Chemistry 125 Seventh Examination Answers **April 5, 2010**

Average Score 74.5/100 1/3 > 83 2/3 > 71
Three Exams 232.9/302 1/3 > 251 2/3 > 221

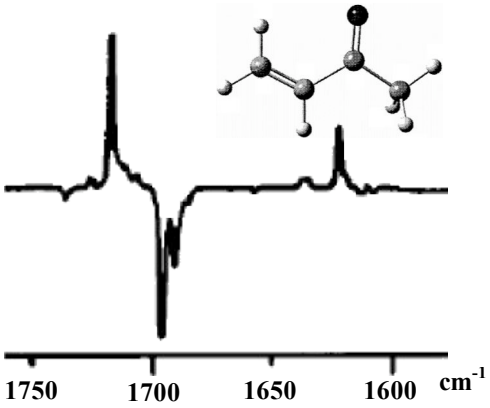
1. (3 min) **Explain** which electronic transition should be easier to achieve by interaction with light of the appropriate wavelength: *1s* to *2s* or *1s* to *2p*.

The electric field of light cannot mix *1s* with *2s*, because this mixing does not generate an electric dipole by shifting the average position of electron density relative to the nuclear position (it just makes the electron density "breathe").

Mixing *2p* with *1s*, however, shifts electron density to one side of the nucleus, creating an electric dipole that interacts with light's electric field.

(Lecture 56)

2. (5 min) The following ***difference*** IR spectrum was obtained after irradiating a sample of methylvinylketone at 308 nm for 2.5 hrs. at 15K . **Describe the normal modes** corresponding to the three largest peaks (2 positive, 1negative).

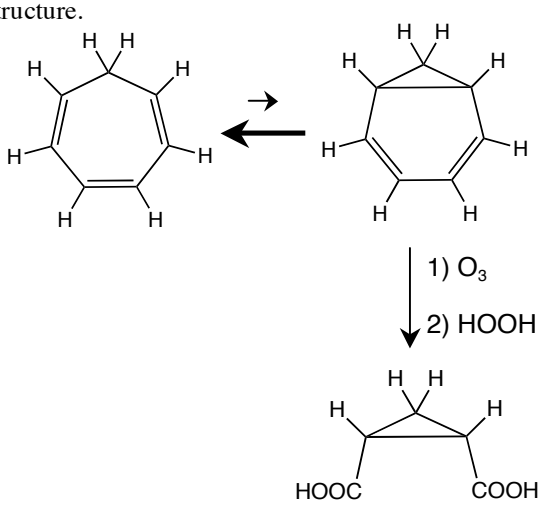


The positive peaks are due to coupled vibration of the C=O and C=C bonds in the molecule shown (with the groups coplanar and *syn* across the single bond, *i.e. s*-syn). The high-frequency mode (~1718 cm^{-1}) is mostly C=O vibration, while the low-frequency mode (~1623 cm^{-1}) is mostly C=C. [These peaks grow during irradiation because the *s-syn* conformer is formed at the expense of the *s-anti* conformer.]

The large negative peak (~1696 cm^{-1}) is the mostly C=O mode (coupled with a little C=C) of the *s-anti* conformer, which is destroyed by irradiation. [The mostly C=C mode is calculated to come at about 1735 cm^{-1}, but it is very weak because the C=O dipole change is largely canceling the C=C dipole change in this mode. The mostly C=C peak of the *s-syn* conformer was reinforced by the C=O vibration.]

(Lecture 57)

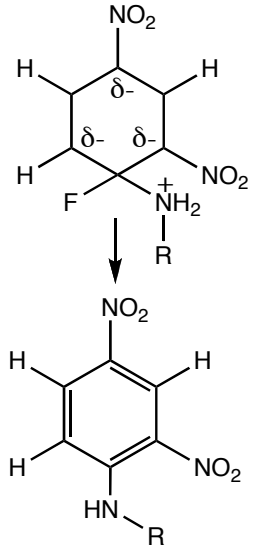
3. (5 min) **Explain how a chemical reaction was used** to assign (erroneously) the "cyclopropane diene" structure shown below, **AND how NMR proved** that the molecule had a different structure.



Ozonolysis/oxidation converted the compound into cyclopropane-1,2-dicarboxylic acid, which supported the "cyclopropane diene" (also called "norcaradiene") structure, but integration of the proton NMR spectrum showed a 3:1 ratio of vinyl to alkyl protons. Thus there must be an equilibrium in which cycloheptatriene predominates, but there is a minor amount of norcaradiene, which must be much more reactive with ozone.

(Lecture 59)

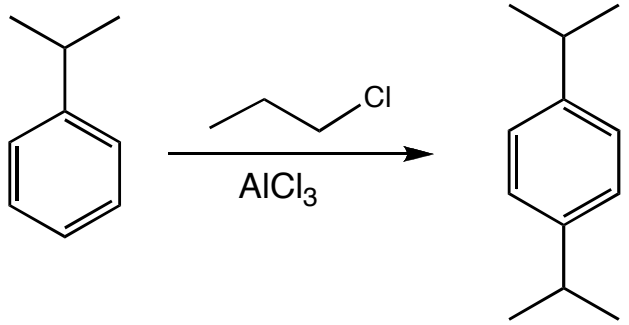
4. (5 min) **Explain three different ways** in which 2,4-dinitrofluorobenzene is perfectly suited for the purpose to which Frederick Sanger applied it (winning Nobel prize). [It would help to draw the reaction intermediate and product.]



1) Electron withdrawal (both sigma and pi) by the two nitro groups in the positions that bear negative charge (participate in the low LUMO) in the pentadienyl anion intermediate help accelerate its formation during nucleophilic aromatic substitution by the high HOMO of an amine group at the terminus of a peptide.
2) Electron withdrawal by the fluoride group also makes the pi-system easy to attack, and because the attack is the rate-limiting step, the overall reaction is faster than with a halogen that is less electron withdrawing but a better leaving group.
3) The product is yellow, which makes it easy to visualize in 2D-chromatography. [The color is due to an aniline with *o,p*-nitro substituents.]

(Lecture 63)

5. (4 min) Give an example of a Friedel-Crafts alkylation with Lewis-acid catalysis that proceeds with *o,p*-orientation and rearrangement.



[There would probably be some unrearranged n-propyl substitution and para should dominate over ortho substitution because of steric hindrance.]

(Lecture 62)

6. (4 min) **Define** a "90° pulse", and **tell why is it required** to make protons "sing out" their precession frequency.

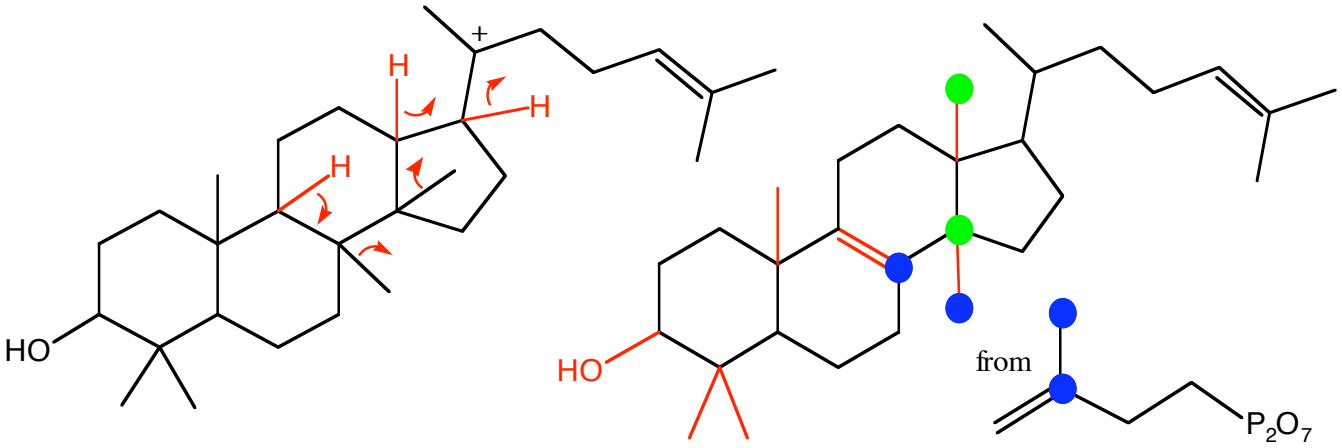
A 90° pulse is irradiation at the precession frequency of the nuclei in question, whose oscillating magnetic vector is perpendicular to the applied magnetic field, that is applied to the sample long enough to rotate the average magnetization of the nuclei from parallel to perpendicular to the applied field. [This is easiest to visualize in the rotating frame. Note that achieving this reorientation requires absorption of energy from the radio-frequency light.]

Without applying this kind of pulse, differences in the precessional phase of the nuclei result in cancellation of the oscillating horizontal component of the average magnetization of the precessing nuclei, which means that no net signal is being broadcast by the sample.

(Lecture 58)

7. (6 min) The cation below left is an intermediate in the synthesis of lanosterol from isopentenyl pyrophosphate.

A) **Elaborate the diagram** (include **curved arrows**) to show the multistage rearrangement that happens next, **and complete the structure on the right** to show its **product**.



[Too many answers included random curved arrows that did not denote electrons moving from one bond to establish a new bond involving a site that formerly housed the low LUMO of a cation. Consider carefully where each curved arrow starts and ends in the above diagram. Note, for example, how the arrows denoting the initial hydride shifts differ from the one denoting the ultimate proton loss.]

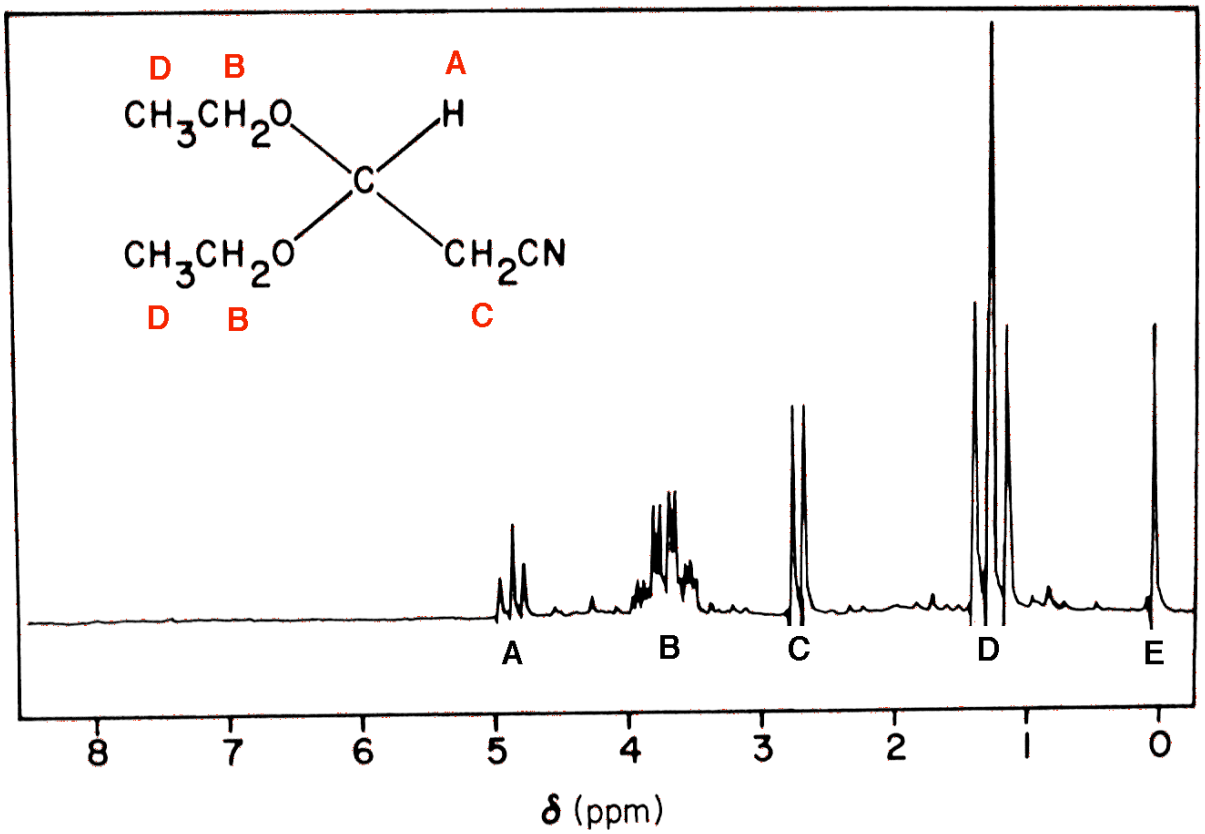
B) **Describe** briefly how an experiment involving NMR was conducted to provide strong confirmation of your mechanism.

Carrying out the biosynthesis beginning with a sample of **dilute double C-13 labeled** isopentenyl pyrophosphate (IPP) shows which pairs of bonded carbons maintain their bond from starting material to product. The **double** label is so that the strong C-13 peaks will show doublet spin-spin splitting in the proton-decoupled CMR spectrum when initially labeled carbons remain bonded to one another. The labeled molecules are **dilute** so that C-13s will not likely be bonded to other C-13s if they originated in different IPP molecules. The two methide shifts in the above mechanism predict, correctly, that the CMR signals for the rearranged methyl groups (and for the carbons from which they migrated) will appear as singlets in the proton-decoupled spectrum of lanosterol. The blue dots in the above structure show a pair of C-13 that came from the same IPP molecule, but that no longer split one another because they are no longer directly bonded. So do the green dots, where

the labels came from a different IPP molecule, and thus appear in a different lanosterol molecule that the C-13 atoms denoted by blue dots.

(Lecture 61)

8. Here is one of the most embarrassing NMR spectra of all time. It was published in 1982 in a paper whose author list included a Chemistry Nobel Laureate (who may not have played a very big role in writing the paper). The spectrum was captioned "Figure 1. Proton magnetic resonance spectrum of 3,3-diethoxypropanenitrile showing the existence of the two conformers." The **paper contended** that unexpected doubling of certain peaks in the spectrum showed that the molecule existed as a mixture of **two different conformational isomers**.



A) (8 min) Each significant signal in the spectrum is labeled with a letter. **Write the appropriate letter above each proton** (or group of protons) in the structural diagram.

In a few words explain the **size, position, and multiplicity** of each of these signals:

A Size: 1 H Position: shifted downfield by electron withdrawal of two oxygens on C
Multiplicity: 1:2:1 triplet split by two "C" protons on next adjacent carbon

B Size: 4 H Position: shifted downfield by electron withdrawal of one oxygens on C
Multiplicity: 1:3:3:1 quartet split by three "D" protons on next adjacent carbon (also "unexpected doubling", meaning that the pattern is more complex that a simple quartet, each line of which is at least doubled. Note that the splitting cannot be some remote interaction with H_A, because the H_A signal is a clean triplet and does not show the same magnitude of splitting by the 4 H_B protons)

C Size: 2 H Position: shifted downfield by electron withdrawal of cyano group (maybe by diamagnetic anisotropy of this group as well)
Multiplicity: 1:1 doublet split by the "A" proton on next adjacent carbon

D Size: 6 H Position: normal 1-2 ppm for methyl group of alkane
Multiplicity: 1:2:1 triplet split by two "B" protons on next adjacent carbon

E Size: from a separate molecule, TMS, added as reference for chemical shift, thus size of peak depends relative to those of the sample depends on how much TMS was used (not much)
Position: Reference of ppm scale – rather high field because Si to which methyls are attached is less electronegative than carbon, so e-density on CH_3 is unusually high.
Multiplicity: Singlet – all methyl protons equivalent

B) (1 min) Which of the five patterns has the **"unexpected doubling"** that suggested the existence of two conformers to the authors? **B** (see above)

C) (2 min) The spectrum was measured at room temperature with a 60 MHz spectrometer. What is the **approximate magnitude** of the "unexpected" doubling **in Hz**?

The scale at the bottom of the spectrum is in parts per million (ppm). One ppm of 60 MHz is 60 Hz. The unexplained doubling separates peaks by a small fraction (less than 1/10) of 60 Hz, perhaps 2 or 3 Hz.

Another point of comparison is the splitting of the methyl triplet, which is normally about 7 Hz. The doublet splitting in B is a little less than half of this value, so again about 2-3 Hz.

D) (5 min) If the authors were correct, what could one say about the **rate of interconversion** of the two proposed conformational isomers from having observed this doubling, and what would this say about the **barrier** (kcal/mole) to interconversion? **How large would you guess** such a conformational barrier should be?

If there are two conformational isomers, each giving one of the quartets which overlap to give the doubling of the quartet, they must be interconverting slowly enough that the peaks for each conformer remain sharp.

Remember that broadening and coalescence occur when the frequency of interconversion is comparable to the frequency separation of the corresponding peaks in the spectrum. Since the separation of the peaks is a few Hz (see part C), that is a few per second, the frequency of interconversion must be much less than 1 per second if the peaks are to remain sharp rather than broadening and coalescing to a single average peak.

So the **rate constant, k, for the conformational isomerization must be less than 1/sec**.

How high a barrier would give a k of 1/sec?

Remember that $k \sim 10^{13}$ /sec * $10^{-3/4 \ * \text{barrier}}$

If $k \sim 1$/sec, then 10^{13} is about equal to $10^{3/4 \ * \text{barrier}}$

Or barrier ~ 4/3 * 13 = 17 kcal / mole

Since the rate is slower than 1/sec, **the barrier must be greater than 17 kcal/mole**.

This is what makes the claim of conformational isomerism so ludicrous. In such simple molecules barriers to conformational change (*e.g. anti*- to *gauche*-butane) are only 3 kcal/mole or so, 5 or 6 times smaller than what would be necessary to explain this doubling in terms of slow interconversion. Even the chair-chair flip of cyclohexane, which you will remember requires substantial bond angle deformation, has a barrier of only about 11 kcal/mole (measured by NMR).]

E) (2 min) Suggest a more probable interpretation of the doubling based on **stereotopicity** relationship between the two protons within each of this compound's methylene groups.

The two hydrogens on the CH_2 group adjacent to CN (the ones labeled "C") are enantiotopic. One can imagine a mirror plane passing through H-C-C-CN on the right of the molecule, and each of these two protons lies in one of these mirror-image environments. Since these hydrogens are enenatiotopic, they have the same chemical shift and their magnetic interaction does not influence the spectrum observed ("they do not split one another"). The only splitting is by the lone proton ("A") which splits the "C" signal into a clean doublet.

By contrast, there is no mirror plane that would pass through the carbon and oxygen atoms of one ethoxy group (C-C-O-C), so the protons of its CH_2 group do not have mirror image environments, they are **diastereotopic**, just plain different in environment. (The same is true for the other CH_2 group.) One trick for seeing that they are diastereotopic is to name the configuration that would result by promoting the priority of one (or the other) of the two hydrogens of the CH_2 group. Doing so would not only make the CH_2 carbon a chiral center**, it would also make the central carbon bearing two oxygens a chiral center** because the two ethyl groups would no longer be equivalent in priority. So diastereomers are involved. [Of course this is a subtle point – as the question warned.]

Since the ethoxy CH_2 protons are in different environments, they have slightly different chemical shifts – hence the "anomalous" doubling of the quartet "B". It is in fact **two quartets with slightly different chemical shifts.**