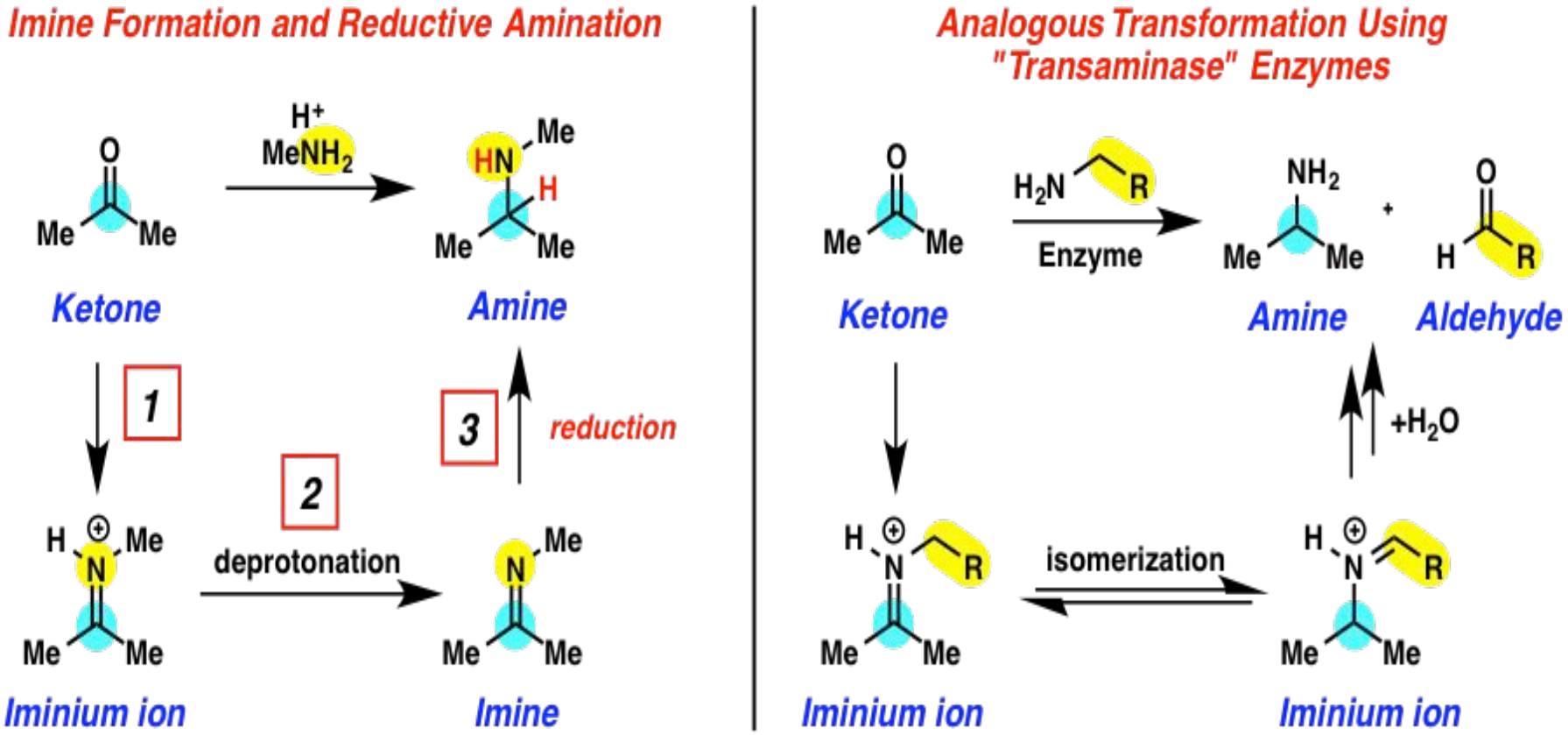
Objective 10. Understand nucleophilic addition reactions of N nucleophiles to C=O compounds.

Skills: Draw structure
ID structural features and reactive sites (alpha C, beta C, LG, etc.)
ID Nu^- and E^+
use curved arrows to show bonds breaking and forming
show delocalized electrons with resonance structures.

Key ideas: imines are common in biology
C=O bond has pi bond but bond is polarized. See resonance.
Carbonyl C = E^+.
Reacts with Nu^- to form tetrahedral intermediate.

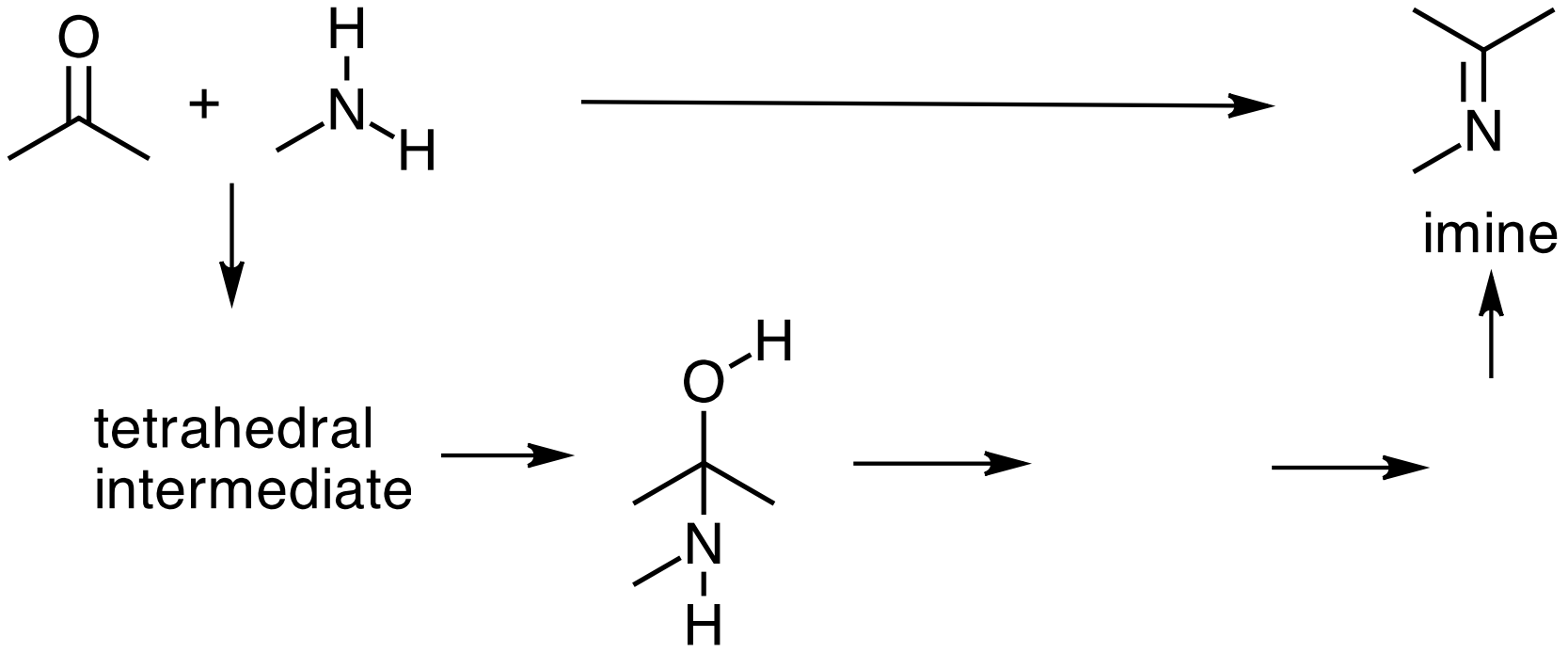
Nitrogen Nu^-: NH_3, RNH_2, R_2NH

Aldehydes and ketones readily react with amines (reductive amination). LearnBacon.com



N Nucleophile - Imine Formation:

Ketone (or aldehyde) + 1° amine → imine



Use curved arrows to show how imine is formed.

How to get rid of –OH? Make it into a better _____.

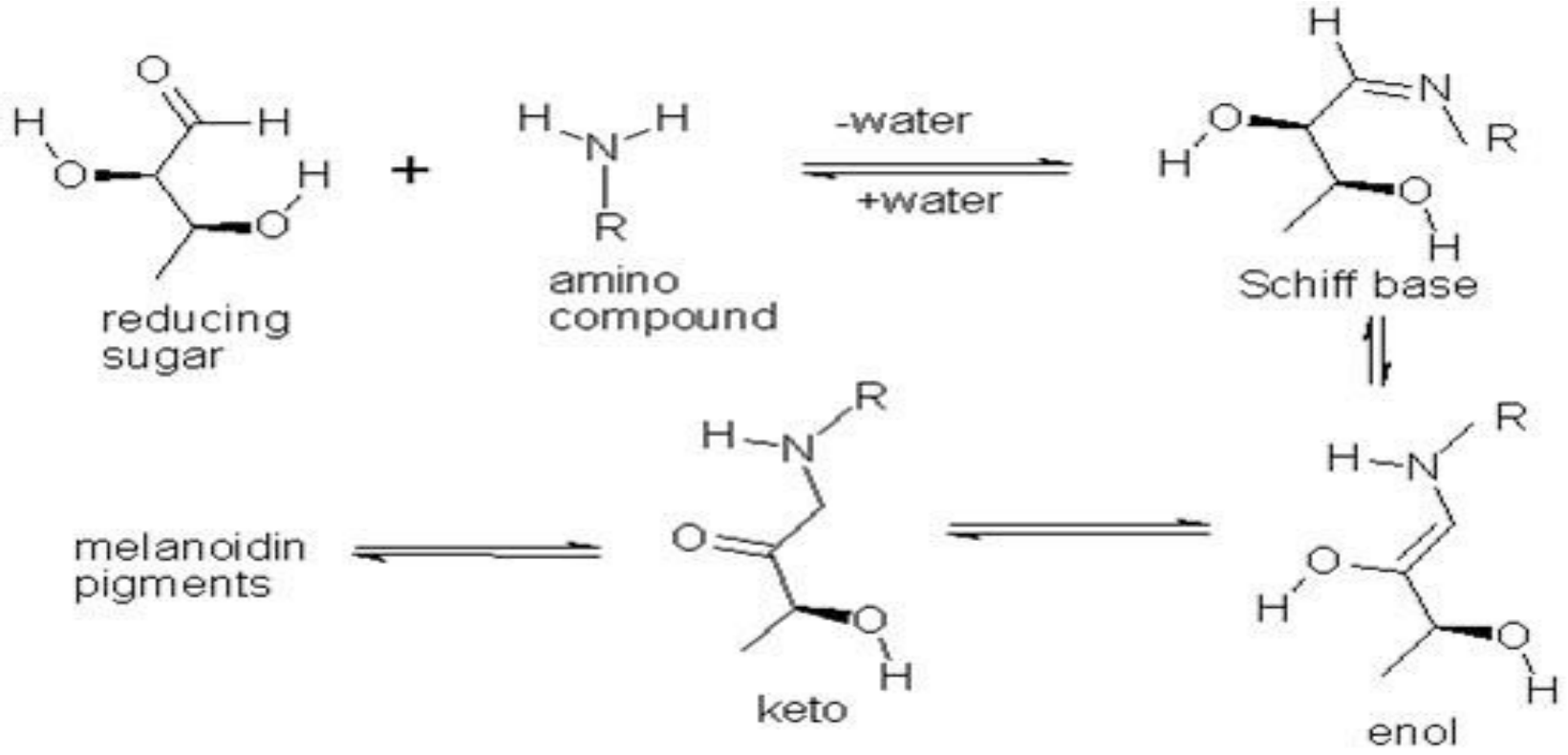
What Do These Foods Have In Common?

Hint: the most widely practiced chemical reaction in the world.

Credit: Shutterstock

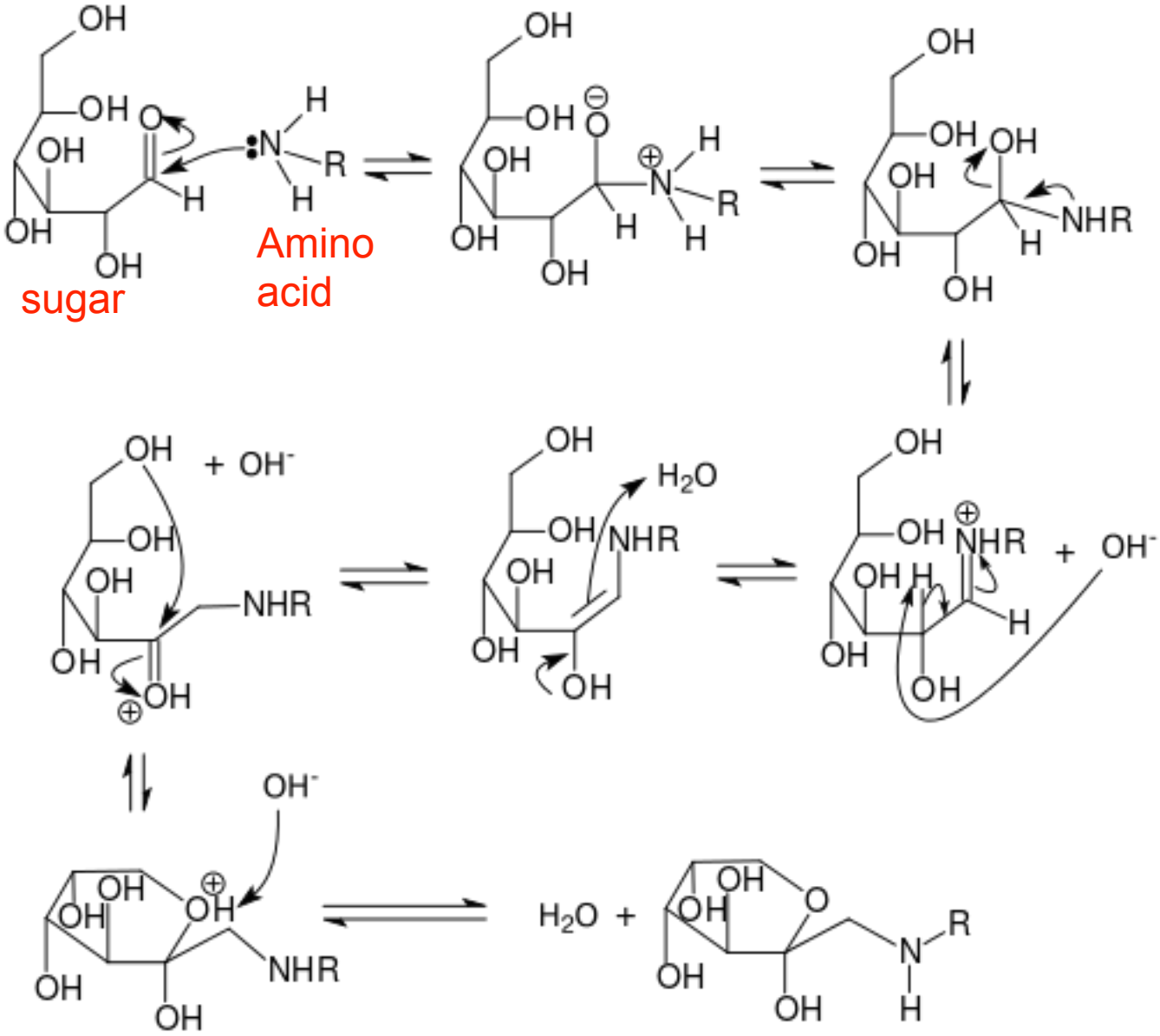
Maillard Reaction produces ***Color***, ***Aroma***, and ***Flavor*** in Grilled Meats, Roasted Coffee, Dark Beer, …

Sugar + Amine (protein) ----> ***imine*** (Schiff base)



http://www.cfs.purdue.edu/fn/fn453/ld_amino.html

Maillard Reaction Mechanism:



1. Circle the tetrahedral intermediate.
2. Box the imine
3. Triangle the hemiacetal
4. What's wrong with Step 3?

https://en.wikipedia.org/wiki/Maillard_reaction

Chemical reactions produce the ***COLOR*** and ***SMELL*** of

Grilled Meat, Roasted Coffee, Dark Beer, Toasted Bread

http://www.starkinsider.com/2009/07/steak-marinade-recipe-tender-juicy-bb.html

http://www.suite101.com/view_image.cfm/1464543

http://www.shutterstock.com/pic-9044662/stock-photo-side-view-of-a-blank-white-plate-with-a-inch-caramelized-sugar-cage-used-as-an-edible-prop-for-an.html

4 types of browning reactions in foods:

Maillard: sugar + amino cpd (protein) ---> aroma, flavor, color

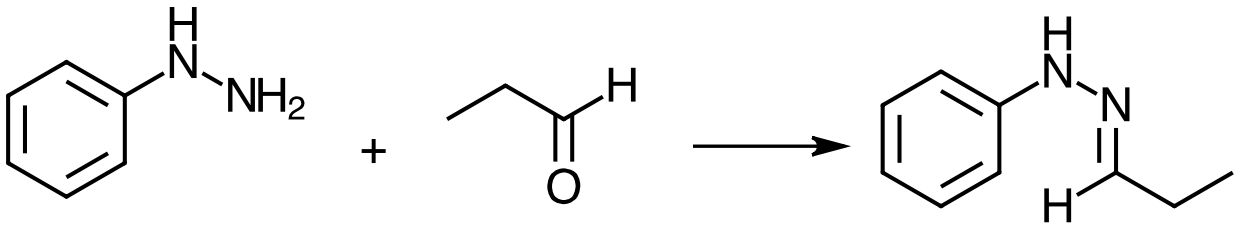
Caramelization: sugar + heat ---> caramel flavor, color

ascorbic acid oxidation: Vitamin C

enzymatic browning (Lab 5): phenolics --- enzyme --> color, flavor

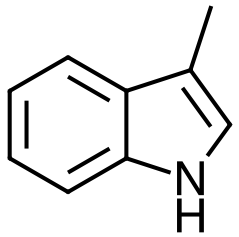
Enzyme is a protein --> amino acid --> acid/base

What do you think Skatole smells like?



phenyl hydrazone

$ZnCl_2$



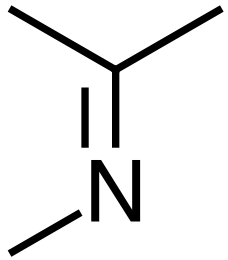
skatole (3-methyl indole)

Fischer synthesis of indoles

Low concentrations: flowery smell (found in flowers and essential oils)
High concentrations: smells like _____ (occurs natural in feces and coal tar)

Imine De-Formation:
Hydrolysis of Imine to amine and ketone

Imine → Ketone (or aldehyde) + amine

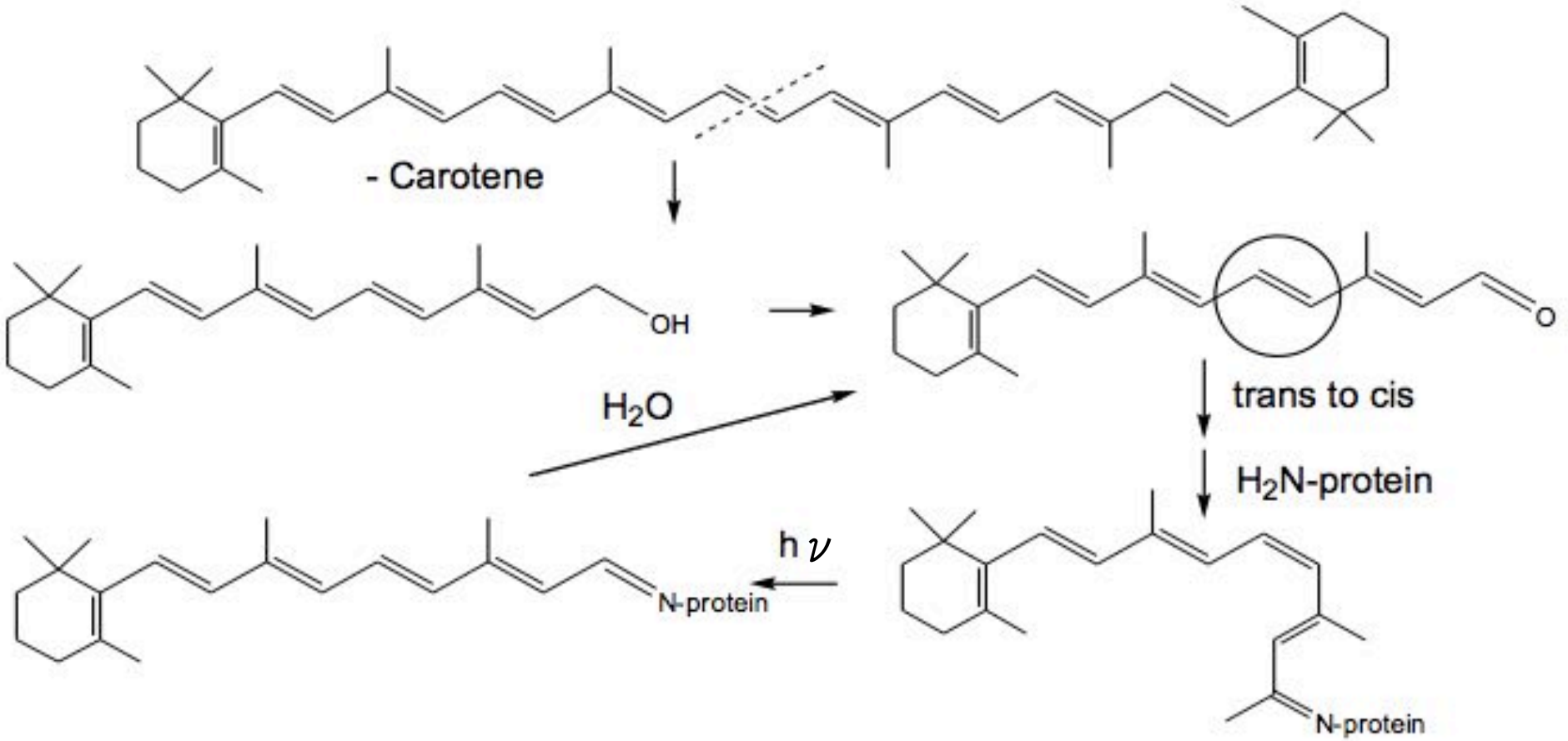


See the C=N bond.

1. Is this bond polar? If so, which atom has a partial negative charge?
2. This atom reacts with H^+ (acid catalyst). Use curved arrows to show product. Draw the resonance structure.
3. Use curved arrows to show how this compound reacts with water. Draw the structure of the intermediate.
4. Use curved arrows to show how this intermediate undergoes a proton transfer step(s) to form a carbonyl compound and amine.

Biological Aldehydes React with Amines (Proteins) → Imines
(Carey, 8th ed., p. 749-750)

What part of your body does this reaction occur?

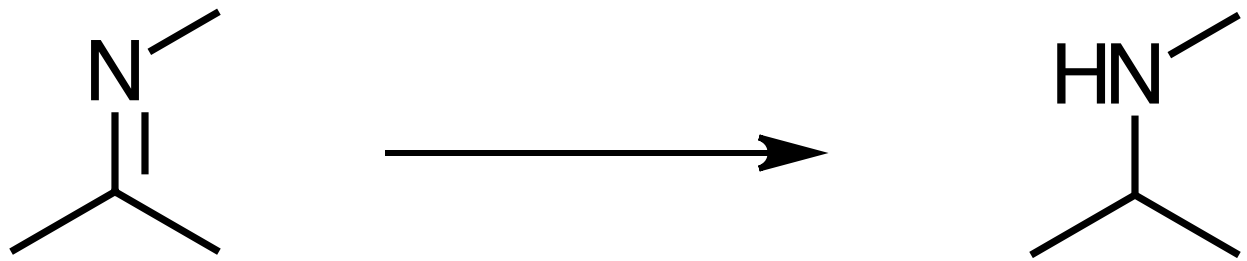


We've covered these reactions in Chem 12.
Identify the reaction types. Support your answer by identifying the structural features in each reaction type.

Transamination – important in biology: ketone ---> amine

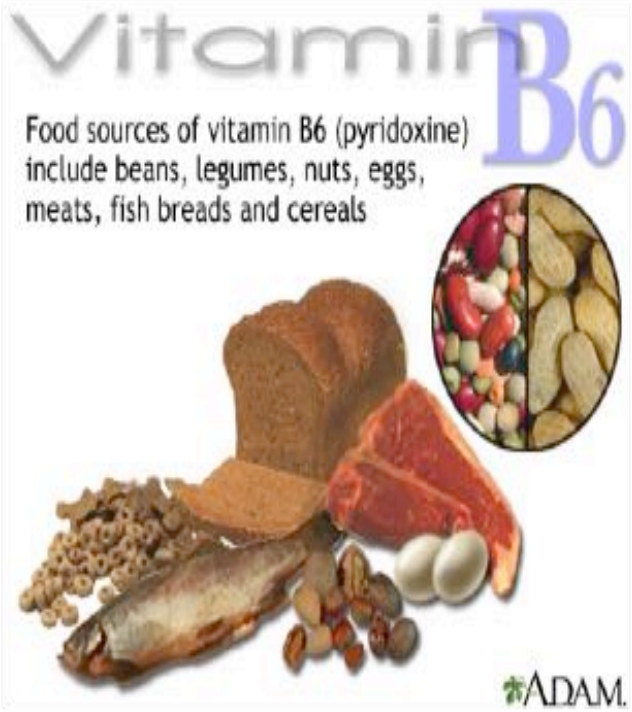
2 steps:

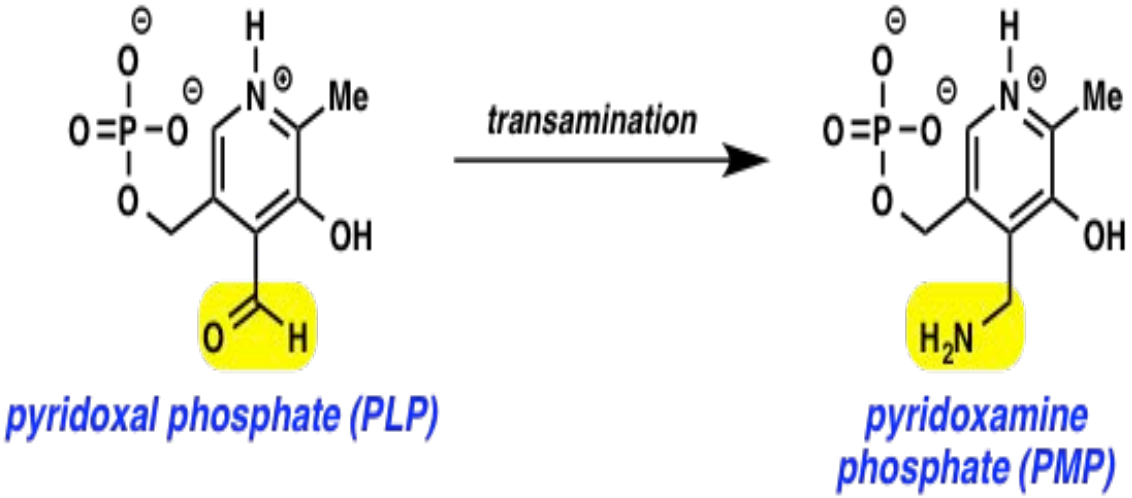
1. Ketone ----> Imine
2. Imine ----> Amine.



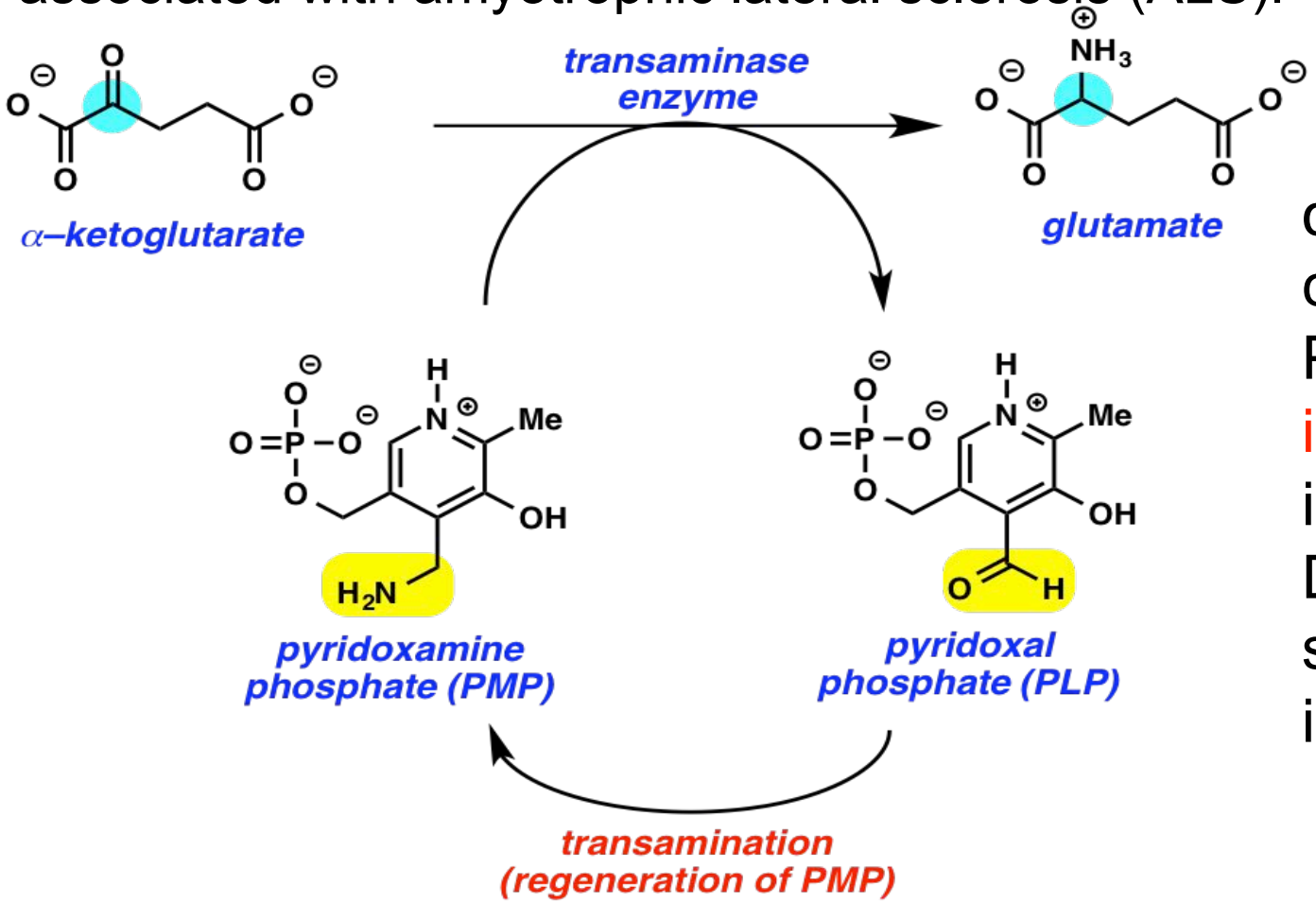
Oxidation or Reduction?

From LearnBacon.com: The conversion of carbonyls to amines is important in our bodies.
Pyridoxamine phosphate (PMP) is an essential cofactor for multiple enzymatic processes including Transamination. PMP is produced from Vitamin B6, which is found in nuts, beans, and meats.



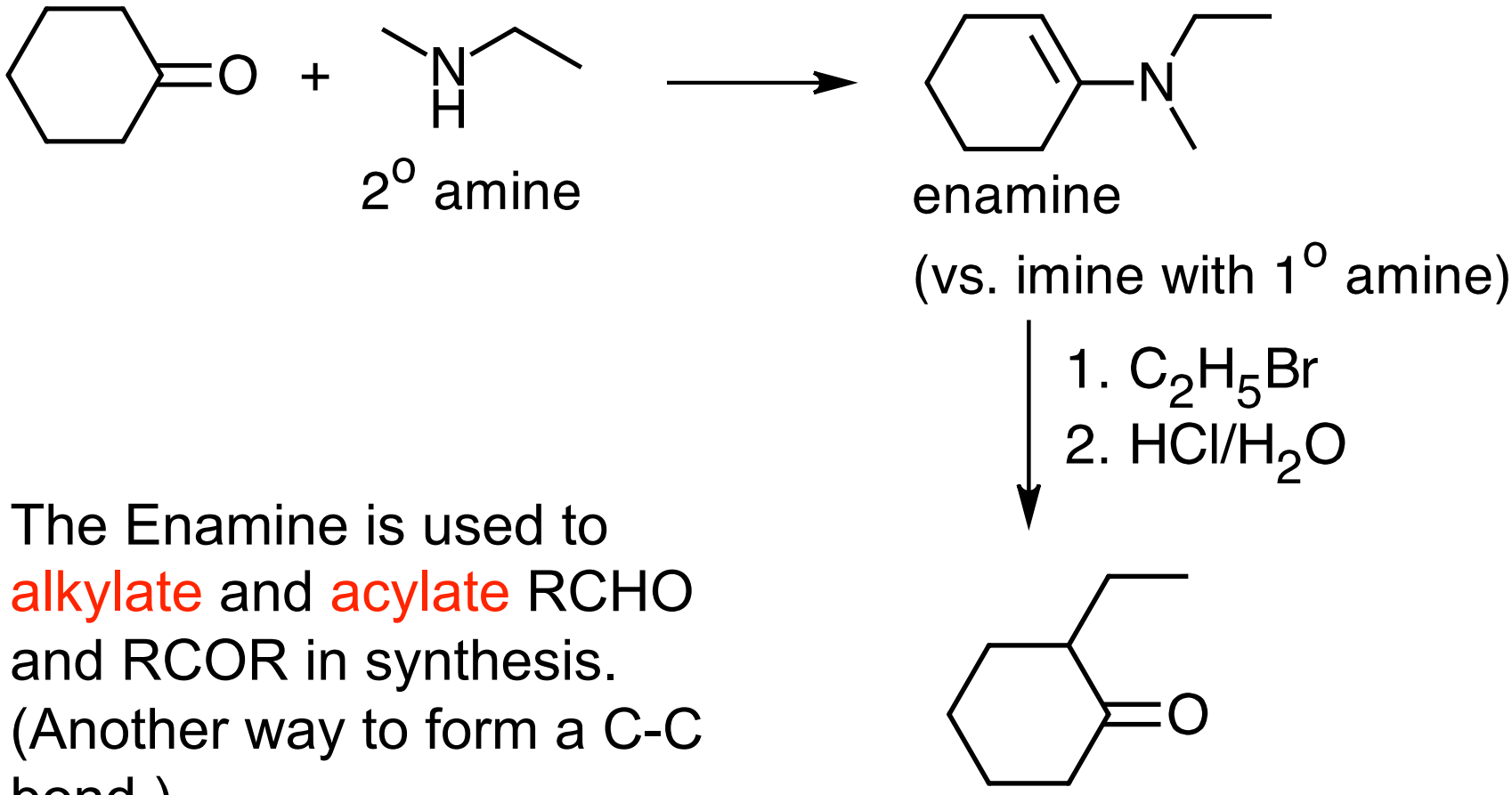


From LearnBacon.com: The conversion of carbonyls to amines is important in our bodies.
Once PMP forms, it converts alpha-ketoglutarate to glutamate (ketone to amine transamination process). This process is used in synthesis of glutamine and in glucose metabolism. Excess glutamate has been associated with amyotrophic lateral sclerosis (ALS).



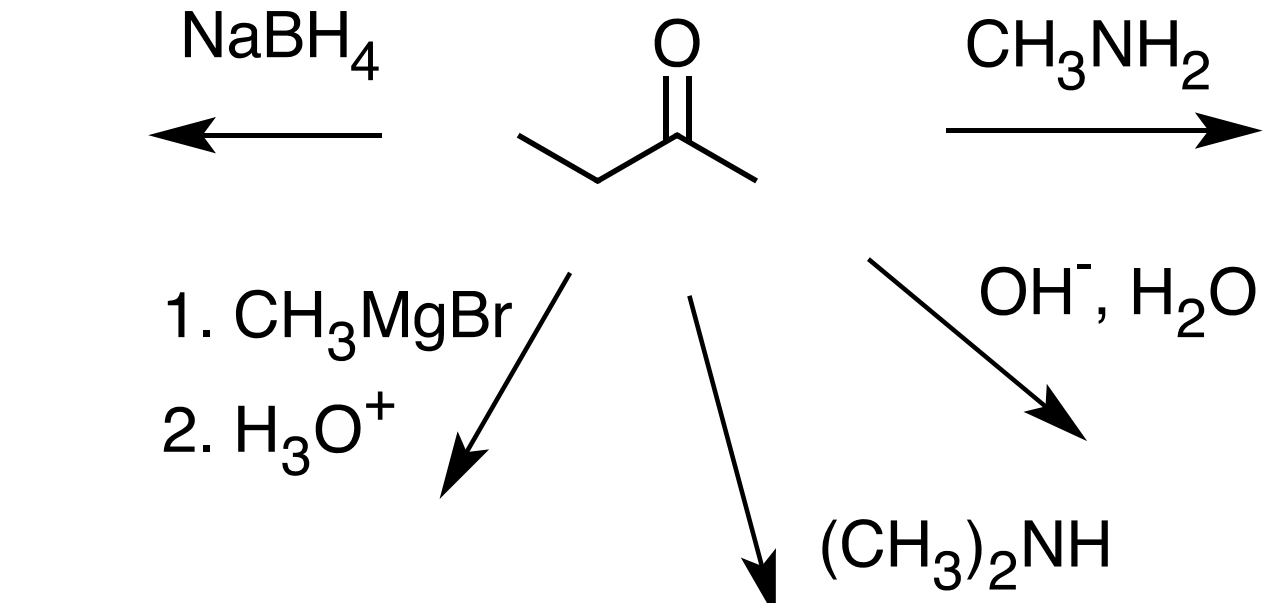
α-ketoglutarate condenses with PMP to give an iminium ion intermediate. Draw the structure of this intermediate.

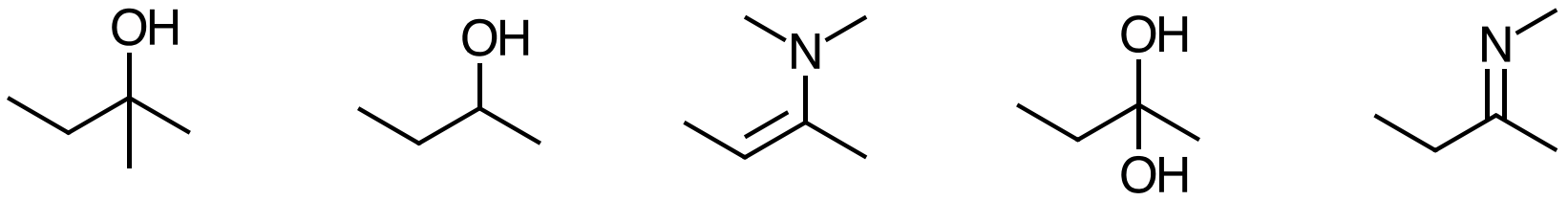
Aldehyde/ketone + 1° amine → Imine
Aldehyde/ketone + 2° amine → Enamine



The Enamine is used to alkylate and acylate RCHO and RCOR in synthesis. (Another way to form a C-C bond.)

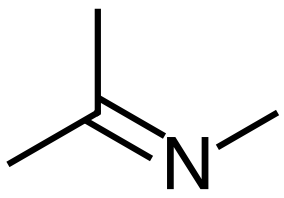
Objective: Predict the product of the following reactions:

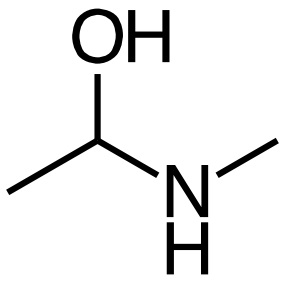


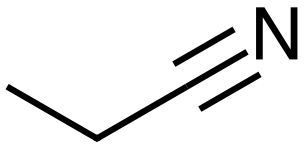


A B C D E

ID the atom that behaves like a $Nu:^-$ or E^+.



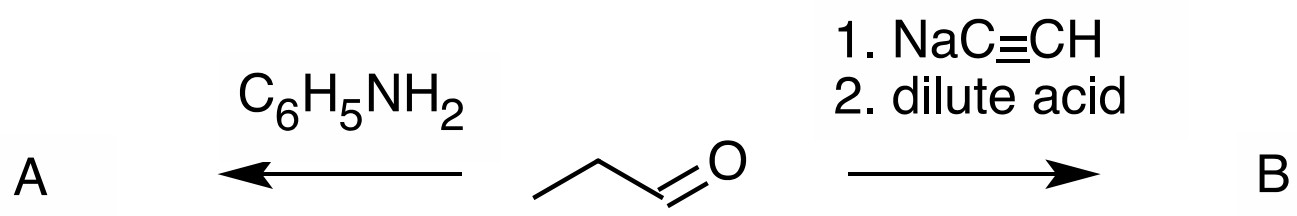


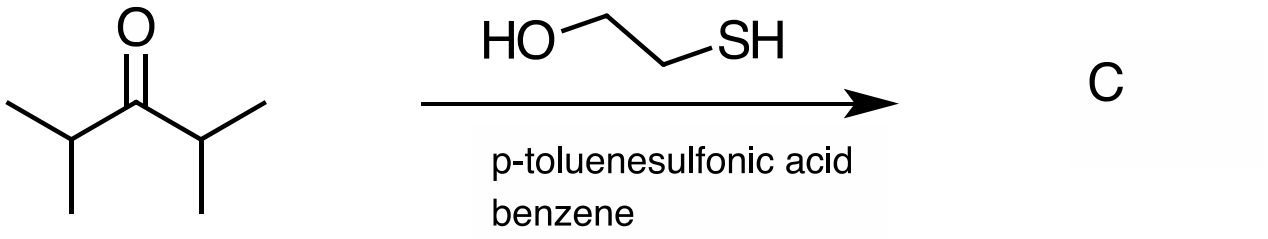


$HO-NH_2$

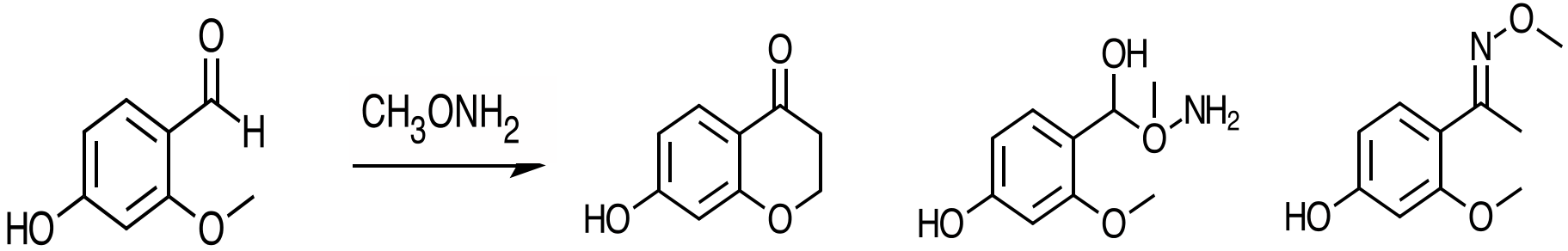
How would you synthesize each compound?

Predict product (A, B, and C)



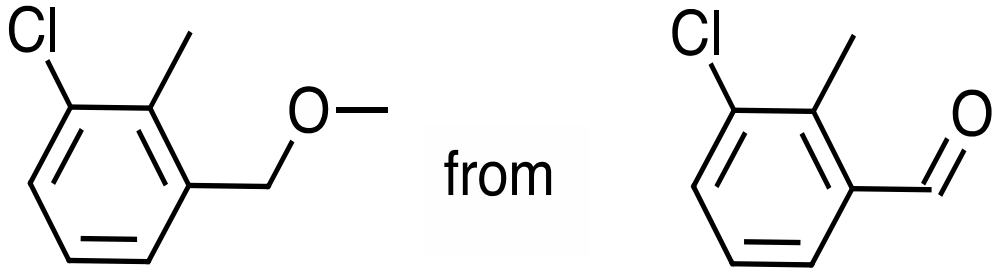


1. Predict the product (A, B, or C) of the following reaction:



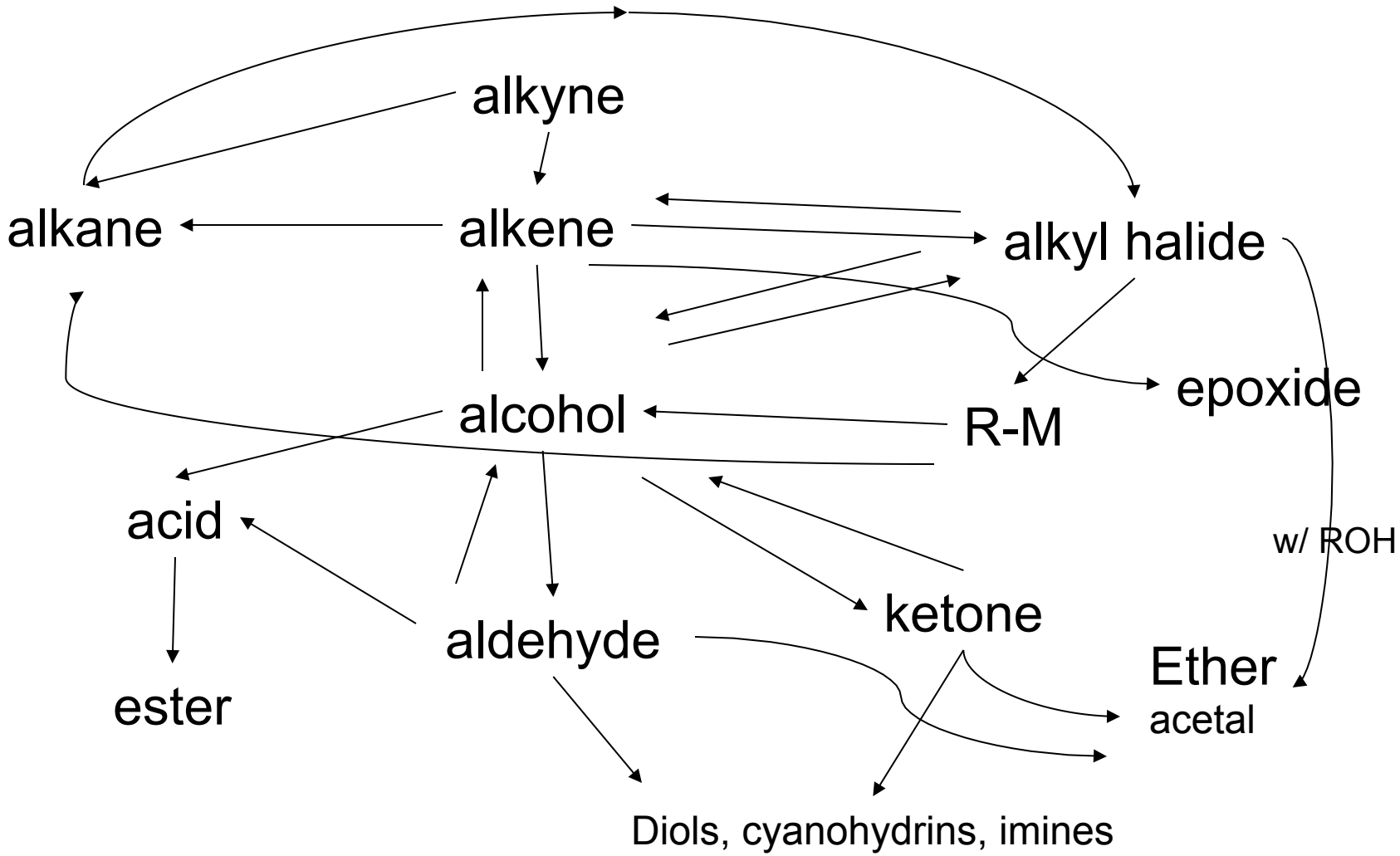
A B C

2. Describe a short, efficient synthesis.



a. (i) CH_3MgBr, H^+, (ii) OH^-, (iii) CH_3Br
b. (i) $NaBH_4$, (ii) OH^-, (iii) CH_3Br
c. CH_3OH in H^+

Reaction Roadmap: Which functional group can be converted into the greatest number of other functional groups?

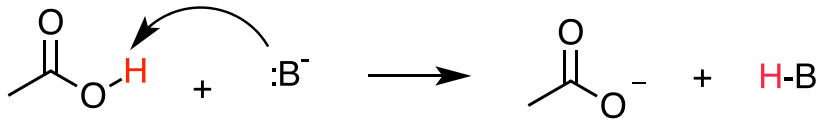


What group undergoes $Nu:^-$ addition? And what group is produced?

Objective: Determine products of a reaction (ID Structural Features)

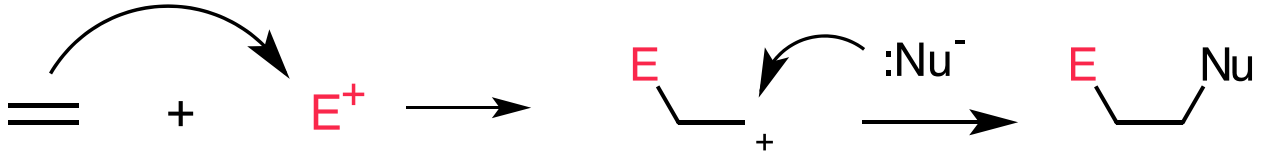
How to figure out how reactants react?

Reaction Type	Structural Feature (reacts with ____)
H^+ transfer	Acidic H^+

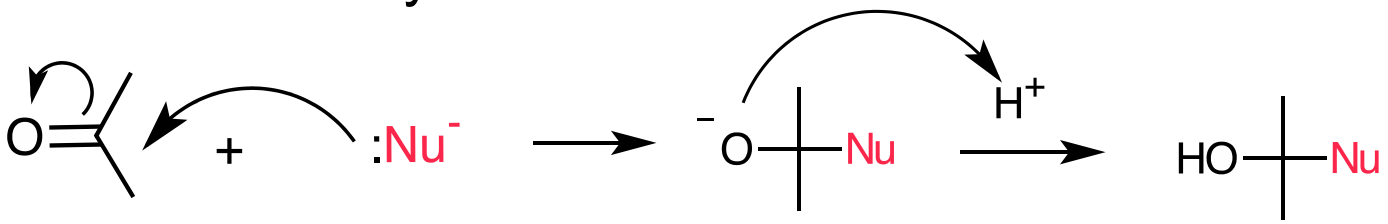


Addition

electrophilic addition pi bond



nucleophilic addition carbonyl C



Objective: Determine products of a reaction (ID Structural Features)

How to figure out how reactants react?

Reaction Type	Structural Feature (reacts with ____)
Elimination	H bonded to β-C; LG
Substitution	
nucleophilic substitution	LG bonded to α-C
electrophilic aromatic substitution	aromatic pi bond
nucleophilic acyl substitution	carbonyl C; LG

Objective: Determine products of a reaction (ID Reactant Function)

How to figure out how reactants react?

Reactant	Function
HX	Acid – reacts with _____
H_2SO_4	E^+
X_2	E^+
OH^-, OR^-	
RMgX	

Predict the product of each reaction:

Compound/ Reagent	HBr	Br_2	CH_3MgBr