

THE VIRTUAL MIXED ALDOL REACTION

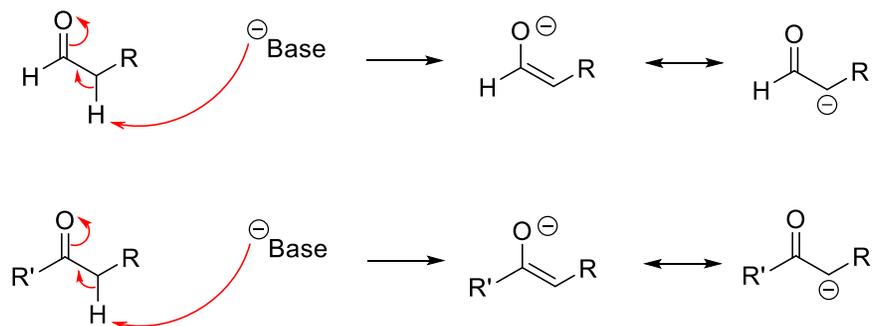
In this virtual experiment, you will use the virtual laboratory to synthesize a beta-hydroxy ketone using a mixed aldol reaction. By making modifications to the reaction conditions, you will try to find conditions that will allow for the elimination of water in an aldol condensation reaction.

Introduction

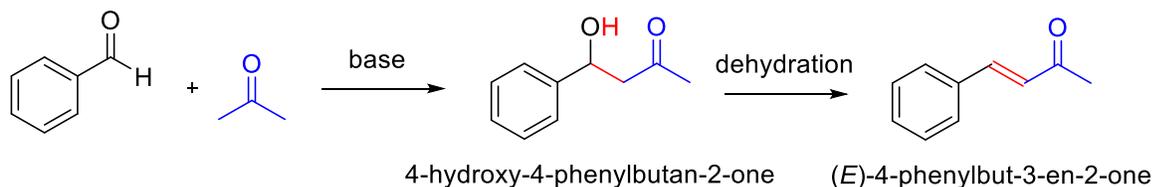
The aldol reaction is an important C-C bond forming reaction that joins two carbonyl containing compounds together by using a base.

The first step in the aldol reaction is the deprotonation of the α -hydrogen (note: α refers to the carbon position next to a C=O bond, β refers to the position 2 carbons away from the carbonyl). The hydrogens at the α position are slightly acidic due to the resonance stabilization of the corresponding enolate (aldehyde $pK_a = 17$; ketone $pK_a = 20$). The high pK_a values indicate that in order to deprotonate the α -hydrogen of an aldehyde, an extremely strong base is required.

This deprotonation was initially done using bases such as potassium hydroxide, (pK_a of water, the conjugate acid of hydroxide = 15.7) which would only deprotonate 5% of the aldehydes ($10^{15.7}/10^{17}$) and 0.005% of the ketones ($10^{15.7}/10^{20}$). The aldol reaction was made a little more efficient by using a slightly stronger base such as potassium *t*-butoxide (pK_a of *t*-butanol, its conjugate acid = 17). Like potassium hydroxide, potassium *t*-butoxide ionizes a small percentage of the carbonyl compound to the enolate ion. Complete and irreversible deprotonation requires a superbases such as lithium diisopropylamide (LDA, pK_a of its conjugate acid = 35.7).



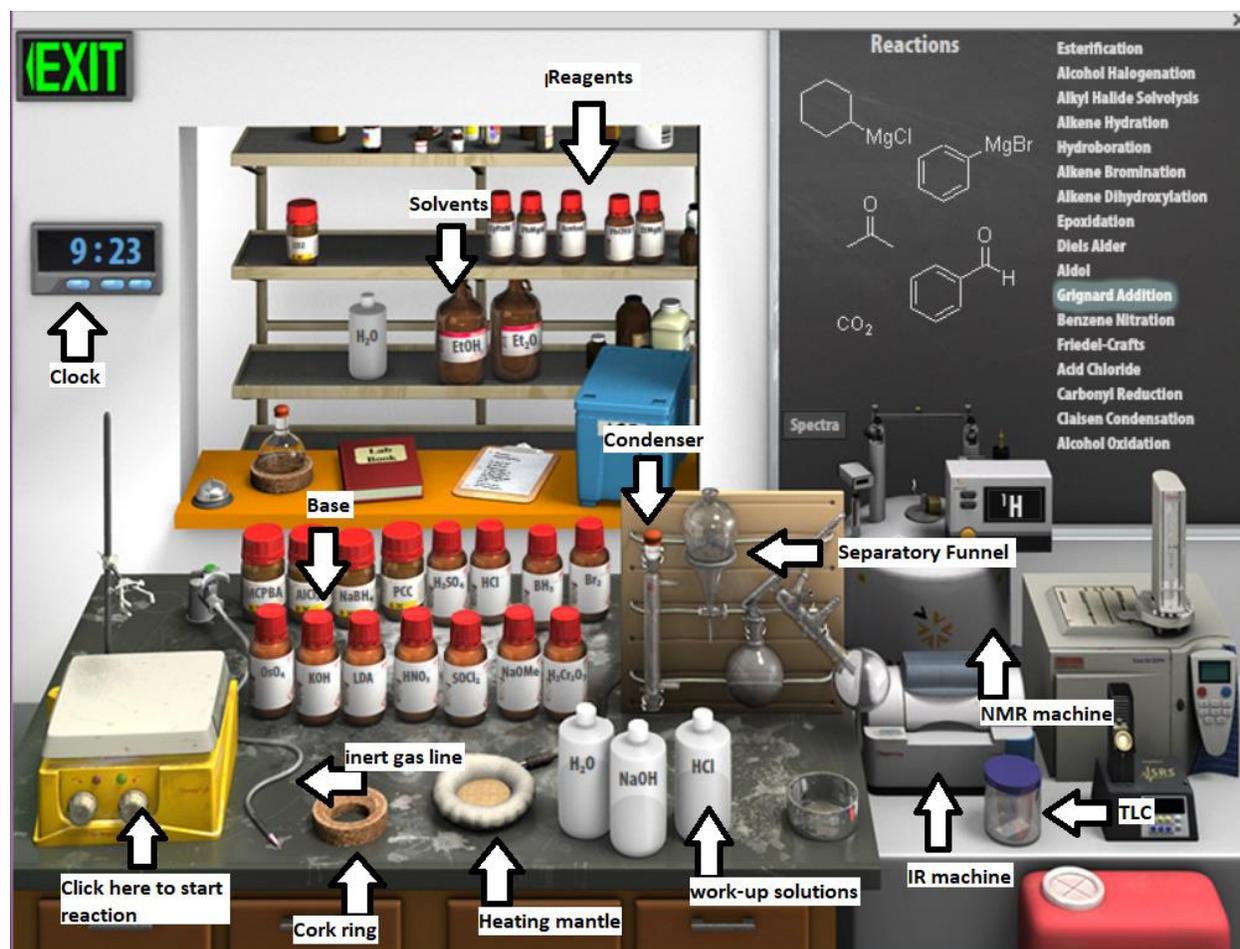
By the addition of a base, you have converted a conventional electrophile (aldehyde or ketone) into a nucleophile (enolate). This newly formed nucleophile can attack a subsequent electrophile like another carbonyl containing compound. This is the basis of the aldol reaction.



Procedure

Using the BeyondLabz platform, enter the virtual organic chemistry lab. Click on the Synthesis button on the top left corner and select the Grignard Addition (not the Aldol tab) on the chalkboard to load the reaction specific reagents onto the stockroom shelves. Click and drag each solvent and reagent to the round bottom flask before moving the flask to the stir plate.

From the stockroom shelves, click on benzaldehyde and drag it to the round bottom reaction flask. Similarly, add 2-propanone (aka: acetone), which will also serve as the solvent for this reaction (no additional solvent required) and place the round bottom flask on the stir plate. Next, add potassium hydroxide from the bottles next to the stir plate. Add a water-cooled condenser, inert gas line, before turning the stir plate on and starting the reaction.



Write down the reaction starting time (use the clock below the exit sign). You can fast forward the reaction time by clicking on the buttons on the clock while paying attention to the chalkboard and taking regular TLCs. Fast forward using only 1 minute intervals for this lab.





When the reaction is ready, you can work up the reaction by double clicking on the separatory funnel and adding some HCl. Click on the organic layer and drag it to the lab bench cork ring to isolate your product.

If you have only one product, take ^1H NMR and IR spectra of the compound by clicking on the NMR or FTIR machine and dragging it to the round bottom flask. Take a screenshot (CTRL + PRN for PC or shift + command + 3 for mac) of the spectra.

If you have more than one product, try to play around with the reaction conditions to obtain only one product.

Discussion

For your report, explain how you might design a synthesis, using Aldol chemistry, to selectively obtain:

- 4-hydroxy-4-phenylbutan-2-one
- 4-phenylbut-3-en-2-one

Attach the ^1H NMR and IR spectra of the two compounds you virtually synthesized and label all relevant peaks.

Questions

What would differ if we used LDA as a base in this synthesis? Explain.

What would differ if we used LDA as a base and ethanol as a solvent in this synthesis? Explain.

