Chemistry 125 First Semester Final Examination Answer Key

December 17, 2008

1. (18 minutes) Give as specific an example as you can for each of 4 of the following 6 items. Make your answers as brief and clear as possible, and try to make them **specific** - *e.g.* real molecules, real numbers, real experiments.

a) Pre-19th Century measurement of a submicron distance.
b) A type of isomerism that was predicted long before it was observed.
c) Evidence that DNA exists as a double helix with major and minor grooves.
d) Evidence for stabilization due to "resonance"
e) Early 19th Century observations supporting the radical theory in organic chemistry.
f) Determination of the heat of formation of an atom.

The following brief summaries give relevant Powerpoint/Wiki links that provide specific ”real molecules, real numbers, real experiments” that make satisfactory answers really good:

a) Either Franklin’s oil-on-pond experiment (lect 4 frame 29 - **Franklin's_Experiment**) or Newton’s rings (lect 4 frame 23 - **Newton's_Rings**)

b) The best example is the van’t Hoff / Kohler chiral allenes (lect 26 frames 8-9 - **Allene_Chirality**). Paternó’s rotational isomers or Sachse’s chair are less clear-cut examples. Many answers misunderstood and used examples where observation of isomerism (*e.g.* of tartaric acid) *preceded* the theoretical explanation.

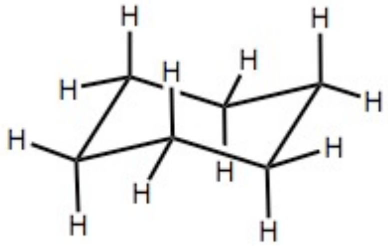
c) The unusual intensity distribution of the “reflections” along the branches of Rosalind Frankland’s “X” pattern (lect 6 frames 13-14 - **Offset_Double_Helix**).

d) The best examples are the special stability or the rotational barrier of amide *vs*. carbonyl-amine (lect 18 frame 4 - **Amide_Group_Resonance**) or the unusual acidity of carboxylic acids due to unusual stability of the carboxylate anion (lect 18 frame 7 - **Acidity_of_Carboxylic_Acids**). Note that other unusual properties attributable to resonance or HOMO-LUMO mixing (*e.g.* unusual bond lengths, and even, arguably, reduced reactivity) do not necessarily relate to thermodynamic stabilization.

e) Liebig and Wöhler’s benzoyl radical (Lect 22 frame 4 - **Benzaldehyde_and_Benzoyl**). Note the specification of “organic chemistry”.

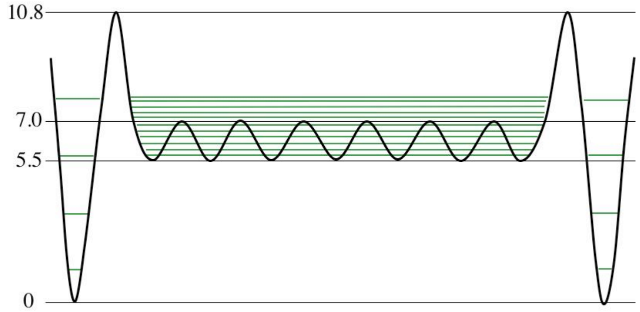
f) Either spectroscopic determination of the energetic “threshold” for formation of H from H_2 or of O from O_2 (lect 35 frame 27 - **Atom_Energy_from_Spectroscopy**) or the Chupka-Inghram oven experiment for C from graphite (lect 36 frames 5-6 - **Heat_of_Formation_of_Carbon_Atom**). A number of answers failed to discuss heat of atomization (substituting heat of formation of a molecule or heat of combustion of an element).

2. (3 min) **Draw** an accurate figure showing the conformation of **chair cyclohexane**.



[Axial bonds should be parallel to the three-fold axis, and equatorial bonds should be antiparallel to next-adjacent C-C bonds. A less idealized, more accurate drawing would have the axial bonds splayed out slightly.]

3. (4.5 min) How does the figure below relate to the **entropy** of cyclohexane?



From the "classical" point of view there are many fewer "structures" (distance along the horizontal axis) corresponding to the chair (deep well) forms than to the twist-boat (shallow well) forms.

From the quantum point of view there are many more quantum states associated with the shallow, low-barrier wells.

The two views agree that there should be a statistical or entropy factor of about 7 mitigating the large Boltzmann bias in favor of the deeper chair-cyclohexane wells.

4. (3 min) Explain the following formula

$$\frac{>1}{2}\left(AO_A^{\,2} + AO_B^{\,2} - 2\,AO_A\,AO_B\right)$$

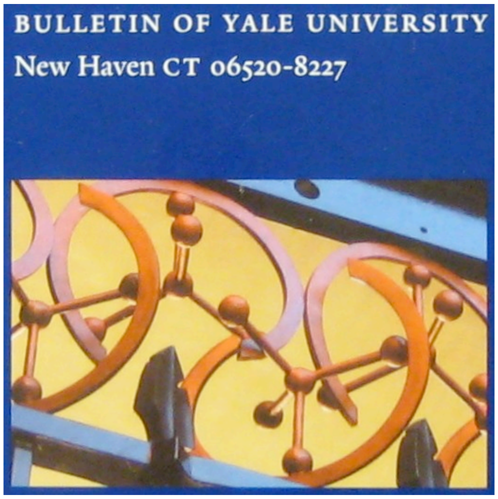
This is the square of the normalized difference between two atomic orbitals, that is, it is the probability density of a symmetrical antibonding orbital. There is a node between the orbitals and, as compared to the isolated atoms, electron density from the overlap region is transferred toward (and beyond) the atomic nuclei.

5. (3 minutes) How many times more stable is a *1s* electron of a C^{5+} atom than a *1s* electron of a H atom?

36 times more stable.

[The energy of a hydrogen-like orbital scales with Z^2, where Z is the nuclear charge.]

6. This figure from the back cover of your course book, *Yale College Programs of Study 2008-2009*, shows icons for organic chemistry from the wrought-iron gate to the Class of '54 Chemical Research Building.



A. (4.5 min) **Explain** how the metal **spirals** surrounding tetrahedral molecules relate to a scheme for **"absolute" systematic stereochemical nomenclature**. (Note: the spirals were positioned to accommodate the aesthetic sensibility of the artist, not for nomenclatural relevance, and he chose not to color the balls).

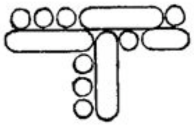
The Cahn-Ingold-Prelog system for giving and unambiguous, absolute name to the configuration of a stereogenic carbon center traces a helix through the substituents on the carbon in order of increasing (or decreasing) priority. The carbon is denoted "R" or "S" according to whether the helix is conventionally right- or left-handed.

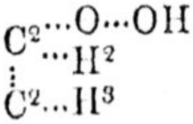
B. (4 min) Describe the **weaknesses of two other schemes** for stereochemical nomenclature.

The"phenomenological" scheme names enantiomers d or l (+ or -) according to whether they rotate the plane of polarized light to the clockwise or to counterclockwise as it passes through the substance toward the viewer. The weakness of this scheme is that it bears no simple relationship to the arrangement of the atoms in space. [It can also vary with wavelength of the light.]

The "genealogical" scheme names the enantiomers D or L according to whether they are synthesized from (or degraded to) d- or l-glyceraldehyde. This scheme is weak because different reaction paths can relate a single enantiomer to either enantiomer of glyceraldehydes.

7. (4 min) Tell how one **(1 only)** of these two figures played a role in 19th century organic chemistry.

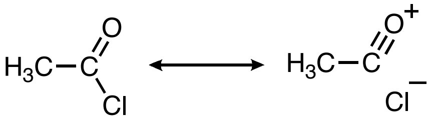




The first is Kekulé's "sausage" structure for isopropyl alcohol. It depicted valence and covalent bonds more or less explicitly, but as he used the system it predicted too many isomers of this constitution. It was thus clearly inferior to the Couper/Crum-Brown (or Lohschmidt) notations and Kekulé soon ditched it without apology.

The second is Couper's initial notation, which, in the French version, showed lines for bonds and easily evolved into the Crum-Brown notation which is in essence what we use today. The doubled carbons were grouped to the correct atomic weight by Couper, and he would presumably soon have done the same with the doubled oxygen atoms if he had kept his health.

8. (5 min) Next semester we will see spectroscopic evidence that the curious "no-bond" resonance structure on the right may have some validity for describing the acyl chloride functional group. Explain **in terms of intramolecular mixing of localized occupied and vacant AOs / MOs** why the triple-bond / no-bond resonance structure might be sensible.



The oxygen atom has an unshared electron pair in an in-plane *p* atomic orbital perpendicular to the C=O bond.

This orbital overlaps with the $\sigma^*_{C\text{-}Cl}$ orbital (which is vacant, large on the C atom, and low in energy because of the high charge of the chlorine nucleus).

Mixing these orbitals stabilizes the molecule, shortens the C=O distance because of the additional bonding, lengthens the C-Cl distance (because of the antibonding character of $\sigma^*_{C\text{-}Cl}$), and shifts electron density from the oxygen atom to the C and Cl. That is, the true molecule has characteristics of the "no-bond" structure.

9. **A.** (2 min) Why did Adolf von Baeyer suggest that cyclopentane is strain-free? (mention **both** experiment and theory)

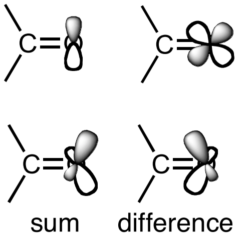
Experiment: The cyclopentane ring is not opened by reaction with HBr, Br_2, or I_2, which open strained cyclopropane and (in the case of HBr) cyclobutane.

Theory: The 108° angles within a regular pentagon are very close to the natural "tetrahedral angle" of 109.5°.

B. (3 min) What does molecular mechanics say about sources of strain in cyclopentane?

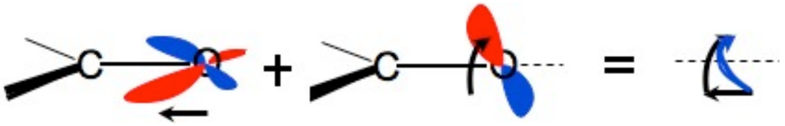
Planar cyclopentane has normal bond angles but high torsional strain (~12 kcal/mole) due to eclipsed interactions. Distortion into the "envelope" conformation reduces this strain (to ~ 6 kcal/mole) at the expense of a small increase in bending strain (~2 kcal/mole).

10. **A.** (3 min) For electron distribution in a carbonyl group what is the implication of mixing a bit of the vacant *3d*$_{xy}$ orbital of its oxygen atom with the occupied *2p*$_y$ orbital of the same atom?



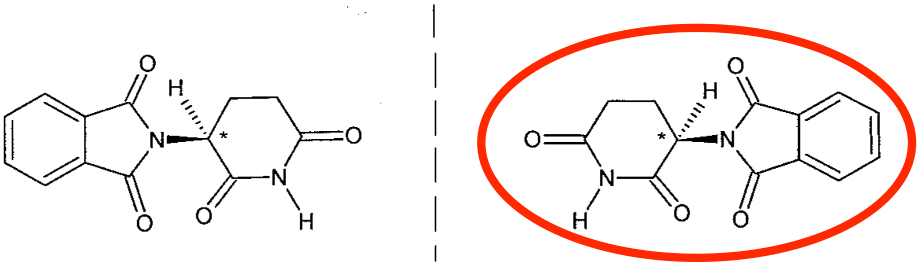
Mixing would shift the electron density along the C=O axis to the right or left (depending on the sign of the mixing - addition or subtraction).

B. (3 min) How is the electron distribution change in Part A related to the optical activity of a chiral carbonyl compound?



Coupling the above electron density shift along the C=O axis with a rotation about the same axis, due to mixing oxygen *2p*$_z$ with *2p*$_y$ orbitals, would generate a helical shift of electron density (see figure from Lecture 29, frame 19). In a chiral molecule right- and left-handed helical shifts will have different probability, giving rise to different interaction with the helical electric fields of right- and left-handed circularly polarized light. This will cause rotation of plane polarized light or "optical activity".

11. **A.** (2.5 min) Circle (R)-thalidomide in the figure below.



B. (3 min) There is a report that the rate constant for isomerization of (S)-thalidomide to (R)-thalidomide under physiological conditions is 0.12/hour (*i.e.* 3.3 x 10^{-5}/sec). Show how to estimate the free energy of activation (*i.e.* the difference in free energy between the transition state and the starting material) for this process.

Physiological conditions means near room temperature, so

k(/sec) ≈ 10^(13 - ¾ ΔG^*)

log (3.3 x 10^{-5}) ≈ -4.5 ≈ 13 – ¾ ΔG^*

ΔG^* ≈ 4/3 x 17.5 ≈ 23 kcal/mole

C. (3 min) The same source reports that the rate for the reverse isomerization (R to S) is 0.17/hour, 1.4 times faster than S to R. In the following list **circle** the free-energy difference between S and R (in kcal/mole) that is consistent with this ratio:

0.002 0.02 [✓ 0.2] 2 20 200

The ratio of rate constants (1.4) is the equilibrium constant K.

1.4 = 10^(3/4 ΔG) or ΔG = 4/3 log(1.4) = 0.195 ≈ 0.2

[An early draft of the exam had also asked whether this difference between enantiomers would be reasonable. At first glance one would think enantiomers must have identical energy, but perhaps not when they are in a chiral biological environment.]

12. French scientist Henri Victor Regnault (1810-1878) was trained as an organic chemist and subsequently made important measurements on gas expansion to show that Boyle's Law was only an approximation. It has been suggested that the constant "R" in PV = nRT be named in his honor. As an avid early photographer, he took this photo of his lab in 1851.

A. (4.5 min) After graduating from the École des Mines in Paris in 1832, Regnault studied organic chemistry in Giessen, Germany. There is a piece of apparatus in this photo that appears to be his own modification of one that he learned to use at that time. **Circle** the piece of apparatus. Speculate on at least **one advantage** and **one disadvantage** of Regnault's design modification(s).

Everyone correctly identified the 8-bulb modification of Liebig's 5-bulb "Kaliapparat". Great!

Presumably the 3 extra bulbs were included in order to make absorption of CO_2 more efficient, on the principle that if a little stirring by bubbling is good, more is better (but in fact all that was needed was enough stirring to assure that all of the CO_2 was absorbed, and Liebig's own apparatus was already sufficient for that purpose).

The genius of Liebig's device was that it was compact and light so that it was easy to weigh and contributed a minimum of weight itself, allowing the absorbed CO_2 to be determined accurately, not as a tiny difference between two large numbers. (Its consequent fragility has meant that only one of Liebig's original devices survives.) Regnault's modification would have been much more cumbersome to weigh and either much heavier or much more fragile.

Regnault does not seemed to have minimized weight by making one of the larger bulbs smaller than the other, and it would appear that he could have achieved better mixing by having narrower connections between the 6 collection bulbs.

The 6-bulbs would have generated greater back pressure when tilted, which would have encouraged leaks, but I cannot see how this design would have required more time for each analysis as many answers claimed.

B. (3 min) Just as Regnault had journeyed to Giessen to study chemistry, young James Thomson, after graduating from Peterhouse, Cambridge, used his fellowship to journey to Paris to study thermodynamics with Regnault. In 1848, as a professor of physics in Glasgow, Thomson devised the "Kelvin" temperature scale in a paper entitled *On an Absolute Thermometric Scale founded on Carnot's Theory of the Motive Power of Heat, and calculated from Regnault's Observations*.

Explain the source of the word "**Kelvin**" **and also** the source of **another word** Thomson coined that remains central to our discussion of stereochemical **handedness**.

As Prof. Barron told us, Kelvin is the name of the river that flows past the University of Glasgow, where Thomson taught. He chose this title for himself when he was made baron. The temperature scale was named for him.

Barron also mentioned that Lord Kelvin had coined the word "chirality", using as a root the Greek word for hand.

C. (5 min) We now know that the reason Boyle's Law fails at high pressure is that molecules, even non-polar ones, attract one another without forming covalent or ionic bonds. Explain the source of this attraction and how it relates to "correlation energy" (which you should define briefly).

This attraction is electrostatic and, in atoms or non-polar molecules, results from the correlated motion of electrons in adjacent species so that their instantaneous dipoles are attractive: (+ -) (+ -) . This attraction has a very short-range, so it becomes important only at relatively high pressure, when the non-bonded species are close to one another.

Self-consistent-field theory in quantum mechanics assumes static electron clouds and thus overestimates the potential energy by ignoring the ability of electrons instantaneously to avoid one another. This error is concealed and dignified by giving it the name "correlation energy".

Both phenomena derive from the correlating motion of electrons to lower the system's energy.

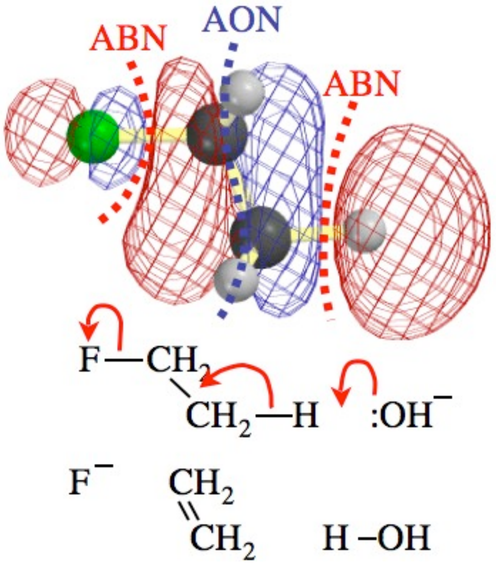
13. During his stay in Germany, Regnault reacted the oil of Dutch chemists ($ClCH_2$-CH_2Cl) with KOH, observing formation of a solid (KCl) and a new gas (H_2C=$CHCl$, **vinyl chloride**). The base hydroxide had removed a proton and chloride from the oil to form this alkene.

A. (4 min) Explain briefly how the presence of a space in the name "vinyl chloride" and the absence of a space in the synonym "1-chloroethene", both derive from the organic chemical theories that were current in the decade surrounding Regnault's discovery of the substance.

According to radical or dualistic theory organic molecules are held together by electrostatic attraction between positive and negative radicals, which were named separately and written with a space between them, thus "vinyl chloride".

According to type, or substitution, or unitary theory they were analogous to wholistic planetary systems and were written as a single word with the root name modified by substituent prefixes, thus "1-chloroethene".

B. (7 min) Propose a form for a LUMO of $ClCH_2$-CH_2Cl and use it to explain formation of vinyl chloride upon this "E2" elimination reaction with hydroxide. (Note that this LUMO will not have the symmetry of the starting material, because bonds will have begun to make and break at the transition state.)

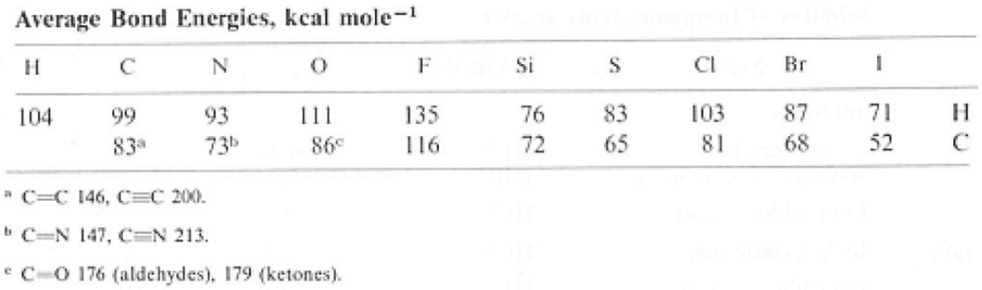


[the figure on the right is from Lecture 17 Frame 4, and the following answer is taken from the Wiki page **Make_2_Break_2_-_E2_Analogy**]

The structure for ethyl fluoride shows the LUMO is the ***favorable*** mixture of $\sigma^*_{F\text{-}C}$ and $\sigma^*_{C\text{-}H}$. There are two antibonding nodes and one atomic orbital node as part of this structure. (In order to make this orbital the LUMO, we stretched the C-H and C-F bonds.)

In this example, when the OH^- group attacks the molecule, electrons are put into a complicated LUMO, which has a node between the hydrogen and the CH_2 group. This bond breaks and the hydrogen and hydroxide groups form water. The electrons that had been a part of this bond are transferred to between the carbons, making a C=C double bond (an alkene), because the LUMO that became occupied was also pi-bonding between the two CH_2 groups. But it is anti-bonding between fluorine and the second CH_2 group, so fluorine breaks off with the single-bond electrons to form a fluoride ion. The reaction therefore results in water, ethylene and the fluoride ions, with a new pi bond between the two carbons in ethylene.

C. (5 min) Use the following table of average bond energies to estimate the heat of atomization of Regnault's vinyl chloride.



Average Bond Energies, kcal mole^{-1}

H	C	N	O	F	Si	S	Cl	Br	I	
104	99	93	111	135	76	83	103	87	71	H
	83[a]	73[b]	86[c]	116	72	65	81	68	52	C

[a] C=C 146, C≡C 200.

[b] C=N 147, C≡N 213.

[c] C=O 176 (aldehydes), 179 (ketones).

H_2C=$CHCl$

C=C	146 kcal/mole
3 x C-H	297
C-Cl	81
Sum	524 kcal/mole

D. (5 min) The actual heat of atomization of vinyl chloride is 518 kcal/mole. Explain **two different sources** of the error in the value you calculated in the previous question.

Two obvious sources of error were mentioned in class:

1) The generic C-H average bond energies from the table may not apply in this case because the sp^2 hybrid orbitals used by C in this case may yield stronger sigma bonds.
2) Vinyl chloride may profit from resonance stabilization due to mixing of an unshared electron pair of Cl with the π^* LUMO of C=C.

[Mentioning these sources of error earned full credit for this question.

BUT the situation is actually more complicated - more complicated than I thought when I wrote the question.

The ***direction*** *of the error seems to be wrong. Both of the corrections above would suggest that vinyl chloride should be more stable than the generic estimate and yield a higher heat of atomization, when in fact the heat of atomization, which I calculated using the vinyl chloride heat of formation from the Streitwieser, Heathcock, Kosower (SHK) table shown in lecture 35 frame 21, is* ***lower*** *than the generic estimate.*

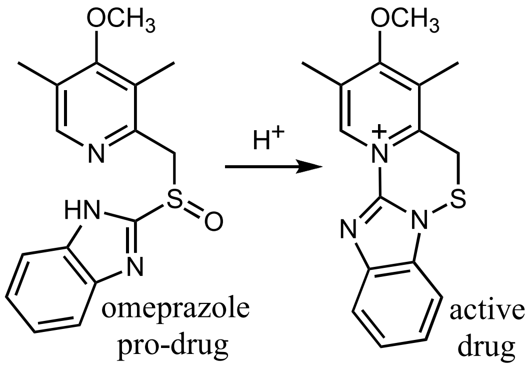
Perhaps the experimental heat of formation is incorrect. The value used from the SHK table is 8.6 kcal/mole, while values of 22 or 29 kcal/mole are given by the National Institute of Science and Technology Webbook (webbook.nist.gov). But these NIST values are even further in the wrong direction, suggesting even less stable vinyl chloride!

What is going on? Perhaps the Average Bond Energy for C=C already incorporates the correction for hybridization change (1 above), and perhaps the correction for C-Cl hybridization should be smaller than those for the C-H and C-C bonds, which the corrected C=C value already incorporates. The "resonance" correction (2 above) should not be very important, because the unshared pair on Cl is not very high in energy.

Whether or not this explanation of the error in the opposite direction is correct, the SNAFU on my part in failing to take the direction into account when writing the question serves to show the kind of difficulties one can encounter in using bond additivity to estimate molecular stability.

If you feel you suffered unjustly by analyzing this question more carefully than I did in writing it, let me know for possible adjustment of your score.]

14. Omeprazole and Nexium



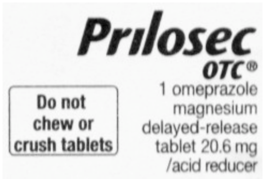
Professor Sharpless mentioned that omeprazole is a "pro-drug", meaning that in the body it undergoes acid-catalyzed transformation into the active drug molecule that actually deactivates an enzyme.

A. (4 min) Explain how this transformation relates to speculation that making a "chiral switch" to a single enantiomer of omeprazole might ***not*** give a more effective drug.

Although the pro-drug is chiral (because of the stereogenic, non-planar sulfoxide group), the active drug is achiral (as the alternative structure shown in class with an R-S-OH group would be). Thus both enantiomers of omeprazole would give the same active drug, reducing the probability that resolution of omeprazole would give a drug with different physiological properties.

B. (7.5 min) The packaging of omeprazole warns that the tablet should be taken without crushing or chewing. Explain the following three points:

(1) how this warning is related to **the design of the tablet** and activation of the pro-drug,



The tablet has an "enteric" coating to protect the pro-drug from activation through catalysis by stomach acid before it dissolves in the gut and makes its way through the blood to the interior of the acid-generating cells in the lining of the stomach, where it is activated in order to react with and deactivate an enzyme to put the "proton pump" our of commission. Crushing would expose the pro-drug to stomach acid too soon and the active drug would react before reaching the target.

(2) how the fact that an enzyme is ***not*** involved in the activation relates to the **likely effectiveness of a chiral switch**, and

If an enzyme were required to activate the pro-drug, then one would expect one enantiomer to be activated at a different rate from the other, which would suggest the possibility of one enantiomer being more effective. If the catalyst for activation is the achiral proton (or H_3O^+), the enantiomers should be activated at the same rate.

(3) **whether**, given the mode of activation, physiological beneficial effect of a chiral switch can be **definitively excluded**.

It cannot be definitively excluded, because the pro-drug is exposed to many single-enantiomer biological molecules on the way to the acid-generating cells [*Cf.* the answer to question 11C above], so there is the possibility that one enatiomer would be more effectively transported (or less extensively metabolized) than the other. [Only a well-designed clinical trial can give a definitive answer.]

C. (5 min) Explain in HOMO/LUMO terms how the active drug on the previous page has a functional group that is well suited to inhibit the "proton-pump" enzyme denoted Enz-S^-.

The functional group is the single bond between N and S, both atoms with high nuclear charge and relatively low-energy atomic orbitals. The unusually low $\sigma^*_{N\text{-}S}$ antibonding orbital, analogous to $\sigma^*_{O\text{-}O}$ (or to the $\sigma^*_{S\text{-}OH}$ in the alternative drug structure that we discussed in class), can be attacked by the HOMO of Enz-S^- to generate a covalent S-S bond deactivating the proton-pump enzyme.

D. (3 min) The Enz-S^- anion in the previous question is in equilibrium with the thiol Enz-SH. Loss of a proton to give the anion is easier than for the R–OH analogue because of the weakness of the S-H bond (see Average Bond Energies on p. 7). **In terms of orbitals, why should S-H be weaker** than O-H?

Orbitals of a second-row atom like S do not overlap as well with H as do the more compact orbitals of a first-row atom like O, that can approach the H atom more closely. So the S-H bond is weak because of poor overlap.

[A number of answers invoked poorer energy-match between S and H than between O and H. There may indeed be better energy match for S-H, but if so it would make breaking the S-H bond into ions (to give H^+) harder, not easier, and breaking into neutral atoms (Average Bond Energy) easier, not harder. See overlap/energy-match discussion of H-H *vs*. HF in Lecture 13, frame 34. This is opposite what is observed experimentally. Decreased overlap is probably the dominant factor, though solvation probably also plays a role, as we'll see later.]

E. (7 min) Explain the **atomic orbital mixing** that justifies drawing an S=O double bond for the sulfoxide group of omeprazole **and** explain why this group is different from the C=O double bond from the point of view of **stereochemistry**.

The single bond between S and O involves one of the two unshared pairs of the S atom. This S is thus pyramidal (as NH_3 is) making the unsymmetrically substituted sulfoxide group chiral. The second bond is formed by mixing an unshared *p*-orbital electron pair on the oxygen with a vacant *d*-orbital of the S atom. In the C=O case the second bond results from mixing *p*-orbitals on the two atoms, which makes the carbonyl functional group planar and achiral.

F. (4.5 min) The Katsuki-Sharpless patent described stereospecific oxidation of allylic alcohols using a Ti-based catalyst. Explain how a diagram in the patent drawn by a lawyer trained as a physical–organic chemist made the patent arguably relevant to the industrial synthesis of Nexium.

In the oxidation of allylic alcohols to epoxides the HOMO that receives the O atom is the pi orbital of the C=C double bond. Bertram Rowland, the patent attorney (who had done postdoctoral work with your chemical "ancestor" P. D. Bartlett), generalized the HOMO by drawing a generic group G with a high-energy "pair of electrons capable of accepting an oxygen atom". Thus the patent could be read as applying to the oxidation of sulfur to sulfoxide with this catalyst.

[See Wiki Bert_Rowland's_Patent_and_Esomeprazole for lecture 34 frame 17.]

G. (3 min) When he was staying in the "Madonna" suite in Munich, what would Professor Sharpless have said about clinical trials of esomeprazole, had he been asked by one of the 1200 gastroenterologists?

He would have said that the clinical trials testing esomeprazole (a single enantiomer) against racemic omeprazole were missing tests with a 40 mg dose of the racemate that would have "given them equivalence against the one enatiomer of 20 mg."

[I was delighted that 84% of the class got a perfect score on this question, since it may be the most important lesson of the course for the pre-meds among us.]

H. (4 min) Answer (i) or (ii) (NOT BOTH – you have a choice)

(i) Choose TWO (2 only) among Stages 0-IV of FDA-approved clinical trials and state their purpose(s).

or

(ii) List three responsibilities of a physician who is using a drug for an "off-label" purpose.

i)

Phase 0:	speed up development of promising agents with microdosing; establish very early on whether agent behaves in human subjects differently than expected from preclinical studies; interrogate and refine a target or biomarker assay for drug effect.
Phase I:	Determine metabolism and excretion in healthy volunteers (N~50)
Phase II:	Study effectiveness for a particular disease or condition in comparison to placebo or to a different drug. Establish safety and short-term adverse effects. (N~100)
Phase III:	Study safety and effectiveness with different populations and different dosages and in combination with other drugs (N~1000)
Phase IV:	Gather additional postmarketing information about product's safety, efficacy, or optimal use.

ii) If physicians use a product for an indication not in the approved labeling, they have the responsibility to ***be well informed about the product***, to base its use on ***firm scientific rationale*** and on ***sound medical evidence***, and to ***maintain records of the product's use and effects***. (see Lecture 30, frame 61)

15. (10 min) Suppose there were people on a planet in a galaxy far, far away, and that their Moses brought **Schroedinger's equation** down from their Mt. Sinai, so that their scientists had learned to solve it for electrons in molecules (at least approximately) **long before they did any experimentation with organic molecules**. Now that they have finally done such experiments, **would you expect bonds to be discussed** in their courses of elementary organic chemistry?

(A) Write a sentence or two supporting the answer "yes".

(B) Write a sentence or two supporting the answer "no".

This question aimed to let you have fun showing that you had thought about the "big" questions posed at the end of the semester's last lecture. There are no cut-and-dried correct answers, and most questions that showed careful thought and invoked some evidence earned about 7 points for each part (with more allowed for those who misread the question and thought only one part needed answering). Not surprisingly no one came up with the astoundingly insightful answers that would have earned 10 points for each part in the time available – remember that Isaac Newton would have earned only 95% on a Chem 125 exam for his correct answer to Pepys).

I personally incline to the conservative view that bonds (for all their inadequacy) would still have been invented, if only as a mnemonic device to provide a quick, easy, human-friendly way for correlating facts about structure, energy, and reactivity for very complex molecular systems (and that they will still be taught on Earth centuries from now).

Perhaps a different quantum-based intuition, based for example on “plum-pudding” molecular orbitals, would have sufficed without bonds (or will replace them, as it has already done for certain “paracyclic” reactions that we will discuss in the second semester), but I don’t have enough imagination to see how that could work out for quick practical purposes in most of organic chemistry.

Maybe one of you will contribute to a radically new formulation of this central science. Good luck.