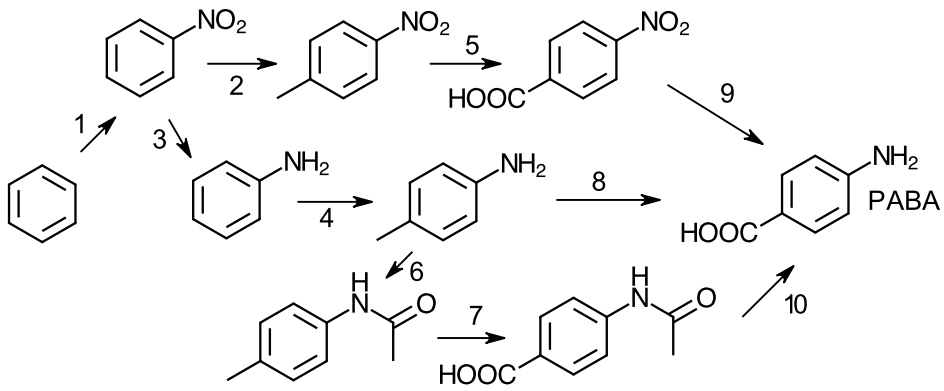
Multi-Objective Question 4 Solutions

1.



a. Path 1, 3, 4, 6, 7, 10

b. Reaction conditions: Step 1 HNO_3/H_2SO_4

Step 2 $CH_3Cl/AlCl_3$

Step 3 reducing agent, e.g., $NaBH_4$

Step 4 $CH_3Cl/AlCl_3$

Step 5 oxidizing agent = $KMnO_4$

Step 6 CH_3COOH and acid catalyst

Step 7 oxidizing agent = $KMnO_4$

Step 8 oxidizing agent = $KMnO_4$

Step 9 reducing agent, e.g., $NaBH_4$

Step 10 hydrolysis (H_3O^+/H_2O or OH^-/H_2O)

c. Step 2: CH_3 substitutes para to NO_2 group but NO_2 group is a meta director.

Step 8: oxidation of CH_3 to COOH but NH_2 is also oxidized to NO_2.

Optional MOQ Solutions

The malonic ester synthesis is used to make amino acids. Compound A is the starting material to make amino acid B.

a. Step 1: acid-base reaction.

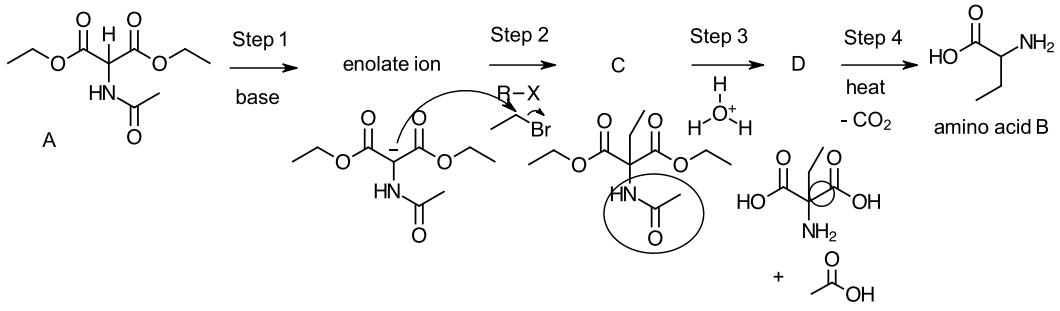
(i) Draw in the H on the alpha C in Compound A. State the pK_a of this acid.

$pK_a = 11$

(ii) Would you use H_2O, $NaOC_2H_5$, or $N(C_3H_7)_2^-$ to remove this proton? Give reasons.

$NaOC_2H_5$ is a strong enough base to remove the H on the alpha C.

(iii) Draw the structure of the enolate ion.



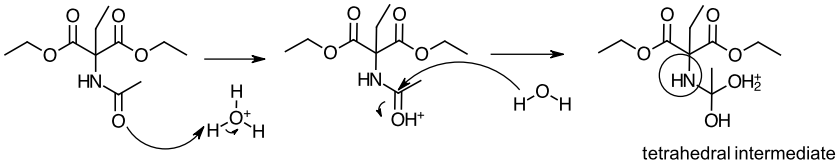
b. Step 2: alkylate the alpha carbon.

(i) Draw the structure of the alkyl halide RX that reacts with your enolate ion in Step 1 that forms amino acid B.

(ii) Use curved arrows to show how the enolate ion reacts with your RX to form Compound C. Draw the structure of Compound C.
Curved arrow from lone pair in enolate ion to alpha C, curved arrow from C-X bond to X to form Compound C.
(iii) The enolate ion can react with your RX in an unwanted side reaction to form a compound that lowers the yield of Compound C. Draw the structure of the compound that forms in this unwanted side reaction.
Unwanted side product is the elimination product: $H_2C{=}CH_2$

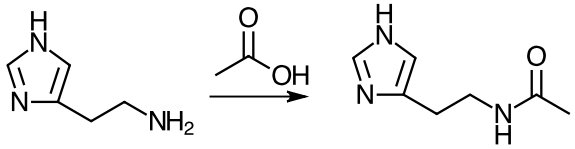
c. Step 3: Convert ester to acid using H_3O^+.
The two ester groups in Compound C are converted to acid groups.
(i) The amide group in Compound C reacts with H_3O^+ to form a ___ group.
Amide group hydrolyzes to form an amine and acid in a nucleophilic acyl substitution reaction.
Ester group hydrolyzes to form an alcohol and acid in a nucleophilic acyl substitution reaction.

(ii) Use curved arrows to show how the amide group reacts with H_3O^+ to form an intermediate and how this intermediate reacts with water to form a tetrahedral intermediate. Circle the group in your tetrahedral intermediate that behaves like a leaving group to form Compound D.
Step 1: curved arrow from carbonyl O in amide group to H in H_3O^+, arrow from H-O bond to O.
Step 2: curved arrow from O in H2O to carbonyl C, arrow from C=O pi bond to O to form tetrahedral intermediate.
Circle NHR group as leaving group.
(iii) Draw Compound D. See reaction sequence above.



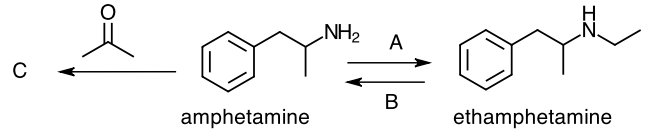
d. Step 4: decarboxylation to form amino acid B. Circle the bond in Compound D that breaks to form CO_2 and amino acid B. See reaction sequence above.

Quiz 11 solutions
1. Histamine is involved in allergic reactions.



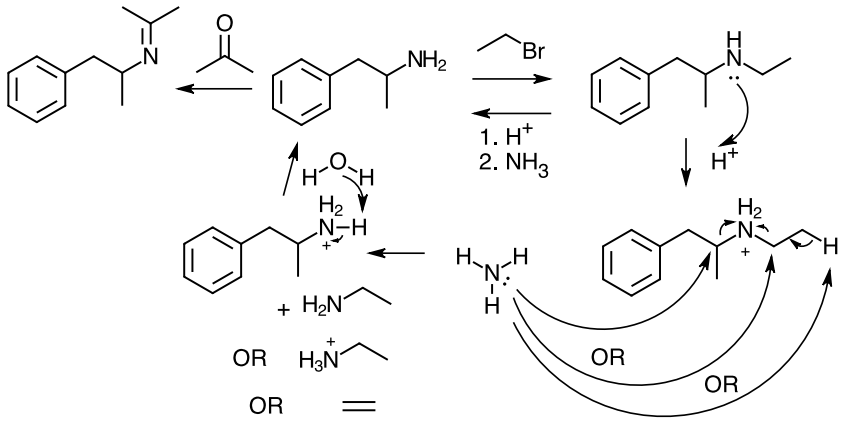
a. The N in the ring is less reactive than the N in the chain because the lone pair on the N in the ring is ____ and the lone pair in the chain is not. Give a one word answer. Delocalized (the ring is aromatic)
b. Acetic acid reacts with the N in the chain (use an acid catalyst). Draw the structure of the product of this reaction.
The amine reacts with the acid to form an amide in a nucleophilic acyl substitution reaction. Lone pair on N in amine reacts at carbonyl C in acid.

2. Amphetamine is a central nervous system stimulant.

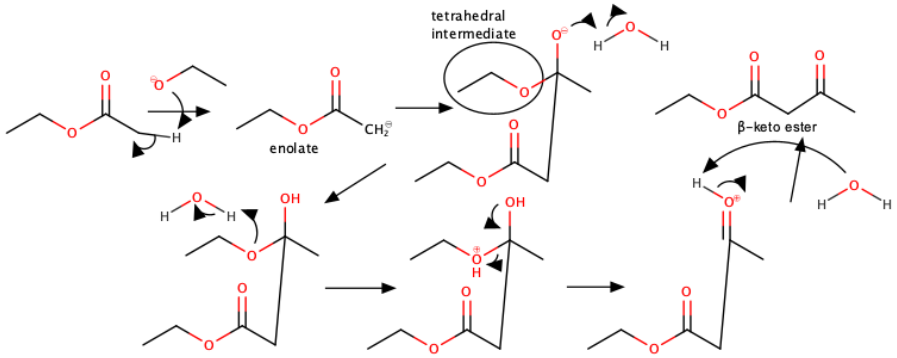


a. Amphetamine reacts with acetone and an acid catalyst. Draw the structure of C.
The 1° amine reacts with the ketone to form an imine in a nucleophilic addition reaction. Lone pair on N in amine reacts at carbonyl C in ketone.

b. Identify Reaction Condition A. C_2H_5X
c. B is 1. H^+, 2. NH_3. Use curved arrows to show how 1. H^+, and 2. NH_3 reacts with ethamphetamine to produce amphetamine.
H^+ makes the amine a better leaving group. NH_3 is a nucleophile and reacts at one of the alpha carbons in a substitution reaction or at the H on the beta carbon in an elimination reaction.
Step 1: curved arrow from N in amine group to H+ to form better leaving group. Step 2: arrow from N in NH3 to alpha C in ethamphetamine, arrow from C-N bond to N so leaving group leaves. Step 3: arrow from O in H2O to H in conjugate acid of amphetamine, arrow from N-H bond to N to form amphetamine.
OR
Step 1: curved arrow from N in amine group to H+ to form better leaving group. Step 2: arrow from N in NH3 to alpha C in ethamphetamine, arrow from C-N bond to N so leaving group leaves to form amphetamine.

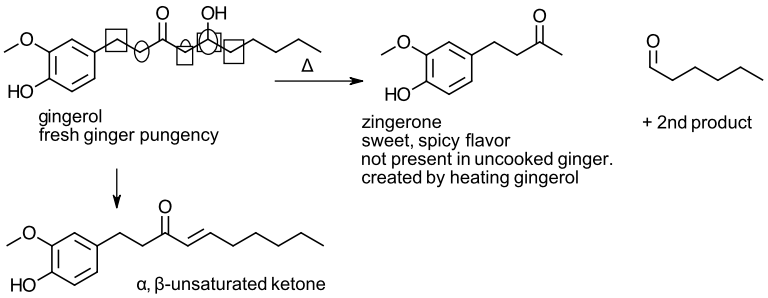


Quiz 10 solutions
1. Ethyl acetate reacts with $NaOC_2H_5$ to form an ester enolate ion.



a. Draw the structure of the ester enolate and tetrahedral intermediate.
b. (i) Circle the leaving group in the tetrahedral intermediate that leaves to form the β-keto ester.
(ii) Use curved arrows to show how the tetrahedral intermediate forms the β-keto ester.
(iii) Draw the structure of the β-keto ester product.

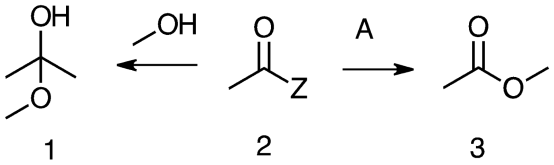
2. If you like cooking with ginger, here is one thing that happens:



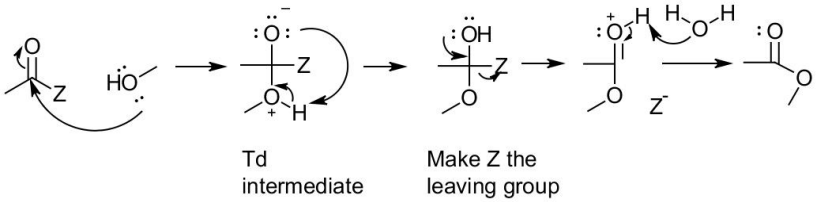
a. There are two types of alpha carbons. Circle the alpha carbon(s) and box the beta carbon(s) in gingerol.
b. When zingerone forms, a second product also forms. Draw the structure of the second product.
c. Can gingerol form an α, β-unsaturated aldehyde/ketone? If so, draw the structure of this compound.
Yes

Quiz 9 solutions
1. Acid (or acyl) chlorides are the most reactive acid or acid derivative whereas amides (Z = NHR) are the least reactive in nucleophilic acyl substitution reactions. Explain how Cl and NHR affect the reactivity of the carbonyl carbon.
Cl is more electronegative than N so a C-Cl bond is more polar than a C-N bond.
The more polar C-Cl bond gives the carbonyl C a greater partial positive charge than the less polar C-N bond.
Greater partial positive charge on C makes it more reactive (better electrophile).

2. Under acidic conditions, if Z = CH_3 in Compound 2, Compound 1 forms.

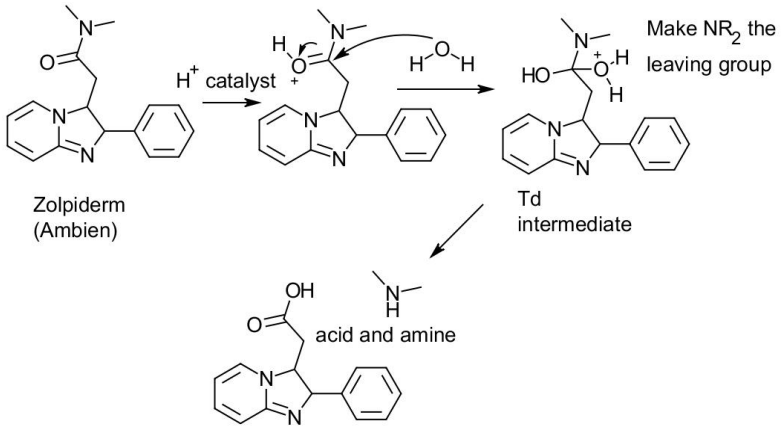


a. If Z = _____, Compound 3 forms.
Identify Z and determine reaction condition A.
Z = leaving group, e.g., -OH, -OR, -NHR, -X.
A = CH_3OH. Use acid catalyst.
b. Use curved arrows to show how Compound 3 forms from Compound 2 using your Z and reaction conditions A from Question 1a.



c. How does Z determine the product that forms?
If Z is not a leaving group, the addition product forms.
If Z is a leaving group, the acyl substitution product forms.

3. Ambien is a prescription sedative. Draw the structures of the metabolic (hydrolysis under acid conditions) products of this compound. Draw the structure of the tetrahedral intermediate.
The amide group hydrolyzes to an acid and amine.


Zolpiderm
(Ambien)
H+ catalyst
Make NR2 the
leaving group
Td
intermediate
acid and amine