Models of Complex Lignin Carbohydrate

Compound Synthesis

Bachelor's thesis in Chemical Engineering

Fabian Krantz
Sanjidul Huda

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Cover: Visualisation of β-O-4 linkage containing complex lignin model compound constructed in MolView.

Abstract

One step in the evolution of working with green chemistry is to develop catalysts for efficient conversion of lignin polymers into chemical compounds for further processing into materials. This requires manufacturing suitable lignin models. The aim of this thesis is to attempt to streamline the synthesis of lignin models by varying different parameters and testing different methods.

In the synthesis of benzyl vanillin, the combination of acetone as solvent and potassium carbonate as base produced the most promising result. Although, since the recrystallization failed, the yield of this step could not be correctly estimated. However, results from NMR and TLC shows that all vanillin had been consumed in the reaction.

The process of synthesis of methyl 3-(4-(benzyloxy)-3- methoxyphenyl) acrylate was successful. An optimisation to the method was able to be achieved by using water as a solvent and performing it in a one-pot reaction, thereby removing one processing step.

Experiments were conducted to determine if it is possible to attach a phenolic group to methyl 3-(4-(benzyloxy)-3-methoxyphenyl) acrylate **(4)** by oxidation into an epoxide. This method was intended to reduce the amount of steps required for the synthesis path and was tested prior to producing **(4)**, by using trans-cinnamaldehyde. Results indicated that it was possible to create the epoxide using trans-cinnamaldehyde, while reacting **(4)** did not work. One cause of this may be the steric hindrance from the protecting benzylic group, since this is a varying factor from the cinnamaldehyde.

Keywords: Lignin models, Complex compounds, Lignin, β-O-4 linkage, Green Chemistry, Biomass.

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Fabian Krantz, Gothenburg, May 2020
Sanjidul Huda, Gothenburg, May 2020

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Introduction

1.1 Background

In recent years, there has been an increasing awareness of saving the Earth's resources and maintaining sustainable work ethics [1]. In addition to reduced consumption, energy-efficient systems and reusable products, interest in green chemistry has also increased. More specifically, the utilisation of biomass for conversion into today's and tomorrow's products. One step in this evolution is to develop catalysts for efficient conversion of lignin polymers into chemical compounds for further processing into usable products. In the design of effective catalysts, it is important to have well-defined chemical lignin structural fragments so that the efficiency of the catalyst can be correlated to the structure of the lignin. The dominant structural feature of the lignin polymer is an extensive network of biological monomers connected via β-O-4 linkages.

1.2 Purpose

In this study, a series of lignin models containing β-O-4 linkages will be produced based on the article *"Synthesis of lignin model compound containing β-O-4 linkage"* by Mukhtar et al [1]. The aim is to understand the connection and theory behind the reaction mechanism through literary studies, as well as laboratory work until the desired lignin models is obtained.

Furthermore, the study will also focus on streamlining the synthesis path by adjusting various parameters, solvents and alternative reactions from the original mechanism. This is to answer the aim of the report, if it is possible to synthesise lignin models in a more time-efficient manner than what the article states, which is achieved by reducing the reaction steps. From a sustainable perspective, fast methods and processes follows the principles of green chemistry. The study will need to be delimited to the time frame, thus the primary focus is on experimentally finding methods to streamline the synthesis path, making it more effective.

1.3   Interpretation

Experimental data and results will be analysed during the laboratory mainly using thin layer chromatography, TLC, as a control that the reactions worked properly by monitoring during reaction time. For further analysis, nuclear magnetic resonance spectroscopy, NMR, is applied for interpretation of molecular compounds and structural fragments of obtained products.

2
Theory

2.1 Pulp and Paper Industry

The pulp and paper industry is still a vital component of the modern world [2]. Products manufactured from papers are widely used in a variety of areas, from newspapers to tissue papers. The wide variety of paper qualities are a product of different industrial processes, preserving sought after properties for the specific product. The characteristics of wood pulp is determined by its final composition. Lignin provides much of the strength in the wood and gives it a yellow colour.

Mechanical pulping is achieved by using mostly mechanical force to break down the structure in the wood, which retains much of the strength of the fiber but makes it more coarse and rough [2]. This is a result of a high amount of lignin and impurities remaining after the process. It is common to use a chemical wash to aid in removing some of the lignin, even in these types of processes. The amount is substantially smaller than in chemical pulping. Examples of common products made from mechanical pulp are newspaper and cardboard.

In chemical pulping, a higher purity of the pulp is achieved by using white liquor, accompanied by washing, to remove most of the lignin and impurities [2]. Lignin is removed by using white liquor which consists of sodium hydroxide and sodium sulphate. After the cooking process, the now black liquor is extracted, composed of the white liquor and mostly lignin. In modern day recovery boiler systems, the liquor is evaporated and burned, providing heat for other parts of the pulp making process. The resulting pulp is a more fine, bright and porous mass, providing a good material for products such as printing paper, toilet paper and napkins.

2.2   Wood

Wood is composed of three main constituents; lignin, cellulose and hemicellulose [2]. These interact with each other to give wood it's structural and mechanical properties via primary and secondary bonds. Proportions of these vary between different types of wood. Softwoods generally contain 25-30 % lignin while hardwoods generally contain less, around 20 %. Even within these categories, the exact lignin content varies between individual species. Due to the fact that this thesis revolves around lignin model synthesis, lignin will be discussed over cellulose and hemicellulose in the following segment.

2.3   Lignin Compounds

The structure of a lignin molecule alter between different types of wood. Nonetheless, the base structure remains the same [3]. Lignin is a biopolymer made up of three phenolic alcohol monomers, also known as monolignols; sinapyl alcohol (S), coniferyl alcohol (G) and p-coumaryl alcohol (H). These form bonds between the phenol groups and alcohol groups with a β-O-4 linkage to create a large amorphous web-like structure. Lignin provides structural rigidness through interactions with cellulose and hemicellulose in the cell wall. Long strands curve around the cells in varying ways, which additionally creates a porous configuration that aids the liquid absorbing qualities of the wood.
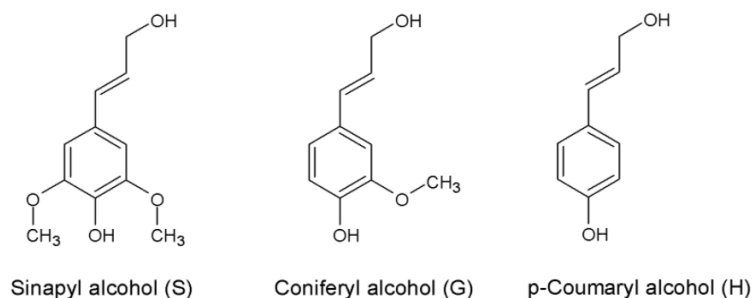
Figure 2.1: The three phenolic alcohol monomers that builds up the lignin compound [3]

Lignin and its macro structure varies between softwood and hardwood [3]. The differences lie in what monolignols make up the lignin. The main constituents of hardwood are sinapyl (S) and coniferyl alcohols (G). The two monolignols are in approximately equal amounts to there being three times as much sinapyl alcohol. Softwood contains almost exclusively coniferyl alcohol, with traces of p-coumaryl alcohol.
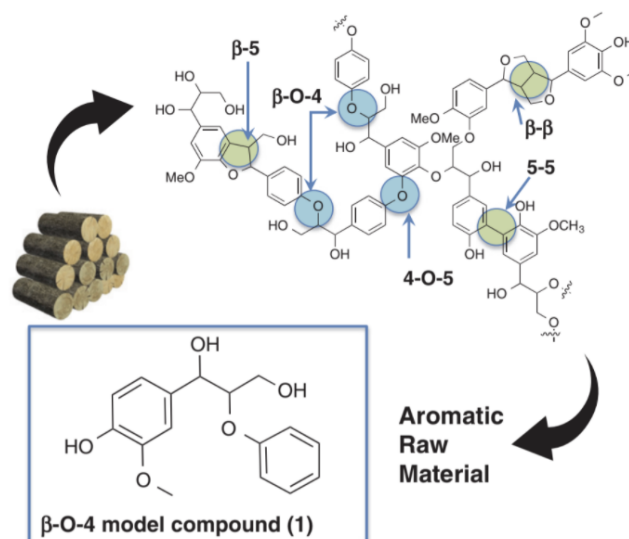
Figure 2.2: β-O-4 linkage in a large amorphous web-like structure [1]

2.4 Green Chemistry

The drive to develop and engineer sustainable and green ways of using the earth's resources is growing amongst consumers and producers alike. Signs of the greenhouse effect has been showing more and more and awareness of it has grown with it. This study contributes to sustainable uses of wood pulp through research towards using lignin in a more efficient way than the modern way of burning it for heat energy. The field has been researched for many years, producing promising results, such as one by where lignin shows promise for being turned into biofuel [4]. Although these studies have made such advancements, further research continues to be a necessity. Through working towards streamlining the synthesis of lignin models, continued work in the field of lignin research is made more available.

Green chemicals, meaning materials which are inexpensive, have low environmental impact and are less toxic, are preferable when attempting to streamline any chemical process. Finding greener substitutes for example solvents in a reaction is a good way to improve the environmentally friendly nature of a process. Method factors are similarly important, producing similar results as chemical substitution. Limiting the amount of steps or using a greener solvent serves the same purpose. In this report, efficiency has been attempted to be achieved in various ways, including reducing the number of steps by using a "one-pot", where two steps are made into one, eliminating the use of evaporation equipment, solvent and possible more for that part of the process. Furthermore, by using greener and safer solvents, such as deionized water, the environmental impact of the process is reduced [5]. Many solvents used today are produced through finite sources, such as through extraction of fossil materials. An example of such a solvent is toluene, which is found in crude oil and is extracted during petroleum production process.

Working towards making the synthesis of β-O-4 model more streamlined, is important to the ongoing effort to improve the state of the environment. Creating affordable, effective and green synthesis paths will hopefully contribute to finding more effective uses of lignin obtained from the paper pulp process. The focus for this thesis has been on improving efficiency by substitution with greener solvents and reducing the amount of steps required.

2.5   Reaction mechanism

This section will give a detailed overview of all steps required for the complete synthesis of the β-O-4 model from vanillin. Due to lack of time, all of the steps were not able to be completed. Altough, describing the full intended synthesis is of contextual importance for understanding the synthesis. The following sections will be divided into two parts, one containing all performed reactions and one with all that were not completed. The yield for the different steps was not the main focus, although this is also something that would benefit the synthesis in terms of green chemistry, by reducing the amount of starting material required.
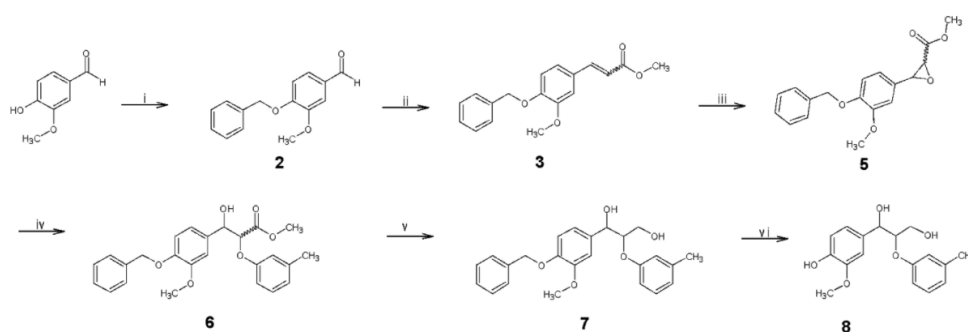
Figure 2.3: Intended synthesis of the reaction for producing complex lignin compounds

2.5.1   Reaction flow i - ii
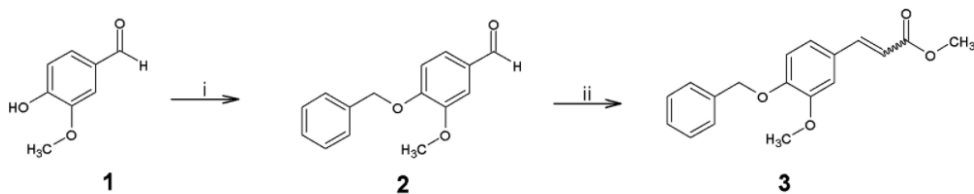
Figure 2.4: Reaction scheme to successfully produce intermediate for i - ii

The first step in the synthesis involves vanillin **(1)** in a solvent, which is deprotonated by a base. A nucleophilic reaction with benzyl bromide occurs, resulting in a benzylated derivative, benzyl vanillin **(2)**. This benzyl group acts as a protective group to the vanillin, preventing unwanted reactions.

Synthesis of 3-(4-(benzyloxy)-3-metaoxyphenyl)acrylate **(3)** is made in accordance with an article by El-Batta et al [6]. The article includes a synthesis of an α-β-unsaturated ester via a wittig reaction, with water as solvent. The synthesis is performed through a reaction with triphenylphosphine and methyl 2-bromoacetate in a saturated solution of $NaHCO_3$.

2.5.2 Reaction flow iii-vi
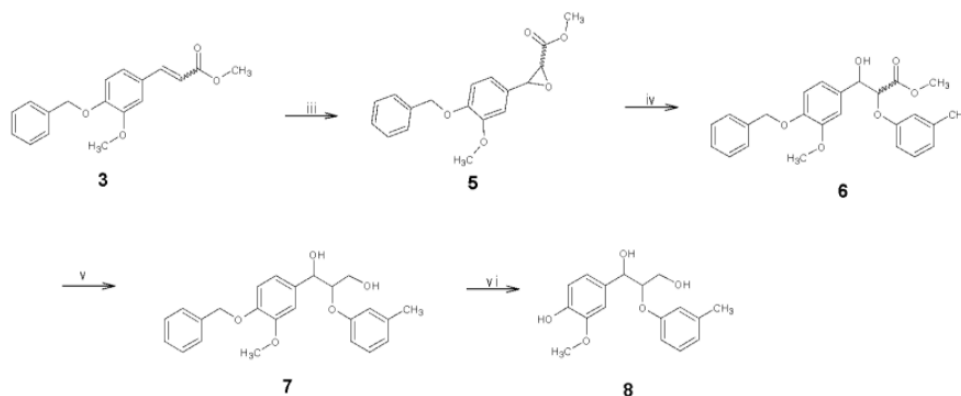
Figure 2.5: Reaction scheme for **(3)** to **(8)**

The following section will cover the reaction flow of the reactions that either were attempted and failed or not attempted at all. Reaction iii was attempted but failed while steps iv-vi were never performed.

The synthesis of methyl 3-(4-(benzyloxy)-3-methoxyphenyl) oxirane-2- carboxylate **(5)** is made in accordance with an article by Gak Yang et al regarding the oxidation of an olefin into an epoxide [7]. The oxidation agent used here is tetrabutylammonium peroxydisulfate **(4)**. The oxidant is synthesised through a reaction with tetrabutylammonium hydrogensulfate and potassium persulfate in water.

Further, **(3)** and **(4)** react together with hydrogen peroxide and sodium hydroxide, in order to produce **(5)**. Hydrogen peroxide and sodium hydroxide react to form HOO- which reacts with **(4)** to form a peroxysulfate anion intermediate. The strong nucleophilie oxidizing properties of this intermediate towards **(3)** will result in a 1,4-addition to an α-β-unsaturated ester. The double bond of **(3)** will thereby be replaced by an epoxide group.

By deprotonating m-cresol through introducing KOH, a nucleophilic attack will be initiated on the epoxide **(5)**, resulting in the addition of the phenol group, producing methyl 3-(4-(benzyloxy)-3-methoxyphenyl)-3-hydroxy-2-(m-tolyloxy)propanoate **(6)**.

The last two steps, v and vi, include reductions. The planned method would have followed the process used by Mukhtar et al [1], which involves well-established reduction methods. It is therefore safe to assume that now unwanted reactions would take place in these steps. Although, it is possible that further optimisation to the product would be necessary, prior to achieving a successful result. The reactions start with **(6)**, an α-β-unsaturated ester, being reduced to a primary alcohol through the use of $LiAlH_4$ in diethyl ether. Now, 1-(4-(benzyloxy)-3-methoxyphenyl)-2-(m-tolyloxy)propane-1,3-diol **(7)** has been attained.

Secondly, the protecting group, in this case the benzyl group, is removed with Pd/C and H_2 gas. 1-(4-hydroxy-3-methoxyphenyl)-2-(m-tolyloxy)propane-1,3-diol **(8)** has now been attained.

2.5.3 Reaction mechanism for wittig salt
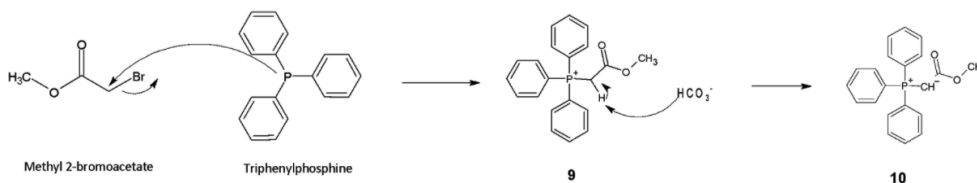
Figure 2.6: Synthesis of the wittig reaction part 1

In this section, the overall reaction mechanism for the wittig salt on the benzyl vanillin will be described more precisely. First of all, an nucleophilic attack will occur on the methyl 2-bromoacetate by triphenylphosphine. This will cause the bromide to leave the molecule and form (2-methoxy-2-oxoethyl)triphenylphosphonium cation **(9)**, before HCO_3 depronates the α-hydrogen and cause a negatively charged α-carbon. The product **(10)** has now been formed.
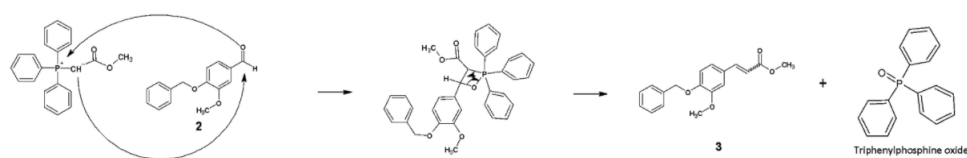
Figure 2.7: Synthesis of the wittig reaction part 2

Subsequently, the α-carbon will make a nucleophilic attack on to the aldehyde carbon in **(2)**. Due to this attack, a double bond of oxygen will be released to O-P with phosphorus. At last, the linkage between C-P and C-O will break to form double bondings between C=C and O=P, and the product **(3)** together with triphenylphosphine oxide has been produced.

3
Methods

3.1 Experimental

3.1.1 Benzyl Vanillin

Following the method from the article by Mukhtar [1], in a 100 mL round-bottom, a small magnet stirred solution of vanillin (5 mmol) and 20 ml of acetone, 8 g of K2CO3 and benzyl bromide (5.30 mmol) was added respectively. The suspension was then stirred for 3 h and monitored by TLC during the reaction time.

After the reaction was completed, the suspension was filtered and evaporated in order to remove the base and solvent. The remaining oil was extracted with dichloromethane and water three times (10 mL at a time of each substance) in a separation funnel. The residual organic phase was dried over sodium sulphate before evaporated under reduced pressure to furnish a white solid. NMR is taken for further analysis.

^{1}H NMR (CDCl$_3$): $\delta = 9.84$ (s, 1 H, aldehyde), 7.46 - 6.95 (m, 7 H, Ph), 6.98 (s, 1 H, Ph-H), 5.25 (s, 2 H, CH$_2$), 3.95 (s, 3 H, CH$_3$).

Table 3.1: Precise amount chemicals used in Benzyl Vanillin reaction

Chemical Substance	Precise amount used in Experiment
Vanillin	8.5 g
K_2CO_3	8.00 g
Benzyl bromide	0.63 mL
Sodium ethoxide	386.0 mg

3.1.2 Wittig Reaction

Procedure for Wittig Reaction without One Pot

For the procedure containting wittig reaction without one pot was achieved by following the method from the article by Mukhtar [1]. In a 50 mL round-bottom, a small magnet was added along with a mixture of triphenylphosphine (6.7 mmol) and 10 mL ethyl acetate. To the mixture, a solution containing methyl 2-bromoacetate (6.5 mmol) in ethyl acetate were added, and the content reacted for 17 h at room temperature. The progress was continuously monitored by TLC.

When the reaction was complete, a white precipitate was collected by filtration. The mixture was transferred to a separation funnel where it is being extracted with diethyl ether three times (25 mL at a time). The organic compound is being collected and dried with sodium sulphate before evaporated under reduced pressure to furnish a white solid.

The white solid, phosphonium bromide (4.81 mmol) was added to a suspension of sodium ethoxide (340 mg) in 30 mL ethanol in 100 mL round-bottom with a magnet. To the mixture, aldehyde from previous reaction (1.0 mmol) were added and stirred at room temperature for 1 h, before further stirring at 50 - 55 ° for 1 h. The progress was monitored by TLC during the process.

After completed reaction, water was poured and the solution was transferred to a separation funnel where it was being extracted with diethylether four times (25 mL at a time). The organic compound is being collected and dried with anhydrous sodium sulphate before evaporated under reduced pressure to furnish a white solid. NMR is taken for further analysis.

The reaction was performed in a one pot, meaning using one vessel for the reaction with no processing in between. This differs from the method used in the article from Mukhtar et al [1], where the synthesis of the wittig salt and synthesis of **(3)** were performed separately. The product was thereafter washed with sodium bisulphate and separeted. This extracts any remaining aldehyde, which is the premise of this extraction method used in accordance with an article by Furigay et al [8].

Table 3.2: Precise amount chemicals used in Wittig reaction without One Pot

Chemical Substance	Precise amount used in Experimment
Triphenylphosphine	8.5 g
Methyl 2-bromoacetate	4.97 g
White solide (phosphonium bromide)	5.22 g
Sodium ethoxide	886.0 mg

Procedure for Wittig Reaction with One Pot

By a one pot reaction, all the chemicals are added simultaneously and allows the mixture to react at instant [6]. This type of method is more time efficient regarding that intermediate steps and minor work-ups are overlooked. Following the method from an article by El-Batter et al. in a 20 mL scintillation vial, a small magnet was added along with a mixture of triphenylphosphine (1.4 - 1.5 mmol), saturated aqueous NaHCO3(5 mL), an appropriated - bromoester (in this experiment methyl 2-bromoacetate were being used, 1.6 - 1.8 mmol) and aldehyde from previous reaction (1.0 mmol). When the chemicals were applied to the vial, it was capped and the content reacted for 4 hours. During the reaction time, the progress was continuously monitored by TLC.

When the reaction is complete after being controlled by TLC that all the initial chemicals has dissolved, 25 mL of deionized water is added and the mixture is transferred to a separation funnel where it is extracted with diethyl ether three times (25 mL at a time). The organic compounds is being collected and allowed to dry with sodium sulphate before filtration. Thereafter, it is being evaporated under reduced pressure to furnish a solid residue. NMR is taken for further analysis.

^{1}H NMR (CDCl$_3$): δ = 7.60 (d, J = 16.0 Hz, 1 H, olefinic proton), 7.46 - 7.28 (m, 6 H, Ph), 7.22 (dd, J = 1.6, 8.3 Hz, 1 H, Ph-H), 7.05 (d, J = 8.3 Hz, 1 H, Ph-H), 6.56 (d, J = 16 Hz, 1 H, olefinic proton), 5.13 (s, 2 H, PH-CH$_2$, 3.77 (s, 3 H, CH$_3$), 3.67 (s, 3 H, CH$_3$)

Table 3.3: Precise amount chemicals used in Wittig reaction with One Pot

Chemical Substance	Precise amount used in Experiment
Triphenylphosphine	0.482 g
$NaHCO_3$	5.0 mL
Methyl 2-bromoacetate	0.34 g
Aldehyde	2.60 mg

Purification

The solids produced from the wittig reactions with, and without one pot, are mixed and prepared all together for purification by using a column chromatography (ethyl acetate : hexane, 3:7). When the chromatography was completed, the product was possessed and reduced under pressure to evaporate. The produced white solid was dissolved in a solution of 25 mL diethyl ether and small amounts of saturated $NaHSO_3$, before extracted by using a separation funnel. Organic phase was collected and reduced under pressure and the purified solid were analysed by NMR.

3.1.3 Oxidizing Agent

For producing the oxidant that were later used in the epoxidation, method was followed from an article by Gan Yang [7]. In a 50 mL round-bottom, a small magnet was added along with tetrabutylammonium hydrogensulfate (64.0 mmol) and potassium persulfate (32.0 mmol). The chemicals were dissolved in deionized water and the solution was stirred for 60 min at room temperature.

When the reaction is complete the solution was moved to a separation funnel where it was extracted with dichlormethane three times (30 mL at a time). The combined organic layers was collected and washed with deionized water, dried over anhydrous sodium sulphate before filtration. Afterwards, it was evaporation under reduced pressure to furnish a oxidant as a white solid. NMR is taken for further analysis. The oxidant received from the reaction is tetrabutylammoinum peroxydisulfate.

^{1}H NMR (CDCl$_3$): $\delta = 3.31$ (t, 8 H, CH$_2$), 1.63 (t, 8 H, CH$_2$) 1.45 (m, 8 H, CH$_2$), 0.98 (t, 12 H, CH$_3$)

Table 3.4: Precise amount chemicals used in Oxidation Agent reaction

Chemical Substance	Precise amount used in Experiment
Tetrabutylammonium hydrogensulfate	21.2 g
Potassium persulfate	8.70 mL

3.1.4 Epoxidation

The following method was performed but never produced the wanted results. It is therefore important to view the following segments as a trial, not as a functioning method for epoxidation of this form of molecule. Furthermore, NMR results will not be shown in this section but will instead be discussed in the Results and Discussion section.

The epoxidation follows the method B from the article from Gan Yak [7]. To a stirring solution **3** (0.50 mmol) and 10 mL methanol, along with tetrabutylammoinum peroxydisulphate, oxidant (0.50 mmol) from previous reaction and NaOH (0.50 mmol) were added. Hydrogen peroxide (0.50 mmol) was thereafter added dropwise and stirred for 120 minutes. The reaction was monitored by TLC.

After finished reaction, the mixture was quenched with 30 mL saturated ammonium chloride and the solution was moved to a separation funnel where it was extracted with diethyl ether three times (30 mL at a time). The combined organic layers were dried with anhydrous sodium sulphate and evaporated to produce white crystals. The crystals were dissolved and run through a flash column chromatography to procure a pure product after another evaporation.

Table 3.5: Precise amount chemicals used in Epoxidation reaction

Chemical Substance	Precise amount used in Experimment
Substance (3)	0.746 g
Potassium persulfate	8.70 g
Oxidant (tetrabutulammonium peroxydisulphate)	1.70 g
$NaOH$	100 mg
Hydrogen peroxide	2.5 mL

3.1.5 Epoxidation with trans-cinnamaldehyde

The previous method was tested beforehand using trans-cinnamaldehyde in place of product **(3)** from the Wittig Reaction. The decision was made based on the fact that low amounts of **(3)** was produced from previous reaction. Trans-cinnamaldehyde was therefore chosen because of the similarity in both being α-β unsaturated.

Table 3.6: Precise amount chemicals used in Epoxidation reaction

Chemical Substance	Precise amount used in Experimment
Trans-cinnamaldehyde	0.740 g
Potassium persulfate	8.72 g
Oxidant (tetrabutulammonium peroxydisulphate)	1.70 g
$NaOH$	100 mg
Hydrogen peroxide	2.5 mL

4

Results and Discussion

All the earned NMR data and results from the experiment are represented in the appendix section of this thesis.

4.1 Benzyl Vanillin

In the step of synthesising benzyl vanillin, different solvents and bases were used. In the original procedure, DMF was used as a solvent, and K_2CO_3 was used as the base. However, the process did not go as expected.

The suspension had not successfully reacted after it had been stirred, when it was being monitored via TLC. Furthermore, having been dissolved in water, the solution was not able to be properly evaporated, creating further difficulties in regards to processing the solution after the reaction. The solution also contained excessive amounts of K_2CO_3, which lead to the observation of three distinct layers during extraction with an extraction funnel. In addition to the organic and water phases, a mixed layer was observed. These problems provoked additional attempts with different solvents and an increased amount of filtration steps.

The solvents that were used instead of water were ethanol and acetone. This decision was based on a article by Nakatsubo et al [9], where synthesis of benzyl vanillin was conducted using ethanol. Acetone was chosen because of the similarity in polarity to ethanol. The base was also replaced with KOH as an alternative base. Results are presented in table 4.1. Recrystallization was problematic because of the presence of remaining benzyl bromide. To combat this, the rate was decreased from (1:1.7) vanillin:benzyl bromide to (1:1.05). This turned out to be problematic since all vanillin was not able to react, according to NMR results.

Table 4.1: Results from analysing different solvent and bases

Samples	Solvent	Base	Results
(1)	DMF	K_2CO_3	All vanillin consumed
(2)	Ethanol	K_2CO_3	Some vanillin was left
(3)	Ethanol	KOH	Some vanillin was left
(4)	Acetone	K_2CO_3	All vanillin consumed
(5)	Acetone	KOH	Failed attempt

4.1.1 NMR interpretation

Sample 1 - DMF with K_2CO_3

NMR for sample 1 displays a signal at 9.8 ppm, indicating the presence of an aldehyde proton on both vanillin and the product, benzyl vanillin. The signal at 5.2 ppm indicates the presence of double protons in the product and the signal at 4.3 ppm indicates double protons on the benzyl bromide. If all vanillin had been consumed, the signal on 5.2 ppm should be shown as a double for the signal on 9.8 ppm.

The result from this sample is hard to compare with the other three because the reaction was processed differently from the other three. Reasons that the DMF was difficult and problematic to evaporate, as well as it blended with water while extraction. The reason for the presence of water was the method used, which utilises water for precipitation of the desired product.

Sample 2 - Ethanol with KOH

NMR for sample 2 shows total consumption of benzyl bromide, which is a perplexing result since vanillin is the limiting factor in this reaction.

Sample 3 - Ethanol with K_2CO_3

NMR for sample 3 shows that the intensity of product signal is almost as double as the aldehyde signal. Thus indicating that there still are vanillin left from the reaction.

Sample 4 - Acetone with K_2CO_3

What is evident in analysis of NMR results for sample 4 is that the intensity of the aldehyde signal is approximately half of that off the product. This is a good indication that all the vanillin had been consumed.

Sample 5 - Acetone with KOH

Failed attempt, no NMR data was attained.

4.2 Wittig Reaction

Procedure for Wittig Reaction without One Pot

NMR results indicate the presence of an aldehyde. Signals for benzyl vanillin were absent, indicating that it had reacted fully. Even though the reaction could be considered successful, the overall time required for the procedure was long and included external processing phases that penalises the time efficiency aspect of the thesis. Therefore, an alternative synthesis was tested and evaluated where all the chemicals was put inside a scintillation vial, as an one pot reaction, and stirred only once for a reduced reaction time.

Procedure for Wittig Reaction One Pot

The NMR result confirms that the alternative synthesis method was successful, yet a signal at 9.8 ppm was observed after the reaction, indicating the presence of benzyl vanillin aldehyde that had not reacted. Even though some aldehyde was still present, the product that has been obtained would still be used in further steps. This is because of the small amount of aldehyde remaining and if attempts to purify the product were to be applies, the risk that the desired product yield is reduced or its fragments are excreted increases. Thus, the decision was made that it was better to proceed with the product obtained in the synthesis path.

One important factor to be acknowledged is the fact that if the stirring during the reaction goes further than mentioned time, the risk that the fragments and particles in the molecule were to be destroyed, increases substantially. That is one source of error in the experiment that can cause the final product to be demolished or produce unwated results. Therefore, it is vital that the solution is being controlled and monitored by TLC during the process, minimising the risk of harming the product. The fragments can also be harmed even before expected time of finished reaction if the temperature or pressure used are too harsh. For a optimal stirred solution, the parameters should be unchanged and be kept same during the whole process.

4.3 Oxidizing Agent

The reaction was carried out without notable problems and NMR data corresponds to the reference data, thus indicating a sucessful result. The next phase on the synthesis is an epoxidation of general and electron-rich olefins, and by achieving electrophilic oxidants, the synthesis is facilitated. Therefore, the oxidizing agent obtained is a versatile reagent for useful transformations, especially for further epoxide reactions in the synthetic pathway.

4.4 Expoxidation

The possibility of reacting **(3)** into an epoxide was examined through the use of a similarly structured α-β-unsaturated aldehyde. The chemical used was trans-cinnamaldehyde. After the finished reaction, the epoxide was to react with a phenol, m-cresol, to introduce a β-O-4 linkage to the molecule. Different solvents were tested and reaction times varied.

Epoxidation of 3-(4-(benzyloxy)-3-metaoxyphenyl)acrylate

NMR results from trials using **3** shows significant amounts of residual starting material in all attempts, indicating that the epoxide was not sucessfully produced. One cause of this may be the steric hindrance from the protecting benzylic group on **3**, since this is a varying factor from the cinnamaldehyde. This would cause the oxidising agent to not be able to approach the double bond, thus preventing the epoxidation from occurring. Another varying factor is the fact that **3** is an ester, providing a possible interpretation that the reactivity of an ester to this reaction is less than that of an aldehyde. This was not able to be further investigated due to lack of time.

Epoxidation of trans-cinnamaldehyde

The reaction was stopped after TLC analysis indicated that all starting material was consumed. Trans-cinnamaldehyde was easily recognisable via TLC and when the solution did not include any indication of containing trans-cinnamaldehyde, the reaction was considered complete. Although, this produced conflicting results with the NMR data obtained, showing varying degrees of cinnamaldehyde signals. The consistency of the product varied, ranging from coloured to uncoloured liquids to moist white crystals. In the cases where NMR showed strong signals for cinnamaldehyde, the liquid retained some of the colour and smell of cinnamaldehyde. Some NMR results showed low intensity in signals for cinnamaldehyde but the product was still a viscous liquid. In these cases, a signal for benzaldehyde was identified. This indicates that the cinnamaldehyde had reacted into an epoxide, which further reacted into benzaldehyde. The result which showed the least signals for any aldehyde produced a white solid, showing promise for having created the epoxide.

NMR signals at 10.0 ppm indicates the presence of benzaldehyde. This is an interesting observation which supports the theory of trans-cinnamaldehyde reacting into benzaldehyde. The way this transpired could not be tested due to lack of time, although it could be theorised. On breakage of the double bond of the cinnamaldehyde, a possible result is the creation of a vicinal diol forming in the presence of the activated oxidising agent. This could further be subject to a cleavage of the coal bonds between the hydroxide groups [10] [11], thus resulting in an aldehyde with one less coal in it's chain, which is this case is benzaldehyde.

Due to the time scope of this thesis, the main focus was on improving methods by substitution with greener chemicals and reduction of the amount of steps required. Further improvements could be made to increase yield, which would similarly improve efficiency in terms of green chemistry.

Taking into consideration that earlier trials using trans-cinnamaldehyde were more successful than later ones, it is possible that it had been contaminated, since it is sensitive to light.

5

Conclusion and Future Outlook

Due to lack of time, a complete synthesis was not able to be achieved. A few optimisations to some of the reactions were accomplished but further experimentation would have been desired, provided more time was available.

5.1   Solvents

A mixture of acetone and potassium carbonate were the most promising combination for use in reaction i. TLC and NMR analysis indicated complete reaction from vanillin to benzyl vanillin. What was troubling was the fact that re-crystallisation was not successful and therefore, yield could not be determined. The mixture of ethanol and potassium carbonate was not easily evaluated, because of the fact that it produced confusing results. In other words, there was no way to tell if this mixture had a positive or negative effect on the reaction.

5.2   Wittig Reaction

The decision to perform the wittig reaction with one pot in order to reduce time, energy and solvent required, was successful. As was evident from the results, some aldehyde was still present though. Further trials would be beneficial to perform, in order to minimise, or preferably eliminate, any remaining aldehyde in the product. The substitution of toluene with water as a solvent is beneficial to improving the method in terms of green chemistry. Toluene, made from fossil fuels, is a finite resource, which contributes to the increasing amounts of emitted greenhouse gases by emission of carbon dioxide. Meanwhile, water exists in greater abundance and the environmental impact is much lower.

5.3 Epoxidation

Attempts with **(3)** to create an epoxide and further react with m-cresol were not successful. The most probable cause of this seems to be the inability for the oxidant to perform a nucleophilic oxidation with the protective benzylic group on the benzyl vanillin molecule. There was not enough time to confirm that this was the only cause. Tests with trans-cinnamaldehyde were not able to provide enough information about the reaction, because of the fact that results varied greatly, suggestively due to contamination of the trans-cinnamaldehyde sample.

5.4 Alternate reaction paths

Performing flash column chromatography on **(2)** would have been a valid route for extracting any remaining benzyl bromide. Persistent benzyl bromide in the product was the main reason behind the inability to recrystallise. A TLC analysis indicated that benzyl bromide was emulable in hexane while **(2)** was not. This would make flash column chromatography, with hexane as the appropriate eluent, suitable.

Processing for the wittig reaction with one pot was most likely largely unnecessary. The method was to perform a flash column chromatography, followed by extraction with sodium sulphate, finished off with a recrystallising. By using another eluent, which results in better separation, all aldehyde would be removed in one step, eliminating the use for extraction and recrystallising.

The theorised cause for the failure of the epoxidation, the protective benzyl group, could be attempted to be eliminated by simply adding it after the epoxide has been created. Possible consequences for previous steps would need to be examined.

5.5 Final remarks

Due to the time scope of this thesis, the main focus was on improving methods by substitution with greener chemicals and reduction of the amount of steps required. Further improvements could be made to increase yield, which would similarly improve efficiency in terms of green chemistry.

As has been mentioned several times during this thesis, a substantial amount of testing and synthesis steps had to be put off, due to lack of time. Although promising results were achieved in several parts of the synthesis, there is much research left to be done. The future of the field of lignin research looks promising and this thesis work contributes to a small, yet vital, path forward to a more sustainable society.

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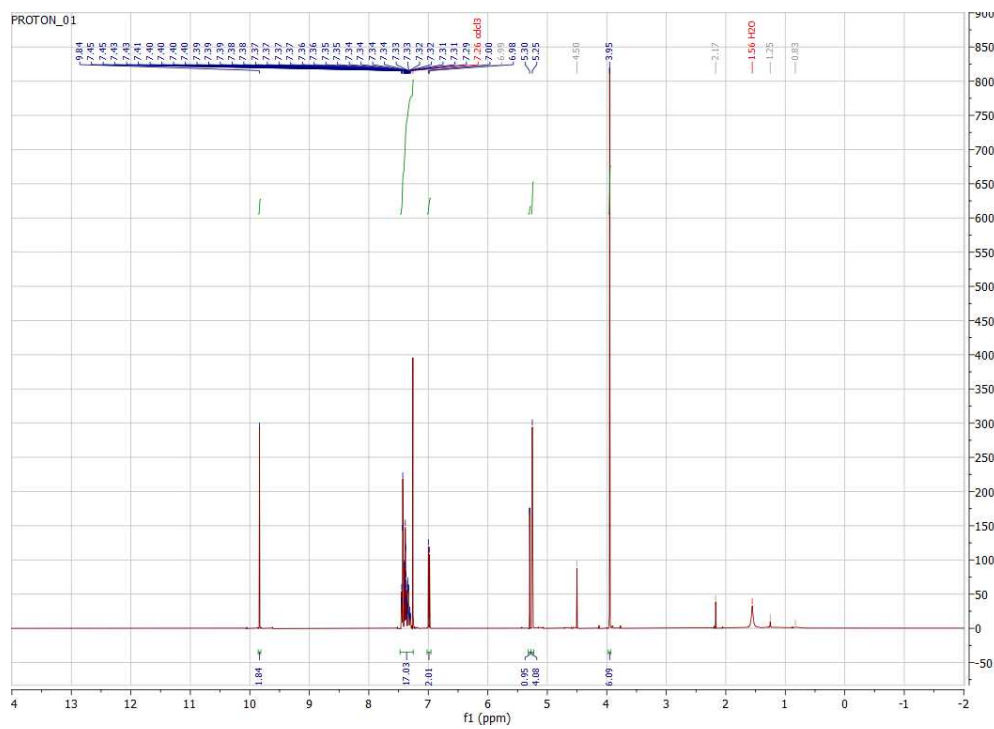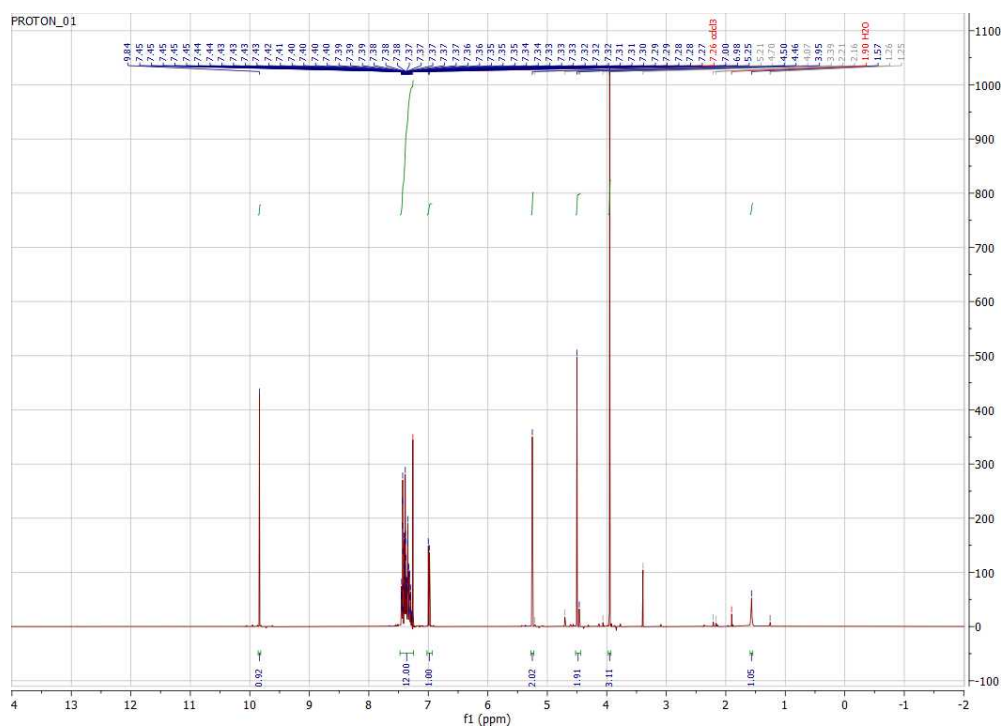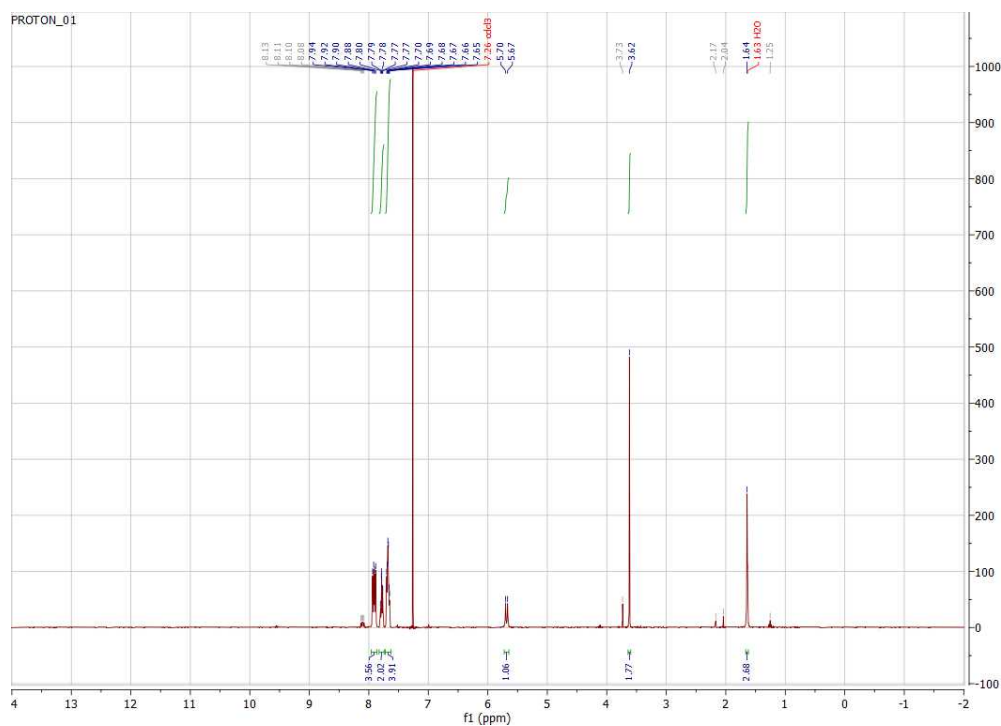
A

Appendix 1

Figure A.1: NMR data for Benzyl Vanillin (Sample 1)

Figure A.2: NMR data for Sample 2

Figure A.3: NMR data for Sample 3

Figure A.4: NMR data for Sample 4

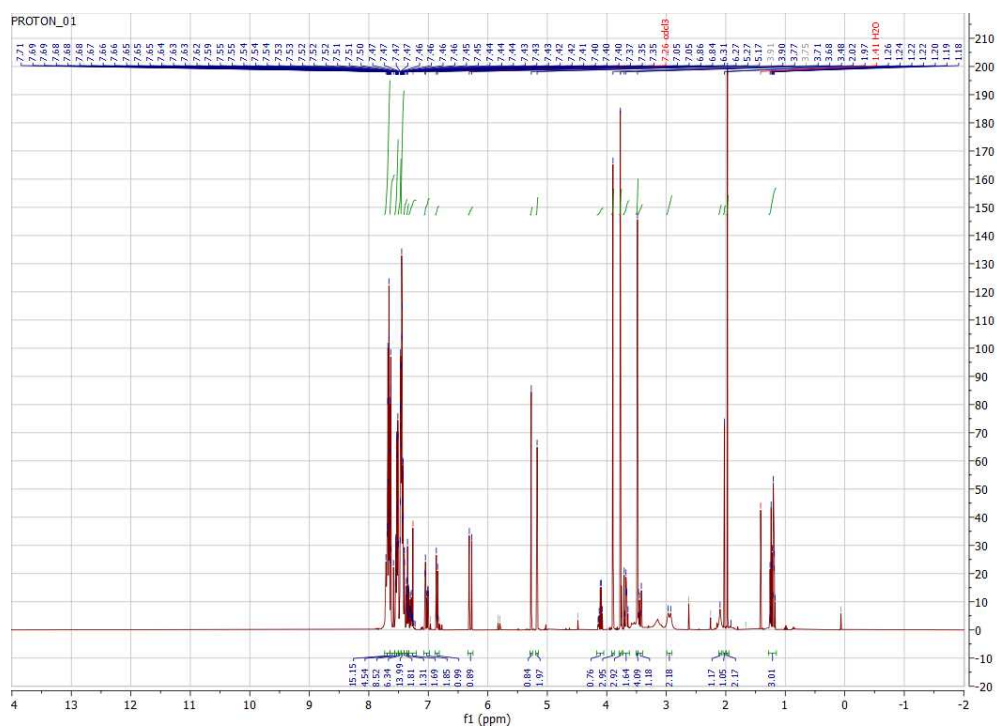**Figure A.5:** NMR data for wittig reaction without one pot
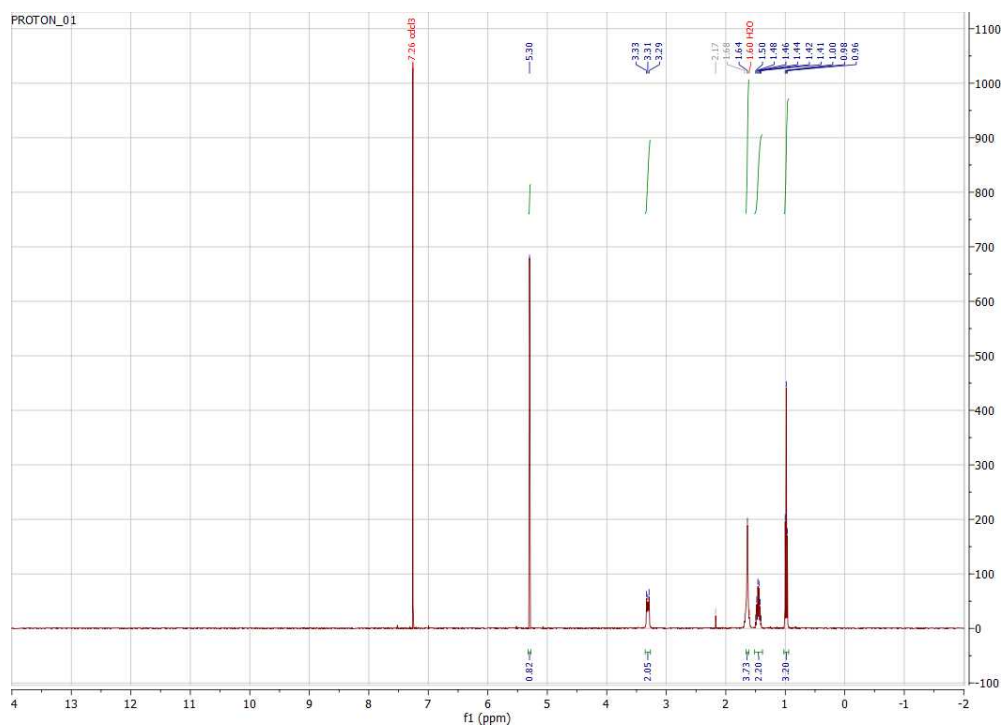
Figure A.6: NMR data for wittig reaction with one pot
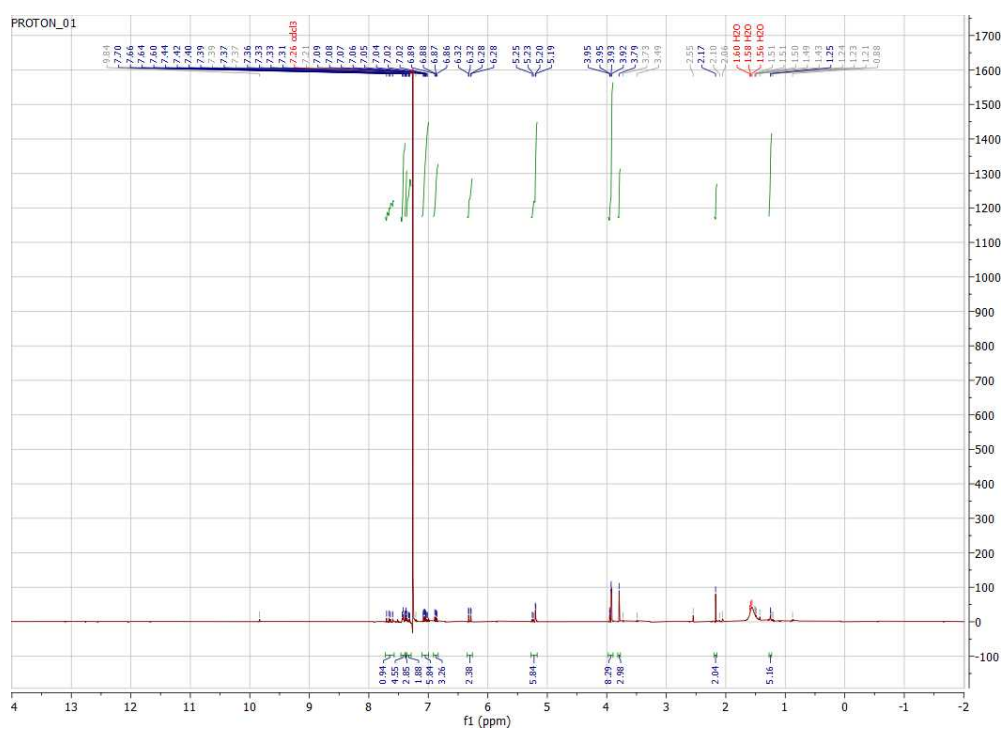

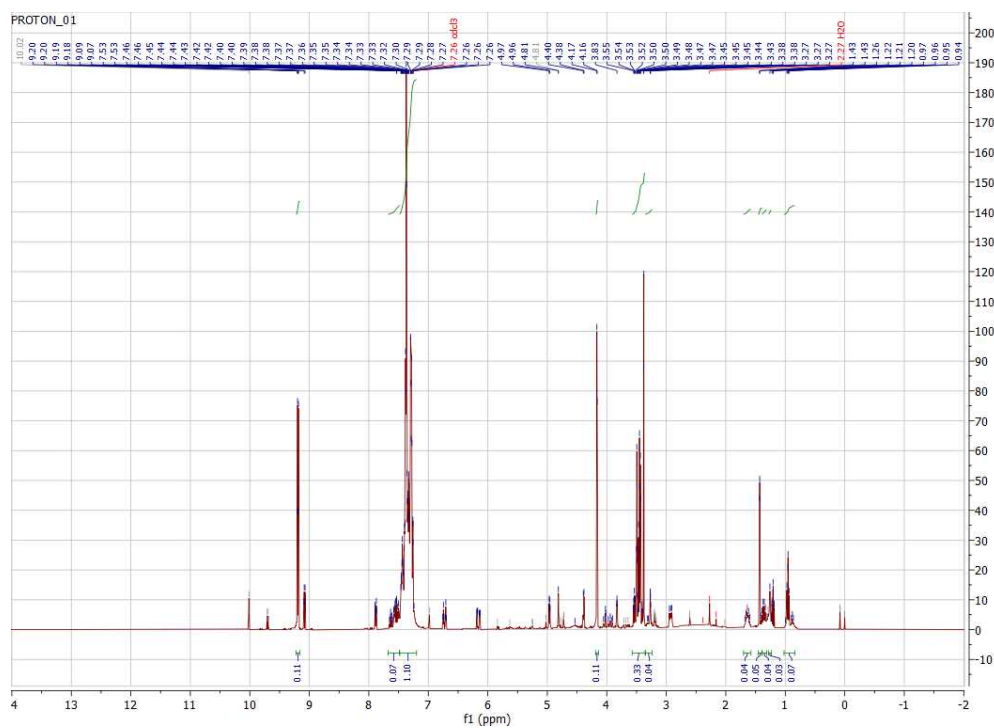**Figure A.7:** NMR data for oxidizing agent

Figure A.8: NMR data for Epoxidation

Figure A.9: NMR data for Epoxidation using trans-cinnamaldehyde