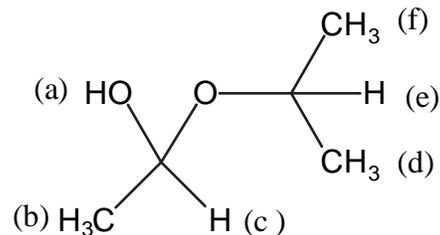


Chemistry 125 Seventh Examination Answers April 16, 2004

1. (3 min) **Name** the functional group in the molecule on the right **and** suggest **reagents and conditions** for its preparation (no mechanism necessary).

The functional group is hemiacetal (or, more loosely, hemiketal)

This hemiacetal is formed by reacting acetaldehyde with isopropanol using either acid or base catalysis (or by reacting the full ketal with water using acid catalysis).



2. (9 min) Sketch the proton nmr spectrum you would expect for the compound in Question 1. Say a few words about your selection of **chemical shift** and **splitting pattern** for each of the 6 labelled (sets of) protons.

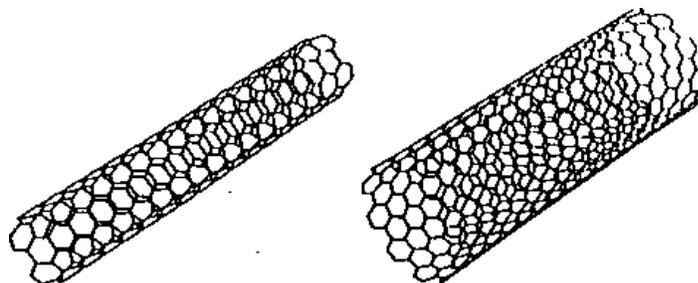
Group	Chemical shift	Splitting
a	almost anywhere (δ 1-6) depending on concentration and temperature (averaged H-bonding)	Probably no splitting (broad singlet) because of rapid OH proton exchange among molecules
b	slightly deshielded by two oxygen atoms on neighboring carbon. δ 1-2 (a real analogue is at δ 1.3)	1:1 doublet from single H on neighboring carbon (J about 7 Hz)
c	deshielded by two oxygen atoms on the same carbon δ 4-5 (a real analogue is at δ 4.7)	1:3:3:1 quartet from 3 H atoms on neighboring carbon (J about 7 Hz)
d	slightly deshielded by oxygen atom on neighboring carbon. δ 1 (a real analogue is at δ 1.1)	1:1 doublet from single H on neighboring carbon (J about 7 Hz)
e	deshielded by oxygen atom on the same carbon (but less than c) δ 4 (a real analogue is at δ 3.8)	seven line multiplet from 6 H atoms on neighboring carbons (J about 7 Hz)
f	slightly deshielded by oxygen atom on neighboring carbon. δ 1 (a real analogue is at δ 1.1)	1:1 doublet from single H on neighboring carbon (J about 7 Hz)

NOTE: d and f should have slightly different chemical shifts, because they are **diastereotopic**.

Note that your drawing should show approximately correct relative sizes of the patterns, as well as reasonable chemical shifts and correct multiplicity. The integrated total area for a, c, and e should be 1 proton each (meaning that the septet for e should have very small peaks), while areas for b, d, and f should be three times as large.

3. (9 min) Answer **ONE (1 only)** of the following TWO questions about NMR:

- A) Carbon “nanotubes”, are isomers of diamond or graphite, whose cylindrical walls are hexagons of carbon as shown on the right. A recent issue of the journal “Nature” reports that a magnetic field along the axis of such tubes causes electron circulation about the axis of the tube. These hollow cylinders can contain other molecules, such as a methane.



Explain how in a solution containing freely tumbling nanotubes and methane you might **distinguish methane molecules inside and outside the nanotubes by their NMR spectra.**

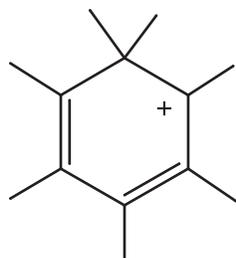
Point out an analogy with the curious chemical shift of the protons in acetylene.

If easy diamagnetic circulation of electrons is about the long axis of these nanotubes, then when the tubes are freely tumbling, the magnetic field due to diamagnetic circulation will not average to zero. The dominant effect will be when the tube is parallel to the applied field, and it will be such as to oppose the applied field inside the tube and reinforce the applied field outside the tube. Thus methane molecules within the tube should be unusually shielded, and their NMR signals should appear “upfield”, to the right, at small or even negative δ values.

The analogous effect due to the cylindrical symmetry of the acetylene triple bond, causes acetylenic protons to appear at much higher field than would be expected for a proton bonded to an sp -hybridized carbon atom.

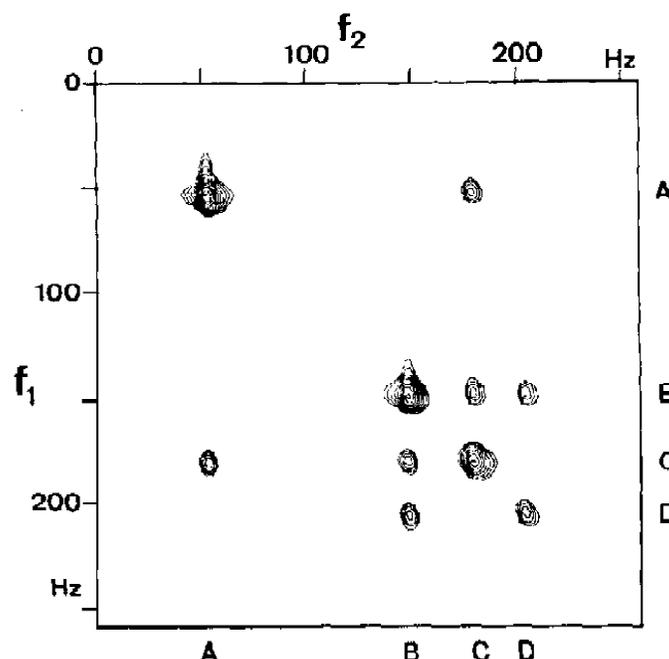
- B) Explain what this 2D NMR spectrum shows about “heptamethylbenzenonium” ion (Note that higher frequency denotes shift downfield from TMS)

The 2D NMR spectrum shows how a radio frequency signal that excites protons at one frequency influences the radio signal that emerges from the sample at the same, or a different, frequency.



Peaks on the diagonal show that exciting at a particular frequency influences the same frequency, which is not surprising, because the same protons in the same location are involved. Those at the highest two frequencies (C and D) are those that are least shielded because they are at locations where electron density is lowest (+ charge in resonance structures).

The most interesting features are the off-diagonal signals, which result because protons that have been excited at one frequency (one chemical location) emit at a different frequency (a different chemical location)

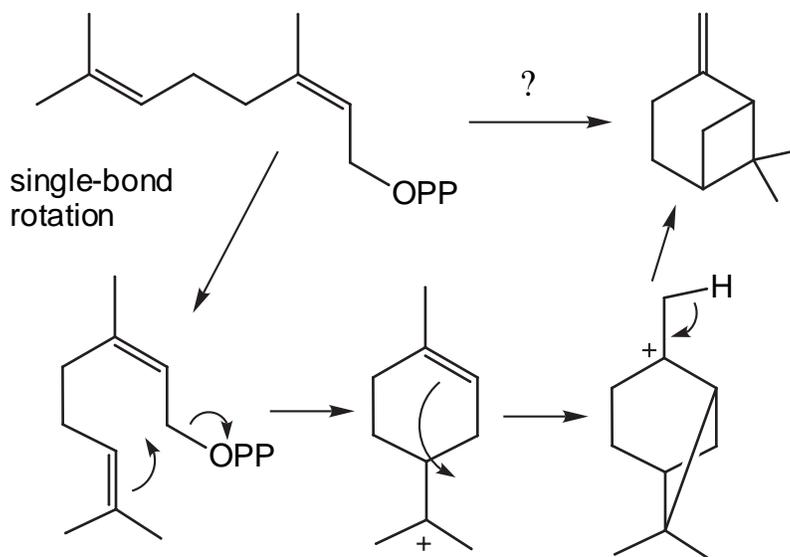


because of molecular rearrangement. Thus, for example, methide shift to the adjacent position leaves one of the original A (gem dimethyl) groups in a C position, which has a + charge in the resonance structure shown. It also changes one B methyl group into C and the other into D (and vice versa).

Thus, this 2D NMR spectrum confirms rearrangement by motion of one of the gem-dimethyl groups to an adjacent carbon. A different rearrangement would have given a different pattern of interchange (e.g. loss and readdition of the methyl group would give all possible cross peaks).

4. (9 min) Draw a detailed mechanism of **several steps** with carefully drawn **curved arrows** to show a plausible mechanism for converting neryl pyrophosphate to β -pinene.

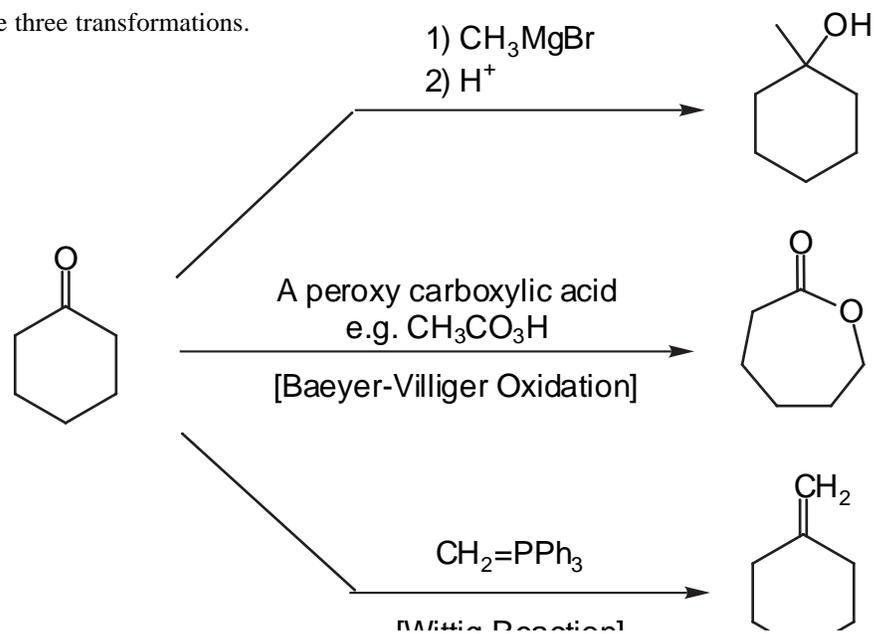
[The three steps are an internal S_N2 displacement of pyrophosphate by the alkene nucleophile (to generate the more stable tertiary cation version of the intermediate); addition of the carbon cation to the second alkene (to generate the more stable tertiary cation version of the intermediate); and loss of a proton from the methyl group next to the carbon cation (to generate the LESS stable, less substituted alkene product – presumably



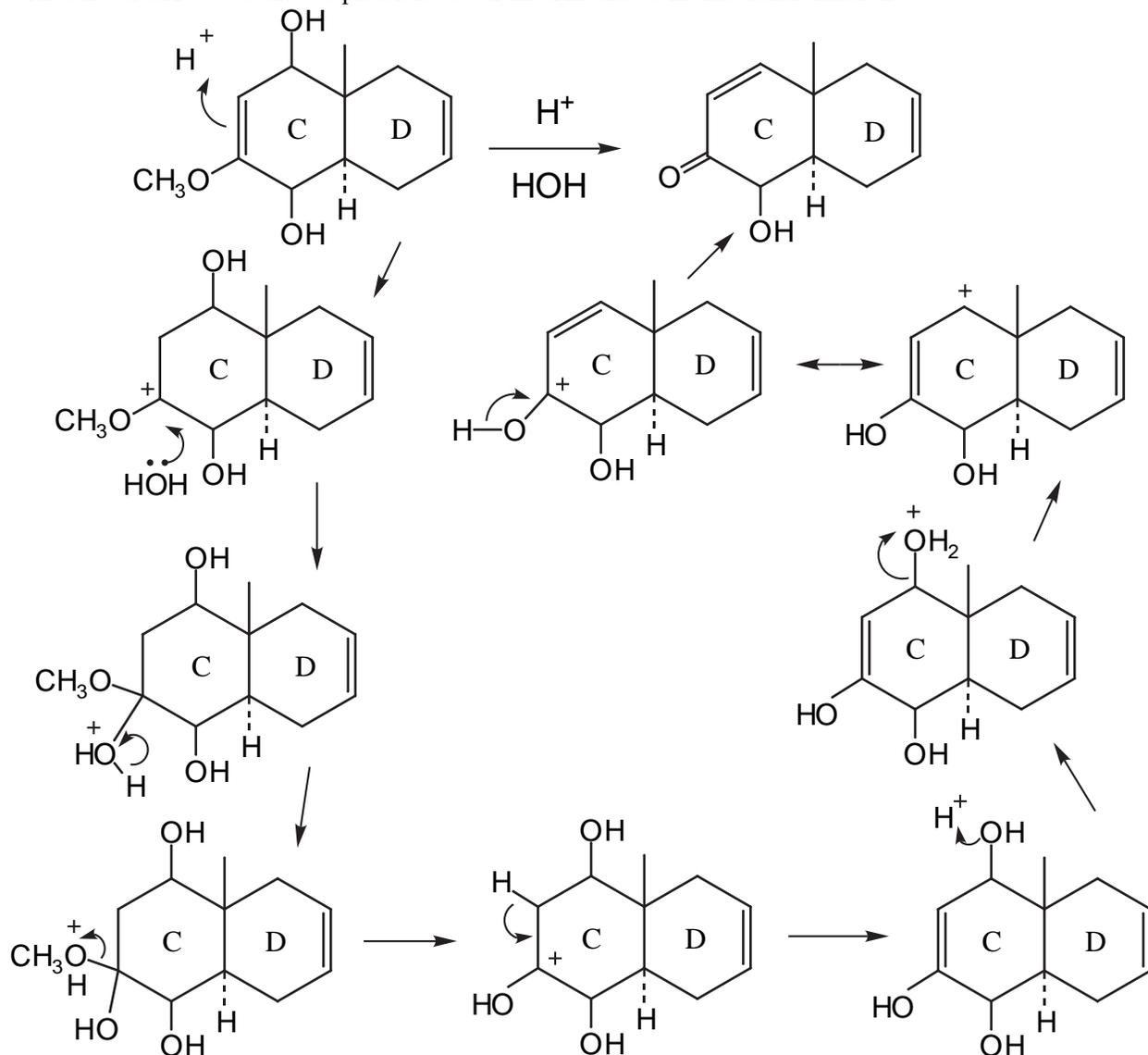
Nature has a properly situated base to extract this proton selectively). **Note** that β -pinene is chiral, because one of the carbons of the cyclobutane ring has two methyl groups, but the product structure as drawn does not specify the absolute handedness. Some answers included complicated and implausible, but unnecessary, steps to shift the methyl groups from one carbon to another. It is a good exercise to figure out which step of the mechanism establishes the chirality of the ultimate product.]

5. (6 min) Suggest **reagents** for each of these three transformations.

(No mechanisms necessary, just reagents)



6. (8 min). One step in Woodward's synthesis of cortisone involved the following transformation. Draw a mechanism with **curved arrows** to show a plausible **set of intermediates** in this transformation.



NOTE: it is possible to reverse the order of removing the OH and OCH₃ groups.

7. (6 minutes) Had protection not been necessary, Woodward might have been able shrink the size of ring D by two reactions. Complete the scheme below by drawing the **intermediate compound** for this transformation and the **reagents** involved in the two steps. (No curved arrows necessary, just one intermediate compound and the reagents. The squiggly line means we are ignoring the rest of the molecule.)

