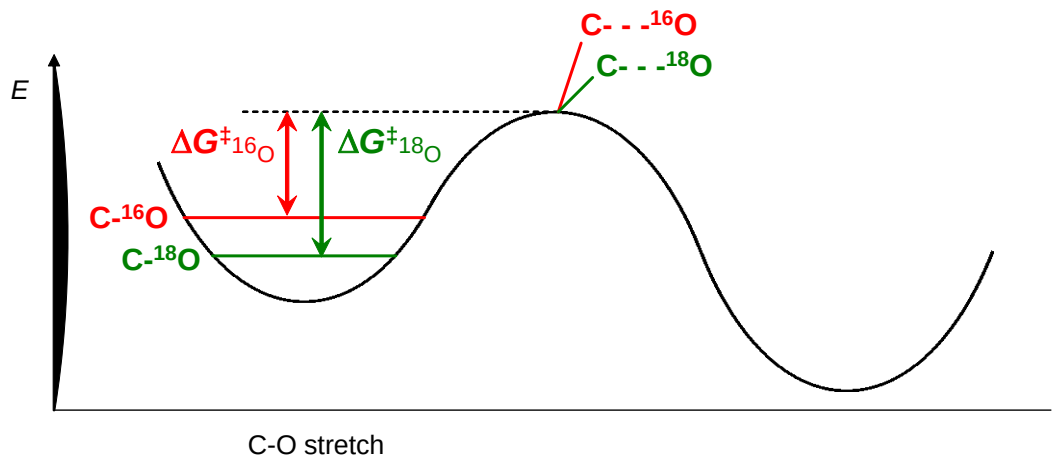
In this case, we are looking at the difference between $\mathbf{E{\bullet}1_{diax}}$ and $\mathbf{E{\bullet}TS^{\ddagger}}$. I stated that, for this part of the problem, the enzyme doesn't stabilize the transition state any different than it stabilizes $\mathbf{1_{diax}}$; this means $\Delta H^{\ddagger}_{\text{step 2,cat}} = \Delta H^{\ddagger}_{\text{step 2,uncat}}$, but both of those values are still lower than the overall $\Delta H^{\ddagger}_{\text{overall,uncat}}$ (by ~6 kcal/mol). For $\Delta S^{\ddagger}$, this case does not involve a change of molecules between $\mathbf{E{\bullet}1_{diax}}$ and $\mathbf{E{\bullet}TS^{\ddagger}}$. The constraints on the transition state here are probably the same as in the uncatalyzed reaction, but here $\mathbf{E{\bullet}1_{diax}}$ is also constrained, by the enzyme. I might expect $\Delta S^{\ddagger}$ to closer to zero than in the uncatalyzed case. So,

	>, < or =	
$\Delta H^{\ddagger}_{\text{overall,cat}} - \Delta H^{\ddagger}_{\text{overall,uncat}}$	**<**	0
$\Delta S^{\ddagger}_{\text{overall,cat}} - \Delta S^{\ddagger}_{\text{overall,uncat}}$	**=** or **>**	0

Rubric:

3 points for one box correct,
2 points for the other.

d. This is a primary isotope effect for a bond that is breaking, and the maximum isotope effect would be observed if all of that breaking were reflected in the transition state. (Transition-state theory in fact says that this will be so; see the answer to part (e).)



Here,

$$\frac{k_{16O}}{k_{18O}} = \frac{\frac{k_B T}{h} e^{-\Delta G^{\ddagger}(16O)/RT}}{\frac{k_B T}{h} e^{-\Delta G^{\ddagger}(18O)/RT}} = e^{\frac{\Delta G^{\ddagger}(18O) - \Delta G^{\ddagger}(16O)}{RT}} = e^{\frac{ZPE(C-16O) - ZPE(C-18O)}{RT}}.$$

From Workshop 10,

$$\text{ZPE(any vibration)} = \frac{1}{2}h(c)\nu$$

$$= \frac{1}{2}(6.626\times10^{-34}\ \text{J sec})(3.00\times10^{8}\ \text{m/sec})(100\ \text{cm/m})$$

$$\times(6.022\times10^{23}\ \text{/mol})(\nu\ \text{ in cm}^{-1})$$

$$= (5.99\ \text{J cm/mol})(\nu\ \text{ in cm}^{-1}).$$

ZPE(^{12}C – ^{16}O) = (5.99 J cm/mol)(1000 cm^{-1}) = 5.99 kJ/mol.

We can calculate ZPE(^{12}C – ^{18}O) using reduced masses:

$$\frac{\text{ZPE(C-}^{18}\text{O)}}{\text{ZPE(C-}^{16}\text{O)}} = \frac{\nu_{\text{C-18O}}}{\nu_{\text{C-16O}}} = \frac{\frac{1}{2\pi}\sqrt{\frac{k}{\mu_{\text{C-18O}}}}}{\frac{1}{2\pi}\sqrt{\frac{k}{\mu_{\text{C-16O}}}}} = \sqrt{\frac{\mu_{\text{C-16O}}}{\mu_{\text{C-18O}}}} = \sqrt{\frac{\left(\frac{m_{\text{C}}m_{16\text{O}}}{m_{\text{C}}+m_{16\text{O}}}\right)}{\left(\frac{m_{\text{C}}m_{18\text{O}}}{m_{\text{C}}+m_{18\text{O}}}\right)}} = \sqrt{\frac{\left(\frac{(12)(16)}{12+16}\right)}{\left(\frac{(12)(18)}{12+18}\right)}}$$

= 0.976.

ZPE(^{12}C – ^{18}O) = (0.976)(5.99 kJ/mol) = 5.846 kJ/mol.

$$\left(\frac{k_{16\text{O-}7}}{k_{18\text{O-}7}}\right)_{\text{max}} = e^{\frac{ZPE(C-16\text{O})-ZPE(C-18\text{O})}{RT}} = e^{(0.144\ \text{kJ/mol})/RT}$$

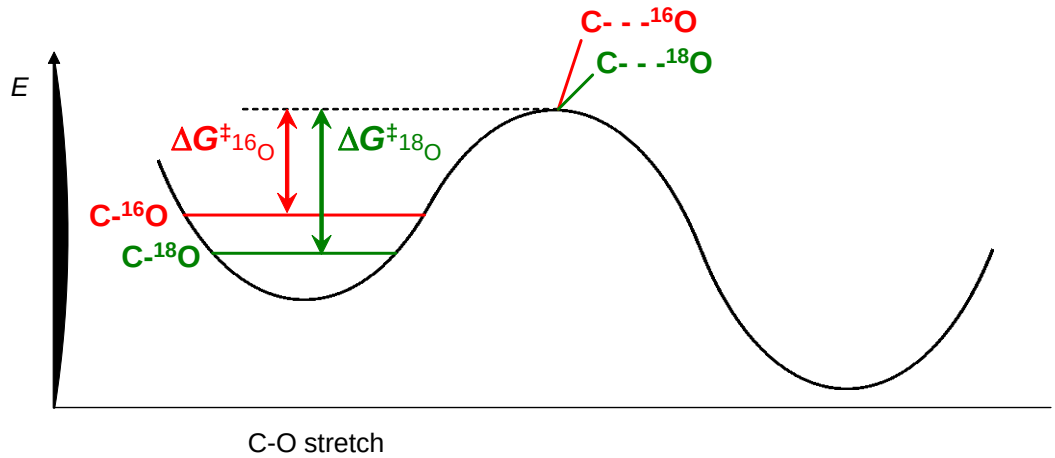
$$= \boxed{1.060}$$

Rubric:

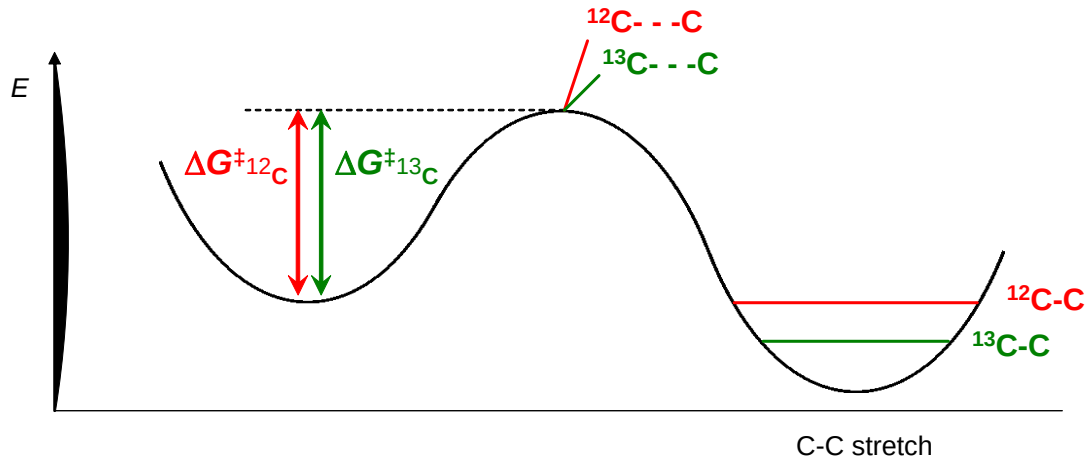
4 points for assuming no ZPE difference in **TS**‡ (either in text or in calculations);
4 points for calculating ZPE(^{12}C – ^{16}O) from ν_{stretch}(^{12}C – ^{16}O) = 1000 cm^{-1};
4 points for calculating ZPE(^{12}C – ^{18}O) using reduced masses;
3 points for using Eyring to calculate answer.
-1 point for each trivial math mistake.

We did not grade the answer you put in the box; propagating errors were too difficult for us to track.

e. When we are thinking about the effects of substitution on reaction rates, we are always thinking about the difference between starting materials and transition states. Transition-state theory says that vibrations involved in the reaction coordinate—here the C5-O7 and C1-C9 stretches—don't really exist in the transition state, and that as a result there should be no zero-point energy differences in the transition state for these modes. If this is true, then the full difference between bond and no bond should be felt for the C-O bond that is breaking:



But there should be virtually no isotope effect for bonds that are *forming*. (I.e., that are going from no bond in the starting materials to no bond in the transition state.)



Here, there is an isotope ZPE difference in the *products*, but that clearly doesn't have any impact on the starting materials and transition states, so TST says there shouldn't be any isotope effect here. (Of course, there still is a small one, because TST doesn't explain everything.) The observed isotope effects are consistent with this TST-based explanation.

Rubric:

5 points for $^{16}O/^{18}O$ potential energy diagram, w/isotope ZPE's drawn correctly;

3 points partial if ZPEs incorrect or $\Delta G^{\ddagger}$'s incorrectly inferred;

5 points for $^{12}C/^{13}C$ potential energy diagram, w/isotope ZPE's drawn correctly;

3 points partial if ZPEs incorrect or $\Delta G^{\ddagger}$'s incorrectly inferred;

5 points for explaining in terms of transition-state theory—for noting that TS has no bond frequency, and thus no ZPE differences.

5 points for connecting to concerted mechanism (where C-O is being broken, C-C is being made.

2. a. In class, you learned that tunneling was a consequence of the de Broglie wavelength for atoms. This can be expressed as

$$\lambda = \frac{h}{mv} = \frac{h}{\sqrt{2mk_{\mathrm{B}}T}},$$

where *m* is the mass of the atom. In the case of carbon,

$$\lambda = \frac{6.626\times10^{-34}\,\mathrm{J\cdot sec}}{\sqrt{2\left(\frac{12\ \mathrm{g/mol}}{6.022\times10^{23}/\mathrm{mol}}\right)\left(1.38\times10^{-23}\,\mathrm{J/K}\right)\left(8\,\mathrm{K}\right)}}$$

$$= \frac{6.626\times10^{-34}\,\frac{\mathrm{kg\cdot m^2}}{\mathrm{sec^2}}\cdot\mathrm{sec}}{\sqrt{4.40\times10^{-45}\,\frac{\mathrm{kg\cdot m^2}}{\mathrm{sec^2}}\cdot\mathrm{g}}} = \frac{6.626\times10^{-34}\,\frac{\mathrm{kg\cdot m^2}}{\mathrm{sec}}}{\sqrt{4.40\times10^{-48}\,\frac{\mathrm{kg^2\cdot m^2}}{\mathrm{sec^2}}}}$$

$$= 3.16\ \text{Å}.$$

I was surprised when I first did this calculation. I had been taught that only hydrogen and deuterium are light enough to exhibit real tunneling at room temperature. I hadn't considered that, with root *T* in the denominator, heavier atoms would tunnel more at extremely low temperatures.

Rubric:

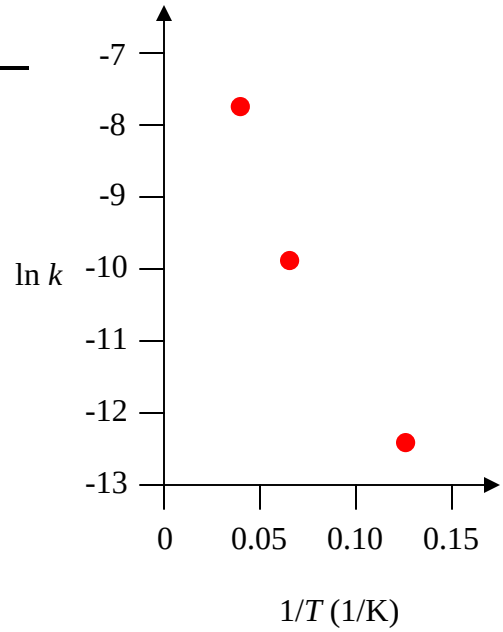
5 points for using de Broglie relationship to calculate tunneling distance. (Or even just writing down the de Broglie relationship.)

5 points for correct answer (+/-5%, +/-0.15%).

b. Tunneling throws off Arrhenius/Eyring behavior because the reaction no longer goes through the transition state. In lecture, I described how a typical Arrhenius plot (of ln *k* vs. 1/*T*) for a reaction that exhibits tunneling will show a non-linear shape, and will have a slope at low temperatures that is much less than the E_a/R that you would calculate from classical (through-the-transition-state) Arrhenius behavior.

To answer this problem, it was easiest to actually calculate ln *k* and 1/*T* for the three data points, and then draw them on a makeshift graph:

T (K)	$1/T$ (1/K)	k (s^{-1})	ln k
8	0.125	4×10^{-6}	-12.4
16	0.0625	5×10^{-5}	-9.9
25	0.04	4×10^{-4}	-7.8



You didn't need to make this graph to get full credit for this problem, but it does help to visualize things.

<u>Reason #1:</u> The slopes are too low to correspond to sensible Arrhenius E_a values. Using the top two points in the table to calculate,

slope = $-E_a/R$ = -40 K;
E_a = 0.08 kcal/mol.

Clearly, that doesn't make sense; the computational study estimated E_a = 6.4 kcal/mol for this reaction. The only reason the Arrhenius slope would be that low is if tunneling were involved.

Another way of putting this would be to say that the k values are too high to correspond to realistic $\Delta G^{\ddagger}$ values. At 8 K, the Eyring equation would put the k for a reaction with (calculated) $\Delta G^{\ddagger}$ = 6.4 kcal/mol at

$$k = \frac{k_B T}{h} e^{-\Delta G^{\ddagger}/RT}$$

$$= (1.49 \times 10^{11}\ s^{-1})(2.6 \times 10^{-175})$$

$$= 3.9 \times 10^{-164}\ s^{-1},$$

which, let's face it, is really low. The reported k values are much higher than this.

<u>Reason #2:</u> The graph is not linear. If we assume the data is very accurate, the calculated "E_a" for the second segment (0.18 kcal/mol) is still low, but over two times higher than the first segment (0.08 kcal/mol, above). That's a big jump, and suggests that these values may be in the curved part of the Arrhenius graph where behavior switches from tunneling to normal. In any case, the curve definitely doesn't follow typical linear Arrhenius behavior, and this is consistent with the reaction not going over the typical thermal barrier.

Rubric:

Reason 1

4 points for arguing slopes are too low, or that values of *k* are too high, using math. (Not okay to just say it.)

4 points for calculating what E_a would be/slope should be.

2 points for comparing to computational study.

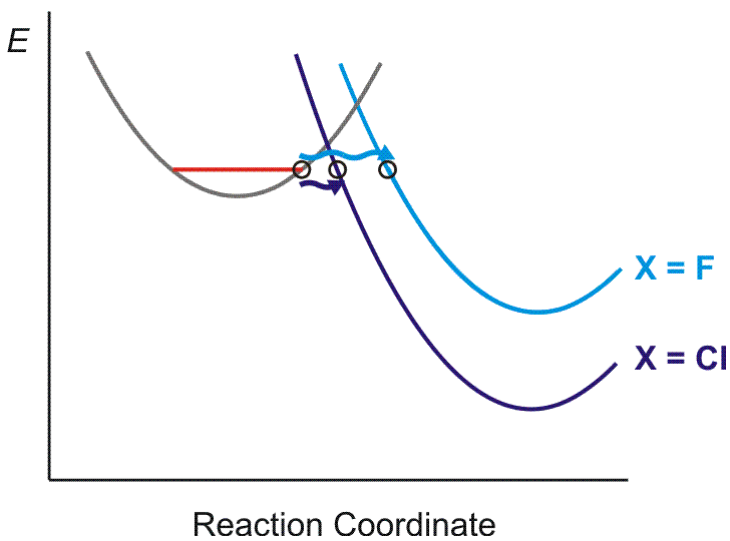
Reason 2

5 points for arguing non-linear, using math. (Again, not okay to just say it.)

5 points for saying not consistent with Arrhenius/Eyring.

c. Exothermicity, by itself, doesn't have anything to do with the rate of tunneling; the efficiency of tunneling is only affected by the width of the energy barrier that separates reactions from products. The thinner the barrier, the shorter a distance the atom has to tunnel, and the faster it will go.

I treated the effect of ΔG^0 on the potential energy surface using Marcus theory graphs:



If the reaction becomes more exothermic (going from X = F to X = Cl), the barrier width between the ν_0 vibrational level in the starting material and the product energy surface decreases. As a result, tunneling should happen more frequently (have a higher rate) for the more exothermic chlorocarbene rearrangement.

Some answers to this problem used Hammond postulate instead to justify these same arguments. Intuitively, it makes sense that if (1) the reaction is more

exothermic, and (2) if transition state is closer to starting materials, then (3) the barrier should be thinner. But while Hammond explicitly connects (1) and (2), it makes no logical connection to (3). We gave partial credit for this explanation.

Rubric:

6 points for arguing that an exothermic reaction should lead to a narrower barrier.

4 points for explaining this in terms of Marcus theory, either using words or a picture of parabolae;

2 points partial for using Hammond Postulate instead.