

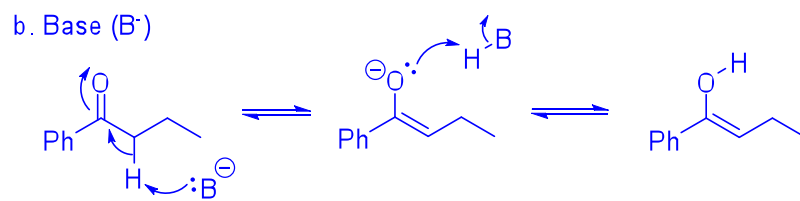
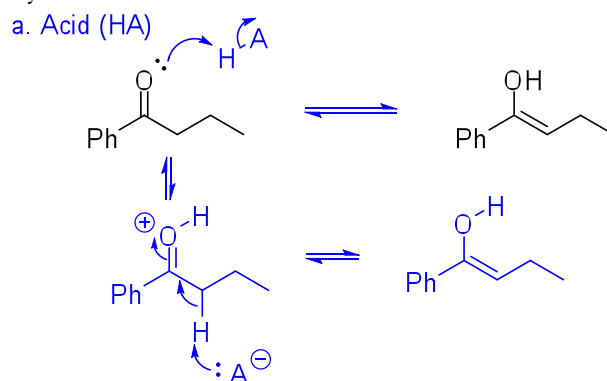
CHM 2120 – Assignment 7 -- ANSWERS

In this Assignment:

- The Aldol reaction
- Haloform Reaction
- Synthetic applications

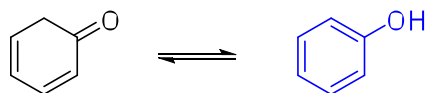
Note: many questions incorporate earlier material

1. Draw the mechanism for the tautomerization of 1-phenyl-1-butanone (also known as butyrophenone and phenyl propylketone) by
 - a. acid catalysis
 - b. base catalysis



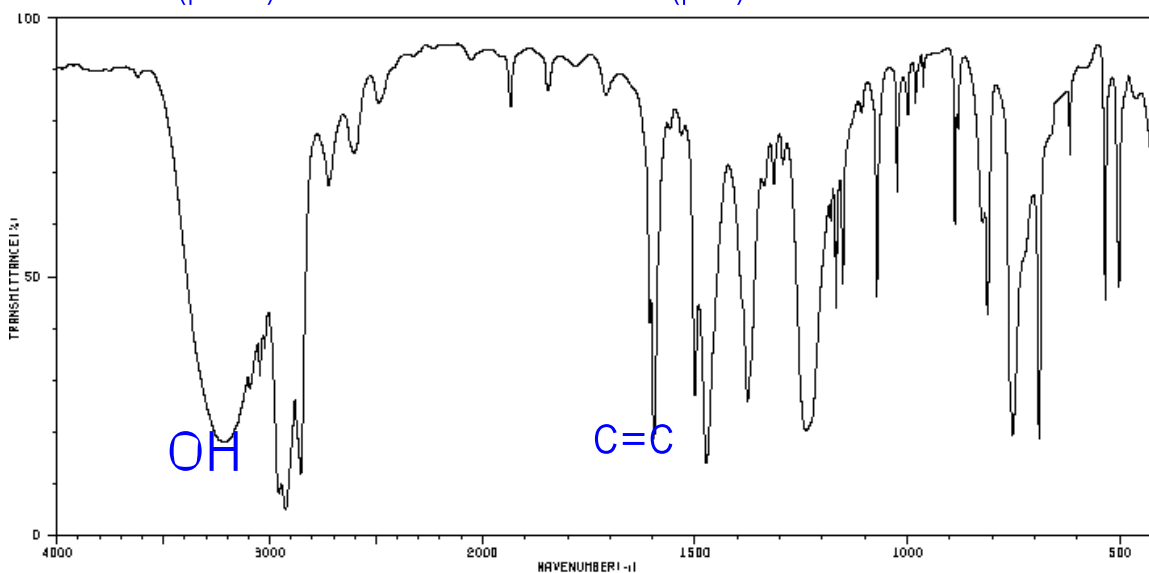
2.

- What is the key tautomer of the molecule shown below?
- Which would be the major tautomer at equilibrium? Why?
- How could you prove the structure of the major tautomer by IR?

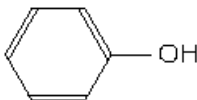


more stable tautomer is aromatic

IR: keto form: would see C=O stretch (peak) at about 1715 cm^{-1} -- NOT observed
 enol form (phenol): would see the broad OH stretch (peak) at about 3200 cm^{-1} - OBSERVED

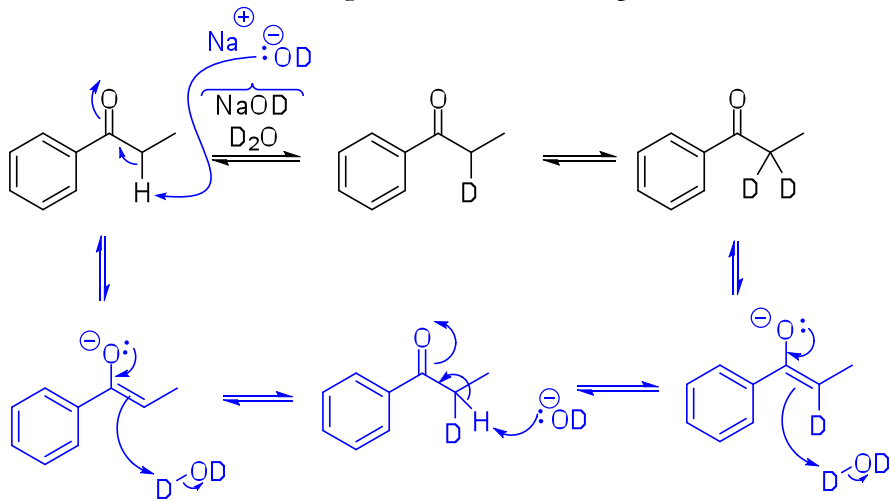


3226	17	2926	4	1600	26	1181	68	823	68
3215	17	2855	11	1474	13	1168	42	812	41
3206	17	2723	64	1376	24	1153	46	753	18
3094	26	2602	70	1337	66	1072	44	690	18
3047	29	1608	39	1315	66	1024	64	617	70
3023	35	1598	17	1294	66	888	57	535	43
2966	7	1532	74	1238	19	881	77	603	46



3.

a. Draw a mechanism for the generation of the compounds shown below.



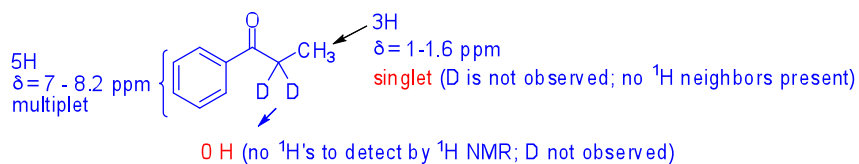
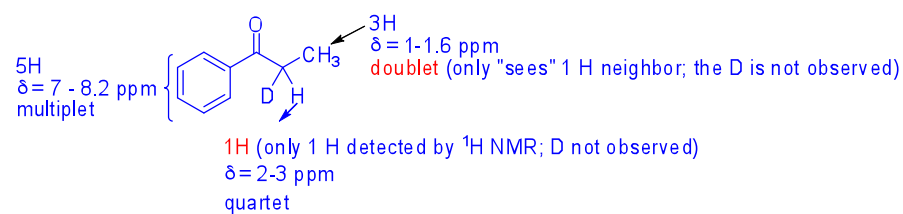
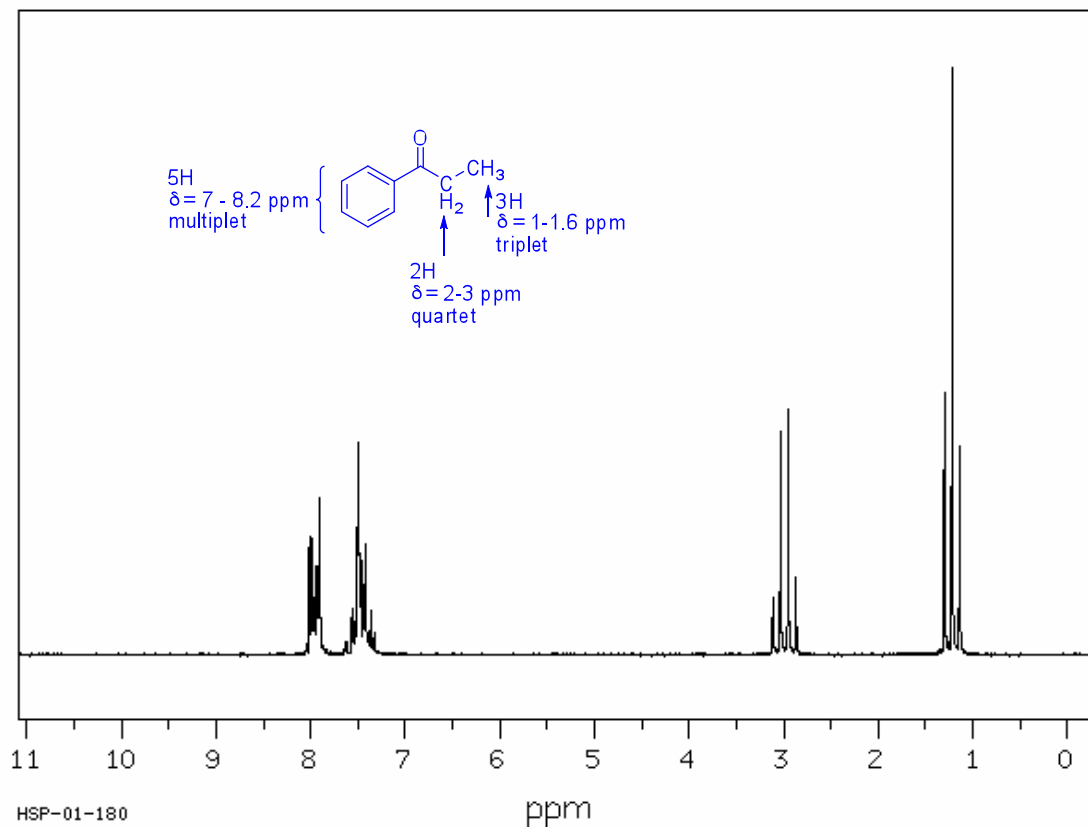
Assignment 7 – Enols/Enolates and related reactions

ANSWERS

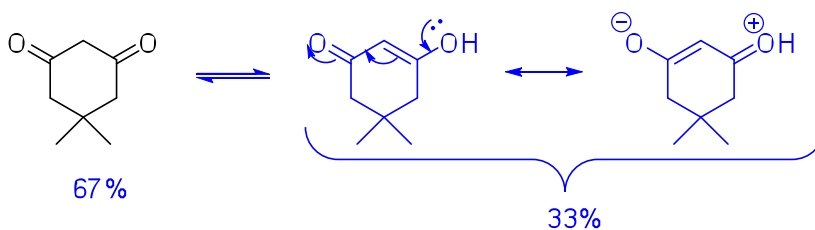
- b. (3. b.) Describe how the ^1H NMR of the starting material would differ from the ^1H NMR of the two products.

Note: H = ^1H \rightarrow detected by ^1H NMR (peaks are seen)

D = ^2H \rightarrow not detected by ^1H NMR (no peaks)

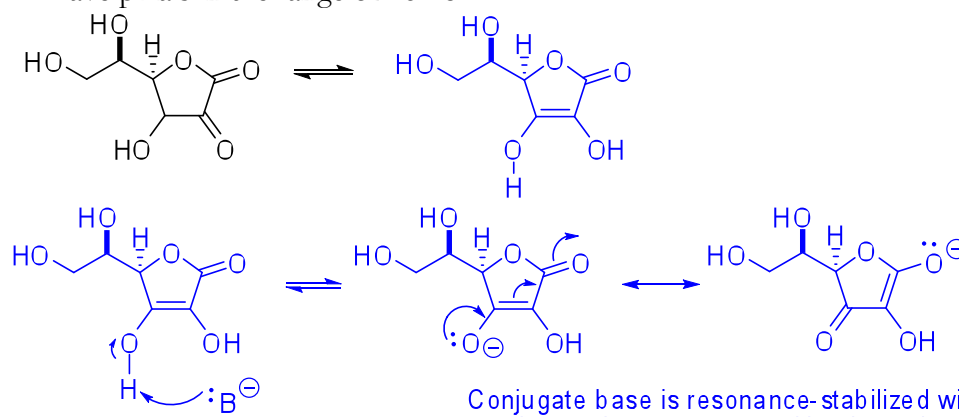


4. A solution of dimedone (5,5-dimethylcyclohexane-1,3-dione) in chloroform contains 33% of an enol tautomer. Draw this tautomer and explain why it is found in much higher proportion than most enols.



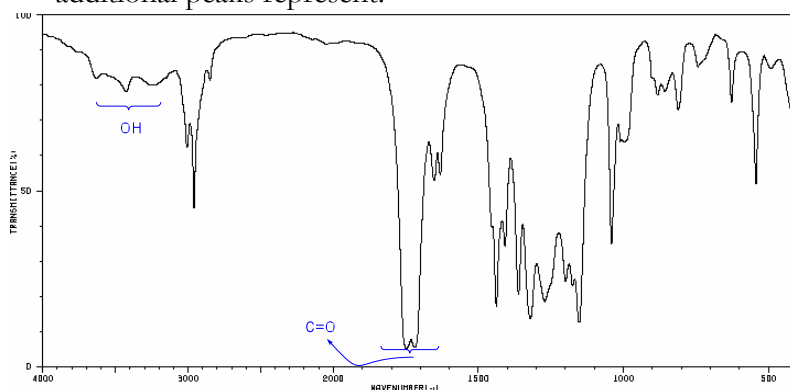
Enol form is resonance stabilized and consequently exists in a detectable amount in a sample of 5,5-dimethyl-1,3-cyclohexanedione

5. The tautomer of vitamin C shown below is not the most stable one.
- Draw the more stable tautomer
 - Why is vitamin C, also called ascorbic **acid**, so acidic? Note: the 1st pKa of vitamin C is 4.6 (similar to that of a carboxylic acid) whereas typical alcohols have pKa's in the range of 16-18.

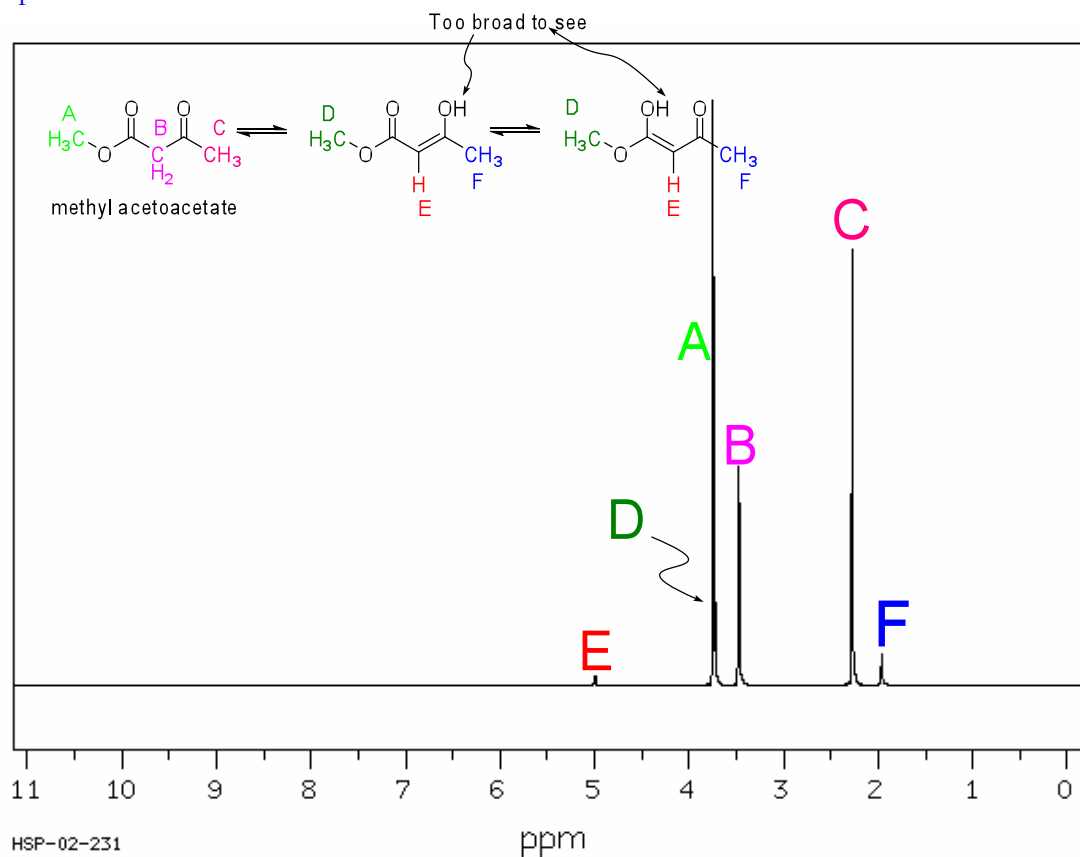


Conjugate base is resonance-stabilized with another carbonyl group, making it much more acidic than a typical alcohol.

6. The following IR of a sample of methyl acetoacetate shows the presence of an OH group. The ^1H NMR of the sample also shows three peaks at 5.00, 3.72, and 1.96 ppm in addition to the expected peaks at 3.75, 3.47, and 2.27 ppm. What do these additional peaks represent?

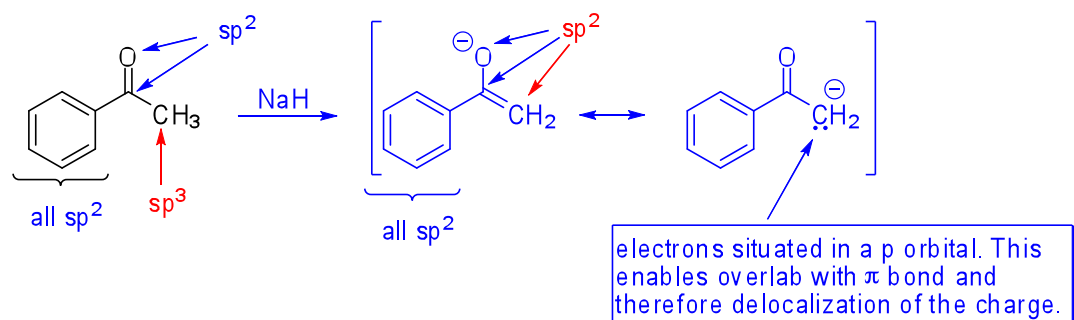


- The enol form of methyl acetoacetate is resonance stabilized, and so an observable amount of it exists (can be detected) in a sample.
- In the IR, we can see a broad peak at about 3300 cm^{-1} which represents the OH stretch (peak). In addition, we can observe two different carbonyl stretches (peaks) for the keto tautomer (ketone and ester carbonyls).
- In the ^1H NMR, peaks E (alkene-type proton) and F represent the small amount of enol present in the sample (Peak D is hidden under peak A). Peaks A, B, and C represent the peaks of the keto tautomer.



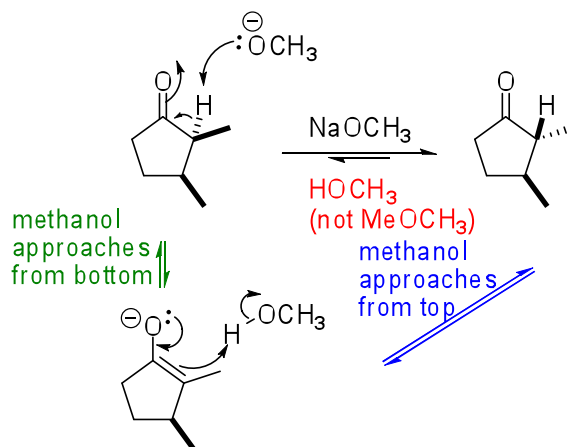
7.

- Give the product of the following reaction
- Draw the resonance forms of the product
- Identify the hybridization of each atom in the starting material and in the product and explain any differences.

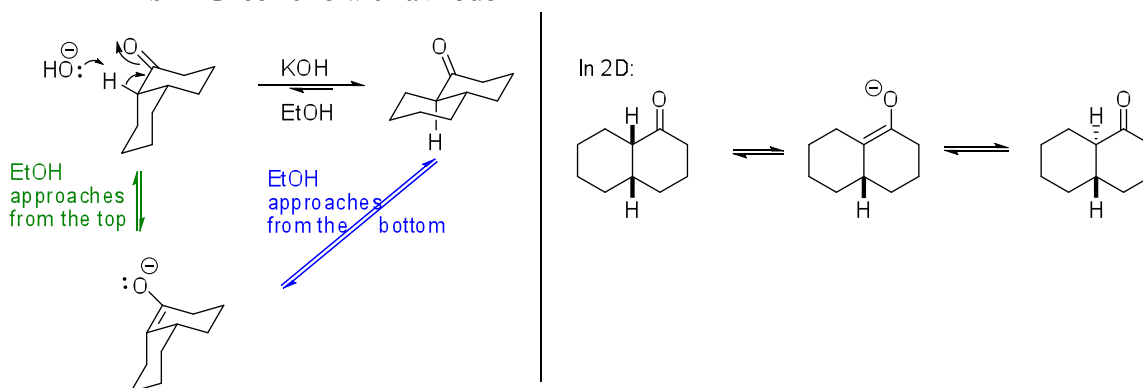


8. Provide a mechanism to explain the following interconversions.

a.



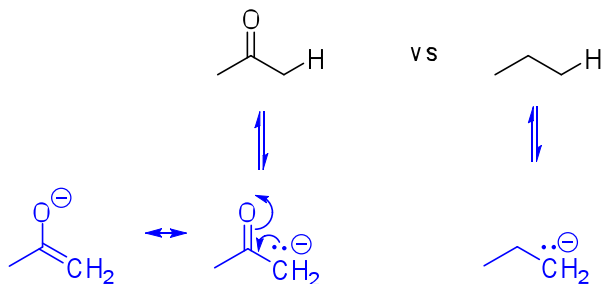
b. Check this with a model:



9. Which of the hydrogens identified in the following pairs is most acidic? Why?

Note: for each response, **FIRST** draw the conjugate base of each acid. Determine which conjugate base is most stable using the 4 criteria outlined at the start of the course (its acid is the strongest).

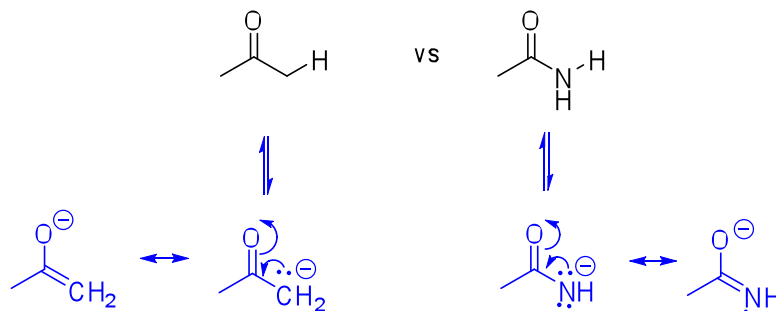
a.



The resonance stabilized conjugate base (first molecule) is more stable than the second conjugate base in which no resonance-stabilization is possible. The indicated proton in the first molecule is consequently more acidic.

Alternatively, this question could be answered by a pKa comparison: The pKa of the indicated proton in the first molecule is about 20, while the pKa of the indicated proton in the second molecule is about 50. The indicated proton in the first molecule is consequently more acidic.

b.



Both conjugate bases are resonance-stabilized, however the negative charge is supported by an "O" and a "N" in the second conjugate base, and by an "O" and a "C" in the first base. Since N is more electronegative than C, the N can stabilize the negative charge better, making the second conjugate base weaker.

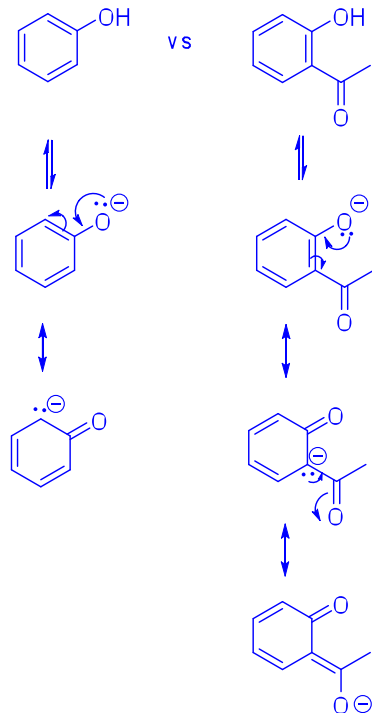
The indicated proton in the amide is more acidic than the indicated proton in the ketone.

Alternatively, pKa's could be used to answer this question. The pKa of the indicated proton in the ketone is about 20, while the pKa of the indicated proton in the amide is about 16, making the amide more acidic.

Assignment 7 – Enols/Enolates and related reactions

ANSWERS

c. (9. c.)



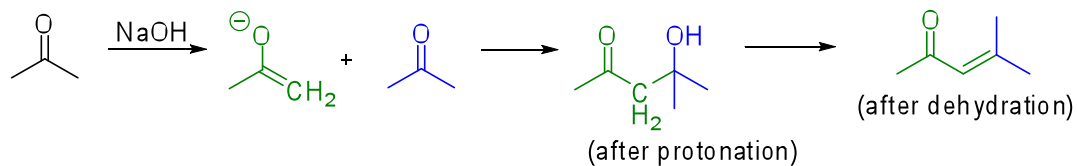
Both conjugate bases are stabilized by resonance with the aromatic ring. The second c.b. is additionally stabilized by resonance with the acetate carbonyl as shown. The second c.b. is consequently more stable than the first, and therefore the second phenol is more acidic than the first.

Note: a pKa comparison of the acids cannot be used in this case since both acids are phenols (pKa about 10).

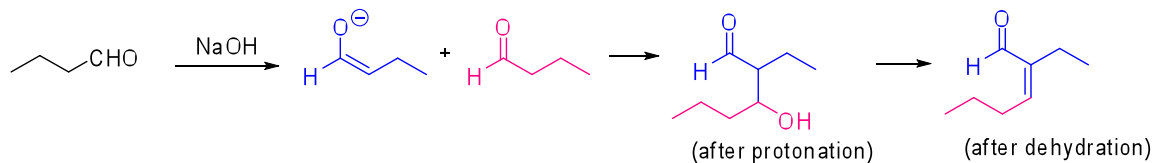
Note: The question could also have asked for a comparison between the ortho, meta and para substituted phenols (or thiols, or anilines).

10. Predict the products of self-condensation:

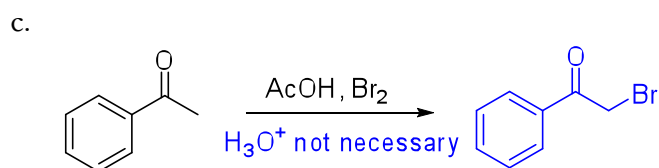
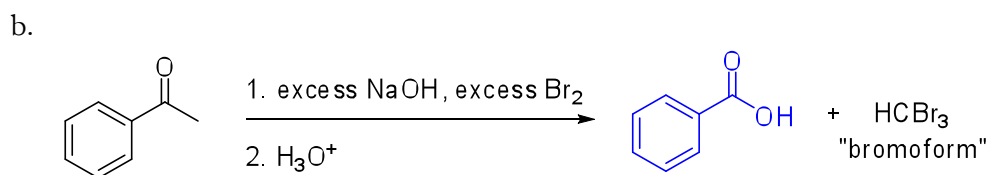
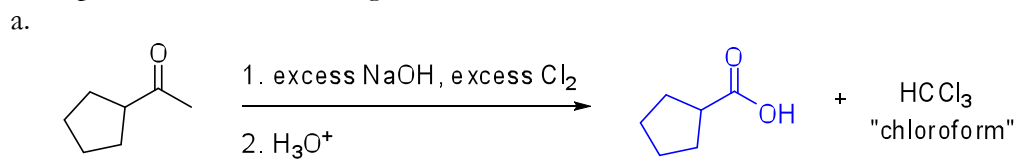
a.



b.

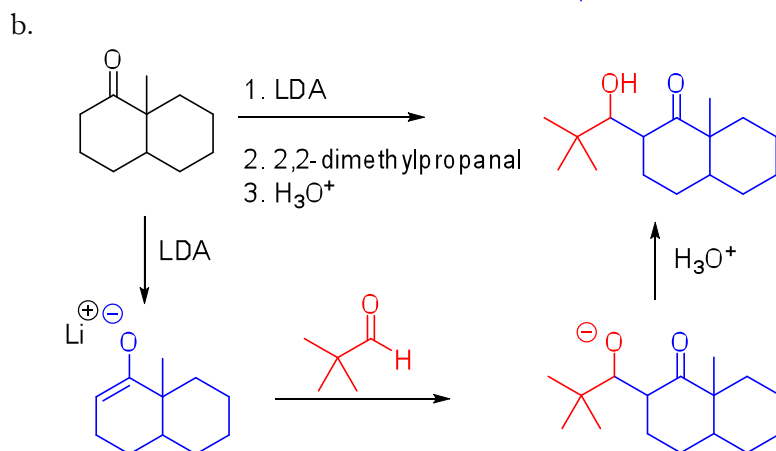
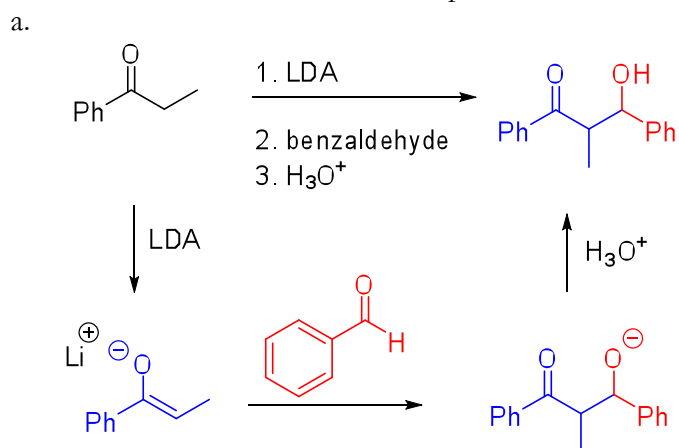


11. Give the product of the following reactions.



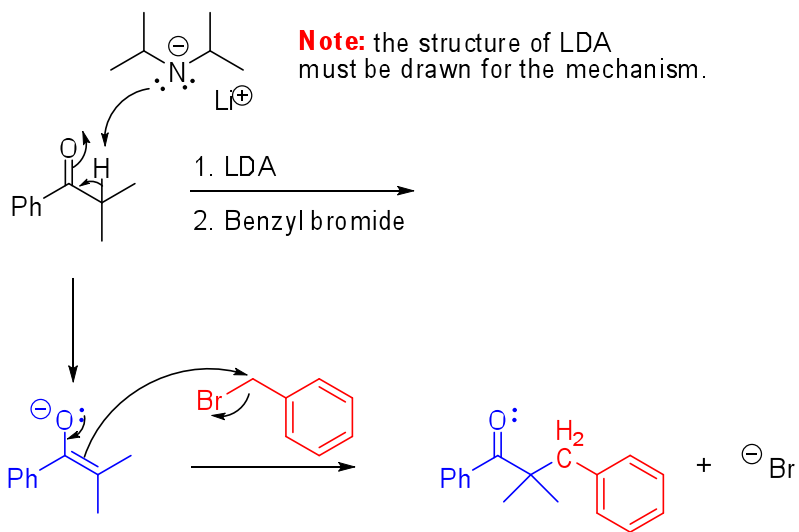
Note: Look at the difference between the products generated in part b versus part c.

12. Predict the crossed aldol condensation products:

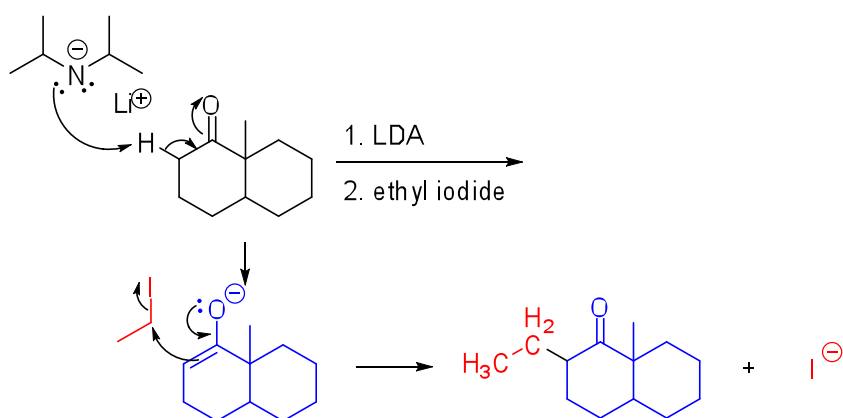


13. Give the intermediate obtained after each step and the final product of each sequence.

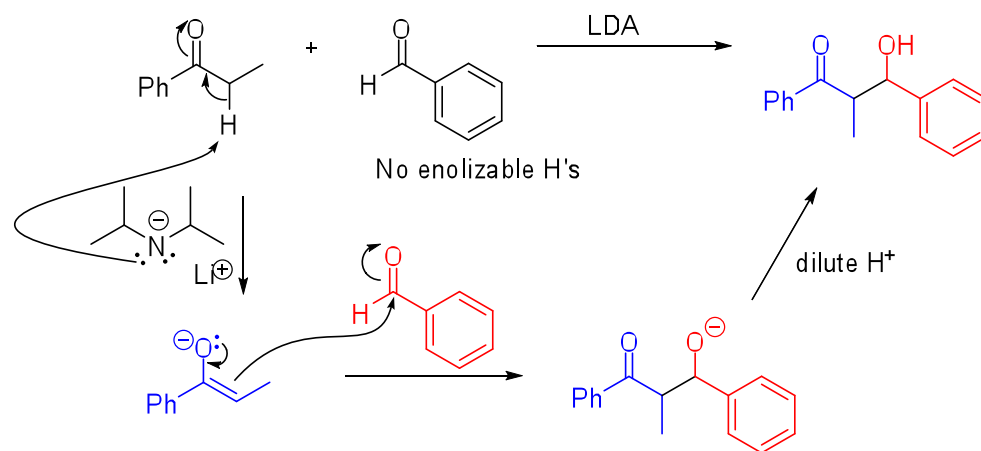
a.



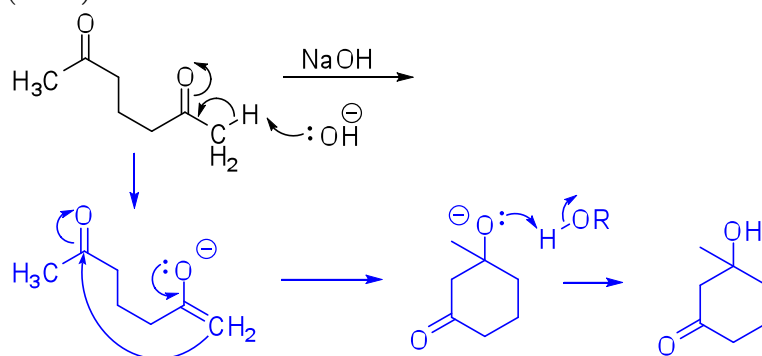
b.



c.

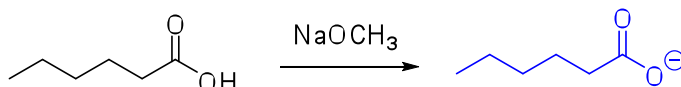


d. (13. d.)

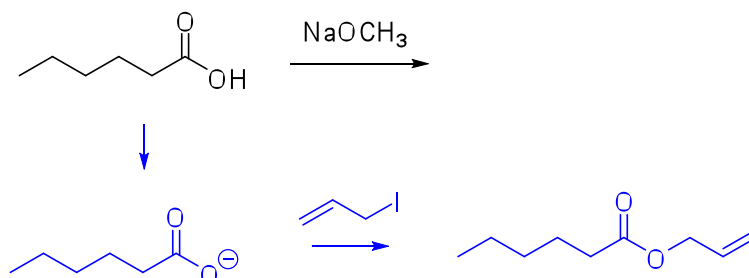


14. Predict the major product expected from each of the following reactions and include a mechanism for each step.

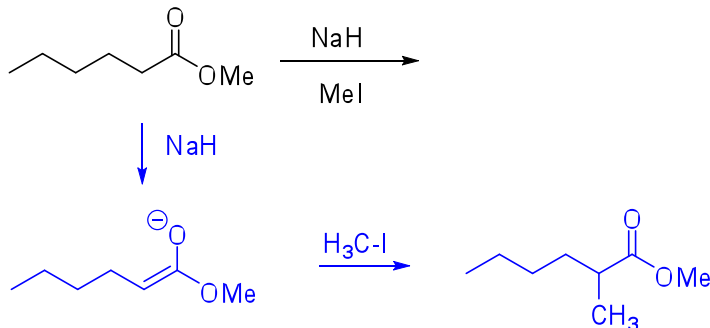
a.



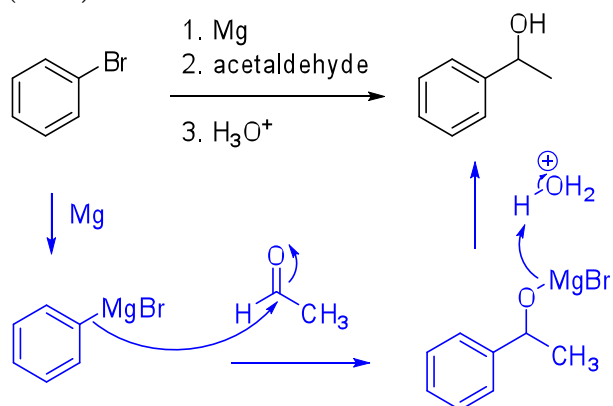
b.



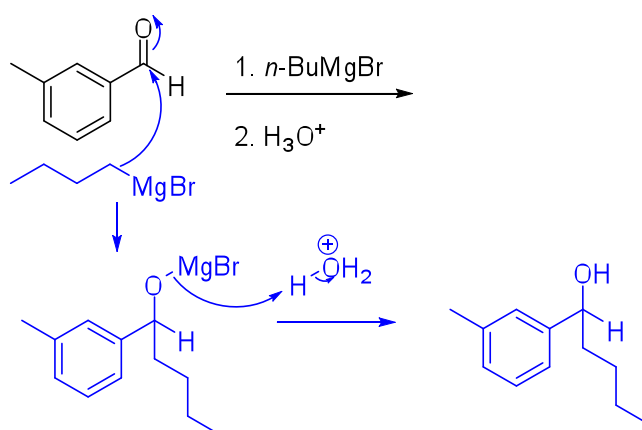
c.



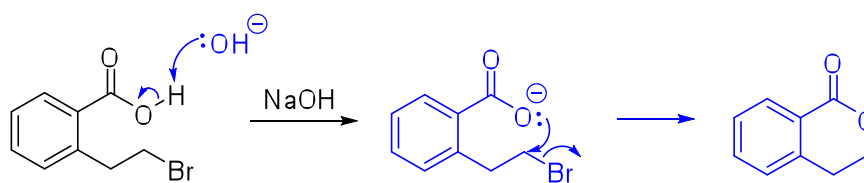
d. (14. d.)



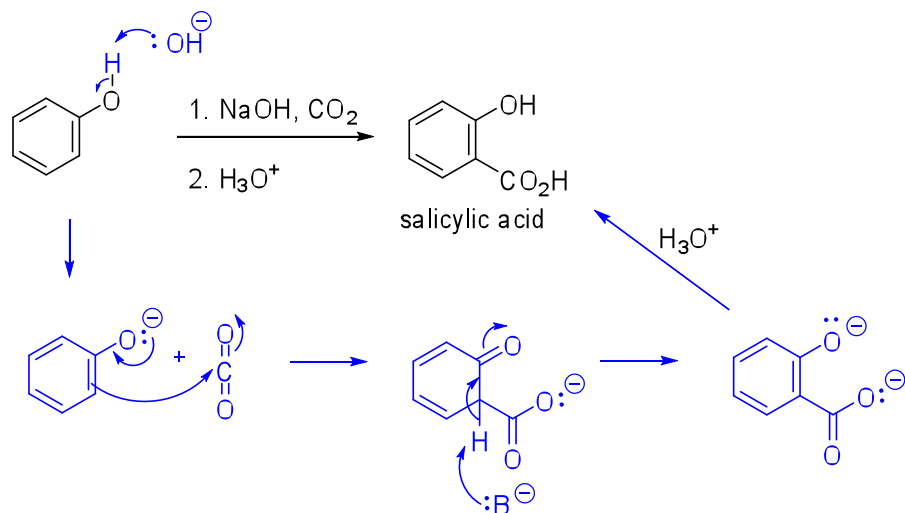
e.



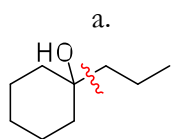
f.



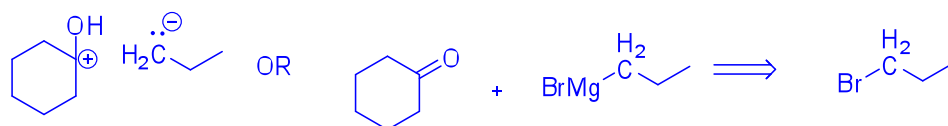
g.



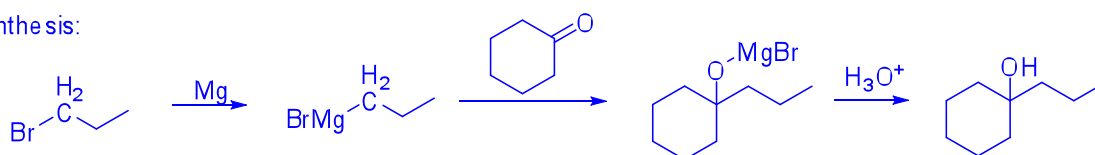
15. Suggest a synthesis of the following molecules. An analysis/brainstorming and retrosynthetic analysis are required.



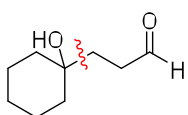
from cyclohexanone and 1-bromopropane



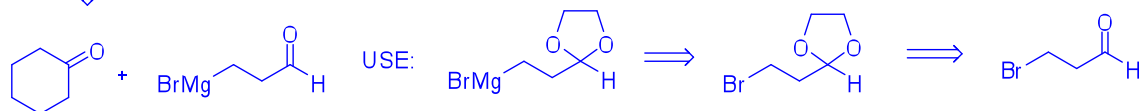
Synthesis:



b.

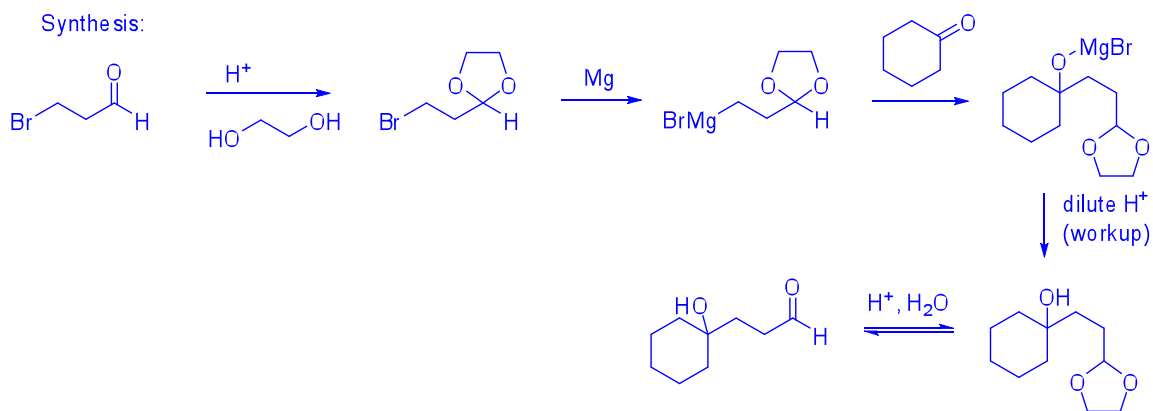


from cyclohexanone and 3-bromopropanal

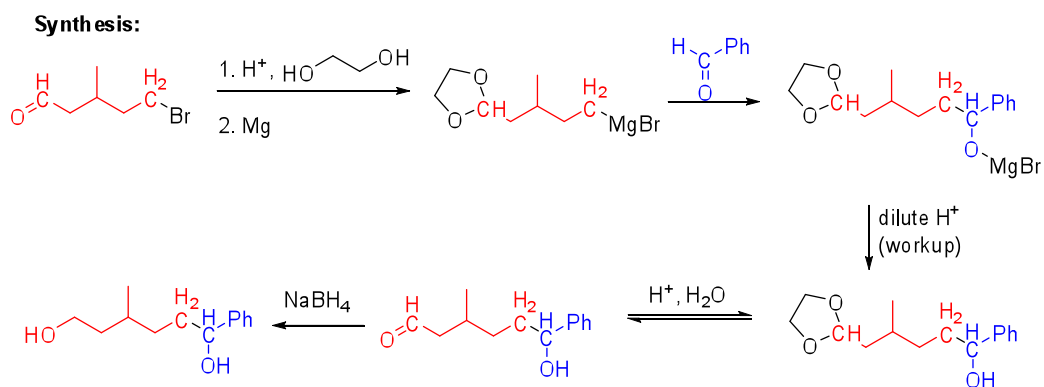
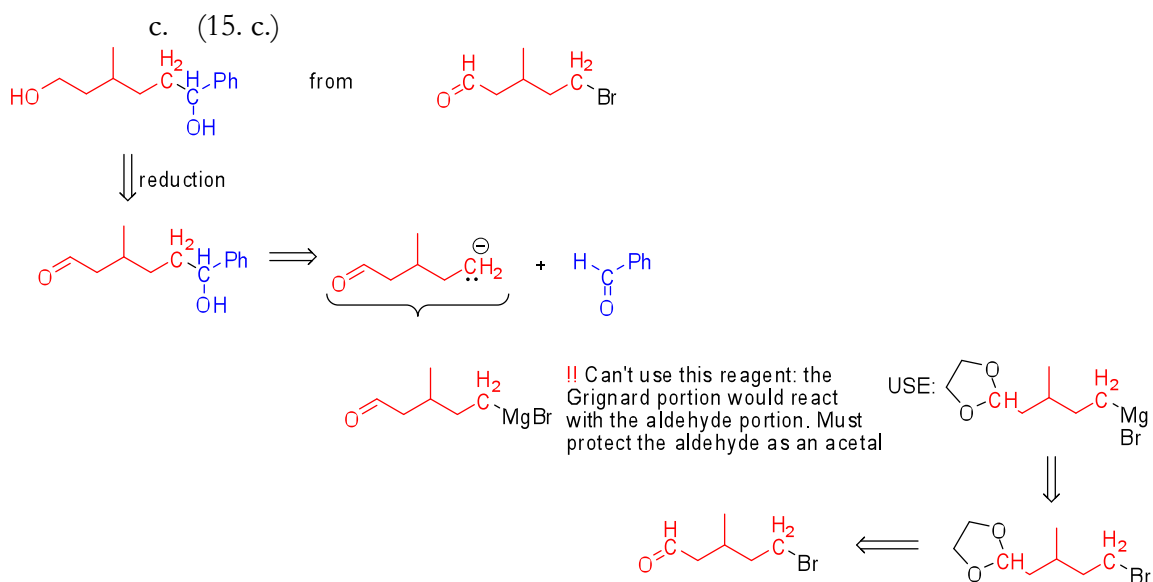


!! Can't use this reagent: the Grignard portion would react with the aldehyde portion. Must protect the aldehyde as an acetal

Synthesis:

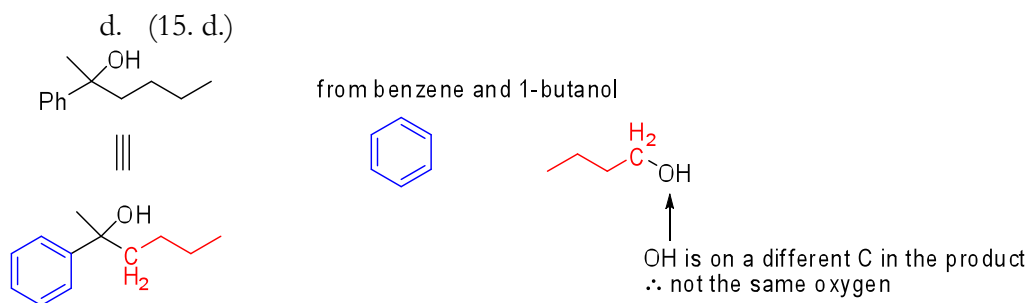


Assignment 7 – Enols/Enolates and related reactions
ANSWERS

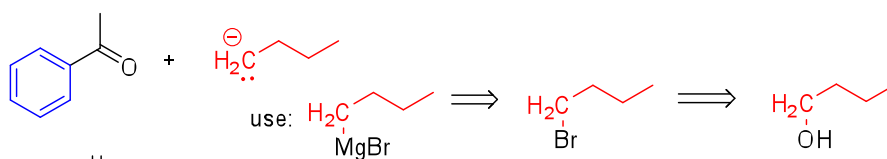


Assignment 7 – Enols/Enolates and related reactions

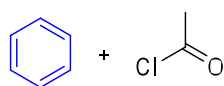
ANSWERS



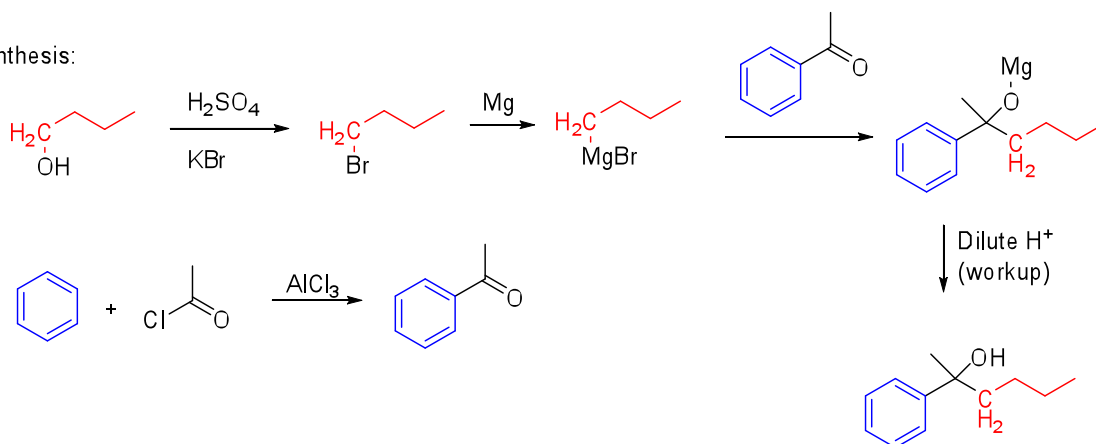
Grignard rxn



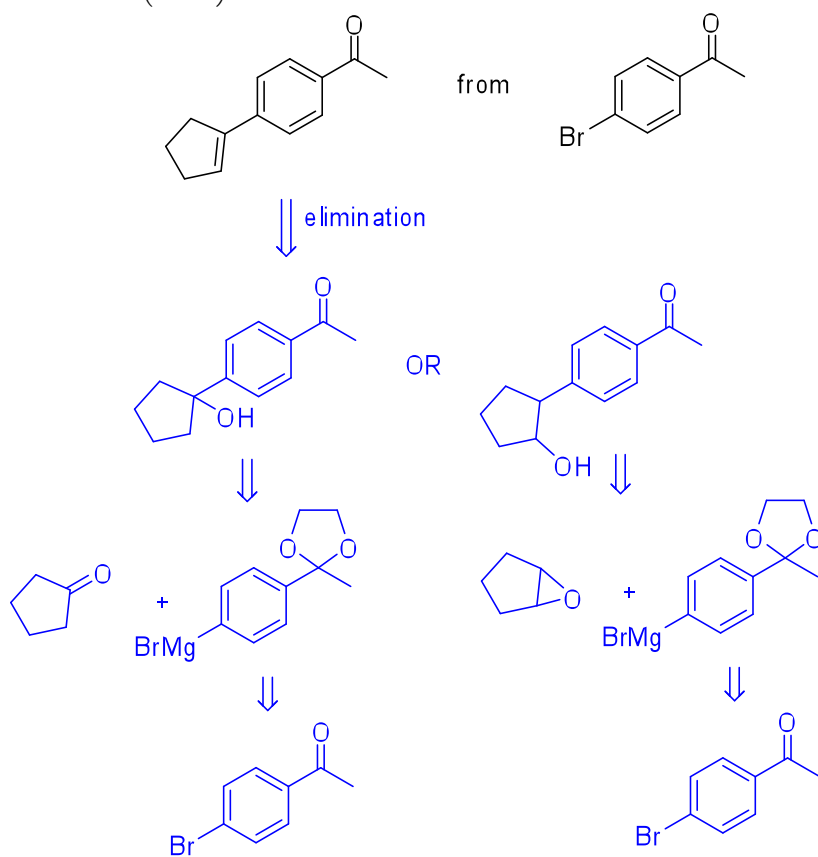
F.C. acylation



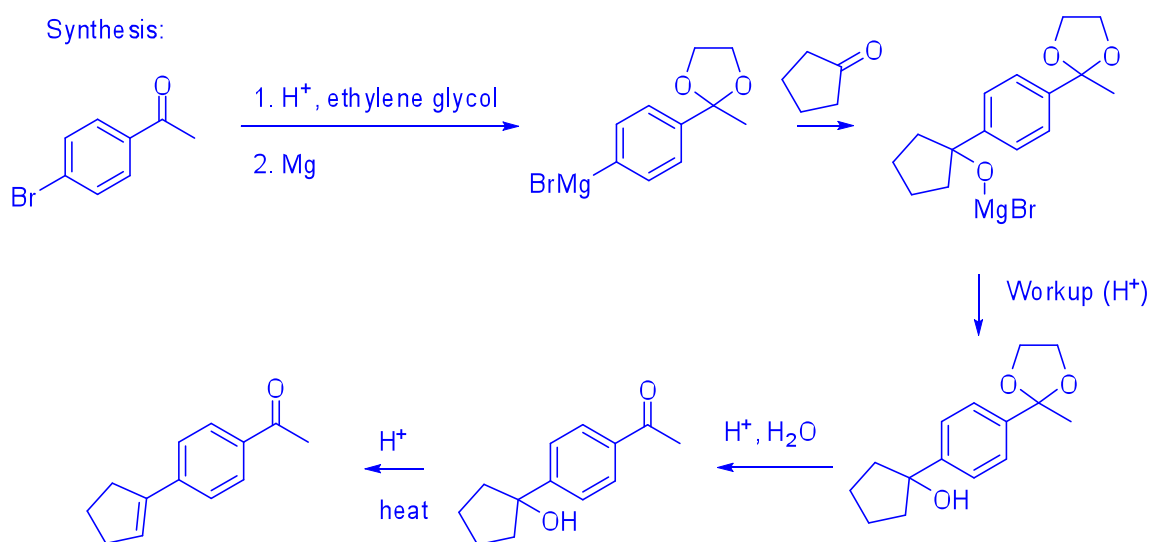
Synthesis:



e. (15. e.)

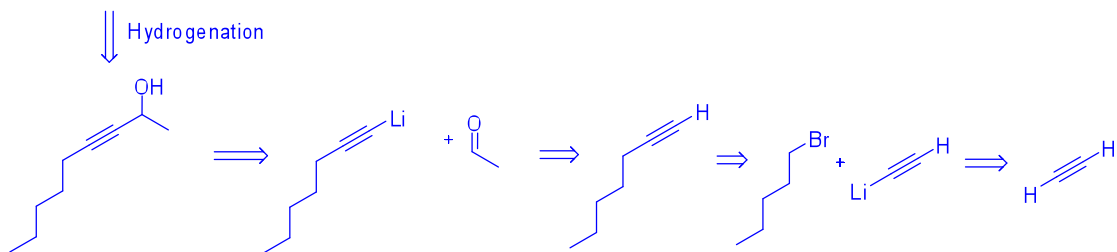
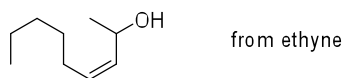


Synthesis:

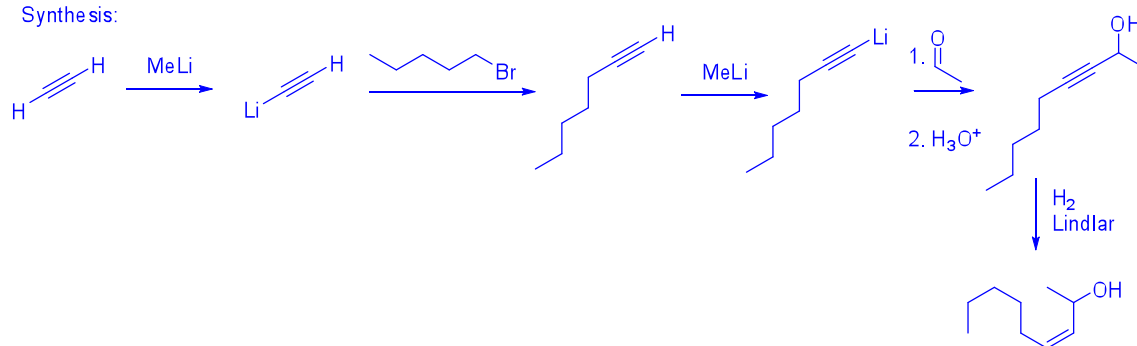


This E1 reaction generates a tertiary and resonance stabilized carbocation—better than in the other synthesis in which only a secondary carbocation would be generated

f. (15. f.)

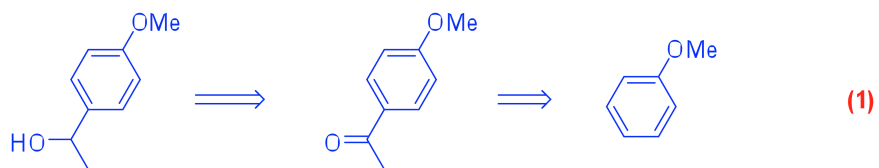
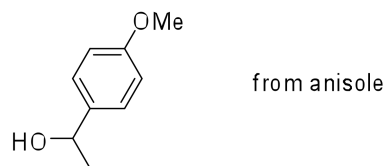


Synthesis:

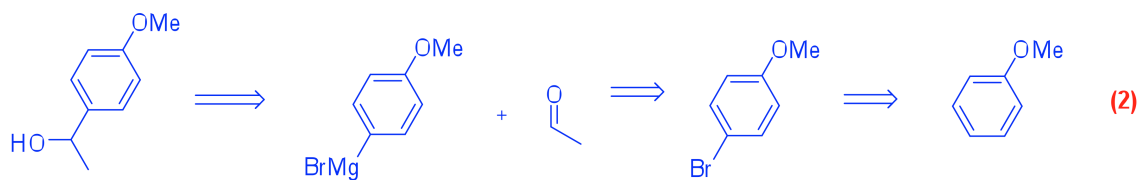


Assignment 7 – Enols/Enolates and related reactions
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g. (15. g.)

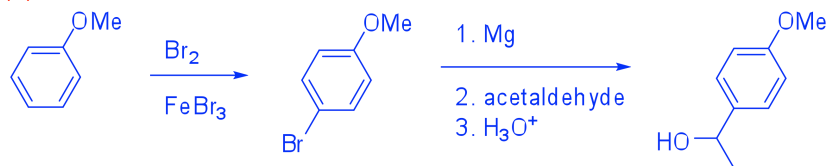


OR



Syntheses:

(2)



(1)

