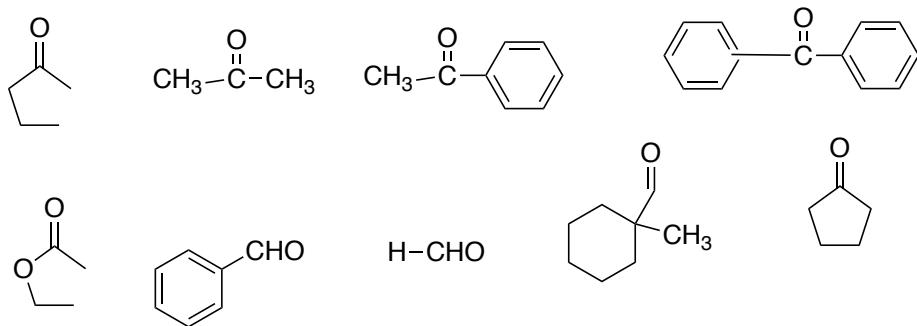


The focus of the next two chapters is an anion called the *enolate ion*. This ion forms when a base removes a proton from a carbon that is adjacent to a carbonyl group. The carbon is called the  $\alpha$  carbon because it is right next door to the carbonyl. Molecule with  $\alpha$ -H's (That is an H attached to an  $\alpha$ -carbon) are called "enolizable." Circle them). Draw an arrow to the carbon(s) with the  $\alpha$ -H.

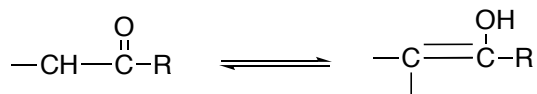


Enolizable molecules have a  $K_a$  of about  $10^{-20}$  which is crazy high for a H on an  $sp^3$  carbon. The conjugate base is called an enolate ion (the star of this lesson!) Draw an enolate ion, then play our game, and explain why  $\alpha$ -H's are so acidic.

Here's a fun fact bout enolizable molecules. They exist as an equilibrium mixture of isomers called the keto tautomer (has a carbonyl) and enol tautomer (has an alkene and an OH). That is:

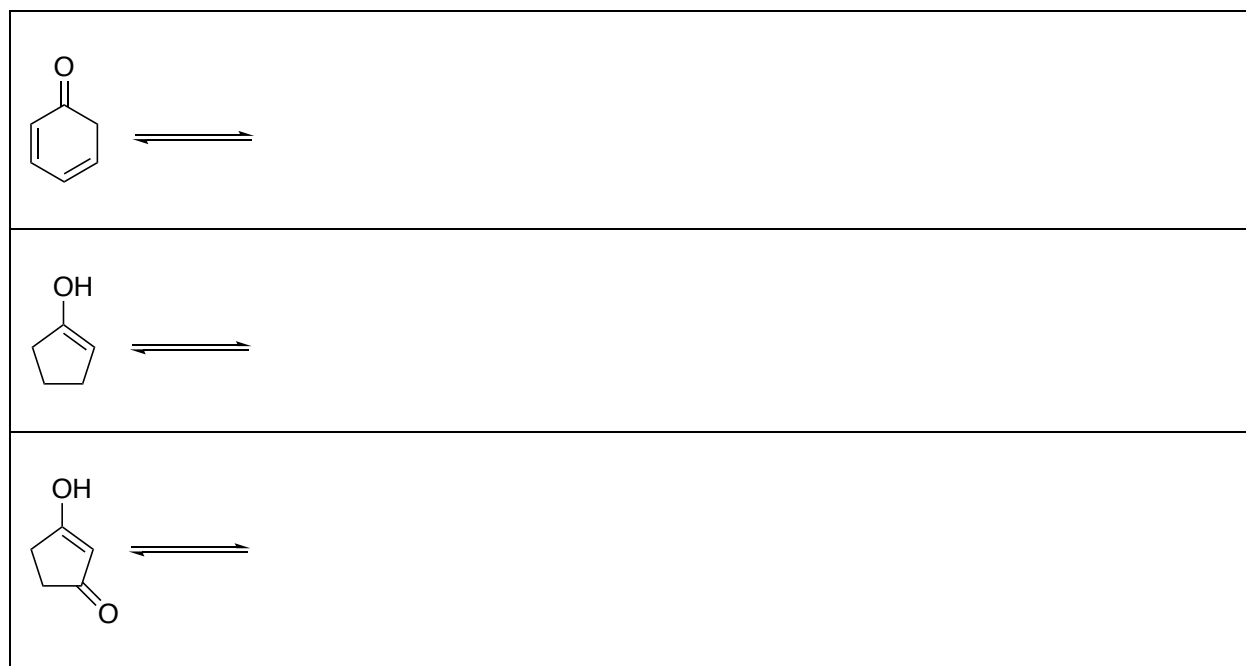
KETO:

ENOL:



Draw acetone (propanone) and show both tautomers.

Usually, the keto isomer is predominate, but not always. For each of these, draw the missing tautomer and circle the most important.



The last example is a special case: the tautomers of a  $\beta$ -dicarbonyl. Why is it called that?

Another fun fact. Every transformation has a mechanism. Some mechanisms are so famous that they get names like  $S_N2$ , EAS or saponification. This mechanism is very famous and its name is TAUTOMERIZATION. Nice, right?

Here's the mechanism in the presence of base. Base removes acidic  $\alpha$ -H, a delocalized anion called enolate forms. Negative oxygen atom takes the proton back from the base yielding the alternate structure i.e. (Keto tautomer becomes enol tautomer). Write out this mechanism as an equilibrium reaction, using acetone to begin. Include all resonance contributors and the hybrid.

Draw the structure for ethyl acetate, then the enolate that would form if ethyl acetate is treated with strongly basic NaOEt.

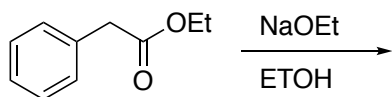
The enolate above will be a minor component in the test tube, so it can react with other things in the tube.

Draw the products that would form if the enolate removes an  $\alpha$ -H from a second ethyl acetate molecule. Does this lead to a new set of substances in the tube?

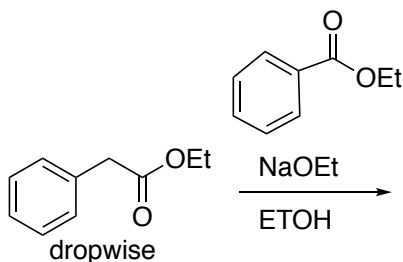
Draw the product that would form if the enolate carbon attacks the carbonyl of a second ethyl acetate molecule in a nucleophilic acyl substitution. Only one mole will react. Does this lead to a new set of substances in the tube?

The reaction on the last page is a famous one called the Dieckmann Condensation. What type of product is formed (we will need to use a Greek letter to completely answer this. Ketones can be referred to a keto groups or as oxo groups).

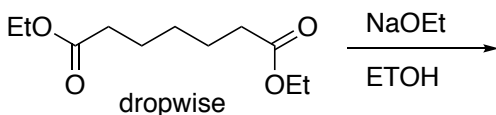
Show the final product for each of these Dieckmann condensation examples:



In this example, only one of the esters is enolizable. It will become an enolate and attack the other ester. The enolizable ester will not react with itself because it is being added slowly.

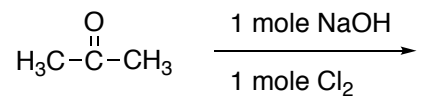


Check this one out. The molecule has two ester groups, one will enolize, then it can react with the other. This is called an intramolecular reaction. Intramolecular reactions usually form a ring in the process. This one does.



Why was it important to add the diester slowly in the last reaction? What might have happened if we added it all at once?

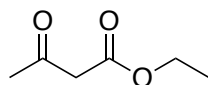
Think about this reaction. What might the product be? Write mechanism to support your answer.



What is different if we use an excess of NaOH and I<sub>2</sub>? Hint: only one of the enolizable carbons will react. And at the end there are two separate products. This is called the haloform reaction.

More specifically, since we used iodine, we call it the iodoform reaction.

One of the carbons on this molecule is 10 billion times more acidic than the others. Which one and why? Play the game to be specific.



ethyl acetoacetate

When the acidic carbon becomes an enolate then it is a good nucleophile.

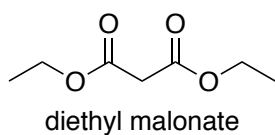
We can use that nucleophile to build other molecules. Draw the product that would form at each step if you treat ethyl acetoacetate with these reagents one after the other.

First an acid/base reaction with NaOEt
Then a nucleophilic substitution with Bu-Cl
Then a saponification with water and base

Then neutralization with  $\text{H}_3\text{O}^+$

Then decarboxylation by heating (see beginning of page 796 in chapter 17 and point 6 on page 799).

Now try it again with a twist. Begin with this molecule:



Here are the reagents. Again draw the product as it will look after each step.

First an acid/base reaction with  $\text{NaOEt}$

Then a nucleophilic substitution with  $\text{Pr-Cl}$

Then an acid/base reaction with  $\text{NaOt-Bu}$

Then a nucleophilic substitution with  $\text{Pr-Cl}$

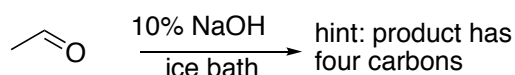
Then a saponification with water and base

Then neutralization with  $\text{H}_3\text{O}^+$

Then decarboxylation by heating. This is a little tricky unless you think very carefully about it. One step after the next.

Now let's extend our thinking from esters to aldehydes (Welcome to chapter 19!)

Think about what would happen in this reaction. Include mechanisms.



This is called the aldol addition reaction.

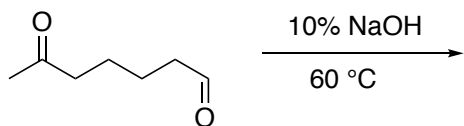
If you run the same reaction at room temperature or warmer, an elimination occurs to form a conjugated alkene. Repeat the reaction above and draw the product that would form if it was run at  $60^\circ\text{C}$ . This is called the aldol condensation reaction.

Now let's play some other games with this reaction: we will include one enolizable aldehyde that is added slowly and one that is not enolizable. This is similar to what we did on handout page 4. Use propanal and benzaldehyde as the two aldehydes. In this case it doesn't matter what the temperature is because conjugation with a benzene ring makes it especially stable and, therefore easy to form.



Now try this intramolecular aldol condensation. Hints: if an enolate tries to react with a ketone, the reaction fails. Enolates only react with aldehydes and esters, and if an enolate reacts with an aldehyde on the same chain, then it reacts most easily if the aldehyde is closer to the enolate.

Other hint: the product is a ring because this is an intramolecular reaction!



Enolates don't react with ketones but ketones can become an enolate that can react with other things. For example, acetone (1 mole) plus benzaldehyde (two moles) with 10% NaOH at room temperature can form a product. This reaction happens on both sides of the ketone. What is the final product? Note: it is much bigger than the starting materials.

Would it matter if we ran this reaction at ice bath temperature? Explain.