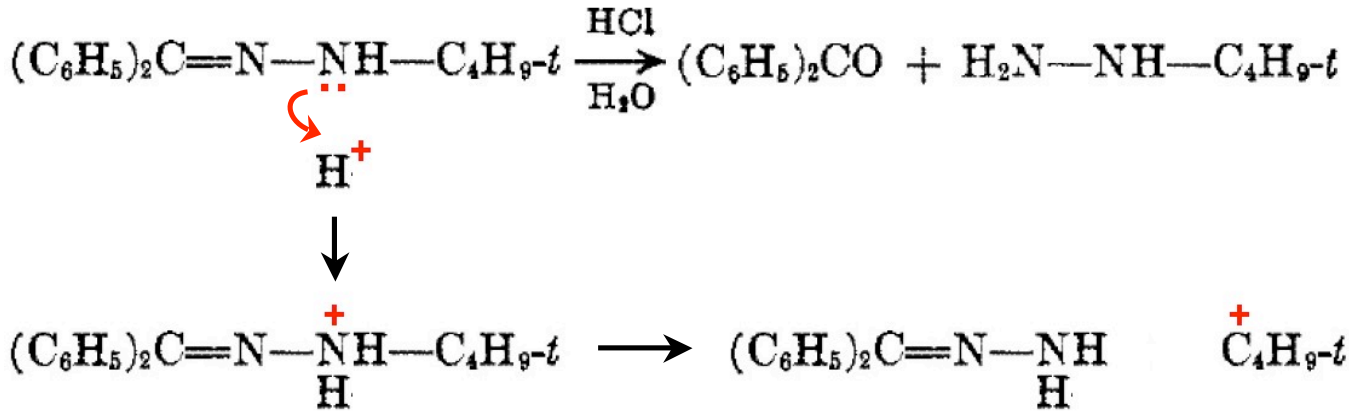
Chemistry 125 Seventh Examination Answers **April 8, 2009**

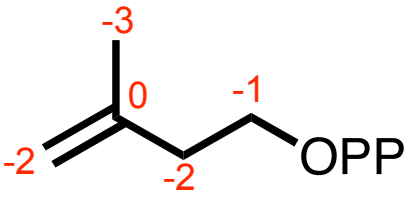
	This Exam	Sum of 3 Hr. Exams +6 Wikis
Average	73.8	220
1/3 of scores greater than	82	238
2/3 of scores greater than	72	212

1. (2 min) Jo-David Fine had fits trying to prepare t-butylhydrazine by repeating the following reaction from the chemical literature. Show what actually happened instead. Use **curved arrows** (**two steps will suffice**).



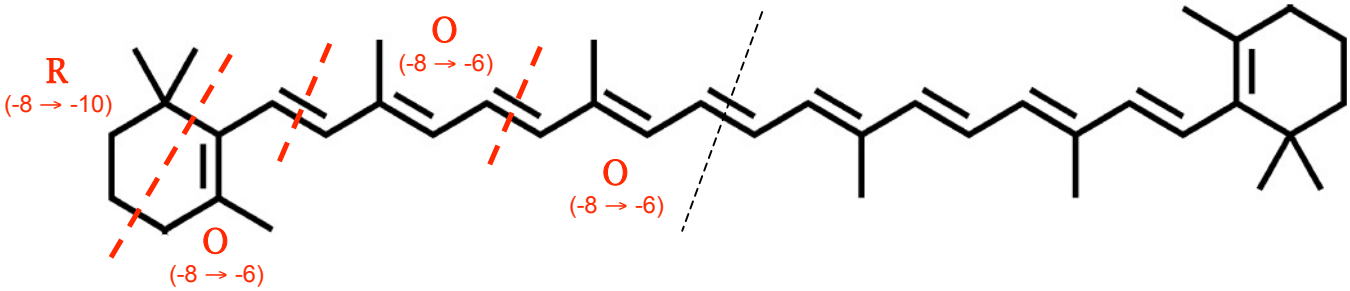
The relatively stable t-butyl cation is lost. Ultimately it adds water to become t-butanol or loses a proton to become isobutylene.

2. The structure below is β-carotene. A dashed line is drawn in the structure to show that the molecule was assembled by head-to-head dimerization of units that were assembled from isopentenyl pyrophosphates (IPP, show on the right).



A. (2 min) Label every carbon of IPP with its oxidation state number.

B. (3 min) Draw **additional dashed lines** to divide the ***left half*** of β-carotene into units from different IPP molecules, Then **label each** unit to show whether overall it was oxidized (O), reduced (R), or neither (N) relative to IPP.



C. (1.5 min) Not surprisingly β-carotene is in the family of "carotenoids". It is also a "tetraterpene". Briefly explain the meaning of the term "tetraterpene".

Terpenes are "essential" oils of formula $C_{10}H_{16}$ that derive from isoprene (2-methyl-1,3-butadiene, C_5H_8). A tetraterpene proper would have the formula $C_{40}H_{64}$.

[This oxidized form is $C_{40}H_{56}$, but is still called a tetraterpene, because it derives from 8 isoprene units.]

3. The following pairs of numbers are relevant for distinguishing spectroscopically between certain (Z) and (E) alkenes:

967 *vs.* 710 cm^{-1} **0-12 *vs.* 12-18 Hz**

A. (2 min) In each pair circle the member that indicates a (Z) alkene.

B. (6 min) Choose **ONE** of the pairs of numbers and explain in detail **WHY** the isomers differ in this direction.

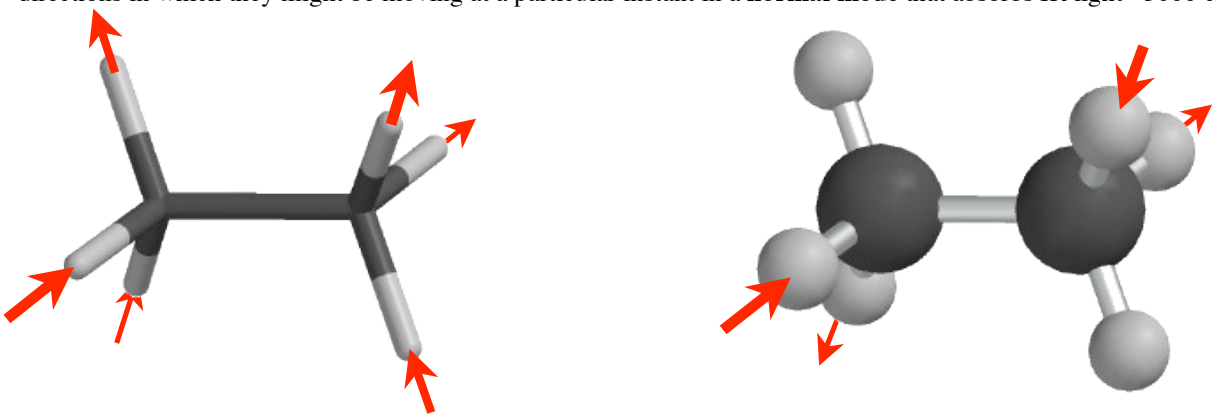
IR: This distinguishing pair of IR peaks is due to simultaneous out-of-plane vibration by H atoms attached to adjacent carbons on the C=C bond. In the two normal modes for each isomer, the two H atoms are both moving simultaneously, that is, their vibrations are coupled. In order to generate a change in dipole moment on vibration, and thus for the normal mode to be active in the IR spectrum, the motion of the two H atoms must be parallel, not anti-parallel. For the (E)-alkene (trans) this motion twists the double bond, reducing pi overlap and contributing extra resistance to the vibration. Thus the (E) isomer vibrates at higher frequency. For the (Z)-alkene the skeleton folds like a book instead of twisting, so the pi bond remains intact, and vibration is easier and at lower frequency.

NMR: Spin-spin coupling between protons attached to adjacent carbons depends on the overlap between the orbitals of the relevant C-H bonds. One might suspect that overlap would be greater between C-H bonding orbitals that point more or less the same direction, but in fact overlap is greater between trans C-H bonds on C=C. This "anomaly" arises because, although s-s and p_σ-p_σ overlap between the atomic orbitals of adjacent carbons is indeed larger for the cis C-H bonding, s-p_σ overlap is dominant and is larger for trans C-H bonding. (see illustration in frame 7 of Lecture 64)

4. Consider the vibrational normal modes of ethane.

A. (2 min) How many such normal modes should the molecule possess? 8 atoms, 3N-6 = 18 normal modes

B. (3 min) **Draw arrows** on appropriate H and/or C atoms or bonds in the structure below (use either or both) to show the directions in which they might be moving at a particular instant in a **normal mode** that absorbs IR light ~3000 cm^{-1}.

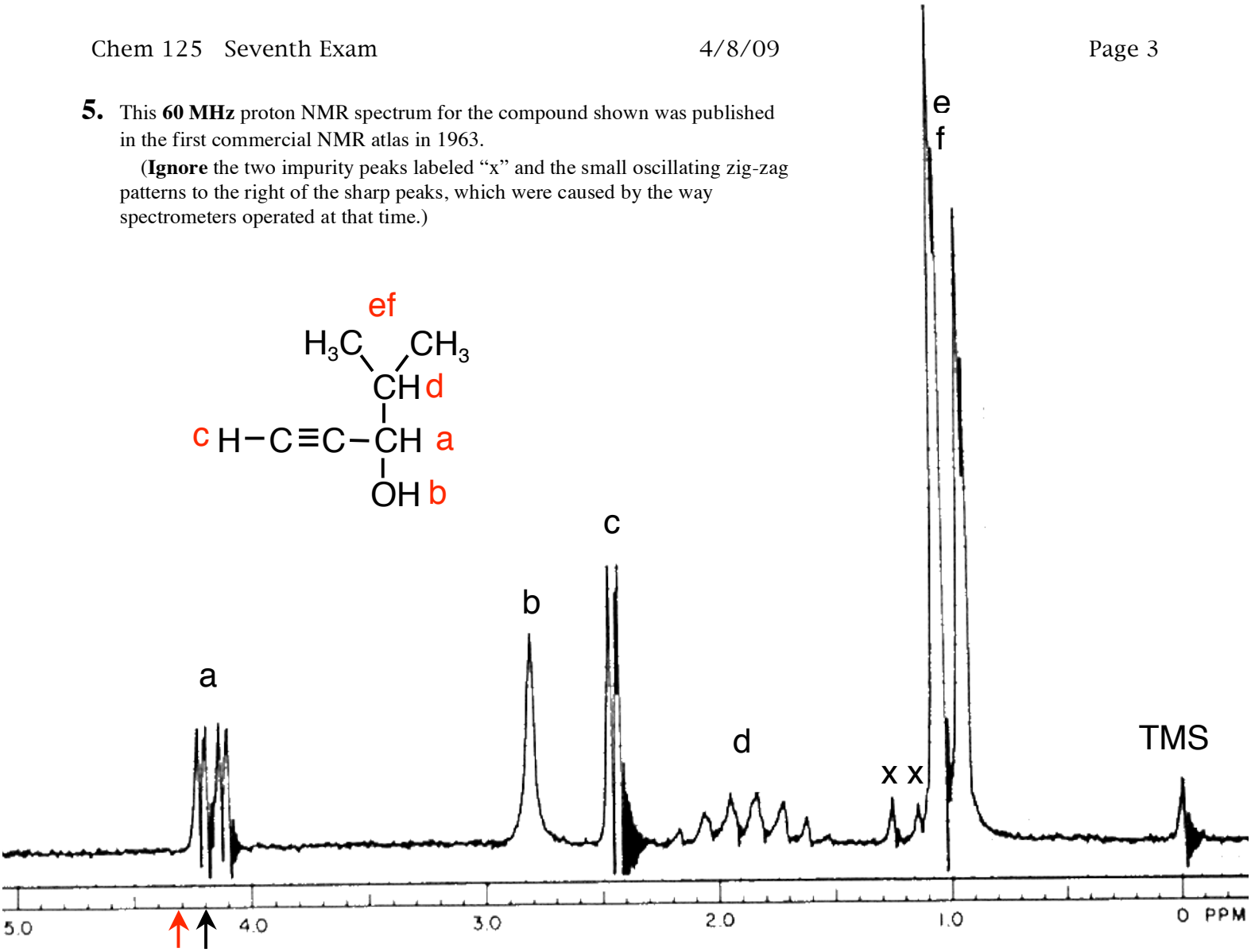


Vibrations near 3000 cm^{-1} involve C-H stretching, in which the dominant motion is of the light H atoms (the C atoms move ~1/12 as much in the opposite direction). IR-active normal modes must involve parallel motion of opposite H atoms, as shown above.

(Since there are 6 C-H bonds, there are 6 normal modes composed of C-H vibrations. Two of the three IR-active modes are illustrated above. In the third active mode, four C-H bonds stretch while two shrink; it comes at slightly lower frequency.)

5. This **60 MHz** proton NMR spectrum for the compound shown was published in the first commercial NMR atlas in 1963.

(**Ignore** the two impurity peaks labeled "x" and the small oscillating zig-zag patterns to the right of the sharp peaks, which were caused by the way spectrometers operated at that time.)



A. (1 min) **Draw a second arrow** beneath the ppm scale that is **7 Hz** from the arrow at 4.2 ppm.

B. (5 min) **Label** the protons in the **chemical formula** with the letters **a-f** to correspond to the labeled groups of peaks.

C. (3 min) Explain why the **chemical shift** of the peak labeled "**b**" is strongly **dependent on concentration** and **temperature**.

This is the OH signal. The proton is rapidly exchanging among differently hydrogen-bonded environments and thus appears at the average of their chemical shifts. The equilibrium distribution of environments changes with concentration (higher concentration : more H-bonding) and temperature (higher temperature : less H-bonding).

D. (3 min) Explain the **spin-spin splitting** of the proton at "**a**".

Proton "a" is split into a double doublet first by proton "d" (normal 7 Hz splitting for protons on adjacent carbons) and second by proton "c" (small 2 Hz splitting through 3 carbons. Normally such splittings are smaller and not observed, but here there is unusually strong electronic communication through hyperconjugation with the pi orbitals of the acetylene). Note that there is no splitting by the OH proton "b" because that proton is rapidly exchanging and one sees the average value of zero.

E. (3 min) **Describe TWO** competing factors that determine the **chemical shift** of the peak labeled "**c**".

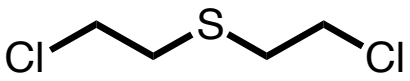
It is shifted downfield by *sp* hybridiztion of the acetylenic carbon (electron withdrawal), but upfield by diamagnetic anisotropy of the triple bond (H above the circulation that is allowed when CC is parallel to magnetic field).

[Incidentally, the methyl doublets e and f are diastereotopic and have very slightly different chemical shifts.]

6. (2.5 min) Explain why the magnetic fields used for medical MRI must be very different from those used for chemical NMR. (Don't worry about their physical size.)

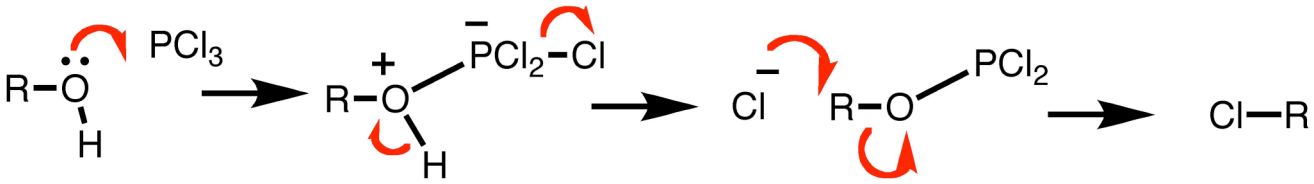
For MRI the applied magnetic field must be inhomogeneous, so that one can tell, by the precession frequency, where the relevant protons are located in 3-D space. For chemical NMR the applied field must be homogeneous (within a small fraction of a part per million) so that the only difference between protons is due to slightly different fields ***within*** the molecule due to chemical shift and spin-spin splitting. There must be no field difference due to location in 3-D space, which would swamp the small "chemical" differences.

7. In 1886 German chemist Viktor Meyer reacted 1,5-dihydroxy-3-thiapentane with PCl_3 to form 1,5-dichloro-3-thiapentane, which ultimately became known as "mustard gas", one of the most notorious chemical warfare agents.



It was used first at Ypres in July 1917 against British soldiers. Although outlawed internationally in 1925, it was used by Iraq against Iran in the 1980s and perhaps by the Sudanese army in the 1990s. Mustard gas functions by dissolving readily in body lipids and then alkylating biological nucleophiles such as R_2NH or ROH, deactivating them and releasing HCl.

A. (1.5 min) Draw a mechanism with curved arrows to show how PCl_3 converts an alcohol to an alkyl chloride.



B. (6 min) Give three fundamental reasons to explain why mustard gas is a much faster in alkylating a nucleophile like ROH than 1,5-dichloropentane is.

An episulfonium ion intermediate is formed rapidly by nucleophilic substitution of S for Cl. This reaction is faster than attack by ROH because:

1) S is a much better nucleophile than O (larger, more polarizable atoms stabilize S_N2 transition states)
2) The attacking S atom is pulled closer than van der Waals distance to the C-Cl sigma* bond being attacked because both groups are bonded to a common C atom.
3) The probability of the S atom being in position to attack within the same molecule is much higher than the probability of an O atom from a different molecule being in position (effective molarity)

The episulfonium ion intermediate is attacked rapidly by the nucleophile because:

1) Ring strain is being reduced as the three-membered ring is opened
2) Neutral RS is a good leaving group from the cationic intermediate

8. (3.5 min) Explain briefly why dilute ^{13}C double labeling NMR experiments are useful for biosynthetic studies.

To discover how precursor molecules are transformed biologically into product molecules, it is of course valuable to know which carbon in the precursor goes where in the product. Because the magnetic isotope of carbon (^{13}C) is rare, only 1% of the product carbons normally appear in a ^{13}C-NMR spectrum. The peaks are weak. If precursor molecules are prepared with an artificially high abundance of ^{13}C in a particular position, the corresponding position in the product will appear as an unusually strong NMR peak.

If precursor molecules are prepared with two adjacent carbon atoms labeled, ^{13}C-^{13}C splitting will appear in the product spectrum, giving a double-doublet pattern for the pair of carbons. Splitting would also be observed from ^{13}C atoms that are adjacent by chance in the product, but if the double-labeled precursors are dilute, it is unlikely that ^{13}C atoms from different precursor molecules will appear adjacent to one another by chance in the same individual product molecule. If there is a strong double-doublet signal, one may safely conclude that that portion of the precursor molecule was incorporated intact into the product. If there had been a rearrangement that separated the labeled carbons, there would be no spin-spin splitting in the product, and a simple doublet pattern would be observed. (For an example see Slide 26 of Lecture 65.)