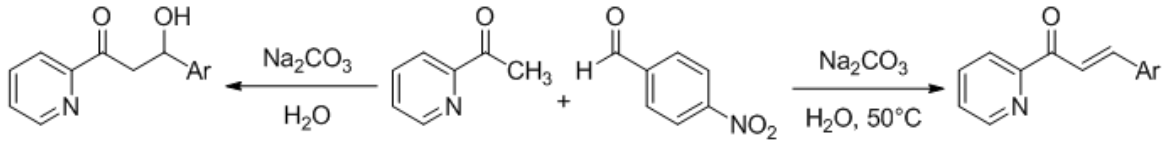
Activity 10: Aldol Addition and Aldol Condensation Reactions: Crossed Aldol Reaction of 2-Acetylpyridine and 4-Nitrobenzaldehyde

The Experiment



Lab Activity Goal

Demonstrate experimentally how reaction conditions can have a dramatic influence on the outcome of aldol addition or aldol condensation reactions. In this context, the base-catalyzed addition of 2-acetylpyridine to 4-nitrobenzaldehyde will demonstrate how aldol addition reactions or aldol condensations reactions can be achieved from identical substrates using slightly modified reaction conditions.

Pre-Laboratory Assignments

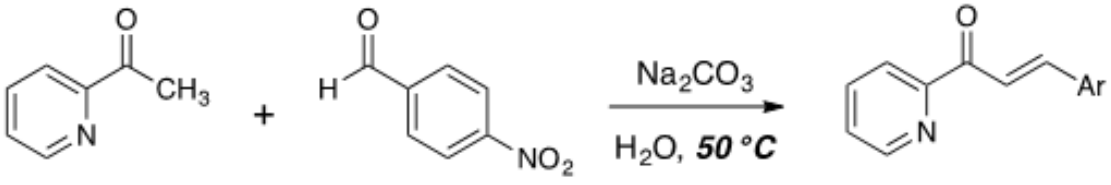
See the Activity 10 Pre-Lab Preparation and Outline document in Labflow.

Experimental Procedure[1]

Note: Part 1 and Part 2 reactions are identical in set-up and work-up except the Part 1 reaction will be heated to 50°C while the Part 2 reaction will remain at room temperature.

- Each student pair will do either Part 1 or Part 2. Part 1 and Part 2 groups will share observations and data and thus **no student pairs can leave lab until they and their complimentary groups are finished**.
- It is important to carefully follow the procedure for setting up the Part 1 reaction for heating. This will prevent an accidental flood (working with condenser) and prevent sand from spilling around the lab.
- It is also important (**for safety reasons**) that while the Part 1 reaction is heating that great care is taken not to let any organic solvent come in contact with the hot sand or heating mantle.
  - Thus, no organic solvents can be measured in the hood that has the hot heating mantle.
  - Organic solvent that has been measured out at the dispensing hood should be kept on the opposite side of the hood from the heated reaction and be used promptly.
  - Any unused organic solvent should be disposed of immediately.

Part 1: Aldol Condensation



1. Tare the balance with a cork ring placed on it. Then, place a stir bar and disposable 1-mL syringe into a 100-mL round bottom flask. Weigh the entire assembly. Record the mass. Take your assembly to the 2-acetylpyridine dispensing station.

Activity 10: Procedure

2. A bottle of 2-acetylpyridine will be secured to the monkey bars at a dispensing station. Remove the reagent bottle cap and using the 1 mL syringe (that was part of the weighed assembly) withdraw ~0.45 mL of 2-acetylpyridine. Place the loaded syringe into your round bottom flask (recap the reagent bottle!) and reweigh your assembly after zeroing the balance with a cork ring that will hold your flask. It isn't necessary to use the same cork ring or balance. Record the mass. Determine the mass of 2-acetylpyridine to be used in the addition reaction.
3. Place a stir plate onto a raised lab jack. Secure the round bottom flask to the monkey bars on top of a stir plate. The lab jack should be high enough that when wound down the stir plate can be easily removed without touching the secured round bottom flask.

Pro-tip **If the stir plate (or any electrical equipment) stops working, check to see if the outlet it is plugged into needs to be reset by pressing the reset button.**

4. Add the 2-acetylpyridine from the syringe into the round bottom flask followed by 40 mL of H_2O. Stir the mixture vigorously.

    - When convenient, back at the dispensing hood, rinse the syringe twice with acetone into the provided waste beaker before disposing of it into the solid waste.

5. Into a 50-mL Erlenmeyer flask add 600 mg of 4-nitrobenzaldehyde and 10 mL MeOH. Swirl the flask over a steam bath to dissolve the solids (if all of the solid does not dissolve, add an additional 2 mL MeOH and continue warming).
6. While the above MeOH solution is still warm, use a funnel to add it to the stirring 2-acetylpyridine solution from step 4. Continue vigorous stirring.
7. Carefully add 20 mL of 0.54% (w/v%) Na_2CO_3 to the stirring reaction mixture using the same funnel.

Activity 10: Procedure

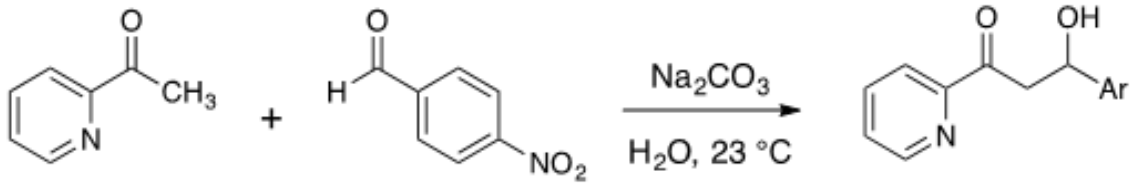
8. Ensure that the reaction flask is properly secured to the monkey bars and then lower the lab jack far enough to insert a heating mantle on top of the stir plate. Raise the lab jack until the bottom of the round bottom of the reaction flask just touches the mantle. Contact between the reaction flask and the ceramic of the heating mantle is critical BEFORE you begin adding sand to the mantle (so that the stir plate can stir through the heating mantle).
    - Follow directions from your instructor to obtain sand:
        - Take a DRY 100-mL beaker to the sand station in the center island. From the stock supply of "clean sand" (that is inside secondary containment) scoop ~75 mL of sand into your DRY 100 mL beaker. Brush off sand stuck on outside of beaker into stock "clean" sand. There is small brush by the station for brushing.
        - Back at your hood, carefully fill in void between the round bottom flask and heating mantle.
        - Avoid spilling sand outside of mantle. Brush any sand stuck in beaker into the red solid waste using the small brush by that trash. Do not put sand into the sink.
9. Attach clear, flexible tubing to condenser nozzles and ensure that the hoses are long enough to reach the cup sink once the condenser is placed on the reaction flask.
    - Attach the hoses (water in the bottom nozzle, drain hose out the top nozzle).
    - A lab partner should carefully hold the hoses on the condenser nozzles while the other partner turns on the water to make a steady stream (not blasting, but not dripping either). Ensure that the drain hose remains secured in the cup sink.
        - Note: Holding the hoses on to the nozzles while turning on the water ensures that the strong water flow rate does not cause the hoses to pop off the condenser nozzles and cause a flood. The strong flow rate ensures a hidden valve inside the hood is properly seated which prevents flooding.

- While a lab partner still holds the hoses on the nozzle, the water flow rate should be adjusted down to a steady drip.
- The dripping flow rate is fast enough to keep cool water continually flowing inside the condenser but will not cause the hoses to pop off the condenser once the lab partner quits holding the hoses on the condenser nozzles.

10. Carefully insert the thermometer into the sand. Support the thermometer leaning it inside an iron ring (or open clamp secured to the monkey bars).
11. **Ask your instructor to inspect your set up.** After inspection, ensure the variac is set at 0%, plug in the heating mantle, and then turn variac to 20%. Be patient. Only turn the variac beyond 20% if the temperature stabilizes below 45°C. Run the reaction anywhere between 45-50°C. Exceeding this temperature can cause unwanted side reactions that produce brown goo (the scientific term for what you will observe if the reaction overheats).
12. Monitor the temperature of the reaction. Once the bath temperature reaches 45-50°C, stir the reaction for an additional 60 min. During the reaction, **do not let the temperature of the bath exceed 50°C**.
    - Controlling the temperature is important for two reasons. First, this avoids unwanted side reactions mentioned above. Second, since the round bottom flask is now more than half full, it is not advisable to reach reflux temperature.
13. After 60 minutes of vigorous stirring, collect the solid product that has formed by vacuum filtration. Wash the solid product with DI H_2O (2 x 20 mL). Continue drawing vacuum for 10 minutes.
14. Scrape the solid product onto a dry piece of filter paper. Label this as the CONDENSATION PRODUCT. Proceed to Part 3.

Activity 10: Procedure

Part 2: Aldol Addition



1. Tare the balance with a cork ring placed on it. Then, place a stir bar and disposable 1 mL syringe into a 100-mL round bottom flask. Weigh the entire assembly. Record the mass. Take your assembly to the 2-acetylpyridine dispensing station.
2. A bottle of 2-acetylpyridine will be secured to the monkey bars at a dispensing station. Remove the reagent bottle cap and using the 1-mL syringe (that was part of the weighed assembly) withdraw ~0.45 mL of 2-acetylpyridine. Place the loaded syringe into your round bottom flask (recap the reagent bottle!) and reweigh your assembly after zeroing the balance with a cork ring that will hold your flask. It isn't necessary to use the same cork ring or balance. Record the mass. Determine the mass of 2-acetylpyridine to be used in the addition reaction.
3. Secure the round bottom flask to the monkey bars on top of a stir plate (that is directly on the hood surface, not on a lab jack). Discharge the 2-acetylpyridine into the round bottom flask followed by 40 mL of H_2O. Stir the mixture vigorously.
    - When convenient, back at the dispensing hood, rinse the syringe twice with acetone into the provided waste beaker before disposing of it into the solid waste.
4. Into a 50-mL Erlenmeyer flask add 600 mg of 4-nitrobenzaldehyde and 10 mL MeOH. Swirl the flask over a steam bath to dissolve the solids (if all of the solid does not dissolve, add an additional 2 mL MeOH and continue warming).
5. While the above MeOH solution is still warm, use a funnel to add it to the stirring 2-acetylpyridine solution from step 4. Continue vigorous stirring.

6. Carefully add 20 mL of 0.54% (w/v%) Na_2CO_3 to the stirring reaction mixture using the same funnel. Continue vigorous stirring for 60 minutes.
7. Collect the solid product that has formed by vacuum filtration. Wash the solid product with H_2O (2 x 20 mL). Continue drawing vacuum for 10 minutes.
8. Scrape the solid product onto a dry piece of filter paper. Label this as the ADDITION PRODUCT. Proceed to Part 3.

Part 3: Product Characterization

1. Once dry, weigh each product. Dissolve a small portion of the product in EtOAc and obtain a TLC using 20% EtOAc in hexanes. Spot each product alongside authentic samples of 2-acetylpyridine and 4-nitrobenzaldehyde.
2. Let the product dry in your drawer until next week. You will obtain an IR spectrum during the next lab.

Clean-Up and Waste Disposal

Activity 10 Specific Clean-Up

- **Organic Liquid Waste**:
  - Excess starting materials
  - Acetone rinse from glassware washing and syringe rinsing.
  - TLC solvent (20% EtOAc in hexane)
- **Aqueous Waste**:
  - $Na_2CO_{3(aq)}$ and methanol
  - Aqueous rinses from glassware washing
- **Solid Waste:**
  - Excess 4-nitrobenzaldehyde
  - Contaminated sand

- Rinsed syringe barrels wash (note that if our syringes had needles, the needles would need to go in a "sharps" waste). Make sure that you wash out the syringe barrels with acetone before discarding.
- Used filter paper
- Used gloves
- Used TLC plates

Routine Clean-Up

- Clean up your hood space of all trash, spilled chemicals, etc. Don't leave a mess for the people who share this hood at other time slots. Up to 24 other people are sharing this space at various time slots throughout the week. Clean up your mess!
- No dirty or clean glassware should be left in the sink. No used filter paper or wadded up dirty paper towels should be left in the sink.
- **Dirty paper towels go into the REGULAR TRASH** not the red solid waste trash. This saves the university a lot of waste disposal money!
- Dispose of dirty filter paper in the red solid waste container.
  - Do **NOT** deposit filter paper in the liquid waste eco-funnel as this will cause a clog which will lead to a messy overflow of waste.
  - Do **NOT** leave filter paper in the sink as this is poor lab etiquette and rude.
- Used gloves should be disposed of into the red solid waste.
- **Ask your instructor if you are in charge of cleaning up the balance area** for this week. If you are in charge do the following:
  - Be sure all reagent bottles are properly capped.
  - Use the small brush to clean off balances.
  - Use small broom and dustpan (located on the wall surrounding the balance area) to remove excess solid from counter. Dispose of excess solids in red solid waste container. Return broom and dustpan to proper location.
  - Wipe down the counter with a moist paper towel.
- **Ask your instructor if you are in charge of making sure the sink area is presentable** for the next lab group.

- Wash any dirty glassware rudely left in the sink. Let clean glassware air dry on rack or windowsill area.
- Dispose of any paper towels, filter paper, or cotton rudely left in the sink.
- **Do not remove broken glass from the drain or the sink**. Rather, tell your instructor and then fill out a "something wrong form" located in the cabinet above the solid waste containers. Be sure to record room number and the Left/Right location of the sink.

Post-Lab Assignment

The Activity 10 Post-Lab Assessment is posted on Labflow and is due according to the deadline posted on Labflow.

References

1. Crouch, R. D.; Richardson, A.; Howard, J. L.; Harker, R. L.; Barker, K. H. *J. Chem. Educ.* **2007**, *84*, 475-476.