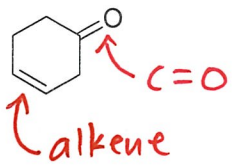
Key - Ex. 2 Summer 2019
3331

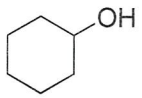
For questions 1 through 5, select the best reagent(s) from the list. *Assume appropriate solvents and aqueous workup after all reactions.* Choices may be used more than once, or not at all.

a. Only $NaBH_4$ would work
b. Only LAH would work
c. Either $NaBH_4$ or LAH would work
d. H_2/Pd
e. H_2/Raney Ni

1.

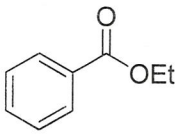


E

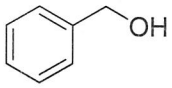


Both C=O and C=C were reduced

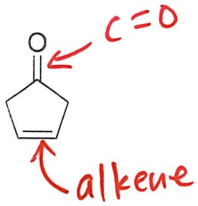
2.



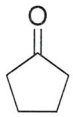
B



3.

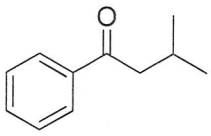


D

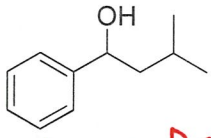


Only C=C was reduced

4.

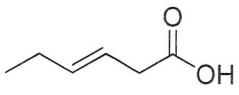


C

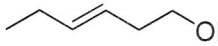


Can't use Raney Ni/H_2 – could affect benzene

5.



B

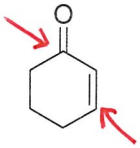


Reduce RCO_2H, not alkene

Each question 6 through 10 shows an organic molecule. Using what you have learned about the ways that organometallic reagents react, select the reagent(s) from the list that will reliably and successfully react with the substrate in each question. "Successful" means a reaction that produces a majority of one organic product (which may include mixtures of enantiomers or diastereomers) with minimal side reactions. Assume you can use as many equivalents of the organometallic reagent as you need and that all reactions are run in appropriate solvents and followed by aqueous workup. Answer choices can be used once, more than once, or not at all.

RMgX = Grignard reagent
RLi = organolithium reagent
R_2CuLi = organocuprate

a. RMgX
b. R_2CuLi
c. RMgX and RLi
d. RLi and R_2CuLi
e. RMgX, RLi, and R_2CuLi



6

Conjugate or direct addition:

D

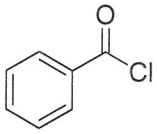
(RMgX not reliable)

7

Epoxide opening

B

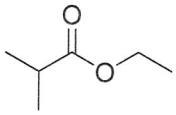
(RMgX/RLi give side reactions)



8

E

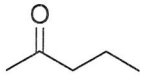
- Can make ROH using 2 eq of RMgX/RLi
- Can make ketone using R_2CuLi



9

C

2 eq of RMgX/RLi

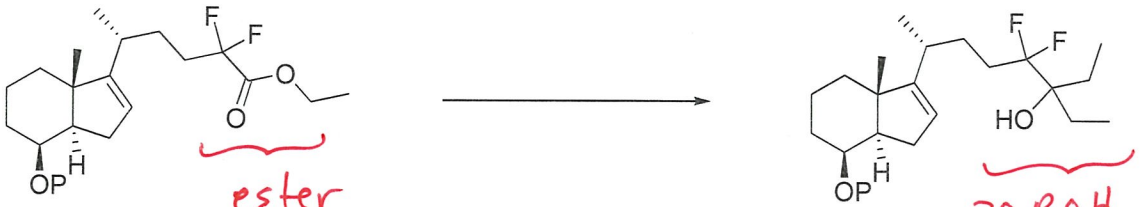


10

C

1 eq of RMgX/RLi → ROH

11. The following step occurred in a synthesis of a derivative of a hormone in the Vitamin D3 family of compounds. (The label "OP" stands for a protected OH group.)



ester

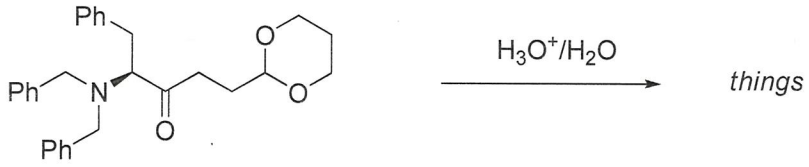
3° ROH, 2 R's the same

E

Which of the following reagents was used in this step? (Assume aqueous workup in all cases.)

a. LAH
b. 1 equivalent of Et_2CuLi
c. 2 equivalents of Et_2CuLi
d. 1 equivalent of EtLi
e. 2 equivalents of EtLi

12. This compound is treated with aqueous acid:

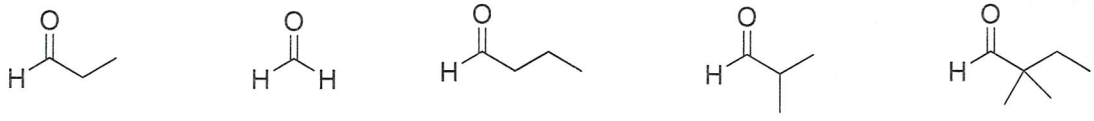


E

Which of the following species would you NOT expect to exist in solution? (Note that this question is not necessarily asking about a final product that is or isn't possible, but rather all the possible structures in solution. Just select the species that would not reasonably form under the conditions shown.)

a. hydrate ketone gets hydrated, as does deprotected aldehyde
b. enol ketone and deprotected aldehyde can tautomerize
c. hemiacetal acetal hydrolysis intermediate
d. aldehyde what you get when acetal is hydrolyzed
e. all of these species could exist under the conditions shown

13. Which of these aldehydes has the smallest value of $K_{hydration}$? (Least favorable — more C=O than hydrate)



A B C D E

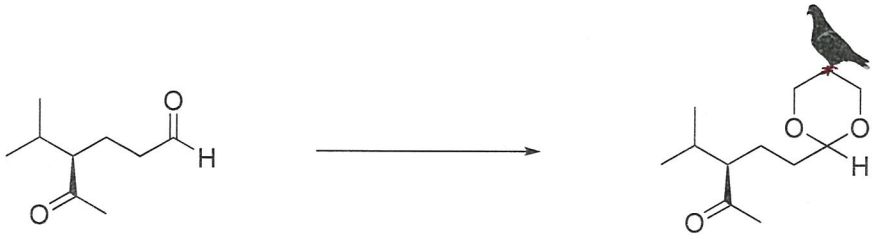
most hindered

14. What is the stereochemical outcome of this reaction?

C

a. Racemic mixture
b. An unequal mixture of enantiomers
c. An unequal mixture of diastereomers
d. An equal mixture of diastereomers
e. A single achiral molecule

15. Distinguished pigeon chemist Professor Burblecoo needed to protect an aldehyde as a cyclic acetal as part of a synthesis:



D

As you know, the reaction calls for the use of molecular sieves, which are shown in the photo to the left. When Professor Burblecoo saw the sieves, he thought they were seeds so he gobbled them all up. After this binge (it took the pigeon about 5 seconds to eat the entire bowl of sieves), the pigeon burped loudly, flew around the lab a few times, and ran the reaction without the sieves.

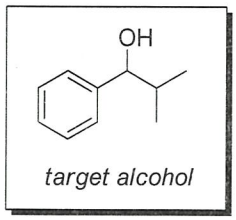
What will be the effect on the reaction of leaving out the molecular sieves?

a. The acetal will not form at all.
b. Both the aldehyde and the ketone will be protected as acetals.
c. The ketone will be protected as an acetal instead of the aldehyde.
d. The pigeon will not get the highest possible yield of acetal.
e. Leaving the molecular sieves out of the reaction will not change the desired outcome.

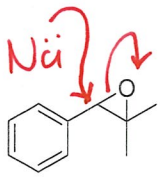
The purpose of the sieves is to remove H_2O (product) and pull the equilibrium to the right.

16. You are trying to make the alcohol shown. From which of these structures can you NOT make the alcohol in one step (reaction + workup = one step)?

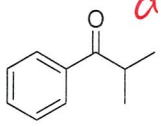
A



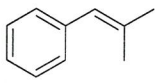
Nü ← Cuprate opening won't produce the desired alcohol.



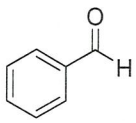
(A)



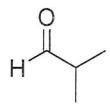
B



C



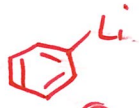
D



E

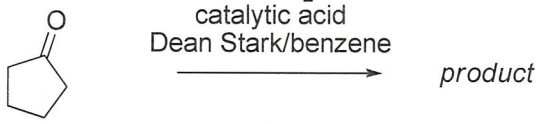
+ $NaBH_4$ MeOH

1. $BH_3 \cdot THF$
2. $H_2O_2, HO^{\ominus}$

1. 

2. $H_3O^{\oplus}$

17. Which of the statements about this reaction is true?

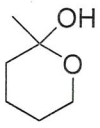


E

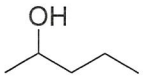
a. An azeotropic distillation is being used to make sure that water is continuously added into the reaction mixture. No - removed
b. The product of the reaction is a cyanohydrin. No - imine
c. If the reaction is run at pH > 5, the nucleophile will be protonated. No
d. Running the reaction at a pH of 2 will ensure that the reaction will proceed at the fastest possible rate. No - too acidic
(e.) There is a carbinolamine intermediate in the reaction.

18. Which of these compounds will be converted to a ketone in the presence of aqueous acid?

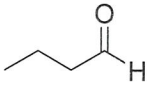
A



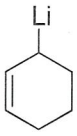
(A)



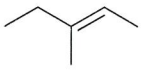
B



C



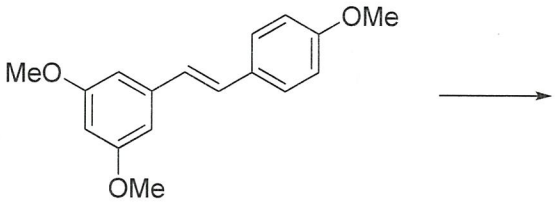
D



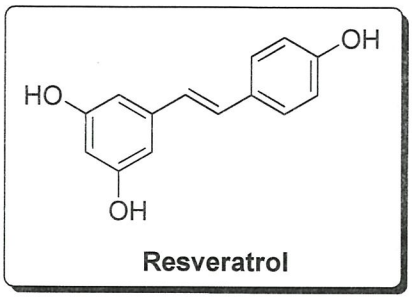
E

hemiacetal

Questions 19 and 20 involve the synthesis of resveratrol, an antioxidant found in red wine. In the CU undergrad lab, two students each proposed a synthesis to make a key intermediate, trimethylresveratrol. In each of the methods shown below, each arrow represents one synthetic step. The product of each step is not shown. "CHO" represents an aldehyde.

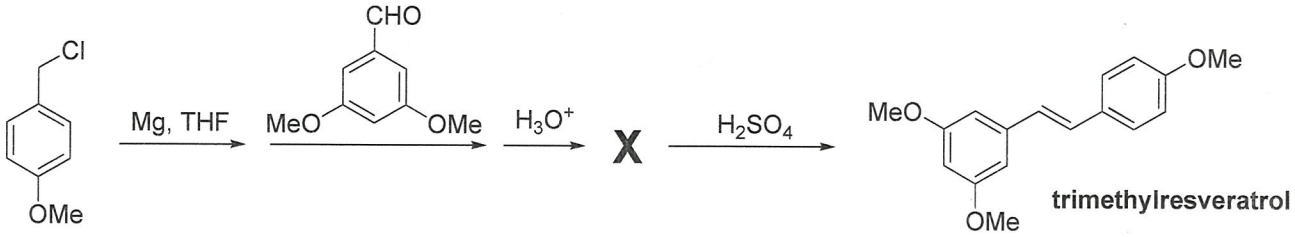


trimethylresveratrol



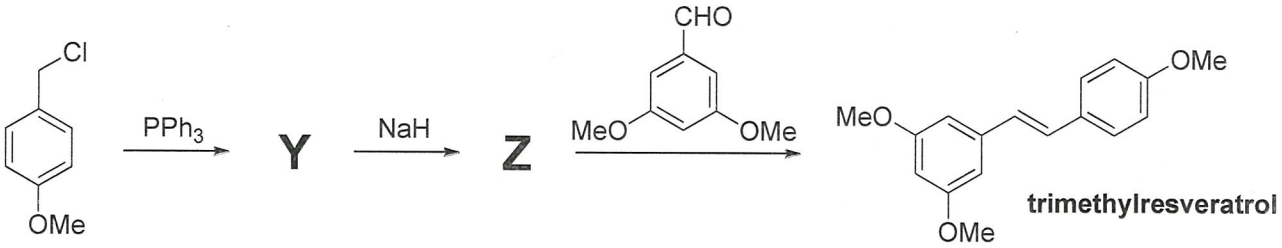
Resveratrol

Method #1:



trimethylresveratrol

Method #2:



trimethylresveratrol

19. In Method 1, which of the following statements is NOT true regarding the steps leading to compound X?

C

T a. The THF solvent in the first step should be free of water to guarantee the success of the reaction. Grignard

T b. In the starting material, if Cl is replaced by Br, the steps that follow will still result in the production of compound X. Not a problem

(c.) If an ester is used instead of an aldehyde, the reaction still generates compound X. No - you'd get a 3° ROH instead

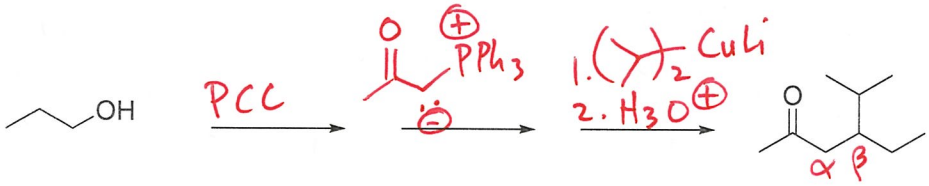
T d. X is produced as an optically inactive racemic mixture.

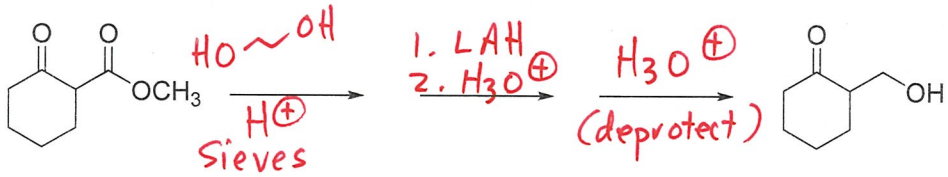
e. None of the statements a-d are true

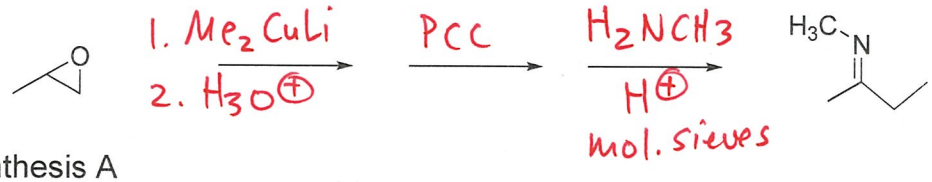
20. Method 2 used a Wittig reaction. Select the TRUE statement about Method 2.

F a. The first step produces Y, which is an ylide. No - it's a phosphonium salt
F b. The base NaH can be replaced by TsOH and the reaction will still generate Z. Need base to convert phosphonium salt to ylide
D F c. A three-membered ring intermediate is involved at the step that converts Z to trimethylresveratrol. Oxaphosphetane = 4-membered ring
T d. In Method 2, the alkene in trimethylresveratrol is produced using a resonance stabilized ylide.
e. All the statements a-d are true.

For questions 21-25, consider these three multi-step syntheses, then use the answer choices below. **Each arrow represents one synthetic step, which may include a workup (e.g. 1. Grignard; 2. H_3O^+ = one step). Answer choices may be used once, more than once, or not at all.** (Hint: Working backwards, particularly with "A" and "C", may be helpful.)

A 

B 

C 

a. Synthesis A
b. Synthesis B
c. Synthesis C
d. More than one of these syntheses
e. None of these syntheses

(See next page for details)

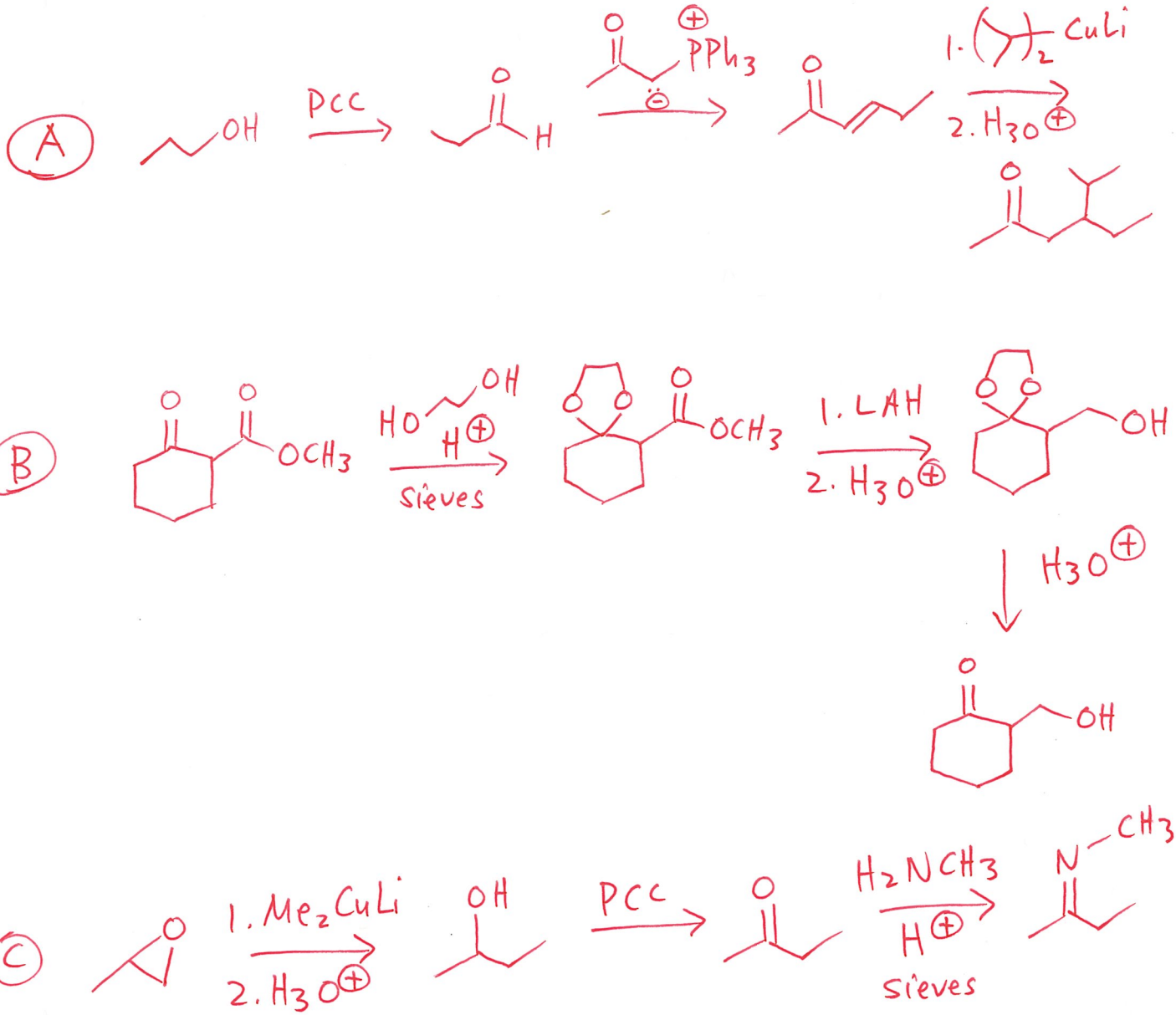
B 21. Which synthesis involves the use of a protecting group?

E 22. Which synthesis involves the use of an unstabilized ylide?

A 23. Which synthesis incorporates a conjugate addition as one of the steps?

D 24. Which synthesis requires the oxidation of an alcohol?

E 25. Which synthesis requires the use of a secondary amine?


A
OH
PCC
H
PPh3
1. ( )2 CuLi
2. H3O⊕
B
OCH3
HO
OH
H⊕
sieves
1. LAH
2. H3O⊕
OH
H3O⊕
OH
C
1. Me2CuLi
2. H3O⊕
OH
PCC
H2NCH3
H⊕
sieves
N
CH3