CHEMISTRY 314-02

MIDTERM # 3 – answer key

April 19, 2005

Statistics:

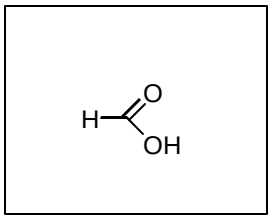
- Average: 67 pts (67%);
- Highest: 99 pts (99%); Lowest: 35 pts (35%)
- Number of students performing at or above average: 25 (56%)

1. (5 pts) Mark as true (**T**) or false (**F**) the following statements. Do not explain!
   - (**T**) The *haloform* reaction requires basic conditions;
   - (**T**) *Fischer* esterification occurs only in acidic conditions;
   - (**T**) Amides are less reactive than acid chlorides and esters;
   - (**T**) *Saponification* is the process of base-catalyzed hydrolysis of esters;
   - (**T**) Lactams are intramolecular amides;
2. Circle all that apply:
   A. (3 pts) The following reactions CANNOT be used to generate esters:
      a. Base-catalyzed reaction of carboxylic acid and alcohol;
      b. Reaction of acid chloride and alcohol;
      c. Reaction of amide and alcohol;
      d. *Baeyer-Villiger* oxidation of ketones;

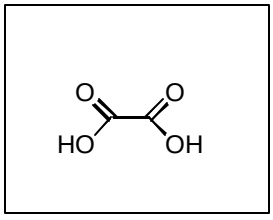
   B. (3 pts) The following reactions DO NOT occur with an intermediate formation of enolates:
      a. *Fischer* esterification;
      b. *Claisen* condensation;
      c. The *haloform* reaction;
      d. Saponification of esters;

   C. (3 pts) The following compounds DO NOT decarboxylate upon heating:
      a. β-ketoacids;
      b. γ-dicarboxylic acids;
      c. β-dicarboxylic acids;
      d. γ-hydroxyacids;

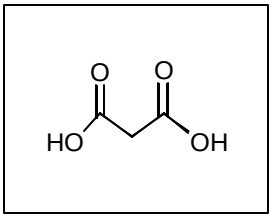
3. (5 pts) Provide the structure of each of the following carboxylic acids, listed with their trivial names:



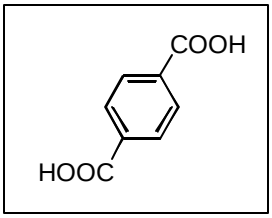
formic acid



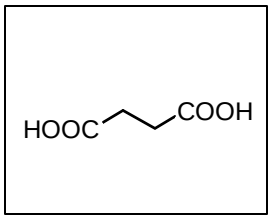
oxalic acid



malonic acid



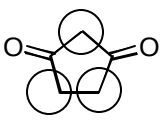
terephthalic acid

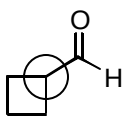


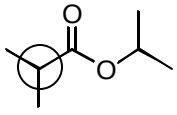
succinic acid

4. (4 pts) Rank the following compounds in order of increasing acidity. Do not explain!
   A. Trichloroacetic acid;
   B. Trifluoroacetic acid;
   C. Propanoic acid;
   D. Isopropanol;
   E. Isopropylamine; **E < D < C < A < B**

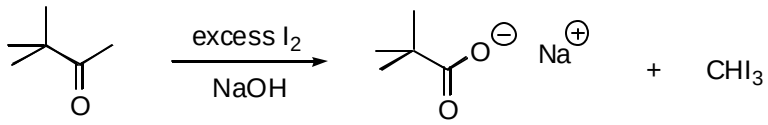
5. (4 pts) Identify (circle) ALL acidic hydrogens (pK_a = 25) in the following molecules:



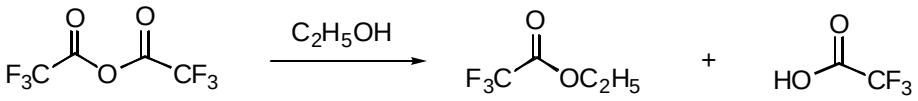




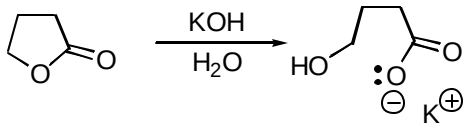
6. Write a complete equation for each of the processes indicated below (NOTE: Do not write mechanisms !!).
   A. (3 pts) Reaction of 3,3-dimethyl-2-butanone with excess I_2 in the presence of NaOH;



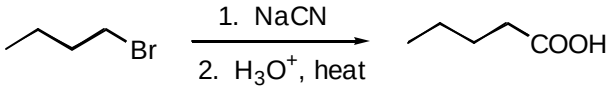
B. (3 pts) Reaction of trifluoroacetic anhydride with ethanol.



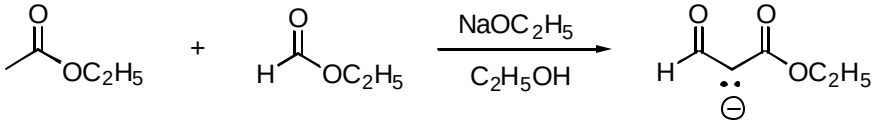
C. (3 pts) Saponification of 4-butanolide (γ-butyrolactone).



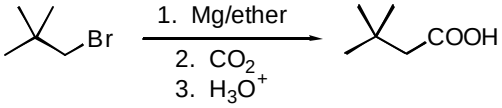
D. (3 pts) Reaction of *n*-butyl bromide with sodium cyanide, followed by acid hydrolysis;

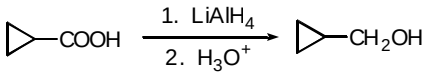


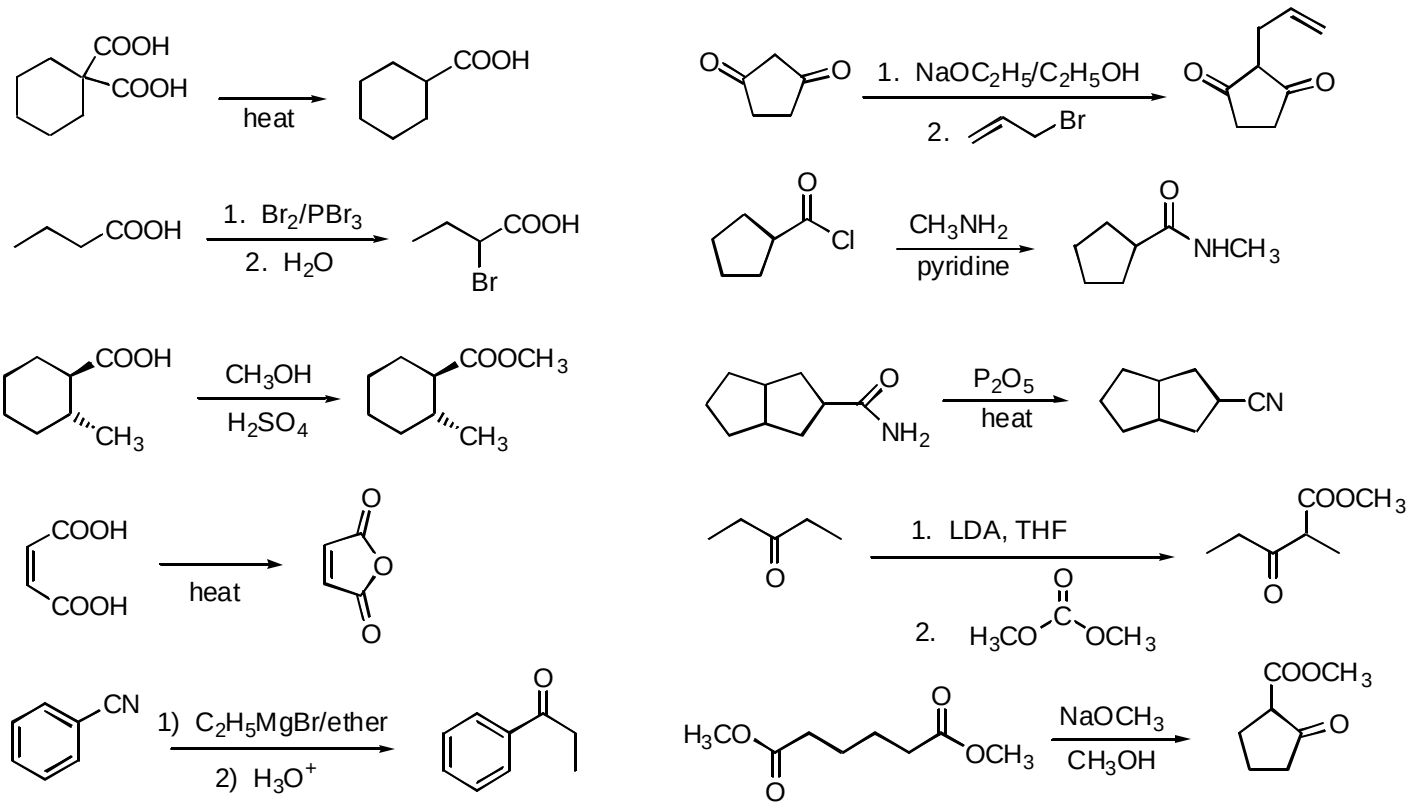
E. (3 pts) Reaction of ethyl acetate with ethyl formate in the presence of NaOEt/EtOH;



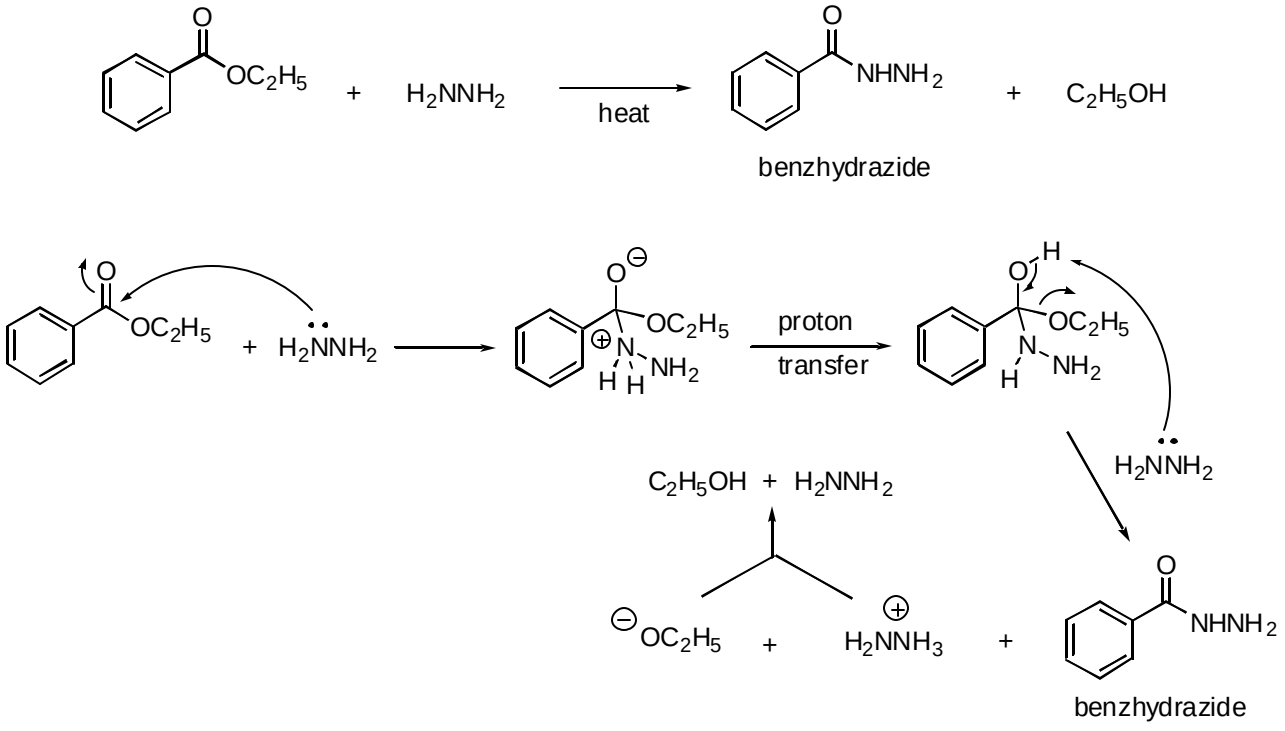
7. (24 pts) Predict the principal organic product in each of the following reactions:



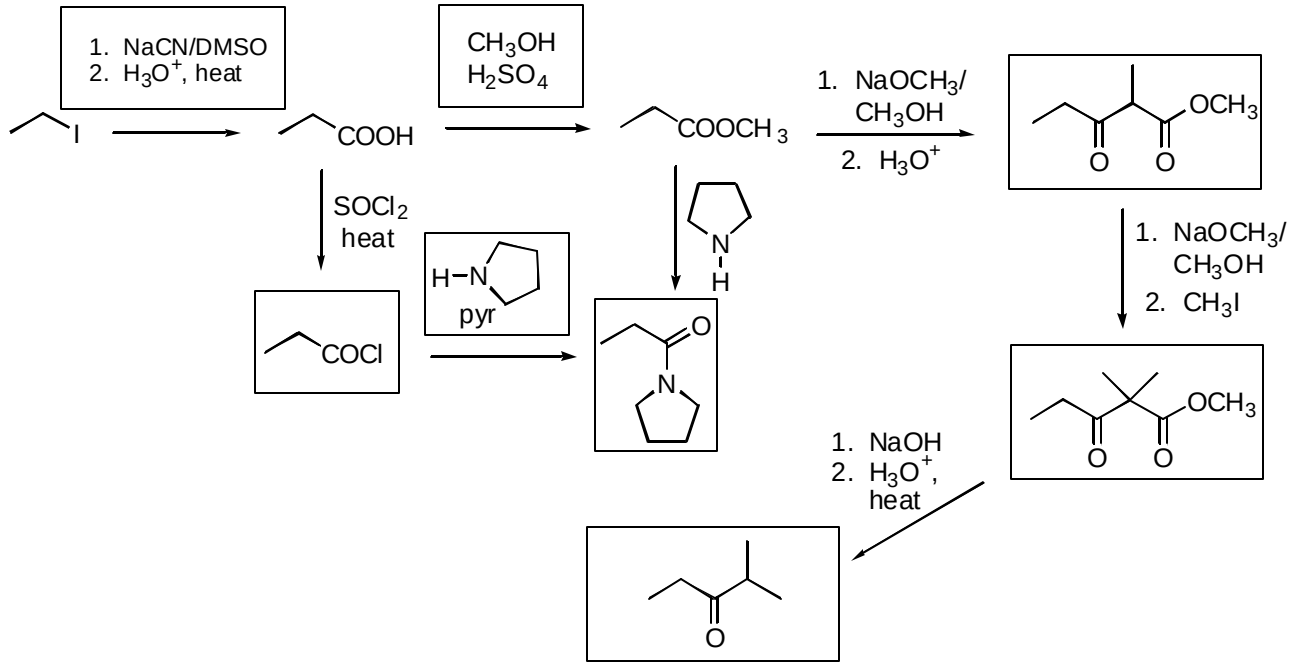




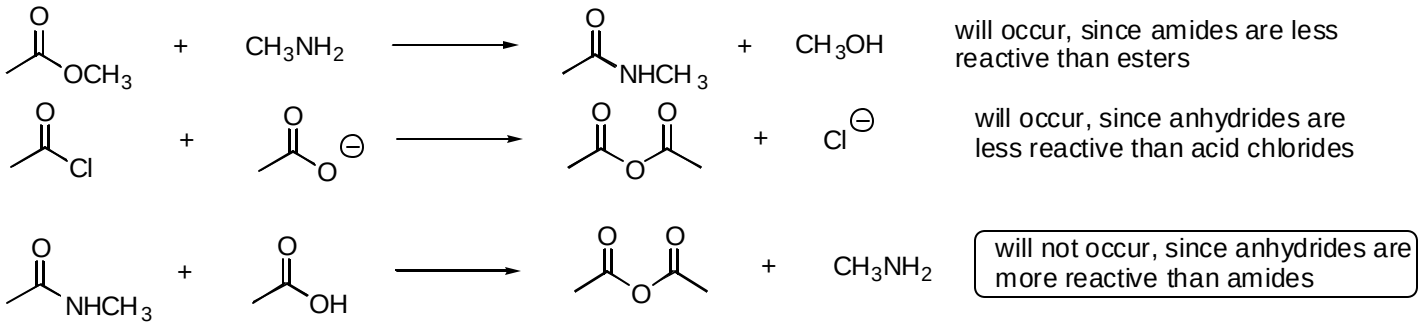
8. (4 pts) Another class of acid derivatives is that of carboxylic acid hydrazides, which can be considered as derivatives of hydrazine. Although not explicitly discussed in class, their reactions are mechanistically similar to those of other derivatives. The reaction below shows the formation of benzhydrazide from ethyl benzoate and hydrazine. Propose a detailed mechanism.



9. (8 pts) Fill in the blanks in the following scheme:



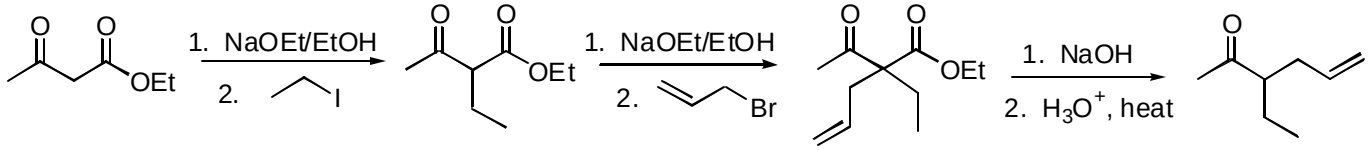
10. (3 pts) Which of the following reactions will not work as suggested?

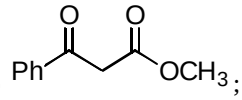


11. You are given four structures below. Propose a synthesis of each of these structures, using any necessary organic or inorganic reagents, and employing **one** of the following synthetic methodologies: **1) Mixed aldol condensation; 2) Mixed *Claisen* condensation; 3) The acetoacetic ester synthesis; 4) The malonic ester synthesis**. Draw the complete synthetic sequence in each case.

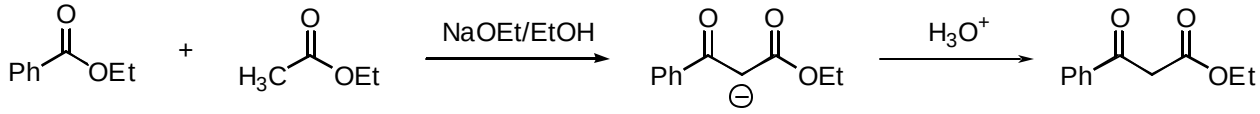
A. (4 pts) 3-ethyl-5-hexen-2-one;

It is generated using the **acetoacetic ester synthesis**:



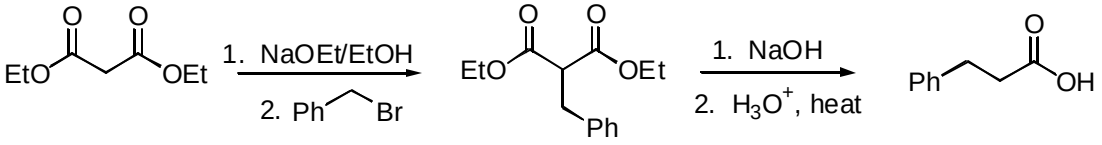
B. (3 pts) 

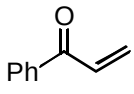
It is generated using a **mixed *Claisen* condensation**:



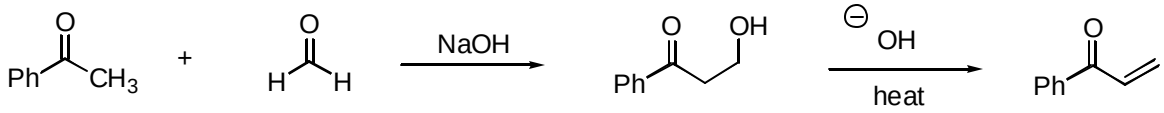
C. (3 pts) 3-Phenylpropanoic acid;

It is generated using the **malonic ester synthesis**:



D. (3 pts) 

It is generated using a **mixed aldol condensation**:

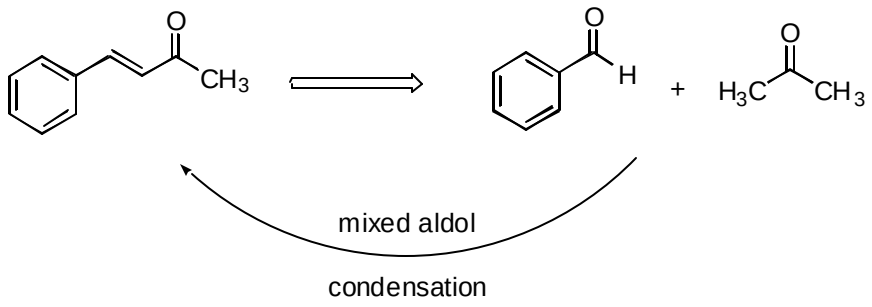


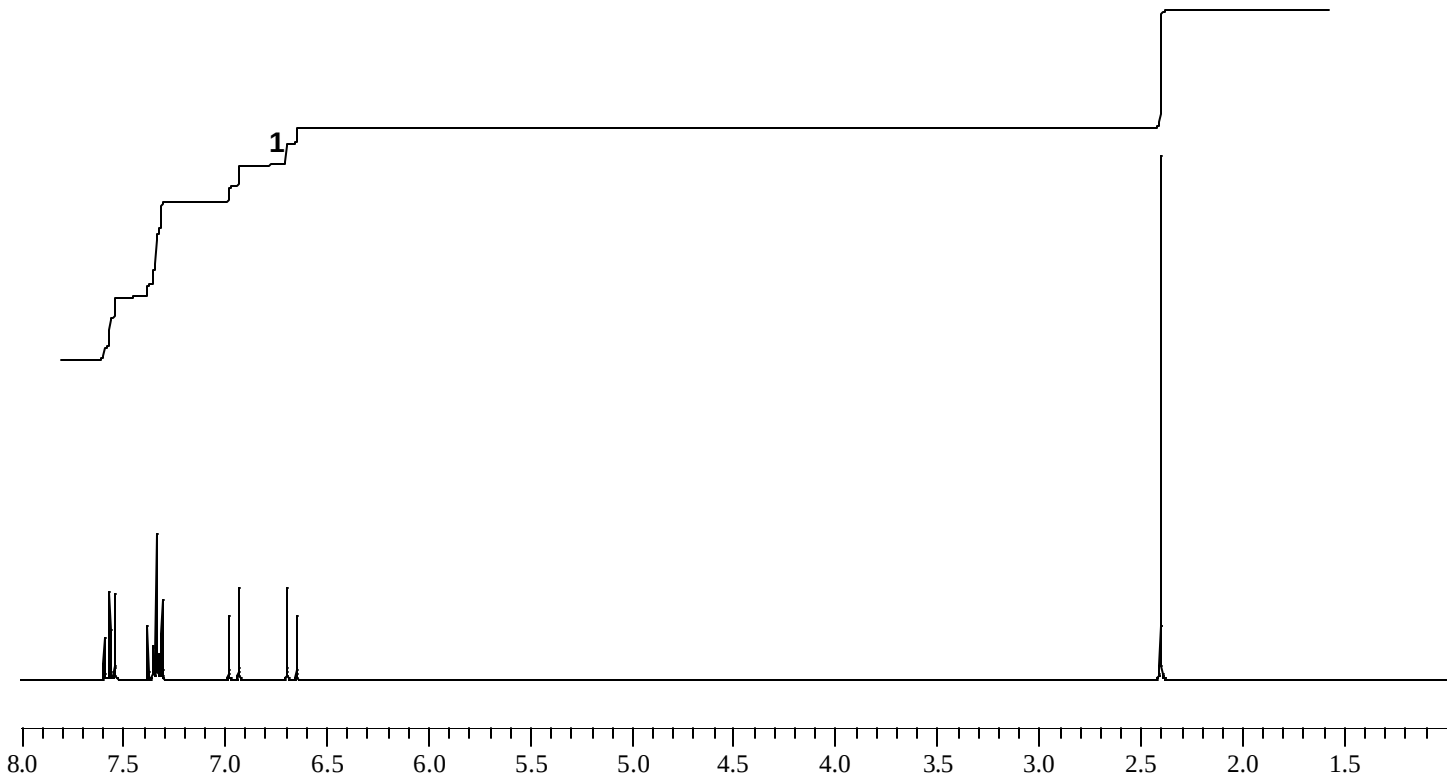
12. (6 pts) Certain compound has molecular formula $C_{10}H_{10}O$ and is prepared using mixed aldol condensation. Its ^1H NMR spectrum is shown below.
    A. Assign the correct structure for the compound.
    B. What carbonyl compounds were used in the aldol condensation?

Solution: First, determine elements of unsaturation: (2 x 10 + 2 – 10)/2 = 6. The NMR spectrum shows clearly the presence of aromatic hydrogens. The presence of a benzene ring accounts for 4 out of the 6 elements of unsaturation. In addition, the compound is a product of aldol condensation. Therefore it must be an a,b-unsaturated carbonyl compound, i.e. it has a carbonyl group and a C = C bond, which are conjugated. Theses two double bonds account for the remaining two elements of unsaturation. Other things to be seen from the NMR spectrum:

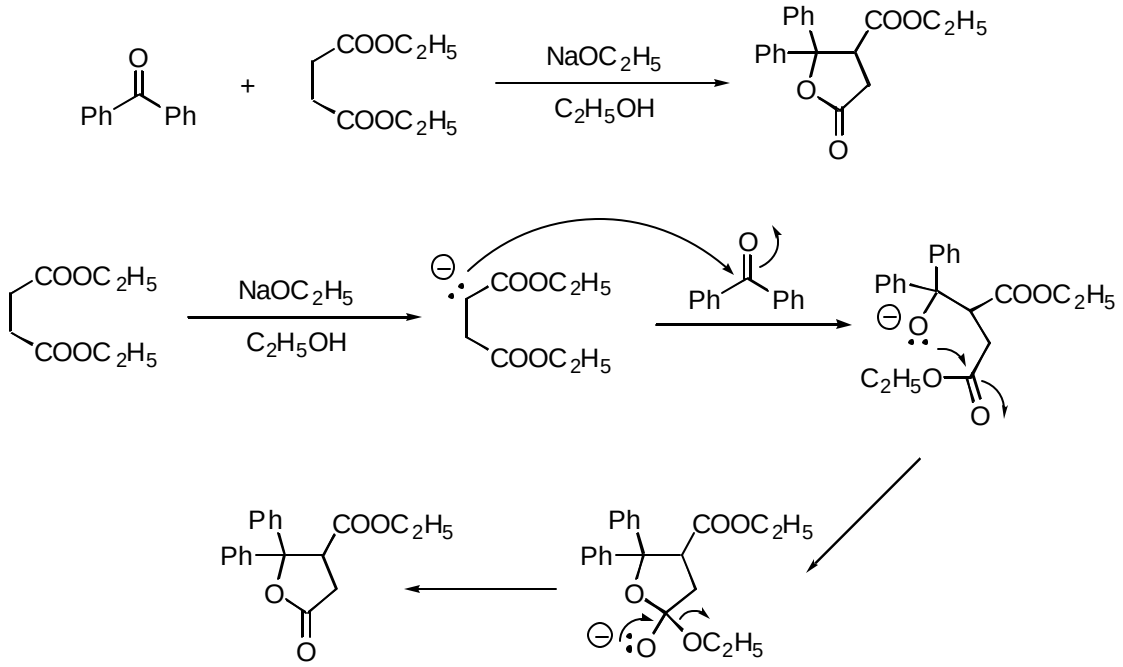
a. two doublets (each for 1H) in the region 6.5 – 7.0 ppm. These belong to alkene-type H-atoms;
b. one singlet (for 3H) at ~ 2.5 ppm. It is most likely a CH_3-group that is not coupled to anything else. By the shift one can expect it to be attached to a benzene ring, or a carbonyl group, or a C = C bond;

These features fit the following structure:





13. (3 pts) **BONUS PROBLEM (In order to receive credit for this problem, it has to be solved entirely!!).** In the *Stobbe* condensation an ester of succinic acid (such as diethyl succinate below) is subjected to base deprotonation and then reacted with a non-enolizable aldehyde or ketone to give a product with a lactone ring. Propose a plausible, detailed mechanism for the *Stobbe* condensation below.


Ph
Ph
O
+
COOC2H5
COOC2H5
NaOC2H5
C2H5OH
Ph
Ph
O
O
COOC2H5
COOC2H5
NaOC2H5
C2H5OH
COOC2H5
COOC2H5
O
Ph
Ph
Ph
Ph
O
COOC2H5
C2H5O
O
Ph
Ph
O
COOC2H5
O
Ph
Ph
O
COOC2H5
O
OC2H5