NMReady

# Aldol Condensation

Incorporating instrumentation into undergraduate laboratories increases students' understanding of fundamental and practical characterization techniques.

The NMReady™ benchtop spectrometer offers a portable and affordable option with a modern, network accessible, easy-to-use interface that can be easily incorporated into teaching laboratories.

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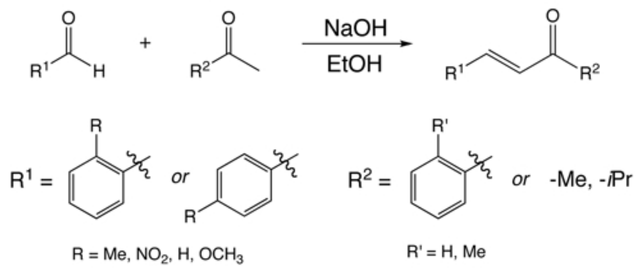
## A Classic Undergraduate Experiment: Mixed Aldol Condensations

Students often perform this quintessential C-C bond forming reaction with unknown aldehyde(s) and/or ketone(s). Chemical structure of the reactants and products is determined by characterization of the final product.




## Procedure:

Dissolve aldehyde (1 mL or 1g) in 95 % EtOH (10 mL). Slowly add 1.5 mL of 2 M $NaOH_{(aq)}$ & mix well. Add ketone (0.04 mL) & mix well. After 15 min a precipitate should form, if no solid is observed heat for additional 15 min.

Cool the reaction in an ice-water bath, collect solid by vacuum filtration & wash with 2 mL of 5 % acetic $acid_{(aq)}$ & cold EtOH. Dry & weigh to determine crude yield.

Determine a suitable recrystallization solvent (EtOH or toluene) by dissolving a small amount of crude material in 10 drops. Once solvent identified, use it to recrystallize bulk crude material. Collect crystals by vacuum filtration, weigh & measure melting point.

### Key Concepts:

organic synthesis, aldol condensations, C-C bond formation, stoichiometry, crystallization, vacuum filtration, percent yield, recrystallization, melting point, unknown identification

## Students' Discussion:

This lab adopts a more advanced structure that starts to mirror a research situation. Students must develop their own purification techniques and then characterize their final product in order to identify it.

However, given the limited accessiblity of NMR spectrometers, instead of utilizing the most prevalent characterization technique avaliable to a chemist, undergraduate students are often required to base their structural assignments on classical techniques such as melting point determination.

## Enhance this Classic Experiment with the NMReady:

Prepare a 0.25-0.5 M NMR sample of each of the following in $d_6$-EtOH or $d_4$-MeOH:

1) unknown aldehyde
2) unknown ketone
3) condensation product

*Additional time: ~1 min per sample = ~3 min*

Measure a $^1$H NMR spectrum for all three samples on the NMReady™ benchtop spectrometer using the following parameters:

| | |
|---|---|
| SW = 16 ppm | ns = 16 scans |
| time per san = 4.6 sec | total time = 1.2 min |

*Additional time: ~1.2 min per sample = ~4 min*

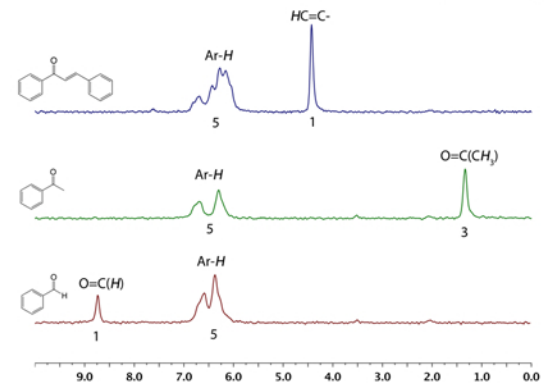
Work-up (*i.e.,* baseline correct, peak pick & integrate) the spectra & either print directly, save to USB drive and/or network folder & include copy in the report *(further details on back).*

### Additional Concepts:

NMR sample preparation, NMR spectrometer operation, NMR characterization

## Example of 60 MHz $^1$H NMR Results:

(for nominal case - benzaldehyde & acetophenone)




## Extended Discussion:

1) Assign peaks in $^1$H NMR spectra and using provided molecular formulas for unknown reactants determine structure & IUPAC names of both the reactants & products.

2) What functional group(s) are present in the final product?

3) What is the mechanism of this reaction? Do you see all the structures that are formed?

4) Assess the purity of the condensation product. How successful was the recrystallization?

5) Can % purity be estimated from a peak integral?

6) What other characterization techniques could be used to identify reactants & products? Which method provides the most conclusive information?

# Modify this Classic Experiment with the NMReady:

Illustrate the versatility of one of the most common C-C bond forming reactions, highlight key concepts through purposeful reactant choice and introduce additional experimental techniques.

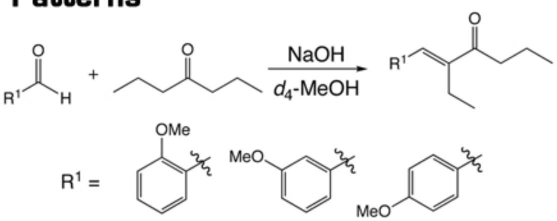
1) microscale experiments
2) NMR tube reactions
3) reaction screening
4) synthesis of derivative series

This allows a guided-inquiry approach while also reducing the

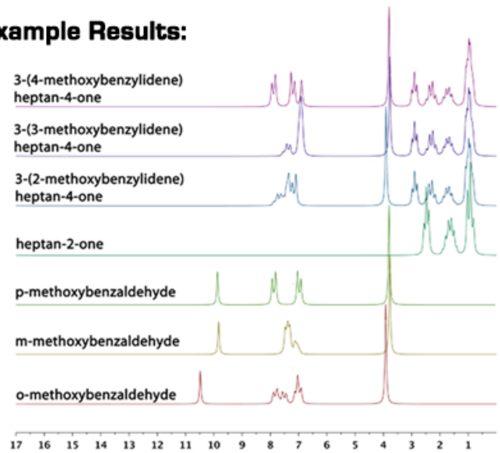
## General Procedure:

Prepare 0.5 M NMR samples of assigned aldehydes in $d_4$-MeOH & measure a NMR spectrum for each. Add NaOH (25 mg) & mix. Calculate how much ketone must be added (0.9 molecular equivalents) & add dropwise via a syringe to each NMR tube, while mixing well. Measure a NMR spectrum for each. If the reaction is incomplete, keep mixing & measure additional spectra every 10 minutes until reaction is complete. Record all results.

## 1) Constitutional Isomers & Substitution Patterns




### Example Results:



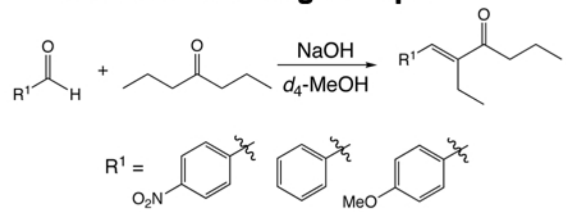

### Discussion:

1) How many 'types of H' are in the aldehyde structural isomers? What splitting patterns do you expect to observe in each $^1$H NMR spectrum?

2) What aromatic splitting patterns do you observe?

3) Can you use reactant or product spectra to distinguish the constitutional isomers?

## 2) Effect of Electron Withdrawing and Electron Donating Groups



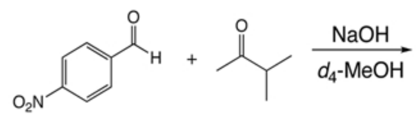

### Discussion:

1) Which reaction reached completion first? Second? Third?

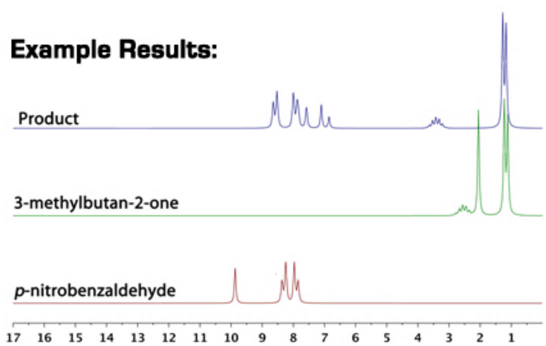
2) Draw the reaction mechanism. Does your proposed mechanism involve intermediates that support the experimentally observed rate of reaction?

3) If so, use your knowledge to rationalize which step is rate determining in the aldol condensation.

## 3) Asymmetric ketones




### Example Results:




### Discussion:

1) What is the final product of your reaction?

2) Is this the only possible product? If not, identify others.

3) Explain what governs the observed reactivity.

## Key Concepts:

NMR tube reactions, microscale reactions, NMR spectrometer operation, NMR characterization, structure elucidation, versatility of aldol condensation, derivative synthesis, steric effects, electronic effects, coupling patterns, kinetics

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## References:


1) Livengood, K., *J. Chem. Educ.* **2012**, *89*, 1001

2) Iler, H. D., *J. Chem. Educ.* **2012**, *89*, 1178

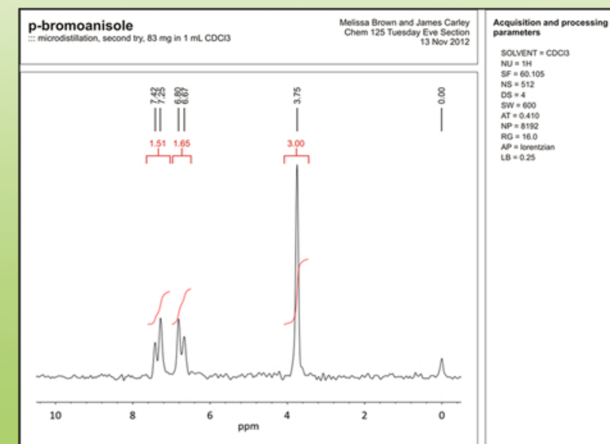
3) Angelo, N. G., Henchey, L. K., Waxman, A. J., Canary, J. W., Arora, P.S., Wink, D., *J. Chem. Educ.* **2007**, *84*, 1816

4) Hathaway, B. A., *J. Chem. Educ.* **1987**, *64*, 367

5) Hawbecker, B. L., Kurtz, D. W., Putnam, T. D., Ahlers, P. A., Gerber, G. D., *J. Chem. Educ.* **1974**, *51*, 64


## Data Accessibility:

NMReady outputs to a networked drive and has a print option. Students can process and print in a third party software, like Mestrelab™, or use the NMReady directly. An example of data to be incorporated into a lab report processed and printed directly from the NMReady is presented below:




For additional ideas of how to incorporate the NMReady™ benchtop spectrometer into undergraduate laboratories please see:

**1) Synthesis of Aspirin**

**2) $S_N2$ Reactions**

**3) Biodiesel**

available at:

**www.nanalysis.com/experiments.html**