Aldol condensation in a continuous flow microreactor

Background

The aldol condensation of benzaldehyde and acetone is a textbook example of an exothermic, spontaneous reaction which is often performed during practical courses at universities and high schools. Due to its exothermic character, the reaction vessel is traditionally cooled in an ice bath, with controlled reagent addition to avoid the formation of side products and evaporation of acetone. The product dibenzalacetone is used as a UV blocker and as a ligand in organometallic chemistry.

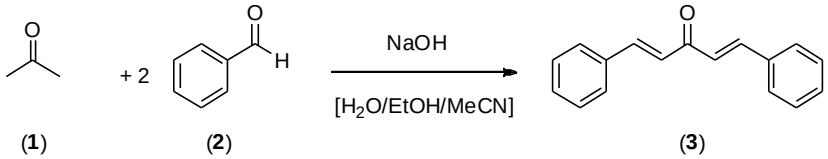

Figure 1: Aldol condensation scheme

Using continuous flow chemistry, aldol condensations are suitable for large-scale, preparative synthesis of unsaturated compounds. In continuous flow, a ketone (1) and an aldehyde (2) are introduced into the microreactor, where they react to form the corresponding aldol condensation product (3).

Setup and method

Material

- *Flow*Start B-200
- B-230 Pump Module
- B-242 Inlet Module
- 3x plastic 10 mL syringe
- Basic Microreactor (internal volume $V_{\mu R}$ = 100 µL)

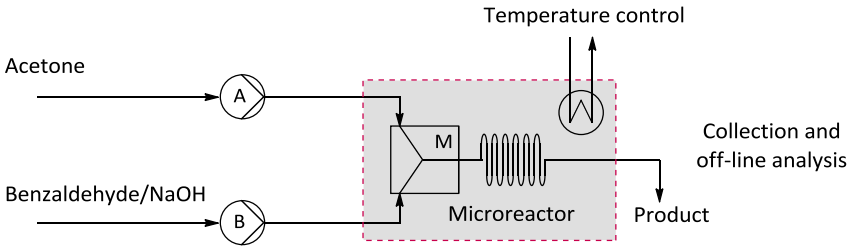

Figure 2: FlowStart setup for the Aldol condensation

Chemicals

Recommended grade: *pro analysi* (p.a.) or *reagent grade*.

- benzaldehyde
- sodium hydroxide
- acetone
- acetic acid
- acetonitrile/ethanol/water

Stock solutions

- **A.** 128 µl acetone (1.75 mmol) dissolved to a total volume of to 10 mL with acetonitrile/ethanol/ water (1:1:1) (corresponding to 0.18 M)
- **B.** 140 mg sodium hydroxide (3.5 mmol) and 357 µL (3.5 mmol) benzaldehyde dissolved to a total volume of to 10 mL with acetonitrile/ethanol/water (1:1:1) (corresponding to 0.35 M)
- **Q.** 3.2 mL acetic acid diluted to a total volume of 100 mL with acetonitrile/ethanol/water (1:1:1) (corresponding to 0.56 M)

Stock solutions are to be prepared at the beginning of the experiments. Make sure to close the flasks which are used to store the solutions, as some of the components are rather volatile.

Analysis

Analysis of the reaction mixture is done using UV-vis. Calibration of the product is done using general methodology. For a quick calibration, make 4 samples with a varying compound concentration. Analyse these samples and 1) setup a calibration curve of absorption against concentration and/or 2) determine the response factor.

Basic experiment

To get acquainted with the reaction and with flow chemistry in general, a so-called *basic experiment* is performed. This experiment is the Aldol condensation at fixed parameters – a reaction time (t_R) of 10 min, a temperature of 60°C and a benzaldehyde molar excess ratio ($ME_{B/A}$) of 2.0. The target volume of solution A to be collected is 2.0 µL, all samples are collected in a vial containing 10.0 mL of solution Q. *The vial must be wrapped in aluminium foil to prevent degradation*. The used setup can be seen in Figure 2.

The corresponding flow rates can be calculated according to the known equations. After preparation of this experiment, the instructor should check if the calculated flow rates and collection time are correct.

Procedure

- Prepare solutions A, B and Q
- Fill the two syringes with solutions A and B
- Slide the microreactor into the holder and connect inlet and outlet tubing
- Connect the inlet tubing to the corresponding syringes, and place the syringes on the pumps
- Set the right flow rates and press start
- Stabilise for 20 minutes
- Collect your sample for the calculated time
- Analyse your sample using UV-vis and calculate dibenzalacetone yield from the calibration curve or response factor
- Rinse the *Flow*Start system by purging the tubing and microreactor with solvent
- Empty, clean and dry the syringes afterwards

Note: Make sure to close the vial after collecting. This is done because some of the reaction components are rather volatile and readily evaporate from the vial.

Questions

1. **Preparation of the experiment:**
    a. **Roughly calculate the cost of the experiment from the prices of the chemicals. In other words, calculate the price (e.g. per gram) of the product.**

b. **Find the safety aspects (including R/S values) of the used chemicals.**

2. **Q: Find the reaction mechanism for the Aldol condensation, and show the essential (sequential) steps from acetone and benzaldehyde to the aldol condensation product dibenzalacetone.**

3. **Q: What advantages in performing the Aldol condensation in continuous flow can you think of? Also, can you think of any disadvantages?**