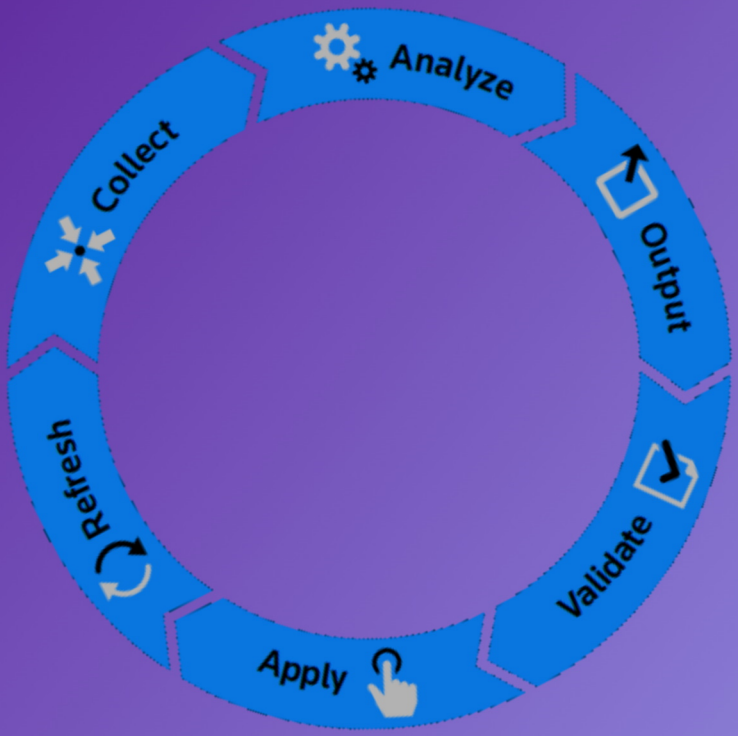
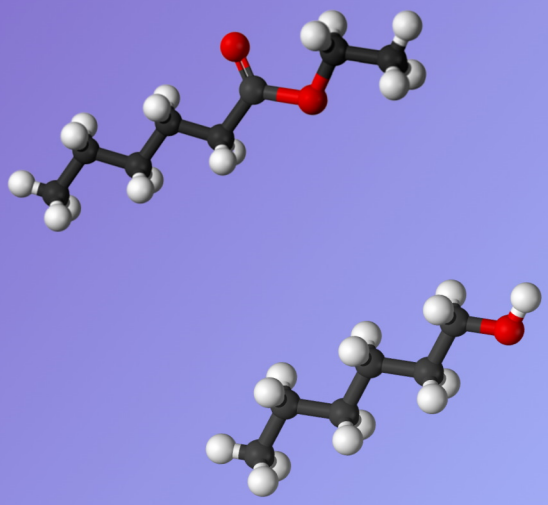
Describing the workflow of high-throuhput kinetic experimentation data

Niels van der Lem

Delft University of Technology





TU Delft

Describing the workflow of high-throuhput kinetic experimentation data

by

Niels van der Lem

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Prof. Dr. E.A. Pidko
Dr. E. Uslamin
Msc. Adarsh Kalikadien

Student number: 5188903/s1839616
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Thesis committee: Prof. Dr. E.A. Pidko, TU Delft, supervisor
Dr. A. Bansode, TU Delft

TU Delft

Abstract

Manual data processing is a tedious task that should be automated. Besides saving time, automated data processing also fights other problems in chemistry. Automated data processing in a normalized way makes data analysis between different experiments possible and can remove biases. In this study, kinetic data workflow is studied and a python script for automated data processing is made. Different experiments on the hydrogenation reaction of ethyl hexanoate using a ruthenium-PNN catalyst have been performed to obtain kinetic hydrogenation data. Reaction temperature was set to either 50, 70 or 110 °C and catalyst loading was either 50, 100 or 200 ppm. In total, nine experiments were performed. Gas chromatography and pressure readings during the reaction are used for analysis. Analysis is done on two different machine that report data in a different template and format. Therefore, a python script was written to automatically process the raw data obtained by these analysis methods. The written script imports obtained data, calculates new normalized parameters, concentration of different species for example, creates different plots of processed data and exports an excel file containing normalized data. This exported excel file was used to further examine catalyst kinetics. It was found for example, that at 50 and 70 °C, the reaction order of the catalyst is below one and at 90 and 110 °C catalyst reaction order is above one. The made processing script has improved data workflow, while data processing time has been reduced.

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1

Introduction

Each day, scientists create a lot of new data, leading to an increase in the amount of data generated each year [2]. Obtained data is never readily for data analysis. Therefore, data processing is needed before data can be analysed. Manual data processing is a time consuming and tedious job. When a series of experiments with slightly different conditions is performed, data is processed almost the exact same way for each experiment. For that reason, a significant amount of data processing can and should be automated. As data is processed, it is important that data is normalized. Data normalization is the process where data is structured to a desired normal form. Benefits of data normalization are less data redundancy and better data integrity [3]. Furthermore, normalized data is easier to read and analyse, especially if data from many different researchers is stored together.

In chemistry, almost every analysis instrument creates data in a digital form. A significant part of data is still not reported however [4]. A consequence of this non-published data is the impossibility for other researchers to use this data. A digital database where processed data is saved in a normalized way can solve this problem. Different efforts have been made to create such a database. The open reaction database (ORD) for example, provides an open-access schema and infrastructure to share chemical reaction data [5]. Using such a database opens up the possibility to use machine-learning. Machine-learning could help scientists better predict possible synthesis routes and reaction outcomes [5]. Important to note is that 'failed' experiments can still be useful for future reaction predictions [6]. At this point, data of 'failed' experiments is almost never publicly published and can therefore hardly be used for other scientific purposes by other researchers and machine-learning. Machine-learning can only learn from published data. As published data is overwhelmingly positive, machine-learning will be biases if it is not able to also learn from negative 'failed' experimental data. Figure 1.1 shows a scheme of how a database with machine-learning could automate and improve experiments and workflow.

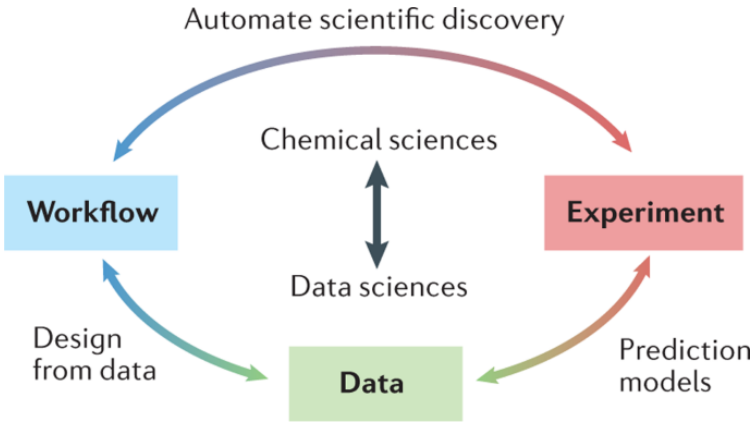

Figure 1.1: Graphical overview of data driven automated experimental workflow [1]

There is still another big problem in chemistry however. Experimental data is often hard to reproduce. A survey in *Nature* (n=1576) showed that more than 70% of researchers have failed to reproduce the experimental results of another scientist's experiments [7]. Furthermore, more than 50% of researchers were not even able to reproduce results from their own experiments. The dangerous result of this is that published data is often not transparent enough [8]. Experimental findings can be and are often greatly exaggerated [9]. Furthermore, exaggeration of findings means that data is biased to some extent. Confirmation bias is defined as the seeking of data to support once's particular beliefs [10]. Automatic data processing and normalization could reduce confirmation bias, as data is reported in a normalized structure without influence of the researcher. Reproducibillity could also be ensured if data is reported in a standardized structure [5].

In this research, the complete life-cycle of high-throughput kinetic experimental data is studied. To do so, complete data workflow of kinetic data is examined. First, raw kinetic data of hydrogenation reactions is experimentally obtained. Afterwards, data processing of experimentally obtained data is studied. At last, a data protocol for data storage and automated data processing is created.

2

Theory

In this chapter, background information used in the thesis will be given. First, the theory behind the studied reaction is provided. Then, theory behind the used analysis methods used is explained.

2.1. Hydrogenation of esters

The catalyzed hydrogenation of esters is an efficient way to produce alcohols. Hydrogenation is a process where hydrogen atoms are added across unsaturated bonds [11]. Traditional reduction of esters to alcohols is achieved by using a stoichiometric amount of metal hydride reagents, LiAlH4 for example [12]. In comparison, traditional reduction of esters produces more waste, whereas catalyzed hydrogenation of esters does not produce any waste [13]. For this reason, catalytic production of alcohols from esters is an environmentally friendly and economically attractive way to produce alcohols. Figure 2.1 shows the general hydrogenation of esters to alcohols.

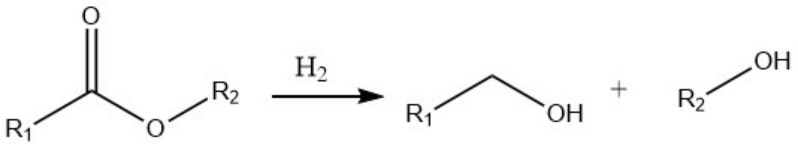

Figure 2.1: Reaction scheme of the general ester hydrogenation reaction

Currently in industry, heterogeneous catalysts are used for the hydrogenation process. A major drawback of this method however, are the harsh reaction conditions under which this hydrogenation process takes place. Typically, temperature ranges from 200 to 300 °C under 200 to 300 atm hydrogen pressure [14]. Homogeneous catalysts allows operation at much lower temperatures, resulting in higher selectivity towards the alcohol products [15].

During hydrogenation, transesterification reactions also happen. Transesterification is the reaction of an alcohol group with an ester to form a new ester and alcohol [16]. The general process is shown in Figure 2.2.

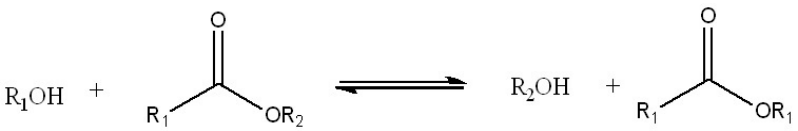

Figure 2.2: Reaction scheme of the general transesterification reaction

As shown in Figure 2.2, a new ester is formed during transesterification. This new ester can again be hydrogenated to alcohols using the same catalyst. Figure 2.3 shows this reaction.

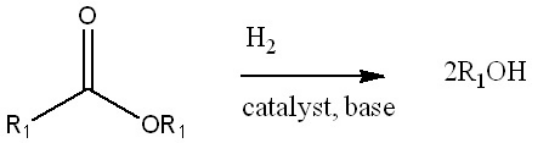

Figure 2.3: Reaction scheme of the hydrogenation reaction of newly formed ester

In this research, a ruthenium based catalyst is used. It has already been proven that many different ruthenium complexes can catalyse hydrogenation reactions. Since the 1970s research has been done on hydrogenation catalysed by ruthenium [17]. Much progress had been made on selective homogeneous catalysed hydrogenation of molecules containing electrophilic carbonyl groups, like ketone and imines [18]. However, progress has been much slower on homogeneous catalysed hydrogenation of molecules containing less electrophilic carbonyl groups, like esters [19]. Early metal containing catalysts could only hydrogenate esters under harsh conditions or activators were needed [20]. However, since the first reported unactive ester hydrogenation catalysed by a ruthenium pincer ligand by Zhang et al [13], more practical homogeneous catalysis systems for ester hydrogenation have been developed [21].

2.2. Analysis methods

To determine the state of the hydrogenation reactions, analysis is crucial. Therefore, gas chromatography and pressure readings are used. During the reaction hydrogen gas is consumed, resulting in a drop in pressure. As pressure is measured every 10 seconds, precise pressure information is achieved over the time span of the reaction. For more quantitative analysis, gas chromatography is used. Gas chromatography can be used to identify different species in a sample. Different calculations are done to process raw experimental data. A scheme of performed data processing is shown in Figure 2.4.

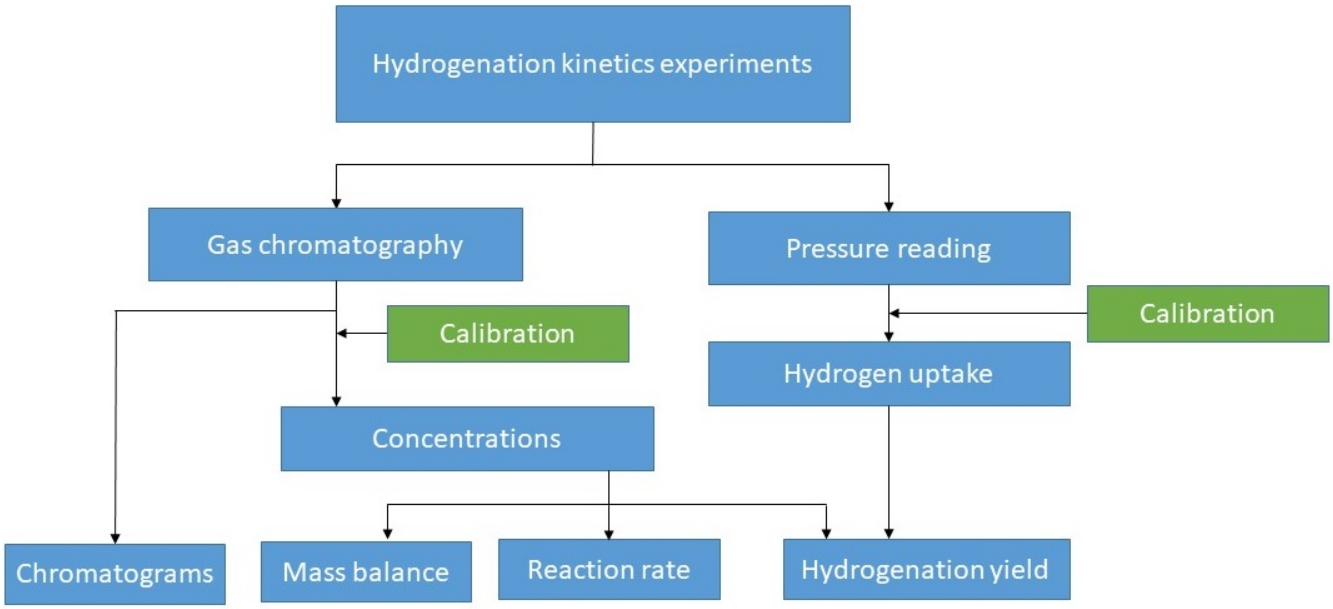

Figure 2.4: Overview of data processing. Starting from the top, raw gas chromatography and pressure data is processed into normalized values shown at the bottom

Figure 2.4 shows that calibrations are needed to transform raw data into useful qualitative data. After calibrations, hydrogen uptake and species concentrations can be determined. Afterwards, normalized values for mass balance, reaction rate and hydrogenation yields can be calculated. In the next sections, calculations will be discussed in more depth.

2.2.1. Pressure readings

A pressure sensor measures pressure in the reaction chamber and reports this data to a computer. For hydrogenation to take place, hydrogen gas needs to be used by the liquid substrate. The reactor is fully pressurized by hydrogen gas. A drop in pressure is therefore the result of hydrogen uptake.

$$\text{Hydrogen uptake (mmol)} = \frac{\Delta P * V_h}{V_m} \tag{2.1}$$

In Equation 2.1, Hydrogen uptake is the number of moles hydrogen gas used during the reaction, ΔP is the difference in pressure in bar, V_h is the reactor headspace. The reactor headspace is the volume of gas above the liquid sample [22]. For this reactor, a value of 40 was obtained. However, this value is uncertain as hydrogen gas can dissolve and the temperature is different under reaction conditions. Therefore, reaction headspace is compensated with a certain experiment dependent factor. These factors are shown in Table 3.1. V_m is the molar gas volume, which corresponds to the volume that one mole of gas occupies. If the amount of hydrogen used during the reaction is known, it becomes possible to determine the hydrogenation yield.

$$\text{Hydrogenation yield (\%)} = \frac{Hydrogen\ uptake}{2 * n_{substrate}} * 100 \tag{2.2}$$

In Equation 2.2, the hydrogen uptake calculated using Equation 2.1 is divided by two times the amount of moles substrate. This results in the ratio between moles of hydrogen gas used during the reaction and the total amount of oxygen atoms. In the case of esters, this amount is equal to two times the amount of moles substrate.

2.2.2. Gas chromatography (GC)

In contrast to pressure data, for gas chromatography only a limited amount of samples are taken. Gas chromatography is an analysis method which identifies compounds based on the interaction of species with the gas chromatography phase [23]. Gas chromatography uses two different phases. The mobile phase is an inert carrier gas and the stationary phase is a silica column. A sample is evaporated into the mobile phase and species are separated based on their interactions with the stationary phase [23]. From the gas chromatography data, a list of compound peak areas is obtained. Peak areas directly correspond to the amount of a certain compound present in the sample. To quantify the compound concentration present in the sample, an internal standard is used. An internal standard is a compound with known concentration added to the reaction mixture. The internal standard does not react and is only used to quantify sample concentrations [24].
Before experiments are run, a calibration GC run is done. Calibration is another way to determine compound concentrations, while calibration runs are used to determine how the gas chromatography machine responds to an analyte [25]. It is important to calibrate a GC machine as different GC machines will not always result in the same absolute peak values, however calibration allows peak areas to be transformed in normalized values that are the same for different machines. To do a calibration run, a mixture of similar compounds, including reaction compounds of interest, is made. Furthermore, the calibration mixture is diluted several times to make sure that the machine response is tested at different compound concentrations. After a calibration run is done, the linear response of the GC machine to different compounds can be determined. The calibration constants for a species is equal to the slope of intensity plotted against species concentration.
When a calibration run is done, and a known concentration of an internal standard is present in the reaction mixture, the unknown sample concentrations can be calculated. Equation 2.3 shows the derived formula to calculate species concentrations.

$$C_x(mol/L) = \frac{PE_x}{PE_{is}} * \frac{k_{is}}{k_x} * C_{is} \tag{2.3}$$

In this equation, C_i is the compound concentration, PE_i is the corresponding peak area of the compound, k_i is the calibration constant of the compound. Afterwards, the internal standard values convert peak area to concentration. C_{is} is the known internal standard concentration in the sample, PE_{is} is the peak area of the internal standard and C_{is} is the calibration constant of the internal standard.

After concentrations are know, hydrogenation yield can be calculated. Hydrogenation yield is the ratio between R1 from Figure 2.1 in the sample and R1 total. In other words hydrogenation yield is the percentage of

R1 that ended up in the products. In formula, hydrogenation yield from concentration can be described as shown in Equation 2.4

$$\text{Hydrogenation yield (\%)} = \frac{C_{R1products}}{C_{R1total}} * 100 \tag{2.4}$$

From hydrogenation yield, reaction rate can be directly calculated. The reaction rate at a certain point is the slope of the hydrogenation yield against time. In other words, reaction rate is the first derivative of the hydrogenation yield.

2.3. Kinetic analysis

Kinetic analysis gives an insight about catalyst performance. Arrhenius equation relates reaction temperature to reaction rates.

$$k = Ae^{\frac{-E_a}{RT}} \tag{2.5}$$

Where k is the rate constant, A is the pre-exponential factor, E_a is the activation energy, R is the universal gas constant and T is the temperature in Kelvin. Arrhenius plots show a linear dependence if the natural logarithm of Equation 2.5 is taken. The Arrhenius equation then becomes:

$$\ln k = \ln(A) - \frac{E_a}{R}(\frac{1}{T}) \tag{2.6}$$

If $\ln k$ is plotted against $\frac{1}{T}$, the slope of the line represents activation energy. Furthermore, intercept at x=0 corresponds to the pre-exponentional factor A. After these two variables are determined, rate constant only depends on the temperature.

3

Experimental

In this chapter, the complete experimental will be discussed. First, experimental setup used will be explained and afterwards, performed experiments will be discussed.

3.1. Experimental setup

Experiments were performed in a homogeneous reactor setup. The reactor chamber is able to handle hydrogen pressure of up to 75 bar. Pressure sensors make accurate measurements of reaction chamber pressure. An external heater is able to heat up the system to desired temperature. An autoclave system is in direct contact with the reactor chamber and is able to take samples from the reaction vial when needed. In the reaction chamber a stirrer is also present to make sure that the reaction mixtures are equally mixed.

3.2. Performed experiments

For this research, the kinetics of the hydrogenation reaction of ethyl hexanoate (EtOHxt) to hexanol (HexOH) and ethanol (EtOH) is studied. Ruthenium-PNN ($C_{38}H_{36}Cl_2N_2P_2Ru$) is used as a catalyst. The structure of Ruthenium-PNN can be seen in Figure 3.1.

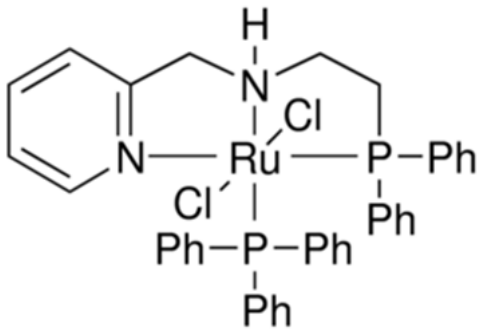

Figure 3.1: Chemical structure of used Ruthenium-PNN catalyst

To enhance catalyst performance, the strong base potassium tert-butoxide (KOtBu) is added to substrate solution. KOtBu activates the ruthenium complex, resulting in higher activity [26]. The total reaction scheme can be seen in Figure 3.2.

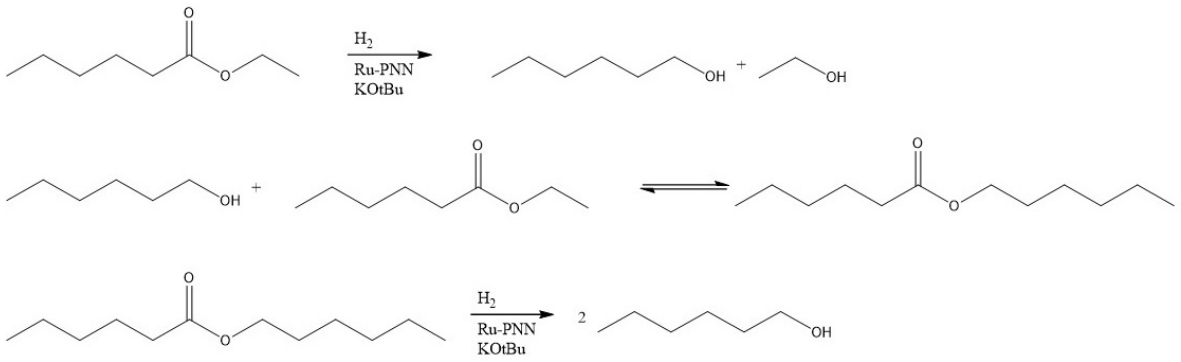

Figure 3.2: Reaction schemes of performed reactions

Catalyst performance is tested under different reaction conditions. Temperature and catalyst loading are different for each experiment. Reaction temperature is either 50, 70 or 110 °C and catalyst loading is 50, 100 or 200 ppm. In total nine experiments are performed, testing each possible set of temperatures and catalyst loadings. Table 3.1 summarizes performed experiments and conditions.

Table 3.1: Performed experiments and corresponding conditions

Experiment name	Reaction temperature (°C)	Catalyst loading (ppm)	Headspace compensation factor
NL1	50	50	1.3
NL2	50	100	1.14
NL3	50	200	1.1
NL4	70	200	1.4
NL5	70	50	1
NL6	70	100	1.4
NL7	110	50	2.5
NL8	110	100	2
NL9	110	200	1.25

3.2.1. Substrate and catalyst preparation

For each experiment, the same substrate mixture is made. In a glovebox, substrate ethyl hexanoate (1.724 mL, 10.401 mmol) and internal standard dodecane (0.100 mL, 0.440 mmol) were added to a vial. 0.208 mL of KOtBu (23.3 mg, 0.208 mmol) dissolved in THF was also added to the vial. Extra THF (6.968 mL) was added to the vial. In total, 9 mL of substrate mixture was created.
Catalyst solution was separately made. Amount of ruthenium-PNN and THF differs based on the desired catalyst loading. For 50 ppm catalyst solutions, ruthenium-PNN (0.4 mg, 0.52 μmol) was dissolved in 0.196 mL THF. Afterwards, extra 0.804 mL THF was added to the vial. For 100 ppm catalytic solutions, twice as much ruthenium-PNN (0.8 mg, 1.04 μmol) was dissolved in 1 mL THF total. For the 200 ppm solutions, more ruthenium-PNN (1.6 mg, 2.08 μmol) was dissolved in 1 mL THF. Substrate and catalyst solutions together result in 1 mL of reaction mixture.

3.2.2. Experimental reactor procedure

Before usage, the whole reactor system is cleaned thoroughly. Afterwards, a clean vial is placed in the reactor chamber and the reactor is closed. Substrate solution is added to the vial through a capillary. Then, the system is put under 40 to 45 bar hydrogen pressure. Stirring is set to 150-200 rpm and the heater is set to the desired reaction temperature. When the system reaches desired temperature, stirring is increased to 500 ppm and pressure is increased to 50 bar hydrogen pressure. Before starting the autoclave software, a sample of the substrate solution is taken, this is the zero sample. Afterwards, autoclave software is started and five seconds later catalytic solution is added to the reaction chamber through the capillary. Now over the next 20 hours, 27 samples are automatically taken. After this time, reaction is stopped. Temperature is set to room

temperature, stirring is stopped and pressure is released from the system. The system is cleaned and the next experiment can be performed. The 28 samples are analysed using gas chromatography.

3.3. Raw data workflow and Jupyter

After an experiment is done and samples are analysed, raw data files are locally created on the lab computers. A backup of the raw data is automatically made on a Synology server. This server saves the raw data in a save environment and allows raw data to be remotely accessed by all users of that server. For an experiment, different analysis machines are used. Therefore, raw data is saved on different locations within this Synology server. Normally, if one wants to process raw data, desired raw data is downloaded from the Synology server. Data of interest is then imported in desired processing software, Origin or Excel for example. Now, a tedious and time consuming jobs is started. However, it is also possible to connect the Synology server to a linux server which runs a JupyterHub. Jupyter is an open souce web-application that allows users to run python scripts in a web-based interface. Connection of Synology to the linux server allows data from the Synology drive to be used in the JupyterHub interface. In JupyterHub, multiple JupyterNotebooks can be run. A JupyterNotebook is an interactive computing platform that combines python code, equations, text and visualizations. In short, a JupyterNotebook allows the possibility to import data from the Synology server, process this data in the web-based environment and visualize processed data. A notebook is however run locally for one specific user only. JupyterHub allows multiple users to use the same notebooks and data. In conclusion, the usage of JupyterHub could allow automation of data processing, resulting in a more efficient data processing workflow.

One conditions is however that raw data has to be reported in a well ordered manner for the data to be usable by a script. Most analysis machines are made by different companies. Due to this fact, most machines have different user interfaces and save data in different formats and templates. Some of these templates do not allow written scripts to use that data. An example of this can be seen in subsection 4.2.2. Jupyter allows all of these different data formats and templates to be used within one single interface. As a result, a convenient and easy to use environment can be created for data processing and analysis.

4

Results & discussion

In this chapter the results of the conducted research is shown and discussed. First, the data processing script is presented and explained. Afterwards, data plots made by the script are presented and at last.

4.1. Data processing script

Figure 4.1 shows how obtained experimental data is transferred to be processed. Obtained experimental data is automatically uploaded to a server. Within this server, the data is saved under the 'Experimental data' tab. In this tab, data from the corresponding lab computer is automatically uploaded. From the performed experiments autoclave, pressure readings and gas chromatography data is obtained. Experimental data is obtained on two different lab computers. Autoclave and pressure readings are done by the same computer. Within this computer's folder, autoclave data is saved in the "Sampler", while pressure data is stored in the "Reactor" folder. Gas chromatography is saved on another computer's folder. In this folder, gas chromatography data is saved in the "Kinetic runs" folder. Here, a new folder is created for each gas chromatography run. To make sure that the JupyterHub can easily get access to all different data files in a simple manner, linux jobs are created to copy data from their original folder to a new shared folder called "automatic_data_processing". In this shared folder reaction conditions and machine calibration files need to be manually added. This is represented in Figure 4.1 by the green box. JupyterHub is connected with this shared folder. This enables the hub to import files from the shared folder, process said data and in the end, export plots and processed data back to the server. Unfortunately, the shared folder has not been able to be connected to the JupyterHub. At this point in time, only one way was found to connect the JupyterHub with the data on the server. This way requires the JupyterHub user to have full access on the linux server that hosts Jupyter. Security concerns arise as all JupyterHub users will have full access on the server, which is not desired. Therefore, it was decided to put full automation on hold for now.

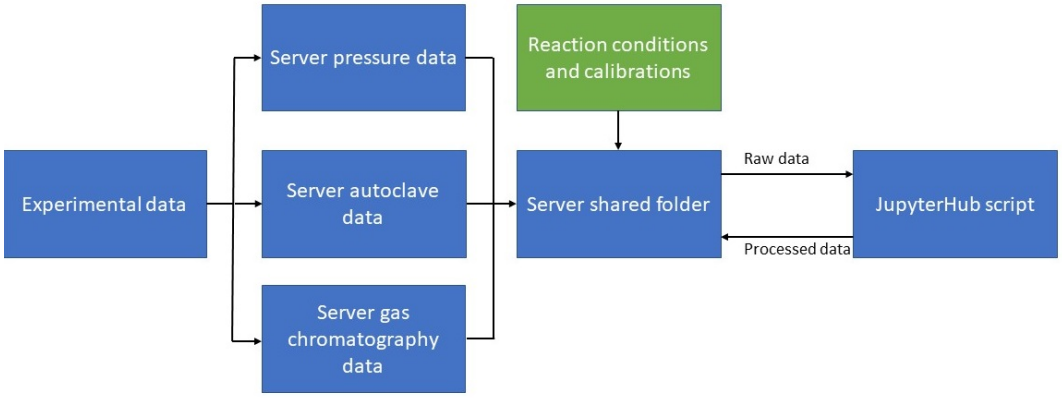

Figure 4.1: Graphical overview of experimental data pathway, experimental data starts from the left and is moved to a shared folder

Two different versions of the processing script are written. The first script is written for full automation on the JupyterHub. Due to the fact that JupyterHub has no access to raw data, this script could not be tested. However, the script is ready in the JupyterHub and can be tested once the problems are resolved. The second version of the script runs locally in JupyterNotebook and requires manual input of which experiment to process. Raw data also needs to be manually downloaded and moved to the raw data locations where the script imports the raw data from.

The two processing script contain the same functions and work process data the same way. A detailed description of how the code works can be found in Appendix A. The processing script can be divided in three different parts: importing data, processing data and exporting data. First, data from all different sources is imported. Calibration, reaction conditions, and autoclave time are first imported. Then, pressure readings and gas chromatography data is imported. Afterwards, imported raw data is normalized using previous imported variables. Chromatograms are also imported and merged into one data frame.

As data is imported, data processing is done immediately after. Calculations are done using formulas discussed in chapter 2. After processing, processed data is visualized in different plots. Created plots are shown and discussed in section 4.2.

After data is processed and visualized, data is ready to be exported. First, a new folder is created for the experiment being processed. All created plots are then saved in this folder. Lastly, an excel file is created and exported to this folder containing all normalized processed data. As the script processes more data, it is important to easily know which data correspond to which experiment. Therefore, different factors are taken into account when a processed file is named. The structure of the file naming is as follows: Experiment name - Catalyst name - Substrate name - Reaction temperature - Catalyst loading. For example, experiment NL4 was done at 70 degrees and the catalyst loading was 200 ppm. The exported data file is called *NL4-Ru-PNN-EtOHxt-70C-200ppm*. Using this naming structure, data will be primarily sorted based on the experiment name. Furthermore, this naming structure makes data comparison of several experiments fairly easy, as all important conditions are present in the name of the data files.

4.2. Data plots

Created plots visualize what the data processing script does. It is important for plots to be easy to read, since plots are to be used to compare different experimental results. In the end, different types of plots are created for gas chromatography and pressure data. All created data plots can be found in Appendix B.

4.2.1. Pressure plots

Three plots are created of processed pressure data. The created plot contains raw pressure readings. Examples of created pressure plots are shown in Figure 4.2.

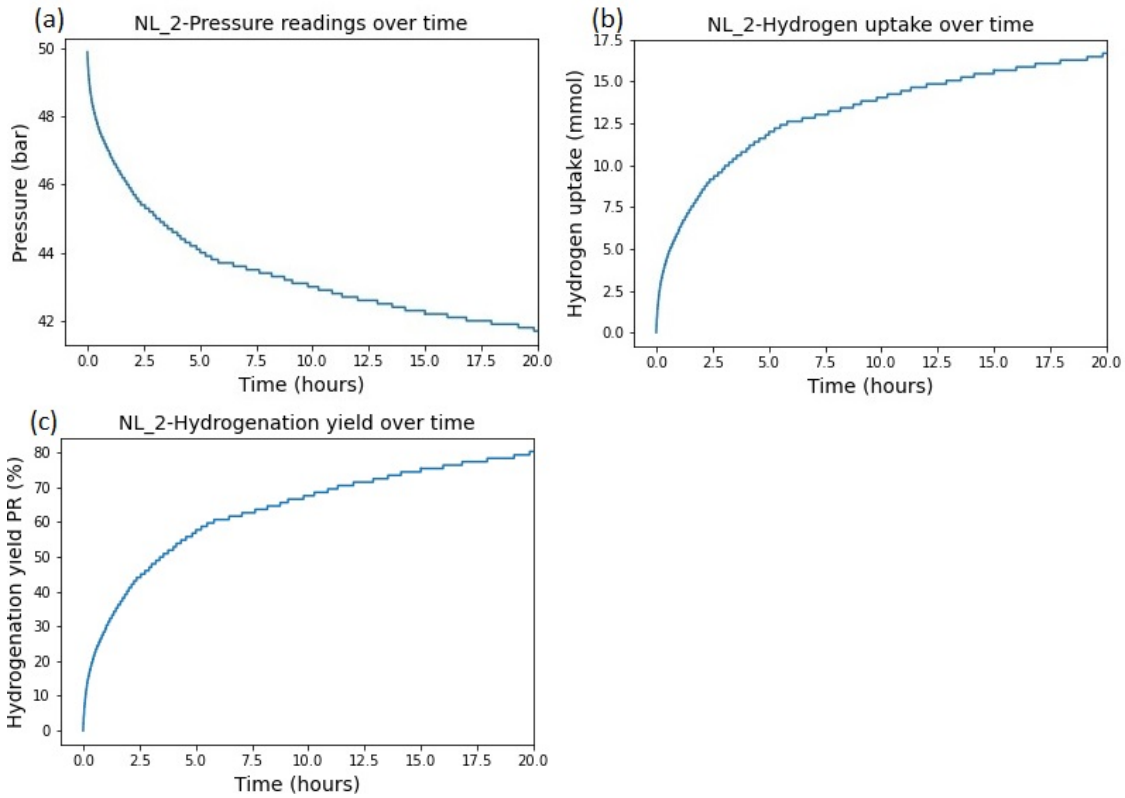

Figure 4.2: Examples of created (a) pressure readings, (b) hydrogen uptake and (c) hydrogenation yield plots

In Figure 4.2a hydrogen pressure over reaction time is visualized. The plots shows a decrease of 8 bar hydrogen pressure over the course of 20 hours. A drop in pressure is the result of hydrogen gas used during reaction. Figure 4.2b quantifies the total amount of hydrogen used during hydrogenation. Hydrogenation yield is visualized in Figure 4.2c. After 20 hours, 17 mmol hydrogen is used, which results in a hydrogenation yield of 80%.

Current pressure sensors can only measure pressure on one decimal, resulting in plotted lines shown in Figure 4.2 to be static. For this reason, reaction rate could not be determined from pressure data, as reaction rate is the slope of the hydrogenation yield over time. In many points, the difference in hydrogenation yield is zero, only to jump up moments later. This problem could be resolved by using better pressure sensors, or by using curve smoothing on pressure plots. In the later case, data will be lost however.

4.2.2. Gas chromatography plots

For gas chromatography plots, five different plots are created. The first two plots are both plotted over time, while the other three plots are different reaction rate plots. Examples of created time plots are seen in Figure 4.3. Reaction rate plots are shown in Figure 4.4. At last, a contour plot of raw chromatograms is created. This plot is shown in Figure 4.5.

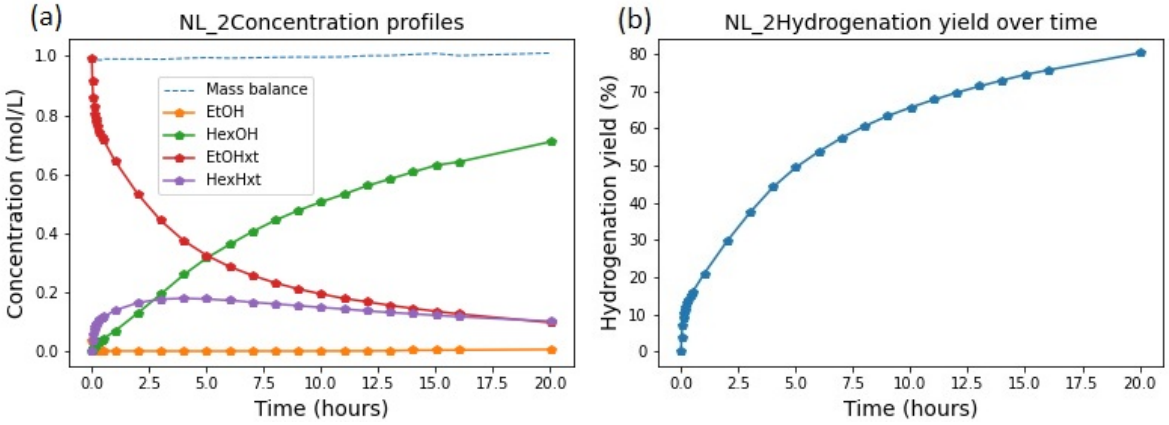

Figure 4.3: Examples of (a) concentration profiles and (b) hydrogenation yield time plots created by the processing script

Figure 4.3a shows the concentration profiles and mass balance of different compounds. At the start of the reaction, only the ethyl hexanoate substrate is present in the sample. In the figure, ethyl hexanoate has concentration of 1 mol/L at the start of the reaction, while other compounds have no concentration. As soon as catalyst is added to solution, hydrogenation and transesterification occur. At the start, more hexyl hexanoate is formed than alchohols. After six hours hexyl hexanoate concentration starts to slowly decrease, while hexanol concentration keeps increasing. After 20 hours, substrate concentration decreased to 0.10 mol/L. Hexanol concentration increased to 0.70 mol/L after 20 hours. The mass balance is shown Figure 4.3 to validate plotted gas chromatography data. The mass balance should always be equal to one for concentrations to be considered valid. If mass balance does not equals one, data may be wrong. Figure 4.3b shows the hydrogenation yield in percentages over time. It can be seen that after 20 hours, a hydrogenation yield of 80% is achieved.

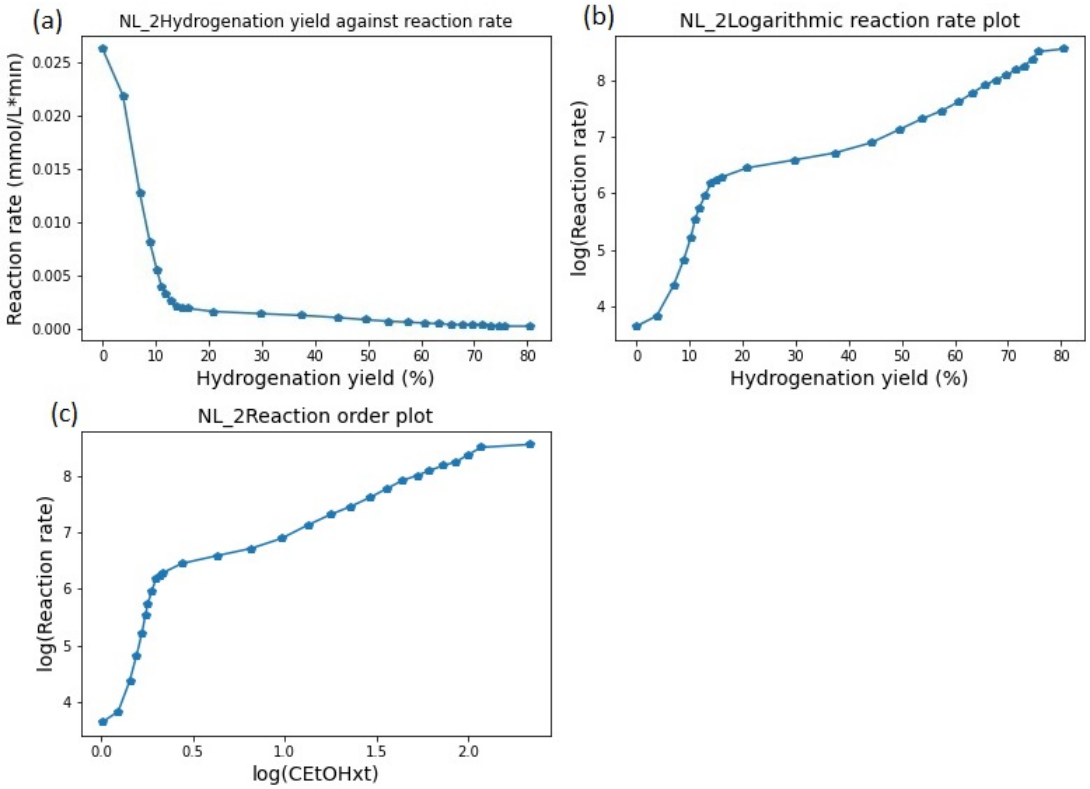

Figure 4.4: Examples of created reaction rate plots created by the processing script

Figure 4.4a shows the how the reaction rate changes as a function of hydrogenation yield. Plotting reaction rate this way instead of plotting over time results in a better representation of the way the reaction rate changes as reaction conditions change. It can be seen that at the start of the reaction, reaction rate is a hundred times higher than at higher conversions. Within the first 10% hydrogenation yield reaction rate becomes 10 time smaller than at the start. As reaction rate is the slope of hydrogenation yield against time, Figure 4.3b confirms the drop in reaction rate. At the start of the reaction, the slope of Figure 4.3b is significantly larger for the first 10% hydrogenation yield then afterwards. Figure 4.4b and Figure 4.4c show how the kinetics change as reaction progresses. Different reaction regimes can be identified based on the slope. If the slope drastically changes, means that reaction order has shifted. For example, Figure 4.4c shows three different reaction regimes.

The last types of plots created from gas chromatography data are contour plots. Previous gas chromatography plots shown in Figure 4.3 and Figure 4.4 are created out of the peak areas of different species. These plots use only a limited amount of gas chromatography data, whereas created contour plots contain complete gas chromatography information. A created contour plot is shown in Figure 4.5.

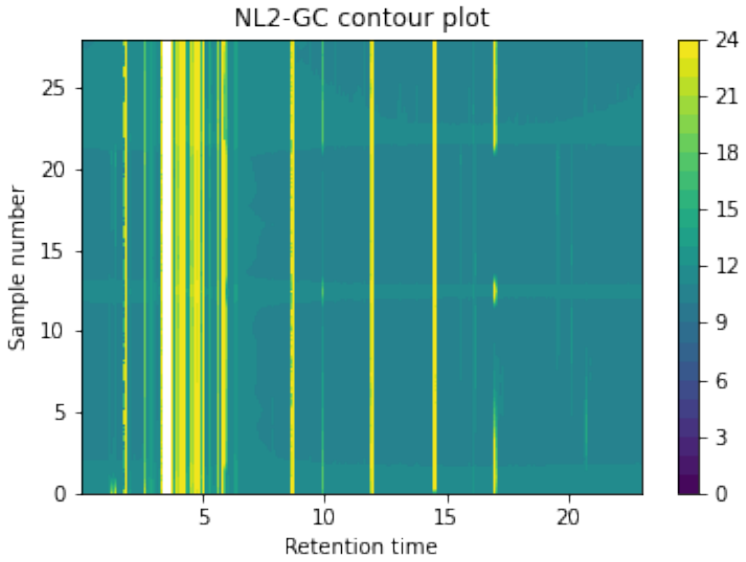

Figure 4.5: Example of created contour plot

In Figure 4.5, different colours represent the intensity of a signal at a certain retention time for a certain sample number. The intensity scale is shown on the right. The brighter the color, the more intense the signal. A yellow line means that a species is present at corresponding retention time. The white and yellow line at a retention time of three to five represents the toluene solvent. In total, four other yellow line can be seen, which corresponds to four species present in the reaction mixture. Other less intense lines can also be observed, which may mean that other species may get formed during the hydrogenation reaction.

During this research, the way gas chromatography sequence data is reported was changed a few times. At the start, a sequence report was created that was not ordered in a numerical order. For automation of data processing this template for GC data reporting was not optimal and therefore changed. The second reporting template was ordered well, however, the file contained numbers saved as text. Scripts are not able to import data from those files without the manual removal of those numbers. This would mean that full automation of GC data processing could not be achieved. The third reporting template seemed to be perfect. From experiment NL5 onward this template was used. However, after all experiments were done and data was being processed it was found that the created files were corrupted and had to be manually saved first before the data could be imported by the processing script. In the end, a template was created and tested that does not create a corrupt file and is ordered in a good way. The final script contains the function that processes files with this created template.

During GC data analysis, it was found at that another species is present in some samples and increases and decreases over time. At this point in time, the species has not yet been identified. The species could be a new ester formed out of two ethyl hexanoate molecules. However, more research is needed to be certain of the identity of this formed species.

4.3. Kinetic results

Kinetics of the used ruthenium-PNN catalyst were studied using the exported processed data that the script created. Initial reaction rate was determined by plotting a linear line over the first four hydrogenation yield points. The slope represents the initial reaction rate. Before this project, experiments at 90 °C had been done. These experiments are also used for kinetic analysis.

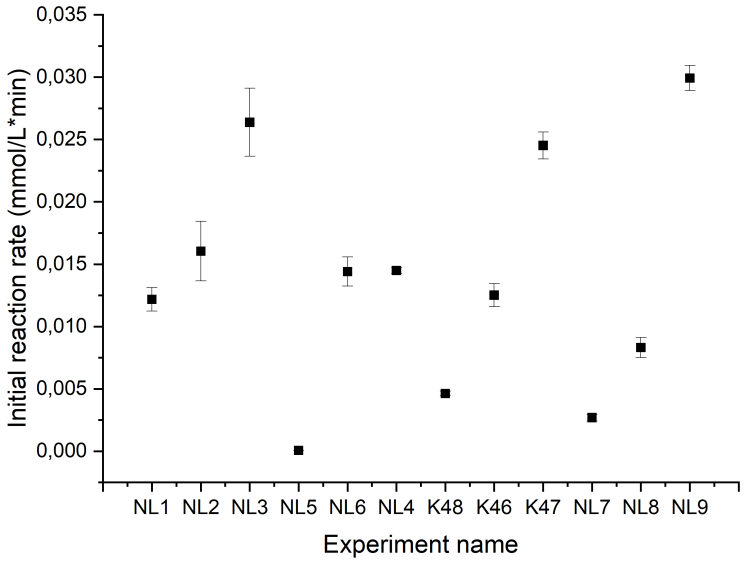

Figure 4.6: Initial reaction rates of all performed experiments. Starting from 50 °C and 50 ppm on the left to 110 °C and 200 ppm on the right

Figure 4.6 shows the initial reaction rates including error bars of performed experiments. Experiments NL1, NL2 and NL3 behave as one might suspect, the increase in initial reaction rate from 50 ppm to 100 ppm is almost the same as the increase from 100 ppm to 200 ppm. NL7, NL8 and NL9 show the same pattern. However, the gap between 100 ppm (NL8) and 200 ppm (NL9) is significantly larger then the difference between NL2 and NL3. A big gap in initial reaction is also observed between NL4 and NL5. This difference however is between 50 ppm and 100 ppm. Unsurprisingly, highest initial reaction rate is observed for the experiment performed at highest temperature containing the most catalyst. What is surprising however, is the result of NL1. This reaction contained 50 ppm catalyst and was performed at 50 °C. Initial reaction rate is higher under these conditions than for experiments performed with the same catalyst loading under higher temperatures. Results from NL5, performed at 70 °C and 50 ppm catalyst, are questionable, Therefore, this data set is not used for further analysis. To be certain of this experimental outcome, the experiment should be redone.

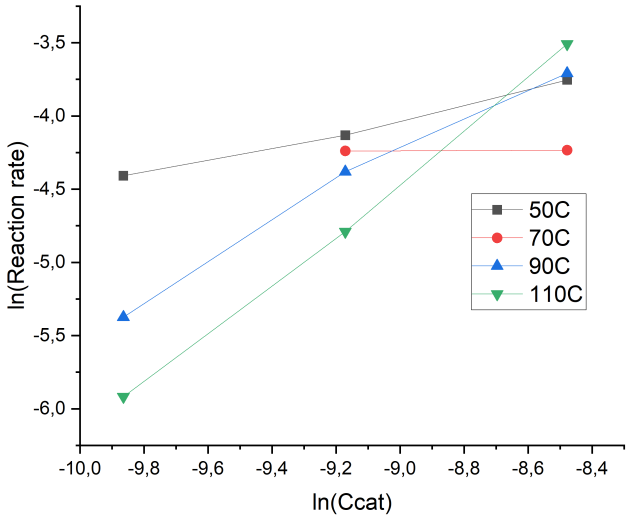

Figure 4.7: Plot of logarithm of initial reaction rate against logarithm of catalyst concentrations

Figure 4.7 shows the natural logarithm of the initial reaction rate plotted against the natural logarithm of the catalyst concentration for different temperatures. Plotting kinetic data this way allows easy calculation of the initial reaction rate of the catalyst, which correspond to the slopes. For 50 °C a reaction order of 0.47 was found, for 70 °C, a reaction order of 0 was found, for 90 °C reaction order is 1.20 and for 110 °C reaction order is 1.74. Reaction order above 1 means that another process, aside from catalyst activation, influences initial reaction rate. A possible process could be product induced activation. These processes have more impact on initial reaction rate at higher temperatures. At 50 and 70 °C, reaction order is below one. At lower temperatures, catalyst activation has less influence on the initial reaction rate.

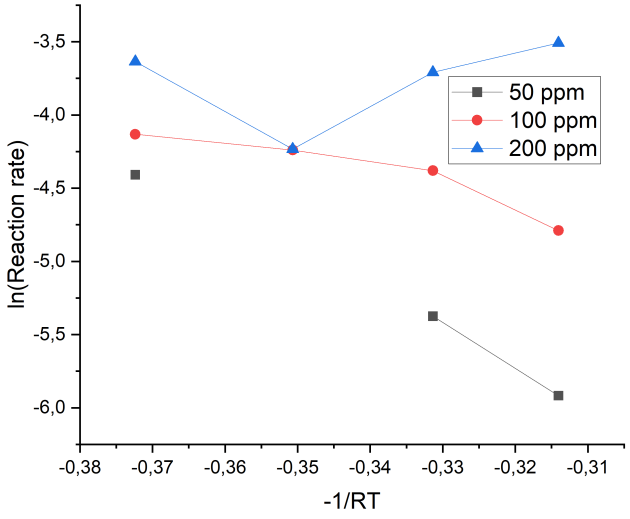

Figure 4.8: Arrhenius plots of performed experiments based on catalyst loadings

In the kinetic plot showed in Figure 4.8, natural logarithm of the initial reaction rate is plotted against minus the inverse of gas constant times temperature. For each catalyst loading a line is plotted. The slope of the line represents the activation energy of the catalyst at that catalyst loading. Activation energies for 50,100 and 200 ppm of -25.48, -10.68 and 19.94 kJ are found. Negative activation energies are not expected. A possible

explanations might be catalyst deactivation. However, more research is needed to confirm this result.

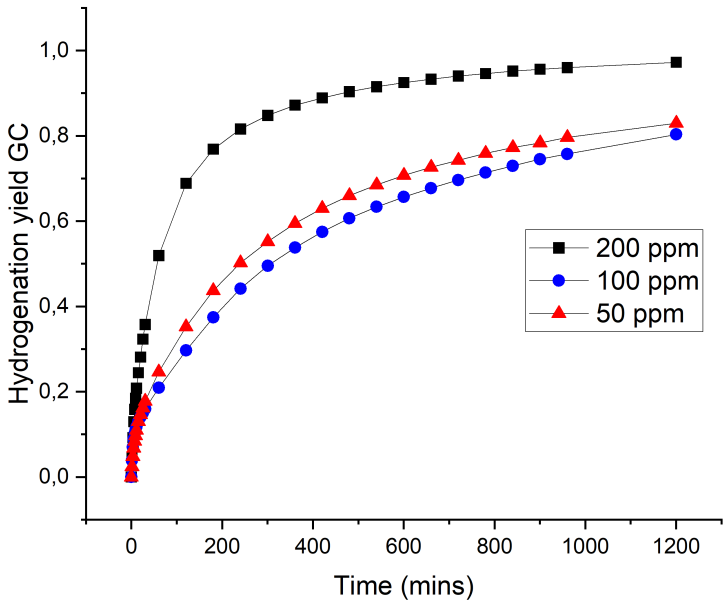

Figure 4.9: Hydrogenation yields of experiments performed at 50 °C

Figure 4.9 shows the hydrogenation yield of experiments done at 50 °C in one plot. It can be observed that after 20 hours a higher yield is obtained for the experiment performed with 50 ppm catalyst in comparison to the experiment performed with 100 ppm catalyst loading. This result is surprising, while the 100 ppm experiment does have a higher initial reaction rate in comparison to the 50 ppm experiment. More research is needed to determine what causes this outcome.

5

Conclusions & outlook

5.1. Conclusions

The goal of this research was to describe the whole 'life cycle' of kinetic experimental data. To study and optimise the data workflow, data of hydrogenation reactions of ethyl hexanoate using ruthenium-PNN as homogeneous catalyst under different conditions has been experimentally obtained. Afterwards, raw data workflow has been examined and improved by the use of a python script was to automate raw data processing. Although full automation has not been achieved, the local processing script is still an improvement over manual data processing. The script allows fairly fast data processing to normalized values and visualizes this data. Data of different experiments can readily be compared after automated processing.

Processed data created by the processing script was used to kinetically compare obtained experimental results. It was found that at 110 °C and 200 ppm catalyst loading the initial reaction rate was highest. Surprisingly, experiment containing 50 ppm catalyst had a lower initial reaction rate at 70 °C then at 50 °C. Catalyst reaction orders were determined for 50, 70, 90 and 110 °C and were 0.47, 0, 1.20 and 1.74 respectively. At last, activation energy has been determined. For most temperatures, activation energy was negative. This result is questionable and should be further investigated. In short, normalized data created by the script allows further kinetic analysis, which resulted in further research possibilities.

5.2. Outlook

The result of this studies is an script made on a platform that opens up many new possibilities. Similar scripts can be written for different reactors and analysis methods. Unfortunately, many different analysis machines do not allow the use of custom written code, meaning that the template and format at which raw data is reported, fully depends on the machine used. Much progress on data progressing efficiency could be made if raw data templates and formats could be customized. Another possibility is the usage of a script to compare different experimental data sets, something that has been manually done in this research. Digital lab notebooks could also improve the data processing script workflow. At this point in time, reaction conditions need to be manually placed in the folder, due to the fact that these files are locally made. A digital notebook could automatically upload these reaction conditions files, which will improve workflow. At last, data mining could be utilized on the processed data. Machine-learning could use the made processed data excel files to learn about which reactions under which conditions have best chance to deliver desired reaction outcomes. In conclusion, a significant amount of new applications and uses can be found using the created processing script and JupyterHub as a basis.

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At last, I would like to thank my family for always supporting and believing in me, even though they did not understand a single thing I was doing, the support was still really appreciated.

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Appendices

A

Processing script details

The first thing the script does is import all needed modules. Then, several variables are created with values and names of species of interest. Then, the experiment name needs to be inputted. Afterwards, the script will check if an processed data folder for this experiment is already made. If not, one is made. Then, data processing is started. Different functions are written to import, process, visualize and export data. These functions are discussed in the next sections. After exporting is completed, a logger updates the log file containing time and name of which experiment is processed.

A.1. Data importing functions

To process all different data files with one script, different functions are written. The first function called get_conditions imports the reaction conditions, which are needed in a later stage for calculations and naming purposes. The imported conditions are: experiment name, catalyst name, catalyst loading, reaction temperature, hydrogen pressure, substrate concentration, internal standard concentration and names of catalyst and substrate.

The second function get_autosampler_time imports the auto sampling time. The function returns the fourth column of the autoclave file. This column contains the real time in seconds after the start of an experiment at which a sample is taken. Imported the sample times allows the processed gas chromatography data to plotted against the sample time.

The third function get_calibrations imports and returns the values of the gas chromatography calibration constants of different compounds. Later, the calibration constants are used in calculations. The calibration data file is the only imported data file that is not experiment dependent, instead, calibration data remains constant if experiments of the same species are performed..

Previous explained functions contain data needed for further calculations. Next two functions import new data and use previous imported data to calculate various The function called get_pressure_data creates a variable which contains the data that the get_conditions imports. Afterwards, pressure data is imported. The pressure readings file contains 37 columns, of which only the first and fifteenth column are of interest. The first column contains the date and time at which a pressure value is taken. Each ten seconds the pressure is read. The fifteenth column contains the pressure value in bars. These are the only two columns which the functions imports. It can happen that the pressure column contains blank spaces. Therefore, the blank spaces are filled with the previous pressure value. Afterwards, date time is converted into delta time in hours. A new column is created by calculating hydrogen uptake. Afterwards, the hydrogenation yield is calculated and stored in a new column. The function returns the data frame containing all processed pressure data.

The get_gc_data function first gets data from both get_conditions and get_autosampler_time functions. For each gas chromatography analysis, a new folder is created containing raw data. To import data corresponding to the performed experiment a list of all gas chromatography raw data folders is created. A for loop over all folders searches for the data folder of the right experiment. Afterwards, GC data is imported from the se-

quence summary file containing peak areas of different compounds for all different samples. The function then creates a data frame consisting of only compounds of interest. It often occurs that at certain samples peak intensity of the molecule was not sufficient enough for the GC machine to detect, resulting in an empty cell. Therefore, the function fills empty cells with a value of zero. Peak areas are then transformed into concentrations using calibrations and internal standard concentration. Afterwards, a new column is added to the data frame which calculates hydrogenation yield. The reaction yield can be directly calculated, as the reaction rate is the slope of hydrogenation yield over time. To check if concentrations are valid, column for the mass balance is created. At last, the function returns a data frame containing all processed GC data.

Previous discussed function only imports peak areas of some chemical species. The function called get_chromatograms imports the complete chromatograms. For every sample taken, a chromatogram is created. The function imports all created chromatograms and creates one data frame containing all signals. Another variable is created, which imports the retention time of only one sample. Retention time only needs to be imported once, as retention time remainst constant for all samples. In the end, the function returns a variable containing retention times, a variable which contains a list of 0 to the amount of samples taken and a variable which contains all intensity information.

A.2. Data plotting functions

After data is imported, several plots of different types of data can be made. Therefore, multiple functions are written to plot all informational data. For pressure data two functions are written to plot data. All different processed pressure data needs to be plotted against time. Therefore, one function creates a general template for pressure data to be plotted. This function is called create_pressure_plots. Several inputs are needed. These inputs are plot number, pressure data frame, column name of the data, label and limit of the y axis and title of the plot. Afterwards, the function will create and export a picture of the plot.

To create pressure plots, data needs to be put in the create_pressure_plots function. A function called get_pressure_plots does that. First, a variable gets pressure data from the get_pressure_data function. Then, three lists are created containing information about which data to plot and corresponding limits and axes names. After all data is created, a for loop puts the data in the create_pressure_plots function. In the end, three plots are created. The first one plots pressure readings. The second plot contains hydrogen uptake data and the last plot contains hydrogenation yield data.

For gas chromatography data plotting one function is written and is called create_gc_plots. First, variables are created which get imported gas chromatography, autoclave time and reaction conditions from the corresponding data importing functions. Then, the first plot of the concentration profiles and mass balance is plotted over time. The second plot, plots hydrogenation yield over time. The third plot contains the reaction rate against hydrogenation yield. For each plot, a picture of the plot is exported.

Another type of plot is created for gas chromatography data. The function called contour_plot creates contour plots for imported chromatograms. On the X-axis, retention time is plotted. The Y-axis represents the sample number and Z-axis represents the intensity data corresponding to aligning sample number and retention time. After creation, a picture of the contour plot is exported.

A.3. Data exporting function

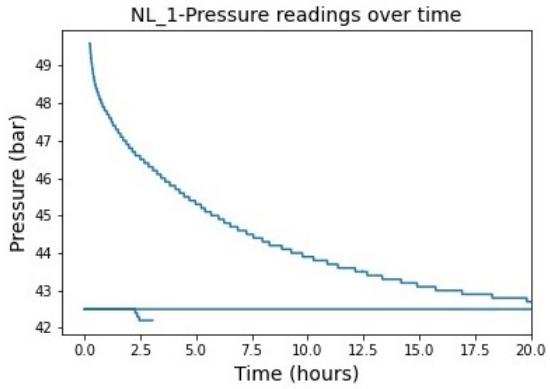
One function is written to export all processed data. This function is called export_data. Variables are created for gas chromatography data, chromatograms and pressure data importing and plotting functions. Each created plot is automatically exported once created. For the data itself, two new data frames are created. One data frame is filled with processed gas chromatography data and the other is filled with processed pressure date. Afterwards, one data frame is created out of the previous two. It is necessary to create two separate data frames for processed pressure and gas chromatography data as both data frames contain a different number of rows. One last column is added to the data frame containing the time at which the data frame is created. At last, the created data frame is exported as a .csv file.

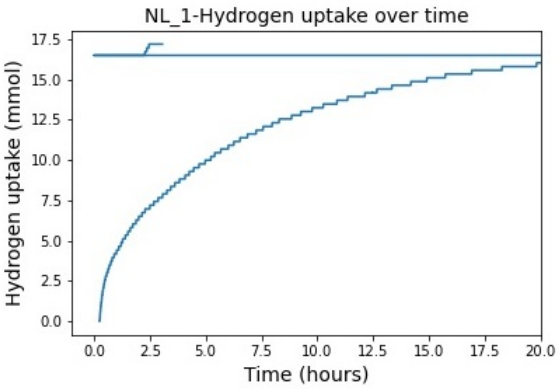
Processed data is exported to a separate folder called “processed_data”. Within this folder all data that the script processed is saved. As the script processes more data, it is important to easily know which data cor-

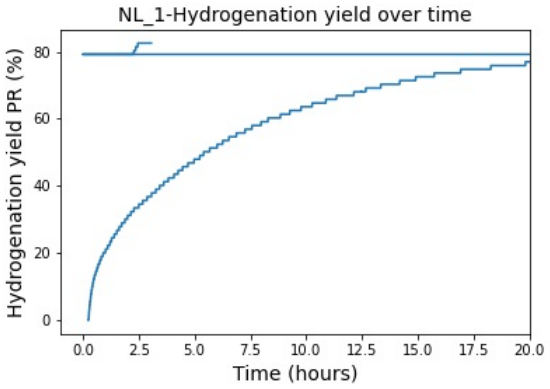
respond to which experiment. Therefore, different factors are taken into account when a processed file is named. The structure of the file naming is as follows: Experiment name - Catalyst name - Substrate name - Reaction temperature - Catalyst loading. For example, experiment NL4 was done at 70 degrees and the catalyst loading was 200 ppm. The exported data file is called NL4-Ru-PNN-EtOHxt-70C-200ppm. Using this naming structure, data will be primarily sorted based on the experiment name. Furthermore, this naming structure makes data comparison of several experiments fairly easy, as all important conditions are present in the name of the data files.

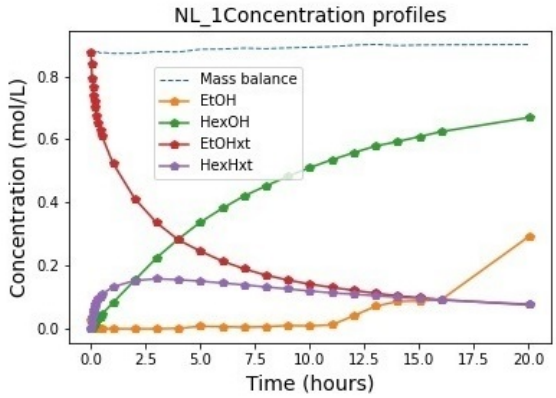
B

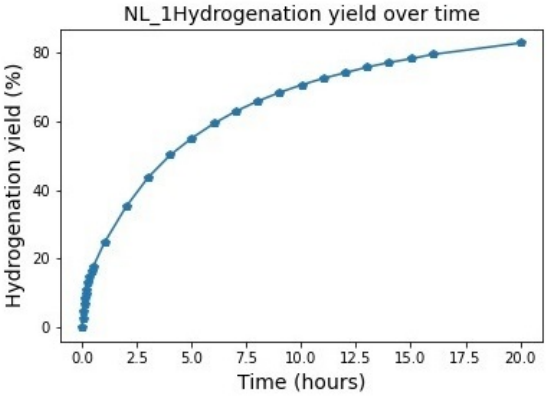
Experimental plots

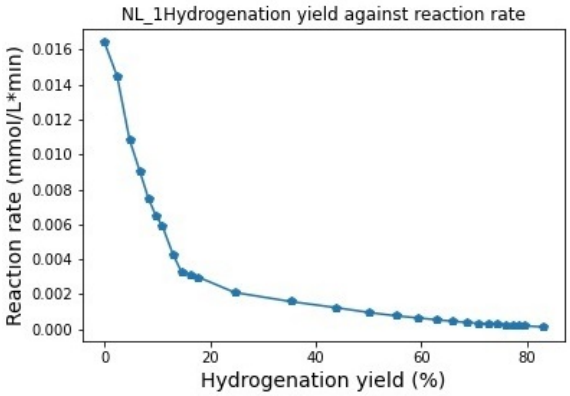


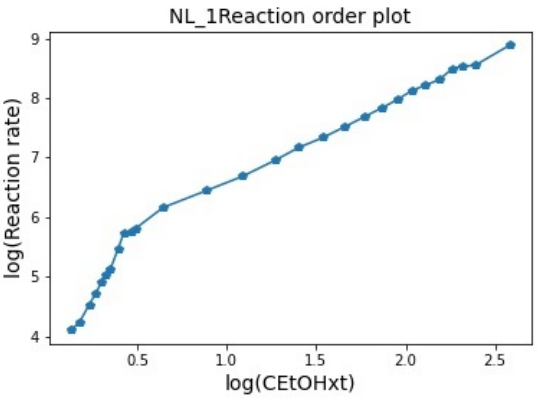


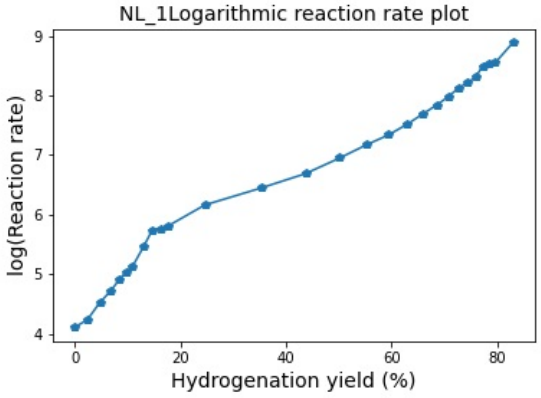


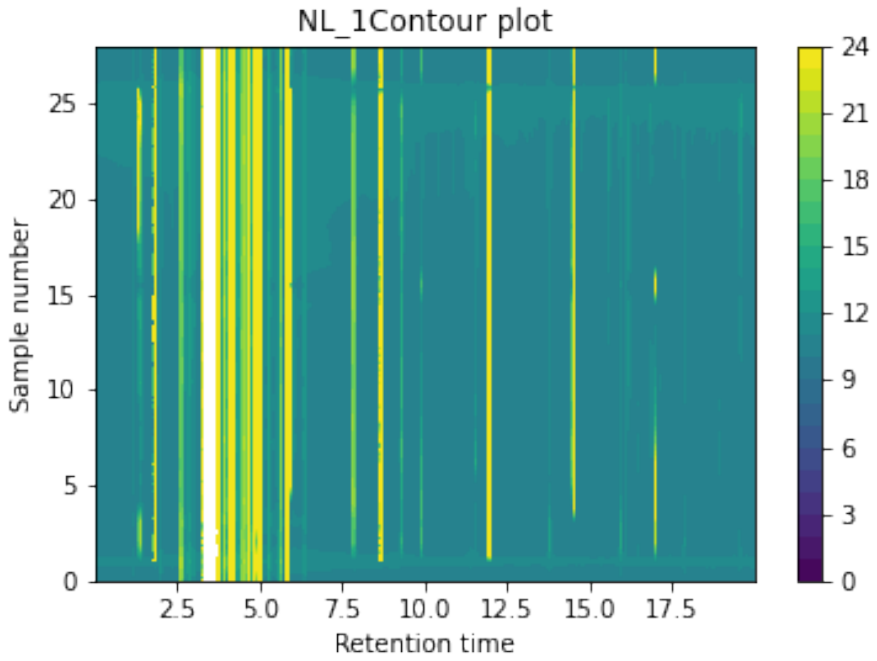

NL_1Concentration profiles
Mass balance
EtOH
HexOH
EtOHxt
HexHxt
Concentration (mol/L)
Time (hours)

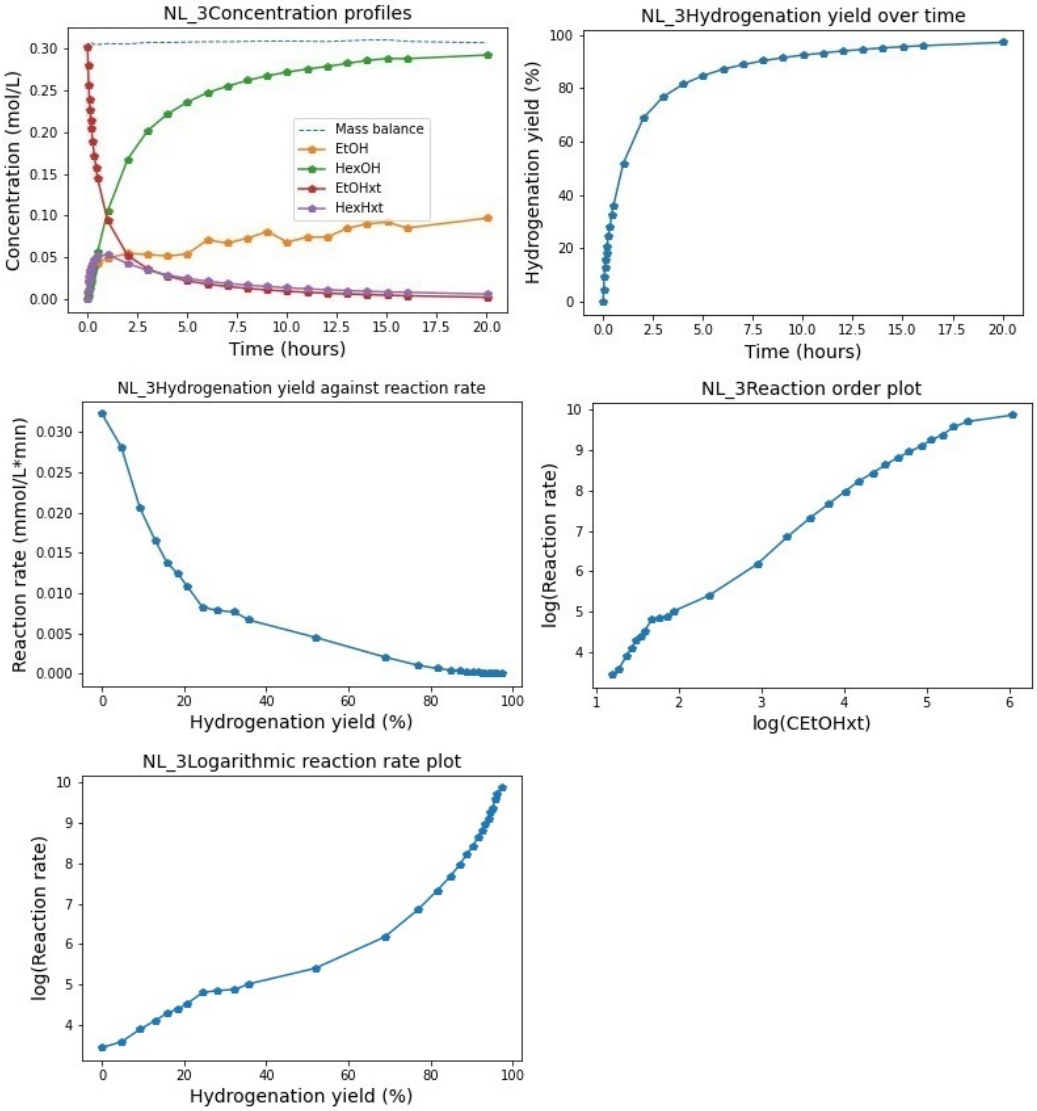

NL_1Hydrogenation yield over time
Hydrogenation yield (%)
Time (hours)

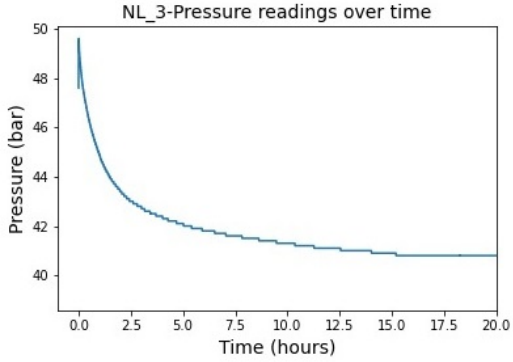

NL_1Hydrogenation yield against reaction rate
Reaction rate (mmol/L*min)
Hydrogenation yield (%)

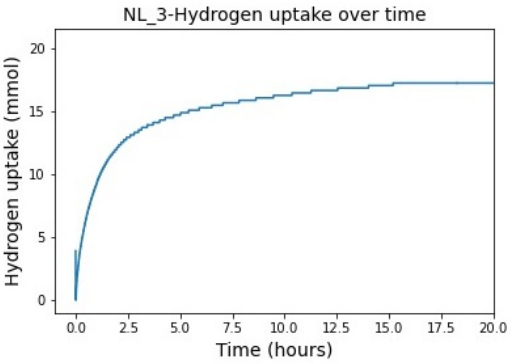

NL_1Reaction order plot
log(Reaction rate)
log(CEtOHxt)

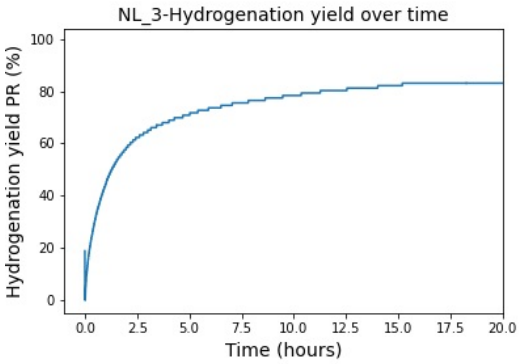

NL_1Logarithmic reaction rate plot
log(Reaction rate)
Hydrogenation yield (%)

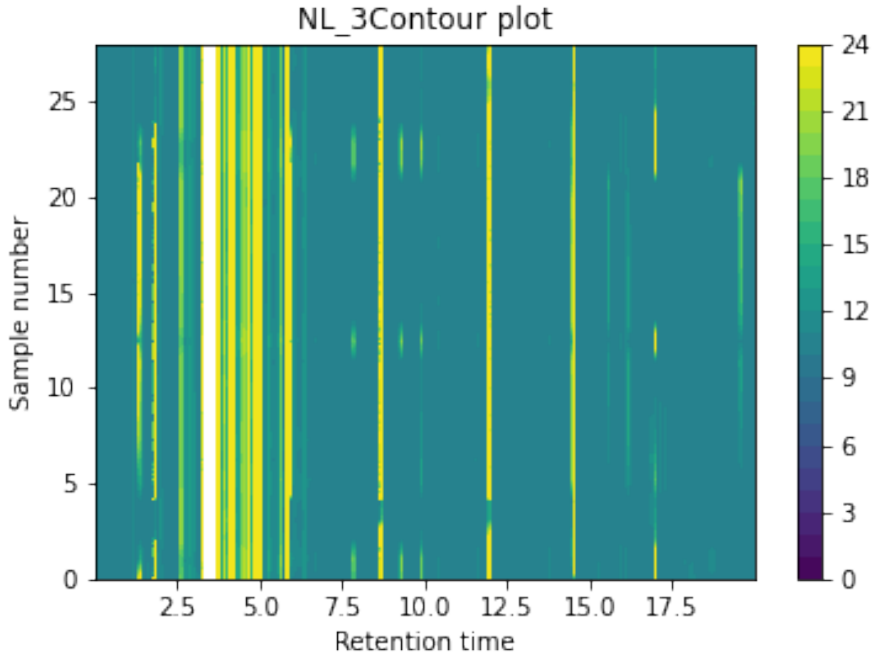

NL_1Contour plot
Sample number
Retention time
0
5
10
15
20
25
2.5
5.0
7.5
10.0
12.5
15.0
17.5
0
3
6
9
12
15
18
21
24

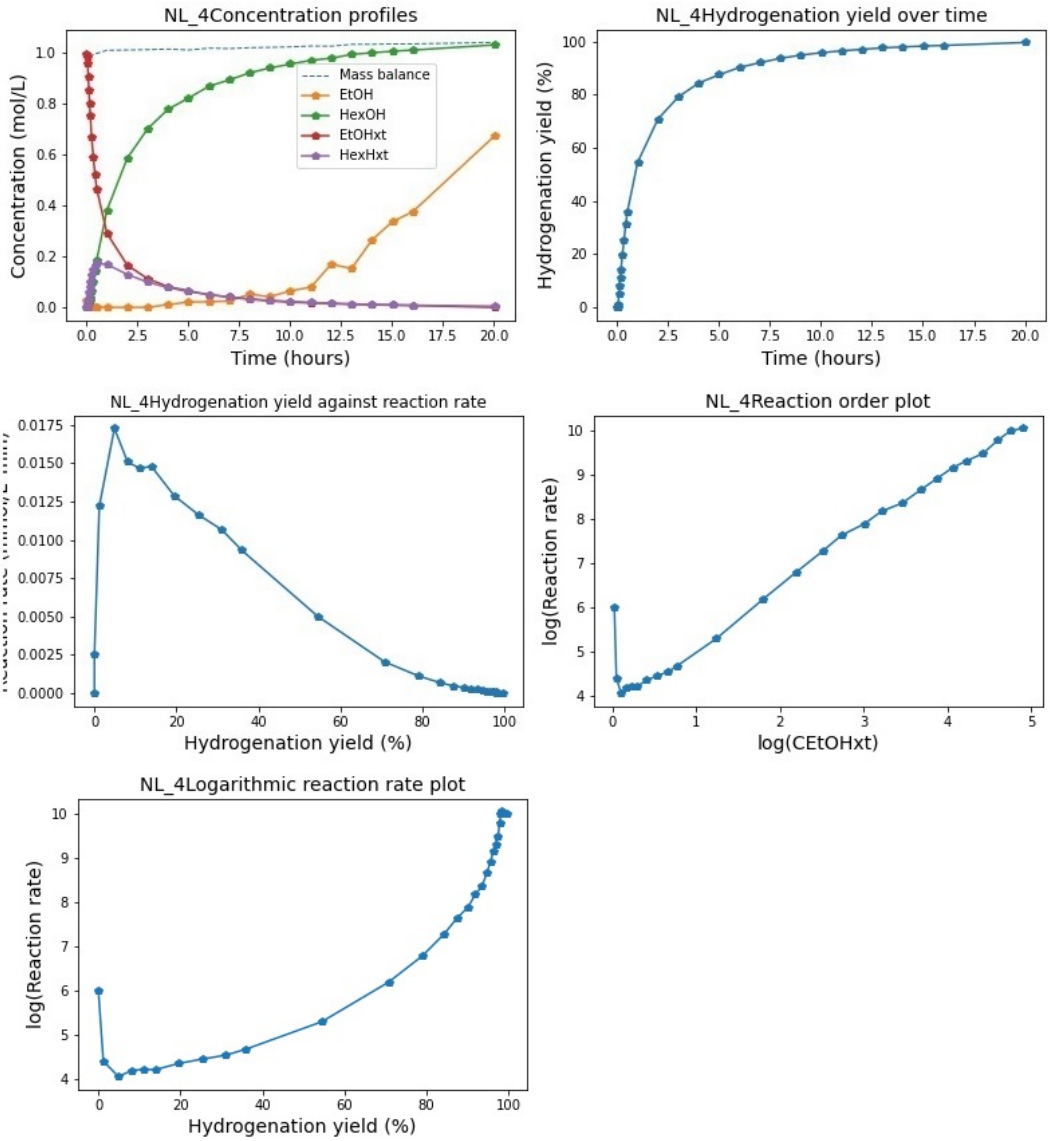

NL_3Concentration profiles
Concentration (mol/L)
Time (hours)
Mass balance
EtOH
HexOH
EtOHxt
HexHxt
NL_3Hydrogenation yield over time
Hydrogenation yield (%)
Time (hours)
NL_3Hydrogenation yield against reaction rate
Reaction rate (mmol/L*min)
Hydrogenation yield (%)
NL_3Reaction order plot
log(Reaction rate)
log(CEtOHxt)
NL_3Logarithmic reaction rate plot
log(Reaction rate)
Hydrogenation yield (%)

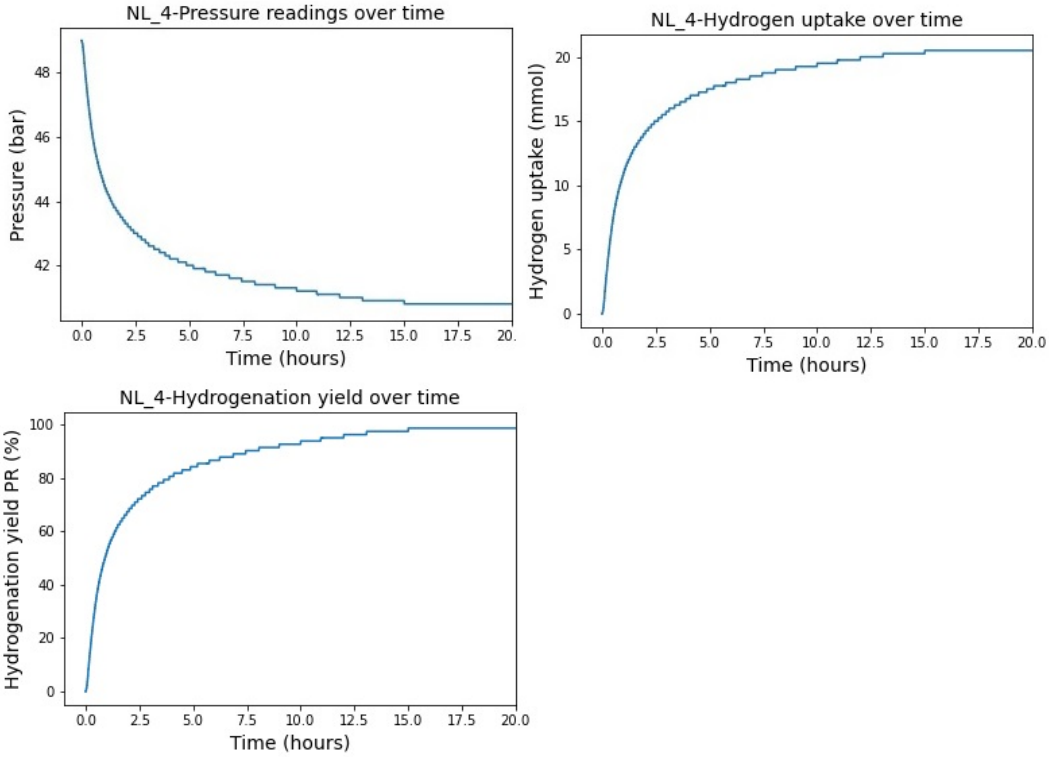

NL_3-Pressure readings over time
Pressure (bar)
Time (hours)

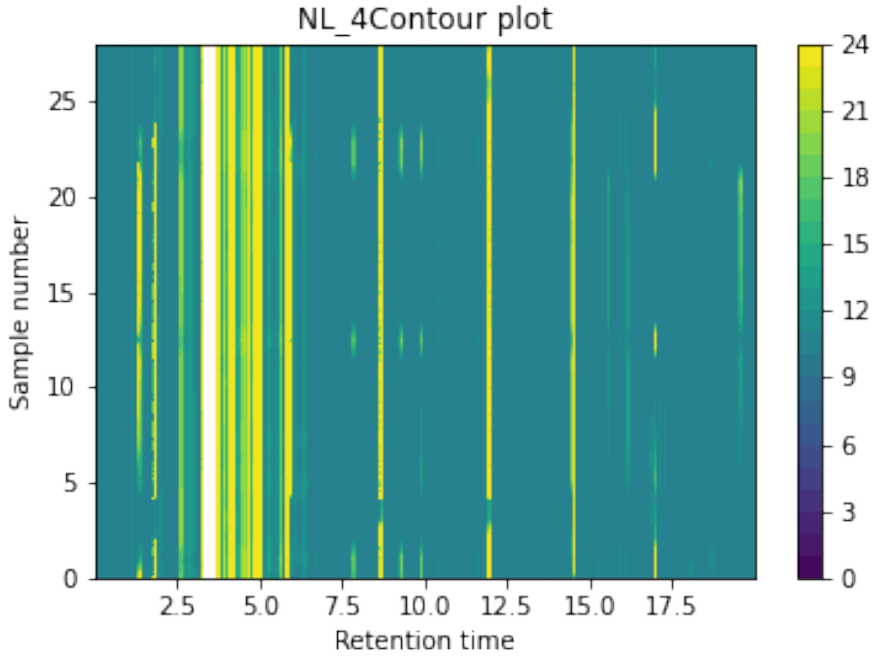

NL_3-Hydrogen uptake over time
Hydrogen uptake (mmol)
Time (hours)

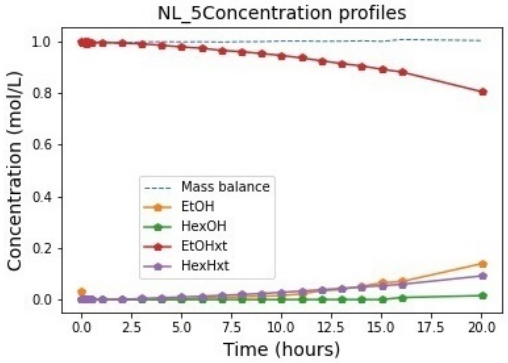

NL_3-Hydrogenation yield over time
Hydrogenation yield PR (%)
Time (hours)

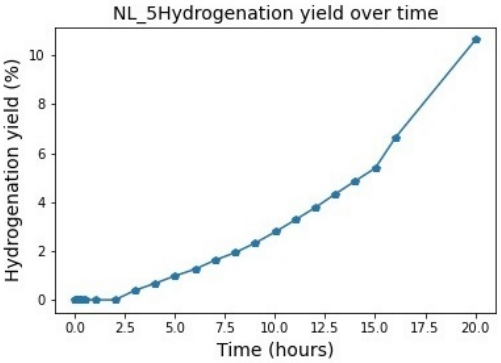

NL_3Contour plot
Sample number
Retention time

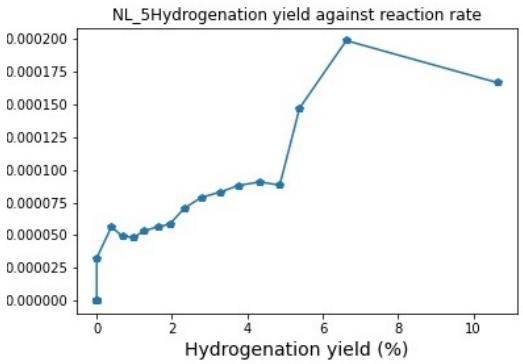

NL_4Concentration profiles
Concentration (mol/L)
Time (hours)
Mass balance
EtOH
HexOH
EtOHxt
HexHxt
NL_4Hydrogenation yield over time
Hydrogenation yield (%)
Time (hours)
NL_4Hydrogenation yield against reaction rate
Hydrogenation yield (%)
NL_4Reaction order plot
log(Reaction rate)
log(CEtOHxt)
NL_4Logarithmic reaction rate plot
log(Reaction rate)
Hydrogenation yield (%)

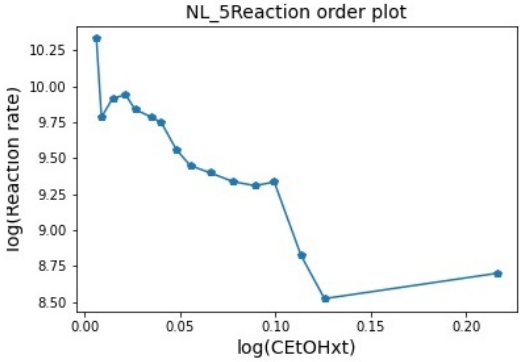

NL_4-Pressure readings over time
Pressure (bar)
Time (hours)
NL_4-Hydrogen uptake over time
Hydrogen uptake (mmol)
Time (hours)
NL_4-Hydrogenation yield over time
Hydrogenation yield PR (%)
Time (hours)

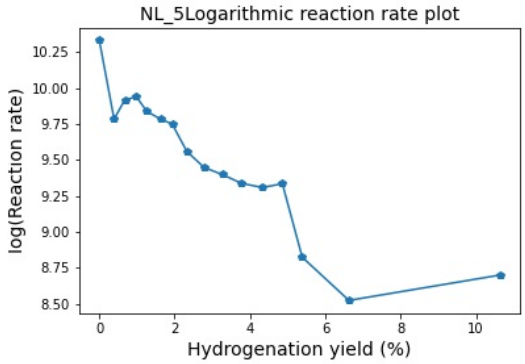

NL_4Contour plot
Sample number
Retention time

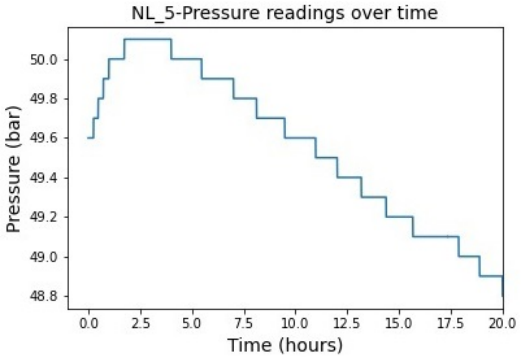

NL_5Concentration profiles
Concentration (mol/L)
Time (hours)
Mass balance
EtOH
HexOH
EtOHxt
HexHxt

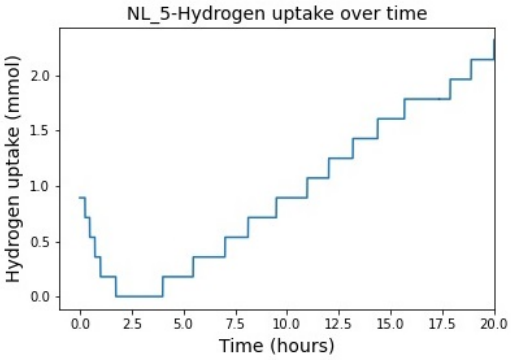

NL_5Hydrogenation yield over time
Hydrogenation yield (%)
Time (hours)

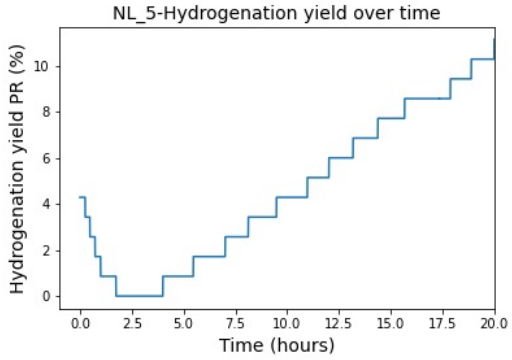

NL_5Hydrogenation yield against reaction rate
Hydrogenation yield (%)

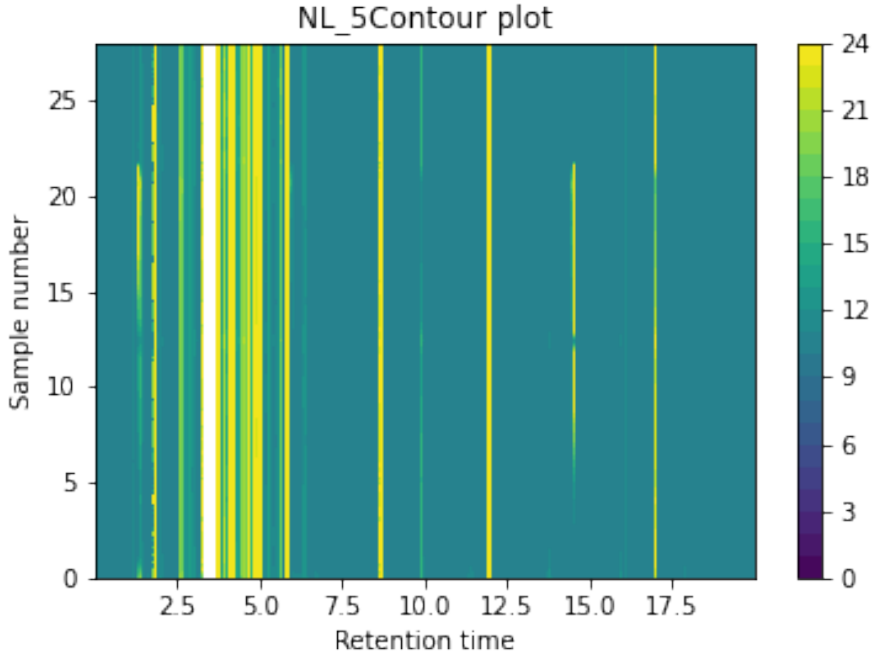

NL_5Reaction order plot
log(Reaction rate)
log(CEtOHxt)

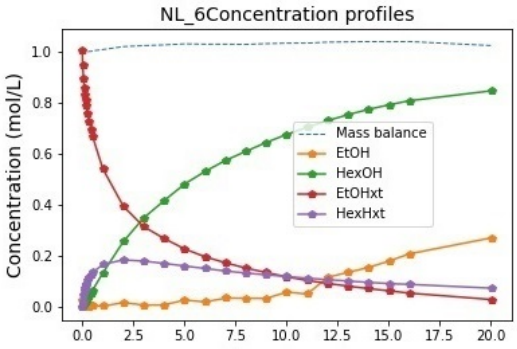

NL_5Logarithmic reaction rate plot
log(Reaction rate)
Hydrogenation yield (%)

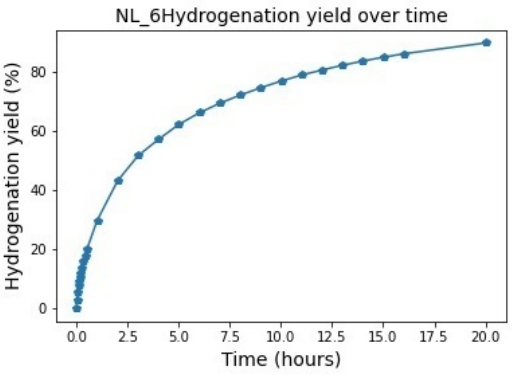

NL_5-Pressure readings over time
Pressure (bar)
Time (hours)

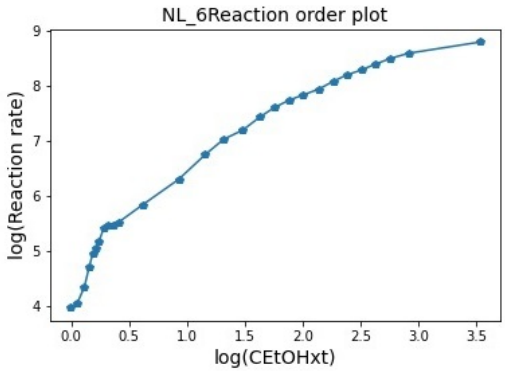

NL_5-Hydrogen uptake over time
Hydrogen uptake (mmol)
Time (hours)

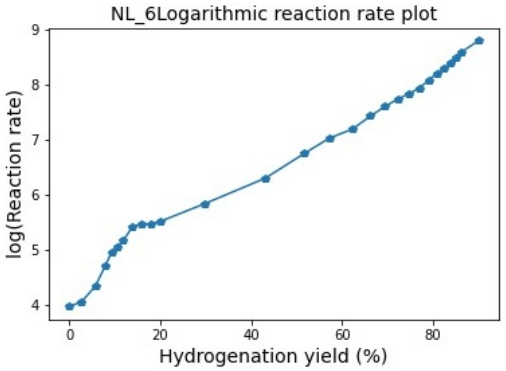

NL_5-Hydrogenation yield over time
Hydrogenation yield PR (%)
Time (hours)

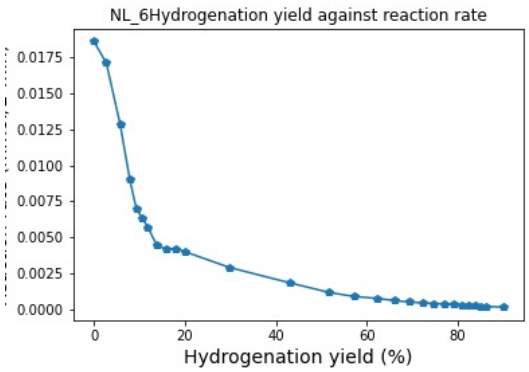

NL_5Contour plot
Sample number
Retention time

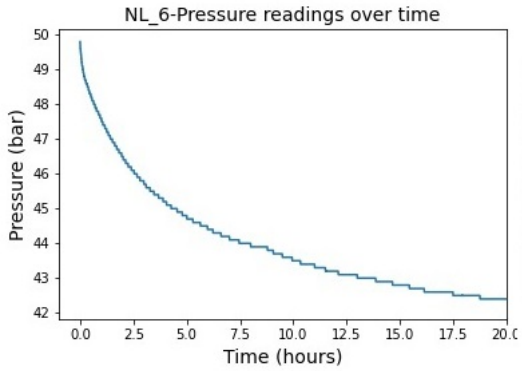

NL_6Concentration profiles
Concentration (mol/L)
Mass balance
EtOH
HexOH
EtOHxt
HexHxt

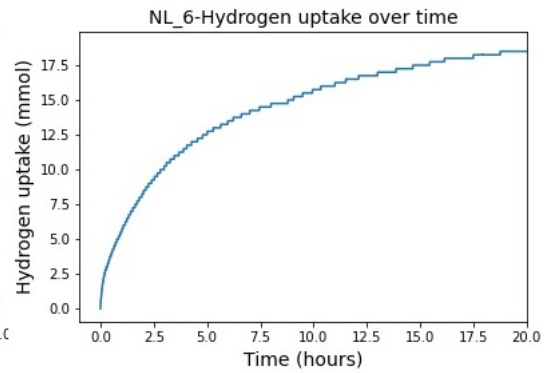

NL_6Hydrogenation yield over time
Hydrogenation yield (%)
Time (hours)

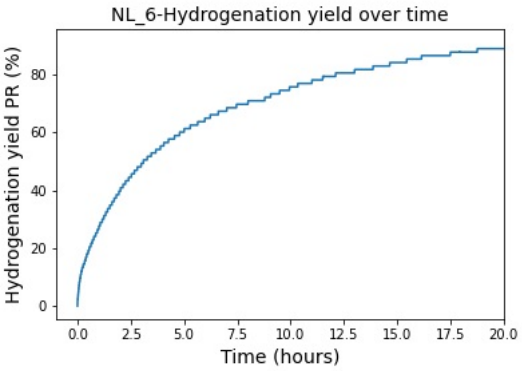

NL_6Reaction order plot
log(Reaction rate)
log(CEtOHxt)

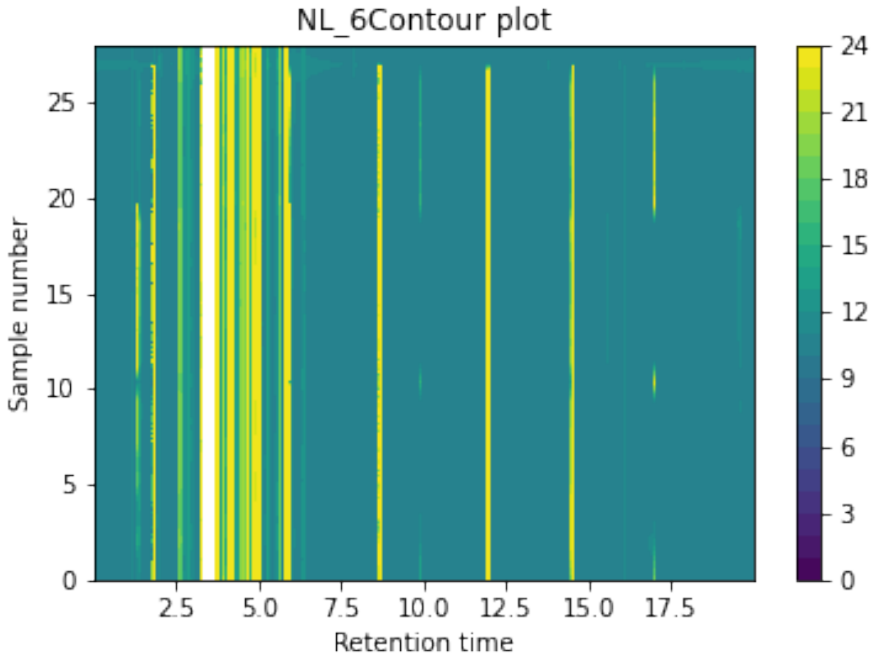

NL_6Logarithmic reaction rate plot
log(Reaction rate)
Hydrogenation yield (%)

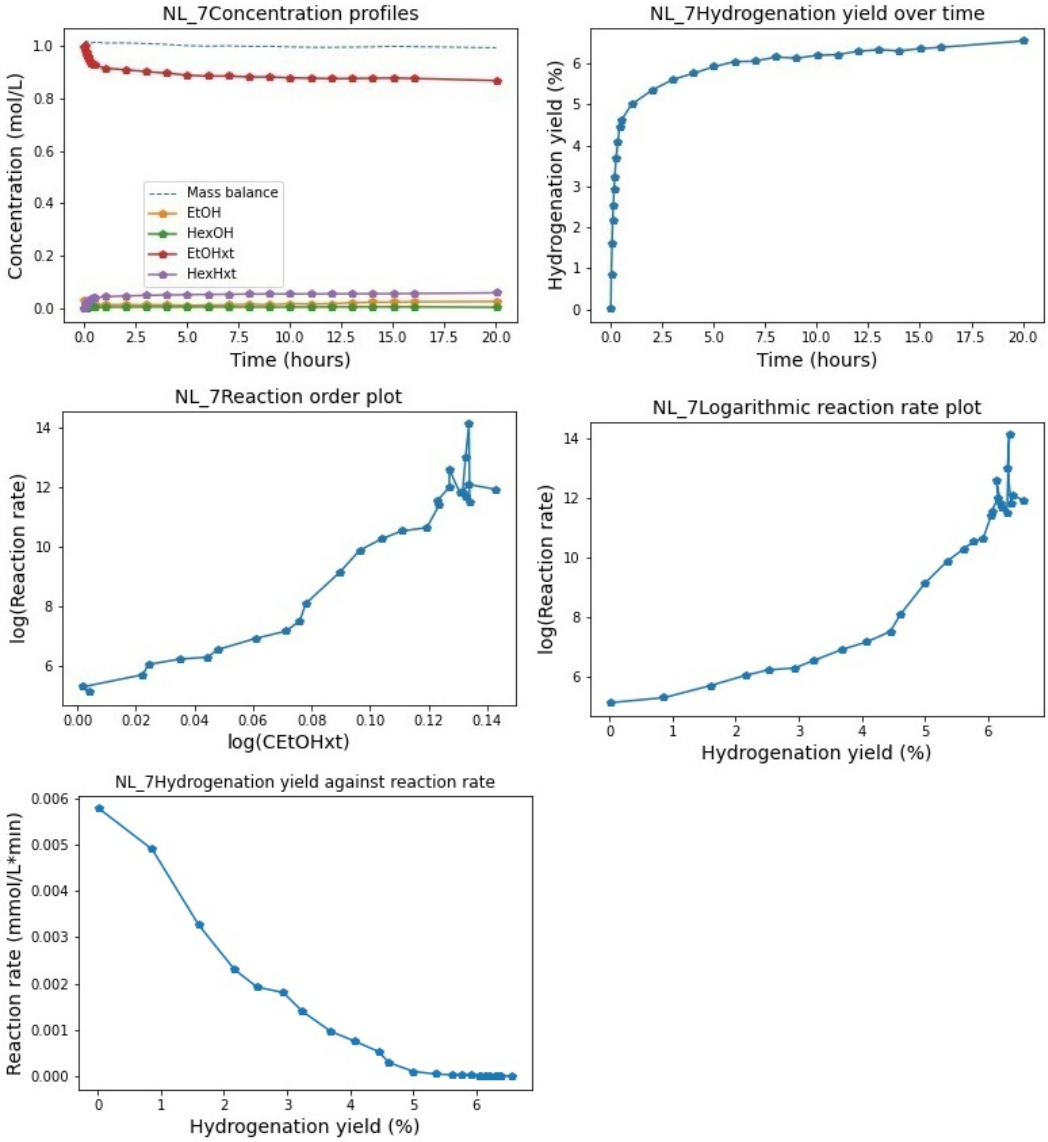

NL_6Hydrogenation yield against reaction rate
Hydrogenation yield (%)

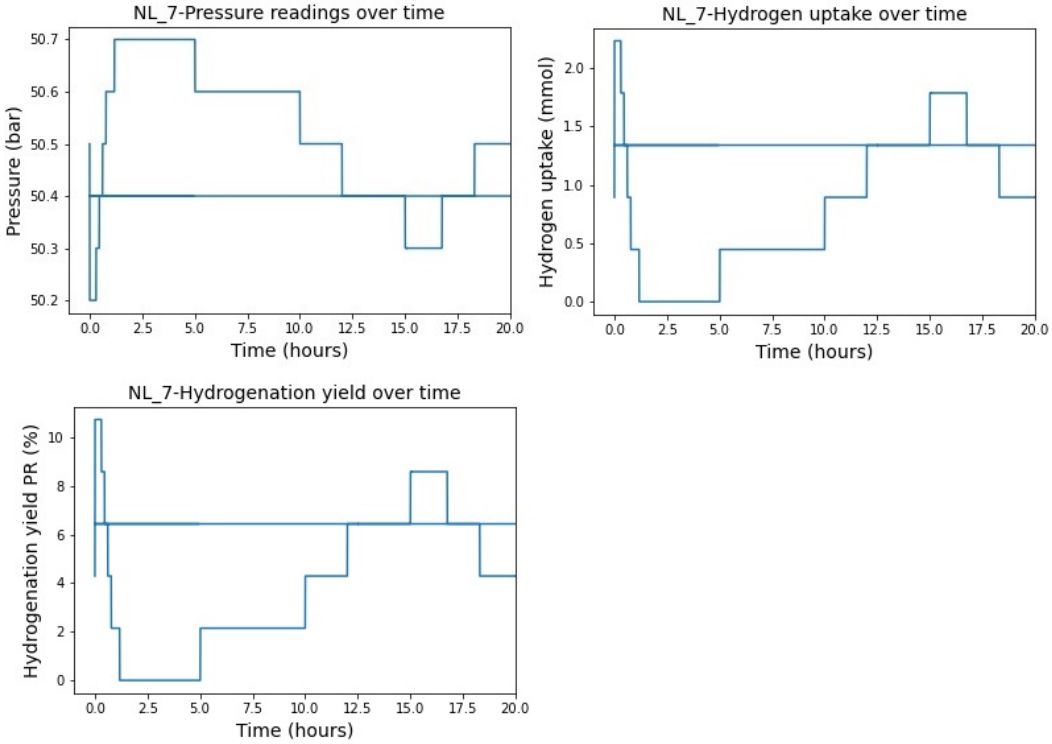

NL_6-Pressure readings over time
Pressure (bar)
Time (hours)

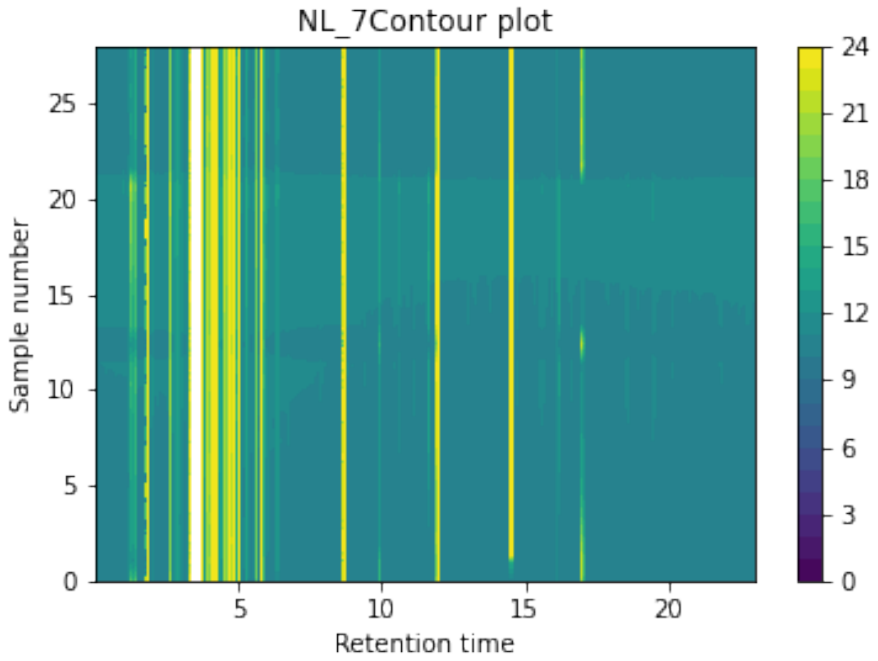

NL_6-Hydrogen uptake over time
Hydrogen uptake (mmol)
Time (hours)

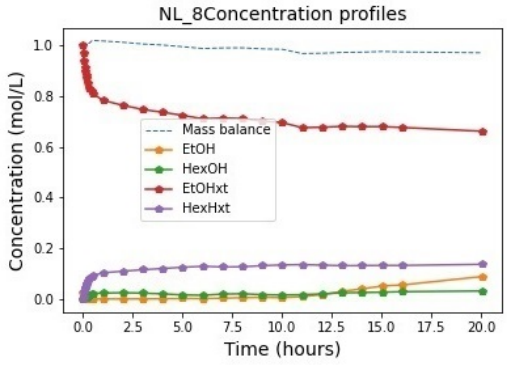

NL_6-Hydrogenation yield over time
Hydrogenation yield PR (%)
Time (hours)

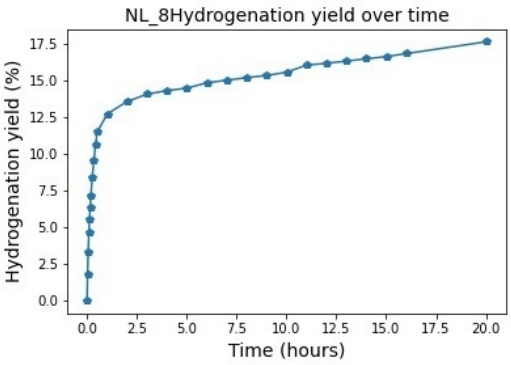

NL_6Contour plot
Sample number
Retention time

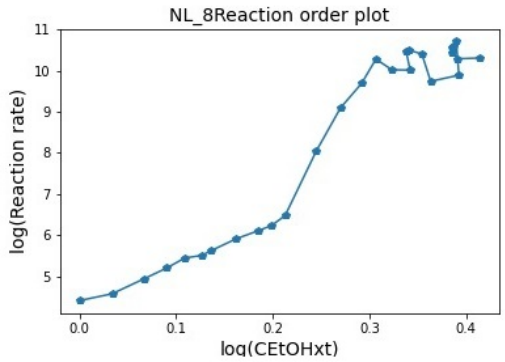

NL_7Concentration profiles
Concentration (mol/L)
Time (hours)
Mass balance
EtOH
HexOH
EtOHxt
HexHxt
NL_7Hydrogenation yield over time
Hydrogenation yield (%)
Time (hours)
NL_7Reaction order plot
log(Reaction rate)
log(CEtOHxt)
NL_7Logarithmic reaction rate plot
log(Reaction rate)
Hydrogenation yield (%)
NL_7Hydrogenation yield against reaction rate
Reaction rate (mmol/L*min)
Hydrogenation yield (%)

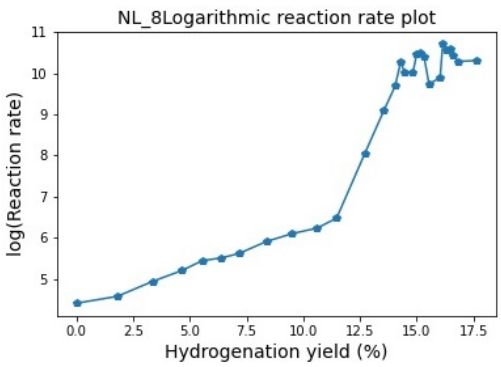

NL_7-Pressure readings over time
Pressure (bar)
Time (hours)
NL_7-Hydrogen uptake over time
Hydrogen uptake (mmol)
Time (hours)
NL_7-Hydrogenation yield over time
Hydrogenation yield PR (%)
Time (hours)

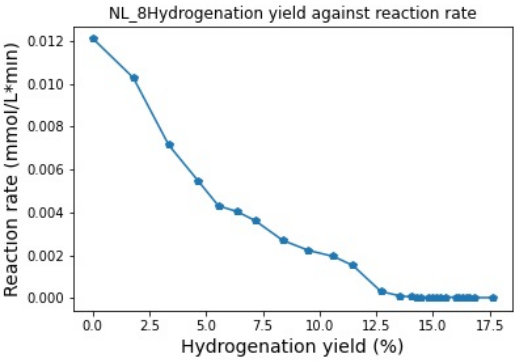

NL_7Contour plot
Sample number
Retention time

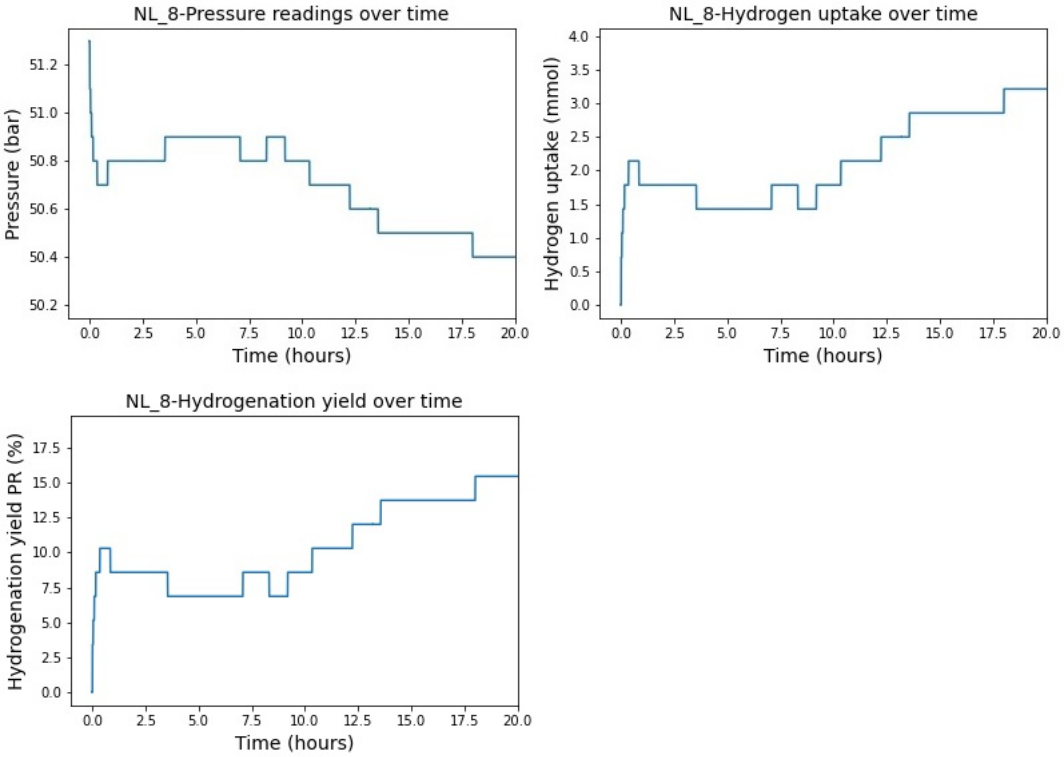

NL_8Concentration profiles
Concentration (mol/L)
Time (hours)
Mass balance
EtOH
HexOH
EtOHxt
HexHxt

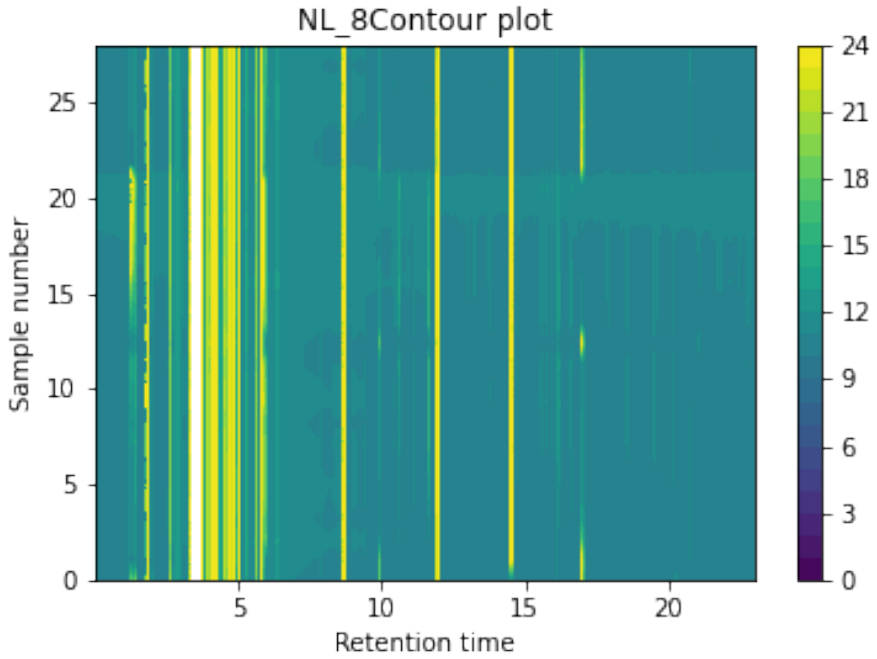

NL_8Hydrogenation yield over time
Hydrogenation yield (%)
Time (hours)

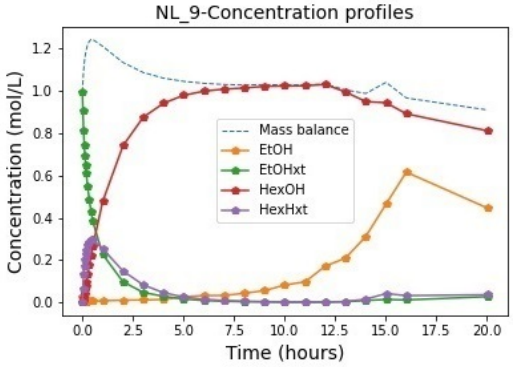

NL_8Reaction order plot
log(Reaction rate)
log(CEtOHxt)

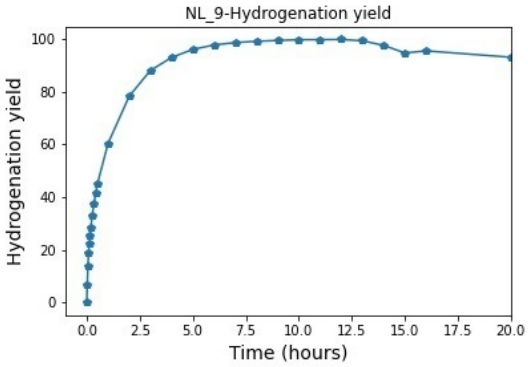

NL_8Logarithmic reaction rate plot
log(Reaction rate)
Hydrogenation yield (%)

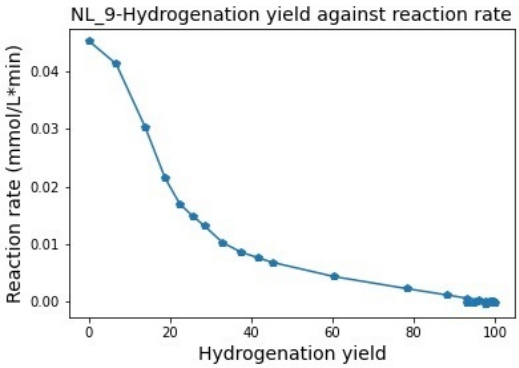

NL_8Hydrogenation yield against reaction rate
Reaction rate (mmol/L*min)
Hydrogenation yield (%)

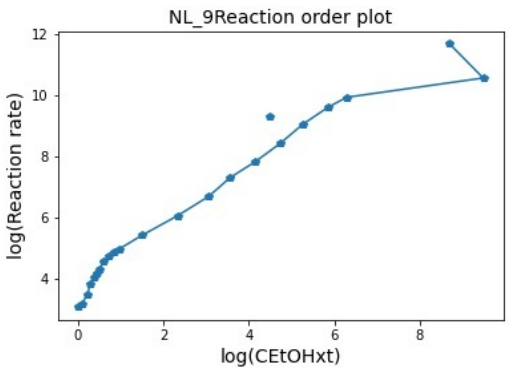

NL_8-Pressure readings over time
Pressure (bar)
Time (hours)
NL_8-Hydrogen uptake over time
Hydrogen uptake (mmol)
Time (hours)
NL_8-Hydrogenation yield over time
Hydrogenation yield PR (%)
Time (hours)

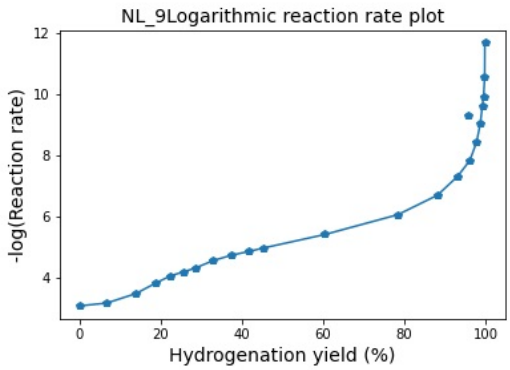

NL_8Contour plot
Sample number
Retention time

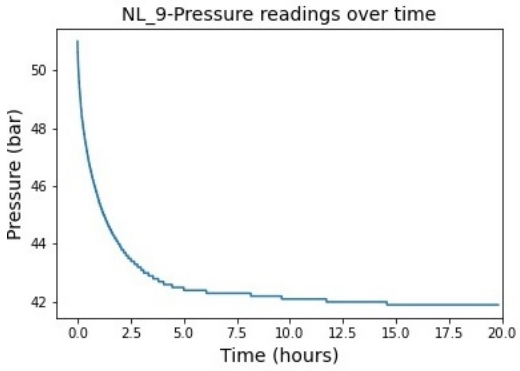

NL_9-Concentration profiles
Concentration (mol/L)
Time (hours)
Mass balance
EtOH
EtOHxt
HexOH
HexHxt

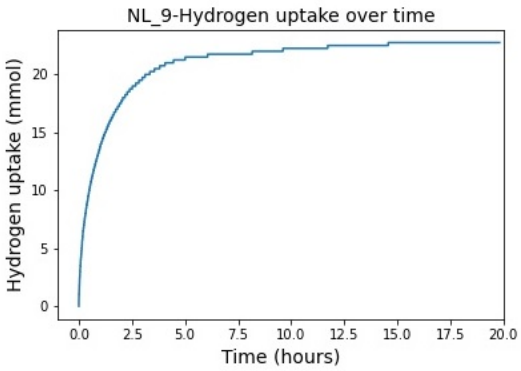

NL_9-Hydrogenation yield
Hydrogenation yield
Time (hours)

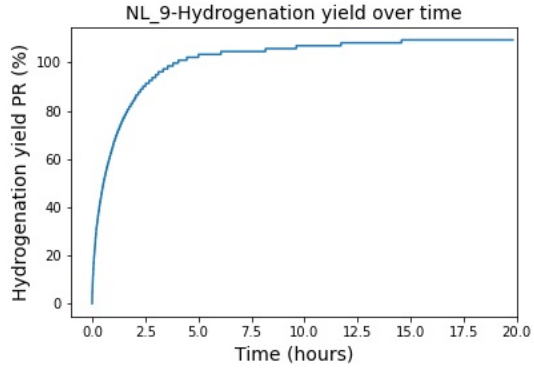

NL_9-Hydrogenation yield against reaction rate
Reaction rate (mmol/L*min)
Hydrogenation yield

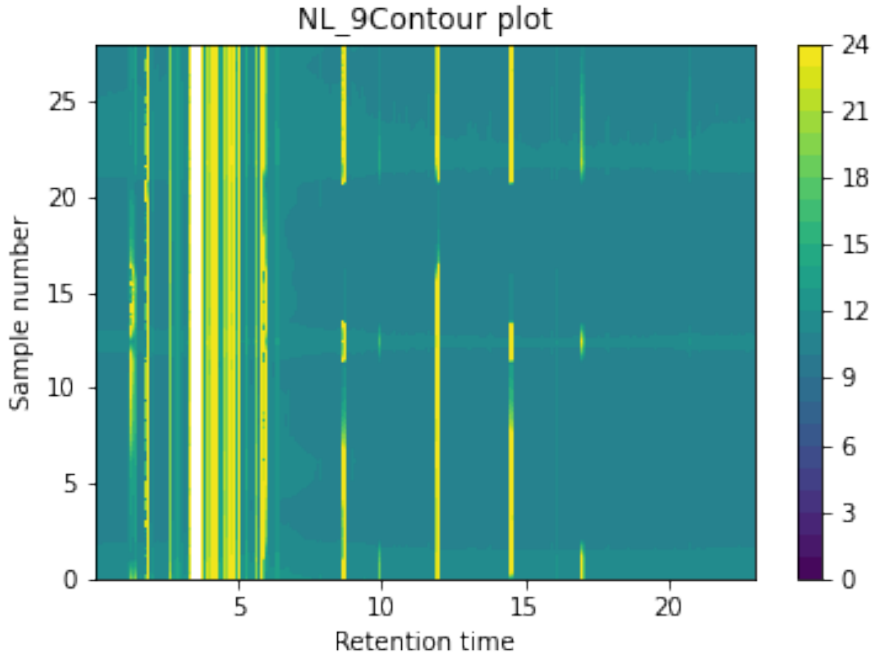

NL_9Reaction order plot
log(Reaction rate)
log(CEtOHxt)


NL_9Logarithmic reaction rate plot
-log(Reaction rate)
Hydrogenation yield (%)


NL_9-Pressure readings over time
Pressure (bar)
Time (hours)


NL_9-Hydrogen uptake over time
Hydrogen uptake (mmol)
Time (hours)


NL_9-Hydrogenation yield over time
Hydrogenation yield PR (%)
Time (hours)


NL_9Contour plot
Sample number
Retention time