

Aldol Condensation

Lab #5

Aldol Reaction

Aldol addition or aldol condensation

“**aldol**” - *al*dehyde/ketone and *alcohol* as starting materials

β -hydroxy aldehyde or ketone - product

Condensation

reaction of two or more molecules
combine into a large molecule with loss of
a smaller molecule (water)

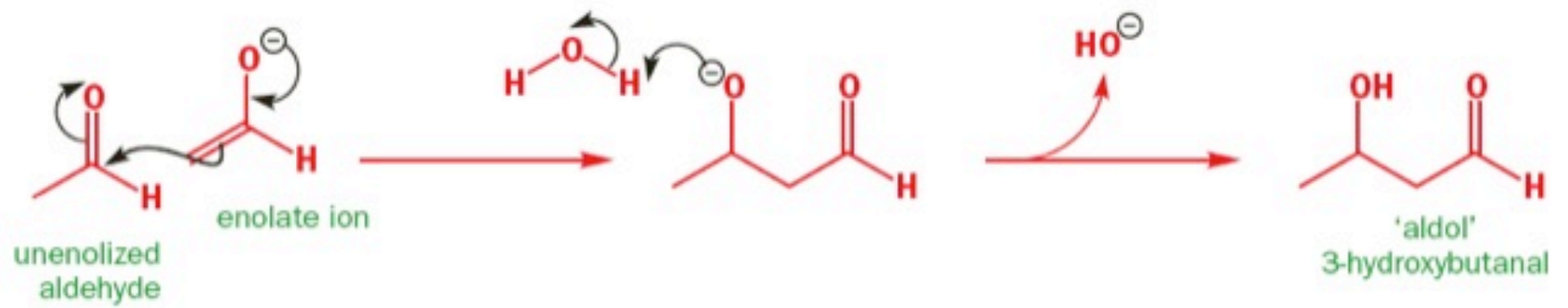
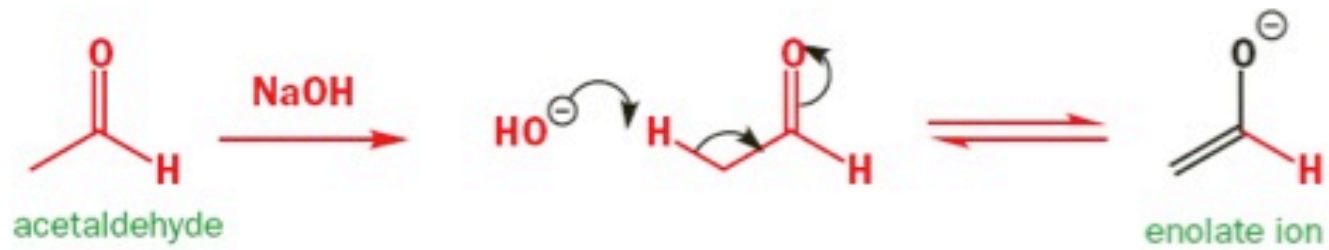
Condensation

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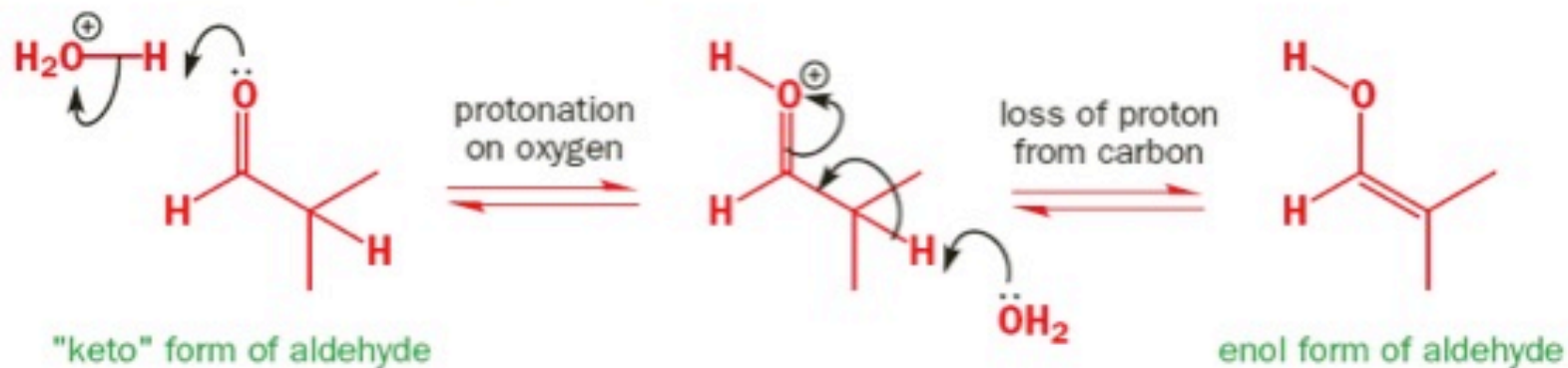
Self-condensation

both partners in the condensation reaction are the same

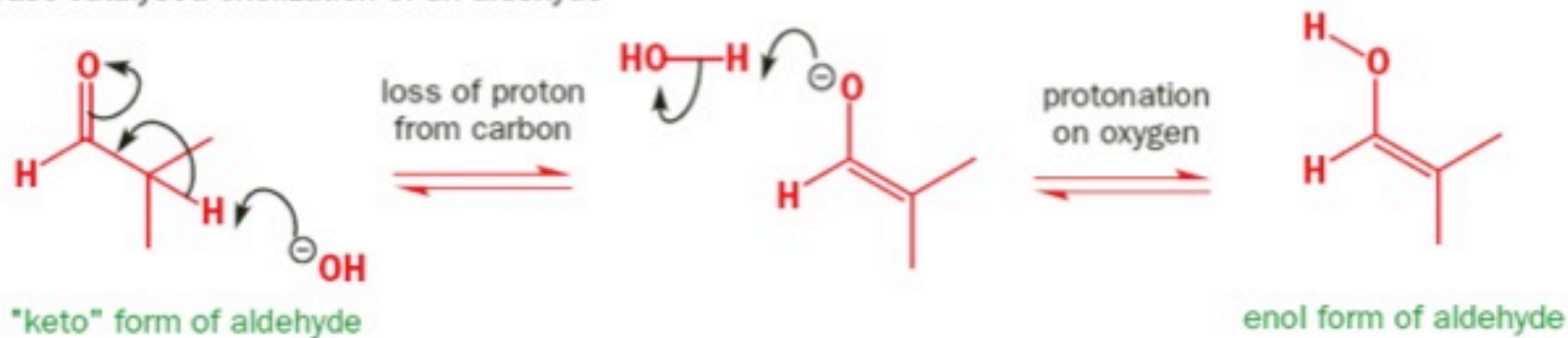
“DIMERIZATION”

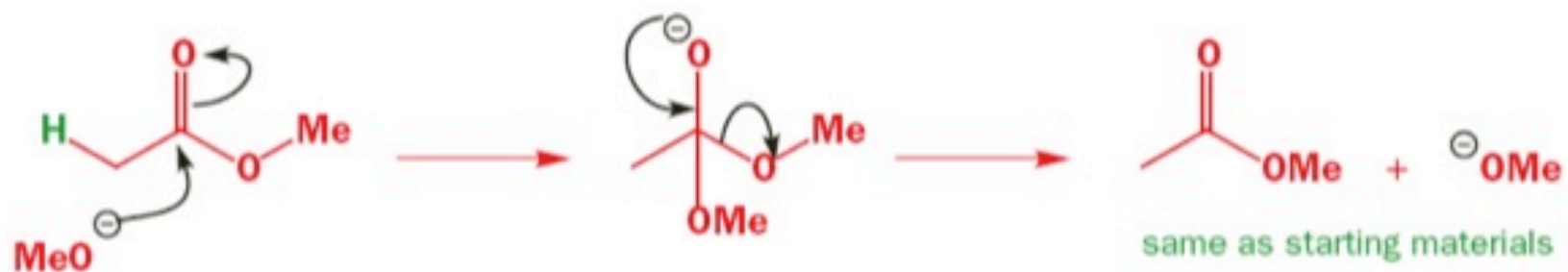


acid-catalysed enolization of an aldehyde

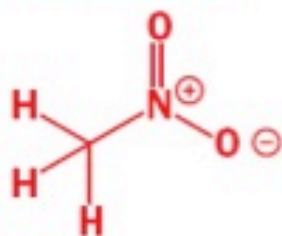


base-catalysed enolization of an aldehyde

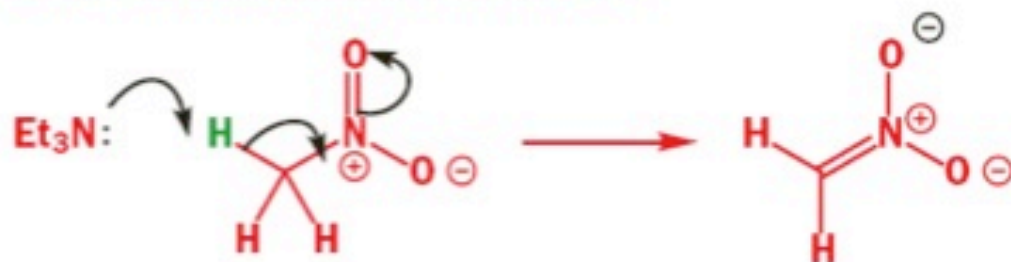


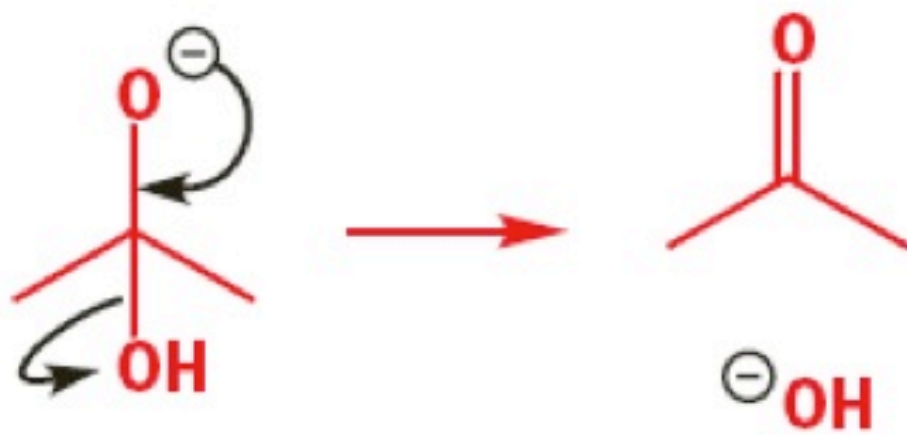
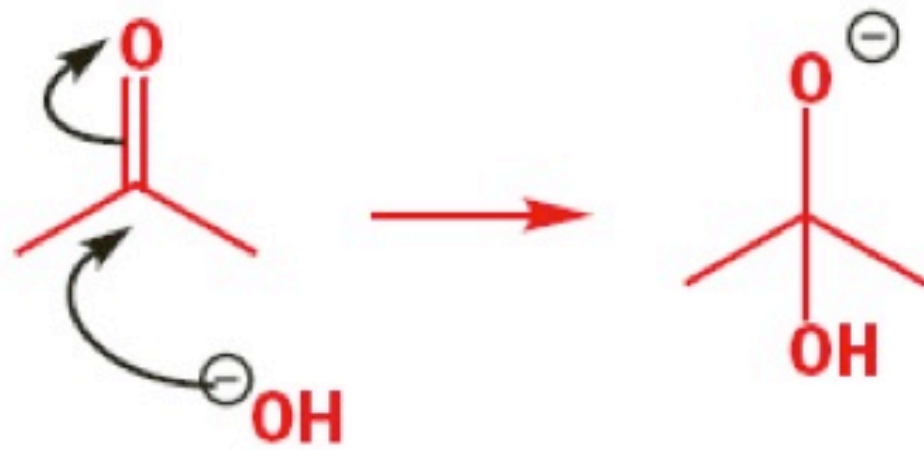


nitromethane



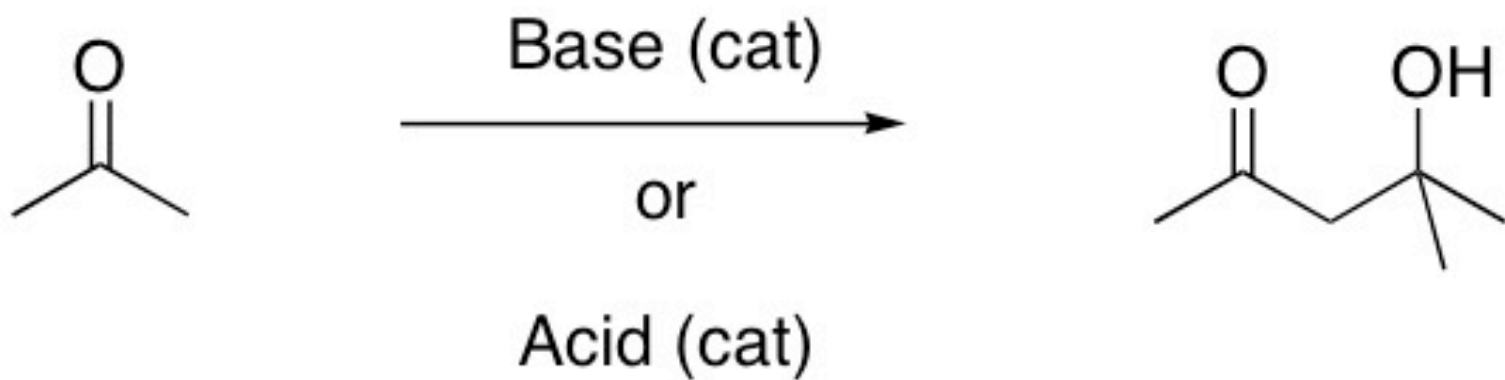
formation of nitromethane anion in base



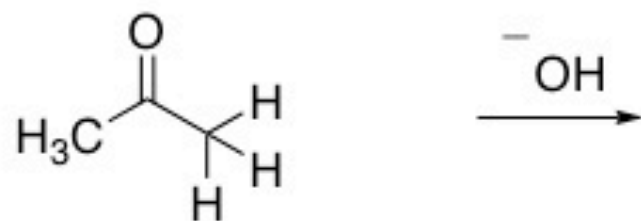


	5
	9
RCH_2NO_2	10
	11
	11
	13
	16
	19-20
	25
	25
	26

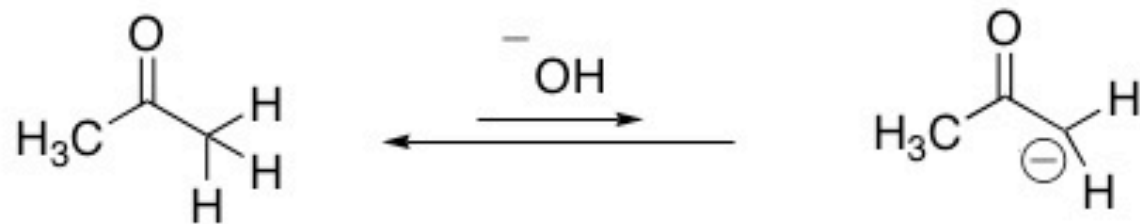
Self-Condensation of Acetone



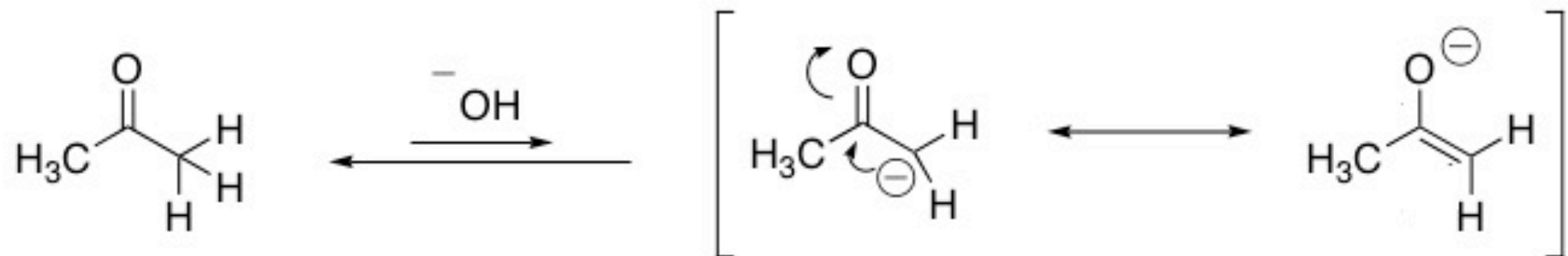
BASE-catalyzed Aldol Condensation



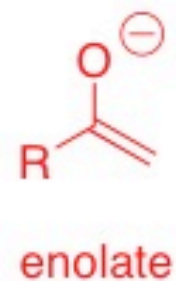
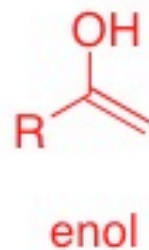
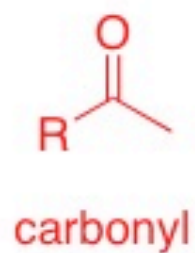
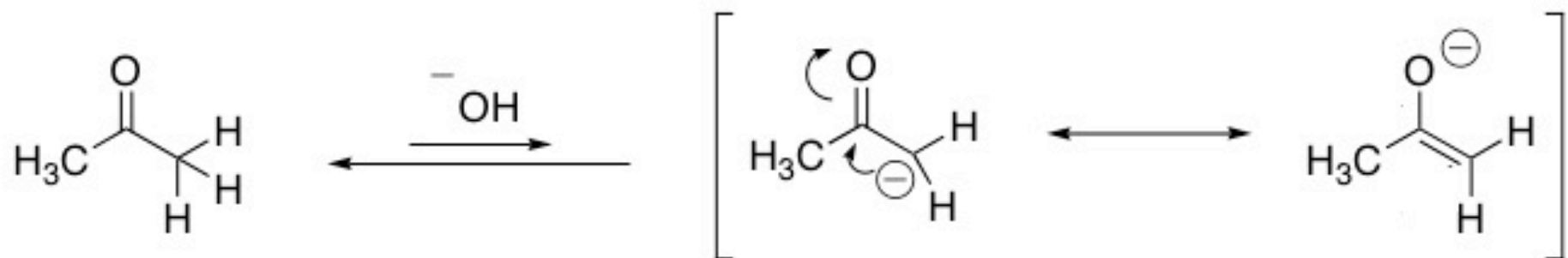
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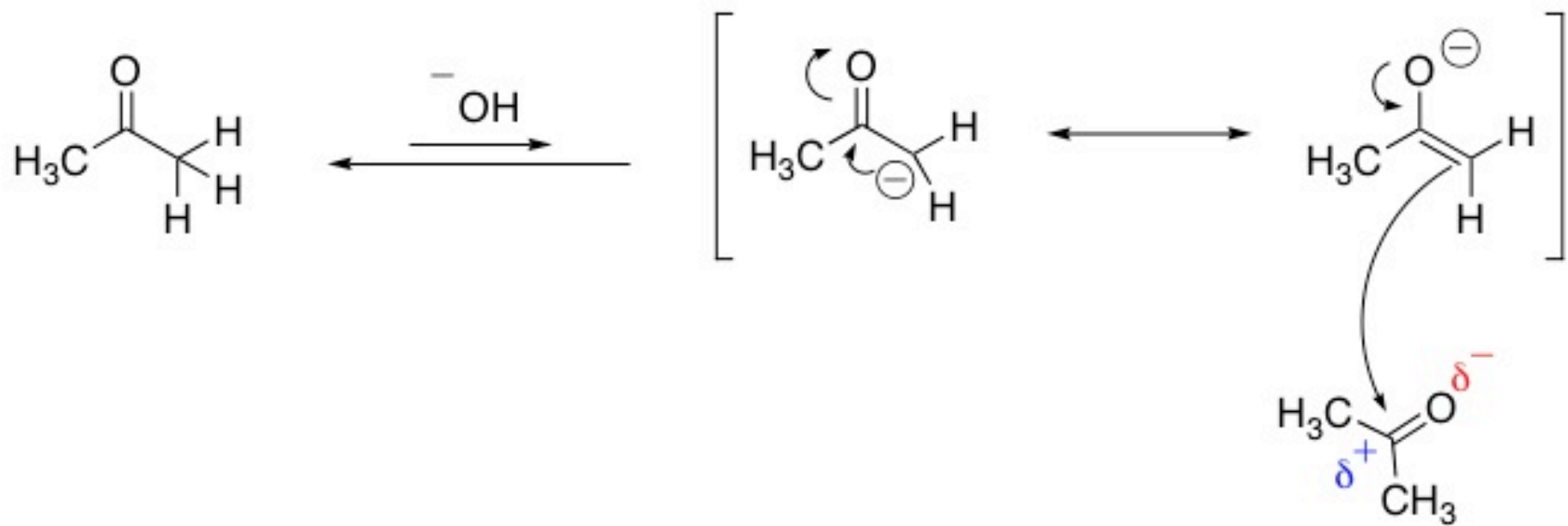
BASE-catalyzed Aldol Condensation



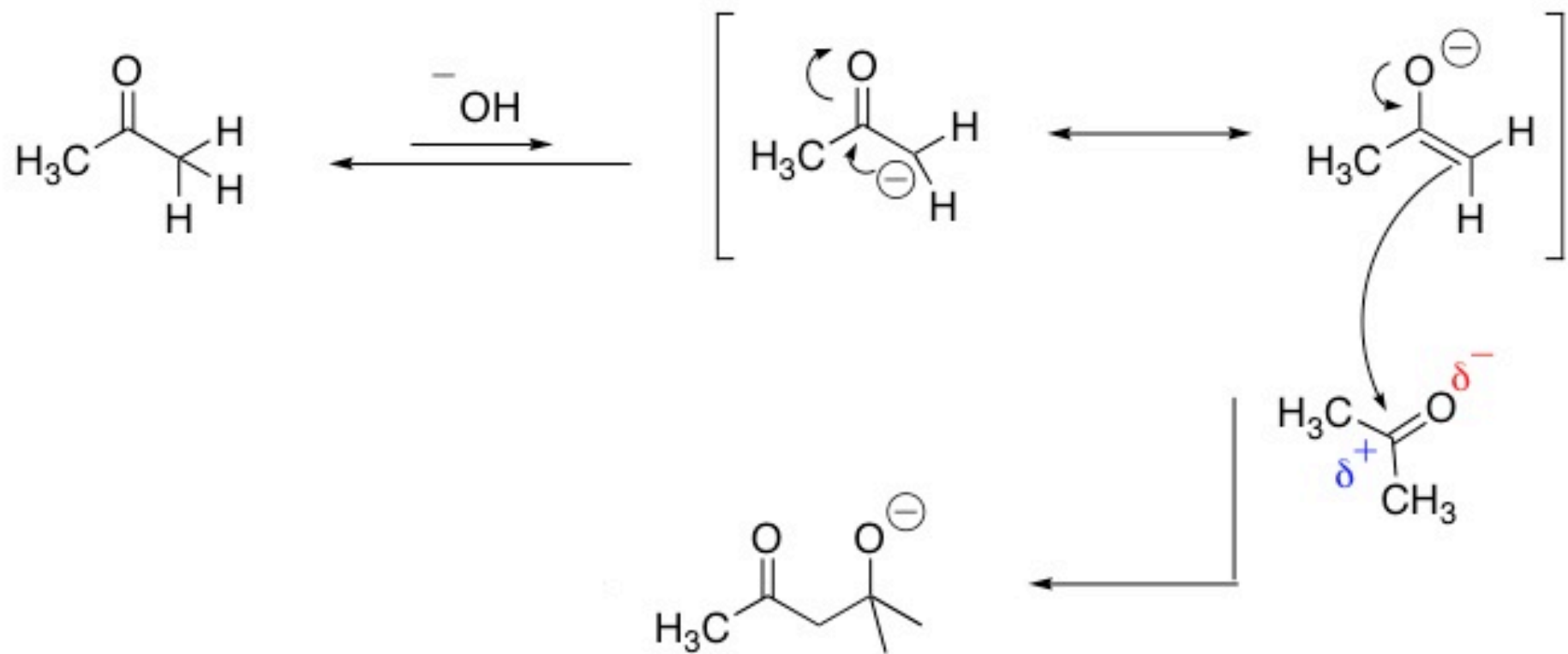
BASE-catalyzed Aldol Condensation



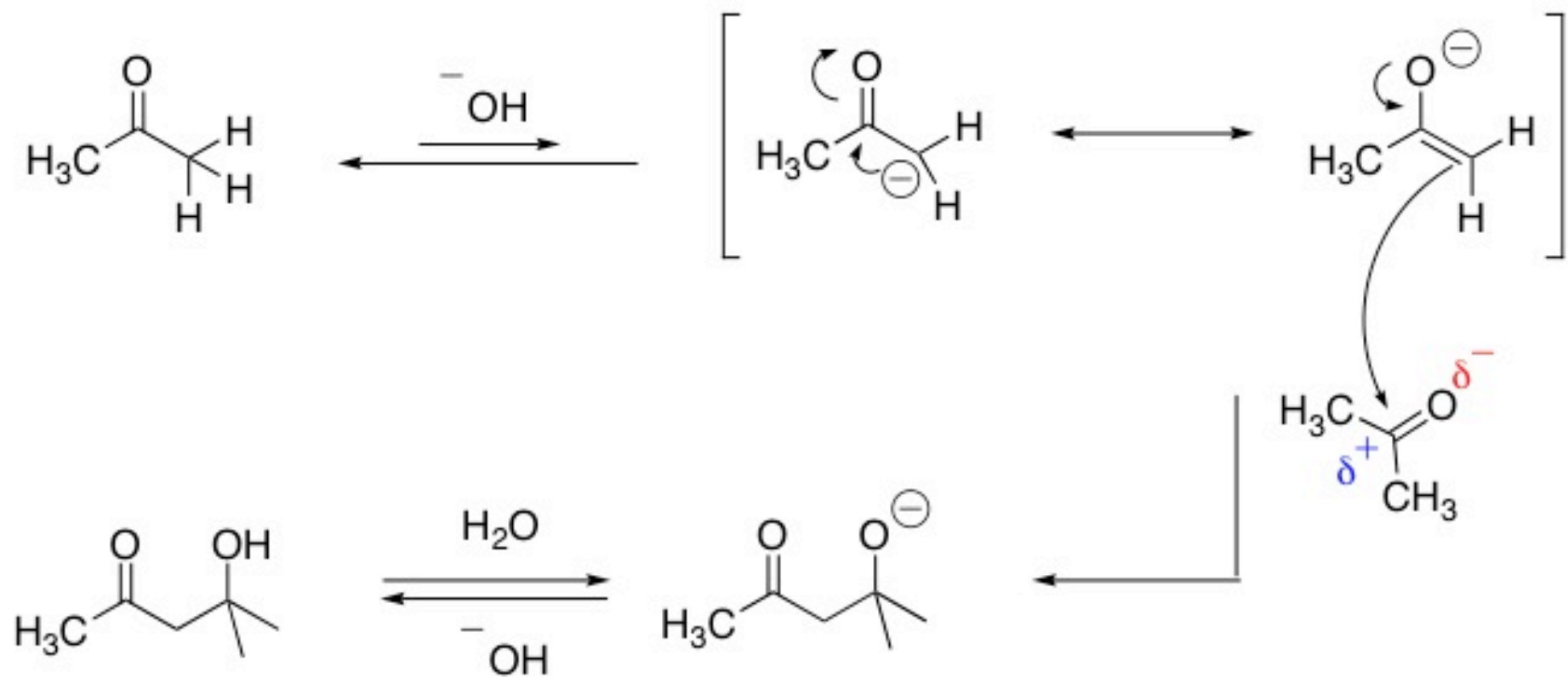
BASE-catalyzed Aldol Condensation



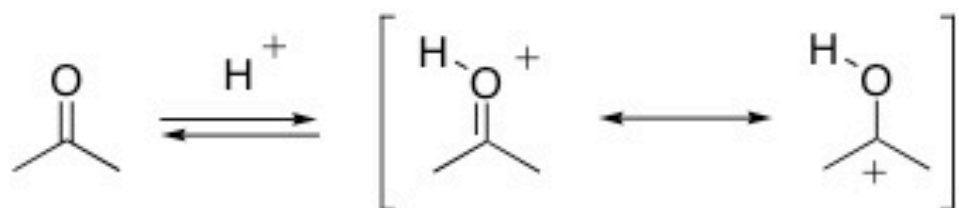
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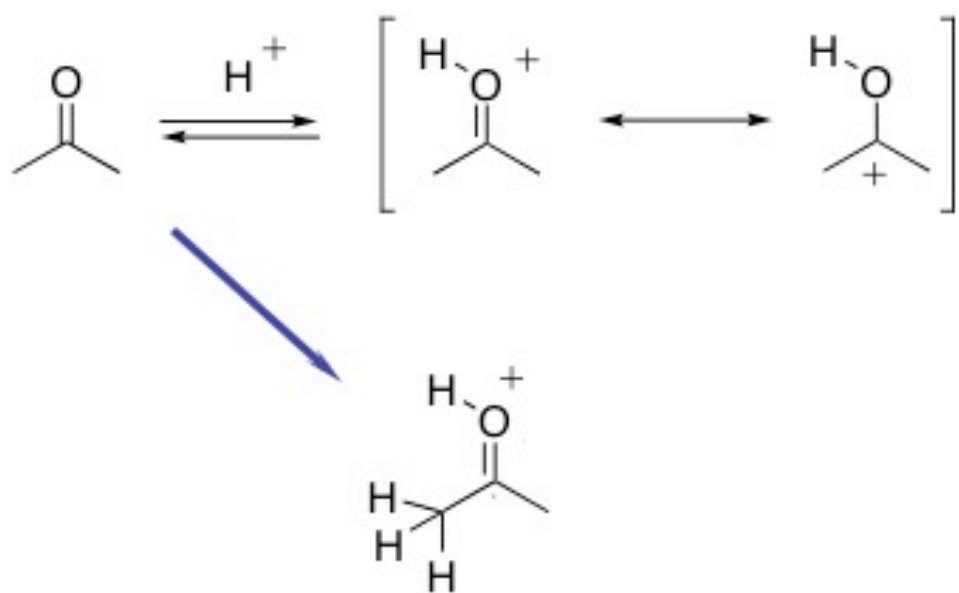
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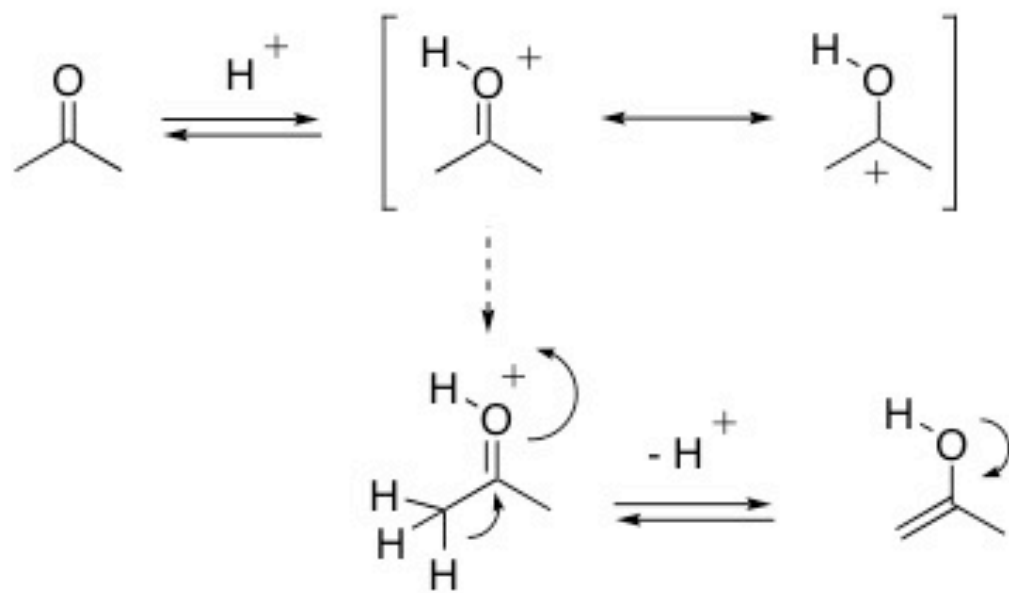
ACID-catalyzed Aldol Condensation



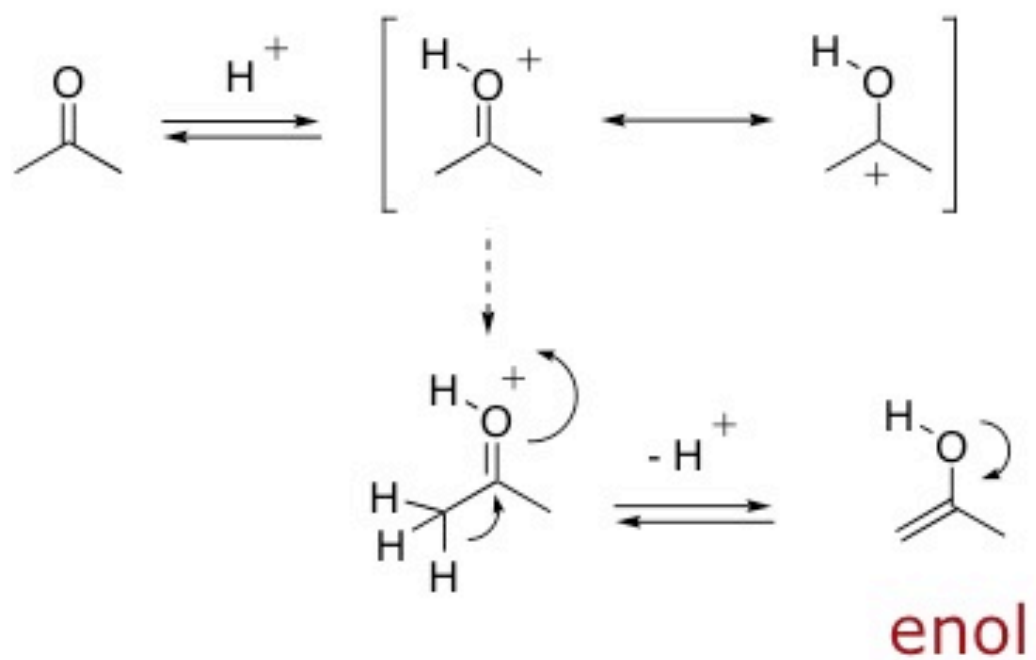
ACID-catalyzed Aldol Condensation



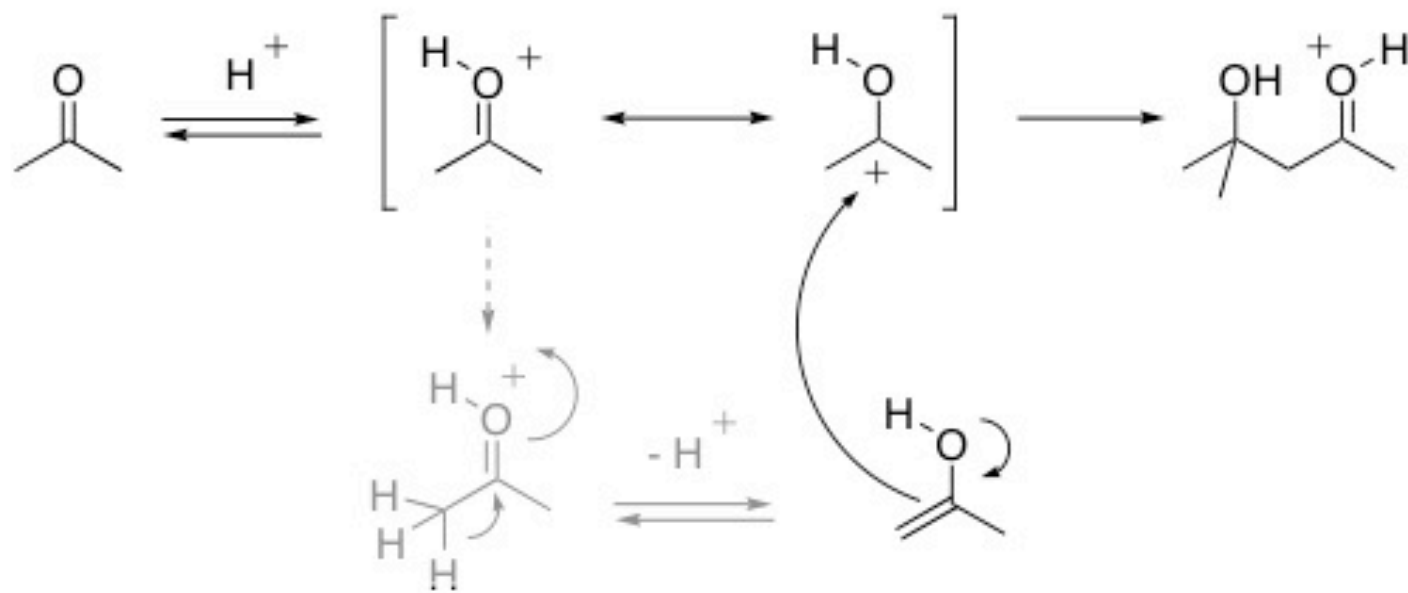
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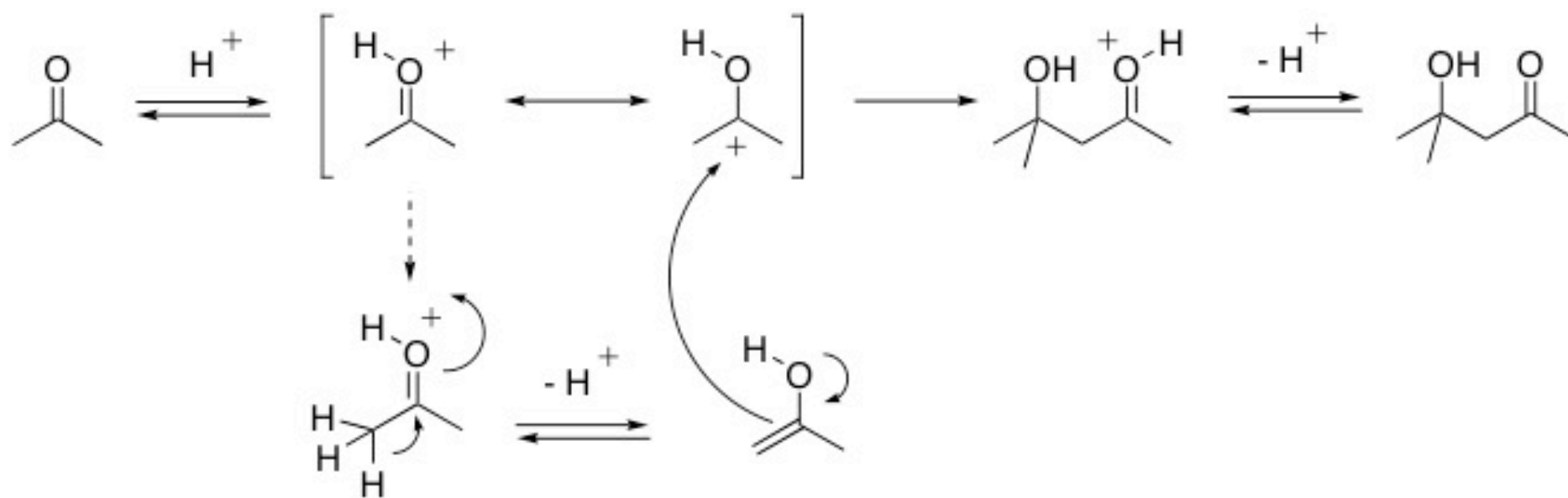
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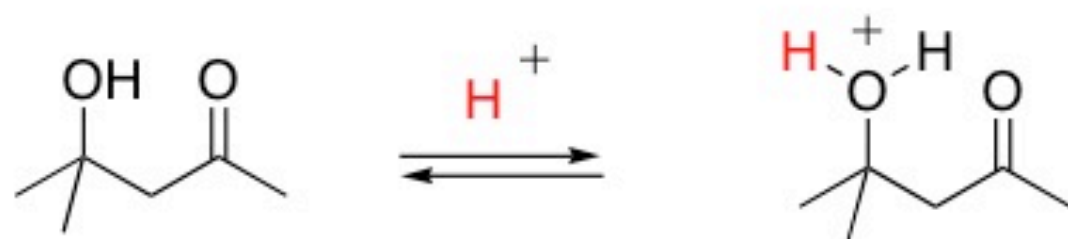
ACID-catalyzed Aldol Condensation



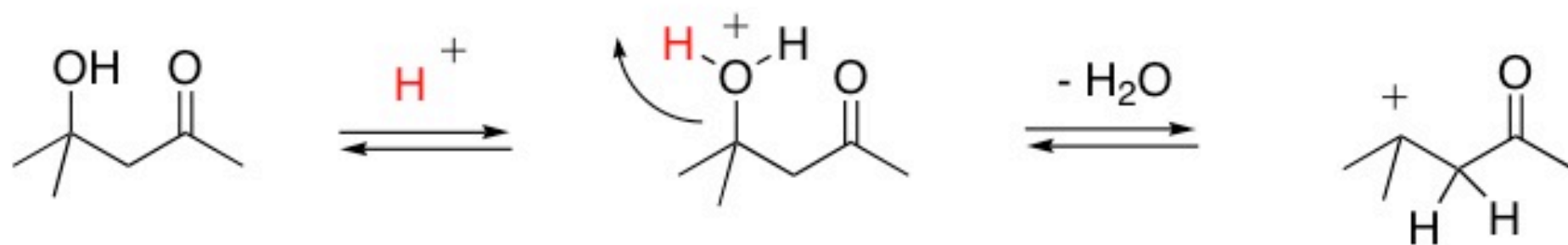
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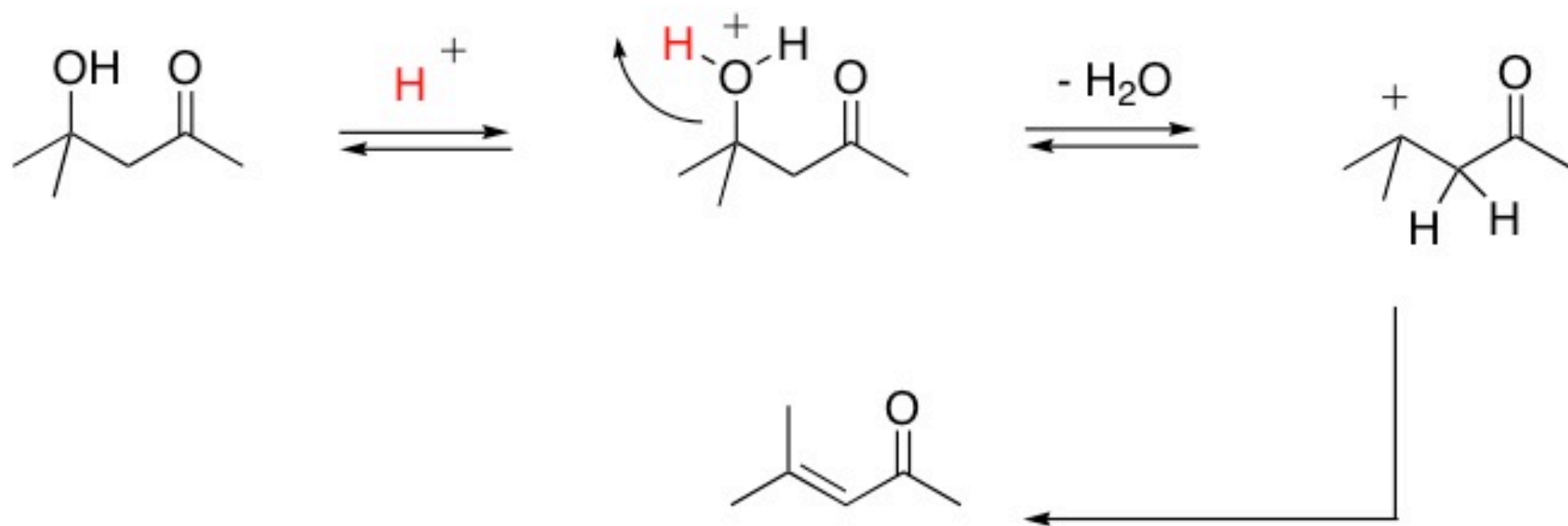
If the aldol is a 3°-alcohol, an elimination (E1) is likely to take place



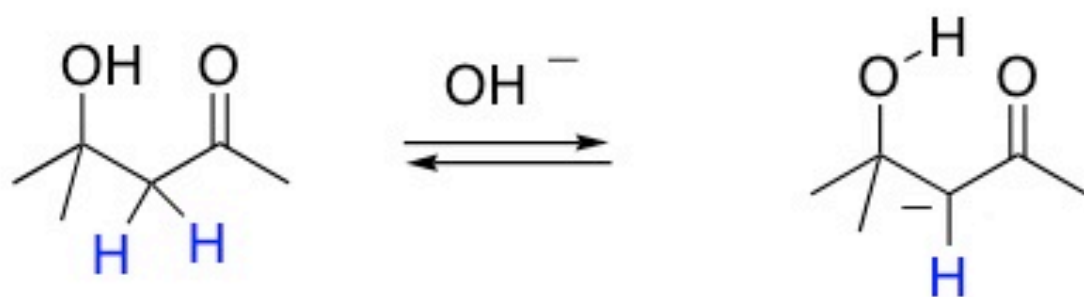
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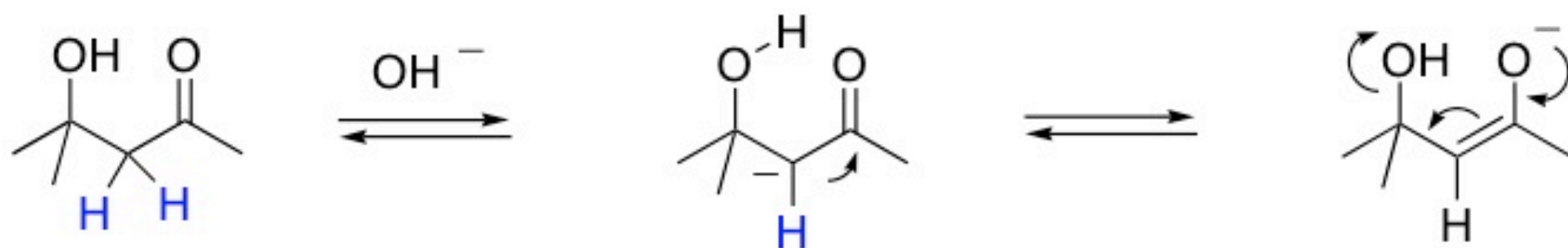
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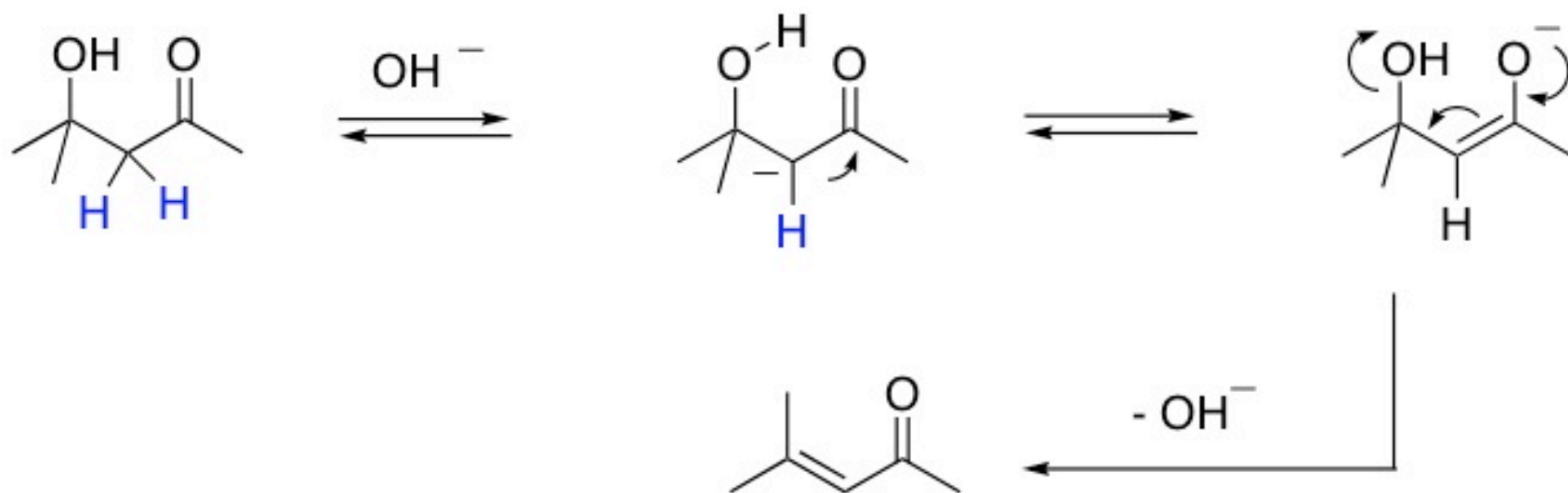
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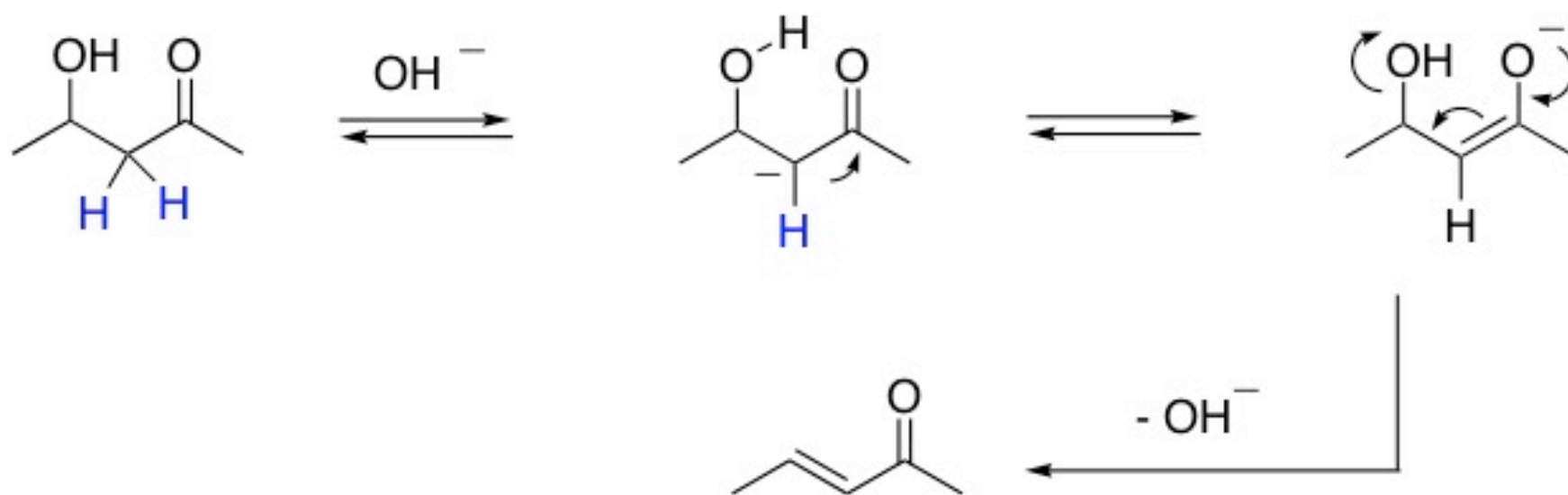


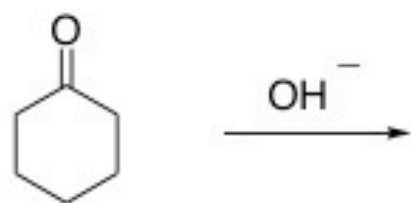
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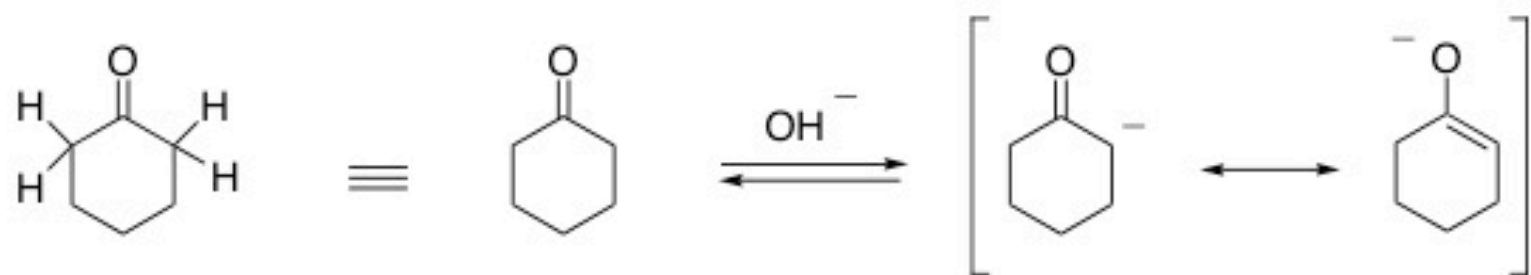


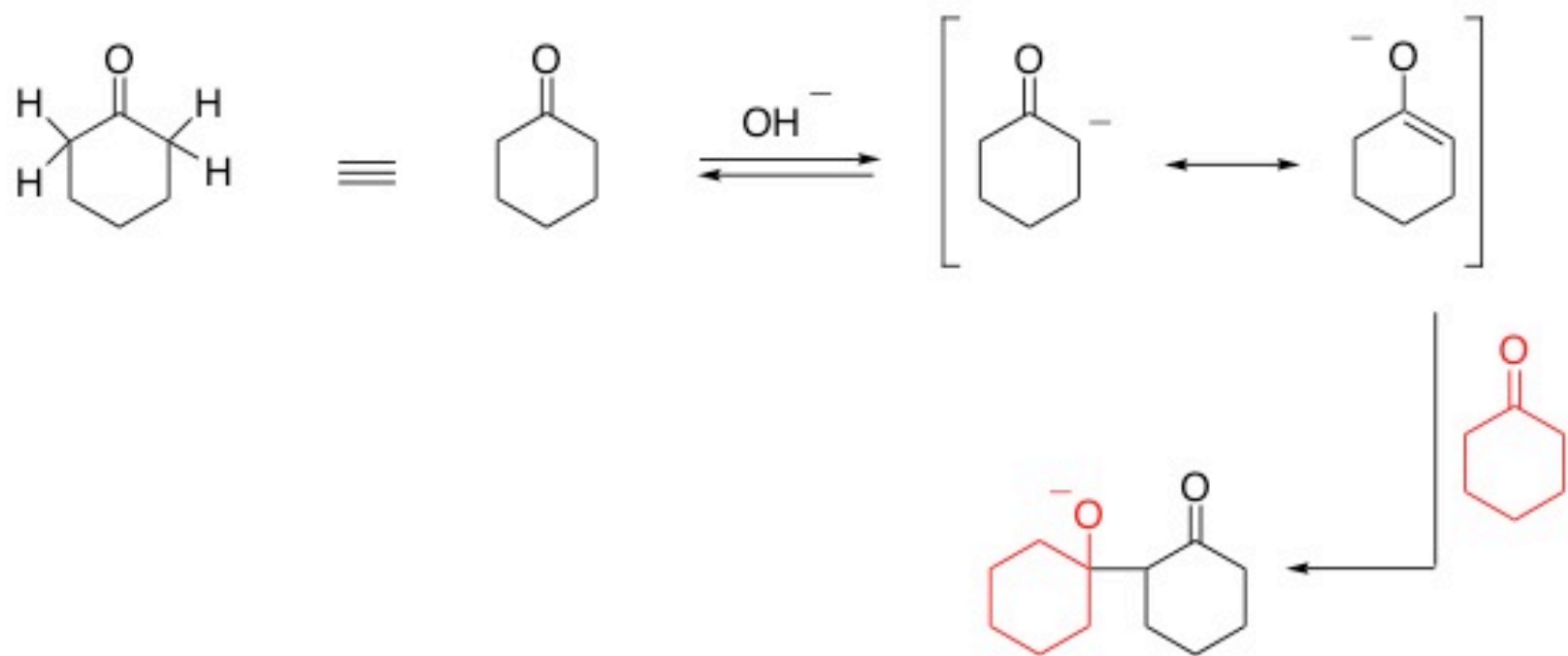
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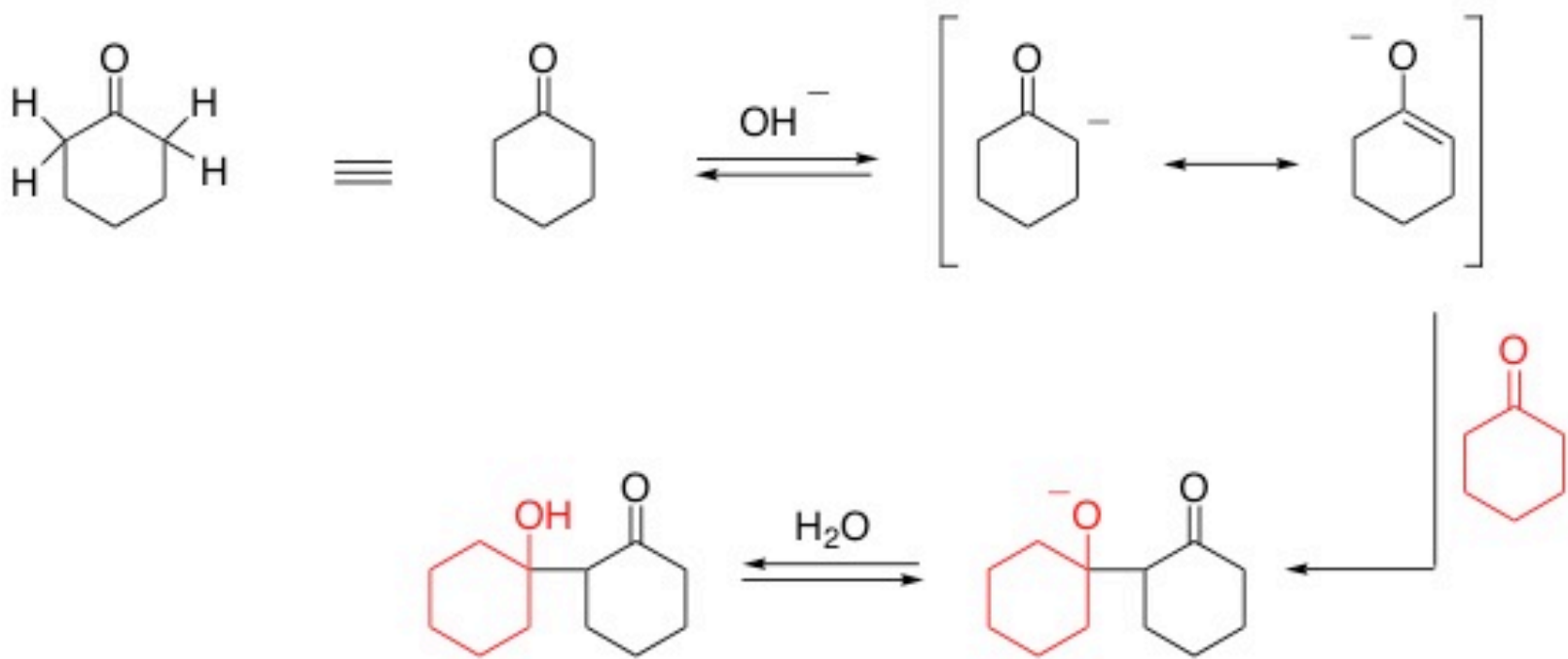
Even 2° can eliminate - conjugated product!!

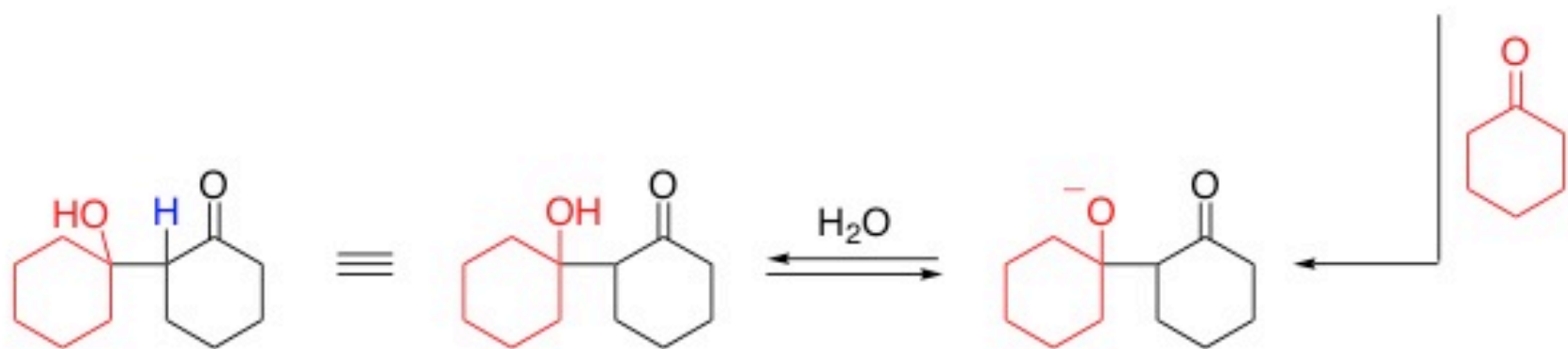
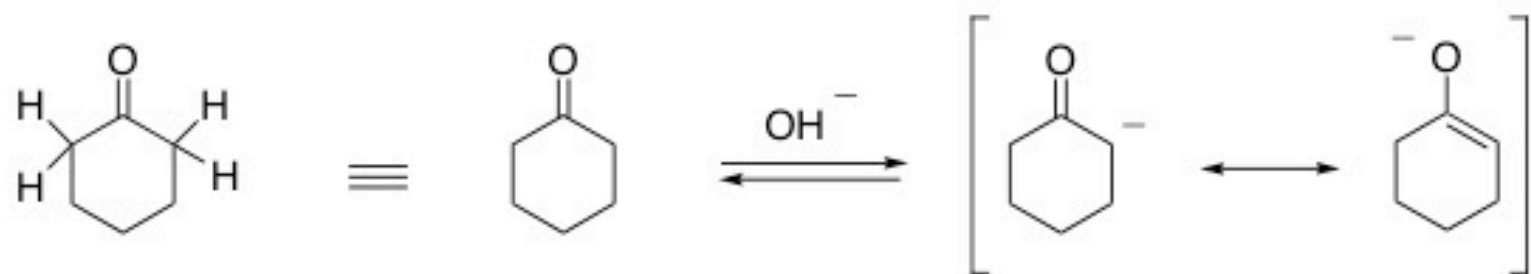


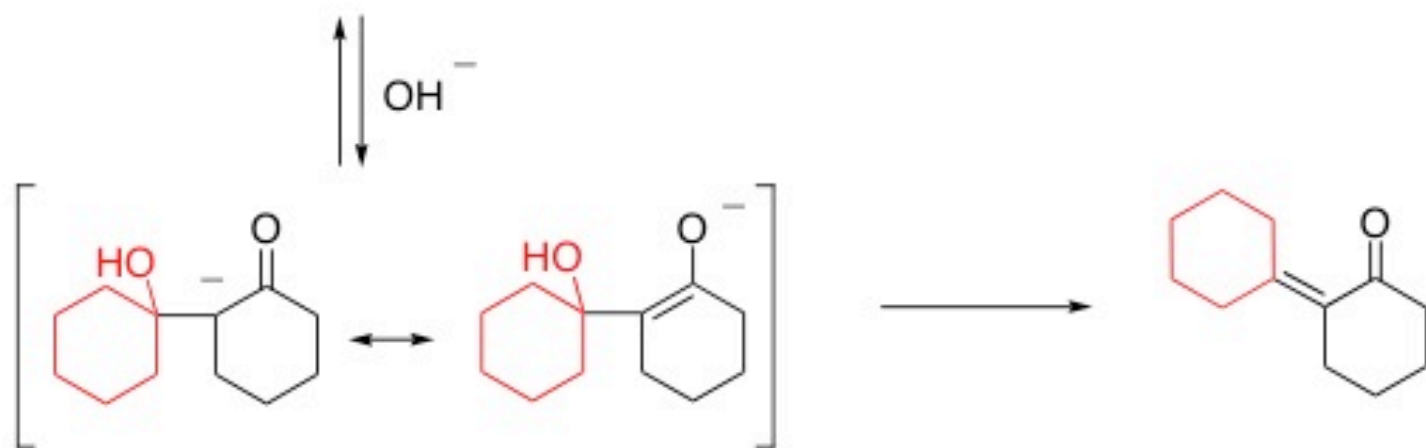
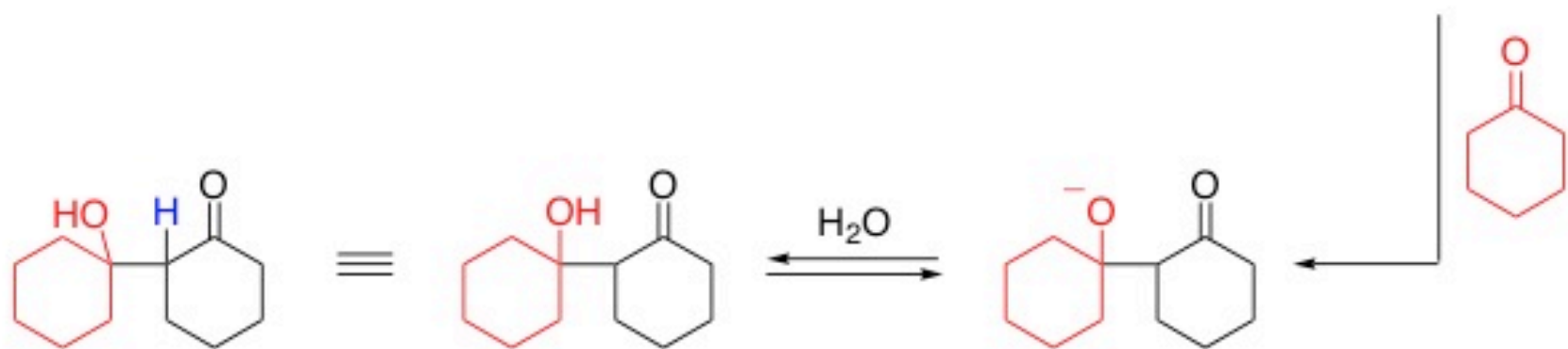
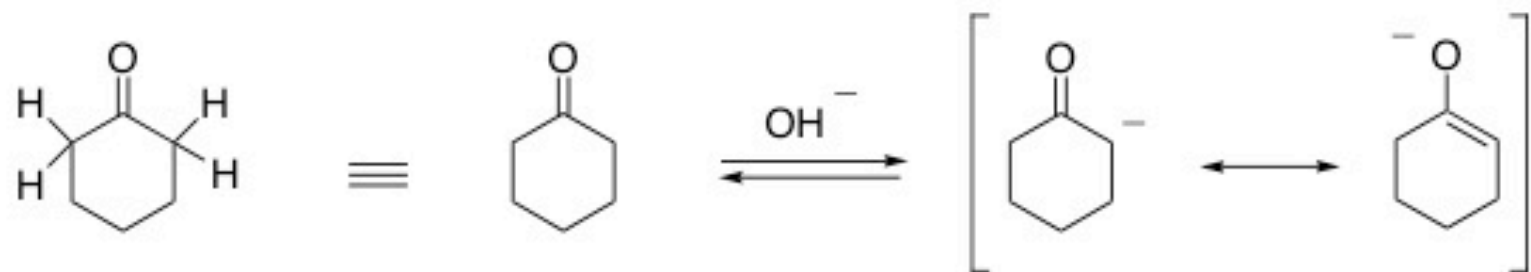












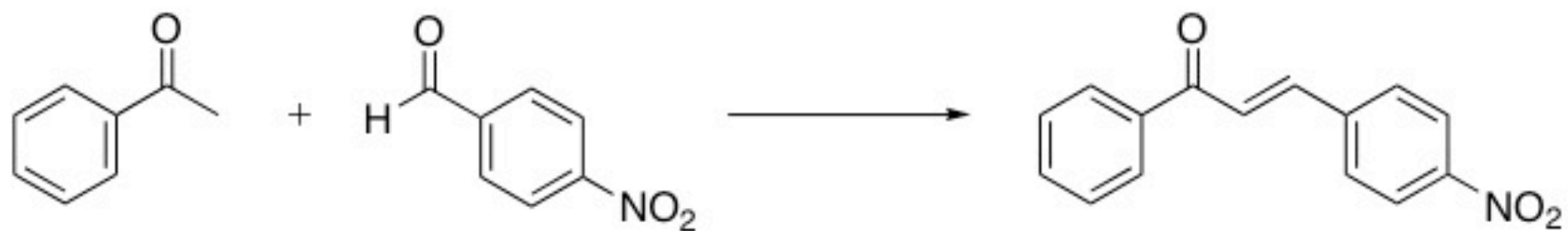
Cross-Condensation

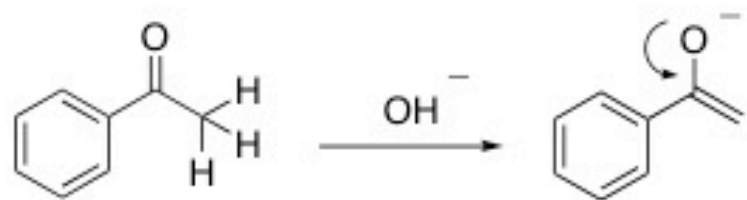
Different carbonyl compounds:

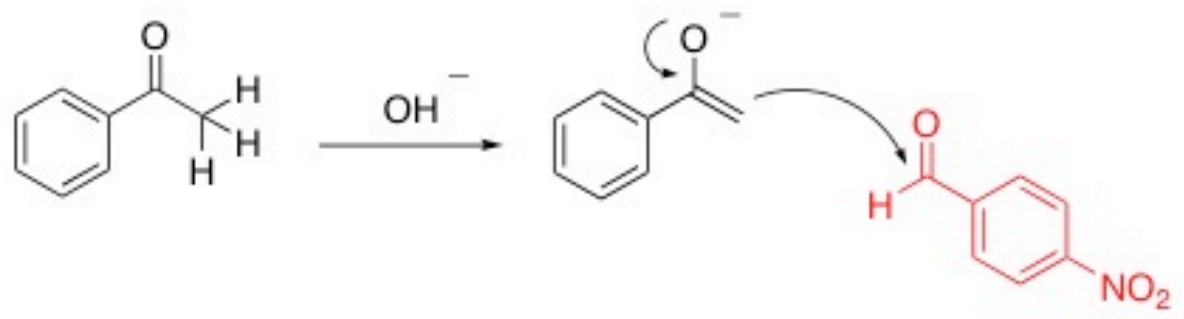
one will act as a nucleophile in
enol/enolate form

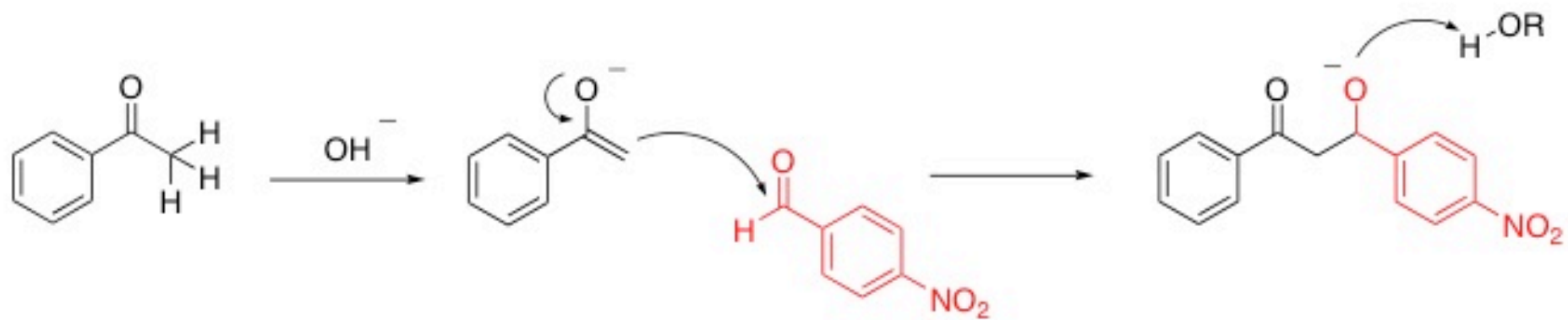
the other will be electrophile

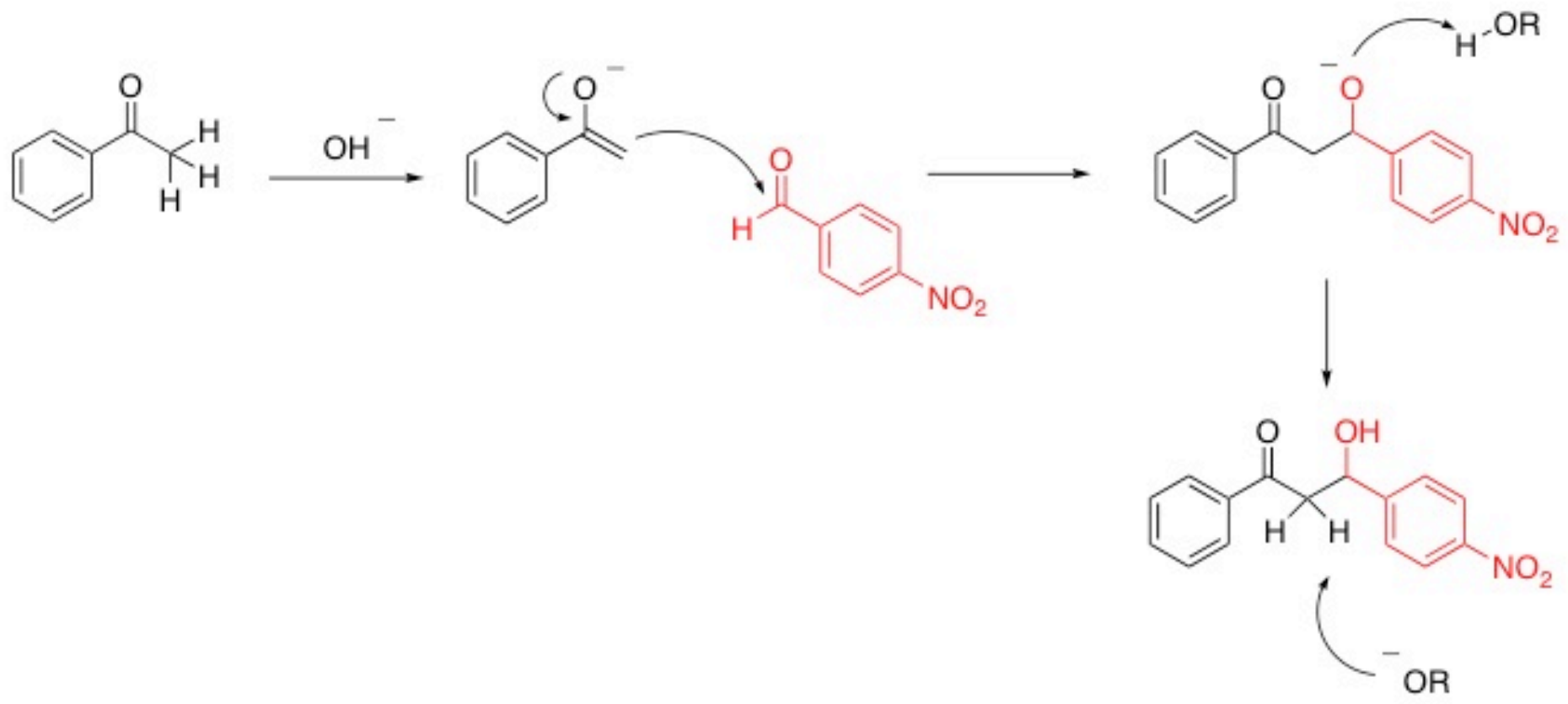
Cross-Condensation

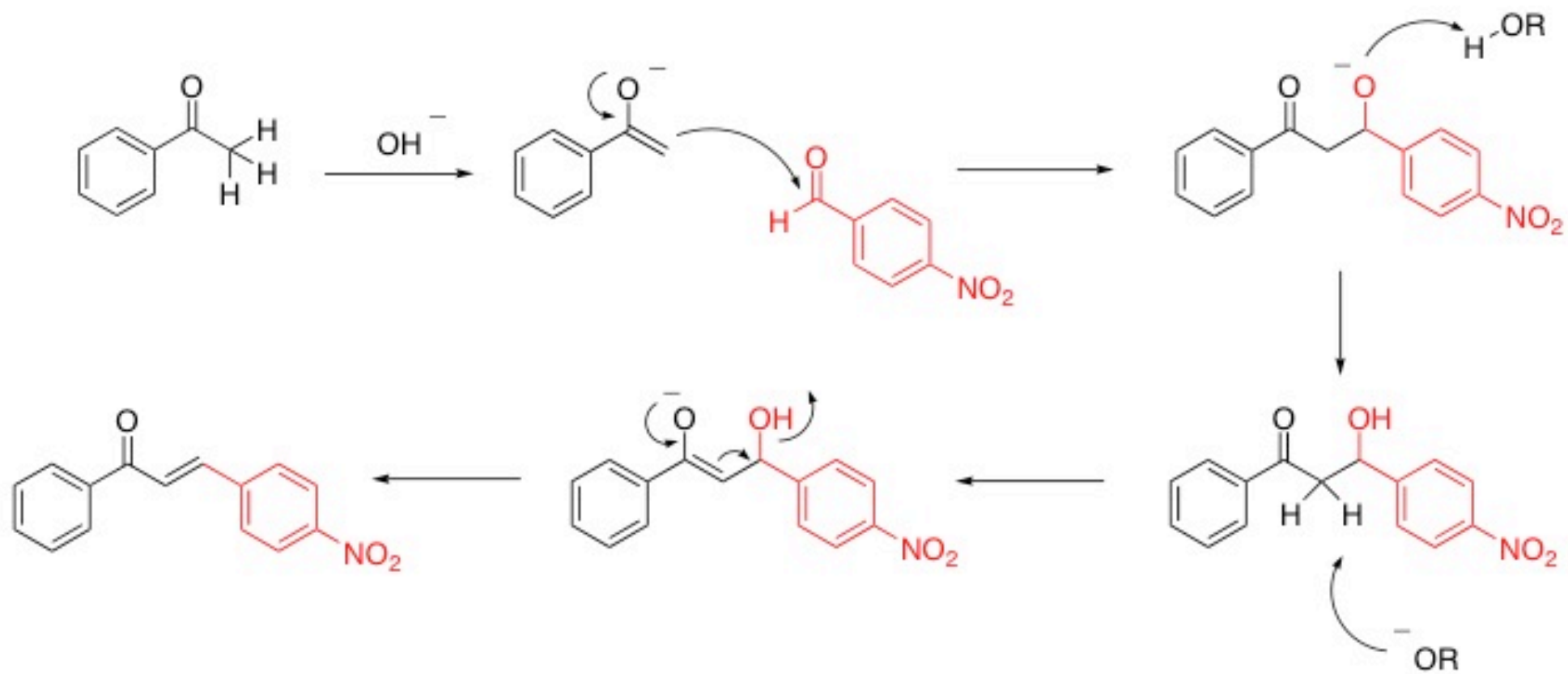




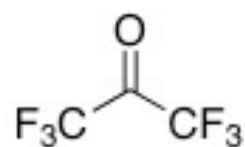
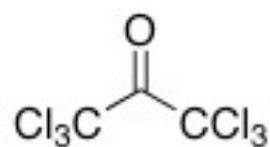




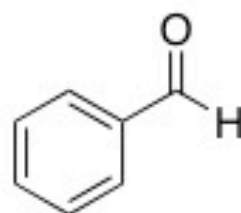
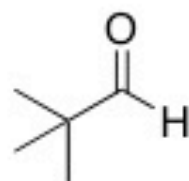
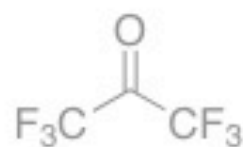
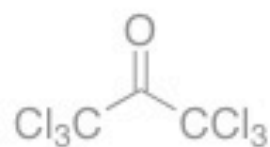




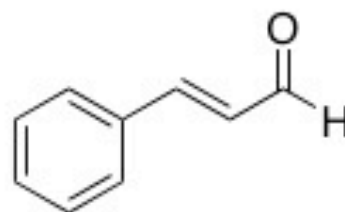
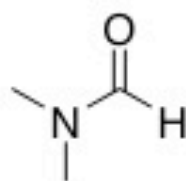
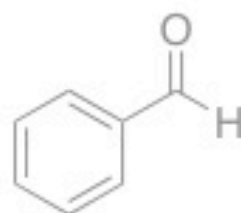
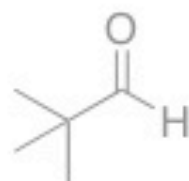
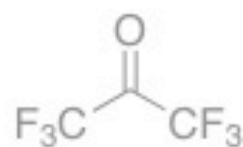
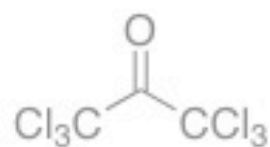
Carbonyl compounds that do not participate in enol formation



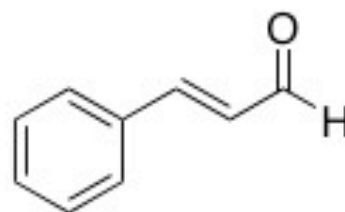
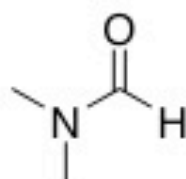
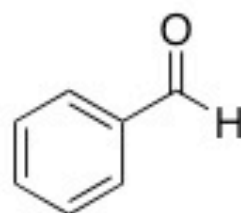
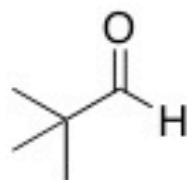
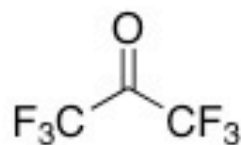
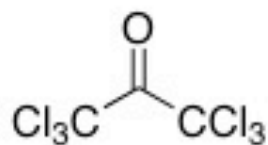
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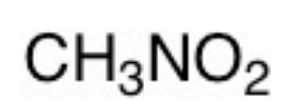
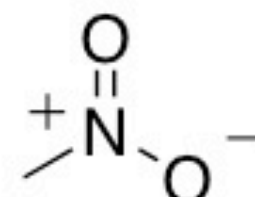
Carbonyl compounds that do not participate in enol formation



No α -hydrogen

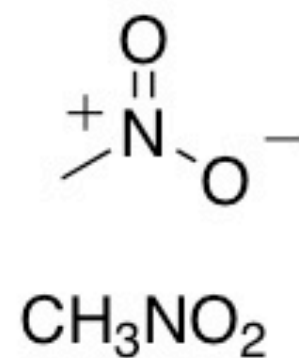
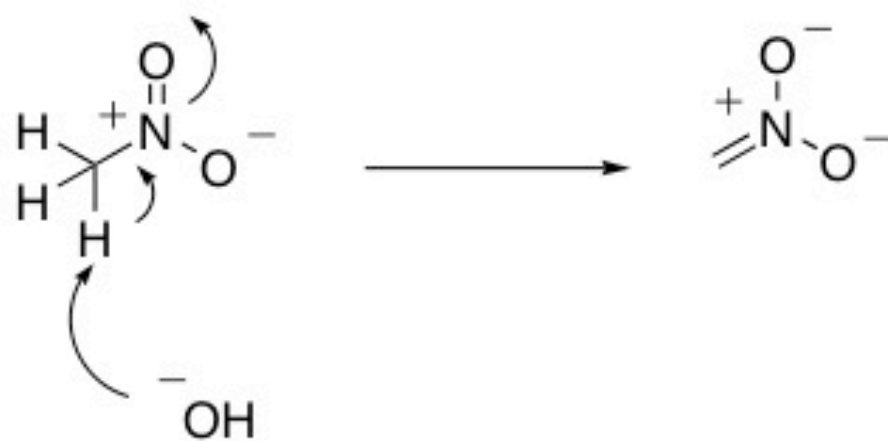
Nitroalkanes

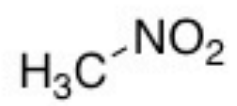
enolization & aldol reaction



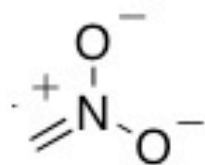
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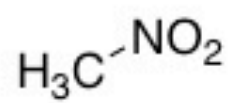
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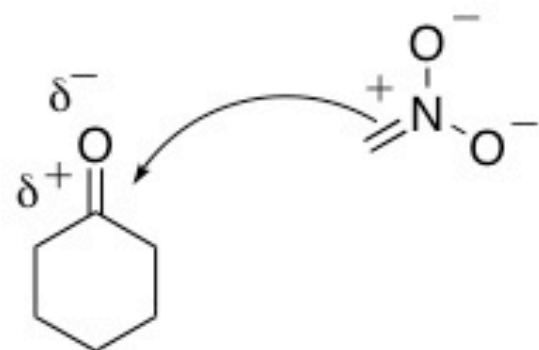


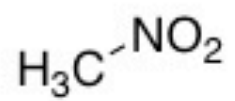
NaOH, MeOH



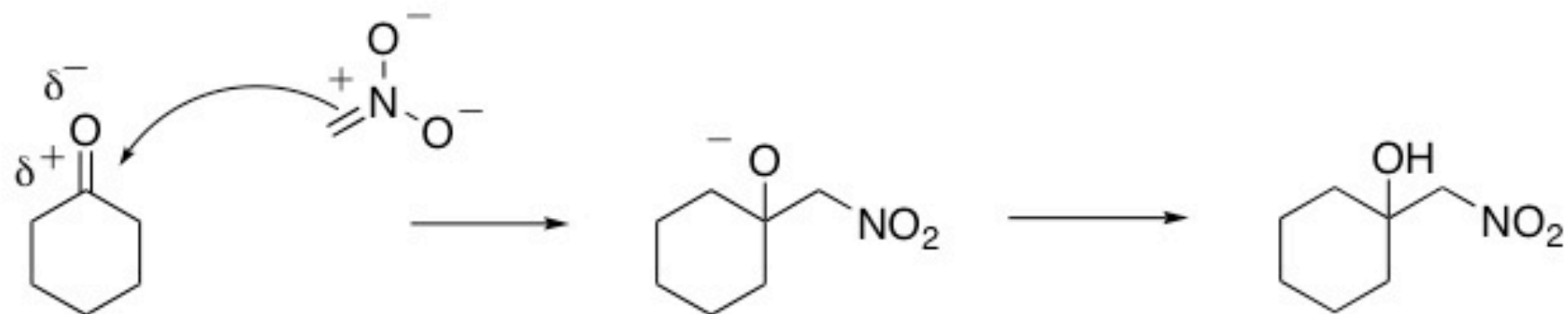


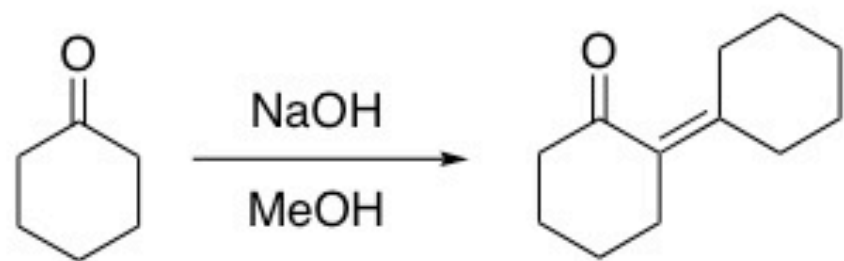
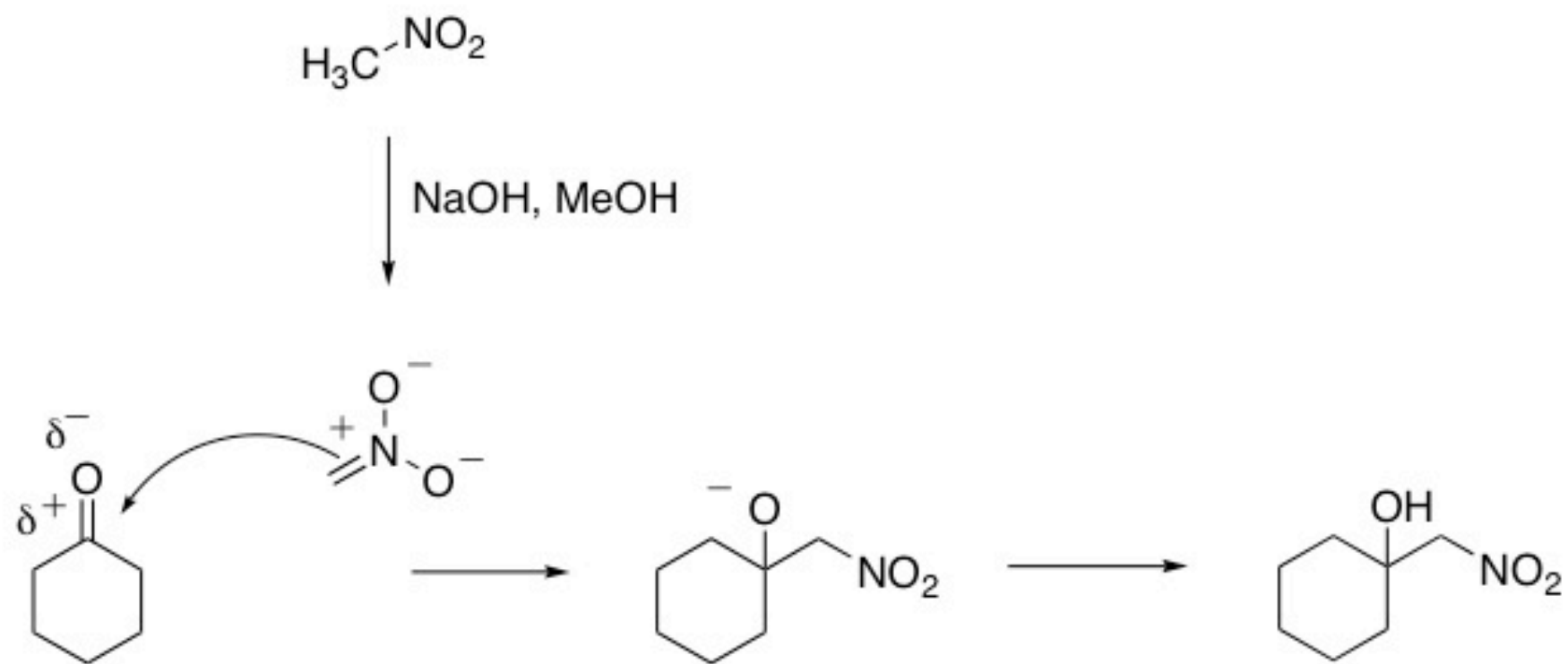
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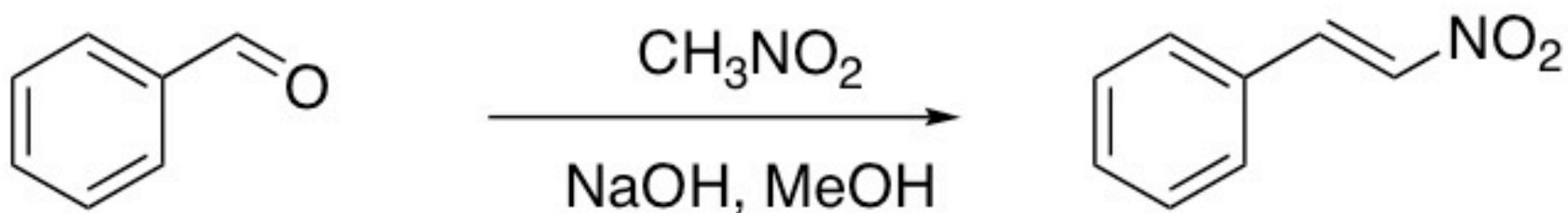


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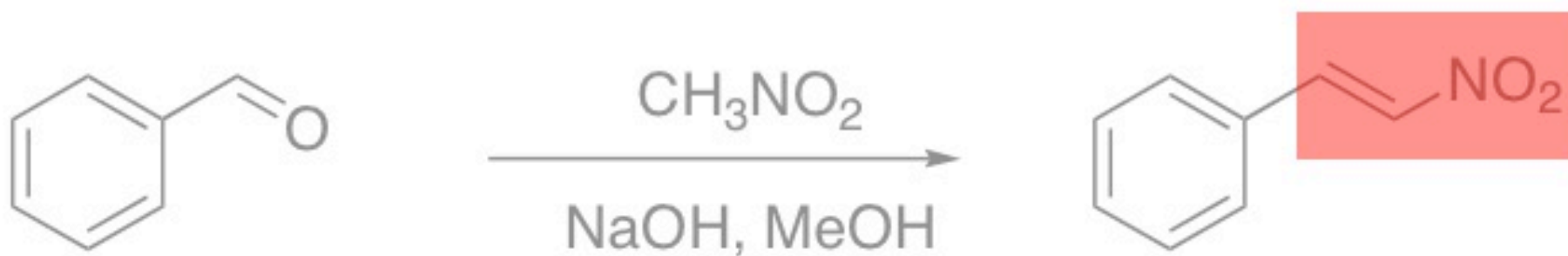




Elimination is very facile, if possible



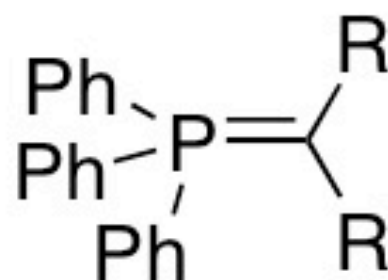
Elimination is very facile, if possible



Enol equivalents

Phosphonium ylides

Wittig reaction





The Nobel Prize in Chemistry 1979

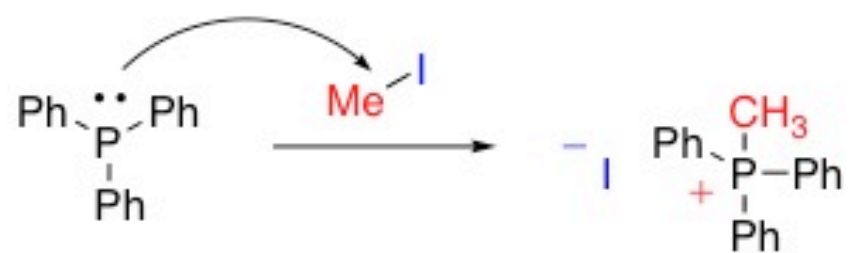
"for their development of the use of boron- and phosphorus-containing compounds, respectively, into important reagents in organic synthesis"

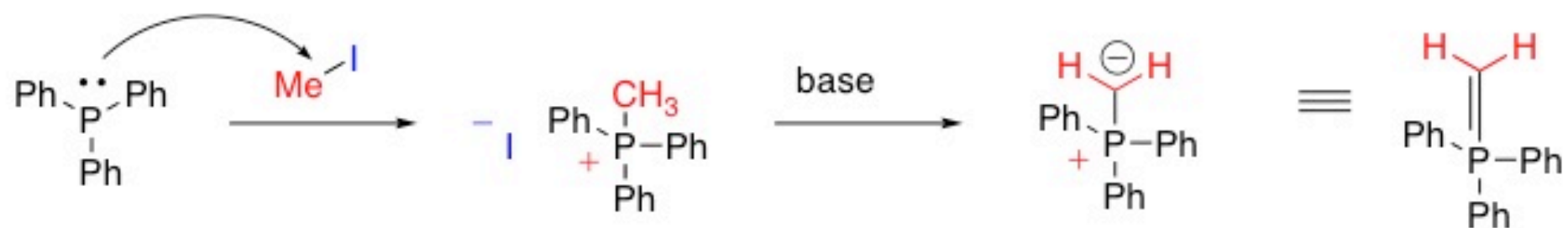


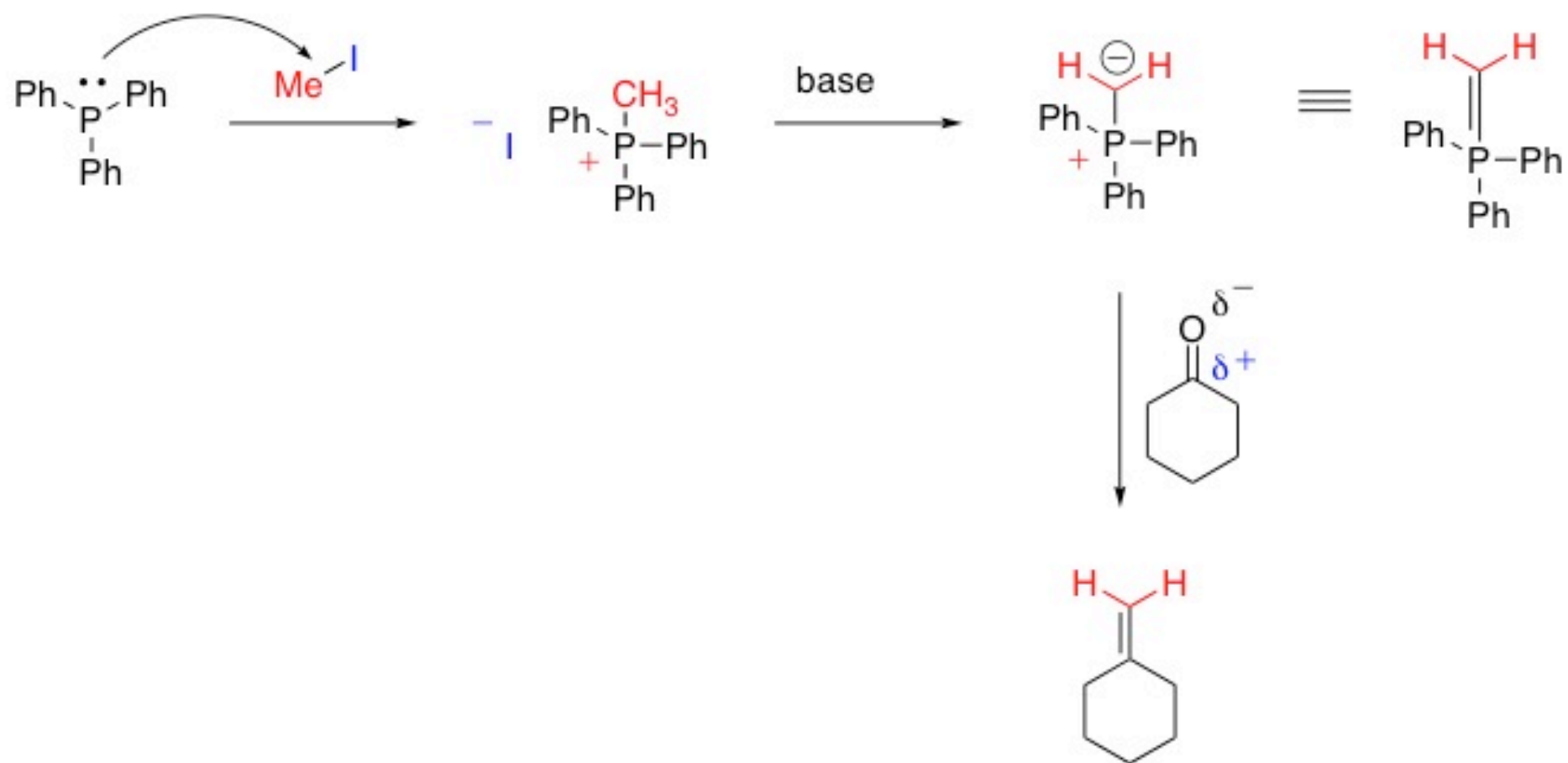
H.C. Brown

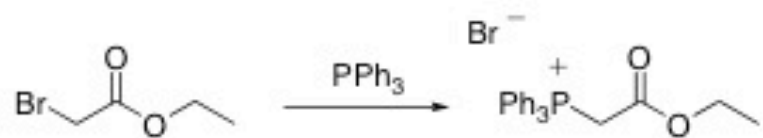


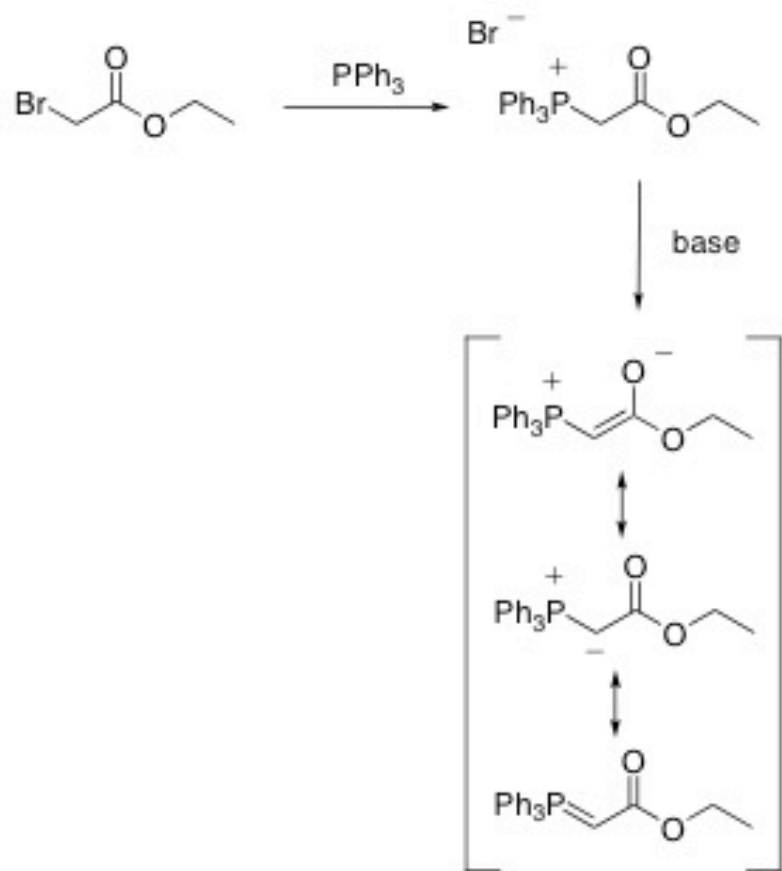
Georg
Wittig

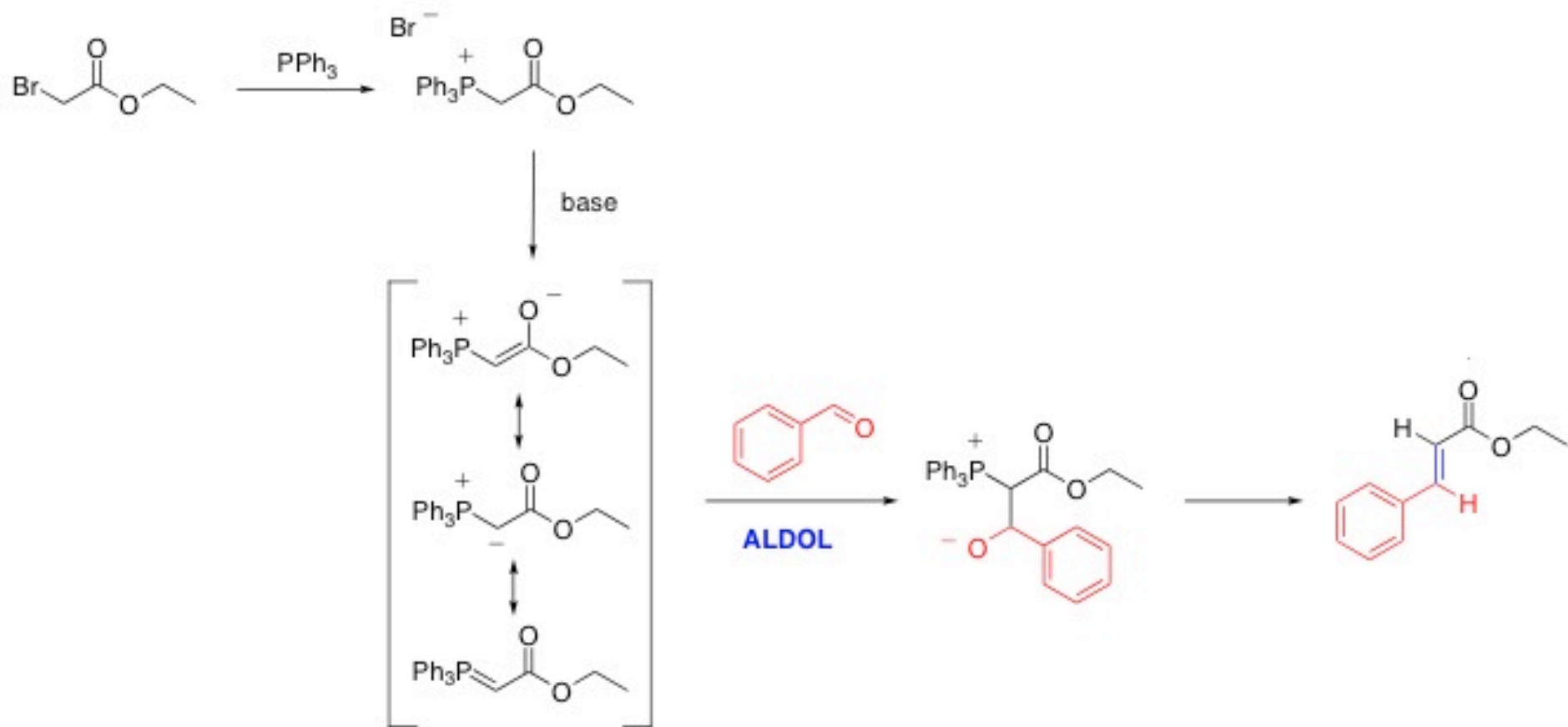


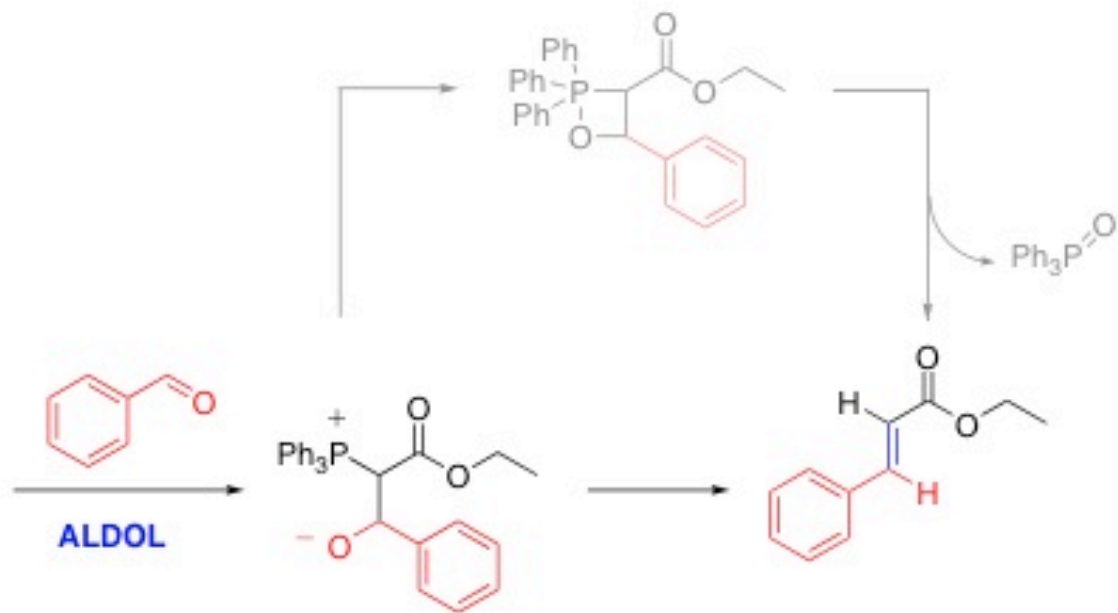
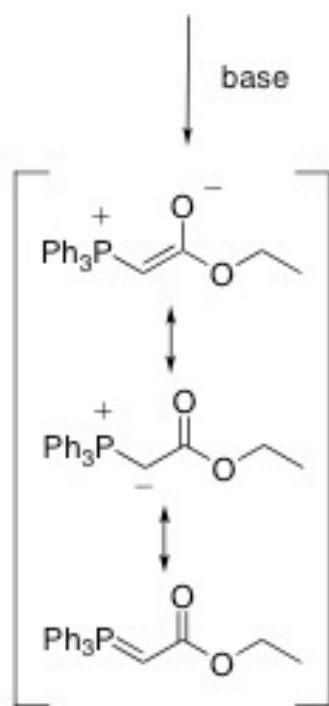
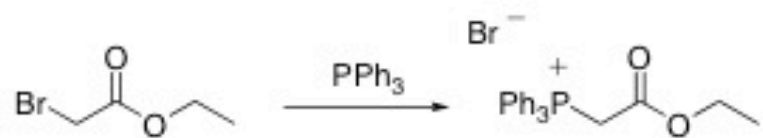


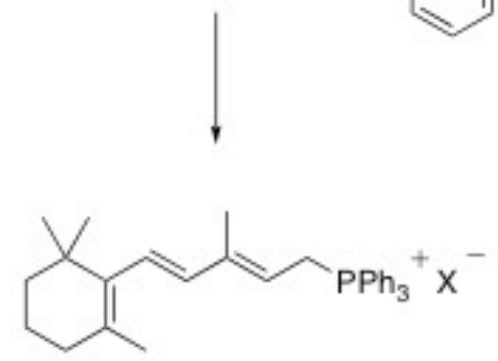
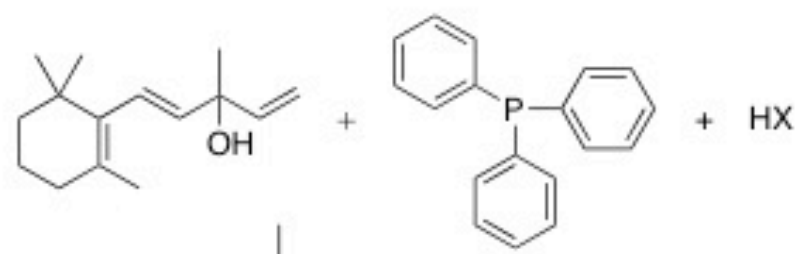




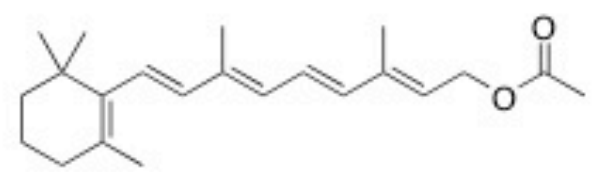
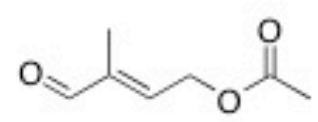
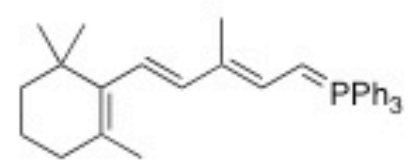








base



Aldol Reaction

Lab #5

Power cords in the hoods

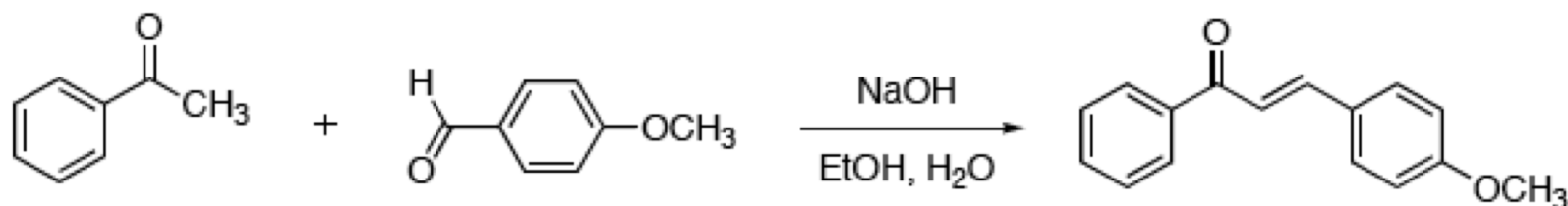
When the hot plate is on - make sure the cords are not touching the plate

Plastic cover melts, and as soon as it is damaged, it will shortcut!

EXPERIMENT 5: ALDOL REACTION (preparative)

WEAR GLOVES! Plan your time carefully and be efficient: you will turn make 2 compounds and you will have to determine 2 melting points.

ALDOL REACTION: synthesis of *trans*-p-anisalacetophenone



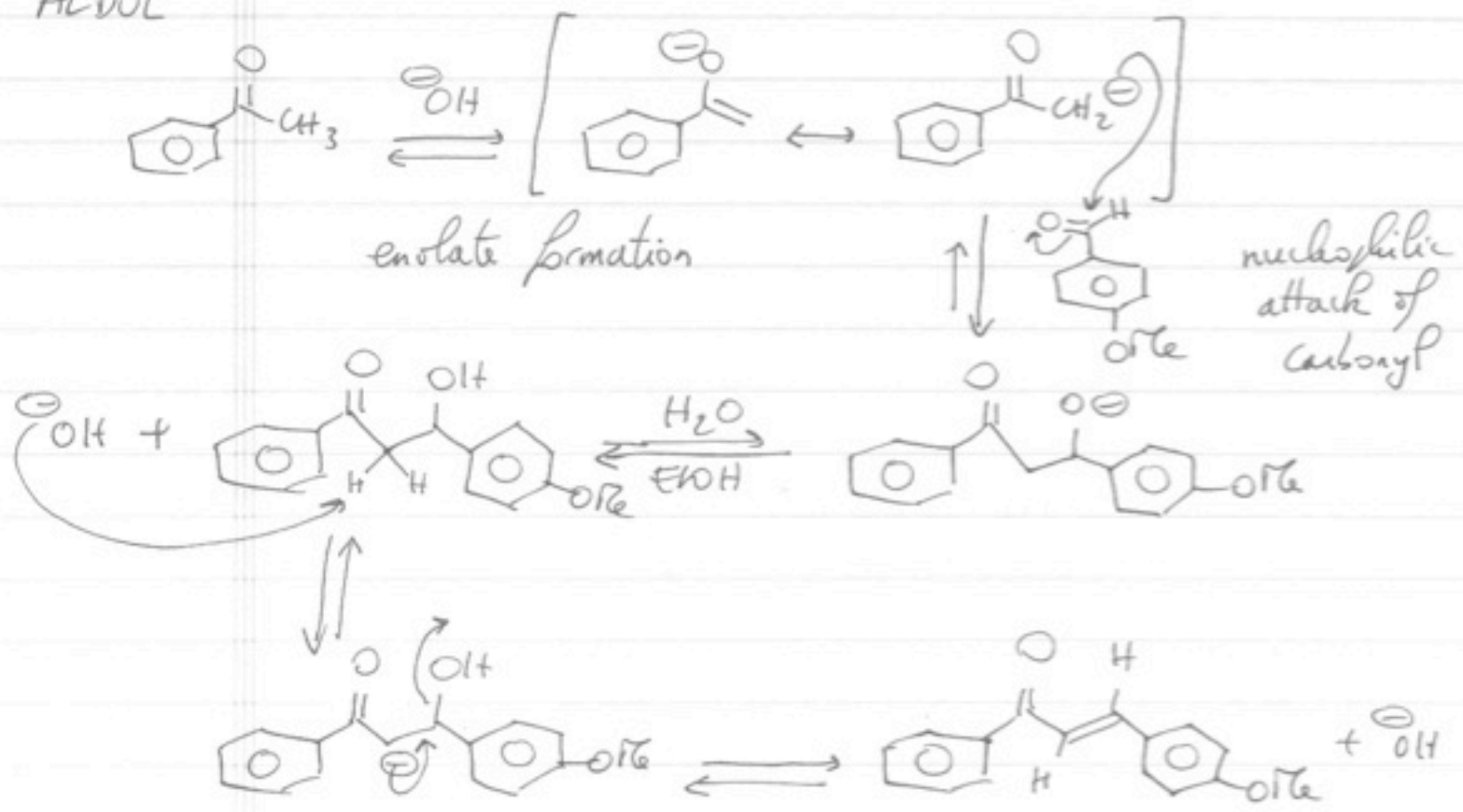
acetophenone

p-anisaldehyde

trans-p-anisalacetophenone

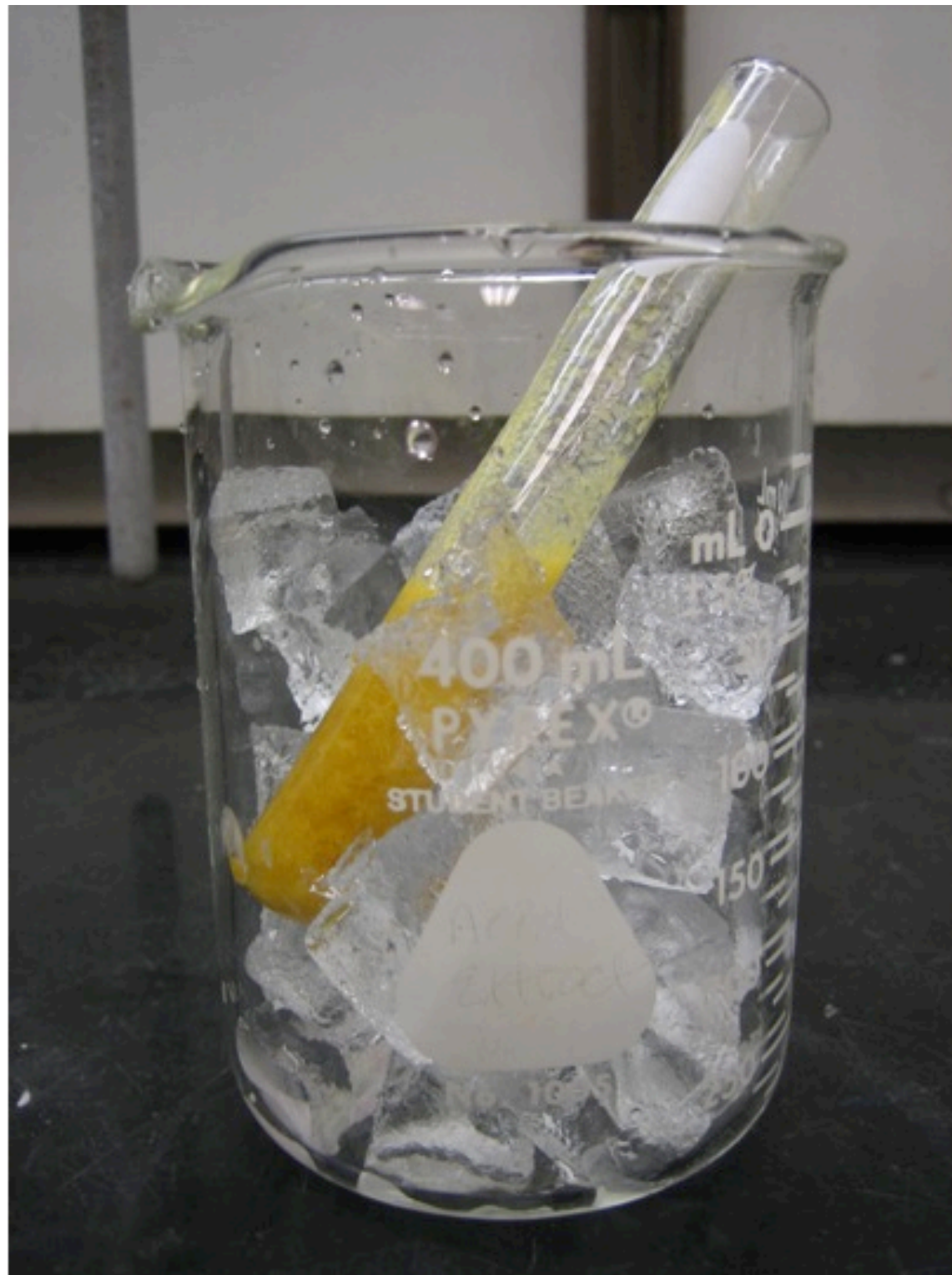
- add 5 mL of a 95% EtOH solution containing a mixture of p-anisaldehyde and acetophenone (50:50 v/v, 1 mL each) [This solution has been prepared by the TA] using the solvent pump to a test tube.
- add 5 drops of 50 wt.% NaOH (1.0 g/mL H₂O) [This solution has been prepared by the TA], to the test tube.
- shake until homogeneous.
- let stand with occasional shaking for 15 min.
- cool in ice-water.
- collect the crystals by vacuum filtration.
- wash with **cold** 95% EtOH (~1-2 mL).
- recrystallize the crude product from MeOH (about 3mL of MeOH per 1g of crude product; don't set the setting on the hot plate higher than 3).
- collect the solid by vacuum filtration, wash with 1mL of MeOH and keep under vacuum for ~15 min, weigh it out, determine the m.p; dispose in the proper container (not a waste bottle).

ALDOL



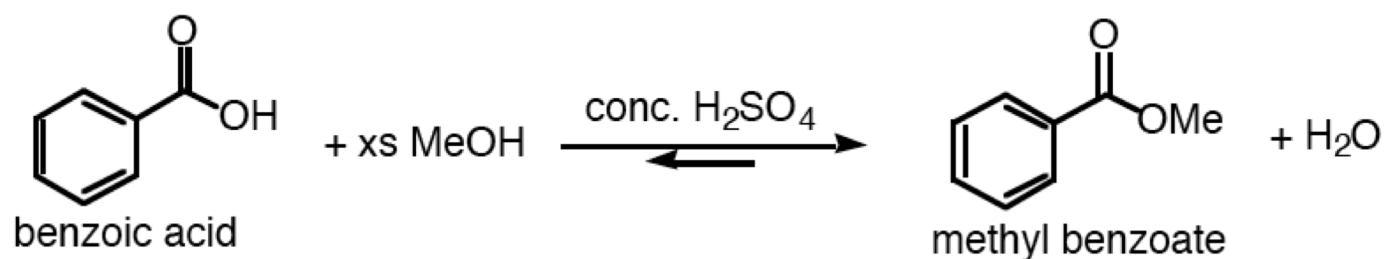
trans-product (4-methoxychalcone) is formed because it is the most stable product and all steps are equilibria. (It is called THERMODYNAMIC CONTROL)

OH^- is CATALYTIC





Lab5: Preparation of Methyl Benzoate



Reaction: Place 6.1 g of benzoic acid and 20 mL of methanol in a 100-mL round-bottomed flask, and carefully pour 2 mL of concentrated sulfuric acid down the side of the flask. Swirl the flask to mix the reagents, attach a reflux condenser, and gently heat the mixture at reflux for 1 hr. (Power controller setting ~ 6. Boiling chips can be used for the reaction.)

Work-up/Extraction: Cool the solution and transfer it to a separatory funnel containing 50 mL of water. Rinse the flask with 40 mL of dichloromethane, and add the rinsing to the separatory funnel. Shake the funnel to extract methyl benzoate and benzoic acid into the dichloromethane layer; **vent the funnel often**. Remove the organic and aqueous layers and wash the organic layer with a 25-mL portion of water. Remove the aqueous layer and wash the organic-layer with 25 mL of 0.6 M aqueous sodium bicarbonate. **CAUTION: foaming may occur**. Swirl the open funnel for a few seconds to assure that no vigorous reaction occurs; then shake the stoppered funnel **with frequent venting**. Separate the aqueous (bottom) layer. Test the aqueous layer to see that it is basic to litmus paper. If not, repeat the washing of the organic layer with an additional 25-mL portion of aqueous sodium bicarbonate. Combine this with the first bicarbonate washing and **SAVE THE SOLUTION**. Wash the dichloromethane layer with a 25-mL portion of saturated sodium chloride, then dry the ether solution with anhydrous magnesium sulfate.

Purification/Solvent removal: Remove the drying agent by gravity filtration into a 100-mL round-bottomed flask. Set up a simple distillation apparatus using the 100-mL flask, as the pot. (Since dichloromethane is very volatile, cool the receiving flask, and a power controller setting at, or below 3). Remove the dichloromethane by distillation and place the distillate in the waste dichloromethane recovery bottle.

Purification/Solvent removal: Remove the drying agent by gravity filtration into a 100-mL round-bottomed flask. Set up a simple distillation apparatus using the 100-mL flask, as the pot. (Since ether is very volatile, cool the receiving flask, and a power controller setting at, or below 3). Remove the ether by distillation and place the distillate in the waste ether recovery bottle.

Purification of the product by distillation: Transfer the crude methyl benzoate into a 50-mL round-bottomed flask, and attach the flask to an apparatus for simple distillation. Distill the ester using *an air-cooled condenser* rather than a water-cooled condenser (which can crack because of the high boiling point of the ester). [Power controller setting at 10] Collect the material boiling above 190° C in a weighed receiver, and turn in the product to your instructor.

Purification of the product by distillation: Transfer the crude methyl benzoate into a 50-mL round-bottomed flask, and setup an apparatus for simple distillation. Distill the ester using *an air-cooled condenser* rather than a water-cooled condenser (which can crack because of the high boiling point of the ester). [Power controller setting at 10. You can use aluminum foil and glass wool.] Collect the material boiling above 190° C in a weighed receiver, and turn in the product to your instructor.

Recovery of unreacted benzoic acid: Recover the unchanged benzoic acid from the aqueous sodium bicarbonate washing by carefully acidifying the basic solution with concentrated HCl. Cool the solution in ice and add the HCl dropwise since the reaction is exothermic and foaming occurs. Collect the precipitate of benzoic acid by vacuum filtration. Determine the weight of the dry benzoic acid and calculate the theoretical yield of methyl benzoate based on the weight of benzoic acid with which you started (6.1 g) less the weight of benzoic acid recovered. Turn in the product to your instructor.

TIPS: - During the extractions, make sure you know which layer you want. In doubt?? SAVE EVERYTHING!!

- Don't forget to answer the problem assignment (first page of the handout) in your notebook. It will be graded.

Problem Assignment

THIS PROBLEM MUST BE ANSWERED IN YOUR LAB REPORT AND WILL BE GRADED.

Assuming the equilibrium constant for the esterification of benzoic with methanol is $K = 3$, calculate the theoretical yield of methyl benzoate expected using the molar amounts used in the experiment (Lab 5, above).

Concentrated sulfuric acid is added as a catalyst in the esterification procedure, even though another acid (benzoic acid) is one of the organic reagents used. Why is the sulfuric acid necessary?



"These homework patches really reduce your cravings. This one is 'Chemistry,' but you can get them in any subject."