Chemistry 125 First Semester Name _____

December 17, 2004 Final Examination

This exam is budgeted for 150 minutes, but you may have 180 minutes to finish it. Good Luck.

1. (31 minutes) **OMIT TWO OF THE FOLLOWING.** Describe briefly how **experimental** observation on **nine** of the following molecules played an important role in the **development of chemical theory in the indicated decade**.

a) Oxygen (1780s)

b) Salts of the fulminate anion, CNO^- (1820s)

c) Benzaldehyde C_6H_5CHO (1830s)

d) Cl_2 (1830s)

e) CH_4 (1850s)

f) Salicylic Acid (1860s)

g) Lactic Acid $CH_3CH(OH)COOH$ (1870s)

h) Cyclopropane (1880s)

i) Ethane (1930s)

j) NaRb-d-Tartrate (1940s)

k) 1,1,4,4-tetraphenylbutatriene (1970s)

Question 1 (continued)

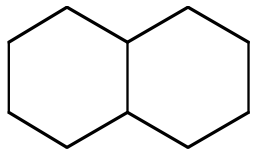
2. (3 min) Give a **chemically relevant** example for each of the following:

A force of the form $F \propto 1/r^2$

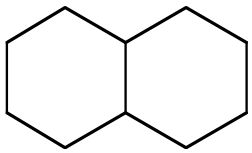
A force of the form $F \propto |x|$

3. **Decalin** ($C_{10}H_{18}$,) occurs as two configurational isomers, called *cis* and *trans*, **without any substituents**.

a) (2 min) **Modify** the two structures so as to show the configurational difference between these two unsubstituted isomers unambiguously.

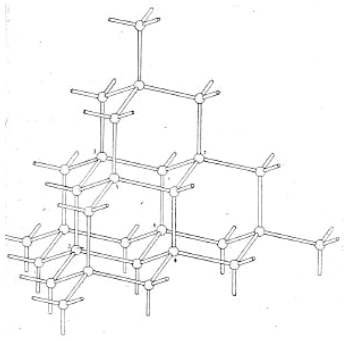


cis

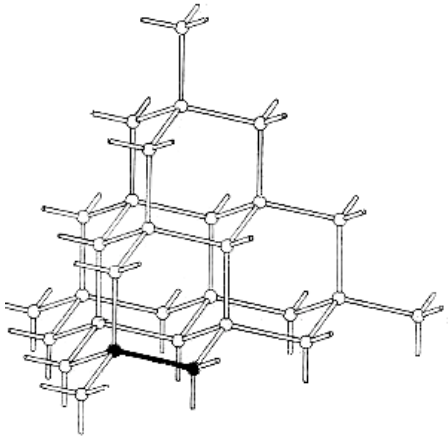


trans

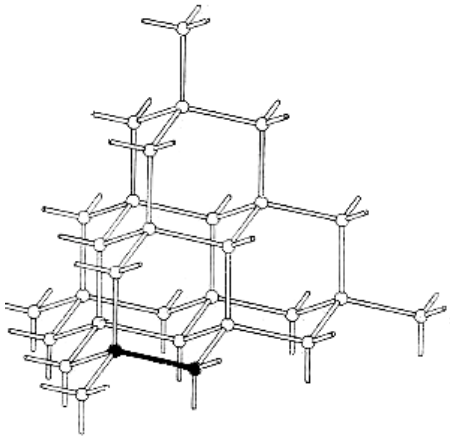
b) (5 min) The figure at the right is from a paper published in 1918. State what the figure shows, and explain briefly how this paper relates to the publications of Hermann Sachse in the early 1890s.



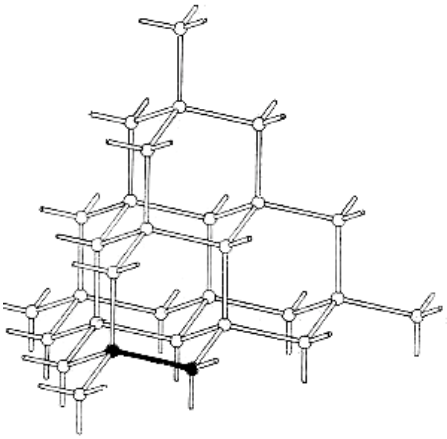
c) (5 min) Here are three copies of the figure above with one bond darkened. **Darken 10 more bonds in each of the first two figures** to show C-C bonds of idealized conformations for *cis*- and *trans*-decalin. (The third is a spare).



cis-decalin



trans-decalin



(for emergency use)

d) (3 min) Draw **Newman projections** to show the arrangement of substituents on the **central pair of carbons** of ***cis*- and *trans***-decalin. (Use H for hydrogen and R for CH_2)

e) (5 min) Use your knowledge of the energy difference between the conformational isomers of normal **butane** to **estimate the energy difference between *cis*- and *trans*-decalin.** (explain briefly)

f) (5 min) The experimental **heat of formation** of *cis*-decalin is –52.5 (±0.2) kcal/mole; that of *trans*-decalin is –55.1 (±0.2). Explain what **experiments** were necessary to determine these numbers.

g) (8 min) Chem3D was used to construct **"idealized"** structures for the decalins (**normal bond distances and angles**). Then it was used to minimize the energy of each isomer. The table below shows the total strain energy (kcal/mole) for idealized *cis* isomer and for the energy-minimized versions of both *cis* and *trans* isomers, followed by the contributions to these energies.

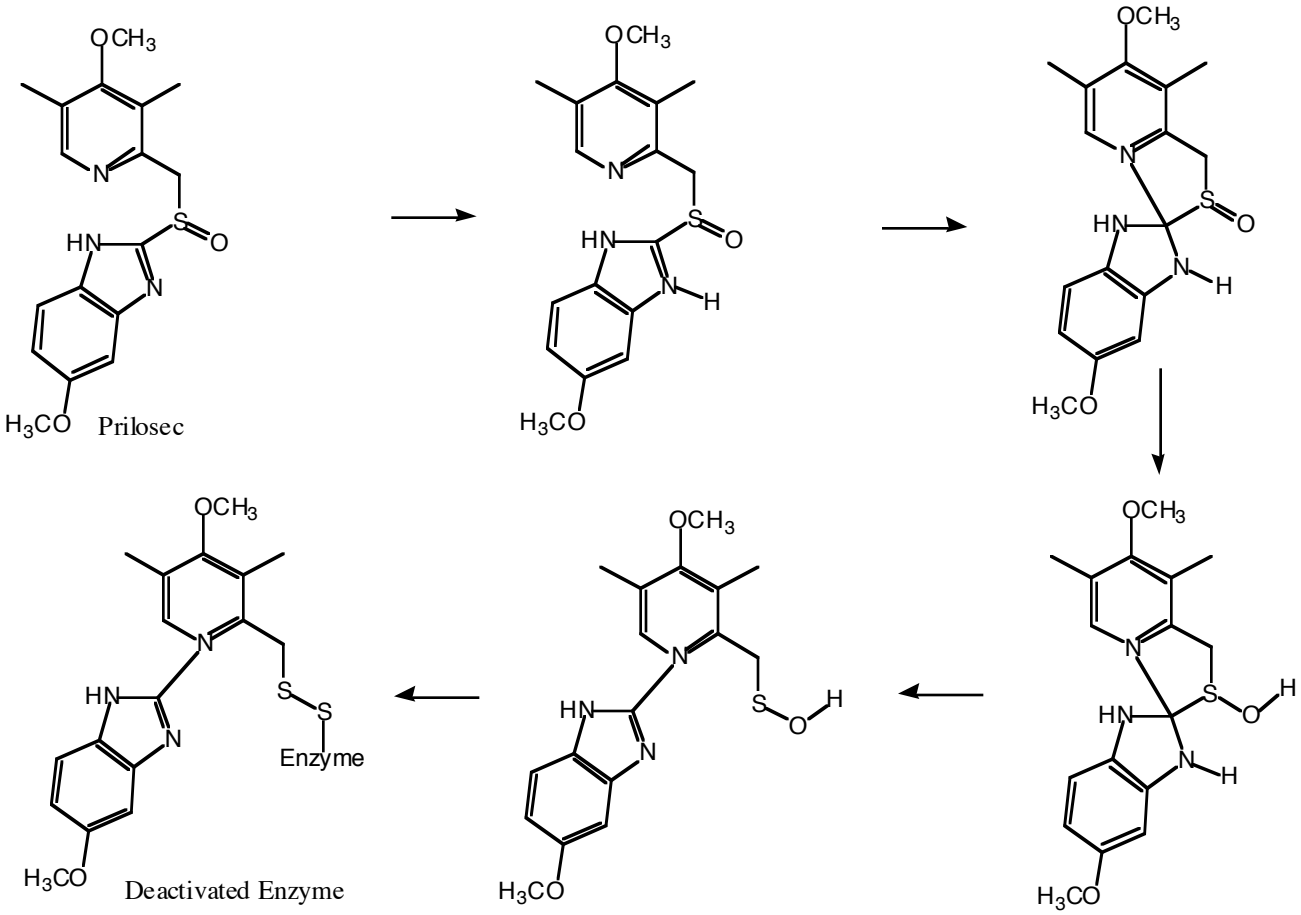
Decalin Model	"Source" of Energy → Total Energy			Bond Stretch			
idealized *cis*	26.3	9.0	0.0	0.0	0.0	5.3	11.9
minimized *cis*	14.1	-2.4	0.2	0.8	1.4	5.6	8.5
minimized *trans*	11.4	-2.6	0.2	0.7	0.7	4.2	8.3

The column for bond stretching energies is labeled. **Complete the top row** by entering an appropriate label for each of the other columns.

Comment very briefly on the **magnitude and direction** of each change in component energy **between the second and third rows** (*i.e.* what happens to minimize the energy of *cis*-decalin, and why?).

4. Prilosec

a) (13 min) The following partial scheme shows how the proton pump inhibitor prilosec may function in cells of the stomach lining to tie up the enzyme that turns on production of HCl. **Complete the scheme** by adding other necessary **reagents, charges, relevant unshared pairs, and carefully drawn curved arrows** to show the making or breaking of each bond that changes.



b) (4 min) Explain why one N is more reactive that the other two in the first step of the scheme above.

c) (4 min) Explain why one C=N group is more reactive that the other in the second step of the scheme above.

d) (4 min) Explain why the S-O bond is reactive in the last step of the scheme above.

e) (3 min) When it was proposed to prepare esomeprazole as a potential drug, there was concern that it would be no different from racemic prilosec, because of the mechanism above. Explain.

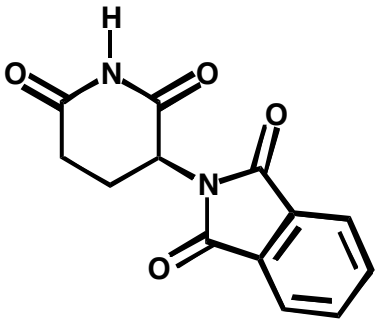
f) (9 min) Three completely different techniques were used to prepare esomeprazole (Nexium) as a single enantiomer. Explain each technique being sure to **say what initial substance** provided the bias that led to a single enantiomer.

i) For preparing a few mg for testing configurational stability

ii) For preparing some hundreds of mg for biological testing

iii) For preparing large quantities for sale as a drug

5. **Thalidomide**



This drug has the structure shown with two "imide" groups (O=C-NH-C=O).

a) (5 min) **List factors** that would favor a coplanar structure for the three bonds to N in an imide, **and** those that would favor a pyramidal structure, and **explain which** structure you expect to occur, perhaps mentioning an analogous compound.

b) (4 min) Explain how you might use infrared spectroscopy to test whether the H attached to N lies in or out of the local molecular plane in thalidomide.

c) (5 min) Modify the structure shown above so that it unambiguously represents (R)-thalidomide. (Explain your thinking for partial credit in case of error)

Researchers who studied interconversion of the enantiomers of thalidomide in human blood reported that the rate for R→S is 0.17/hour, while that for S→R is 0.12/hour.

d) (2 min) Why are these rates particularly interesting for medicine?

e) (4 min) The faster rate for R→S suggests that there should be about 1.4 times as much S as R at equilibrium. **Circle** the most likely value for the excess energy of R over S (in kcal/mole)in the following list: 0.01 , 0.05 , 0.2 , 0.8 , 3 , 8 and **use an equation to explain** your choice.

f) (3 min) **Explain** whether it is conceivable for the R and S isomers to differ in energy in and out of the body.

6. (6 min) Define each of the following terms:

Anti-bonding Orbital

Bürgi-Dunitz Angle

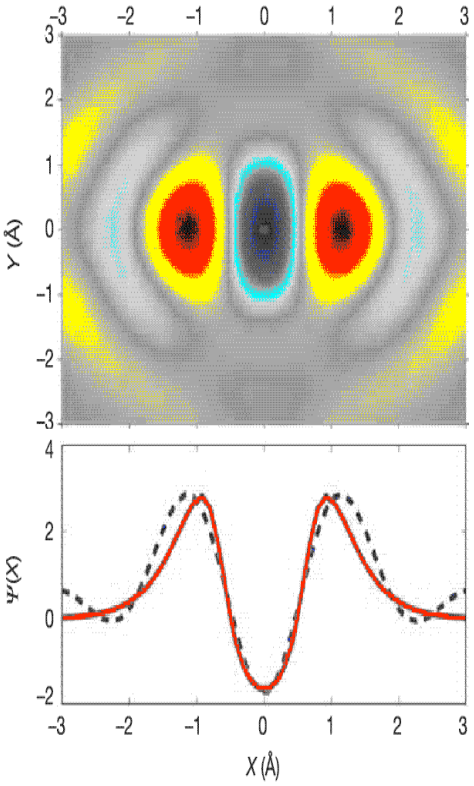
Correlation Energy

7. (2 min) What is typically given, and what to find, in a chemical quantum mechanics problem?

8. This week's issue of *Nature* (vol. 432, p. 867) reports a surprising new experiment that is said to determine the **shape and relative signs(!) of a single molecular orbital**. The figure on the right shows a slice through an orbital of the N_2 molecule as measured experimentally in this way. To interpret the Å scale, **NOTE that the N-N distance in N_2 is 1.09Å**

[The original figure is colored with the dark central blob shades of blue and the flanking "eyes" shades of red to denote the wave function's negative and positive signs, respectively. The lighter surrounding features are probably insignificant beacause of experimental error.]

The lower graph, with the same horizontal scale, plots the MO wave function ψ along the Y = 0 line of the upper graph. The dashed line is experimental, and the solid line is the result of an MO calculation.



a) (4 min) How does this picture differ from what is available from **x-ray** diffraction? (Ignore the difficulty of preparing a crystal of N_2).

b) (2 min) What **atomic orbitals** of nitrogen seem to dominate in making up this MO?

c) (4 min) At the extremes of the lower plot, the calculated (solid) wave function seems to approach Ψ=0 exponentially, while the experimental (dashed) curve has extra wiggles. Explain which behavior makes more sense in terms of reasonable kinetic and potential energy for an electron in this orbital.

d) (4 min) This orbital is said to be the HOMO of N_2. If so, **explain where in the top figure** you would expect H^+ to add to the molecule, **and** whether protonation should make the N–N distance **longer or shorter**.