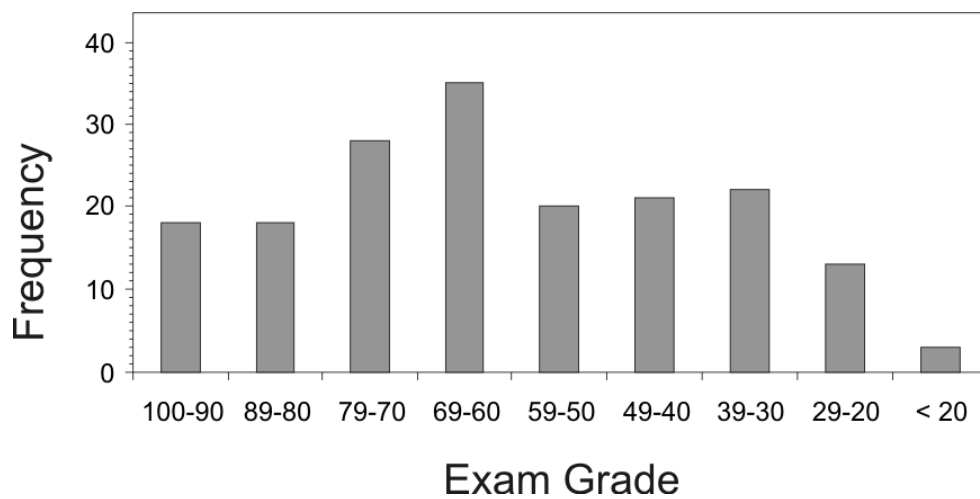


**Exam 4
Answer Key**

Exam 4 Mean: 60
Exam 4 Median: 61
Exam 4 St. Dev.: 21

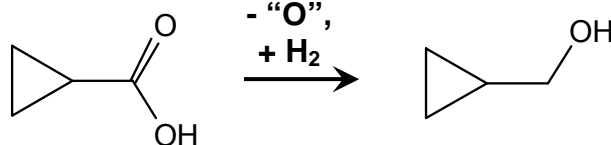


Multiple-Choice Problems

Please answer these problems on the bubble sheet.

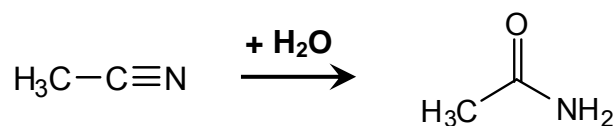
(3 pts each) Identify each of the transformations below as a reduction, an oxidation, or neither.

1.



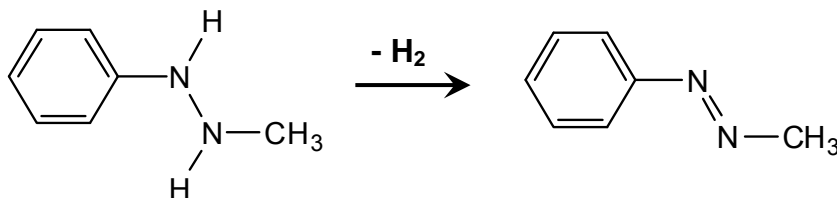
- a. reduction
- b. oxidation
- c. neither

2.



- a. reduction
- b. oxidation
- c. neither

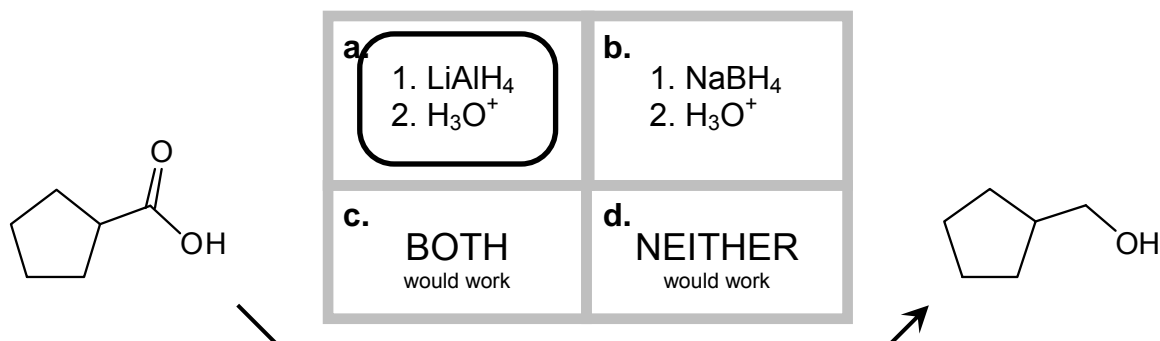
3.



- a. reduction
- b. oxidation
- c. neither

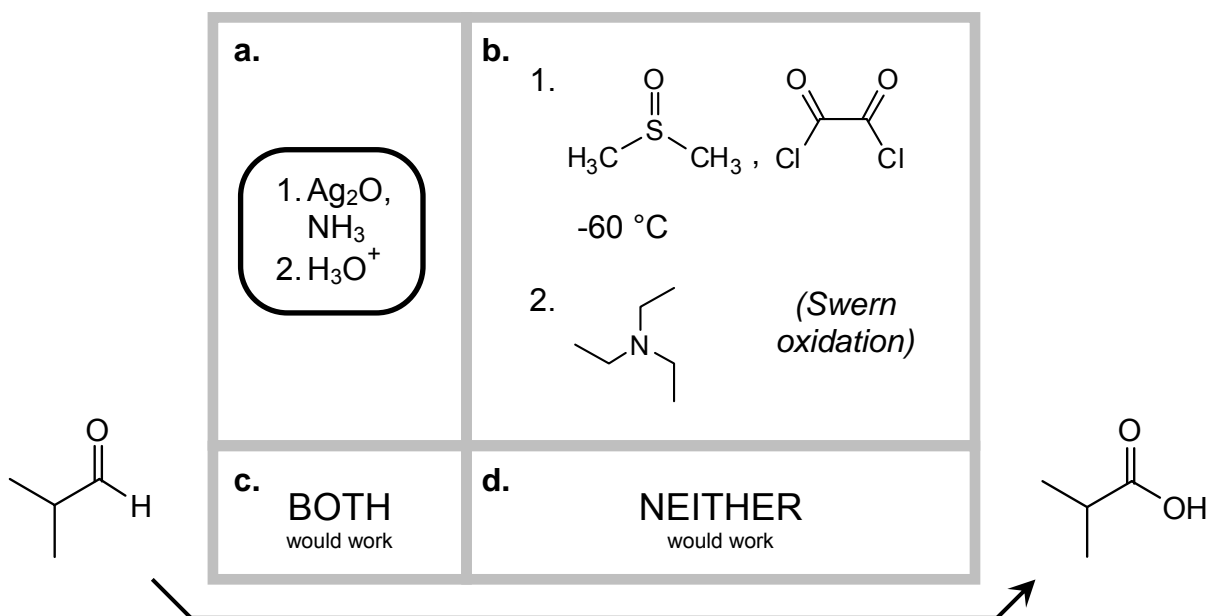
(4 pts each) Each of the reactions below is drawn with two possible reaction conditions. If only one of the two reaction conditions would generate the given molecule as the major product, answer with the corresponding letter. If both sets of conditions would accomplish the reaction, answer (c) "BOTH". If neither set of reaction conditions would succeed, answer (d) "NEITHER".

4.



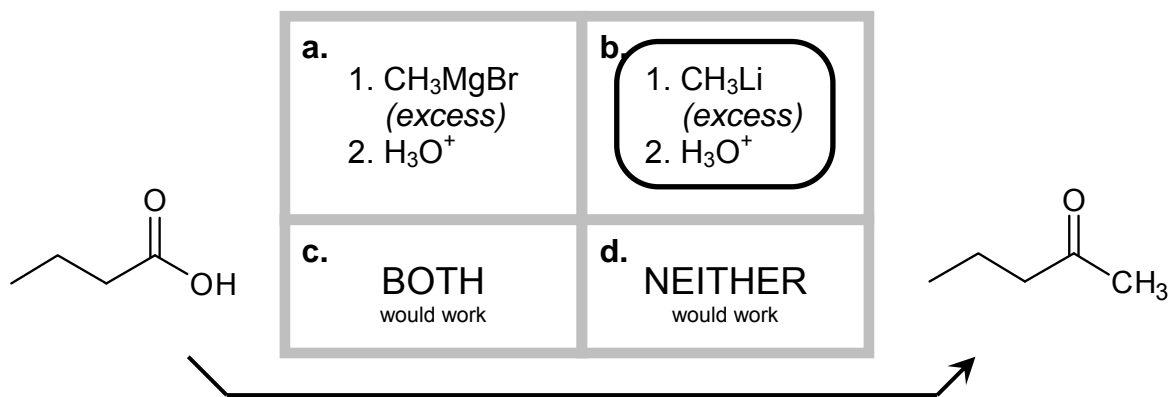
Both of these reagents are reducing agents (sources of "H"). Only LiAlH_4 , however, is strong enough to reduce carboxylic acids. (NaBH_4 will only react with ketones and aldehydes.)

5.



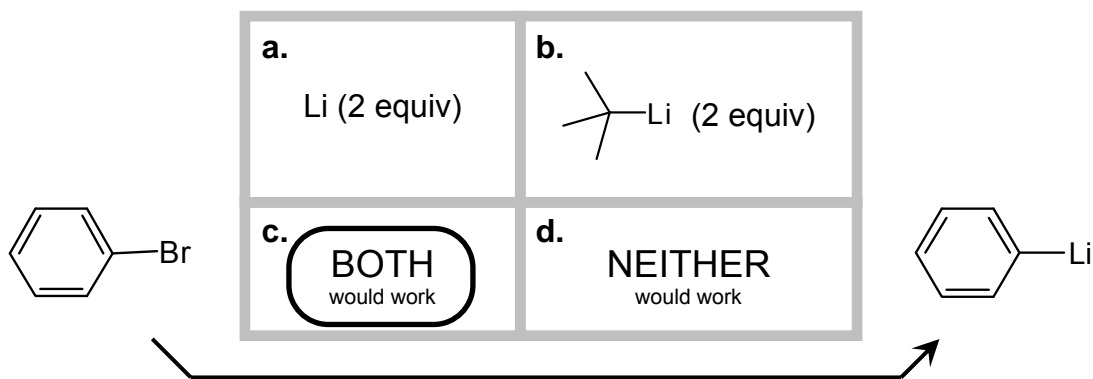
Both of these sets of reagents oxidize molecules. Swern oxidation is a method for oxidizing a primary alcohol to an aldehyde, without further oxidation to a carboxylic acid. Ag_2O , on the other hand, does not react with alcohols but does oxidize aldehydes to carboxylic acids.

6.

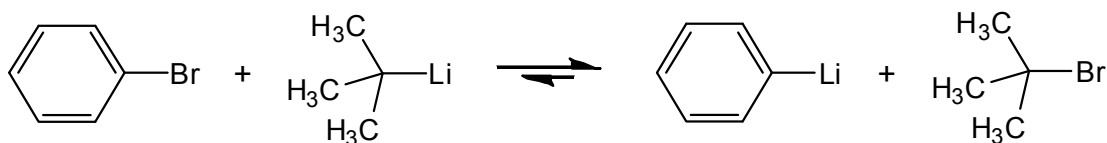


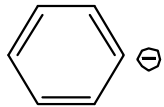
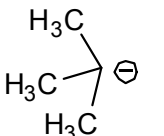
Both of these reagents would deprotonate the carboxylic acid to a carboxylate anion, but only the alkyllithium is strong enough to add to this carboxylate, once, to generate the product ketone.

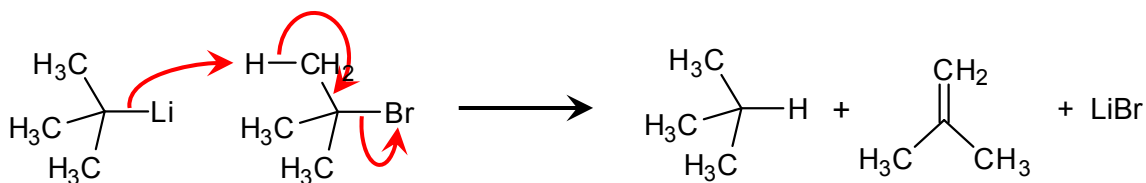
7.



In class, we discussed three methods for generating an alkylmetal species. Of those three, these are methods #2 and #3. Two equivalents of lithium metal will generate the phenyllithium (PhLi) and a molecule of LiBr. One equivalent of $(\text{CH}_3)_3\text{CLi}$ will undergo lithium-halogen exchange with the phenyl bromide, to make PhLi and $(\text{CH}_3)_3\text{CBr}$. This happens because the phenyl anion (at an sp^2 carbon) is more stable than the methyl anion (at an sp^3 carbon). Then, the second equivalent of $(\text{CH}_3)_3\text{CLi}$ reacts with the $(\text{CH}_3)_3\text{CBr}$ via E2 to make an alkane, an alkene, and LiBr.



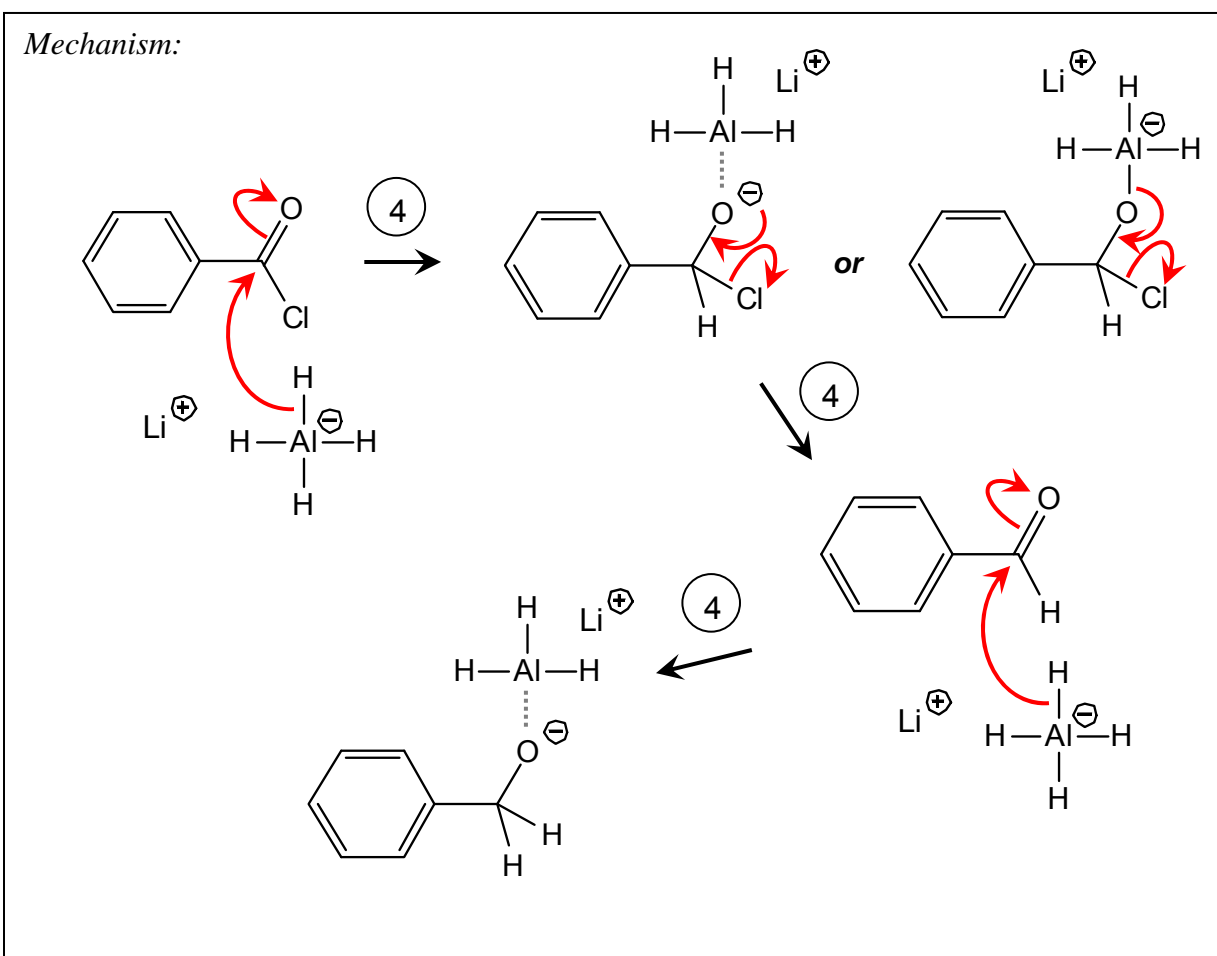
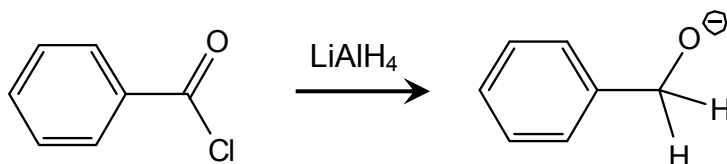
(because  \ominus is more stable than  \ominus)



(equiv # 2)

20. (12 pts) For the reaction shown below, draw a mechanism that explains how the product is generated from the starting material. In your answer, make sure that you:

- Draw each step of the mechanism separately;
- Use “electron pushing” to show where the electrons in each step go;
- Use only the molecules that you are given; do not invoke reactants or solvents that aren't in the problem.



In the mechanism I've drawn above, negatively charged oxygen atoms all have aluminum atoms associated with them—the space in aluminum's octet that used to be occupied by an "H" in LiAlH_4 has been replaced by an RO^- . I did this because that's what really happens. But the oxygen-associated AlH_3 doesn't do anything afterwards, and you could leave it out of your mechanism entirely if you wanted.

Both reduction steps generate aluminum species that have fewer than four hydride equivalents attached (e.g., with chemical formula $\text{LiAlH}_3[\text{OR}]$). Even though these have already donated one equivalent of H^- , the three remaining hydride equivalents are still active. In my mechanism, I only show LiAlH_4 as a hydride donor, but in principle, you could show any $\text{Al}(\text{H})_n$ complex as a donor.

Rubric:

4 points for each of the three steps. (12 points total.) Must be these steps, in this order.

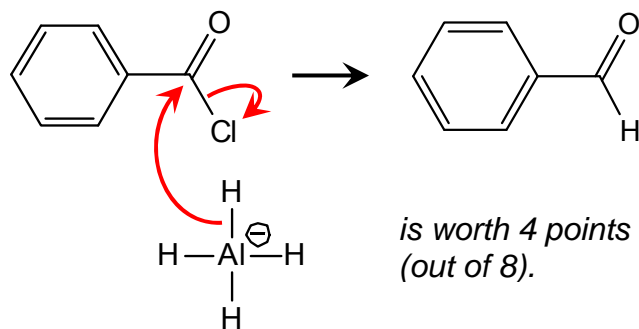
No need to keep track of Li^+ , Cl^- , or aluminum complexes after they are gone.

-1 point for writing " LiAlH_4 " as " H^- ". It really isn't, but we gave almost full credit for it.

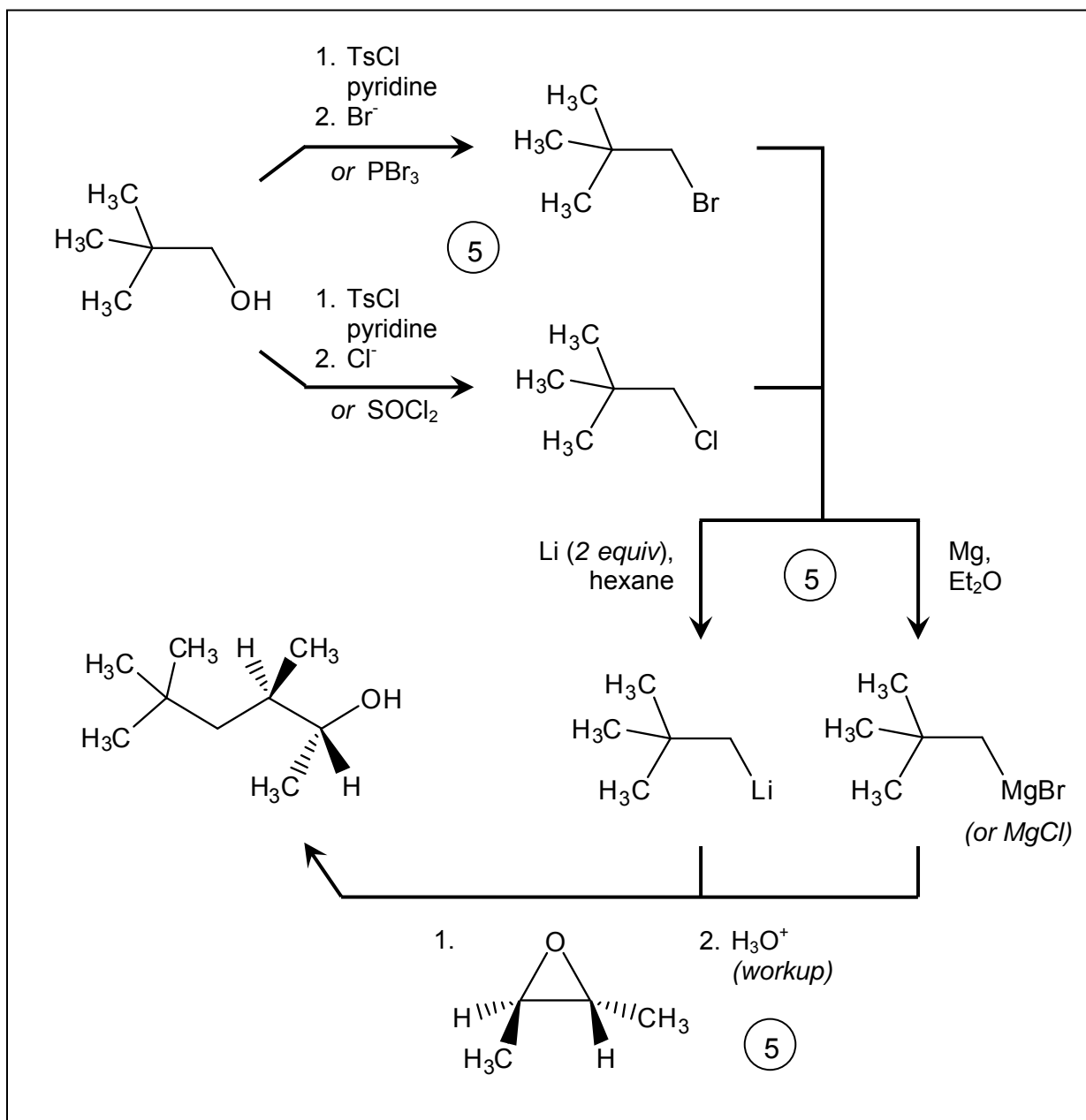
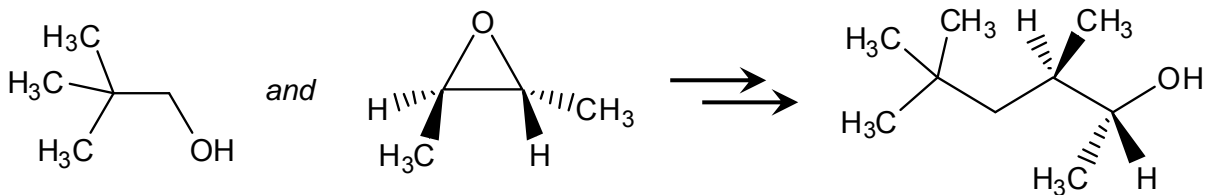
-2 points, for each arrow in each step, for errors in drawing arrows. Arrow must start at an electron pair (or a charge that indicates a pair), and end at nucleus where electrons will newly interact. Can only lose points if you get them.

-1 point for each minor error in charge, valency, structure, base, etc.; if error propagates, points are taken off only for initial error.

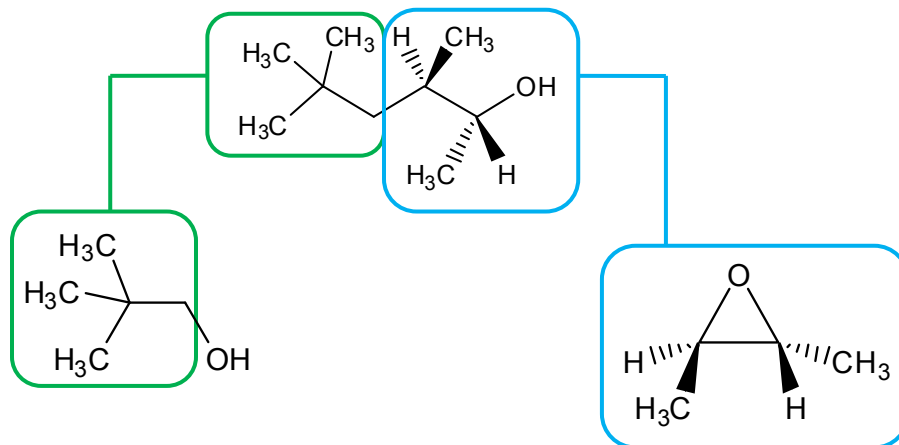
-2 points for each step combined with another. This is counted off of both combined steps. This includes direct $\text{S}_{\text{N}}2$ of Cl^- by $\text{LiAlH}_4/\text{H}^-$:



21. (15 pts) **Propose a multistep synthesis** of the product shown below from the given starting materials, along with any reagents we have covered in class. You might discover multiple answers to this problem; draw only your best (one) synthetic route. Feel free to draw an incomplete route—we will give you partial credit where we can.



I think the easiest way to begin these problems is to try to identify what portions of the product might come from which starting materials. Here, I think it's pretty clear:



These fragments are connected by a carbon-carbon bond in the product. We have learned very few methods for creating carbon-carbon bonds in this class, and they all involve the reaction of an alkylmetal species (an alkyllithium, Grignard, or alkynylsodium) with an electrophile (a C=O containing molecule, an epoxide, a halogen or tosylate leaving group that cannot undergo elimination, or, in the case of alkynylsodiums only, a 1° or 2° halogen or tosylate leaving group). Here we have an epoxide already, which is great; all we need to do is convert our alcohol into an alkylmetal to get us very close to our product.

Many of you tosylated the starting alcohol, and then did things to the tosylate that didn't get you to product. Some tried to convert the tosylate directly into an alkylmetal—this fails, but I can understand where you were going with it, and we gave this partial credit. Others tried to react the tosylate with an alkoxide (which would make an ether, not the target C-C bond). A few others combined the tosylate with the epoxide, assuming the two might react. (They wouldn't.) Our grading of your tosylation step depended on what you were trying to do with the tosylate. If we couldn't figure it out—if it seemed like you were tosylating just because you needed to write something in the box—we didn't give you any partial credit.

Rubric:

This synthesis requires the three tasks described below. Each task is worth 5 points.

Each task is judged separately, and does not require that the synthesis makes sense, or that other tasks are correct.

- 1 point for each minor error in structures or reagents; if error propagates, points are taken off only for initial error.
- 2 points if step reagents are incorrect, but reaction could otherwise be accomplished with correct reagents.

Convert alcohol to a halide.

Any halide other than F is fine.

This step can be done via tosylation in two steps (1. TsCl, pyridine; 2. Cl⁻ or Br⁻ or I⁻), or via one of the single-step methods (SOCl₂, w/ or w/o pyridine, to make chloride; PBr₃, to make bromide; or PI₂, to make iodide).

3 points partial for using HCl or HBr instead of SOCl₂ or PBr₃. These reagents typically work via S_N1, but for primary alcohol, the required primary cation intermediate would be heavily disfavored.

Form an alkylmetal from the halide.

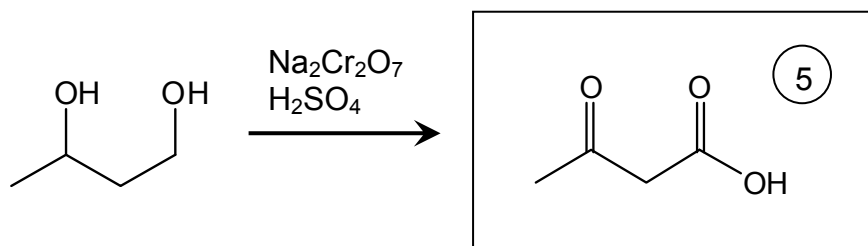
Can be accomplished with Li(s) or tBuLi (2 equiv) to make alkyllithium, or with Mg(s) to make Grignard.

Addition of alkylmetal to epoxide.

-1 point for omitting workup step.

Other routes are possible, but I'm not sure that any others based on the reactions you know would be as short. Graders will have discretion to determine whether other routes are feasible. All reasonable routes require one alkylmetal and one reactive electrophile. I've recommended that syntheses longer than the three steps above receive a maximum of 10 points, and have 5 points removed for each step that doesn't make sense. (You only get points if the synthesis has some merit; if there is no way to do the synthesis the way you've suggested, you may receive 0 points.)

22. (10 pts) Draw the missing reactant or product in the empty boxes. For products, give the predominant, most favored product. Illustrate stereochemistry in your answer where appropriate. For reactions that yield multiple enantiomers, draw only one enantiomer in the box, and include the note "+ enantiomer".

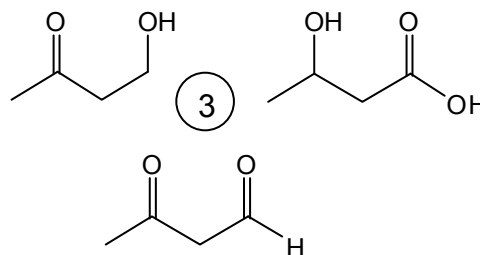


$\text{Na}_2\text{Cr}_2\text{O}_7$ is a strong oxidizing agent; it will oxidize primary alcohols and aldehydes to carboxylic acids, and secondary alcohols to ketones. Here, both alcohols will be oxidized.

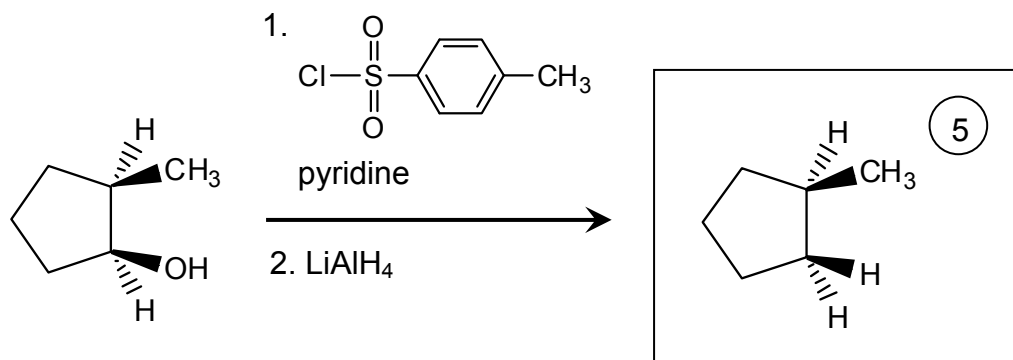
Rubric:

5 points for correct structure.

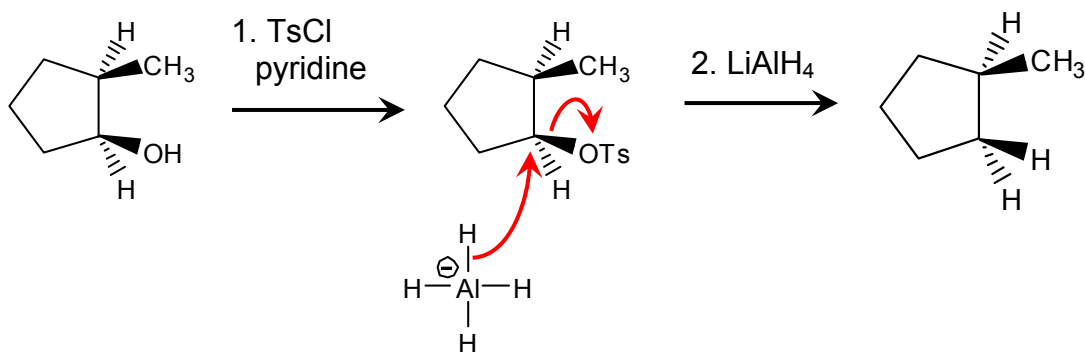
3 points partial for oxidizing only one of two alcohols, or for oxidizing primary alcohol only to aldehyde.



-2 points for each clearly trivial structure mistake.



Tosyl chloride and pyridine convert the alcohol group into a tosylate, which is such a good leaving group that it can be displaced by a source of hydride (H^-):



Rubric:

5 points for correct structure.

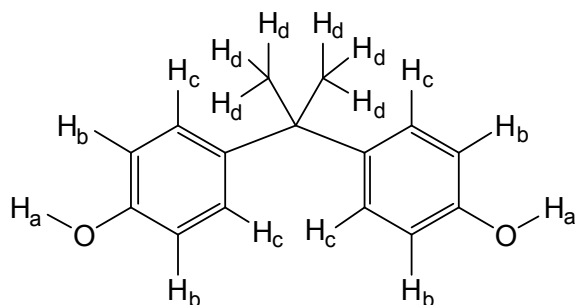
Though I've drawn the methyl group up (with a wedge), the reaction eliminates stereochemistry in the product, and we did not judge stereochemistry in your answer.

2 points partial for tosylate.

2 points partial for replacing alcohol with some other group.

-2 points for each clearly trivial structure mistake.

(3 pts each) How many resonances would you expect to see in the ^1H NMR of each of these additives? In other words, how many inequivalent sets of protons are there in each structure?

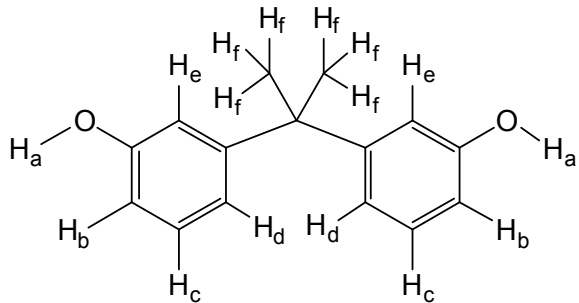


bisphenol A
(BPA)

(in these drawings,
equivalent protons have
the same letter subscript)

8. The ^1H NMR of bisphenol A should show

- a. 3 resonances;
- b. 4 resonances;**
- c. 5 resonances;
- d. 6 resonances;
- e. none of the above.

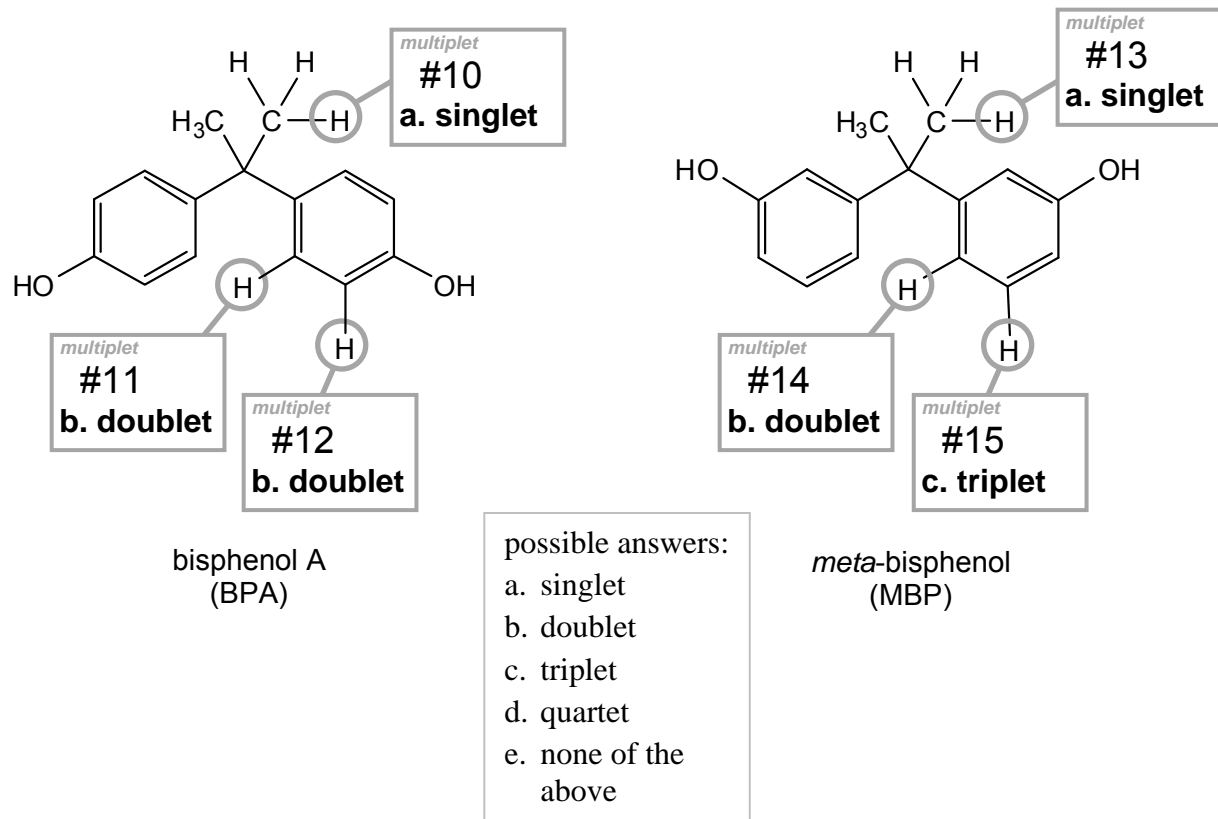


meta-bisphenol
(MBP)

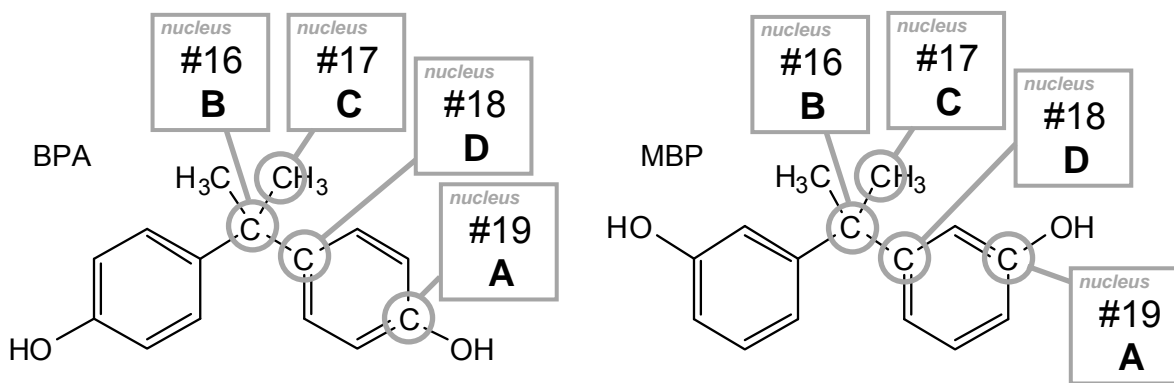
9. The ^1H NMR of *meta*-bisphenol should show

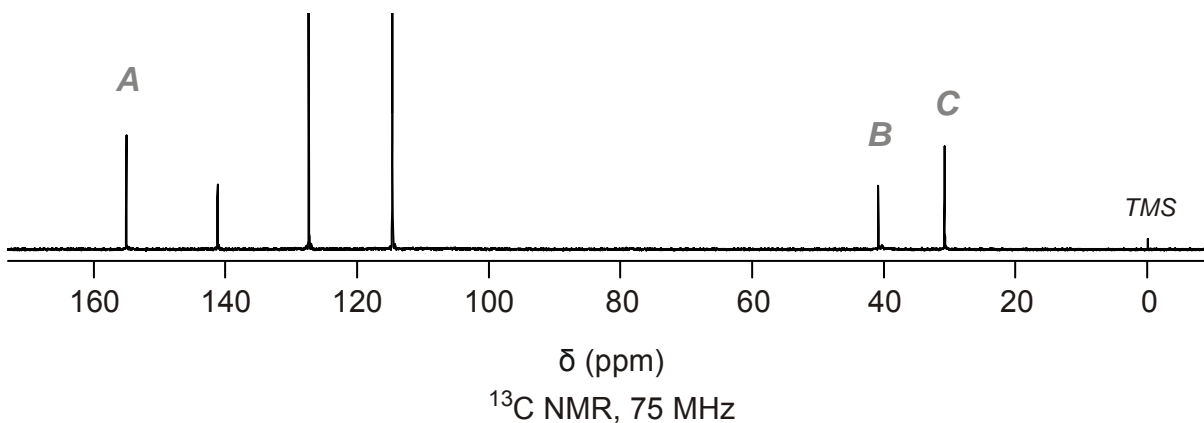
- a. 3 resonances;
- b. 4 resonances;
- c. 5 resonances;
- d. 6 resonances;**
- e. none of the above.

(2 pts each) Each proton circled in the structures below could have its resonance split by neighboring protons. What kind of multiplet should each proton produce in a ^1H NMR spectrum? (Assume that there is no long-range coupling in these molecules.)



(2 pts each) The ^{13}C NMR spectrum of the additive is shown below, and could be consistent with either BPA or MBP. Three peaks on the spectrum are labeled **A**, **B**, and **C**. Which carbons of BPA or MBP could these peaks correspond to? Four chemically similar carbons in the structures of BPA and MBP are circled below. If you would assign one of the ^{13}C NMR peaks to that carbon, fill in the appropriate bubble. If you feel that none of the labeled peaks correspond to the circled carbon, fill in bubble **D** for “none of the above”.

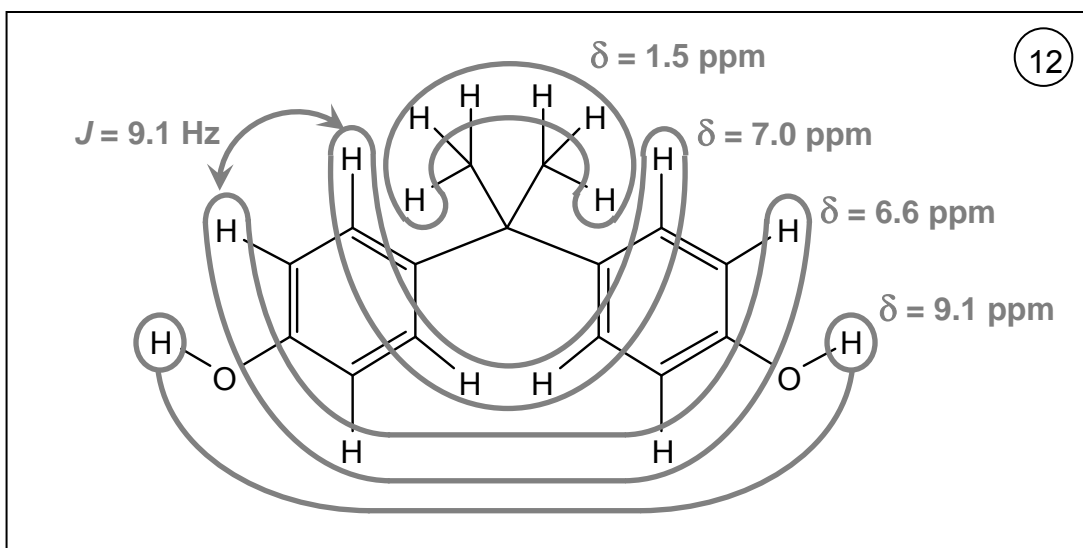
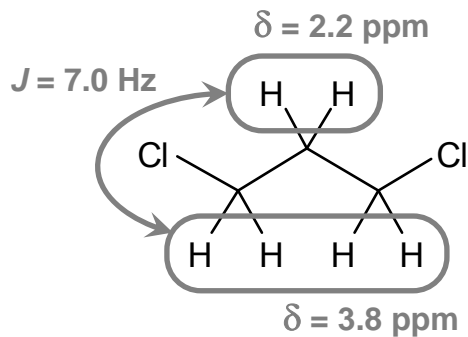




23. (12 pts) Given the ^1H spectrum below, is the additive BPA or MBP? On the unfinished skeleton in the box below, indicate your choice by drawing in the two $-\text{OH}$ groups, as well as all hydrogens. Then,

- Circle each group of equivalent H's;
- Assign a ^1H chemical shift (δ) to each circled group, within 0.1 ppm;
- Connect any pair of coupled, inequivalent groups of H's with a double-headed arrow, and then label that arrow with the corresponding coupling constant (J).

Format for answer to problem 23:



Rubric:

2 points for drawing BPA (the correct molecule choice).

2 points for each set of circled protons and δ values. (8 points total for chemical shift assignment.) To get 2 points, the circle must be perfect (include all the right hydrogens, no less, no more), and the δ value must be correct within 0.1 ppm.

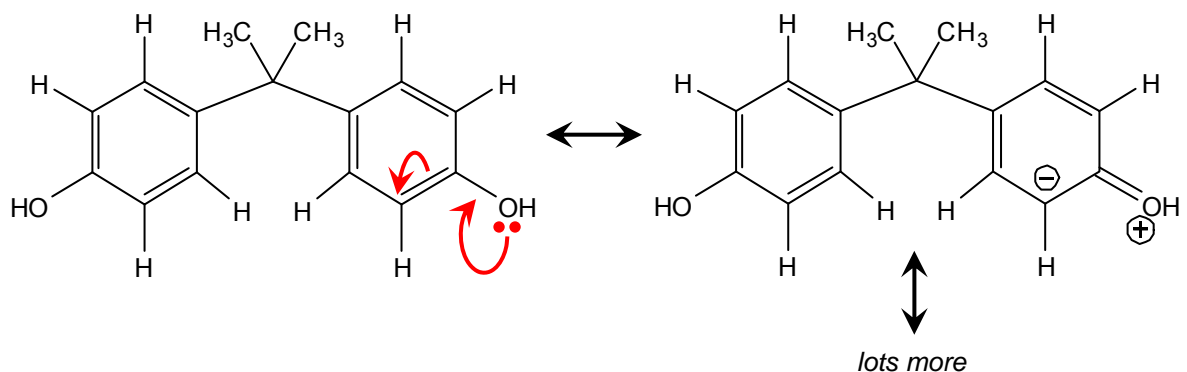
1 point partial for each δ assigned correctly to one correct proton. You get this if circle is incorrect, but δ is correctly associated with one of the protons in the circle.

1 point partial for each circle that is perfectly correct but has incorrect δ assignment.

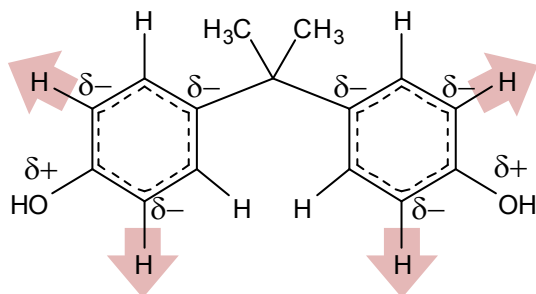
2 points for J assignment. Circles need not be correct to get these points; curved arrow only needs to connect one correct proton with one correct partner. But, both partners need to be correct to get points.

1 point partial if arrow is correct but J value is not.

The chemical shift (δ) assignments for the two benzene-ring protons are not ambiguous; the protons next to the oxygen are upfield (at lower ppm), and the ones nearer the methyl groups are downfield (at higher ppm). Why? The molecule has resonance structures that put partial negative charges at the carbons nearer the oxygen:

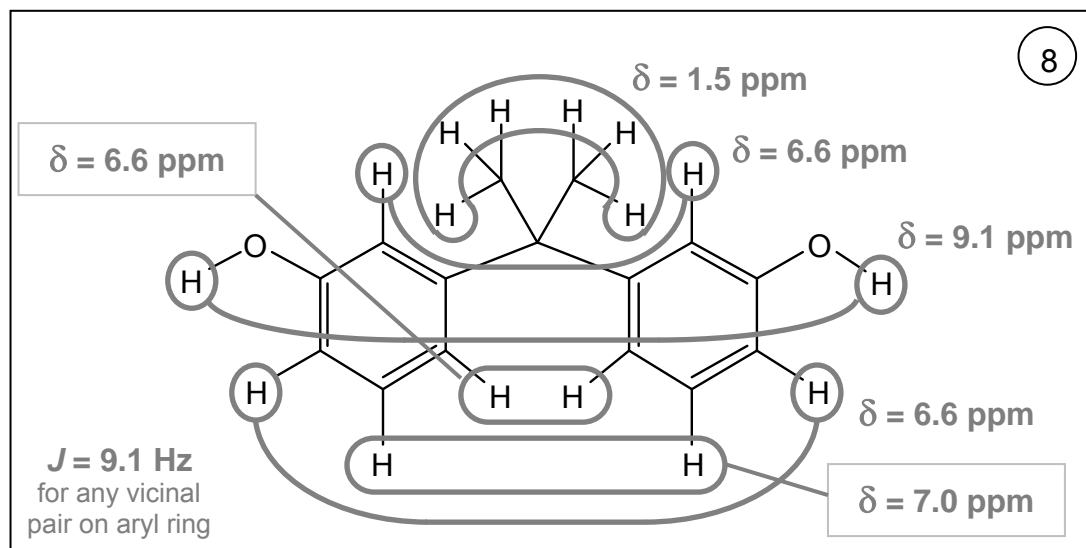


Consensus structure:



Electron density is pushed onto H's by negative charges at these positions, shielding the protons and pushing their chemical shift to lower ppm values (lower frequencies).

If you drew MBP:



Rubric: (maximum 8 out of 12 points)

6 points total for pairs of circled protons and δ assignments.

2 points for 6 methyl protons at 1.5 ppm. Circle must be perfect (include all the right hydrogens, no less, no more), and the δ value must be correct within 0.1 ppm.

1 point partial if circle is incorrect, or if δ value is incorrect, but answer is otherwise correct.

2 points for alcohol protons.

1 point for each assignment of a $\delta = 6-7$ resonance to at least one benzene-ring proton.

2 points for J assignment. Circles need not be correct to get these points; curved arrow only needs to connect one correct proton with a vicinal partner.