

CEM 222

Exam 2

Dr. Berger

March 4, 2010

Name: **Answer Key**

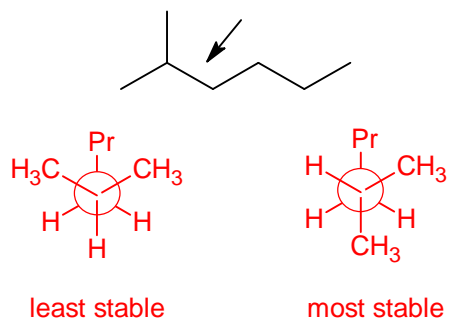
Please write and sign the pledge: *“I am unaware of any aid given or received on this examination.”*

This examination is worth 200 points. Please answer all questions as fully as possible. Partial credit will be given. This examination is closed book. You are expected to do your own work on this examination.

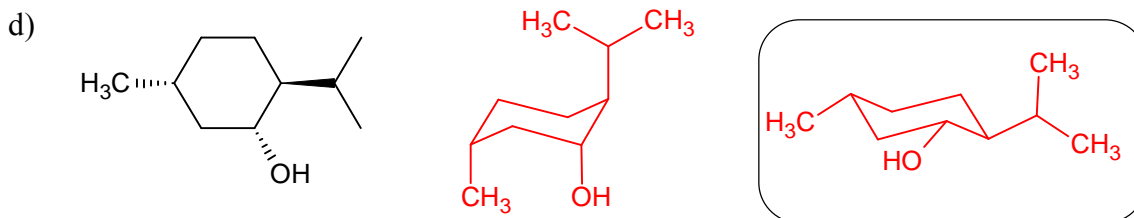
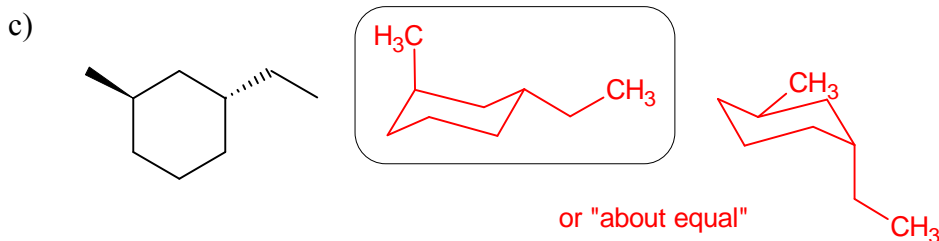
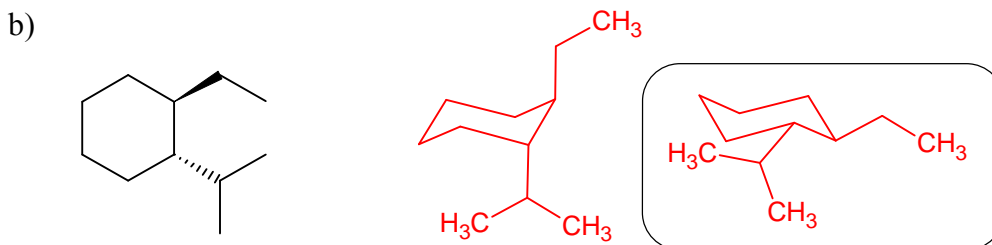
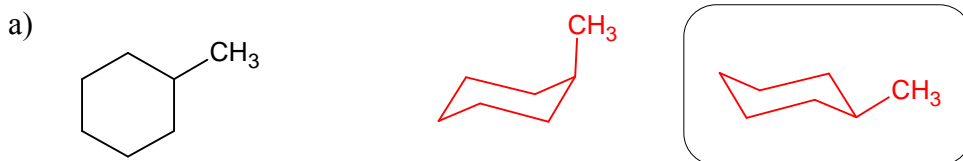
Blank paper will be provided, and you may need it to completely answer some questions. Please place answer pages immediately after the exam pages they correspond to, before stapling. Be sure your name is on all pages turned in!



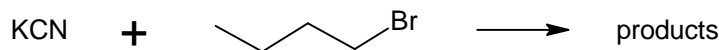
1. Using Newman projections, show the **most** and **least** stable staggered conformations for rotation around the C2-C3 bond in 2-methylhexane. (7 points)



2. Draw both chair forms for each of the following substituted cyclohexanes, and indicate which of each pair is more stable. (7 points each)



3. Answer any **two** of the following four questions. (10 points each; if you answer more than two, only the first two answers will be graded)

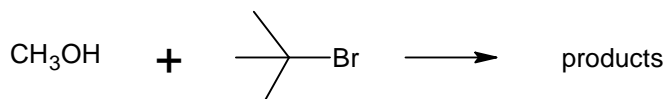


- a) Explain why using a polar aprotic solvent increases the rate of the reaction of potassium cyanide with 1-bromobutane.

Because polar aprotic solvents stabilize cations but not anions, the nucleophile anion is brought into solution but is actually less stable than it is in the solid. This raises the total energy of the reactants. The transition state is not much changed, because its negative charge is much more spread-out. The net effect is to lower the energy difference between the reactants and the transition state.

- b) Explain why using a polar protic solvent decreases the rate of the reaction of potassium cyanide with 1-bromobutane.

Polar protic solvents stabilize both positive and negative charges, but give more stabilization to more concentrated charges. The reactants are stabilized by solvation, but the transition state (because its charge is more spread-out) is not as stabilized as the reactants. The net effect is to increase the energy difference between the reactants and the transition state.



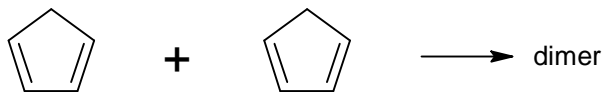
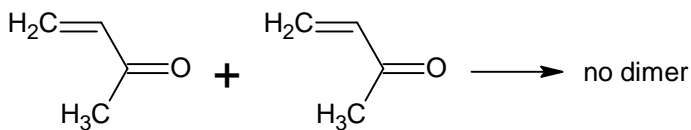
- c) Explain why using a polar aprotic solvent decreases the rate of the reaction of methanol with t-butyl bromide.

The rate-determining step is dissociation of the leaving group from t-butyl bromide, forming a bromide anion. Polar aprotic solvents destabilize anions because the anions are not solvated; this raises the energy of the ion pair and the transition state leading to it. But the reactant energy is not much changed because it has no separated charges. The net effect is to increase the energy difference between the reactants and the transition state.

- d) Explain why using a polar protic solvent increases the rate of the reaction of methanol with t-butyl bromide.

The rate-determining step is dissociation of the leaving group from t-butyl bromide, forming a bromide anion. Polar protic solvents stabilize anions because the anions are solvated; this lowers the energy of the ion pair and the transition state leading to it. But the reactant energy is not much changed because it has no separated charges. The net effect is to decrease the energy difference between the reactants and the transition state.

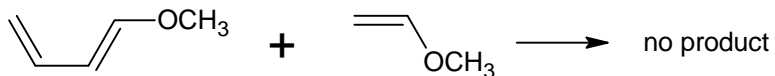
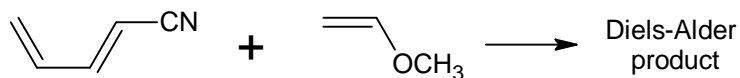
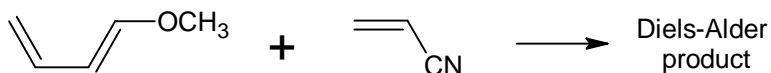
e) Explain why and how cyclopentadiene dimerizes, but 3-buten-2-one does not dimerize.



3-buten-1-one is a dienophile; to dimerize, it would have to form a 4-membered ring via 2+2 cycloaddition. This is not going to happen; it's forbidden by the Woodward-Hoffman rules.

But cyclopentadiene can act as either the diene or the dienophile in a Diels-Alder reaction, and when it dimerizes one molecule of cyclopentadiene acts in each role.

f) Explain the facts shown below:



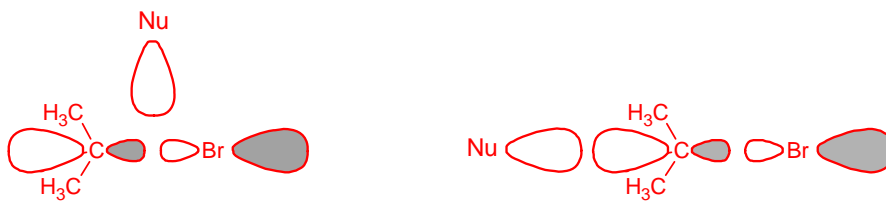
Diels-Alder reactions are promoted when one reactant has an electron-withdrawing group and the other has an electron-donating group; this combination brings the HOMO and LUMO of the two reactants closer together in energy, facilitating the reaction.

But the third set of reactants both have electron-donating groups, and so their HOMO and LUMO are relatively far apart in energy and cannot easily react.

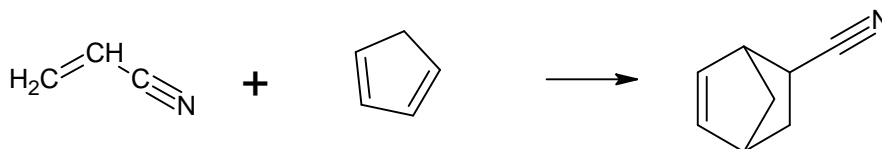
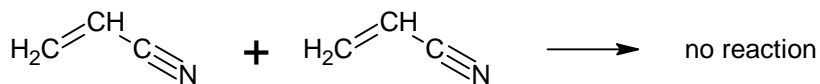
4. Use concepts from valence-bond theory or molecular orbital theory, involving the interactions of atomic or molecular orbitals, to explain **two** of the following five observations. (10 points each; if you answer more than two, only the first two answers will be graded)

- a) An S_N2 reaction always results in the inversion of the carbon at which the reaction happens.

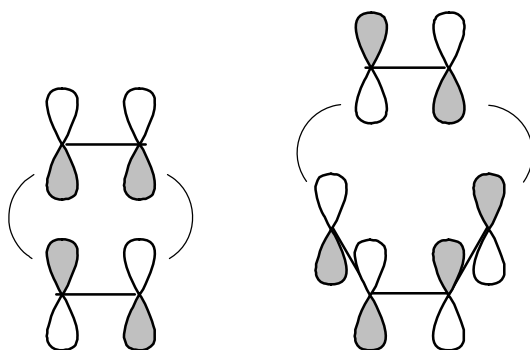
The lone pair (HOMO) of the nucleophile must attack the LUMO of the electrophile, which is the carbon-leaving group antibonding MO. But the antibonding MO cannot be attacked from the front because the overlap is all wrong. Instead, it must be attacked from the backside because there is a large lobe there; this breaks the carbon-leaving group bond and forms a new bond while turning the carbon atom inside-out like an umbrella.



- b) Acrylonitrile will not add to itself, but will undergo cycloaddition with cyclopentadiene to form bicyclo[2.2.1]heptane-2-carbonitrile.



Acrylonitrile would have to add to itself in a 2+2 reaction, in which the HOMO of “ethane” and the LUMO of “ethane” would be trying to overlap—and they can’t, because the ends are out-of-phase with each other:



But acrylonitrile can add to cyclopentadiene, because “ethane” and “butadiene” can have HOMO-LUMO interactions. In this case it would be the HOMO of “butadiene” and the LUMO of “ethylene”.

- c) The reaction of cis-1-bromo-2-methylcyclohexane with potassium t-butoxide is faster than the reaction of the trans isomer.

In an elimination reaction, in order to form the new π -bond, the carbon-hydrogen bond must be parallel to the carbon-leaving group bond, so that the former hybrid atomic orbitals can form the new p atomic orbitals of the new bond. But the only way to make this happen, on a cyclohexane ring, is for the hydrogen and the leaving group to both be axial; if they are equatorial, they cannot line up.

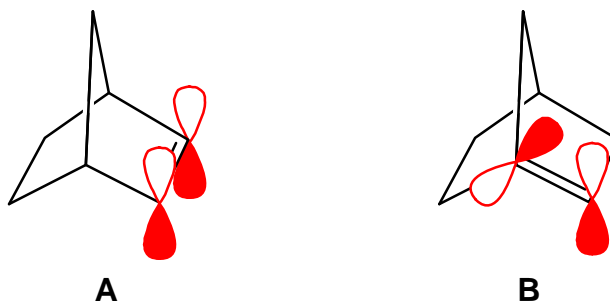
It so happens that the cis isomer of 1-bromo-2-methylcyclohexane has the methyl group equatorial when the bromine is axial, and this is therefore the most stable chair form. But in the trans isomer, the methyl group is axial when the bromine is axial, and this is by far the less stable of the two chair forms:



- d) Alkyl groups geminal to the halogen increase the rate of reaction of alkyl halides with weak nucleophiles and weak bases.

This is because of hyperconjugation. The carbocation has an empty p-orbital that can interact with parallel C-H or C-C bonds on neighboring carbon atoms. This interaction of molecular orbitals lowers the energy of the C-H or C-C bonding electrons, making the carbocation more stable (or less unstable).

- e) Bridgehead double bonds are unstable in small bicyclic systems: for example, compound **A** is stable while compound **B** is unstable (and in fact cannot be isolated).

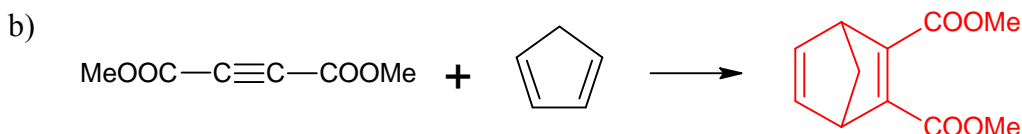


In **A**, the p-orbitals of the double bond are able to be parallel so that a π -bond can form. But in **B**, the geometry of the carbon skeleton constrains the p-orbitals to be almost perpendicular to each other. The overlap between them is very poor, and the result is that the π -bond is pretty much nonexistent.

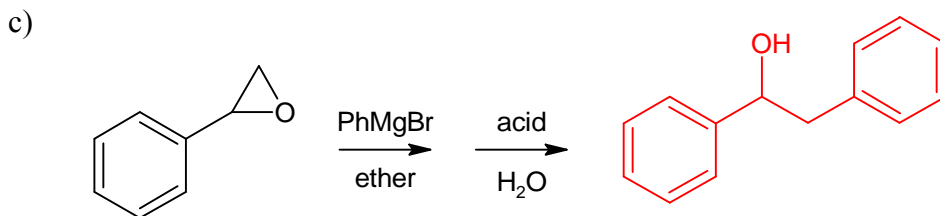
5. Write the expected major product of each of the following reactions. Partial credit will be given for correct minor products, if the correct major product is not given. In other words, it is to your advantage to put down all *correct* expected products for each reaction. (7 points each; points will be deducted for incorrect products)



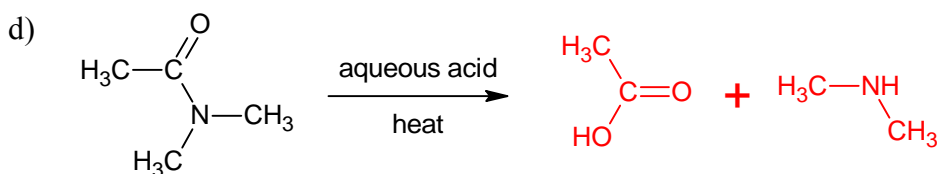
This is an S_N1 reaction because of the tertiary carbon center (and the fact that iodide cannot easily approach the backside). This means that we expect to see both stereoisomers. Full credit if you say that inversion predominates, but ONLY if you give both isomers!



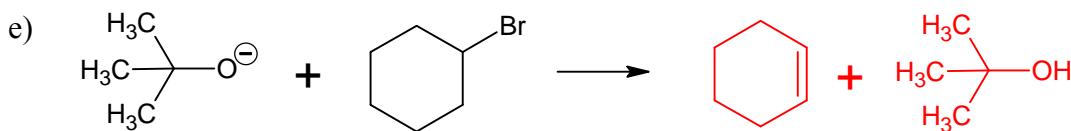
This is a Diels-Alder cycloaddition.



The Grignard reagent, being a strong base, adds to the less-substituted end of the epoxide. Full credit if you claim that elimination happens during acid workup.

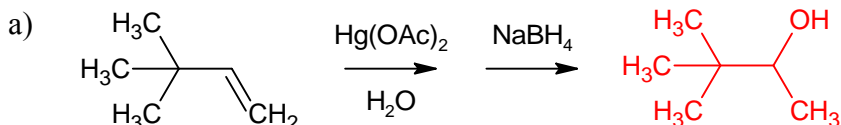


This is hydrolysis of an amide; the product is a carboxylic acid and an amine.

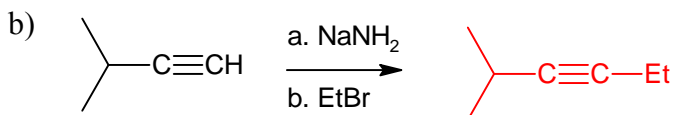


This is an $E2$ elimination reaction. The base is too bulky for an S_N2 reaction on a secondary alkyl halide. No credit for S_N2 product; loss of credit if both substitution and elimination products are given.

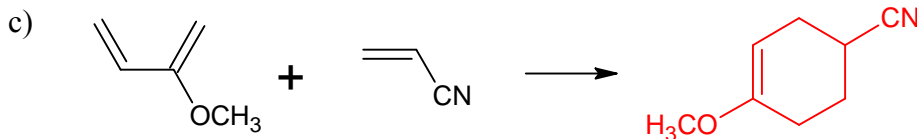
6. Write the expected major product of each of the following reactions. Partial credit will be given for correct minor products, if the correct major product is not given. In other words, it is to your advantage to put down all *correct* expected products for each reaction. (7 points each; points will be deducted for incorrect products)



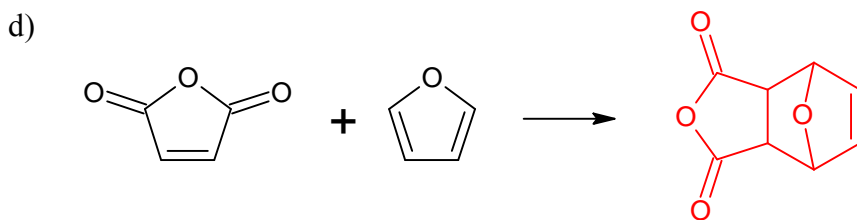
This is an oxymercuration reaction, which gives the Markovnikov alcohol without rearrangement.



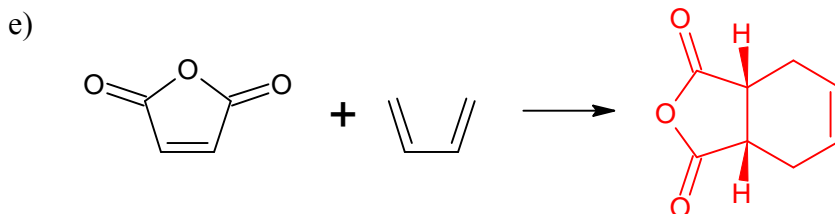
Sodium amide is a strong-enough base to deprotonate an alkyne. The alkynyl anion then does $\text{S}_{\text{N}}2$ substitution on bromoethane.



This is a Diels-Alder reaction. Full credit for the orientation shown, which can be determined from resonance structures as discussed in class.



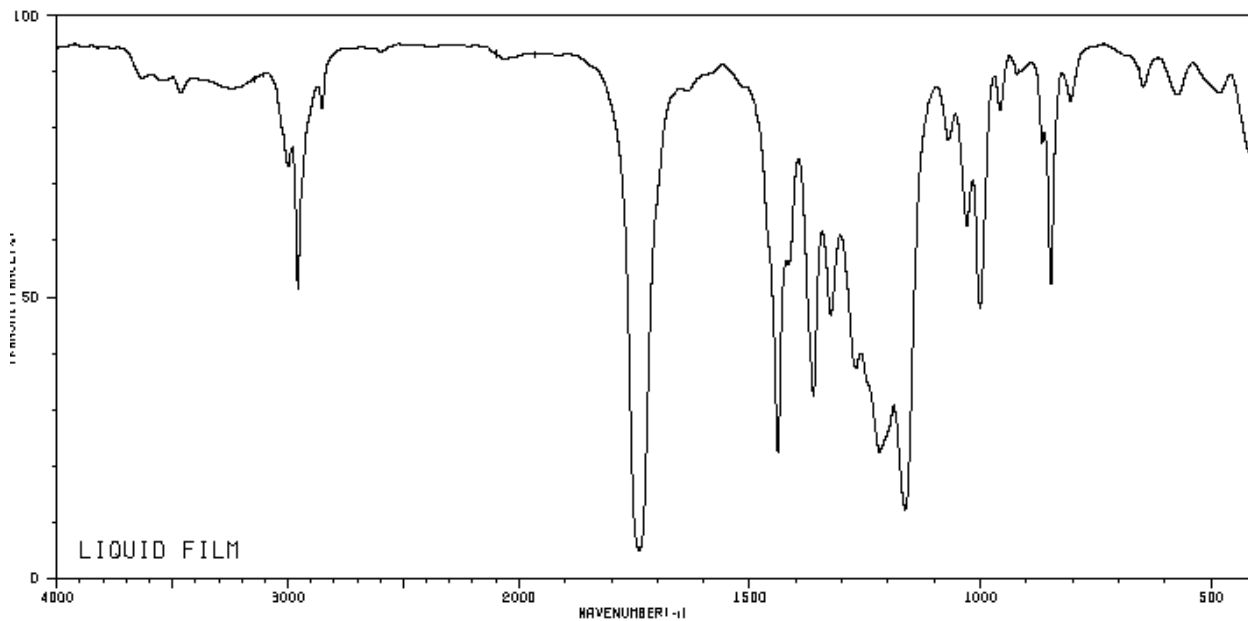
This is a Diels-Alder reaction. The diene is on the right, the dienophile on the left.



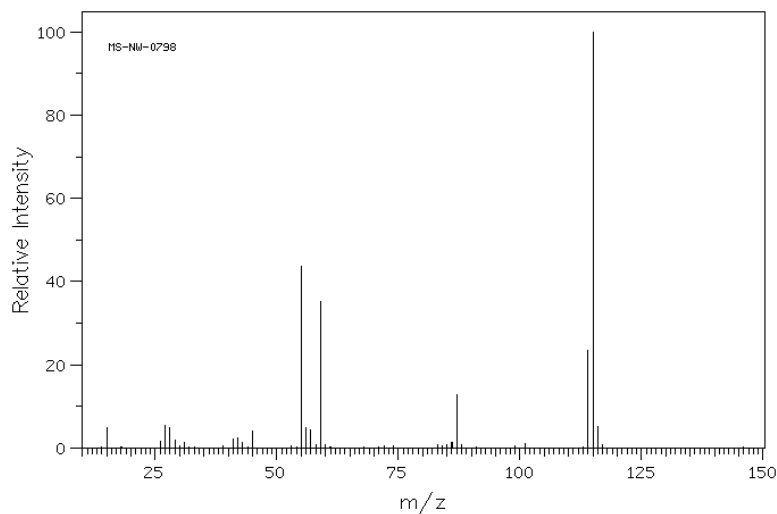
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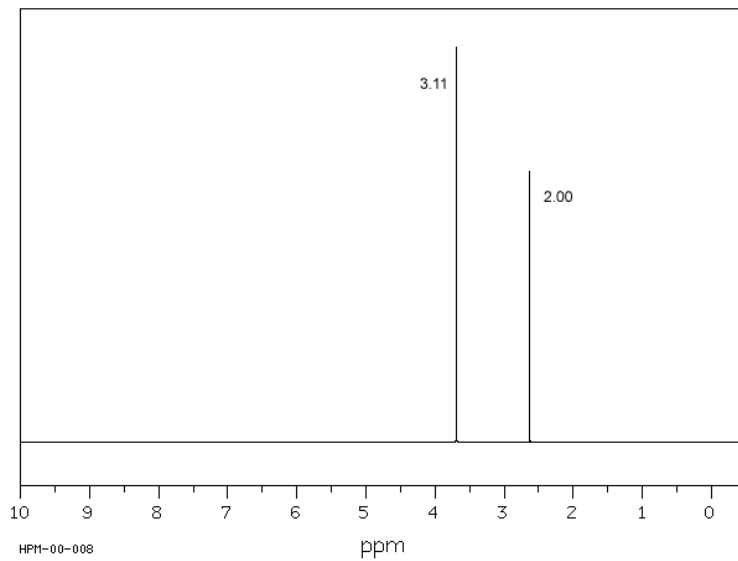
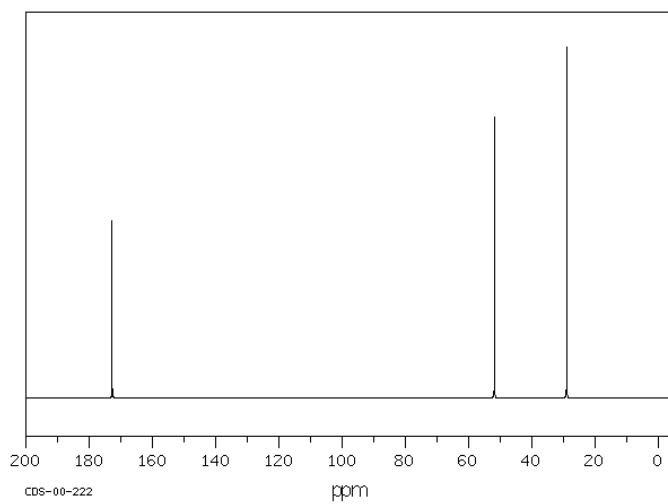
7. When compound A, with the formula $C_4H_4O_3$, is boiled in methanol in the presence of acid, it forms compound B, with the formula $C_6H_{10}O_4$. The spectra of compound B are shown below. Give the correct structures for compounds A and B (5 and 25 points, respectively).

IR spectrum of compound B:



Mass spectrum of compound B:



^1H NMR spectrum of compound B: **^{13}C NMR spectrum of compound B:**

DEPT-45: 51.80, 28.95

DEPT-90: no peaks

DEPT-135: 51.80(+), 28.95(-)

Starting with the spectra of Compound B, we are given the formula: $C_6H_{10}O_4$. This has two points of unsaturation.

The IR shows a strong carbonyl peak at about 1730 cm^{-1} and saturated C-H.

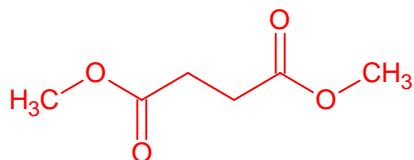
The ^1H NMR shows two types of hydrogen, both singlets, with a 3-H peak at 3.7 ppm and a 2-H peak around 2.6 ppm. $2+3 = 5$, and there are 10 hydrogens in the formula, so the compound is symmetrical with two identical CH_2 groups and two identical CH_3 groups. The CH_3 group is next to something electronegative, most likely oxygen; the CH_2 group is next to (probably) a carbonyl group. Notice that we have two CH_2 -carbonyl combinations, which means two carbonyl groups, and we only have two points of unsaturation.

The ^{13}C NMR shows us three kinds of carbon, with six in the formula, so again we know that the compound is highly symmetrical. But this spectrum gives us one more very important piece of information: the carbonyl group comes at about 172 ppm, so it's an ester.

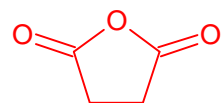
DEPT doesn't tell us anything we don't already know.

So, we have three pieces, which form $\frac{1}{2}$ of the structure; the other half is the mirror image.

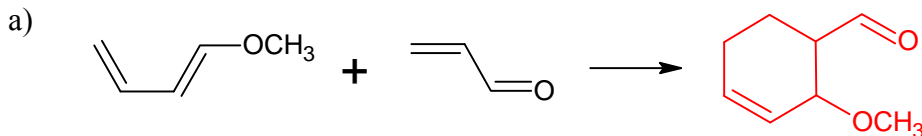
The methyl group is attached to the ester oxygen, while the CH_2 group is attached to the ester carbonyl group (remember that we got this from the hydrogen chemical shifts), so the structure of **Compound B** HAS to be dimethyl butanedioate,



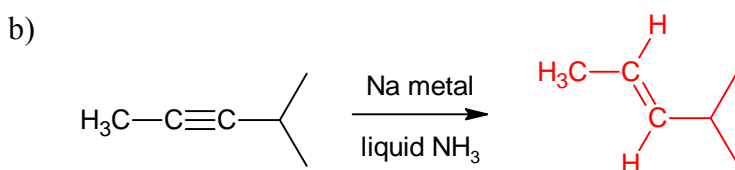
Compound A is a "retrosynthetic" problem: what compound, with a formula $C_4H_4O_3$, would give dimethyl butanedioate when boiled with acid in methanol? The reaction conditions are for esterification, so our first idea would be butanedioic acid, but that has the formula $C_4H_6O_4$. Compound A is missing two H and an O – but what is the result of removing H_2O from butanedioic acid? Why, butanedioic anhydride! And that's the structure of **compound A** (2 points of 5 will be given for butanedioic acid).



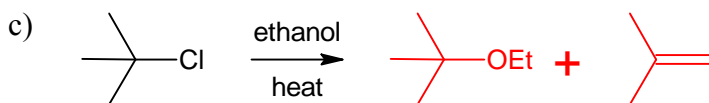
8. Write the expected major product of each of the following reactions. Partial credit will be given for correct minor products, if the major product is not given. In other words, it is to your advantage to put down all *correct* expected products for each reaction. (7 points each; points will be deducted for incorrect products)



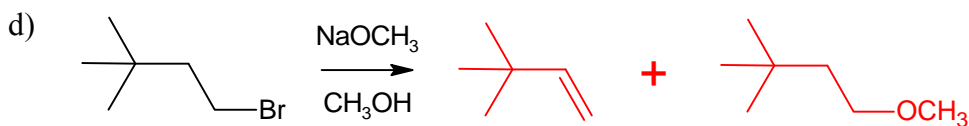
This is a Diels-Alder cycloaddition reaction. Avoiding wedges and dashes allows us to specify both possible products, exo and endo, with one structure.



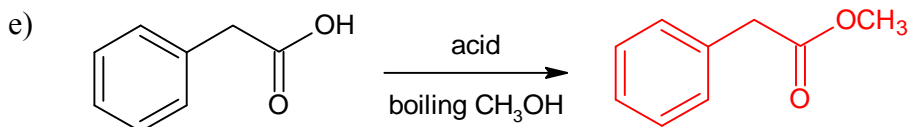
The dissolving metal reduction of an alkyne forms a trans alkene only.



We expect this to be an S_N1, E1 reaction, with both elimination and substitution products. Elimination is probably the major product, but you will get full credit only for both products.



We expect S_N2 here, with a minor E2 product.



This is a Fischer esterification reaction.