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Solvent-Free Synthesis of Glycidyl Ethers

Investigating Factors Influencing the Yield of Alkyl Glycidyl Ethers

Master's Thesis in Materials Chemistry and Nanotechnology

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Abstract

Surfactants are a widely used group of chemicals. With a range of applications from soaps to paints and from hygiene products to asphalt they are one of the most diverse product groups available. AkzoNobel in Stenungsund uses glycidyl ethers as intermediates in the productions of some of their surfactants. These glycidyl ethers are produced with some hazardous compounds, which make the handling complicated and after-treatment expensive. It would therefore be very beneficial to implement a new less hazardous reaction to replace the existing one.

A new reaction presented by Lee et al. has shown promising results. No water or organic solvents are used, instead a solid base and a phase transfer catalyst are involved in the reaction of a fatty alcohol and epichlorohydrin. This reaction opens up new possibilities. For example, the separation of a solid base from the liquid product is a convenient way of purifying the glycidyl ether.

In this thesis, the reaction is investigated by examining the different factors that may influence the yield of the glycidyl ether. The by-products formed in the reaction are identified, and two different alcohols were used; 1-decanol and 1-tetradecanol. Different bases, temperatures, reaction times and concentrations were tested to maximize the product yield. Two Design of Experiment studies were performed to investigate the influence of multiple factors at once.

The results are promising for both of the alcohols used in the reaction, since both of them gives a yield of above 75%. The tetradecanol seems to give a higher product yield in the intervals used in this thesis, and will be interesting for future work. The reaction is clearly possible to optimize, and this was done to some extent. Further optimization should be possible, though.

Keywords: Glycidyl ether, solvent-free, design of experiments, phase transfer catalysis, optimization

Contents

1 Introduction

Today surfactants are used in a wide range of applications, from cleaning products to paints. Their vast opportunities makes them interesting for a number of industries, and their use increases constantly. One area where surfactants have played a significant part is in the recovery of ore from minerals.

The surfactants are used as floatation agents to separate the hydrophilic and the hydrophobic material, forming a froth which is easily separated from the suspension. This increases the efficiency of the separation, making it possible to use ores that previously were discarded. The froth floatation process has, because of its benefits in the mining industries, spread to other industries. An example is the waste water treatment in oil refineries, where process water contaminated with oil is cleaned using a similar technique.

The surfactants for the froth flotation can be produced using glycidyl ethers as intermediates. Glycidyl ethers are compounds with several applications. One of the largest is as a component of epoxy resins, but their reactive epoxide group makes them suitable for further processing. This means that a defined surfactant tail can be paired with the head group of choice, making it possible to optimize the head group for each application. The structure of a general glycidyl ether is shown in figure 1.

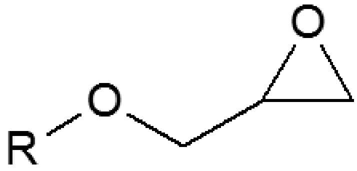

Figure 1: The general structure of a glycidyl ether.

1.1 Background

AkzoNobel in Stenungsund is producing glycidyl ethers using the highly corrosive tin(IV)chloride as a catalyst to react epichlorohydrin with a fatty alcohol. The reaction also involves a concentrated alkali solution, and the waste water from the process is in need of extensive treatment before it is sufficiently clean.

The water treatment is expensive, and large economical benefits can be achieved if the reaction is substituted for another, with similar yields but with cheaper after-treatment. Lee et al. have investigated and patented another possible reaction, without using any solvent or tin(IV)chloride. [1] Instead, they use solid alkali hydroxides with a phase transfer catalyst, all in the environment of the liquid fatty alcohol. Their results are promising, and a successful implementation in the process in Stenungsund could be very beneficial for AkzoNobel.

1.2 Aim

The aim of this thesis is to examine if a new synthesis route for glycidyl ether could bring the yield to an acceptable level of about 80%. This is done by investigating the influence of different reaction conditions, and their combined influence using a Design of Experiments (DoE) study. Factors that will be examined are temperature, time, catalyst concentration, base composition and reactant concentrations.

1.3 Limitations

To be able to investigate the different reaction conditions' influence thoroughly, only one phase transfer catalyst (tetrabutylammonium bromide) will be used. There will not be a detailed investigation of the alcohol chain length dependency. Instead, only 1-tetradecanol and 1-decanol will be tested as the fatty alcohol reactant.

2 Theory

In the following chapters the different components of the glycidyl ether reaction are described, as well as some of the applications of the compound.

2.1 Surfactants

Surfactants are surface active agents which are used to alter the properties at different interfaces. [2] They are used to lower the interfacial tension by having two parts: one part attracted to each phase. The general structure of a surfactant can be seen in figure 2. [3]

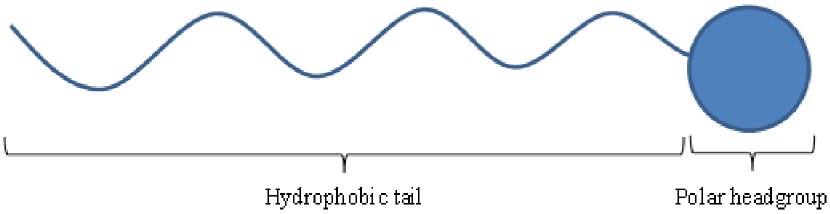

Figure 2: The general structure of a surfactant.

Surfactants can be found in a number of different areas. Soaps and detergents uses surfactants to remove dirt, but a lot of industrial processes also use surfactants. One example is froth flotation, discussed in chapter 2.1.1.

2.1.1 Froth Flotation

Froth flotation is a process where valuable ores are separated from unwanted minerals. The technique used is to selectively hydrophobize one mineral in the presence of another. Blowing air through the suspension will create a foam, enriched in the hydrophobized mineral, that would coalesce fast without surfactants. [4] The flotation can be direct, where the foam contains the desired mineral, or reversed, where the unwanted mineral is removed with the foam. This provides a relatively cheap and easy method of separating minerals. [5] [6] [7]

2.2 Phase Transfer Catalysts

A phase transfer catalyst (PTC) is often a quaternary ammonium salt, but there are also examples of crown ethers and polyethers, among other compounds, that may act as a PTCs. The main purpose of a PTC is that it should show affinity for both phases in the system, thereby making it possible for reactants in the different phases to react with each other. [8] [9]

PTCs are often used for alkylations and other reactions in liquid-liquid systems (LLPTC). [10] [11] Another application is in the use of a solid phase and a liquid phase (SLPTC), where the solid is insoluble in the liquid. An example is the use of a solid base, where the organic compound in solution is deprotonated at the interface of the base and then transported by the PTC into the bulk liquid, while the charge is protected by the catalyst.

2.3 Epoxides and Glycidyl Ethers

The epoxide group is highly reactive because of the built in strain in the structure. The general structure of an epoxide is shown in figure 3. Due to the high reactivity of the group, epoxides are used in a number of applications. An example is as adhesives and as monomers in polymer fabrication. [12] [13] [14]

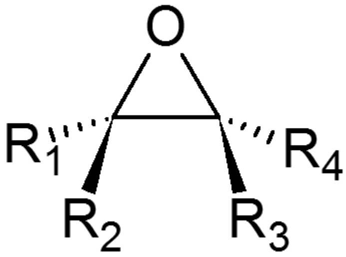

Figure 3: The general structure of an epoxide.

The protons of the epoxide group show three distinctive peaks in an NMR spectrum. This can be seen in the spectrum of epichlorohydrin in figure 4. The three peaks between 2.5 and 3.1 ppm correspond to the protons of the epoxide group. These can be used to identify an epoxide group in a sample.

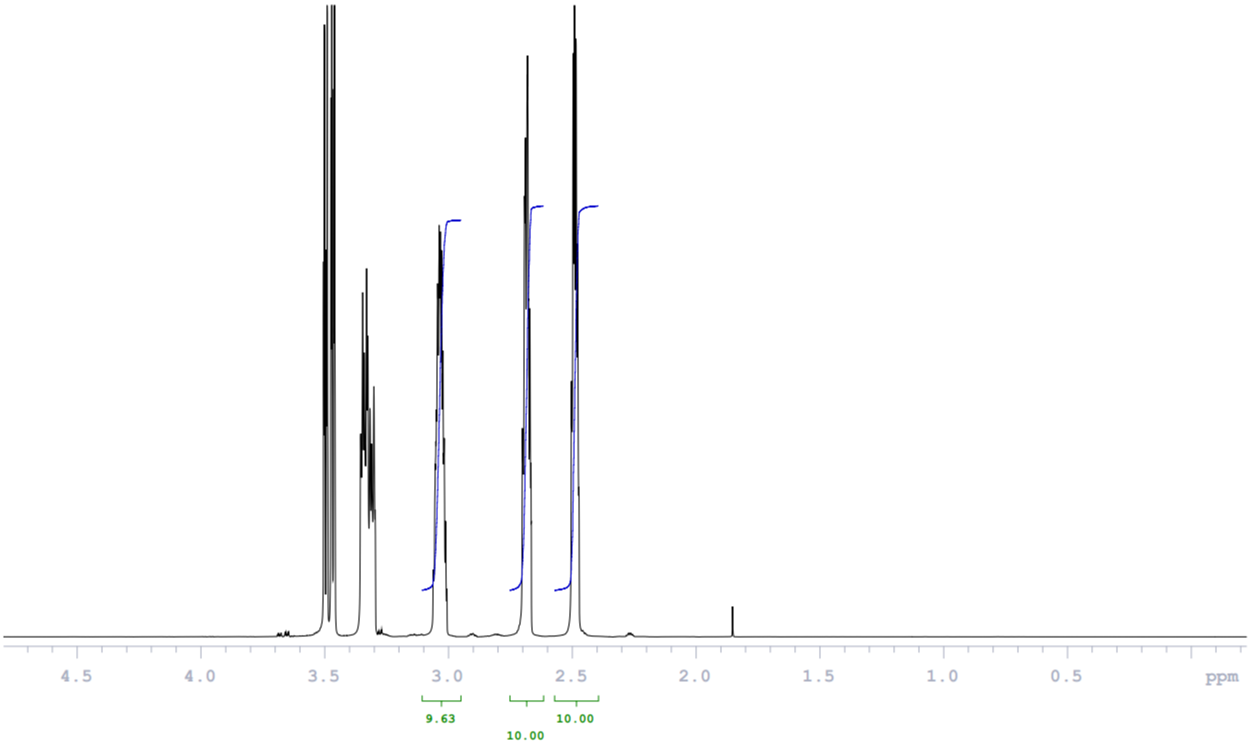

Figure 4: The NMR spectrum of epichlorohydrin. The three peaks between 2.5 and 3.1 ppm correspond to the protons of the epoxide group.

One way of taking advantage of the reactivity of the epoxide group is in the form of glycidyl ethers. Glycidyl ethers are compounds with the functional group shown in figure 1. The glycidyl ethers can, as other epoxides, be used in adhesives, but also as intermediates in surfactant production. The R group of the glycidyl ether can be varied according to the desired application, and the epoxide group can be further reacted with a polar headgroup, forming a surfactant. A way of synthesizing glycidyl ethers is discussed further in chapter 2.3.1.

2.3.1 Synthesis of Glycidyl Ethers

Lee et al. have proposed a reaction where no water or organic solvents are used in the synthesis of an alkyl glycidyl ether. Instead, a solid alkali hydroxide and a PTC is used for the reaction of a fatty alcohol and epichlorohydrin. The reaction takes place in the liquid alcohol, and the unreacted base can be removed along with its salt by filtering the mixture after the reaction. The reaction is described in figure 5. [1] [15]

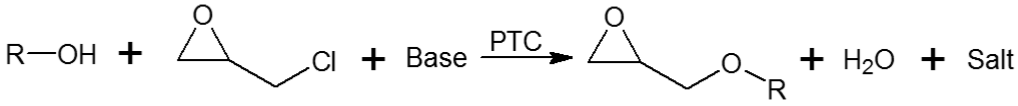

Figure 5: The reaction used for synthesis of glycidyl ether. The R group is in this case a straight alkyl chain.

The base is used to deprotonate the alcohol. Then the PTC transfer the charged alcohol derivative to the liquid bulk, where the reaction with epichlorohydrin takes place. A suggestion of the mechanism of the reaction is that two concerted S$_N$2 reactions occur during the ring opening and closing of the epoxide group. This mechanism is shown in figure 6. In this case the deprotonated alcohol act as a nucleophile, and the chloride ion as a leaving group.

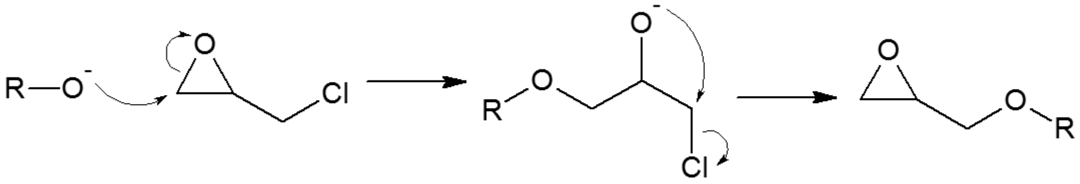

Figure 6: The proposed mechanism for the synthesis of a glycidyl ether, through concerted S$_N$2 reactions.

2.4 Gas Chromatography

Gas chromatography (GC) is used for the analysis of compounds that can be vaporized. The provided sample is diluted and fed to the GC column through an injector. The column is located inside an oven and coated with a stationary phase, often a polymer or inert liquid. [16]

A carrier gas acts as the mobile phase and transports the sample through the column. In the column, the compounds of the sample interacts with the stationary phase in different ways, and are therefore fractioned by their affinity for the stationary phase. [17]

The detectors used varies depending on the analysis desired. Two of the most common are the Mass Spectrometer (MS) and the Flame Ionization Detector (FID). These are described in chapters 2.4.1 and 2.4.2 respectively.

2.4.1 Mass Spectrometry

A mass spectrometer ionizes the molecules, and accelerates these with an electromagnetic field. The ions will have different mass and charge, and depending on their m/z ratio, they will have different paths. In a Time-of-Flight (TOF) detector, this ratio can be determined by measuring the time of flight for the ions: At a certain field strength, the kinetic energy of all ions with the same charge is the same. Therefore, the mass of an ion determines its velocity. With a detector at a known distance, this velocity can be calculated, and translated to the m/z ratio. [17]

2.4.2 Flame Ionization Detector

The flame ionization detector provides a cheap and simple analysis tool for organic compounds. It uses a hydrogen flame to form ions of the compound during its combustion. These ions can be detected using two electrodes with a potential difference, since the ions create a current between them. This current is roughly proportional to the amount of carbon in the sample. [17]

A problem with the FID is that all compounds have slightly different response factors. Another factor to consider is that the FID is sensitive to mass rather than concentration since the number of carbon atoms are measured. This means that a larger compound will give rise to a larger signal than a small compound at the same concentration.

2.5 Nuclear Magnetic Resonance Spectroscopy

Nuclear magnetic resonance (NMR) spectroscopy is an analysis method where the spin transitions of the sample is used. A nucleus with an odd number of protons and/or neutrons will have a magnetic moment because of their spin and charge. The two most commonly used isotopes are ^{13}C and ^{1}H.

An external electromagnetic field, with a frequency unique for the studied isotope, is used to change the orientation of the rotational axis of the nuclei. This will create an oscillating electrical field. The axis can align either with or against the applied field, where an alignment with the field is the orientation with the lowest energy. If a radio wave pulse of the same frequency as the field of the nuclei is applied, the nuclei aligned with the external field can absorb the energy and thus align against the field. The release of energy during the relaxation after the pulse can be measured and analysed. [18] [19]

The old way of applying the radio wave pulse was by scanning through a range of radio wave frequencies. The modern way of doing this is by sending a pulse of all the frequencies at once, exciting all the nuclei, and using a computer to analyse the response using Fourier transformation.

2.6 Design of Experiments

Design of Experiments uses a computer software to optimize a given system. An example is the release of hazardous substances in the combustion of fuel in a truck engine. Given a set of factors that can be changed, the software can model the outcome of different scenarios from the given responses. In this example such factors could be the amount of fuel and air in the combustion. The response would be the amount of the hazardous substances released to the air. [20]

Chemistry is another field where experimental design can be of interest. Since many different factors may influence the end result of a reaction, DoE studies provide an easy way of predicting the outcome of different set-ups. It can detect influences that might be hard to detect by changing one factor at a time, and it also limits the number of experiments compared to investigating each factor one by one, especially when there are many factors to consider.

The software requires data at each of the corners of an n-dimensional analogue of a cube, where n are the number of factors that is being changed, and also three replicates where the mean value of all factors are used. From these data, a model can be fitted, and the reproducibility calculated. The statistical terms R2 and Q2, along with the model validity, is also calculated for each response. The representation of the data points in a three-dimensional (n=3) DoE study can be seen in figure 7.

The reproducibility compares the variation of the three replicates to the variability of the model. This indicates if the reaction is difficult to predict, since a low reproducibility means that different results are obtained despite using the same reaction conditions. A possible solution to a low reproducibility is therefore a more robust reaction set-up. The model validity indicates if there are statistically significant problems in the model. These can be because of for example outliers or a bad model fit.

The R2 value shows the fit of the model, whereas the Q2 value estimates the precision of future prediction. Of these two, the Q2 value is always the best indicator of a good model, since R2 can be forced to fit the provided data, without predictive value. In a good model, the R2 value will be close to the Q2 value. The values of a good model, for each of the parameters, can be seen in table 1. [20]

To improve the model, insignificant model parameters should be removed prior to the fitting. Figure 8 shows an example of significant and insignificant parameters of the model. In this case, the temperature, catalyst concentration and reaction time are significant parameters, whereas the squared time and squared catalyst concentration are insignificant.

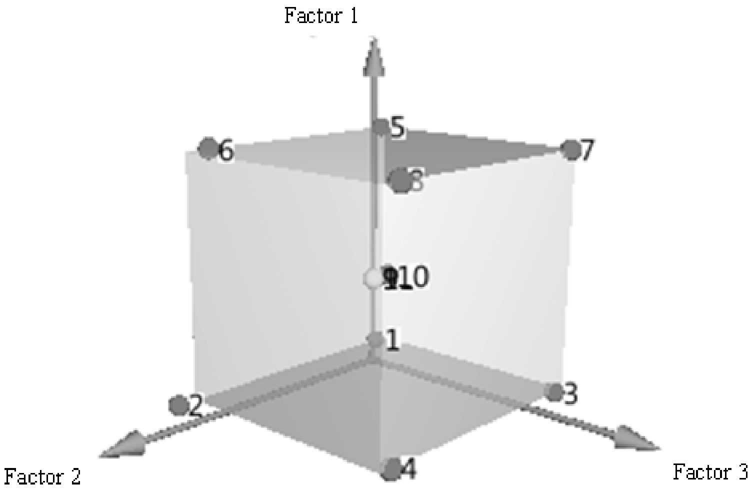

Figure 7: The data points used in a three-dimensional Design of Experiments study.

Table 1: Values of four different parameters indicating a good model.

Parameter	Value for a good model
R2	≫0.5
Q2	>0.5
Model Validity	≫0.25
Reproducibility	>0.5

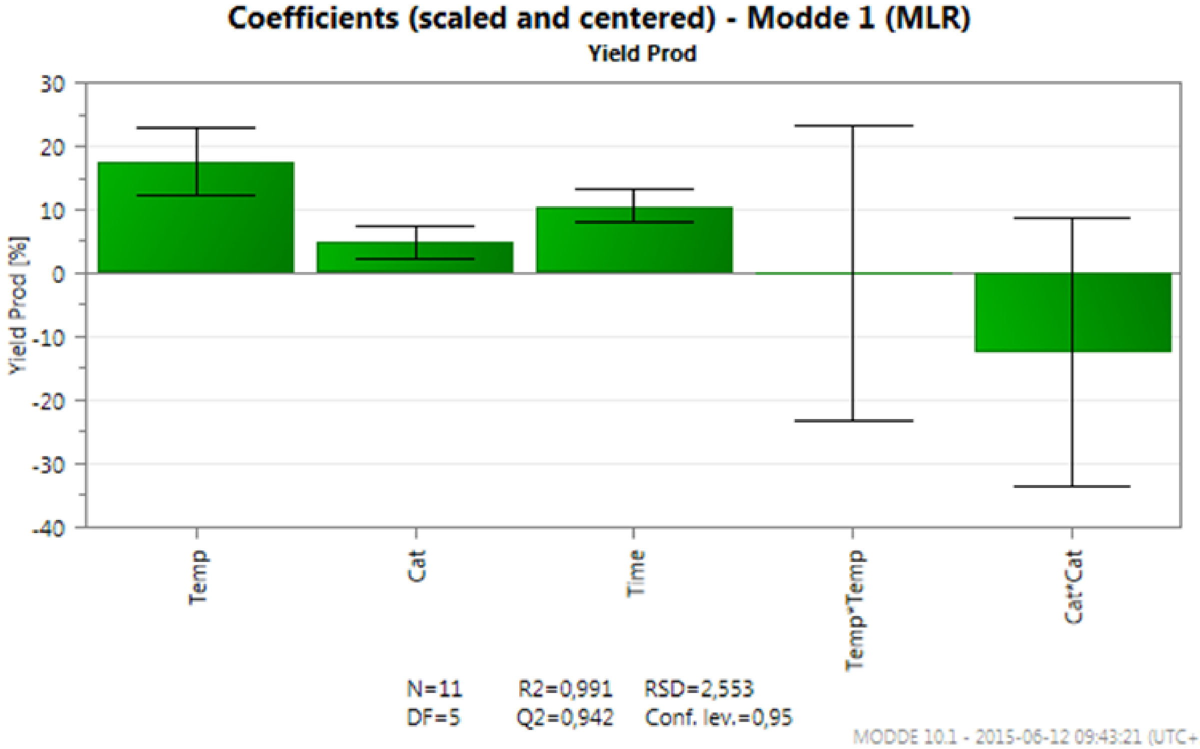

Figure 8: Presentation of some of the significant and insignificant parameters in a Design of Experiments study. In this case the temperature, catalyst concentration and reaction time are the significant parameters for the model.

3 Method

In the following chapters, the materials used for the experiments as well as the experimental approach are presented. The analytical techniques used, and the DoE studies, are explained.

3.1 Materials

The alcohols used in the experiments were 1-tetradecanol or 1-decanol. Epichlorohydrin (ECH) and tetrabutylammonium bromide (TBAB) were used in all of the reactions, whereas a series of different base compositions were used to determine its influence on the yield. The bases used were sodium hydroxide, potassium hydroxide, lithium hydroxide, calcium hydroxide, sodium carbonate and potassium carbonate. The bases were all in the form of pellets, but a powder of the potassium hydroxide was produced by grinding the pellets the pellets in a mortar to determine the influence of the base particle size. All of the compounds used in the experiments can be seen in table 2, along with their purities and manufacturers.

Table 2: The compounds used in the experiments, and their purities and manufacturers.

Compound	Purity (%)	Manufacturer
1-Tetradecanol	>97	Alfa Aesar
1-Decanol	99	Merck
Epichlorohydrin	>98	Fluka
Tetrabutylammonium Bromide	>98	Sigma-Aldrich
Sodium Hydroxide	>99	Merck
Potassium Hydroxidde	>85	Merck
Lithium Hydroxide	>98	Merck
Calcium Hydroxide	>96	Fluka
Sodium Carbonate	>99.5	Merck
Potassium Carbonate	>99	Merck

The molar equivalents of all the reactants compared to the alcohol are presented in table 3.

Table 3: Molar equivalents for the compounds used in the experiments compared to the alcohol.

Compound	Concentration
Alcohol	1 eq
Base	1.3-1.5* eq
TBAB	0.00025-0.05 eq
ECH	1-2 eq

*Note that the equivalent of $Ca(OH)_2$ was 0.75.

3.2 Experimental

The experiments were conducted as follows: 60.0 g of alcohol was added to a flanged flask with a five-necked lid fitted with an overhead stirrer, a thermometer and a reflux condenser. The flask was put in either a water bath or a heating mantle, and the stirrer was set to 60 rpm. When the heating mantle was used, the thermometer in the flask regulated the heat output of the mantle and when the water bath was used, the thermometer in the water regulated the heat output.

When the alcohol reached the reaction temperature, the TBAB and base were added. After this, the stirrer was set to 200 rpm, and the heating source was removed. The ECH was then added drop wise for 5-10 minutes, depending on the heat released in the reaction. The temperature was kept as close to the set temperature as possible, but in the case of a rapid heat increase, resulting in a temperature about 10℃ above the reaction temperature, a cold water bath was used to cool the outside of the flask. When the temperature dropped to the temperature setpoint, the heating source was applied again.

After a fixed time, the mixture was filtered through a Büchner funnel, and samples were taken for GC and NMR analysis. In the case of tetradecanol as starting material, the mixture hade to be heated during the filtration with a heating gun to stop it from solidifying. In this case the Büchner funnel was also pre-heated in an oven at 90℃. When a series of data points were collected over time for the same experiment, these GC and NMR samples were taken and filtered with a syringe. The resulting differences in ratio between the reactants are assumed to be negligible.

3.3 Gas Chromatography

The quantitative measurements of the reaction was done using GC-FID. One drop of sample (about 20 mg) was dissolved in 5 ml of dichloromethane and added to a vial. The GC-analysis was performed with an HP 5890 Series II chromatograph and an Agilent HP-1 column (100% dimethylpolysiloxane). The conditions are presented in table 4 and the temperature program is shown in figure 9.

Table 4: The conditions used for the GC analysis.

Column Gas	H_2
Stationary Phase	Dimethylpolysiloxane
Flow Pressure	40.00 kPa
Flow Temperature	80℃
Split Flow	22 ml/min
Column Length	12.00 m
Column ID	0.20 mm
Film thickness	0.33µmm

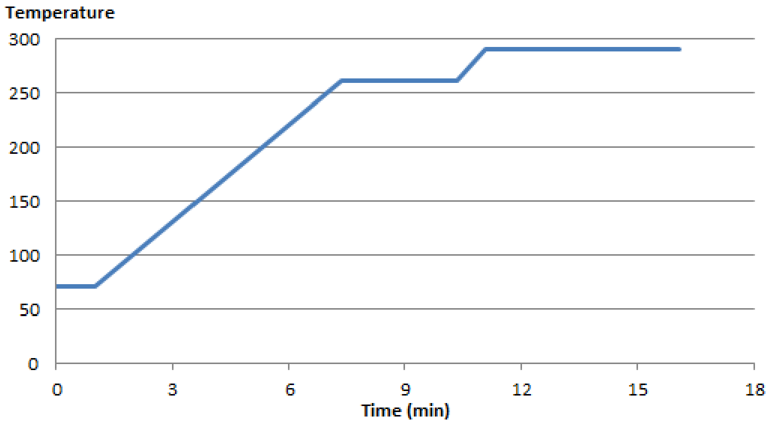

Figure 9: Temperature program used for the GC analysis.

Characterization of the compounds was performed using GC-MS. The sample was dissolved in pyridine and silylated to make the compounds compatible with the GC column. The peaks visible in the chromatogram were then analysed to gain information about the compositions.

3.4 Nuclear Magnetic Resonance Spectroscopy

Proton NMR was used to confirm the results from the GC analysis. The epoxide peaks of the product was compared to the methyl group of the alcohol and product to determine the yield of the product.

A sample was diluted to 10% in deuterated chloroform with 0.5% TMS. The solution was added to an NMR tube and analysed in a Varian VNMRS 400 MHz The analysis of the data collected was performed with the VNRMJ 4.2A software.

3.5 Design of Experiments

The DoE studies were performed with the MODDE 10.1.1 (build 1193) software from Umetrics. Response data was collected with GC-FID, and a model was fitted to the data of each product and by-product. The remaining alcohol was also modelled.

4 Results and discussion

In the following chapters, the GC and NMR results, as well as the dependency of the tested factors, are presented and discussed.

4.1 Gas Chromatography

The GC-MS chromatogram for a mixture of all the products is shown in figure 10.

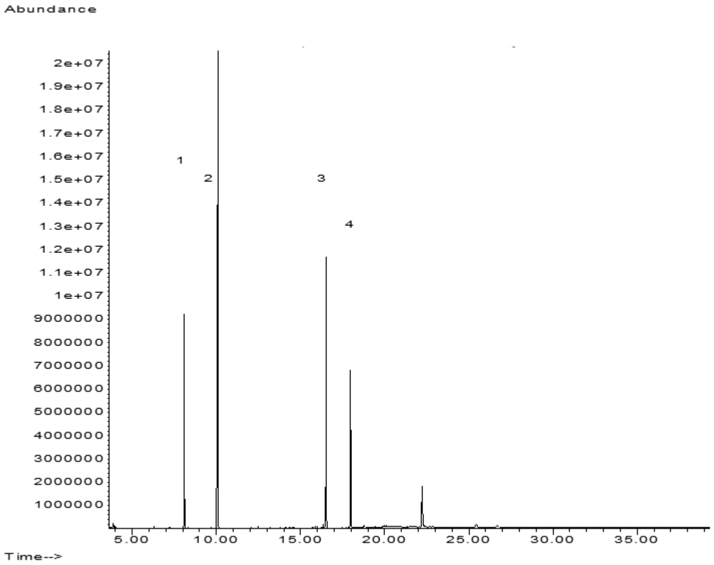

Figure 10: GC-MS chromatogram of the reacted mixture.

Four distinctive peaks where visible in the chromatogram. The GC-MS was used to gain more information about each of the peaks. The resulting spectra are shown in figures 29-32 in Appendix I.

After analysis of the GC-MS spectra, figure 29 was determined to be the alcohol peak, figure 30 the glycidyl ether peak, and figure 31 and 32 by-products. The by-product presented in figure 31 is the glycidyl ether that has reacted with another alcohol, forming didecyloxy propanol. This could either be a 1,3-didecyloxypropan-2-ol (figure 11a)), or a 2,3-didecyloxypropan-1-ol (figure 11b)). Which one of these isomers that has been formed was investigated by NMR, and is discussed in chapter 4.2.

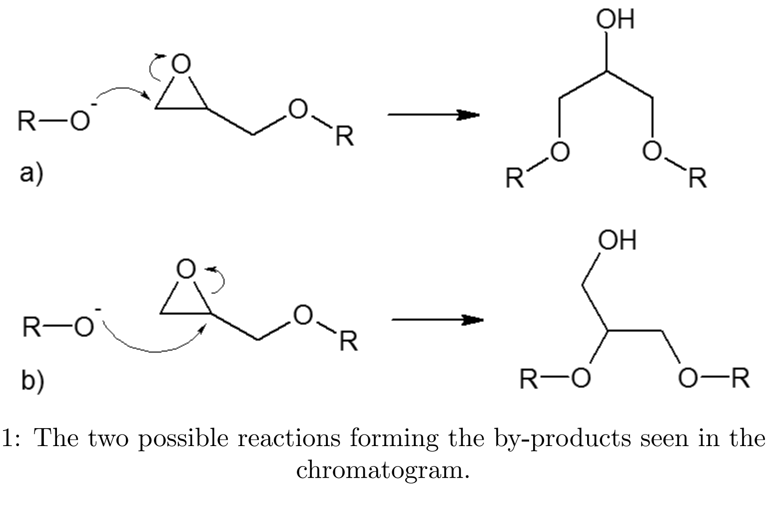

Figure 11: The two possible reactions forming the by-products seen in the GC-MS chromatogram.

The by-product generating the spectrum in figure 32 is formed when the first by-product reacts as an alcohol with an epichlorohydrin molecule according to figure 6, thus forming a didecyloxy propyl glycidyl ether. Which isomer of the glycidyl ether that has been formed is discussed in chapter 4.2.

4.2 Nuclear Magnetic Resonance Spectroscopy

The NMR spectra for the 1-tetradecanol and a reacted mixture is shown in figures 12 and 13. The spectrum of epichlorohydrin is shown in figure 4. The methyl group on the alcohol and glycidyl ether, with its corresponding peak at 0.9 ppm, was used to normalize the peaks. Since there are three equivalent protons giving this peak, its integral was set to 300.00. Then the protons of the epoxide group on the glycidyl ether, at 2.6, 2.8 and 3.1 ppm, could be used to calculate the yield of the product. In figure 13 it can be seen that the yield is between 73.64% and 78.90%. The remaining unreacted epichlorohydrin is also clearly visible.

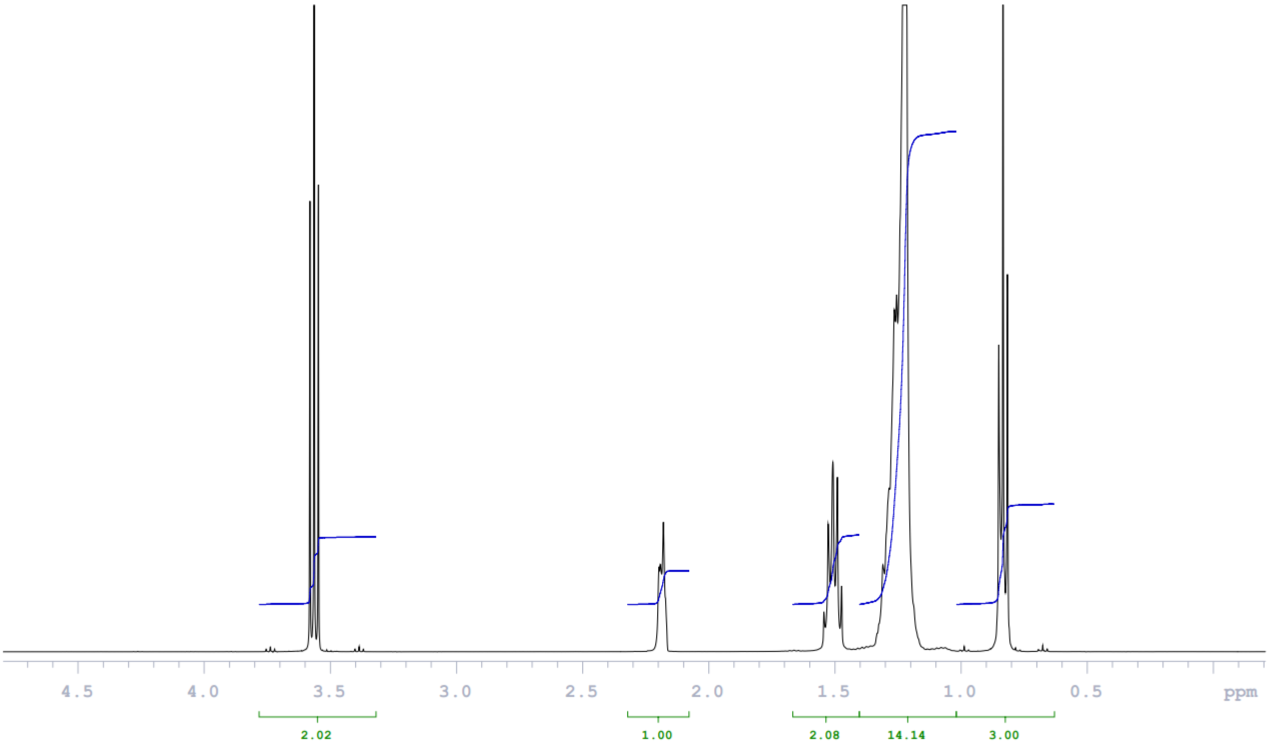

Figure 12: The proton NMR spectrum of 1-tetradecanol.

To determine the structure of the by-products, a ^{13}C-NMR and an HSQC was run for the same sample as for the spectrum in figure 13. The resulting spectra are shown in figure 14 and 15. The amounts of the by-products are 6% and 4% respectively according to GC-FID analysis. The amount of the desired product is 76.5% and the remaining 13.5% is the amount of unreacted alcohol.

Since the epoxide group and the carbon chains of all the products appears at the same chemical shift, the easiest way of determining the by-products' structure is to examine the propanol group. Calculations made by Advanced Chemistry Development, Inc. (ACD/Labs) Software V11.01 shows that the by-product with a primary alcohol should have a peak at 64 ppm in its ^{13}C spectrum. In figure 14 there is only one peak at 63 ppm, but according to the HSQC spectrum in figure 15 this peak corresponds to the carbon closest to the hydroxyl group on the alcohol.

The prediction also says that there will be a peak at 76 ppm, but in the ^{13}C spectrum of the reacted mixture, there is a high peak, which is much higher than what a peak for a by-product of less than 10% would be. Therefore no information is gained about the structure of the by-products from this peak. The predicted ^{13}C spectra can be seen in figure 33 and 34 in Appendix II.

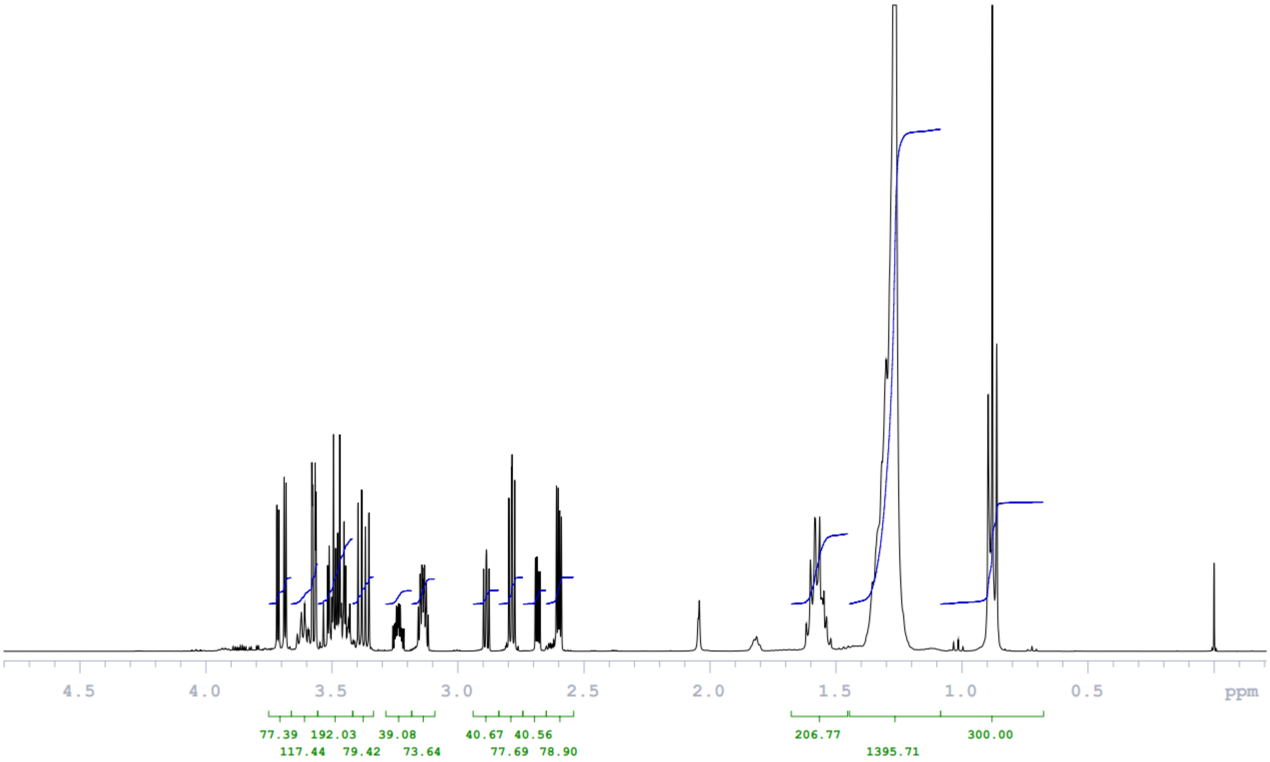

Figure 13: The proton NMR spectrum of the reacted mixture.

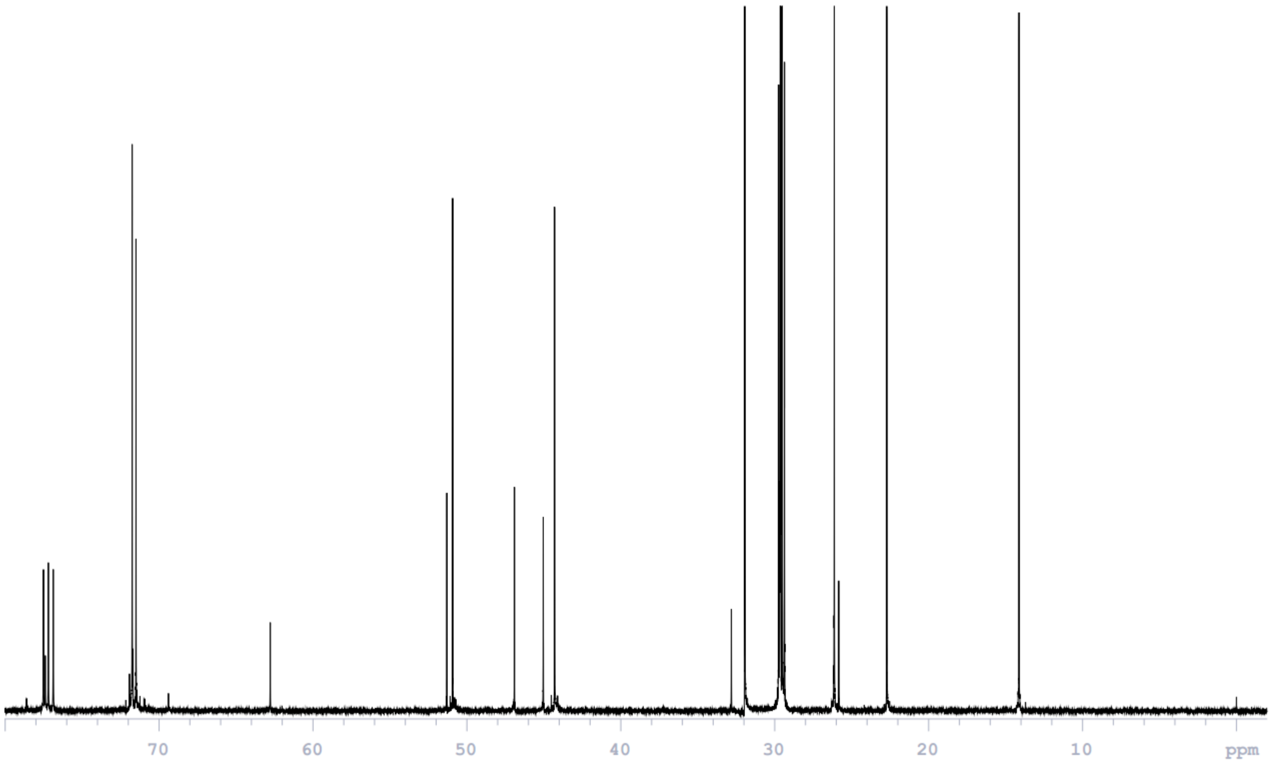

Figure 14: The ^{13}C-NMR spectrum of the reacted mixture.

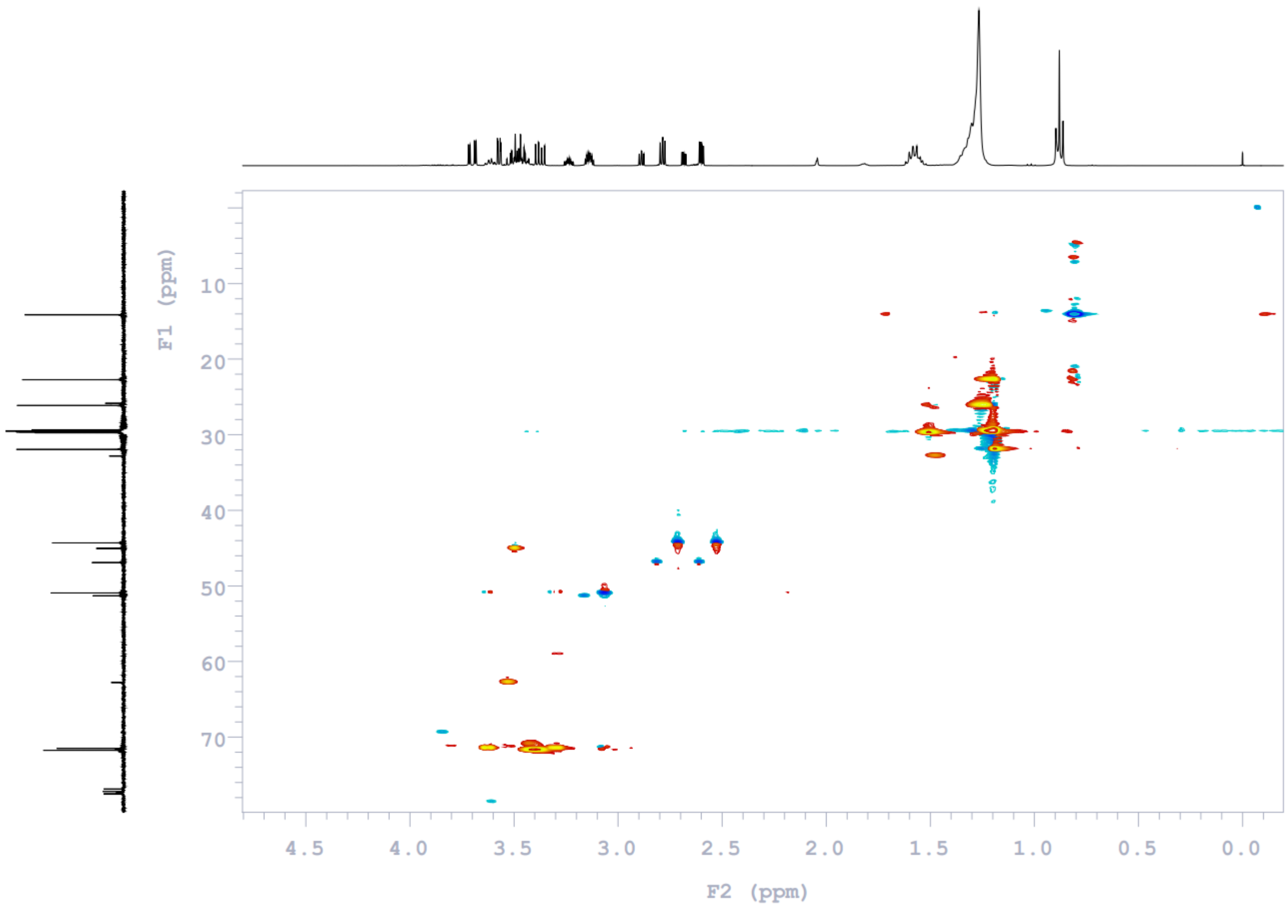

Figure 15: The HSQC spectrum of the reacted mixture.

Due to the lack of a peak at 64 ppm for the by-product, and that the by-products with a secondary alcohol is more likely because of the less sterically hindered structure, it is assumed that the by-products that are formed is 1,3-didecyloxypropan-2-ol (figure 11a)) and 1,3-didecyloxy-2-propyl glycidyl ether.

4.3 Alcohol Chain Length Dependency

The experiments were first carried out with 1-tetradecanol. However, since the melting temperature of 1-tetradecanol is above room temperature, filtering the mixture was problematic. To achieve a decent filtering, heating the mixture with a heating gun was necessary during the filtering. This made it difficult to control the temperature, and for some of the experiments unreacted epichlorohydrin boiled, which means that the temperature was above 117℃, well above any reaction temperature used during the experiments.

To deal with this problem 1-decanol was used instead. Being a liquid at room temperature, 1-decanol would not cause any problem while processing the reacted mixture. The decanol should behave similarly to the tetradecanol, since both of them are primary alcohols with relatively long, straight, carbon chains.

Because of the use of two different reactants, an experiment was run with the decanol, at the same reaction conditions as a previous experiment with tetradecanol. For this experiment 1.05 eq of ECH and 1.3 eq of KOH was used, along with 0.25% TBAB at 55℃. This gives an indication of the difference in yield from the two alcohols. The result of this experiment is shown in figure 16.

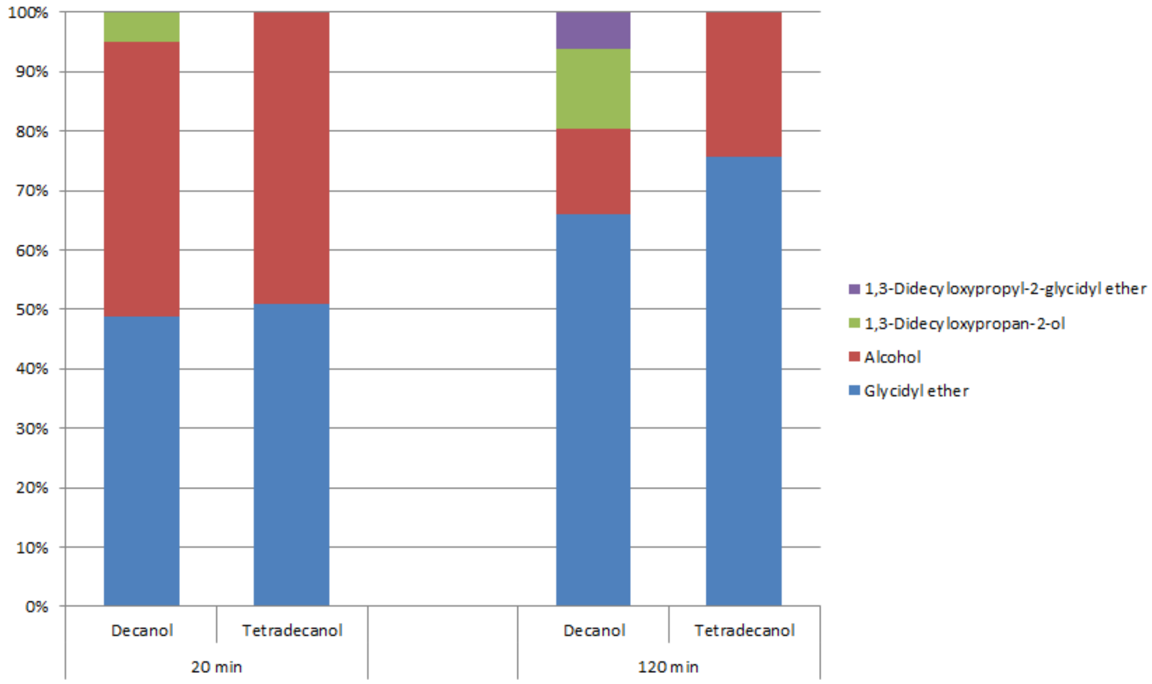

Figure 16: Comparison of the yields of glycidyl ether when using either 1-tetradecanol or 1-decanol as starting material.

As can be seen in figure 16, the yield after 20 minutes is relatively independent of the two alcohols. But after two hours, the tetradecanol yields about 10% more product than the decanol. The figure also shows that the decanol leads to the formation of a larger amount of by-products than the tetradecanol. In fact, the experiment with tetradecanol shows no formation of by-products at all.

The tetradecanol was used for the determination of base composition dependency, base particle size dependency and time dependency, but in further experiments 1-decanol was used as the fatty alcohol reactant.

4.4 Base Composition Dependency

The base counterion was the first factor to be evaluated as a possibly important parameter for the yield of glycidyl ether. Figure 17 shows the product yields from the tested bases. The reactions were carried out with tetradecanol as the alcohol, 1.07 equivalents of ECH and 1.5 equivalents of the base (0.75 for the $Ca(OH)_2$). The catalyst loading was 5%.

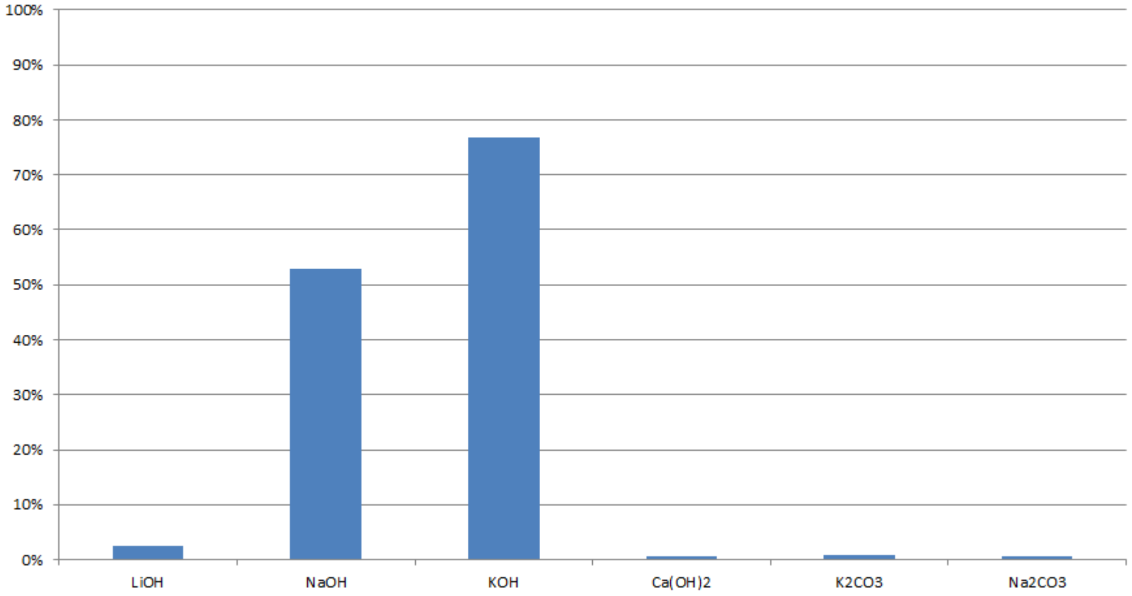

Figure 17: The yield of glycidyl ether for the tested bases.

As can be seen, there are two main candidates for the final reaction: potassium hydroxide and sodium hydroxide. Both of them have relatively low pK_b values and a relatively weak ion bond. This is important, since the dissociation of the base is a crucial step for the reaction. Of the other bases tested, only lithium hydroxide has a lower pK_b value. The low yield resulting from the lithium hydroxide shows that pK_b values might give an indication of the result of the base, but other factors are also important.

An experiment of five hours were performed for the potassium hydroxide and the sodium hydroxide, to decide on which base to use for further experiments. The results from these experiments can be seen in figure 18. It is clear that the reaction is faster with potassium hydroxide, than with sodium hydroxide. Both of them seem to have the same final yield, but the potassium hydroxide was chosen because of the benefit of a faster reaction. Due to this, the potassium hydroxide was used for further experiments.

4.5 Particle Size Dependency

The contribution of the KOH particle size was determined by measuring the product yield for KOH pellets and KOH powder during the same time and reaction conditions. These conditions were 300 minutes reaction time, 40°C, 1.5 eq KOH, 0.2% TBAB and 1.05 eq ECH, using tetradecanol as the fatty alcohol.

According to figure 19, the increased surface area of the KOH had no obvious effect on the yield. This might be due to that the KOH pellets was continuously eroding because of the stirring in the reaction flask. The pellets tended to stick to the glass wall of the flask, and were therefore subjected to a lot of friction from the stirrer. This helped removing the outer, reacted, layer of the pellet, exposing fresh KOH to the reaction mixture.

Due to the small difference in reactivity, the pellets were used in the following experiments. The reason for the choice of pellets instead of powder was for practical reasons; the powder fabrication is time consuming, and provides no obvious benefit.

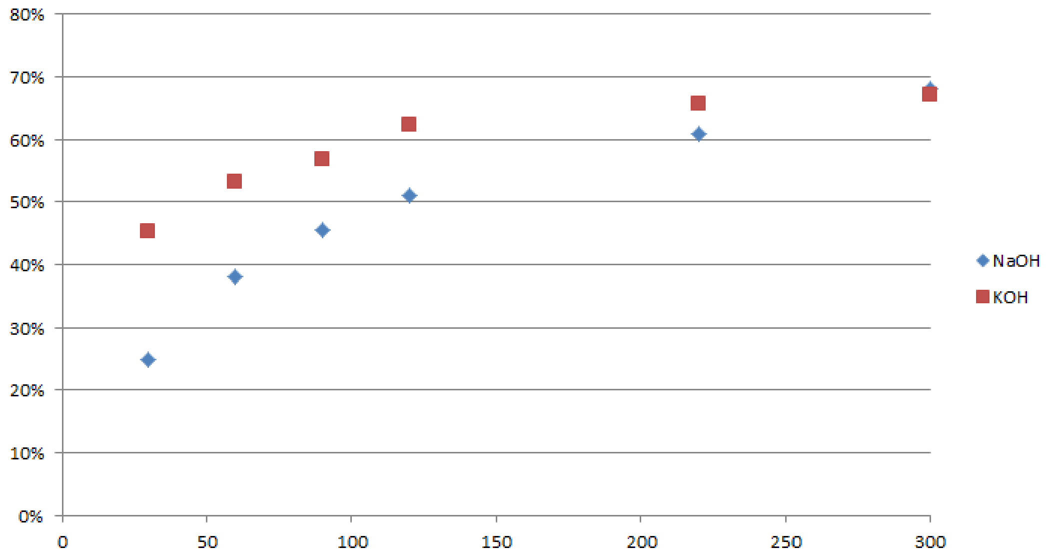

Figure 18: The yield of glycidyl ether as a function of time, for KOH and NaOH as base. The experiment was run for 300 minutes.

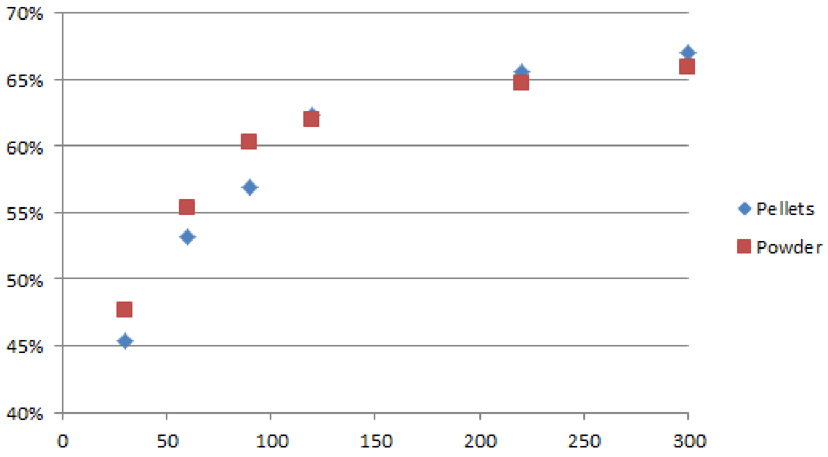

Figure 19: Comparison of the yield of glycidyl ether for KOH pellets and KOH powder. The experiment was run for 300 minutes.

4.6 Time Dependency

With a high amount of PTC (5%), 5% excess of ECH and 50% excess of KOH, the time dependency of the reaction was investigated. 1-tetradecanol was used as alcohol and the temperature was 50°C. The experiment was run for 30 hours, and the results are shown in figure 20.

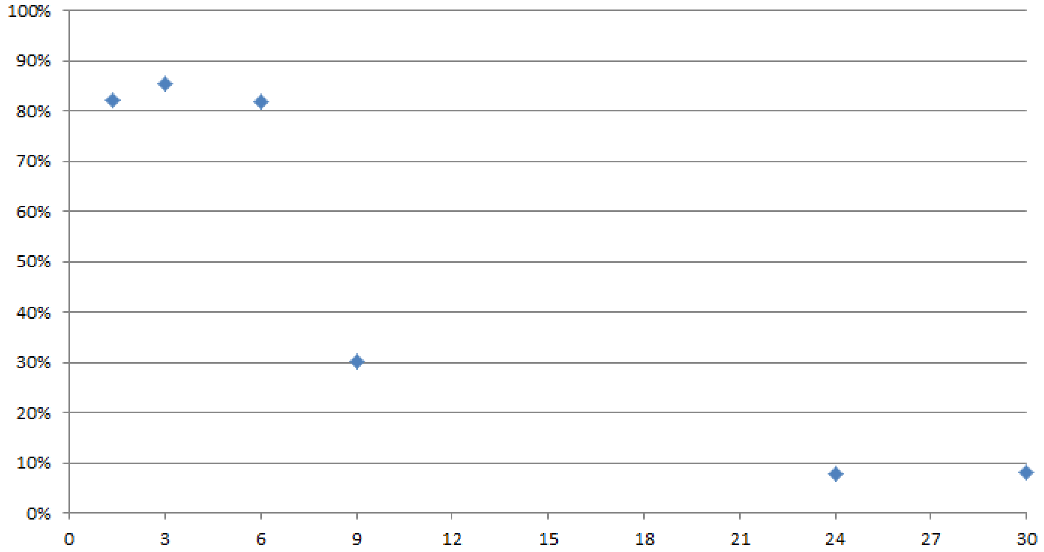

Figure 20: Time dependency for the reaction. The experiment was run for 30 hours.

As can be seen in the figure, there is an optimal time for the reaction to produce a maximal yield of product. With the reaction conditions used here, the amount of product compared to alcohol decreases rapidly after six hours. Lee et al. has shown that a small amount of the alcohol might be formed at the right conditions, but most likely the product is either degraded or by other means reacted making it undetectable in the GC. [15] No further investigation in this phenomenon was performed. The time dependency was further investigated in two DoE studies, discussed in chapter 4.7.

4.7 Design of Experiments studies

The dependency of the reaction on ECH and TBAB concentration as well as its temperature dependence was investigated through two DoE studies, presented in the following chapters. The data collected in the experiments are presented in Appendix III.

4.7.1 First study

In the first study, the TBAB concetration, reaction temperature and reaction time were varied. The intervals are presented in table 5.

Table 5: The intervals used for the first design of experiments study.

Parameter	Interval
Time	20-120 minutes
Temperature	20-50°C
TBAB	0.025-0.25%
ECH	1.05 eq
KOH	1.3 eq

The significant parameters for the yield of the product can be seen in figure 21. The figure shows that the temperature, catalyst concentration and reaction time had a positive influence on the yield, which was to be expected. But the model also shows that the squared reaction time has a negative influence on the yield in the chosen interval. This is what was observed in chapter 20. This means that it should be possible to find an optimal reaction time to optimize the reaction.

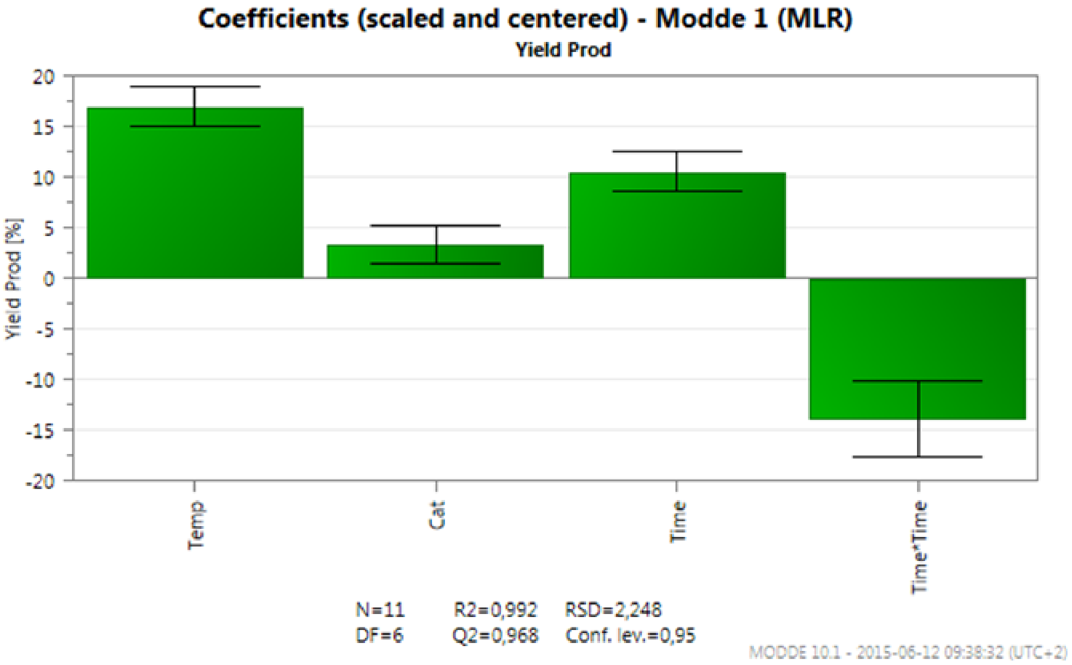

Figure 21: The significant parameters for modelling the product yield.

The fit of the model for the different responses is shown in figure 22. The fit was acceptable for all the models, except in the case of the model validity parameter for the 1,3-didecyloxypropyl-2-glycidyl ether. The yield of this by-product is not considered to be important to model, and the main focus will be the glycidyl ether model.

Figure 23 shows the modelled product yield at different catalyst concentrations with reaction time and temperature on the axes. The optimal reaction time seems to be within the interval chosen for the study, but the optimal temperature and catalyst concentration appears to be outside the intervals used. The temperature interval was adjusted for the next study, to 35-75°C. The catalyst is relatively expensive, and its presence in the final product should be minimized. Therefore it was kept constant at 0.25% of the alcohol for the next DoE study. Instead, the ECH concentration was varied between 1 and 2 equivalents, as the third factor.

4.7.2 Second study

The intervals for the second DoE study is presented in table 6, and the significant parameters for the yield of the glycidyl ether are shown in figure 24.

Table 6: The intervals used for the second design of experiments study.

Parameter	Interval
Time	20-120 minutes
Temperature	35-75°C
ECH	1-2 eq
TBAB	0.25%
KOH	1.3 eq

The second study corresponds well with the first. Both temperature and reaction time has a positive influence on the yield, and the squared reaction time has a negative influence. New is that the yield

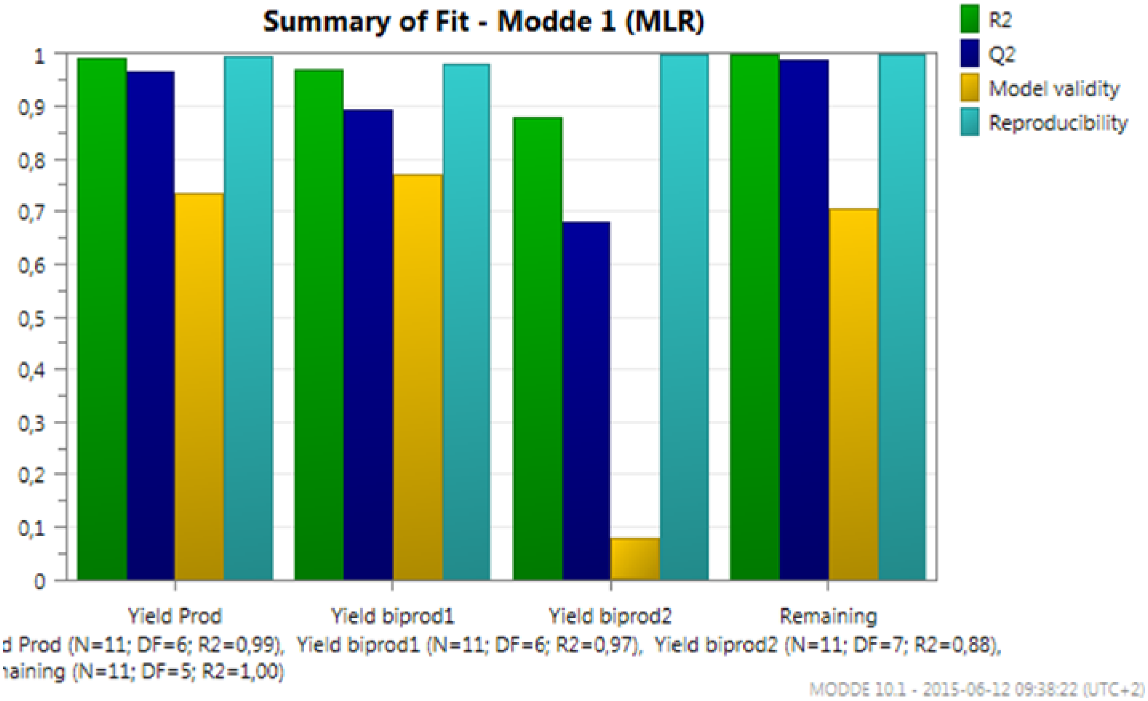

Figure 22: The statistical parameters used to determine the fit of the models.

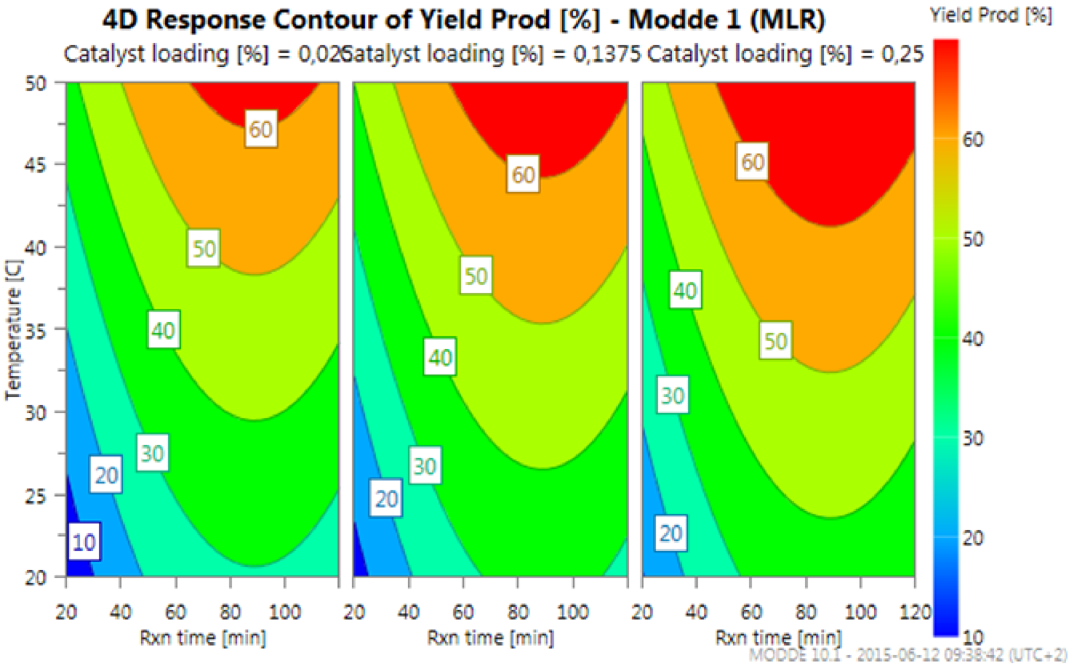

Figure 23: The modelled yield of the product within the intervals used for the study.

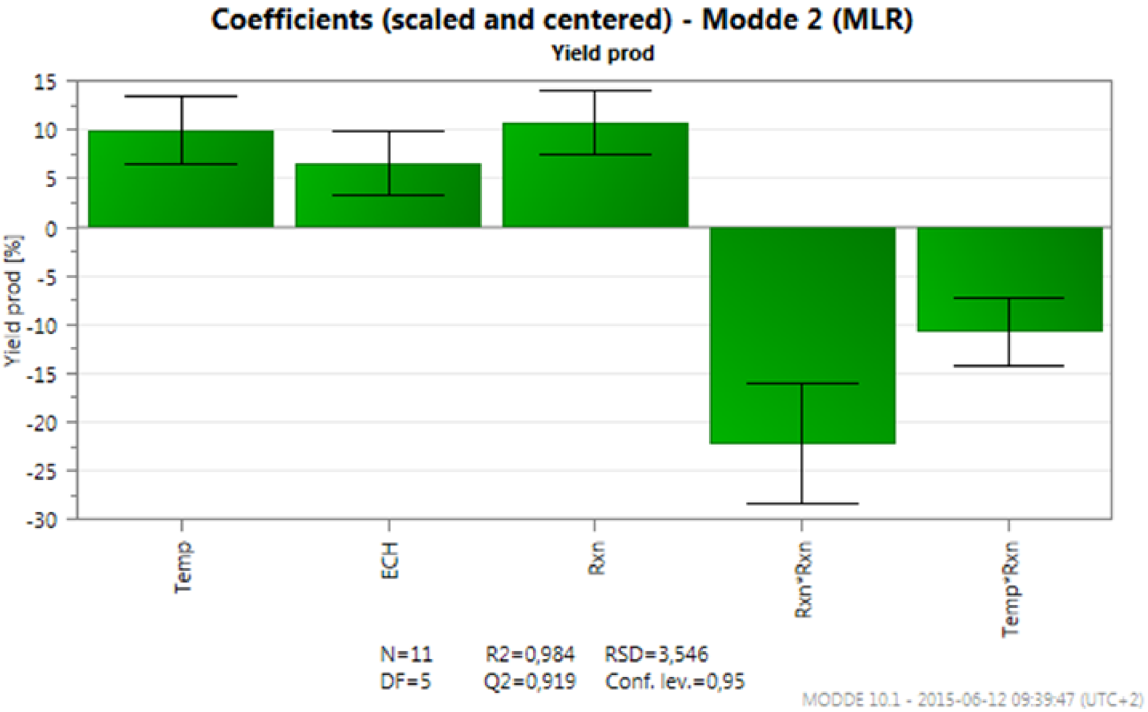

Figure 24: The significant parameters for modelling the product yield.

increases with the ECH concentration, and that the product of the reaction time and temperature has a negative influence on the yield. Since the temperature has both positive influence (by itself) and negative influence (in the temperature and reaction time product), it should be possible to optimize it for maximum yield.

The fit of the models for the different responses is shown in figure 25.

As can be seen in figure 25, all model parameters are sufficient, except the model validity of the glycidyl ether model. However, the model validity is a comparison of the model fit (Q2) and the reproducibility. Since the reproducibility is close to 1.0, the model fit will never be close to that, and therefore the model validity will always be low. Umetrics has a disclaimer regarding this in their software:

> ”Note: Model validity might be low in very good models (Q2 > 0.9) due to high sensitivity in the test or extremely good replicates.”

So despite the low level of model validity, the model can be accepted.

The model for glycidyl ether is shown in figure 26, with temperature and reaction time on the two axes, and for three different concentrations of ECH. It is obvious that the time interval is enough to find an optimal reaction time, since the yield decreases after about 80 minutes.

The ECH concentration interval was set due to the negative impact of residual ECH in the product. A concentration as high as 2 equivalents will not be considered in an industrial process. Therefore it is not interesting in this case to evaluate if there is an optimal ECH concentration before a decrease in yield, but figure 26 shows that a larger amount of ECH, in the range of 1-2 equivalents to the alcohol, will increase the yield.

4.8 Optimization

To optimize the reaction, the results from the second DoE study was used. To keep the amount of ECH low, 1.15 equivalents was used. As can be seen in figure 27, this should be enough to get a yield above 80%.

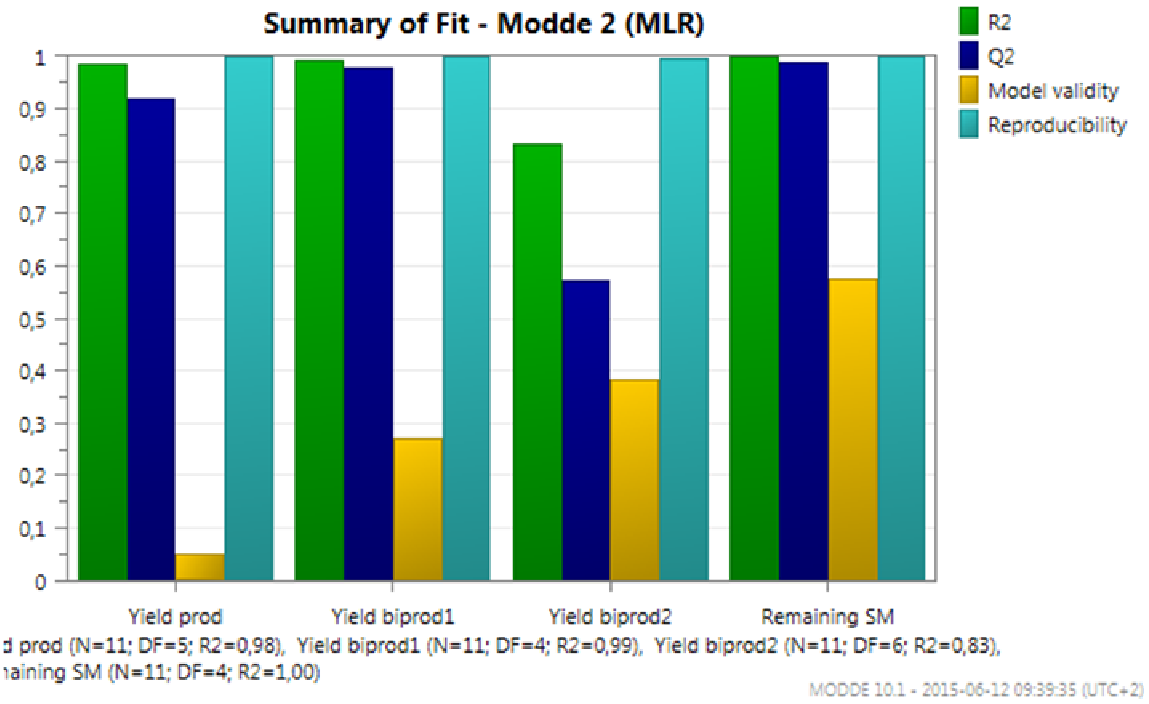

Figure 25: The statistical parameters used to determine the fit of the models.

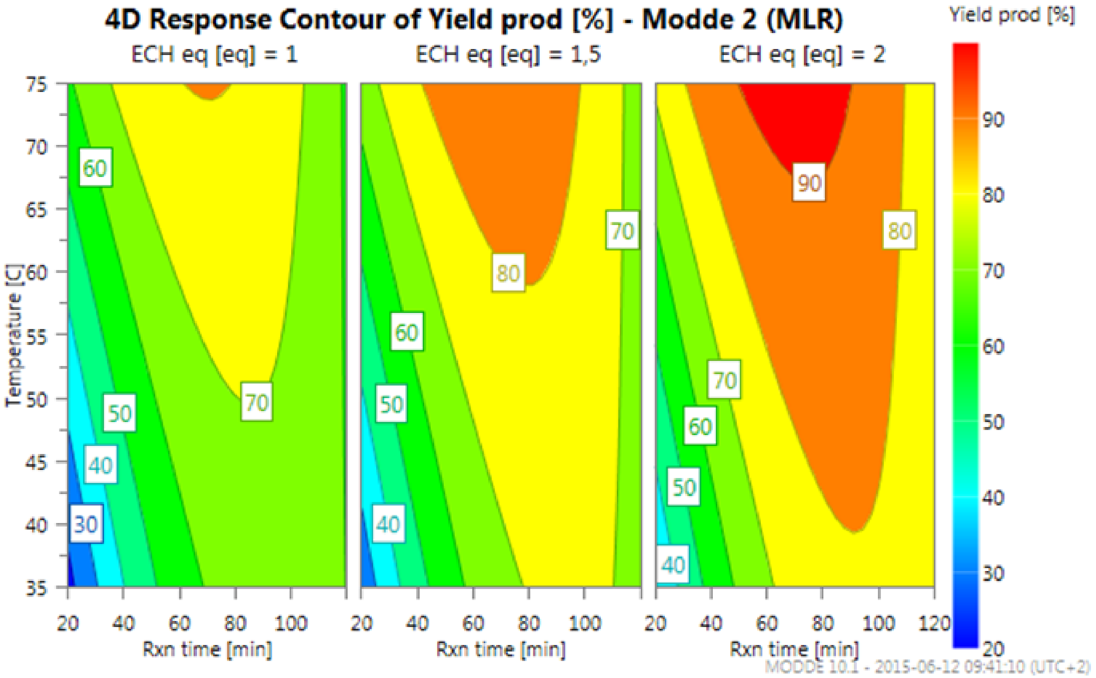

Figure 26: The modelled yield of the product within the intervals used for the study.

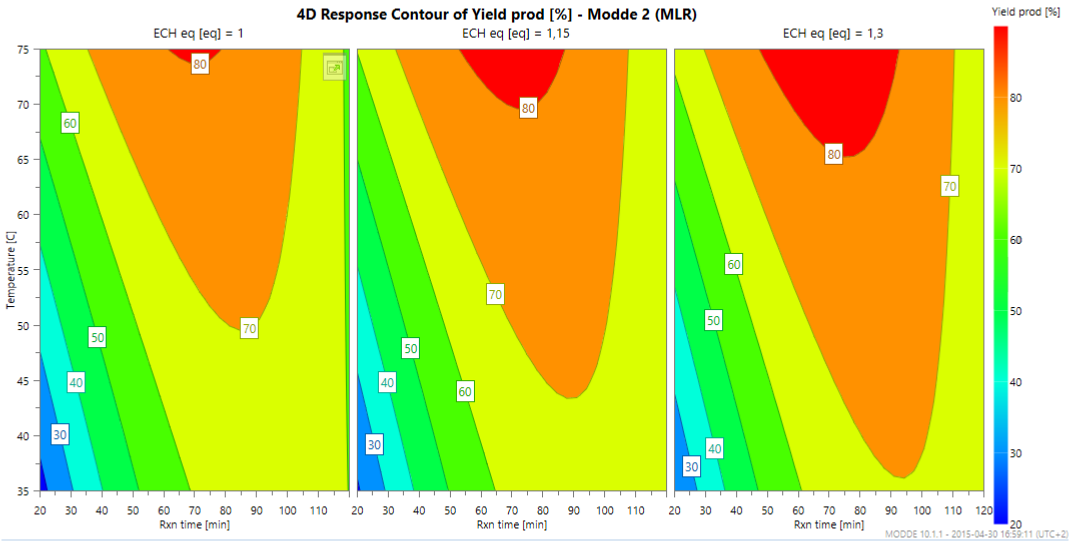

Figure 27: The modelled yield of the product for 1, 1.15 and 1.3 equivalents of epichlorohydrin.

The model was tested with an experiment using 1.15 eq of ECH, 1.3 eq of KOH, 0.25% TBAB with 1-decanol, at 75°C for 70 minutes. This resulted in a yield of 69.0% of the product. This value is far below the predicted value, of about 82.6%.

The reason for the low yield, compared to the predicted, might be the way the software models the reaction. The product, by-products and the remaining alcohol are all modelled individually, without taking into account that the sum of the models should be 100% at all times. That this is the case can be seen in table 7, where the predictions are added and normalized for the reaction conditions mentioned above. The normalized prediction of 67.5% of the product corresponds well with the result from the experiment.

Table 7: Predicted yield, normalized prediction and actual yield of product and by-products, as well as remaining alcohol.

Compound	Predicted Yield	Normalized Prediction	Yield
Product	82.6%	67.5%	69.0%
1,3-Didecyloxypropan-2-ol	13.6%	11.1%	10.8%
1,3-Didecyloxy-2-propyl glycidyl ether	4.6%	3.7%	4.3%
1-Decanol	21.5%	17.5%	15.9%
Sum	122.3%	100.0%	100.0%

Because of time constraints, no thorough investigation of this was performed. However, four different experiments were performed to try to increase the yield of the product. The conditions for these experiments are presented in table 8, along with the product yield.

Table 8: Reaction conditions for the four reactions.

Exp No	Alcohol	Time (min)	Temp. (°C)	ECH (eq)	KOH (eq)	TBAB (%)	Yield (%)
1	1-Decanol	300	55	1.5	1.3	0.25	76.4
2	1-Decanol	180	55	1.5	1.3	0.25	60.0
3	1-Decanol	40	55	1.5	1.5	0.25	76.5
4	1-Tetradecanol	120	50	1.05	1.3	0.25	75.6

In Experiment 1, a high amount of ECH was used, to increase the yield, which reached 76.4%. However, as figure 28 shows, the reaction reaches 75% already after 60 minutes. The following four hours, only another 1.4% of products and by-products are formed. NMR shows that there are still unreacted ECH left in the mixture, but the reaction seems to have reached an equilibrium.

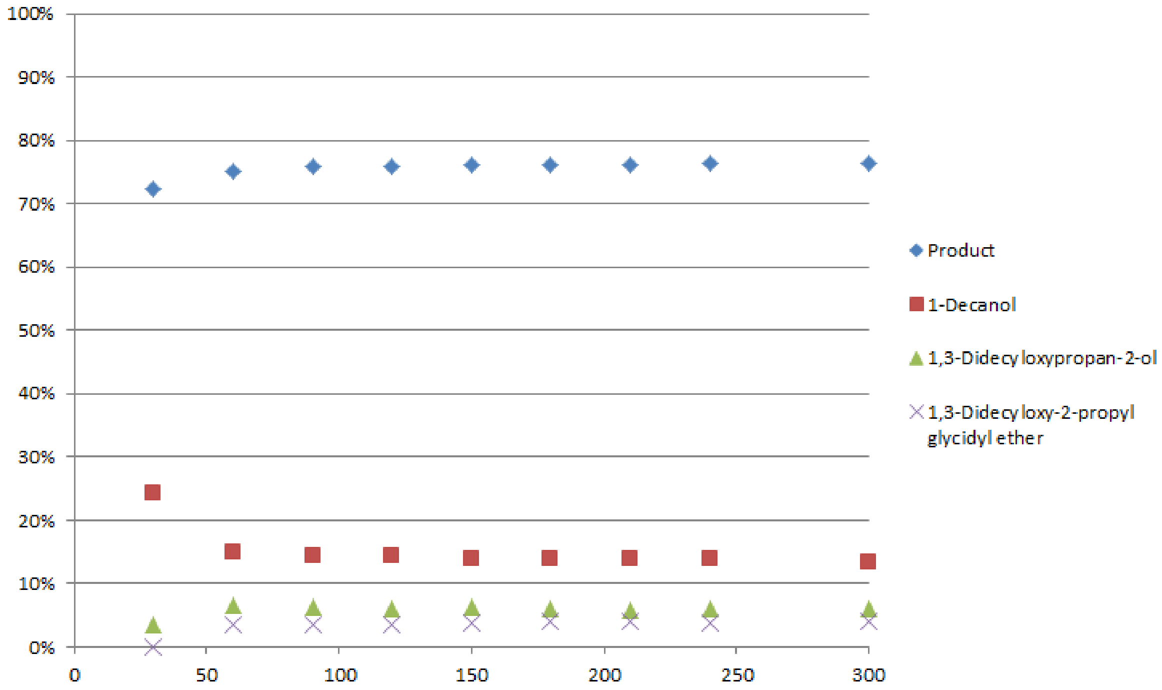

Figure 28: The yield of product over time with 1.5 equivalents of epichlorohydrin. The experiment was run for 300 minutes.

An explanation for this behaviour might be that the water formed in the reaction adsorbs to the surface of the potassium hydroxide, and therefore prohibits further reaction with the base. To test this theory, the following two experiments were performed. In Experiment 2, instead of adding the ECH over time, the base was added in three portions; at the initiation of the reaction and after 30 and 60 minutes respectively. This experiment was unsuccessful, since the yield was a mere 60%. The third experiment used a larger excess of potassium hydroxide. If the theory was true, then this would increase the yield noticeably. However, only 0.1% more product was formed than with less excess, which concludes that the potassium hydroxide is not the limiting factor.

As a last experiment, 1-tetradecanol was once again used for the synthesis. During two hours, it was allowed to react with 1.05 equivalents of ECH and 1.3 equivalents of KOH. Compared to Experiment 1-3, the excess of ECH is very low, but the yield is still 75.6%. Due to time constraints, no further investigation of the 1-tetradecanol reaction was made.

5 Conclusions

This thesis has shown that an alkyl glycidyl ether can be synthesized from a fatty alcohol and epichlorohydrin, without using any water or organic solvents. Both the reaction with 1-decanol and with 1-tetradecanol shows promising results, where the tetradecanol in this initial stage seems slightly more promising.

The reaction was modelled using two design of experiments studies, but this did not bring the yield above the targeted 80%. The misfit of the model was suspected to be because of the way the software model each component separately.

However, it has been made clear that it is possible to optimize the reaction to reach a maximum yield, where the amounts of reactants are minimized to reduce costs.

6 Future work

The results of this thesis lead to new questions that would be interesting to be able to answer. For example, the 1-tetradecanol shows promising results with a relatively low amount of starting material. Another experiment set-up, where filtering is made possible by a controlled external heating process, would make it possible to study the reaction of the longer-chained alcohol, and its benefits over 1-decanol. An alternative is to enclose the solid material inside reaction vessel, and to use a flow of the other reactants through the solid, to remove the problematic filtering. This would in some extent resemble a large scale process equipment.

Another possible study is to examine the influence of the composition of the phase transfer catalyst. There are a lot of commercially available PTCs, and a comparative study would be easy to conduct. The concentration of the PTC is also a factor that is possible to examine further. Every new chemical process has to consider the costs, and it would be possible to compare the PTC concentration to the higher yield it could give rise to, and thereby the increased profits.

The concentration of potassium hydroxide did not show an increased yield of the product. However, if the limiting factor of the reaction is established and dealt with, it may be possible to increase the yield further, with a larger excess of potassium hydroxide. This concentration is also a question about costs. It is relatively easy to remove the base from the final product, but it would be a large waste to increase the excess further, without taking care of the unreacted material. An after-treatment of the solid waste should therefore be considered.

Before a possible implementation of the reaction in the existing process, the reactions should be tested in a larger scale.

7 Acknowledgements

I would like to send a special thanks to some people who made the last months possible:

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Karin Sahlin for being my opponent during my presentation.

8 References

[1] Lee BM, Kang HC, Park J, Yoon JH. Method of synthesizing glycidyl ether compounds in the absence of water and organic solvents; 2002. US Patent 6392064.

[2] Holmberg K, Jönsson B, Kronberg B, Lindman B. Surfactants and Polymers in Aqueous Solution. 2nd ed. Chichester: Wiley; 2003.

[3] Rosen MJ. Surfactants and Interfacial Phenomena. 3rd ed. New York: Wiley; 2004.

[4] Ives KJ. The Scientific Basis of Flotation. 1st ed. The Hague: Martinus Nijhoff Publishers; 1984.

[5] Atkins P, Jones L. Chemical Principles. 5th ed. New York: Freeman and Company; 2010.

[6] Fuerstenau MC, Jameson G, Yoon RH. Froth Flotation: A Century of Innovation. Littleton, Co: Society for Mining, Metallurgy, and Exploration Inc.; 2007.

[7] Leja J. Surface Chemistry of Froth Flotation. 1st ed. New York: Springer; 1982.

[8] Sasson Y, Neumann R. Handbook of Phase Transfer Catalysis. 1st ed. London: Blackie Academic & Professional; 1997.

[9] Makosza M, Fedoryński M. Phase transfer catalysis. Cat Rev - Sci Eng. 2003;45(3-4):321–367.

[10] Clayden J, Greeves N, Warren S, Wothers P. Organic Chemistry. New York: Oxford University Press; 2001.

[11] Starks CM, Liotta C. Phase Transfer Catalysis: Principles and Techniques. New York: Academic Press; 1978.

[12] Yudin AK. Aziridines and Epoxides in Organic Synthesis. Weinheim: Wiley-VCH; 2006.

[13] Jacobsen EN. Asymmetric catalysis of epoxide ring-opening reactions. Acc Chem Res. 2000;33(6):421–431.

[14] Brewis D, Comyn J, Tegg J. The durability of some epoxide adhesive-bonded joints on exposure to moist warm air. Int J Adhes Adhes. 1980;1(1):35–39.

[15] Kang HC, Lee BM, Yoon J, Yoon M. Improvement of the phase-transfer catalysis method for synthesis of glycidyl ether. J Am Oil Chem Soc. 2001;78(4):423–429.

[16] Skoog DA, West DM, Holler FJ, Crouch SR. Fundamentals of Analytical Chemistry. 8th ed. Belmont, CA: Brooks/Cole; 2004.

[17] Harris DC. Quantitative Chemical Analysis. 8th ed. New York: Freeman and Company; 2010.

[18] Berg JM, Tymoczko JL, Stryer L. Biochemistry. 6th ed. New York: Freeman and Company; 2002.

[19] Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 5th ed. New York: Garland Science; 2008.

[20] Eriksson L, Johansson E, Kettaneh-Wold N, Wikström C, Wold S. Design of experiments: principles and applications. 3rd ed. Umeå: MKS Umetrics AB; 2008.

9 Appendix I

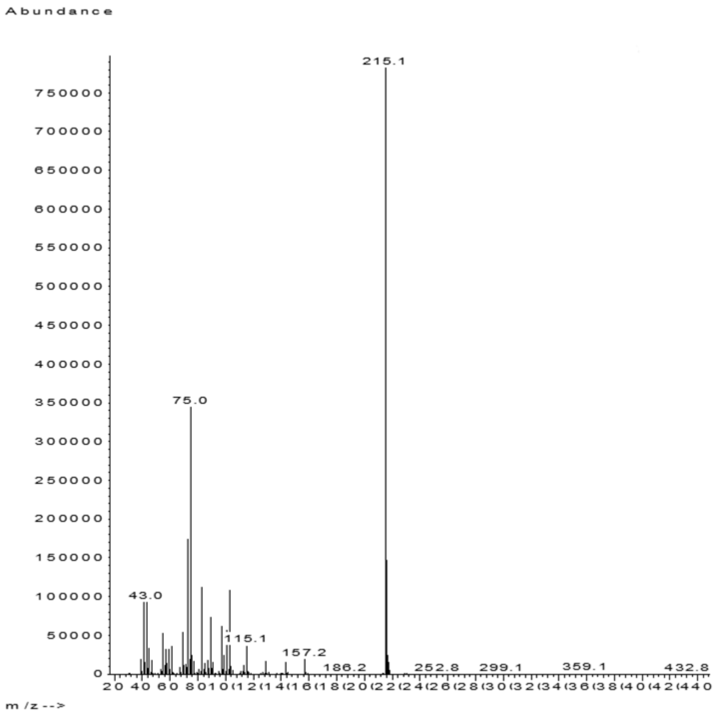

Figure 29: GC-MS spectrum of the fatty alcohol.

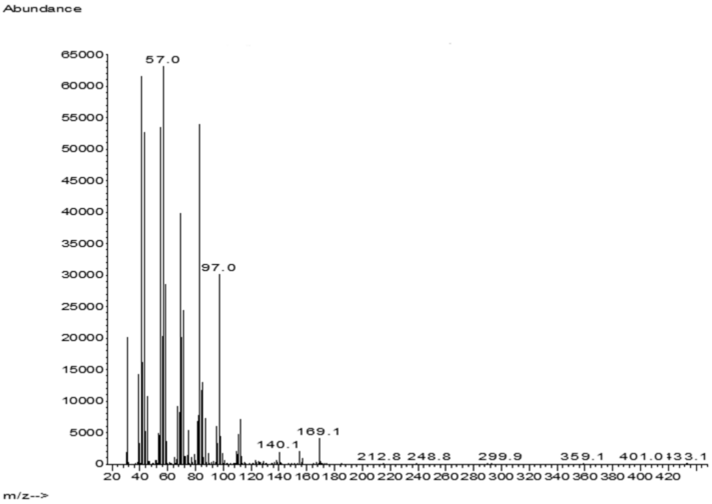

Figure 30: GC-MS spectrum of the product.

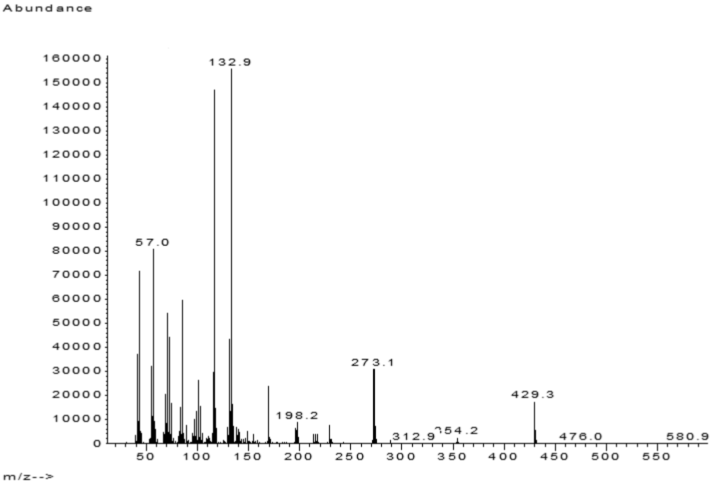

Figure 31: GC-MS spectrum of the first by-product.

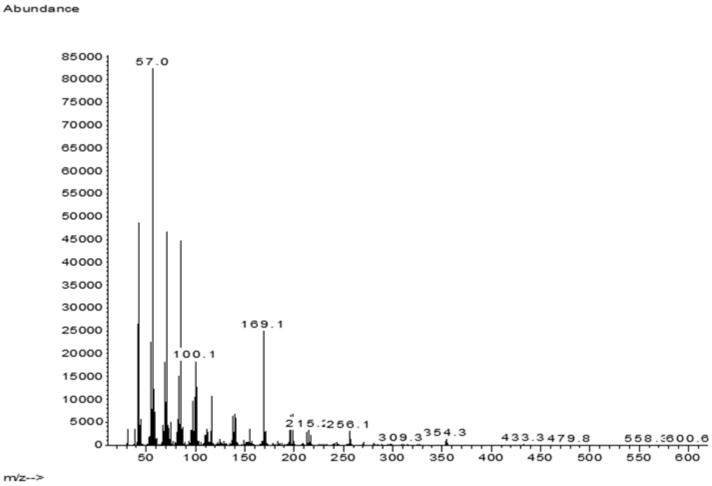

Figure 32: GC-MS spectrum of the first by-product.

10 Appendix II

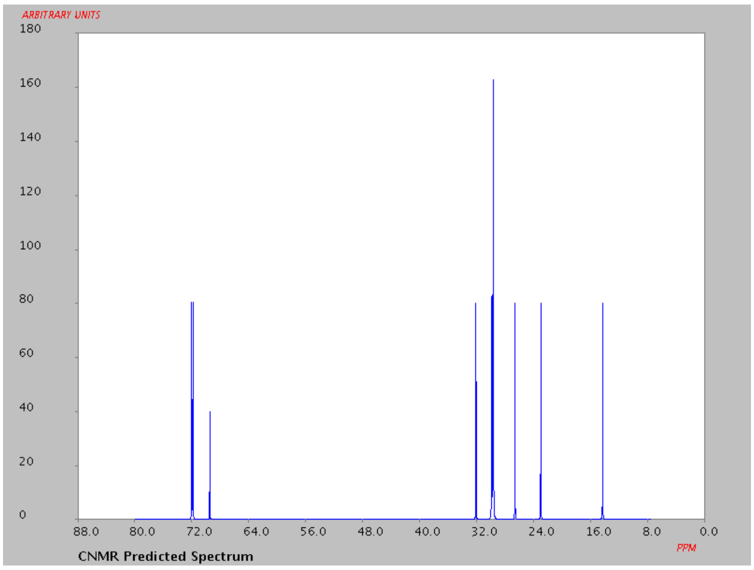

Figure 33: Predicted ^{13}C NMR spectrum of 1,3-didecyloxypropan-2-ol.

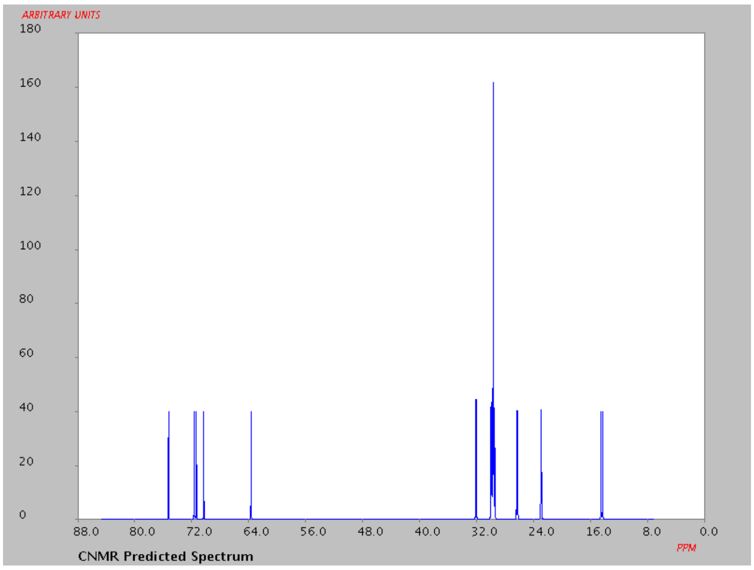

Figure 34: Predicted ^{13}C NMR spectrum of 2,3-didecyloxypropan-1-ol.

11 Appendix III

Table 9: The factors and responses for the first DoE study.

Exp No	Run Order	Temperature (°C)	Catalyst Loading	Reaction Time (min)	Decyl Glycidyl Ether	1,3-Didecyloxy-propan-2-ol	1,3-Didecyloxy-2-propyl Glycidyl Ether	Remaining 1-Decanol
1	1	23	0.0269%	20	7.66%	1.78%	0%	90.56%
2	5	52.5	0.02398%	20	40.41%	3.72%	0%	55.87%
3	10	21	0.26%	20	7.62%	0%	0%	92.38%
4	8	53	0.268%	20	48.69%	5.00%	0%	46.31%
5	2	22.5	0.0269%	120	26.58%	2.32%	0%	56.30%
6	6	51	0.02398%	120	56.88%	16.10%	3.90%	23.13%
7	11	21	0.26%	120	34.42%	2.81%	0%	62.77%
8	9	51	0.268%	120	65.99%	13.53%	6.20%	14.28%
9	4	36.5	0.1367%	70	50.88%	6.78%	0%	42.35%
10	3	36.5	0.1596%	70	48.45%	8.51%	0.86%	42.18%
11	7	36	0.1367%	70	48.68%	7.58%	0%	43.74%

Table 10: The factors and responses for the second DoE study.

Exp No	Run Order	Temperature (°C)	ECH (eq)	Reaction Time (min)	Decyl Glycidyl Ether	1,3-Didecyloxy-propan-2-ol	1,3-Didecyloxy-2-propyl Glycidyl Ether	Remaining 1-Decanol
1	6	37	1	20	22.15%	3.75%	0%	74.1%
2	4	78	1	20	60.31%	14.07%	3.73%	21.89%
3	10	37	2	20	28.6%	3.57%	0%	67.83%
4	2	73	2	20	71.1%	3.62%	1.06%	24.21%
5	7	36	1	120	57.58%	11.58%	1.82%	29.02%
6	5	71	1	120	58.87%	20.13%	6.66%	14.34%
7	11	36	2	120	74.91%	4.30%	1.86%	18.92%
8	3	72	2	120	71.49%	4.62%	2.15%	21.75%
9	8	57	1.5	70	76.15%	5.88%	2.83%	15.13%
10	1	54	1.5	70	80.97%	3.43%	0%	15.6%
11	9	57	1.5	70	75.98%	5.78%	2.65%	15.59%