Solventless Aldol Reaction

The aldol reaction is widely used, both in synthetic organic chemistry and in biochemical reaction pathways. Its wide use is a consequence of the properties of aldehydes and ketones and of the fact that the reaction results in the formation of a new carbon-carbon bond between the substrate molecules, which is frequently useful in making larger organic compounds, and which is frequently difficult to accomplish.

In general, aldol reactions take advantage of the carbonyl group in aldehydes and ketones. The presence of the carbonyl alters the properties of the adjacent carbons (the carbons in positions α to the carbonyl); one altered property is the great reduction in $pK_a$ value of protons attached to the α carbon, which are called α protons.\(^1\)

As with many reactions, aldol reactions are much more efficient in the presence of a catalyst. Base-catalyzed aldol reactions take advantage of resonance stabilization of an enolate to create an effective nucleophile, which is then capable of attacking the carbonyl of another molecule.

The result of the aldol reaction is the formation of a β-hydroxy-aldehyde (where $R_2$ in the scheme above is a hydrogen) or β-hydroxy-ketone (where $R_2$ in the scheme above is an alkyl group).

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\(^1\)Protons on carbons without nearby functional groups have $pK_a$ of ~50; in contrast, α protons have $pK_a$ values of 16-20 depending on other factors.
While this may be the end of the process, frequently the immediate aldol product (note that the name “aldol” implies the presence of an aldehyde and an alcohol) undergoes dehydration to form an α,β unsaturated aldehyde or ketone.

While most aldehydes and ketones can undergo aldol reactions, the synthetic usefulness of the process is sometimes limited by the multitude of possible products. (Note that, in the above generic reaction, both substrates have α protons, and therefore each molecule could also react with another of the same molecule.) However, if one carbonyl containing molecule lacks α protons, then the only possible reactions are either the α proton containing molecule reacting with itself (homocoupling) or the desired cross-coupling product. Thus, benzaldehyde cannot react with itself, but can react with acetophenone. Because homocoupling of ketones is reversible (as long as dehydration has not occurred), and typically not very favorable, the major product is the cross-coupling product shown.

One major cost in many organic chemistry reactions is the organic solvent required to solubilize the reactants. For some sets of reactants, however, the solvent may not be necessary. As you will recall, mixing dissimilar materials alters the melting point of the species involved. If the mixture formed by two solid compounds has a melting point below room temperature, mixing the two solids will result in a liquid; in effect the mixing process creates the solution, with the reactants acting as their own solvents.

**Procedure:**

Place 0.25 g (1.5 mmol) of 3,4-dimethoxybenzaldehyde and 0.2 g (1.5 mmol) 1-indanone in a 13 x 100 mm test tube. Mix the two solids together with a stir rod or spatula until the compounds form an oil. Add 0.05 g (1.25 mmol) of powdered NaOH (use a mortar and pestle to powder the NaOH. Mix until the compounds in the test tube solidify. Allow the reaction to proceed for an additional 15 minutes. Add 2 mL of 10% aqueous HCl, and mix with the stir rod or spatula. Check to ensure that the solution is acidic.
Use vacuum filtration to collect the product. Recrystallize the product using 90%:10% ethanol:water (you can rinse the test tube with hot ethanol:water to add to your recovery).

Determine yields of crude and recrystallized products. Obtain and analyze an infrared spectrum for your product. Can you use this to tell which product(s) formed? What other methods might be useful?

References:


Questions:
1. Report the physical properties and yields for your crude and purified products in a well laid out table.
2. Draw the mechanism for the reaction, and predict the product(s) that might form.
3. Based on your data, which product or products did you synthesize?
4. Calculate the atom economy for your reaction.
CHEM 251L Week 3: Report for Solventless Aldol Reaction (30 points)
DUE: beginning of your lab, week 5

Submit one neatly typed report per pair (this sheet does not need to be included)
The Report should use the grading rubric sheet available for download on Moodle as the title page.

Please include the following on the rubric:
• both partner’s names and a campus mailbox to which the report may be returned
• date experiment was performed
• Lab section day and time (e.g., Wednesday, PM)
• both lab partners should initial on the first page to indicate co-responsibility for work

Report:
Describe your experimental procedure using complete grammatical sentences in past tense. Avoid the temptation to be overly verbose, but be sure to include every detail (such as real numbers that you used) for a student with your level of training to execute the lab. Include observations on all significant changes during the course of the reaction.

Create a table of your results, including amounts used and theoretical yield of product, and melting point ranges for crude and purified product. (The purified product has an expected melting point of 178-181°C.)

Show calculations for percent yield.

Attach an analyzed infrared spectrum of the product.

Draw a reaction mechanism, showing the electron movement using curved arrows.

Discuss (briefly) whether your results are consistent with having obtained the expected product, and whether the recrystallization achieved purification of the product.

Attach hard copies of each lab partner's lab notebook to the report.