Paal-Knorr reaction in a continuous flow microreactor

Analysis method setup

This experiment describes the setting up of an analysis method to quantify the components in a reaction mixture that is obtained when performing the continuous flow experiments of the Paal-Knorr reaction. The methods below describe the analysis methods as used by *Future*Chemistry and act as a starting point or reference when setting up an analysis method on location.

GC method

GC analysis was performed on a Shimadzu GC 2010 GC-FID equipped with a Quadrex 007 1701 column (length: 10 m, internal diameter: 0.1 mm, film thickness: 0.1 mm).

Table 1: GC program

Parameter	*Value*	*Parameter*	*Value*
Temperature program		**Split temperature**	250°C
Start temperature	70°C	**Injection volume**	0.2 µL
0.0 – 0.4 min	25°C/min	**Split**	666.8
0.4 – 2.33 min	150°C/min	**Column flow**	1.79 mL/min

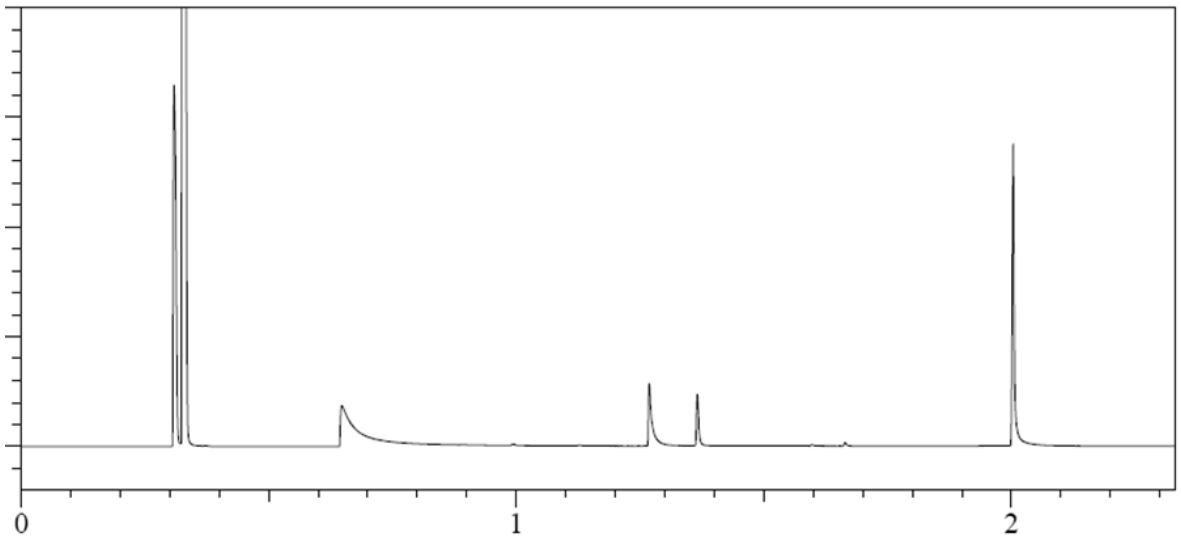

Figure 4: Example GC chromatogram

Table 2: Retention times of internal standard and products

Compound	*Function*	*Retention time [min]*
Ethyl amine	substrate	0.40
Ethanol amine (2)	substrate	0.68
2,5-Hexadione (1)	substrate	1.26
2-Bromotoluene	internal standard	1.36
N-ethyl-2,5-dimethylpyrrole	product	1.41
N-(β-hydroxyethyl)-2,5-dimethylpyrrole (3)	product	1.99

Procedure:

- To set up a valid GC analysis method, first try to analyse a mixture of all components (i.e. a reaction mixture from your Basic Experiment) until all peaks are properly separated. A

reference GC program is stated above, which acts as a starting point for your analysis method.

- Find the substrate and internal standard peaks by injecting these compounds (in acetone) onto the GC.
- How to solve?
    - If peaks overlap, decrease the temperature gradient (or use isocratic temperature).
    - If analysis takes too long, increase column starting temperature (and vice versa).

Calibration

To measure percentage conversion of the formed product, a calibration is set up of the diketone substrate against an internal standard as in Table 2, using the concentrations from Table 3.

Table 3: Internal standard/substrate combination

Substrate	***Internal standard***	***Product***
2,5-hexadione	2-Bromotoluene	N-(β-hydroxyethyl)-2,5-dimethylpyrrole

Table 4: Calibration samples

Sample	***Int.standard***	***Substrate***	***Acetone***	***Corresponding conversion***
1	5.0 µL	15 µL	800 µL	66.7%
2	5.0 µL	30 µL	800 µL	33.3%
3	5.0 µL	45 µL	800 µL	0%
4	5.0 µL	60 µL	800 µL	-33.3% (imaginary conversion)

Procedure:

- Prepare stock solutions of the internal standard (2-bromotoluene) and the substrate (2,5-hexadione) in acetone. Use concentrations that can be diluted to the required sample concentrations using the pipettes available in your laboratory. (*The minimum amount you can accurately dispense from a pipette depends on the type and volume.*)
- Prepare four samples as in Table 4.
- Make sure you can analyse your samples with the GC analysis setup. If not, modify the analysis setup until valid chromatograms are obtained.
- From the obtained chromatograms, obtain peak areas.
- Set up a calibration method according to the literature.