

Imperial College London
Department of Chemistry

Lignin Depolymerisation in Acidic Ionic Liquids

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The work described in this thesis was carried out at Imperial College London between October 2012 and October 2015. The entire body of work is my own unless expressly stated to the contrary and has not been submitted previously for a degree at this or any other university.

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Abstract

In this thesis, mechanistic insights into lignin depolymerisation and more specifically, the hydrolysis of the abundant β -O-4 ether linkage was gained. This was accomplished by exploring the reactivity of different lignin model compounds in acidic ionic liquids. Reported herein are investigations into the reactivity of 2-phenoxyethanol in 1-butyylimidazolium hydrogensulfate with varying amounts of sulfuric acid. Ring sulfonation was observed with the ether bond remaining intact. A similar study was then conducted using 1-ethyl-3-methylimidazolium bromide in the presence of hydrobromic acid. A Hammett plot confirmed the mechanism of ether cleavage proceeding *via* an A2 mechanism, yielding the phenolic product and 2-bromoethanol. The preparation of an array of lignin model compounds bearing the full β -O-4 linkage was also accomplished. Mechanistic studies indicated that the rate-determining step involves substrate dehydration followed by hydrolysis in ionic liquid media. This is analogous to the mechanism reported in acidic aqueous media, however was found to proceed 25 times faster. The reactivity of guaiacylglycerol- β -guaiacol ether was compared between hydrogensulfate ionic liquids. An Eyring investigation showed a consistent mechanism in all ionic liquids with full isokinetic compensation observed between the $\Delta H^\ddagger$ and $\Delta S^\ddagger$ components. The differences in the absolute values of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ were deduced to be due to the interaction of the hydrogensulfate anion with the protonated substrate, influenced primarily by the associative forces between the cation and anion, namely hydrogen bonding and sterics. A final study explored the oxidative depolymerisation of ionosolv lignin using a polyoxometalate catalyst in 1-butyylimidazolium hydrogensulfate. Vanillin and syringaldehyde were identified to be the products of highest abundance and it was observed that shorter pretreatment times led to higher aldehyde yields. Preliminary studies identified that a 5 wt % POM loading with hydrogen peroxide at 100 °C provided the optimal conditions to yield the aldehydes.

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Nomenclature

AIL Acid Insoluble Lignin

DMBQ 2,6-dimethoxybenzoquinone

EDX Energy Dispersive X-ray Spectroscopy

EE Dehydrated intermediate of GG:
3-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-2-propenol

FAB Fast Atom Bombardment

FTIR Fourier Transform Infra-red Spectroscopy

GC-MS Gas Chromatography - Mass Spectrometry

GG Guaiacylglycerol-B-guaiacyl ether

GPC Gel Permeation Chromatography

HPLC High Performance Liquid Chromatography

HSQC Heteronuclear Single Quantum Correlation Spectroscopy

IEA International Energy Association

IL Ionic Liquid

LC-MS Liquid Chromatography - Mass Spectroscopy

MPa Mega Pascal

MTBE Methyl-tert-butyl ether

NMR Nuclear Magnetic Resonance

NOESY Nuclear Overhauser effect spectroscopy

OAc Acetate

OTf Trifluoromethanesulfonate

p-TsOH para-Toluenesulfonic acid

PDA Photodiode Array

PILs Protic Ionic Liquids

POM Polyoxometalate

ROESY Rotational frame nuclear Overhauser effect spectroscopy

SD Standard Deviation

THF Tetrahydrofuran

TLC Thin Layer Chromatography

TMDP 2-chloro-4,4,5,5-tetramethyl-1,3,2-dioxaphospholane

TPES Total primary energy supply

VG veratrylglycerol-B-guaiacyl ether

Chapter 1

Introduction

1.1 The current global energy make up

Our global population is expected to exceed 9 billion by 2050 and with climate change widely recognized as the major environmental issue plaguing the 21st century there is increasing interest in the investment in carbon neutral, sustainable energy technologies.^[1] The 2013 key world energy statistics report from the International Energy Agency describes the current composition of the global energy make-up, with the current supply, transformation and consumption of all major energy sources.^[2] The world's total primary energy supply (TPES) has shown limited changes in energy source over the past 40 years. Crude oil dominates 31.5 % of total fuel shares, followed by coal (28.8%), natural gas (21.3%), biofuels (10 %) and other renewable technologies contributing to only 3.3 %.

Most of the current renewable energy technologies such as wind, photovoltaic, hydro, geothermal and tidal technology, while under constant development, only generate electricity. According to the IEA, almost a third of the global energy make-up is consumed in the transportation sector, which is largely reliant on petroleum liquid fuels such as diesel, gasoline and kerosene. Petroleum based feedstocks also provide the majority of our chemicals and materials. Replacing fossil fuels with sustainable and renewable sources will satisfy three important challenges that remain at the forefront of modern society. The well-established correlation between fossil fuel combustion and the increase in atmospheric CO₂ concentration emphasizes the advantage of using renewable energy in reducing greenhouse gas emissions. Moreover, harnessing renewable energy would alleviate the geopolitical implications that accompany the exploitation of petroleum energy resources. Finally, with the perpetual increase in the demand for energy and materials, renewable feedstocks will ensure a reliable, secure and cost-efficient delivery of fuels and chemicals.^[3] One raw material that has been deemed a suitable candidate for such purposes is lignocellulosic biomass.

1.2 Lignocellulosic Biomass

1.2.1 The modern biorefinery

In addition to mitigating climate change through implementing a carbon neutral energy economy, the 2011 IEA report on biofuels for transport claims that biorefineries will ensure promotion and sustainment of biomass resources and will also have the potential to reduce conflicts and competition over land and feedstock.^[4] The modern biorefinery has been defined by Mikkola *et al* as “a facility where different low-value renewable biomass materials are used as the feedstock in processes where they are transformed to several higher value bio-based products”.^[5] These products include electricity from the combustion of biomass, bioproducts from sugar intermediates and lignin and most importantly, biofuels. The main concepts pertaining to biorefining are analogous to those in oil refining with the sole difference that the latter uses raw materials that come from fossil resources. Figure 1.2.1 gives an example of a fully integrated biorefinery, where the energy produced is used directly for the conversion of biomass feedstocks into different value product streams.

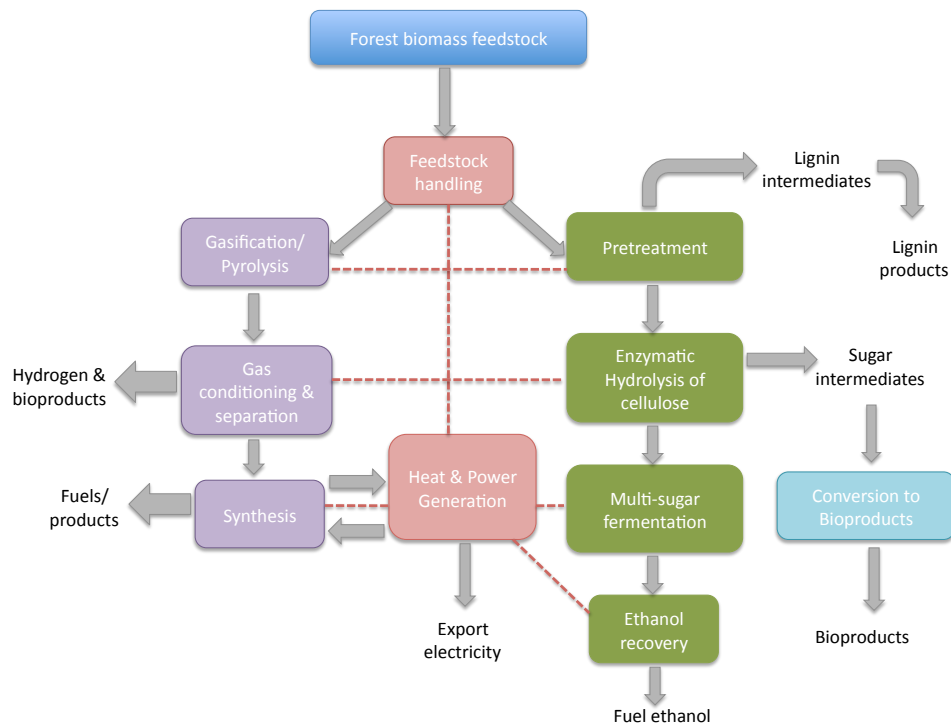


Figure 1.2.1 – Advanced biorefinery converting lignocellulosic biomass to a range of product streams

1.2.2 Second generation biomass

Currently, commercial biofuels are produced from edible components of food crops such as grains, sugar and vegetables where the starch component is fermented into low molecular weight alcohols. The USA and Brazil are currently the primary producers of biofuels, producing 49.6 % and 38.3 % of the 2007 global production respectively.^[6] The main advantage of using these feedstocks is the ease of processing into fermentable carbohydrates, but their major drawbacks centre around the competition for arable land, encouraging the displacement of food-crops and energy-intensive farming practices. The increasing criticism of these so-called “first generation” feedstocks has raised attention to the potential of second generation biofuels.^[7] Second generation biomass feedstocks offer the advantages of consuming agricultural by-products or being cultivated on non-arable land, thereby alleviating competition with food crops. As well as its potential for high CO₂ emission savings, second generation biomass offers rural development and improving economic conditions in emerging regions through offering employment and biofuel export. The considerable amount of research and the installation of a number of pilot plants around the world illustrates the growing interest of these feedstocks as suitable candidates for renewable energy production.

1.2.3 Lignocellulosic biomass: an introduction

Lignocellulosic biomass encompasses a variety of second generation biomass feedstocks including dedicated energy crops and agricultural residues. These feedstocks contain sugars which can be released by acidolysis or cellulytic enzymes.^[8] Agricultural residues such as corn stover, rice straw and sugarcane bagasse provide the benefit of having short harvest periods and being available in large quantity, providing a consistent supply for bioethanol production.^[6] In terms of dedicated energy crops, angiosperms are amongst the most promising due to the high solar energy efficiency, low nutrient and water uptake and high abundance.^[9] Examples of such plants include maize, *Miscanthus*, sorghum, sugarcane and switchgrass with *Miscanthus* being of greatest interest in the United Kingdom due to the ease of growth and cultivation in low temperature climates.^[10]

Softwood and hardwood trees can also be considered as energy crops due to their low nutrient requirements. Softwoods such as Pine and Spruce are fast-growing and abundant in the northern hemisphere hence their commercial use in the timber and wood-pulp industries.^[11] Hardwoods such as Willow offer ease of vegetative propagation, are short-rotation woody crops and are able to resprout after multiple harvests.^[12] These feedstocks are also under current investigation for their projected use in bioethanol production.



Figure 1.2.2 – *Miscanthus Giganteus* or Elephant grass

1.2.4 Composition of lignocellulosic biomass

Lignocellulose is a composite material that makes up the cell walls of woody plants and trees and is made up of three biopolymers: the carbohydrate polymers cellulose and hemicellulose and the aromatic polymer lignin. The arrangement of these polymers relative to each other is depicted in Figure 1.2.3, showing a cross section of a plant cell wall.^[13] The relative amounts of each polymer depends on the type of species and growth conditions. In addition to these polymers synthesized within the plant cells, small amounts of inorganic compounds and extractives such as waxes and lipids are also present.

1.2.5 Cellulose and Hemicellulose

Cellulose accounts for between 35 and 50 % of the dry composition of lignocellulosic biomass, therefore being the largest single component and amongst the most abundant polymers available in nature. The linear polymer is made up exclusively of glucose units, attached by β 1-4 glycosidic bonds as shown in Figure 1.2.4, with up to 10,000 glucosyl units in one chain.^[14] The high degree of linearity and rigid structure of the polysaccharide allows the chains to form flat sheets due to increased intra and intermolecular hydrogen bonding.^[15] These sheets then interact with each other *via* Van der Waals forces, packing the cellulose strands into fine crystalline microfibrils, contributing to the overall high stability of cellulose.^[16] Whilst the glucose monomer and short oligosaccharide chains are water soluble, the high molecular weight as well as the highly-ordered, rigid packing of the cellulose microfibrils renders the polysaccharide water insoluble. Upon successful dissolution or swelling of these microfibrils, the crystallinity of cellulose changes from the original cellulose I configuration to cellulose II, where hydrogen-bonding occurs between sheets, offering a more thermodynamically stable form of the polymer.^[17] Cellulose is currently the component in lignocellulosic biomass that has attracted the most interest. It can be depolymerised

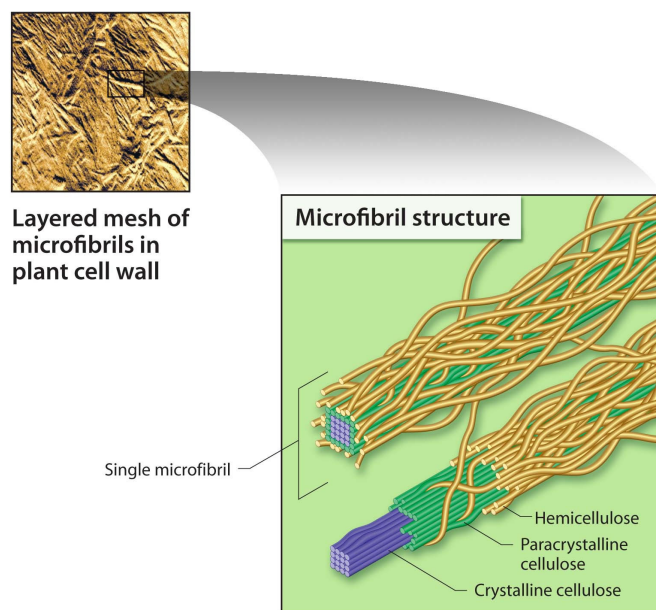


Figure 1.2.3 – Structural arrangement of the major components in the cell walls of lignocellulosic biomass taken from reference [13]

via enzymatic saccharification to yield glucose, which can then be either fermented for the production of bioethanol used in transport fuels or converted to useful platform chemicals such as hydroxymethylfurfural (HMF).^[18, 19, 20]

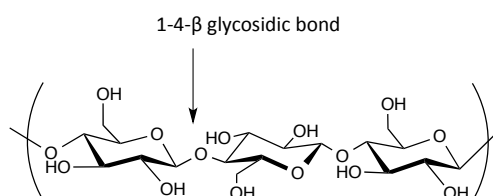


Figure 1.2.4 – The β 1-4 glycosidic bond in cellulose

The second carbohydrate hemicellulose constitutes up to 25 % of lignocellulosic biomass and is composed of polymers of lower molecular weight than cellulose, with a degree of polymerization of between 100 and 200 sugar units.^[21] Hemicellulose is composed of a number of hexose and pentose sugars and depending on the species of plant, are present in different ratios. Hemicellulose in hardwoods mainly contain xylose, whereas softwoods mainly contain mannose. Bonding in hemicellulose involves a range of different bonding motifs, depending on the sugar monomer and is thought to bind to cellulose non-covalently by providing an amorphous matrix material which holds the cellulose fibrils in place.^[16]

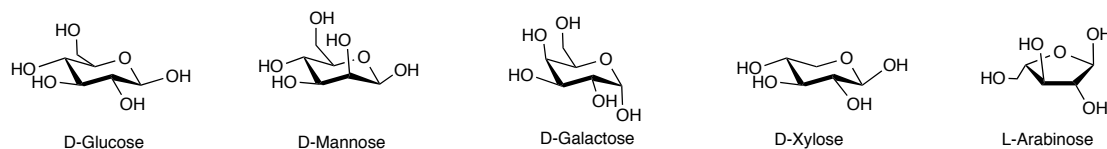


Figure 1.2.5 – The hexose and pentose sugars typically found in hemicellulose

1.2.6 Lignin: Structure and Bonding

The final component of lignocellulosic biomass is the aromatic and non-uniform polymer lignin. Lignin provides structural reinforcement to the plant, decreases the permeation of water through the cell walls whilst protecting the plant material from degradation by microbial attack. Lignin has been defined as a random, three-dimensional network comprised of various phenylpropane units, linked together *via* an array of C-C and C-O bonds.^[22] It is built from up to three building blocks known as “monolignols”, monomers based on a phenylpropanoid backbone derived originally from the amino acid phenylalanine.^[23] These monolignols differ purely in the degree of methoxylation around the para hydroxy group and are presented in Figure 1.2.6.^[24] Once incorporated into the lignin macropolymer, the monomers can be identified by their unmodified aromatic structure and are labelled guaiacyl, syringyl and p-hydroxyphenyl subunits respectively. Like hemicellulose, depending on plant species, the relative ratio of abundance of these monomers affect the structure and bonding within the lignin macropolymer, with softwood containing guaiacyl subunits almost exclusively whereas hardwoods contain mostly syringyl groups.^[25]

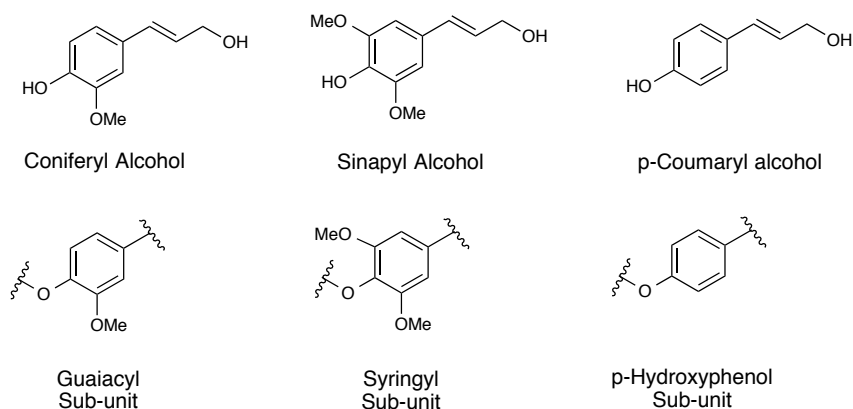


Figure 1.2.6 – Monolignols and their respective subunits identified in lignin

Lignification occurs by the $\cdot\text{H}$ abstraction at the terminal hydroxy groups present on the monolignols by laccases or peroxidases,^[23] forming resonance stabilized phenoxy radicals^[24] as shown in Figure 1.2.7.

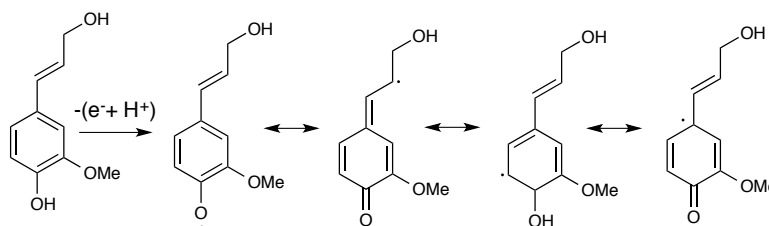


Figure 1.2.7 – Resonance stabilized phenoxyl radicals in coniferyl alcohol by enzymatic oxidation

These monolignols undergo radical coupling reactions *via* propagation through the conjugated monomers with other free radical monolignols and upon termination, forming a variety of dimers known as dilignols. One example of the free-radical reaction mechanism is given in Figure 1.2.8 showing the formation of the β -O-4 linkage. Depending on the site of termination, these reactions allow a number of linkages to form between monolignols, with the β -O-4 and β -5 coupling leading to linear polymerization. The most common linkage in all lignins is the β -O-4 ether bond, where roughly 50% of all inter-subunit linkages are of this type. Upon successful termination, hydration of the intermediate occurs, saturating the quinone methide intermediate, ceasing any further reactivity of the phenylpropanoid.

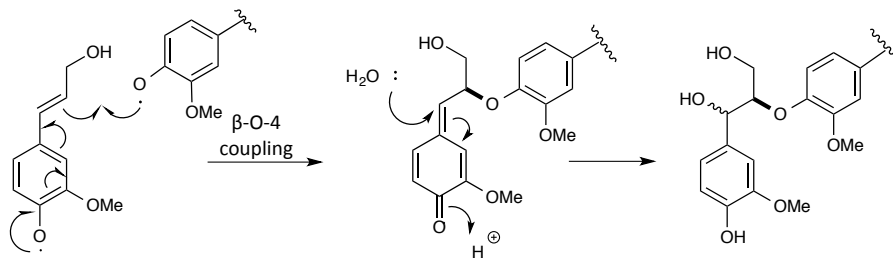


Figure 1.2.8 – Mechanism for the formation of the β -O-4 linkage

Through the nucleophilic attack of other hydroxyl groups on the quinone methide intermediate, branching of the polymer occurs. This allows lignin to adopt a three dimensional and highly branched structure.^[26] Figure 1.2.9 presents the wide range of linkages formed during polymerization and Figure 1.2.10 is a schematic representation of softwood lignin, first proposed by Adler in 1977.^[27] The illustration shows the phenolic alcohol groups occupied in bonding with neighbouring phenylpropane linkages.

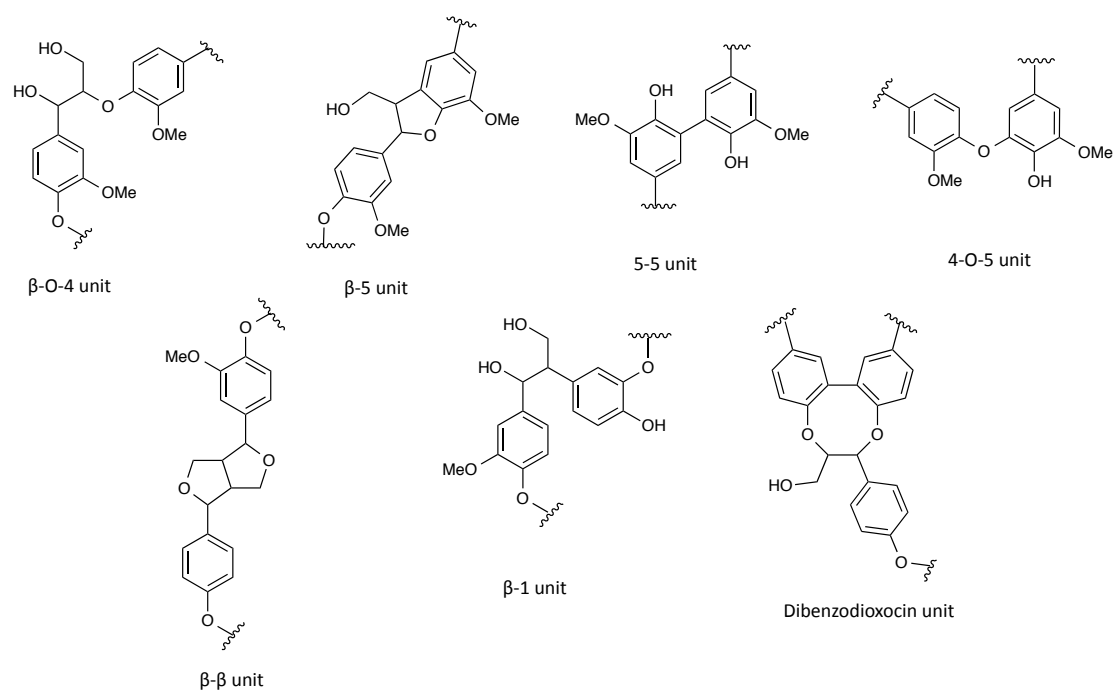


Figure 1.2.9 – Common phenylpropane linkages in lignin

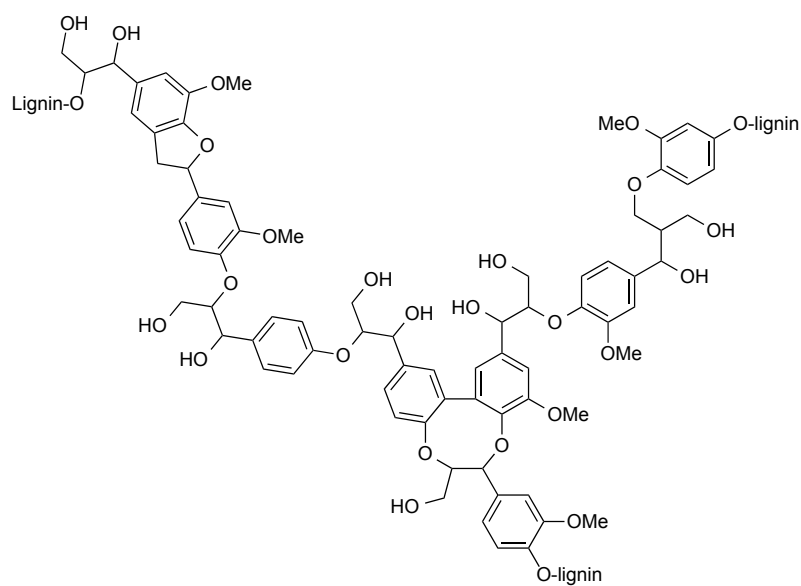


Figure 1.2.10 – Adler's representation of softwood lignin^[27]

1.2.7 Bonding between lignin and carbohydrates

The lignin and the hemicellulose components of biomass are bridged covalently through ester bonds and it has been noted that in grasses, these linkages are composed of feruloylated arabinoxylans present on hemicellulose that attach to lignin during cell wall development.^[28] This process occurs during the lignification process, where the ferulate is actively incorporated into the lignin polymer *via* oxidative coupling, where the aromatic ring couples with the electrophilic ketone methide intermediates that form during lignification. Figure 1.2.11 displays the lignin-carbohydrate complex that forms once the ferulate linkage in hemicellulose couples with lignin.

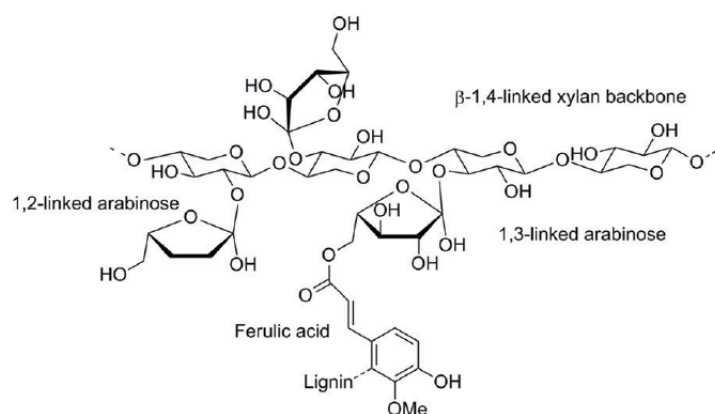


Figure 1.2.11 – Lignin-carbohydrate complex involving ferulic acid taken from reference [16]

1.3 Biomass deconstruction

Biomass deconstruction, or pretreatment, is the process of making the components of lignocellulosic biomass accessible for further processing, e.g. for fermentation into bioethanol or catalytic transformation into value-added products. An efficient pretreatment process has the overall aim of reducing the recalcitrance of biomass and this can be summarised *via* the following:^[16]

- The break down of the compact cell wall by removing any association of the cellulose with lignin
- The decrease in lignin content
- The increase of the surface area and therefore accessibility of substrates
- The reduction of cellulose crystallinity

This allows easy access to the cellulose component and it has been reported that optimal enzymatic hydrolysis is achieved when successful pretreatment occurs.^[29, 30] In the context of a biorefinery, the main objective of pretreatment can be summarised as enabling the release of sugars and hence, the formation of a range of products. A successful pretreatment strategy would minimize the costs in downstream cellulose processing, i.e. through obtaining high enzyme hydrolysis rates during saccharification and reducing the required enzyme loadings.^[31] Efficient fractionation of the biomass components by deconstruction has therefore been highlighted as the key obstacle limiting the progress of cellulosic ethanol as a viable energy source.^[32]

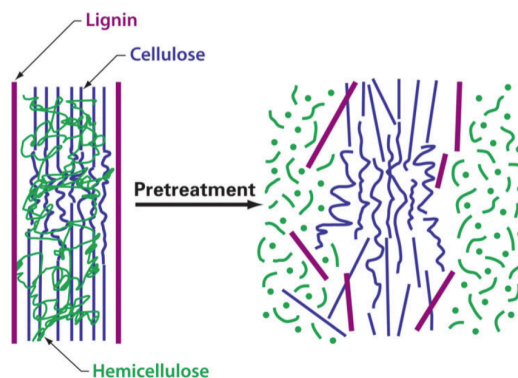


Figure 1.3.1 – Illustration of efficient pretreatment taken from reference [33]

1.3.1 Current biomass deconstruction technologies

Two current commercial pretreatment methods to separate the lignin and carbohydrate components of lignocellulosic biomass include the Kraft pulping process and the organosolv method.

1.3.1.1 The Kraft process

The Kraft pulping process is currently the dominant global process, with the objective to remove enough lignin to separate cellulosic fibers, producing a pulp suitable for the manufacture of paper and other related products.^[34] The process typically involves wood chips being placed in an aqueous mixture of sodium hydroxide and sodium sulfide and left to heat between 150 to 170 °C. During the reaction, the lignin dissolves in the highly basic reaction media, undergoing base-catalysed hydrolysis thereby causing the lignin to depolymerise. This yields a cellulose pulp which can be removed for further processing whereas the lignin and hemicellulose liquor are then burned for energy or chemical recovery.^[35]

1.3.1.2 The Organosolv process

The organosolv process is another method for successful fractionation of biomass and involves the extraction of lignin from lignocellulosic feedstocks with organic solvents or their aqueous solutions.^[36] The process of delignifying biomass typically occurs in organic solvents such as methanol and ethanol at temperatures between 100 to 250 °C with the possibility of adding acid catalysts. This yields the cellulose rich fibers as a solid product whilst the lignin fraction remains in the organic liquor which can then be precipitated on the addition of water. The major advantages of the organosolv process include the reduced air and water pollution, the wide range of woody and non-woody biomass that can be used as a feedstock and the ability to recover the solvents by distillation.^[37] However, the organosolv process also has inherent drawbacks, including the use of expensive organic solvents and the requirement of greater control due to the high volatility of the solvent. Of both pretreatment methods, the organosolv process has been deemed most promising in the context of a biorefinery as the high purity lignin obtained can be used as a renewable source for aromatic chemicals.^[38]

1.4 Ionic liquids

Ionic liquids, otherwise known as molten salts or simply as ILs, are made up entirely of cations and anions.^[39, 40] They have the unique property of being a low melting salt with melting points at or below 100 °C. The low melting point of these fused salts is dependent on the nature of both the cation and the anion. Common inorganic salts such as NaCl are renowned for having especially high melting points due to the regular packing within a well ordered lattice, owing to the high symmetry of both ions and their high charge densities. On the contrary, IL cations and anions generally exhibit low symmetry, weak ionic interactions, and charge delocalisation, therefore discouraging any lattice assembly and decreasing their melting points.^[41]

1.4.1 Ionic liquid structure

The most common cations in ILs include aliphatic ammonium and phosphonium ions and *N*-heterocyclic ions, such as those based on pyridine and imidazole. A selection of these cations are presented in Figure 1.4.1. While the aliphatic cations have their positive charge located on the nitrogen or phosphorus centre, the pyridinium and imidazolium based cations have their charge delocalised within the ring system. The addition of alkyl chains of different lengths to the cation core contributes to the lowering of the melting point. This is caused by the reduced symmetry of the cation as well as the introduction of rotational degrees of freedom active at lower temperatures.^[42]

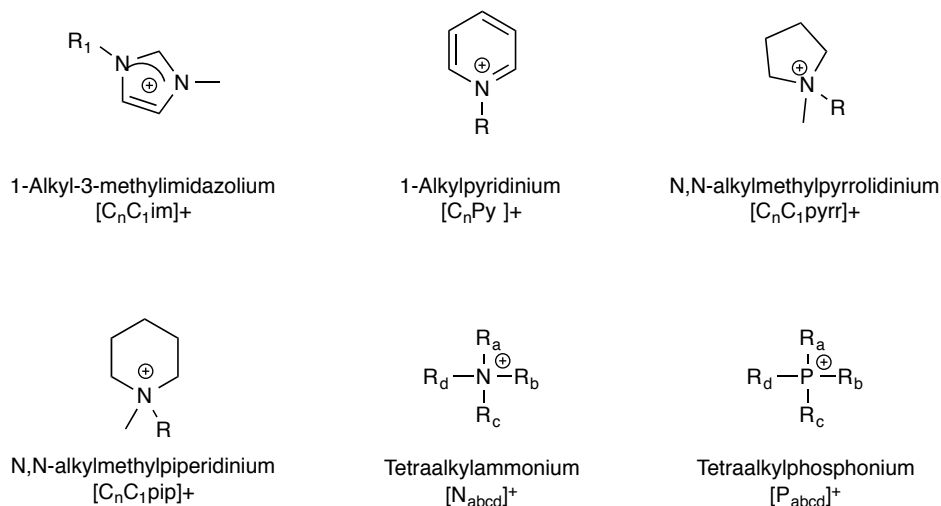


Figure 1.4.1 – Common cations used in modern ionic liquids with their abbreviated notations

The most commonly used anions are composed of a range of inorganic ions such as halides, where the charge is localized on one atom or organic ions such as acetate (OAc) or trifluoromethane-

sulfonate (OTf) where the negative charge is delocalised. A selection of anions is presented in Figure 1.4.2. It is important to note that the most interesting chemical properties of ILs are dependent on the choice of anion whereas the cation is usually selected to obtain specific physical properties such as controlling viscosity, melting point, water miscibility and overall cost of the IL.

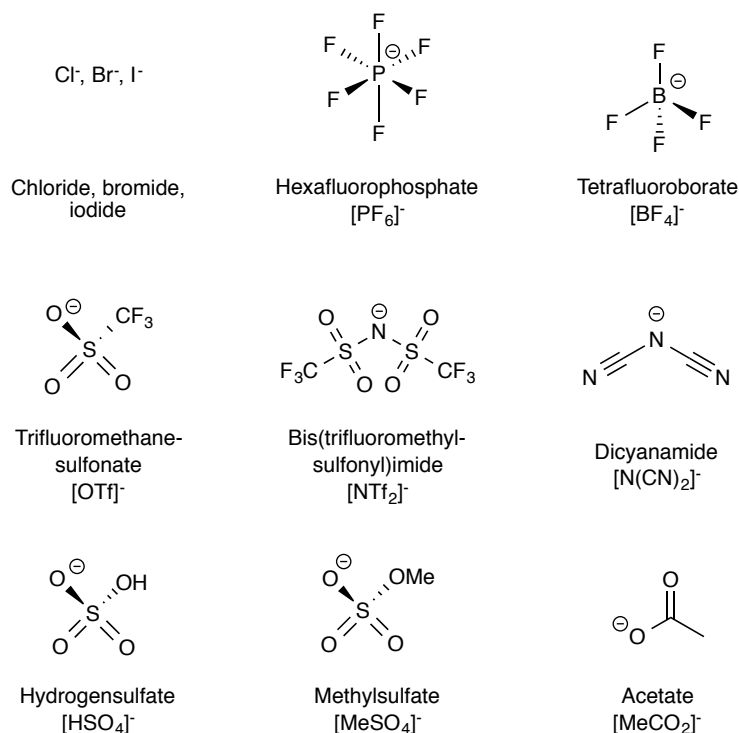


Figure 1.4.2 – Common anions used in modern ionic liquids with their abbreviated notations

Due to their complex structures, ILs tend to have long names. It is therefore conventional to shorten their names using a systematic abbreviation scheme. These abbreviations define the cation core, stipulates the degree of alkylation and the anion included as a suffix. Abbreviations for the common cations and anions are included with their structures in Figures 1.4.1 and 1.4.2. For example, 1-butyl-3-imidazolium hydrogen sulfate is labelled as [C₄C₁im][HSO₄]. This notation will be used throughout this thesis for simplicity.

1.4.2 Applications and properties of ionic liquids

ILs have found a range of applications in various industries over the past few decades. They have seen most use as alternatives to traditional organic solvents^[39] and as catalysts for a range of synthetic transformations.^[41] The BASILTM process implemented by BASF in 2002 is currently the most successful example that demonstrates the capability of IL technology in the chemical industry. This process involves the use of imidazole as an acid scavenger in the production

of alkoxyphenylphosphines, forming imidazolium chloride as a discrete phase that can be easily removed.^[43] Other examples of the applications of ILs include their use as solvents for organic reactions, electrolytes, performance additives, lubricants and dispersants.^[44] The multi-functional uses of ILs have also seen applications in biomass processing, notably in biomass fractionation and cellulose dissolution,^[16, 45] areas which will be explored in greater detail later in this chapter.

The sustained interest in the use of ILs has been due to a number of specific properties unique to this class of solvents that render them suitable for industrial applications:^[39]

1. ILs are effective solvents for a range of inorganic and organic materials. The variety of possible combinations of cations and anions as well as their modifiable functionalisation make them an extremely versatile class of solvents.
2. ILs are composed of poorly coordinating ions whilst also being highly polar. This allows them to alter reactivity in organic reactions by enhancing stabilization of starting materials or transition states.
3. ILs are immiscible with some organic solvents, therefore providing a non-aqueous polar alternative for two-phase systems.
4. The negligible vapour pressure of ILs eliminates containment problems, therefore reducing any flammability or toxicity hazards and also allowing them to be used under reduced pressure.
5. The high thermal stability of ILs provides significant advantages over flammable organic solvents, extending their applications to high reaction temperatures whilst avoiding the use of complex pressure equipment.
6. Being composed of cations and anions, ILs are concentrated electrolytes. Many ILs have wide electrochemical windows of approximately 5-6 V or more, unlocking their potential to be used as high-voltage cathodes with high power density.^[46]

1.4.3 Synthesis of ionic liquids

The first reported synthesis of an IL involved the addition of nitric acid to ethylamine, forming ethylammonium nitrate. The simple acid-base addition with the remaining water removed by distillation, yielded the product as a pure liquid.^[47] This pioneering method remains the most simple and popular procedure for the preparation of ionic liquids, however this only provides a strategy to obtain a small number of protic ILs, with pyridinium chloride being the most widely used.^[48] Other strategies have been developed in order to obtain a range of ILs with a range of different anions and functionality on the cation. The general synthesis of ILs can be split into two sections:

1. The formation of the desired cation, either by quarternisation or protonation yielding an initial salt.
2. The anion exchange of the above salt to form the desired product.

Figure 1.4.3 summarises the steps involved in synthesizing ILs as illustrated by Welton and Wassercheid,^[49] where NR_3 represents an initial amine substrate.

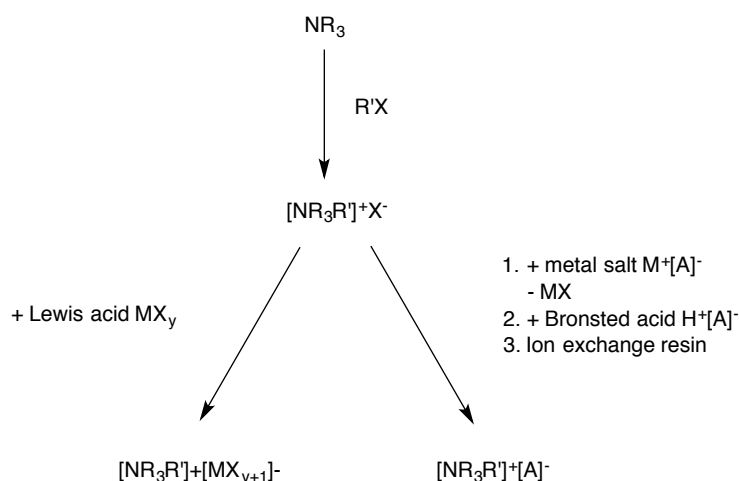


Figure 1.4.3 – Typical synthetic pathways for the preparation of ILs

1.4.3.1 Acid-base neutralization

Protic ionic liquids (PILs) are the most straightforward family of ionic liquids to prepare. The synthesis involves the addition of stoichiometric quantities of a Brønsted acid to a Brønsted base. The PIL forms upon successful protonation of the base, with the extent of protonation dependent on the difference in pK_a between the acid and the base. In all cases, due to the exothermic nature of these reactions, it is recommended to dilute and cool the amine before addition of the acid. The protic nature of these ILs make them suitable for studies involving varying acid concentration where the IL's anion is the conjugate base of the acid added. Another added feature of PILs is the structural preservation of the initial substrate once the cation is formed after protonation.

1.4.3.2 Quarternization reaction

In addition to protonation, cations can be formed by direct alkylation of a tertiary amine or phosphine. The most common alkylating agents for quarternizing the starting materials tend to be haloalkanes due to their inexpensive price, the ease in replacing the halide salts formed post reaction by other anions as well as the short reaction times and low temperatures required for alkylation. In general, chloro, bromo and iodoalkanes are used with ease of alkylation increasing

in the order $I > Br > Cl$, as can be expected for nucleophilic substitution reactions.^[49] The procedure involves mixing the desired amine or phosphine starting material with the haloalkane in a dry organic solvent. The mixture is then stirred and heated.

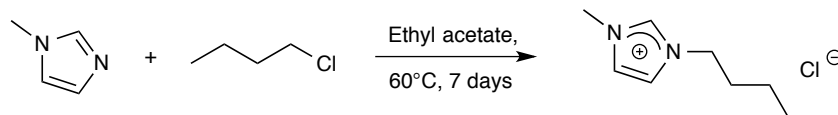


Figure 1.4.4 – Alkylation of 1-methylimidazole in order to form $[C_4C_1im]Cl$

The length of reaction required to obtain complete alkylation is dependent both on the anion and the length of the alkyl chain, with shorter chains reacting the fastest. The most important requirement for the initial alkylation reactions is the anhydrous conditions employed at all steps of the reaction, as the halide salt products tend to be hygroscopic. Once the reaction goes to completion, the IL can be obtained in its crude form by decanting the organic phase from the reaction mixture and recrystallizing as necessary from organic solvents. Other alkylating agents include trimethyl phosphate and dimethyl sulfate, which also quarternise the starting material leaving dimethylphosphate and methylsulfate anions. Unlike the haloalkanes, these alkylating agents can be hydrolyzed post alkylation forming methanol and the acidic hydrogen phosphate and hydrogen sulfate anions.

1.4.3.3 Synthesis of ionic liquids *via* metathesis

Two distinct categories exist for the anion-exchange of ionic liquids. Direct treatment of the halide salt with a Lewis acid allows speciation of the anion with the Lewis acid and anion metathesis allows complete replacement of the original anion. As this thesis includes examples of anion metathesis, the latter will be discussed briefly. The most common metathesis procedures involve mixing the IL precursor obtained during initial alkylation with the lithium salt of the required anion in dry dichloromethane. During anion exchange, the formed lithium chloride salt precipitates out of the solution whilst the IL product remains in solution, driving the reaction to completion.

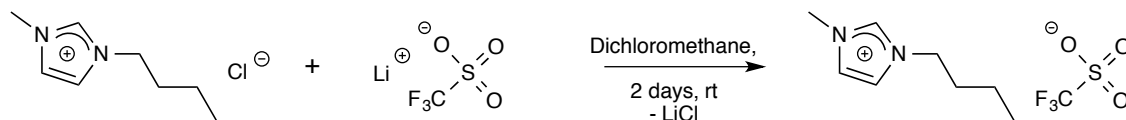


Figure 1.4.5 – Metathesis of $[C_4C_1im]Cl$ with lithium trifluoromethanesulfonate to form $[C_4C_1im][OTf]$

Usually, a slight excess of the halide salt is added to ensure that all the lithium salt containing the desired anion has exchanged with the IL precursor. Washing the organic phase with water,

once the reaction mixture has been left to stir at room temperature for a few days, ensures that the excess unreacted halide salt is removed.

1.4.3.4 Purification of ionic liquids

The negligible vapour pressure of ILs prevents any purification by distillation, therefore purification of the starting materials is essential prior to synthesis. Efficient drying and distillation of the starting materials ensures that the fewest amount of impurities are present, thereby preventing the occurrence of side reactions. A range of drying agents can be employed, sodium hydroxide is routinely used to dry 1-methylimidazole whilst the haloalkanes are dried over phosphorus pentoxide. Equally, all organic solvents used in all steps of the reaction must be distilled and dried. Such precautions ensure that pure colourless ionic liquids can be obtained, a fundamental requirement if the IL is used in investigations involving UV-Vis.

ILs formed after metathesis often have halide anions present as the most common impurity. Even after filtration of the lithium chloride waste product, some may remain dissolved in the organic phase. Washing the organic phase with small portions of water removes the waste salt with minimal losses of the water-soluble ionic liquid product. This washing step is carried out until the formation of the white precipitate no longer happens upon addition of silver nitrate, indicating complete removal of the chloride salt.

1.4.4 Biomass deconstruction in ionic liquids

Ionic liquids have experienced a significant surge in interest for their use in biomass deconstruction processes. The complexity in structure and chemical make up of the lignocellulose structure has allowed ILs to flourish in their ability to be easily tuned in both functionality and cation-anion selection to achieve specific fractionation objectives. ILs offer a promising alternative to pretreatment, either by the swelling and selective extraction of selected components or by dissolving biomass in its entirety. Two recent reviews of note which provide thorough insight into the current deconstruction strategies using ILs are provided by Brandt *et al* and Hossain *et al*.^[16, 50] In this section of the introduction, only major findings and reported investigations that have been highlighted in these reviews will be presented to provide a comprehensive background, introducing the scope of this thesis' objectives.

1.4.4.1 The dissolution process

The first attempts to utilize ILs in the dissolution of lignocellulosic biomass were demonstrated by Rogers *et al* using $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ ^[51] and later by Sun *et al* using $[\text{C}_2\text{C}_1\text{im}][\text{OAc}]$.^[52] In addition to IL choice, successful biomass dissolution was shown to depend on many variables including feedstock type, substrate particle size, dissolution time and temperature. An interesting observation further made by Rogers *et al* is the ability to selectively fractionate the cellulose component from the dissolved biomass through the addition of an acetone-water anti-solvent mixture. This causes a cellulose rich fraction to precipitate from the pulp of lower crystallinity, therefore being in a suitable form for enzymatic saccharification to yield the readily fermentable glucose.

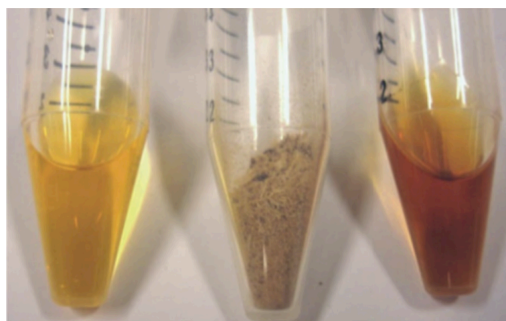


Figure 1.4.6 – Dissolution of beech power in $[\text{C}_2\text{C}_1\text{im}][\text{OAc}]$; left: IL, middle: beech power, right: solution taken from reference [53]

The effectiveness of the dissolution process revolves around the ability of cellulose to dissolve or decrystallise in the IL. Many reported investigations have highlighted the importance of the anion to engage in hydrogen bonding with the hydroxyl groups of cellulose and investigations correlating the Kamlet-Taft β parameter suggest that higher β values offer high cellulose dissolution.^[54] Although 1,3-dialkylimidazolium cations have been consistently employed in such studies, the cation has less of an impact in determining solubility. It has been noted however,

that the lengthening of the alkyl chain and the incorporation of hydroxyl groups reduce cellulose solubility.^[16] Furthermore, due to stronger cation-anion association, protic ILs also prevent solubilization^[55, 56] as the hydrogen bond basic anion is less able to interact with the cellulose.

One major drawback for the dissolution process is its high sensitivity to water, even at quantities as low as 0.15 wt %.^[57] Water has shown to inhibit efficient dissolution of cellulose and causes precipitation due to preferential interactions with the IL anion. This therefore prevents hydrogen bonding between the reaction medium and the cellulose substrate. This is particularly problematic due to the high hygroscopicity of the ILs and the inherent moisture content in biomass.

1.4.4.2 The ionosolv process

The ionosolv process is an alternative approach that successfully disrupts the composition of lignocellulose. Instead of the complete dissolution of the biomass feedstock, ILs are used in order to achieve the partial and selective dissolution of the lignin and hemicellulose components, leaving the cellulose polymer largely intact.

Once again, the correct selection of anion is paramount in order to selectively dissolve and depolymerise lignin. Like cellulose, the efficient dissolution of lignin is governed by the physical parameters of the anion when combined with dialkylimidazolium cations. Previous studies have shown that moderately hydrogen bond basic anions such as methyl sulfate, chloride, bromide, acetate and triflate all exhibit high lignin solubility^[58, 59, 60] with further dissolution reported at higher temperatures.

The highly random and complex nature of lignin as well as the difference in structure depending on species and growth conditions make direct comparison of the efficiency of lignin dissolution difficult. However, studies on softwood lignin have shown that lignin solubility is highest in ILs bearing triflate or methyl sulfate anions and lowest when non-coordinating anions such as [BF₄] and [PF₆] are employed.^[58] A hypothesis exists that combining these mildly hydrogen bond basic anions with 1,3-dialkylimidazolium cations further aids solubility of lignin due to the π - π interactions between the aromatic cation and the aryl groups in lignin.^[53, 61]

Significant features in the ionosolv process have been successfully demonstrated by previous members of the Welton group, where in addition to successful lignin dissolution, lignin depolymerisation also occurs.^[54, 62, 63] Initial studies showed that 1,3-dialkylimidazolium ILs containing methyl sulfonate, hydrogen sulfate and methyl sulfate anions successfully managed to delignify ground lignocellulose from *Miscanthus*, Pine and Willow feedstocks. Even with the presence of 20 wt% water, the lignin and the hemicellulose fractions were dissolved and compositional analysis indicated over 90 % delignification and high lignin recovery of *Miscanthus* when the [HSO₄]⁻

Table 1.4.1 – Lignin solubility in different ILs taken from reference [16]

IL	Lignin Substrate	Solubility (wt/wt) %	Temp °C
[C ₂ C ₁ im][MeCO ₂]	Kraft lignin (Indulin AT)	30	90
[C ₁ C ₁ im][MeSO ₄]	Residual Softwood lignin	26	50
[C ₄ C ₁ im][MeSO ₄]	Residual Softwood lignin	26	50
[C ₆ C ₁ im][OTf]	Residual Softwood lignin	22	70
[C ₄ C ₁ im]Cl	Residual Softwood lignin	13	75
[C ₄ C ₁ im]Cl	Kraft lignin (Indulin AT)	10	100
[C ₄ C ₁ im]Br	Residual Softwood lignin	14	75
[C ₄ C ₁ C ₁ im][BF ₄]	Residual Softwood lignin	12	100
[C ₄ C ₁ im][PF ₆]	Kraft lignin (Indulin AT)	4	90
[C ₄ C ₁ im][PF ₆]	Kraft lignin (Indulin AT)	1	90
[C ₄ C ₁ im][PF ₆]	Residual Softwood lignin	0	120
[C ₄ C ₁ pyrr][PF ₆]	Residual Softwood lignin	0	120

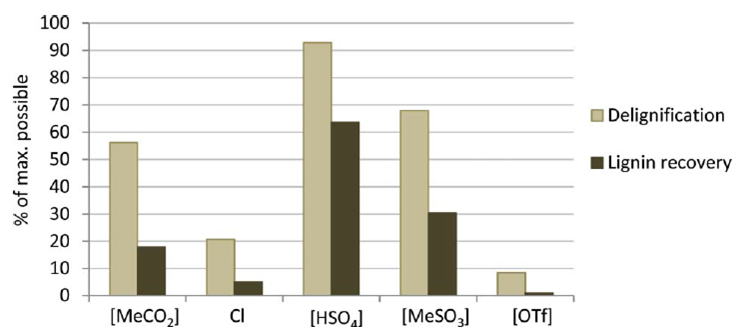


Figure 1.4.7 – Effect of anion on lignin removal and precipitate yield after pretreatment of *Miscanthus* with 80/20 vol% IL- water mixtures taken from reference [54]

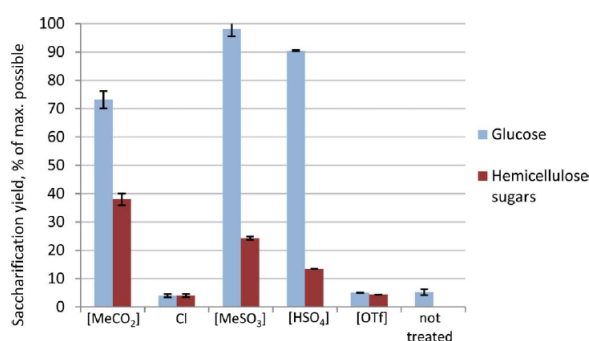


Figure 1.4.8 – Impact of the IL anion on glucose and hemicellulose sugar yields after enzymatic saccharification of *Miscanthus* pulp. Taken from reference [54]

anion was employed. Figure 1.4.8 taken from reference [54] shows a comparison of the activity of different anions on the delignification and precipitation of the lignin fraction. In terms of saccharification yield, the highest glucose yields were obtained with the [MeSO₃][−] and [HSO₄][−] containing ILs where yields exceed 90 %, whereas ILs containing [OTf][−] and Cl[−] anions give low saccharification yields.

The activity of [C₄C₁im][HSO₄] and notably the hydrogen sulfate anion in pretreatment encouraged the idea of using PILs, where instead of ILs bearing dialkylated imidazolium cations, the monoalkylated IL [HC₄im][HSO₄] was prepared. The use of PILs are highly beneficial from an industrial point of view due to the ease in their preparation as well as the lower cost of the starting materials.^[64] A deconstruction process involving the fractionation of lignin in the IL liquor with a cellulose enriched pulp was employed as summarised in Figure 1.4.9. Results showed more advanced delignification of *Miscanthus*, where an excess of 1 mol% of sulfuric acid showed better activity in both delignification and lignin recovery.^[62] Fortunately, the presence of water was beneficial to the deconstruction process using PILs, as lower yields of precipitated lignin occurs

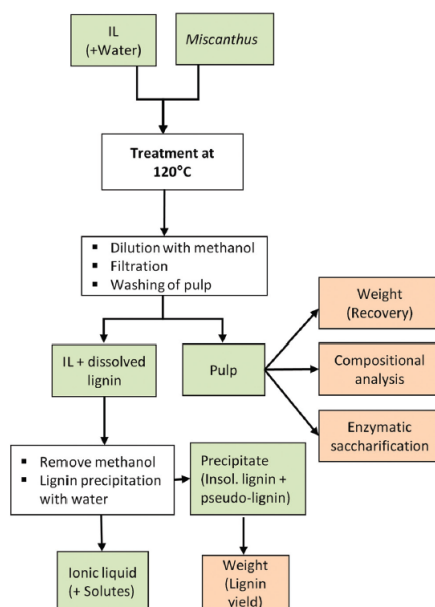


Figure 1.4.9 – Process flow for deconstructing lignocellulosic biomass taken from reference [62]

when the IL is dry, therefore offsetting any issues with IL hygroscopicity. In addition to the ease in preparation and low cost, it was concluded that $[\text{HC}_4\text{im}][\text{HSO}_4]$ is the most interesting IL for biomass pretreatment, due to the ability to tune its acidity and the increase in lignin precipitation compared to its dialkylimidazolium counterpart.

1.4.4.3 Structural changes in lignin during pretreatment

Successful delignification has been highlighted as the predominant objective in any deconstruction process. A number of investigations have been reported within the past few years that aim to unveil the fundamental chemical changes of lignin during pretreatment. A report by El Hage *et al* looks at the changes in organosolv lignin during deconstruction,^[65] Wen *et al* and Sathitsuksanoh *et al* focus on the structural changes in lignin when $[\text{C}_2\text{C}_1\text{im}][\text{OAc}]$ is employed as the IL^[66, 67] and finally the most recent report by Brandt *et al* employs $[\text{HC}_4\text{im}][\text{HSO}_4]$ in their study.^[63] All reports apart from Wen *et al*'s study use *Miscanthus giganteus* as the biomass feedstock, aiding comparison and better understanding of delignification between different pretreatment processes. Common techniques to track changes in lignin include HSQC (Heteronuclear Single Quantum Correlation) spectroscopy, ^{13}C NMR, ^{31}P NMR *via* the use of a phosphitylating agent and GPC (Gel Permeation Chromatography). Such techniques provide insight on lignin functionality with HSQC focusing on the β -O-4, the β - β and the β -5 linkages within the lignin macrostructure, as well as the arabinose carbohydrate, the linkage responsible for the hemicellulose-lignin complex.¹³C NMR and ^{31}P NMR provide quantitative insights into the changes in the aliphatic and aromatic regions of lignin as well as the chemical environments

of specific hydroxyl groups. GPC determines the molecular weight, polydispersity index and average number molecular weight of the lignin polymer, which is used to establish what structural features of lignin change during depolymerisation.

Whilst all studies employ different reactions conditions, temperatures and reaction media, a number of common changes were observed in all systems. Most importantly, regardless of the pretreatment process employed, HSQC data show that lignin undergoes degradation of side chains with aromatic signals increasing with pretreatment time. These have been attributed to the dehydration of the α -hydroxyl group, the removal of the γ -methylhydroxyl group to form formaldehyde and the cleavage of the β -O-4 linkage, observations that have also been made when model compounds are used in acidic conditions.^[68, 69] The mechanism for the hydrolysis of the β -O-4 linkage with acidic ILs is presented in Figure 1.4.10.

This is further supported by results obtained *via* ^{31}P NMR where reduction in the aliphatic hy-

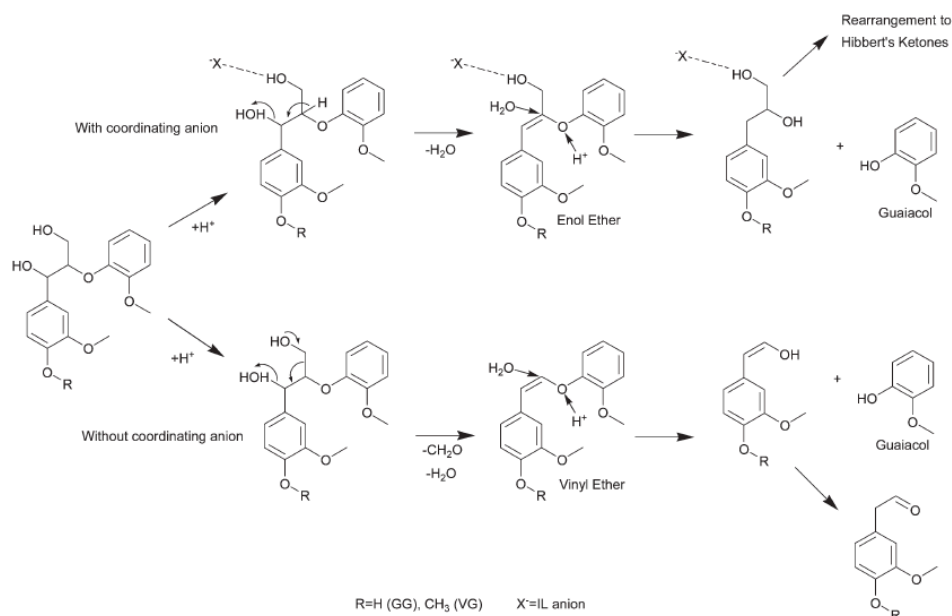


Figure 1.4.10 – Pathways of guaiacylglycerol- β -guaiacyl ether degradation in acidic ILs^[70]

droxyl groups are observed and an overall increase in phenolic hydroxyl groups. Sathitsuksanoh *et al* took the investigation further and established that successful delignification allowed up to a 90 % yield of glucose from the enzymatic saccharification of cellulose after 24 h pretreatment, compared to 10% of untreated biomass.^[67]

Brandt *et al*'s investigation presents a thorough and detailed analysis of the modification of

lignin at different pretreatment times, with the overall goal aiming to understand what conditions are necessary to structurally alter the precipitated lignin.^[63] The most important observations made are based on the hydrolysis of the β -O-4 linkage and the removal of the arabinose ester, the two major changes that cause a significant decrease in the molecular weight of the lignin. Also, lignin was shown to repolymerise *via* condensation reactions which was postulated to occur in competition with the hydrolysis of the β -O-4 linkages, all of which were made by observations through ^{13}C NMR, ^{31}P NMR and HSQC techniques. ^{13}C NMR shows that after a 12 h pretreatment time, all carbons were deemed aromatic or vinylic and integrations of O-alkyl groups decreased by 2.7 alkoxyl groups per aryl ring to 0.3. Furthermore, an increase in aromatic C-C bond signals indicated the occurrence of condensation reactions between cleaved aryl groups. After phosphitylation of the lignin post pretreatment, ^{31}P NMR showed that the hydroxyl groups in lignin attached to aliphatic carbons decreased over time, while aromatic hydroxy groups increased in intensity. The simultaneous increase in the phenolic hydroxy content occurring during condensation reactions, proves that once the β -O-4 linkages are cleaved, the phenolic hydroxy groups remain inert and do not participate in the repolymerisation mechanism.

The HSQC data further supports the hypotheses made with the other NMR techniques. The disappearance of the arabinose carbohydrate during the first hour of pretreatment indicates that the hydrolysis of the ester linkage between lignin and hemicellulose is the starting point for successful delignification. The side chain region of the HSQC spectra provides valuable information on the linkages found within the lignin polymer. The linkage that underwent significant cleavage was deemed to be the β -O-4 linkage, with almost quantitative disappearance occurring after 12 hours, an observation supported by Sathitsuksanoh *et al* and Wen *et al*.^[66, 67] This can be seen in Figure 1.4.11 taken from Brandt *et al*'s published paper.^[63]

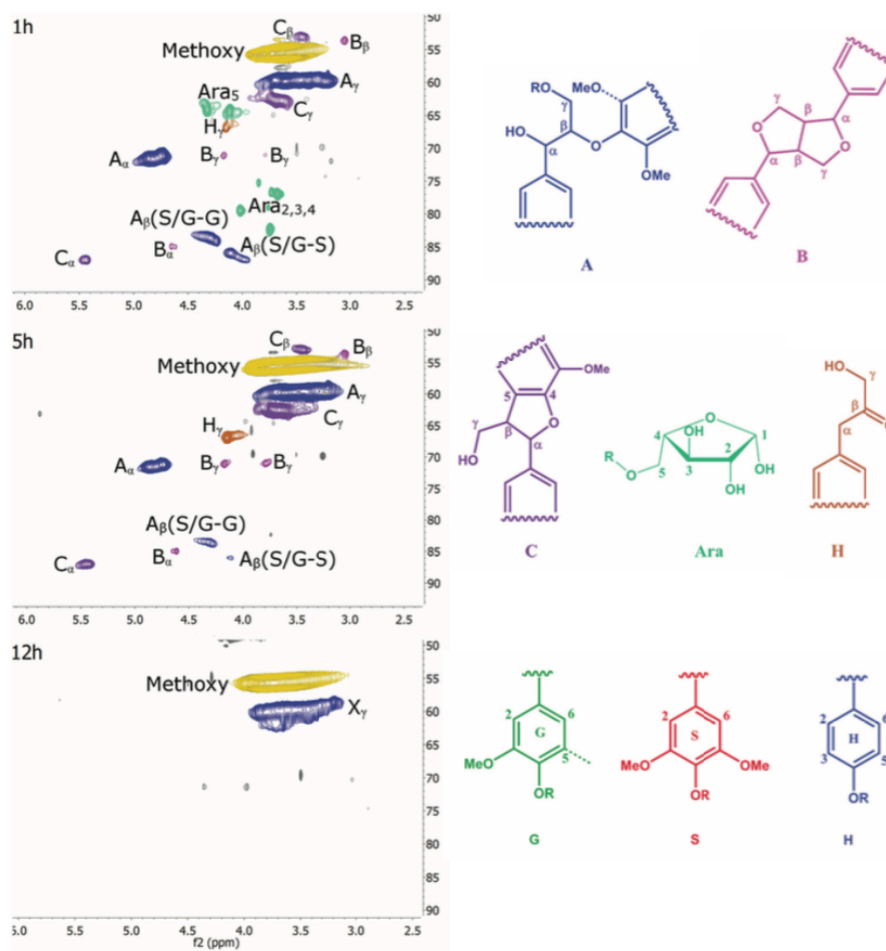


Figure 1.4.11 – The HSQC spectra of the side chain region of Ionosolv lignin after different pretreatment times. Taken from reference [63]

The presence of the Hibbert ketone product (H) is of significant importance, providing insight into product distribution post cleavage of the β -O-4 linkage. However these signals disappeared after 12 hour pretreatment. The most important observation made by Brandt *et al* regarding the aromatic region of the HSQC spectra is decrease in the G6 signal, indicating that this may be the site for condensation reactions. GPC analysis on molecular weight and average molecular number of lignin confirm depolymerisation followed by condensation.

To conclude, the major structural changes occurring in lignin that are responsible for depolymerisation occur due to the hydrolysis of the lignin-hemicellulose complex and the cleavage of the β -O-4 linkage. Successful delignification allow high enzymatic saccharification yields of the

cellulose whilst also allowing different structures of lignin to form. Thorough analysis of the precipitated lignin confirms the lignin fractions to be of different heterogeneities, depending on the degree of depolymerisation and the extent of repolymerisation through condensation reactions.

1.5 Scope of thesis

The use of acidic ILs in biomass pretreatment has introduced an innovative strategy which can potentially render lignocellulosic biomass a commercially viable and sustainable feedstock for the production of biofuels and platform chemicals. In order to optimise such processes, it is important to fully understand the mechanisms in which the IL promotes delignification, the major obstacle for any deconstruction process. The work described in this thesis aims to answer key questions regarding the reactivity of lignin in acidic ILs and more specifically, the nature of the β -O-4 linkage. These findings will then be compared to reported mechanistic studies in aqueous acidic conditions currently available in literature. Due to the high complexity of the lignin macropolymer, the investigations reported herein include a series of fundamental studies using an array of model compounds as well as an applied study using ionosolv lignin. The direction of this thesis follows the degree of complexity presented in the lignin structure and will be set out as follows, with each point representing an individual chapter:

1. A literature review on ether cleavage, exploring the different methods and synthetic strategies employed in traditional organic chemistry for the cleavage of simple ethers. This will then be compared with how ethers typically react in ILs, assessing any correlations in mechanism between the two.
2. An initial investigation looking at the reactivity of simple alkyl aryl ethers in IL systems to elucidate the mechanism of ether cleavage by means of a Hammett study. This will then draw initial conclusions on the importance of reaction medium, substrate electron density and substrate functionality for efficient ether cleavage.
3. An in-depth investigation to glean mechanistic insights of ether cleavage using model compounds bearing the β -O-4 linkage. This will also explore the influence of different functional groups on the lignin model compounds as well as different acidic ILs bearing the hydrogen sulfate anion. Through conducting an Eyring study, the role of the cation on the activation parameters for the reaction will also be assessed, providing a point of reference for suitable IL design.
4. The final chapter will explore how ionosolv lignin can be catalytically upgraded into compounds of higher value, including vanillin and syringaldehyde. Using ILs and different oxidants and oxidation catalysts, this hitherto unprecedented investigation will further evaluate the potential applications of ILs in downstream lignin processing.

Chapter 2

Literature review: Ether cleavage

2.1 Ether formation

The ether bond is the most prevalent inter-unit linkage in the majority of biosynthesised polymers, from the conjoining of glucose units to form the larger cellulose polymer to the formation of aryl-alkyl ethers during the termination stage of lignin formation.^[23] The name “ether” itself can simply be referred to as any compound with two alkyl or aryl groups linked through an oxygen atom.^[71] Ethers are generally considered to be relatively stable compounds with bond dissociation energies of the simple compounds diphenyl ether and phenyl vinyl ether measuring 329.7 kJ mol⁻¹ and 320.5 kJ mol⁻¹ respectively at room temperature.^[72]

The earliest recorded preparation of simple ethers was conducted by Alexander Williamson, in his 1850 publication “Theory of Aetherification”^[73] where diethyl ether was obtained *via* the combination of potassium alkoxide salts with alkyl iodide electrophiles. This protocol was then generalised to the use of a mineral base with a small enough pK_b to deprotonate the alcohol (usually a carbonate), typically proceeding *via* an S_N2 mechanism. This implied an overall second order rate expression, with the rate depending on the concentrations of both the nucleophile and the alkylating agent.^[74] The alkylating agent in question tends to be of a primary structure possessing an effective leaving group including halides (namely chlorides, bromide and iodides) and sulfonates e.g. tosylates and their derivatives. This route has remained a popular and effective method in both industry and academia for the preparation of dialkyl and aryl alkyl ethers, allowing a broad range of alcohols to be etherified including primary, secondary, tertiary and aryl alcohols with a range of alkylating agents. Moreover, the conversion of alcohols to ethers, together with the cleavage of these bonds, is an important method in synthesis for the protection of hydroxy groups.^[75]

2.2 Ether cleavage

The most notable reviews which comprehensively assess the methods and mechanism of ether cleavage have been published originally by Robert Burwell in 1954,^[76] Bhatt and Kulkarni in 1983,^[77] Ranu and Bhar in 1996^[78] and most recently by Weissman and Zewge in 2005.^[79] Burwell defined the meaning of ether cleavage as the case in which “two alkyl groups joined together by an oxygen end up attached to two different functional groups”^[76] and these reactions can be classified into a number of subgroups that have been repeatedly used to provide a reference point in finding different routes for the reaction.

- Cleavage by acidic reagents, primarily passing through a protonated oxonium intermediate
- Cleavage by nucleophilic reagents, in the absence of acids
- Cleavage by protophilic basic reagents, leading to elimination products
- Cleavage using heterogeneous catalysts and Lewis acids, *via* the polarisation of the C-O bond

The mechanism of all the reactions listed above can be conceptualised with existing mechanistic theorems in organic synthesis, namely protonation, deprotonation and metal chelation followed by bimolecular and unimolecular nucleophilic displacement reactions. In each case, these principles will be exemplified with a range of studied substrates and reaction media. As the main objectives of the investigations reported in this thesis involve the use of acids, the focus of this review will be on ether cleavage in acidic media, with a brief discussion of other synthetic approaches using nucleophilic, basic and Lewis acidic reagents.

2.3 Ether cleavage in acidic media

2.3.1 The oxonium intermediate

The oldest and perhaps the most studied route towards ether cleavage involves the use of acidic reagents where the acidic species has two roles: initial protonation of the ethereal oxygen, forming an oxonium cation, followed by the nucleophilic attack of the conjugate base onto one side of the alkyl chain. Upon successful protonation, the positively charged oxonium group allows for the departure of the alkyl group either through the formation of a stabilised carbocation or through the attack of a nucleophilic species as would occur in a common S_N2 type reaction.

An interesting property of the oxonium species in acidic media is the ability to form ion-paired complexes with the acid and no subsequent cleavage, therefore forming a pseudo acid-base complex. This is exemplified with simple alkyl ethers such as diethyl ether in sulfuric acid as shown in Figure 2.3.1. As sulfuric acid can be considered a species in equilibrium between sulfuric acid and the hydrogensulfate anion, this complex can be named diethyloxonium hydrogensulfate

which also sits in equilibrium.

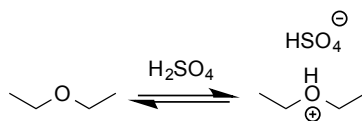


Figure 2.3.1 – Conjugate acid complex of diethyl ether in sulfuric acid

Other ether conjugate acid complexes studied include the use of hydrogen halides, forming ion pairs between the protonated oxygen and the anion. Such complexes include $(\text{CH}_3)_2\text{OH}^+\text{Br}^-$ and $(\text{CH}_3)_2\text{OH}^+\text{Cl}^-$. It can be argued that the basicity of an ether, influenced primarily by the electronic properties of the structure, is paramount in ether cleavage.

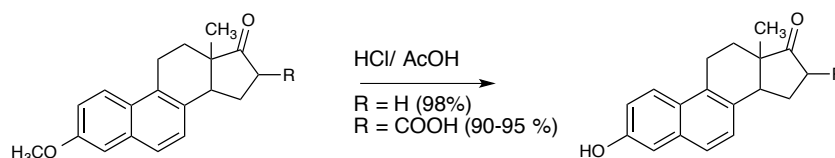
2.3.2 Cleavage by halide acids

Studies into the characteristic features of ether cleavage by halide acids were largely conducted during the nineteenth century, with the first clear example of acid catalysed cleavage demonstrated by Butlerow in 1861^[80] whereby α -ethoxypropionic acid reacted with concentrated hydroiodic acid at 100 °C to yield lactic acid and ethyl iodide. Other early examples including the cleavage of *p*-methoxybenzoic acid to *p*-hydroxybenzoic acid and methyl iodide were also reported soon afterwards with similar observations occurring with concentrated hydrochloric acid.^[76] The use of hydrobromic acid was explored extensively with a range of phase transfer catalysts such as trioctylmethylammonium chloride in order to shorten reaction times and maximise yields. Aryl alkyl ethers such as anisole and its longer chained analogues were seen to cleave to the aryl alcohol and the alkylated bromide in high yield within 24 hours at 115 °C when 0.1 molar equivalents of the catalyst were added.^[81] Relative to hydrobromic and hydroiodic acids, hydrochloric acid participates in very few successful cleavage reactions due to its less strongly acidic proton ($\text{p}K_a$ of -7 compared to -9 and -10 respectively). This is particularly evident in the case of anisole, whereby only hydroiodic acid and hydrobromic acid were shown to cleave the substrate to phenol and the methyl halide,^[82] with the ether bond remaining unaffected by hydrochloric acid. The potency of these acids to cleave ethers can therefore be postulated to follow the order of acidity as shown in Table 2.3.1, with the most acidic hydrohalides being able to cleave the majority of ethers and hydrochloric acid cleaving specific substrates such as benzyl ethers.^[77]

Table 2.3.1 – pK_a values of hydrohalic acids in water at 25°C

Acid	pK_a
Hydroiodic (HI)	-11.0
Hydrobromic (HBr)	-9.0
Hydrochloric (HCl)	-6.1
Hydrofluoric (HF)	+3.5

One example of successful cleavage of an alkyl aryl ether in hydrochloric acid was reported to occur on benzylphenyl ether at 100 °C offering scope for further studies in the use of this acid.^[83] A more recent application of hydrochloric acid in the cleavage of an alkyl aryl ether was presented by Bachmann whereby naphthyl methyl ethers cleaved to the corresponding phenol in excellent yields, with one example shown in Figure 2.3.2.^[84]

**Figure 2.3.2** – Ether cleavage using hydrochloric acid to form Equilenin

Regarding the cleavage patterns of aryl alkyl ethers by halide acids the following observations were made:^[77]

- Regardless of the basicity of the ether oxygen, diaryl ethers are resilient to cleavage due to the steric hindrance of the ring structures.
- Cleavage of alkyl aryl ethers occurs with alkyl-oxygen fission, forming a phenol moiety and the alkyl-halide product.

Regarding the cleavage patterns of the halide acids with di-alkyl ethers, the first substantial study on ether cleavage was carried out by Silva^[85] whereby the reactivity of a range of aliphatic ethers with varying molecular weights and structures were cleaved in concentrated hydroiodic acid with the products analysed. Along with further developments by Lippert^[86] the following observations were made:

- Ethers involving a methyl group and a group of higher molecular weight are cleaved to the methyl halide and the higher molecular weight alcohol.
- Ethers containing simple groups such as methyls are prone to cleave more rapidly than ethers containing groups of higher molecular weight

- In general, the higher molecular weight alkyl moiety will bear the alcohol after cleavage with the lower molecular weight moiety bearing the iodide.
- The rate of reaction declines with increasing molecular weight, even in situations where the alkyl moiety is seen to inductively render the oxygen more electron rich.

This final conclusion, which can be argued to contradict the oxonium intermediate theory, was observed to occur when the oxygen is bonded to a secondary alkyl group or a primary group with a branch adjacent to the ether bond itself, inferring the dominating effects of sterics on cleavage. In terms of the mechanism, Bonhoeffer and Reitz proposed that the reactions of primary alkyl or allyl ethers in aqueous acids proceed by a bimolecular nucleophilic displacement (S_N2) reaction.^[87] Hughes and Ingold concluded that with a secondary or tertiary alkyl group, the reaction proceeds *via* the generation of an inductively-stabilised carbocation, which rapidly undergoes nucleophilic addition by the halide therefore being an S_N1 type reaction (Figure 2.3.4).^[88] The S_N1 / S_N2 mechanistic balance is also influenced by the nucleophilic character of the anion and its concentration. Consequently, an acid with a poorly nucleophilic anion would be more likely to promote a unimolecular nucleophilic displacement.

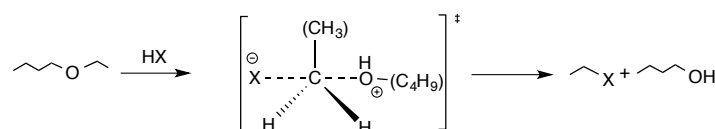


Figure 2.3.3 – S_N2 mechanism for ether cleavage

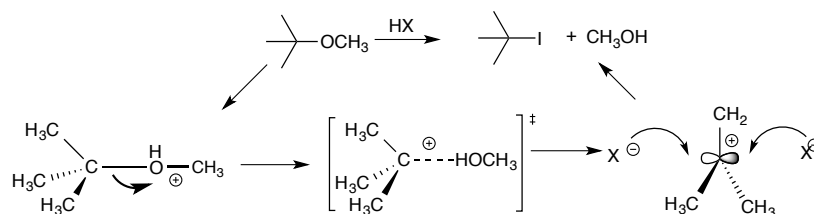


Figure 2.3.4 – S_N1 mechanism for ether cleavage

2.3.3 Cleavage by other acids

Studies towards the use of concentrated sulfuric acid in ether cleavage have been exhaustively investigated. Its weak acidic properties together with the poor nucleophilic character of the hydrogensulfate anion renders sulfuric acid a poor reagent for ether cleavage.^[76] A notable example is shown with simpler phenolics, such as anisole whereby no cleavage occurs at all with only sulfonation occurring at the ortho and para positions, even when concentrated sulfuric acid is

used.^[89] Due to the poor nucleophilicity of the anion, if any cleavage were to occur this would most likely proceed with water acting as the nucleophile. Nonetheless, there are some selected examples whereby phenolic ethers have been shown to be cleaved by sulfuric acid. Namely the cleavage of 2-bromo-4-nitrophenetole to phenol has been achieved with 80% sulfuric acid at 100 °C as well as the cleavage of anthraquinone derivatives tetrahydroxymethanthraquinone and anthragallol dimethyl ether shown in Figure 2.3.5.^[90] In all three of these cases the inclusion of electron withdrawing groups ortho to the ether increase the electrophilicity of the alkyl chain.

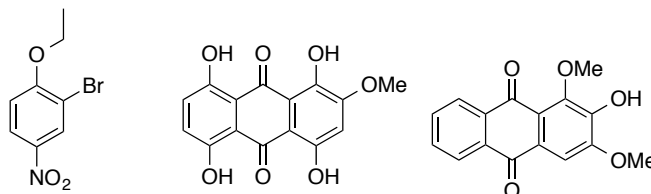


Figure 2.3.5 – Phenolic ethers that undergo cleavage using sulfuric acid

Similarly, like sulfuric acid, some isolated examples of ether cleavage have been demonstrated with phosphoric, nitric and *p*-toluenesulfonic acid. However these acids also suffer from poor nucleophilicity and in the case of phosphoric and nitric acid, poor acidity and are therefore not commonly used.^[76, 77]

2.4 Ether cleavage using basic reagents

2.4.1 Cleavage using alkali hydroxides

The basicity of alkali hydroxides aids ether cleavage *via* reacting selectively with protic solvents, forming nucleophiles which can then cleave the ether. In the same way bond polarisation is achieved in acid catalysed ether cleavage *via* the generation of the oxonium intermediate, basic reagents also require the increased electrophilicity of the alkyl leaving group. However in these basic systems there is no indication that deprotonation of the proton alpha to the ether occurs prior to the breaking of the C-O bond. A simple example of this is shown with both anisole and phenetole whereby both ethers in a concentrated solution of potassium hydroxide in ethanol heated to 200 °C yield phenol as the only identifiable product, with no detection of elimination products.^[91] In this case, the potassium ethoxide nucleophile is formed *in situ* by the basic nature of the anion deprotonating the weakly acidic alcohol, allowing nucleophilic attack of the aryl alkyl ethers by the ethoxide. A similar example has also been demonstrated with sodium methoxide with anisole which yielded similar products.^[92]

Mechanistic insights showing the importance of nucleophilicity, or conversely, the increased electrophilicity of the alkyl groups have been gained when a range of electron withdrawing and

deactivating groups were incorporated into aryl alkyl ether substrates. The cleavage of bis(*p*-methoxyphenyl)ethylene (as shown in Figure 2.4.1) by sodium methoxide and sodium ethoxide in dry alcohol yields the mono-dealkylated product;^[93] the initial dealkylation occurring due to the extended conjugation of the ring, aiding bond polarisation and rendering the alkyl group more electrophilic. However, the generation of the phenoxide post deprotonation of the newly formed phenol reestablishes high electron density in the aromatic system, therefore inhibiting further cleavage.

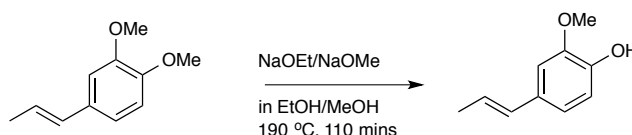


Figure 2.4.1 – Cleavage of bis(*p*-methoxyphenyl)ethylene in basic media

Kinetic studies using a range of *para*-substituted anisole and methoxynaphthalene substrates further explored the nature of ethers in basic media. Substrates with the electron withdrawing nitro, chloro and bromo groups were subjected to ether cleavage. *p*-chloroanisole was seen to react in a solution of sodium methoxide in absolute methanol at 180 °C to form *p*-chlorophenol and dimethylether^[94] whilst the hydrolyses of chloro, bromo and nitro substituted methyl naphthyl ether in potassium hydroxide and absolute ethanol were seen to increase in rate following that order, showing the importance of reducing the electron density of the ether in basic conditions.^[95]

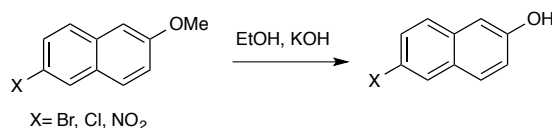


Figure 2.4.2 – Cleavage of substituted methylnaphthyl ethers in basic media

Aryl alkyl ethers with deactivating substituents such as carboxylic acids also show similar trends. 2-hydroxy-3-methoxybenzoic acid in aqueous basic media containing potassium hydroxide and sodium hydroxide yielded successful dealkylation at 250 °C.^[96] The above examples consequently emphasize the importance of ring deactivation in aryl alkyl ethers, with electron withdrawing groups on the aryl moiety promoting nucleophilic attack of the alkyl ether *via* an S_N2- like mechanism on the alkyl group.

The cation in alkali reagents equally plays an important role in ether cleavage. A study conducted by Roberts *et al* proposed the formation of ether-cation adducts with a series of metal carbonates on benzyl phenyl ether.^[97] The high electron density of the ether forms an adduct with the metal cation therefore polarising the ether bond, rendering it more prone to heterolytic

cleavage. This adduct, analogous to the formation of the oxonium intermediate in acidic media, increases the susceptibility of the alkyl ether to nucleophilic attack.

2.4.2 Cleavage using strong bases

Unlike the nucleophilic properties of alkali-metal bases, protophilic cleavage can also be achieved using organo-alkali metal compounds. These reagents have shown to be potent enough for ether cleavage, where an alkene and metal alkoxide are liberated post alkyl deprotonation. Examples using strong organic bases such as sodium *bis*(trimethylsilyl)amide and lithium diisopropylamide are presented when used for the dealkylation of 1,2-dimethoxybenzenes and for selectively debenzylating benzyloxylanisole at 185°C in THF.^[98] With dialkyl ethers, a number of different mechanisms may occur in the presence of organo-alkali metal bases, each involving deprotonation of an alkyl proton close to the ether:^[99]

- attack of an alkyl α -hydrogen by the base (α elimination)
- attack of an alkyl β -hydrogen by the base (β elimination)
- α,β -elimination

In each case, unlike with the nucleophilic bases, deprotonation of the proton on the carbon either α or β to the ether occurs. Ethers with β methyl groups are more likely to undergo β C-H deprotonation *via* an E2 mechanism, whereby the proton removal occurs simultaneously to C-O cleavage. One example includes 2-methoxyoctane with isopropylolithium yielding 1-octene^[100] whereas butylmethyl ether and dimethyl ethers undergo α elimination yielding butanol and methyllithium.^[101] An example of an aryl alkyl ether cleavage involves of phenetole in ethyllithium, whereby as well as α and β - elimination, trans metalation at the ortho position of the ring can occur as described in Figure 2.4.3, which is then followed by the slow decomposition of ethene and the formation of lithium phenoxide *via* either an α or β -elimination.^[102]

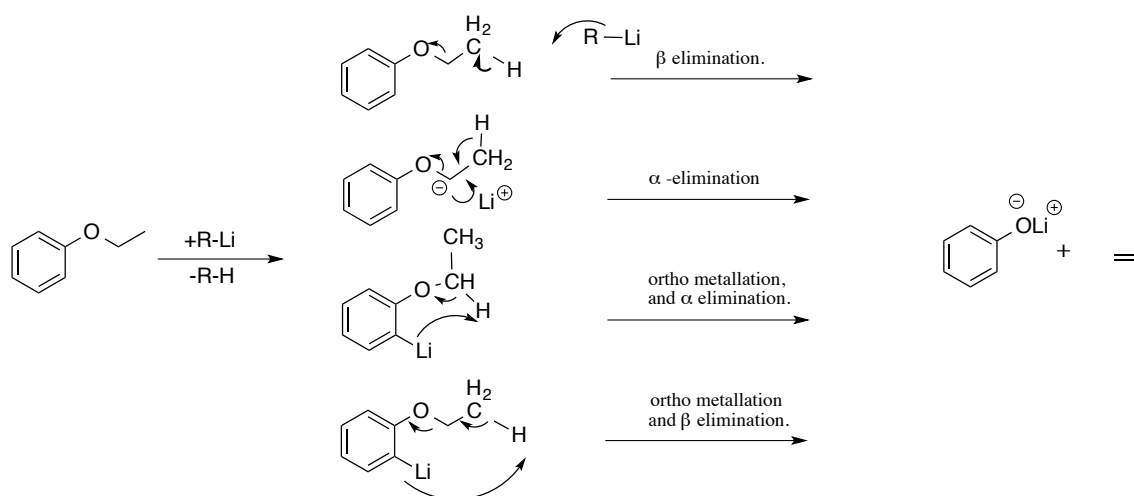


Figure 2.4.3 – Cleavage of phenetole in ethyllithium

2.5 Cleavage using Lewis acids

More recent synthetic approaches that follow similar mechanistic pathways to acid-catalyzed ether cleavage involve the use of Lewis acids bearing a range of cationic metals and halide anions. Both dialkyl and alkyl aryl ethers initially form an addition compound between the basic ethereal oxygen and the Lewis acidic metal forming an $\text{R}_2\text{O}^+:\text{MX}_n^-$ complex which, like other conjugate acid-ether adducts, undergoes nucleophilic displacement *via* either an $\text{S}_\text{N}1$ or an $\text{S}_\text{N}2$ mechanism (see Figure 2.5.1).^[76]

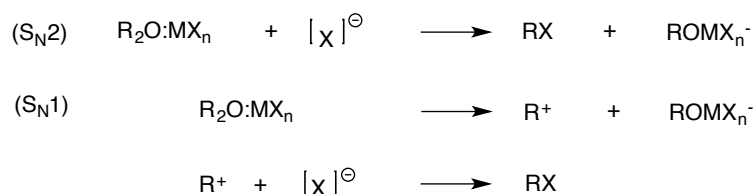


Figure 2.5.1 – Ether cleavage in Lewis acids

Due to the ready cleavage of most aryl alkyl ethers regardless of the electronic effects from substituents on the aryl ring, the basicity of the ether is shown to have a negligible effect due to the polarising ability of the Lewis acid, which is sufficient to increase the ether's susceptibility to ether cleavage. This would infer an $\text{S}_\text{N}2$ mechanism, whereby a halide anion can nucleophilically displace the lower molecular weight alkyl group.

A number of different Lewis acids following this mechanism have been investigated with the

most common being aluminium halides (bromide and chloride). Studies by Harmann and Gattermann showed the formation of an anisole and aluminium chloride adduct, which after heating to 100 °C produced methyl chloride and the Lewis acid-phenoxide adduct.^[103] Similar results were also obtained with aluminium bromide.^[104] Dialkyl ether-aluminium chloride adducts have also been shown to decompose at higher temperatures yielding ethanol, ethyl chloride as well as the elimination products ethylene and hydrochloric acid; whereas aluminium bromide yields mostly ethyl bromide and the alcohol.^[105] Furthermore, addition of sodium iodide salt to aluminium halides and aryl alkyl ethers have seen to increase reaction rate of dealkylation of acetophenone derivatives even at 0 °C.^[106]

Trivalent boron compounds are currently regarded as the reagents of choice for the deprotection of alcohols and dealkylation of ethers due primarily to their high activity under mild conditions and also due to their ability to be selective to ether functionality.^[77] The empty p-orbital in boron is the source of its electrophilicity and accommodates the oxygen lone pair. As with aluminium halides, an oxonium is formed which can then be attacked by the halide anion *via* an S_N2 reaction (see Figure 2.5.2).^[74]

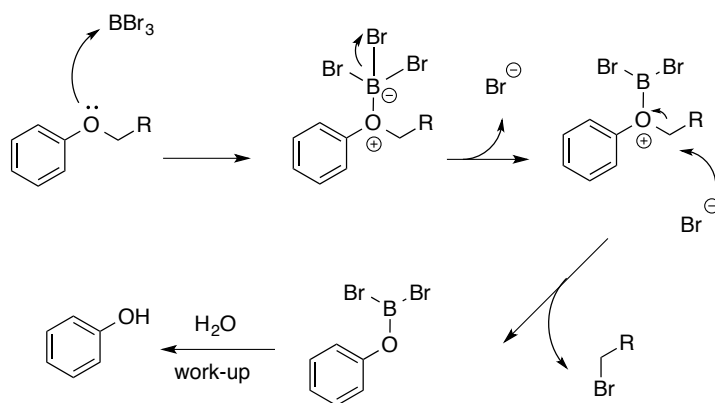


Figure 2.5.2 – Cleavage of aryl-alkyl ethers in BBr₃

The use of boron tribromide was first introduced by Dillon and Benton on a range of common dialkyl and alkyl aryl ethers^[107] and a number of examples showing its current importance in synthesis for the selective dealkylation of aryl alkyl ethers exist in the literature.^{[108],[109],[110]} Equally, boron trichloride has also seen useful applications in synthesis as it exhibits high activity at low temperatures on a range of ethers.^{[111],[112],[113]} Other Lewis acids which have enjoyed niche uses in selective dealkylation include nickel chloride,^[114] zinc bromide,^[115] and beryllium chloride.^[116]

2.6 Ether cleavage in ionic liquids

The use of ILs has seen a significant surge over the past decade, especially in organic synthesis. Studies toward ether cleavage have been extended from the mechanistic understanding of substrate reactivity in organic solvents, to the general exploration of the use of task-specific ILs on a range of dialkyl and aryl alkyl ethers. The fundamental modes of action of these solvents replicate the above mentioned reactions *via* mechanisms described in traditional organic chemistry, however the benefits of these systems lie in optimising activity or promoting selectivity of more complex substrates. In all cases, akin to previous studies conducted on nucleophilic substitution reactions, the activity of the IL is based on the properties of the anion^[117] with the cation largely aiding solubility. Protonation, oxonium intermediate formation and nucleophilic displacement all feature in dealkylation within ILs however the added versatility of modifying acid strength and nucleophile concentration in the medium have allowed numerous investigations on the cleavage of simple ether substrates to be carried out.

2.6.1 Ether cleavage using acidic ionic liquids

As mentioned previously, hydrobromic acid and hydrochloric acid have both seen uses in their aqueous form for ether dealkylation. When incorporated into an IL their nucleophilic ability can be enhanced. Driver *et al* reported that the anhydrous protic ionic liquid (PIL) 1-methylimidazolium bromide ([Hmim]Br), prepared by the addition of 1-methylimidazole to hydrogen bromide gas, demonstrated efficient cleavage of a range of cyclic, dialkyl and aryl alkyl ethers, forming the alcohol and alkyl bromide.^[118] Through doubling the stoichiometry of the acid to the imidazole during the initial synthesis of the IL, speciation of the anion from Br⁻ to [HBr₂]⁻ and [H₂Br₃]⁻ was observed, therefore providing a means to increase acid strength and promoting further cleavage. Anisole and *p*-methylanisole both gave relatively good yields of *p*-cresol, phenol and methylbromide at room temperature within 24 hours using these IL systems with increased concentration of acid.

A similar study exploiting the highly nucleophilic character of the bromide anion was conducted by Boovanahalli *et al* whereby [C₄C₁im]Br was added to a range of ILs along with a Brønsted acid to cleave a range of naphthyl ethers as shown in Figure 2.6.1.^[119]

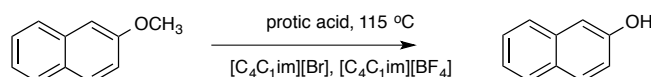


Figure 2.6.1 – Demethylation of 2-methoxynaphthalene

The addition of simple Brønsted acids such as *p*-TsOH, sulfuric acid, hydrochloric acid, acetic acid and methanesulfonic acid in [C₄C₁im][BF₄] and [C₄C₁im]Br was shown to give almost

quantitative yields of the 2-hydroxynaphthalene product within a 24 hour reaction time. Other substrates with longer alkyl groups attached to the ether also displayed similar reactivity under the same conditions. Although the use of the spectator ILs was shown to enhance reactivity, the role of the ionic liquid as a reaction solvent is not well understood.

Hydrochloric acid incorporated in the PIL system *H*-pyridinium chloride was also shown to successfully cleave simple aryl alkyl ethers.^[120, 121] Anisole derivatives with a range of electron withdrawing and electron donating groups cleaved successfully when submitted to microwave irradiation in the IL with yields ranging between 65 % for *o*-nitroanisole and 87 % for anisole itself after a 14 minute reaction time.^[121]

Table 2.6.1 – Microwave assisted demethylation of methylaryl ethers based on anisole with pyridinium chloride

Entry	R	MW heating time (min)	Yield (%)
1	H	14	87
2	<i>o</i> -Me	14	82
3	<i>m</i> -Me	14	82
4	<i>p</i> -Me	14	81
5	<i>p</i> -CHO	16	78
6	<i>p</i> -MeCO	16	74
7	<i>p</i> -Br	16	78
8	<i>p</i> -Cl	16	82
9	<i>o</i> -NO ₂	16	65
10	β-Naphthyl	14	95

^aYields refer to pure isolated products.

The high efficiency of the same IL was reproduced on 4-methoxyphenylbutyric acid and scaled up to a 32 kg scale. After a 3 hour reaction time at 180 °C, successful extraction of the demethylated product was achieved using the organic solvent MTBE with yields ranging between 87 % and 97 %. Additionally, after full consumption of the starting material, the IL solidified when cooled to 75 °C, therefore allowing ease of recycling. This study consequently demonstrated how PILs could potentially be used on an industrial scale for ether cleavage.

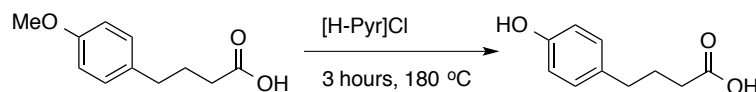


Figure 2.6.2 – Demethylation of 4-methoxyphenylbutyric acid

2.6.2 Ether cleavage using lewis acidic ionic liquids

As with PILs bearing nucleophilic anions, the reactivity of ILs with metal chloride anions mimics the Lewis acids commonly used in ether cleavage. Chloroaluminate ILs with a range of cations have shown to cleave cyclic and acyclic ethers and in some cases have also displayed enhanced selectivity on substrates with numerous ether functional groups. The preparation of these Lewis-acidic ILs typically involves the addition of 2 molar equivalents of aluminium chloride to the organic halide salt (Figure 2.6.3). The first equivalent of aluminium chloride reacts directly with the chloride anion. This forms aluminium tetrachloride which then forms a complex with the remaining amount of aluminium chloride, yielding a range of complexes sitting in equilibrium with one another, where the most common anion is $[\text{Al}_2\text{Cl}_7]^-$.^[122]

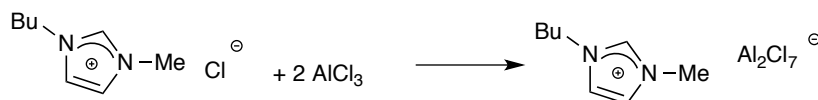


Figure 2.6.3 – The preparation of the Lewis-acidic ionic liquid $[\text{C}_4\text{C}_1\text{im}][\text{Al}_2\text{Cl}_7]$

One example of a Lewis acidic IL is 1-ethyl-3-methylimidazolium heptahalodialuminate, which was shown to successfully cleave a range of ethers including tetrahydrofuran, diethyl ether and anisole when stoichiometric amounts of benzoyl chloride is also added.^[123] A similar study was also conducted using a range of different cations including trimethylammonium, 1-ethyl-3-methylimidazolium and 1-butyl-3-methylimidazolium together with the chloroaluminate anion. The complex diether substrate 4,5-dimethoxyindanone was shown to selectively cleave at the 4-methoxy position with reaction time drastically shortened compared to the use of aluminium chloride alone.^[124]

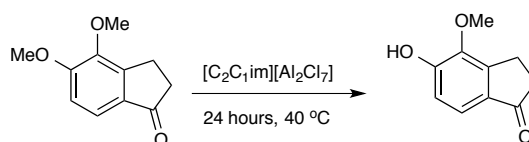


Figure 2.6.4 – Selective demethylation of 4,5-dimethoxyindanone

The enhanced activity of Lewis acidic ILs compared to neat aluminium chloride can be explained

mechanistically. Both the neat Lewis acid and the chloroaluminate anion coordinate to the etheral oxygen on the methoxy functional group therefore activating the bond between the methyl group and the oxygen, allowing the attack of the chloride on the methyl carbon. As this is the rate determining step of the process, the IL which contains a higher concentration of the Lewis acid with more labile chloride ions would therefore proceed faster in cleaving the ether. Kemperman explains this mechanism by showing the interaction of the chloroaluminate with anisole as the substrate as shown in Figure 2.6.5.

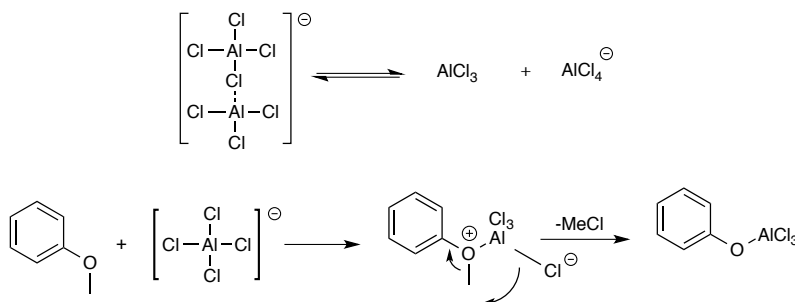


Figure 2.6.5 – Demethylation of anisole with a chloroaluminate ionic liquid

2.7 Cleavage of lignin model compounds

2.7.1 Lignin model compounds and the β -O-4 linkage

One current area where understanding the nature of ether cleavage is imperative involves the cleavage of ethers in bioderived polymers such as lignin and cellulose. ILs have recently been shown to be a promising alternative for biomass pretreatment and processing whereby, through correct selection of the cation and anion, complete or selective dissolution of the components found in lignocellulosic biomass can be achieved at high efficiency as explored in chapter 1. Both $[\text{C}_2\text{C}_1\text{im}][\text{OAc}]$ and $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ are most commonly used in pretreatment^[51, 125] to dissolve both the lignin and carbohydrate rich material without disrupting the inter-unit bonding in cellulose and lignin due to the high hydrogen-bond basicity of the anion. The versatility of ILs has allowed investigations into exploring the use of acidic ILs in pretreatment, whereby both the dissolution and chemical transformation of the lignin component occur concurrently in order to optimise the retrieval of the carbohydrate rich material.^{[58][54]}

Considering the complexity and non-homogeneity of the lignin super-structure, a considerable amount of research aimed at understanding lignin depolymerisation has been conducted in both ionic and aqueous media^[68, 69, 70, 126, 127] using lignin model compounds bearing the β -O-4 linkage, encompassing between 45-60 % of all monomer linkages present in lignin.^[65] The most

common lignin model compound bearing the full functionality of the β -O-4 linkage include the phenol-based guaiacylglycerol- β -guaiacyl ether (GG) and its anisole analogue veratrylglycerol- β -guaiacyl ether (VG), with the former representing a unit at the terminus of the lignin polymer and the latter representing a unit included in the lignin macrostructure.

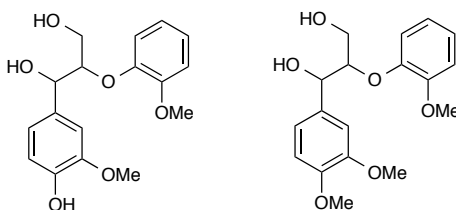


Figure 2.7.1 – GG and VG model compounds

In both cases, the yield of guaiacol (2-methoxyphenol) is indicative of the degree of successful ether cleavage. However, other simpler model compounds resembling the native monomers in lignin biosynthesis have also been studied in order to focus solely on the nature of the ether bond.

2.7.2 Reactions of lignin model compounds in ionic liquids.

A 2012 review published by Hossain *et al* outlines the multifunctional uses of ILs in the context of a biorefinery and directs a great deal of focus on the interactions of ILs with lignin.^[50] Most investigations feature model compounds bearing the β -O-4 linkage and a range of Brønsted acidic and metal chloride catalysts are explored and reported to develop a fundamental understanding of how the ether bond cleaves in the presence of water. Binder *et al* studied the reactivity of three simple lignin model compounds whereby the high electron donating functionality found in lignin is included in each substrate, however the β -O-4 linkage itself does not feature and a simple alkyl aryl ether bond is included instead.^[128] Eugenol (2-methoxy-4-(2-propenyl)phenol), 2-phenylethylphenyl ether and 4-ethyl-2-methoxyphenol were subjected to a range of Brønsted acid catalysts in $[\text{C}_2\text{C}_1\text{im}][\text{OTf}]$ at 180 °C for 2 hours with 3.4 MPa psi H_2 . The results of this study are presented in Table 2.7.1.

Despite the high conversion of the model compounds in acidic conditions, only small amounts of cleaved products were detected with no guaiacol or phenol obtained when the same conditions were repeated on organosolv lignin. This study concluded that the choice of lignin model compound is critical in understanding ether cleavage with substrates as complex as lignin whereby functionality, both sterically and electronically, must be taken into consideration when selecting an appropriate model. However, the study did provide insight on the use of ILs with Brønsted acids in ether cleavage.

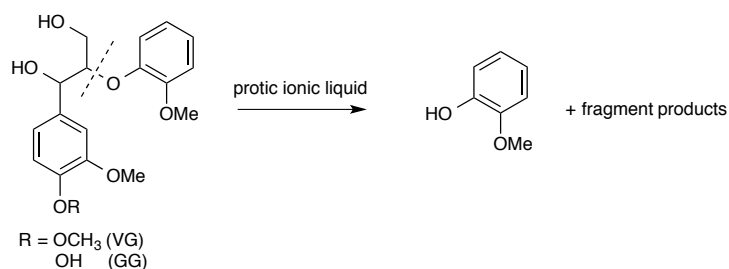
The full functionality of the β -O-4 linkage in lignin can be best depicted by the VG and GG model

Table 2.7.1 – Conversion of model compounds and organosolv lignin in IL taken from reference [128] .

Substrate	Catalyst	Conversion (%)	Guaiacol yield (%)	Phenol yield (%)
Eugenol	H ₂ SO ₄	100	7.8	-
Eugenol	HOTs	100	8.6	-
Eugenol	Nafion	100	11.6	-
4-Ethylguaiacol	H ₂ SO ₄	43.0	-	-
4-Ethylguaiacol	HOTs	16.0	-	-
4-Ethylguaiacol	Nafion	63.7	-	-
2-Phenylethylphenyl ether	H ₂ SO ₄	46.6	-	4.3
2-Phenylethylphenyl ether	HOTs	12.4	-	1.2
2-Phenylethylphenyl ether	Nafion	62.9	-	6.7
Lignin, organosolv	H ₂ SO ₄	n/a	-	-
Lignin, organosolv	HOTs	n/a	-	-
Lignin, organosolv	Nafion	n/a	-	-

Conditions: 10 wt % substrate in [C₂C₁im][OTf], 10 mol% catalyst, 180 °C, 2 h, 3.4 MPa psi H₂. Conversions and yields assessed by GC

compounds, as reported in a series of investigations by Ekerdt *et al.* [70, 126, 127] The use of PILs prepared by the addition of a Brønsted acid to methylimidazole forming 1-methylimidazolium with bromide, chloride, tetrafluoroborate and hydrogensulfate anions was studied for reactions with VG and GG.[70]

**Figure 2.7.2** – Hydrolysis of GG in protic ionic liquids

In each case, after a 20 minute reaction time at temperatures between 110 °C and 130 °C almost stoichiometric consumption of the substrate was observed with guaiacol yields of up to 80% with [HC₁im]Cl. Although all of these ILs are protic and therefore acidic, the trend in hydrogen-bond basicity of the anion is reflected directly in the degree of ether cleavage. The hydrogen bond ba-

sicity of the anions following the series $\text{Cl}^- > \text{Br}^- > \text{BF}_4^-$ predicts the ability of the IL to dissolve biomass^[129] and in this case coordination of the anion is seen to stabilise the hydroxyl group in γ position to the ether bond, preventing any degradation to formaldehyde and promoting ether cleavage. Nevertheless, no correlation between Hammett acidity of the acid system and yield of guaiacol in each reaction was observed, presumably due to the large difference in nucleophilicity of the anions, especially in a complex hydrogen-bond network.

A study of the β -O-4 linkage was conducted in the PIL $[\text{HC}_1\text{im}]\text{Cl}$ whereby a mechanism for VG and GG hydrolysis was proposed and the decomposition products characterised by LC-MS and FTIR.^[126] In IL media, it has been observed that prior to hydrolysis, the initial dehydrated intermediate 3-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-2-propenol, abbreviated to EE, is formed due to protonation of the hydroxy group on the α carbon and examples of its presence have been previously detected and characterised *via* two dimensional NMR.^[130] This unstable intermediate then promptly hydrolyses in the presence of water to form guaiacol and the little understood “Hibbert ketone” a product that has yet to be fully characterised due to the complex distribution of products formed after substrate decomposition. Ekerdt’s mechanism emphasizes the importance of the acid in these PILs, whereby both protonation of the hydroxyl group sitting on the α carbon and protonation of the ether post dehydration occur in sequence, allowing facile cleavage of the β -O-4 linkage *via* an $\text{S}_{\text{N}}2$ mechanism. Figure 2.7.3 shows Jia *et al*’s interpretation of this mechanism.

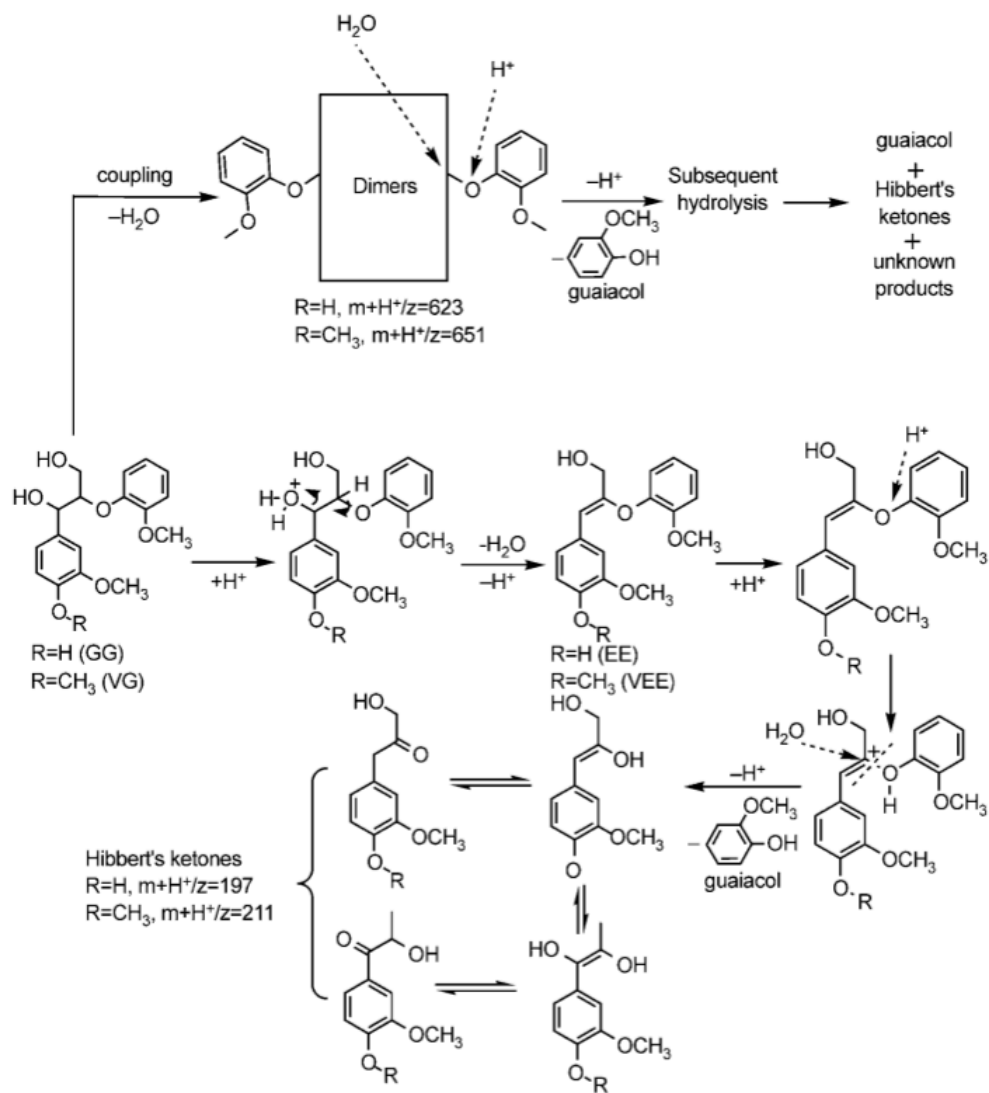


Figure 2.7.3 – Proposed acid-catalyzed mechanism for hydrolysis of GG and VG as presented by Jia *et al*^[127]

Whilst guaiacol is observed in each reaction, analysis of the decomposition products showed the presence of newly formed carbonyl stretches in the FT-IR and molecular masses of 197 for GG and 211 for VG, with the difference in mass accounted for by the addition of a methyl group. Furthermore, after extending the reaction time to 60 minutes, LC-MS analysis showed products with masses of 303 m/z (the EE dehydrated intermediate), 498 m/z and 623 m/z, masses that far exceed that of the original substrate, indicating further reactivity occurring on the ketone moiety once cleavage has occurred.

The addition of metal chlorides such as FeCl₃, CuCl₂ and AlCl₃ to [C₄C₁im]Cl with 2 wt.% water have also shown to be effective in the ether hydrolysis of GG and VG *via* similar mechanisms to Lewis acidic ILs, with AlCl₃ offering the highest activity, giving 100 % conversion of GG and 70 % yield of guaiacol.^[127] When further aliquots of water were added to the metal chloride - IL system, the rate of hydrolysis increased, which was postulated to be a two-fold effect; initially contributing to the hydrolysis of the metal chloride forming hydrochloric acid *in situ*, therefore promoting protonation and also through water nucleophilically hydrolysing the oxonium intermediate.

2.8 Conclusion

The history of ether cleavage using a range of inorganic reagents has offered a solid foundation for understanding the chemistry of ether bonds in simple, small etherified molecules and more recently, in larger bioderived polymers. While functionality and sterics both contribute in determining the susceptibility of any ether to cleavage, this review highlights the mechanistic features common to all cleavage routes regardless of substrate, involving the same two step processes:

- Initial polarisation of the C-O bond, be it through the formation of an oxonium intermediate, coordination of metals to the ethereal oxygen or the removal of a proton on the α or β carbon with respect to the ether.
- The nucleophilic attack of the electrophilic alkyl moiety, either *via* an S_N1 or S_N2 pathway, yielding an alcohol and the newly substituted alkyl product.

In the case where nucleophilic displacement occurs, the reagent must be able to either adopt both roles in order to achieve successful cleavage or be present with a second nucleophilic reagent such as water. Consequently, the most common reagents used in ether cleavage frequently contain halide anions, both in Brønsted acidic reagents for acid catalysed ether cleavage and Lewis acidic reagents involving the formation of a metal-oxygen adduct. With protophilic base-catalysed ether cleavage, as no nucleophile is needed, the only necessary feature of the reagent is the ability to deprotonate the alkyl proton adjacent to the ether *via* an E2 mechanism, yielding an alkoxide salt with an unsaturated alkyl product.

These same principles are applied once again to the activity of ionic liquids. The current growth in interest in the applications of ILs in synthesis has adopted these traditional methods of dealkylation by incorporating the acidic and nucleophilic components of these reagents into a system whereby the overall activity can be optimised and the system potentially recycled as described previously in this review. The additional interest in harnessing the potential of lignocellulosic biomass to obtain bioethanol and aromatic platform chemicals has synergistically enhanced our desire to understand the interactions and mechanism of ether cleavage by these task-specific ionic liquids using more complex, multi-functionalised ethers that undergo a series of chemical transformations both prior to and simultaneously to ether cleavage.

Chapter 3

Hammett study on 2-phenoxyethanol using acidic ionic liquids

3.1 Aims and Objectives

One novel application of IL in biomass processing is the deconstruction of lignocellulosic biomass into cellulose, hemicelluloses and lignin. With the use of Brønsted acidic anions, preferential dissolution and depolymerisation of lignin can be achieved. This has been demonstrated through the use of 1-butyl-3-methylimidazolium hydrogensulfate ($[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$) in an 80:20 wt % IL: water composition, where lignin and hemicellulose can be solubilised, leaving a solid enriched with cellulose.^[54, 62] Investigations on the chemical transformation of lignin during the pretreatment process confirmed the cleavage of the highly abundant β -O-4 linkage, indicating that successful pretreatment occurs when the lignin macropolymer is depolymerised.^[63]

The importance of these results has led to further investigations into the application of these ILs in areas outside biomass deconstruction, with one objective being their use as reaction medium for the valorisation of lignin. This interest has led to the use of ILs as both a solvent and reagent in the depolymerisation of lignin, primarily through the simple cleavage of the β -O-4 linkage between the subunits as outlined in Chapter 1.

The aim of this investigation is to glean mechanistic insights into ether cleavage in simple aryl alkyl ethers through the use of a Hammett study. This involves the use of simple model compounds with functional groups of varying electronic properties and investigating their reactivity in acidic ILs. $[\text{HC}_4\text{im}][\text{HSO}_4]$ with additional sulfuric acid was selected as the solvent of choice

investigated in this study, whereby the IL can act dually as a solvent and nucleophile while the acid can act to protonate the ether. These initial results will then be compared to the reactivity of the same model compounds in the more acidic ILs system: $[\text{C}_2\text{C}_1\text{im}]\text{Br}$ containing hydrobromic acid. From these initial studies, the transition states and reaction pathway for lignin depolymerisation in acidic ILs can be determined which ultimately; will provide insight into what functionality in lignin is responsible for successful ether cleavage.

3.2 Hammett mechanism

3.2.1 Derivation of the Hammett equation

Chapter 2 detailed the most efficient acids and nucleophiles used in the cleavage of alkyl-alkyl and alkyl-aryl ethers. While acid strength and nucleophilicity have been identified as the most important properties in selecting a suitable reagent for cleavage, there are very few reports on the mechanistic pathway and more specifically, the effects of substrate functionality on the reactivity of ether cleavage. Louis Hammett devised an equation that is amongst the most widely used physical organic tools to study and interpret organic reactions and their mechanisms.^[131] Hammett's success in establishing a linear free-energy relationship (LFER) between electronic effects of substituents and reaction rates has allowed studies to be conducted in which the electronic, steric, hydrophobic, hydrophilic and hydrogen-bonding parameters are used to derive quantitative structure-activity relationships.^[132] The overall purpose of these studies is to identify the charge of the transition state of a simple reaction through varying the electronic effects of the reactants and as a result, provide insight into the reaction mechanism.

Hammett originally postulated that a relationship could potentially exist between the rate constant of a reaction and the equilibrium constant between groups of closely related reactions. For example, the equilibrium constant of ionised substrates and the rate of formation of new bonds. In the case of an acid catalysed reaction a generic reaction can be identified in equation 3.2.1 where S is the substrate and HA is the acid catalyst.



As the rate of acid catalysed reactions is related to the dissociation constant, the rate of reaction can be correlated to the equilibrium constant of proton dissociation by the equation 3.2.2 where k is the rate of reaction, K is the equilibrium constant and G and x are constants:

$$k = \text{GK}^x \quad (3.2.2)$$

One of the earliest examples of the LFER given in equation 3.2.2 considers the rate constant for the base catalysed hydrolysis of ethyl esters to form carboxylic acids and the equilibrium constant of the protonation of water by the corresponding acids (see Figures 3.2.1 and 3.2.2). Although the reactions are entirely different, requiring significantly different enthalpies and entropies of activation, the systematic variation of the meta and para functional groups on both the benzoate and benzylic acid substrates causes similar changes in both the rate and equilibrium constants.

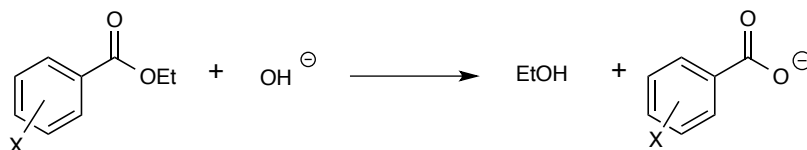


Figure 3.2.1 – Base catalysed hydrolysis of ethyl benzoate

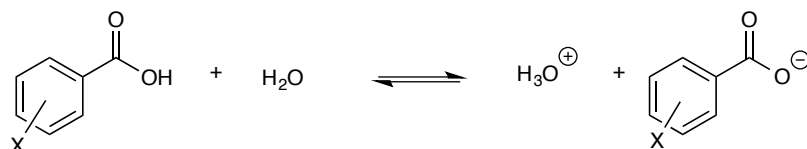


Figure 3.2.2 – Dissociation of benzoic acid in water

The added substituents (X) on both the benzoate and benzoic acid substrates can be either electron-withdrawing or electron-donating with the transmission of electronic density through the ring to the reactive site. The physical meaning and effects of these electronic properties will be explored later.

Through plotting the rate constants of the base catalysed hydrolysis of meta and para functionalised ethyl benzoates ($\log k$) against the equilibrium constants of water ionisation in similarly functionalised benzoic acids ($\text{p}K_a$), a direct relationship can be established between both sets of reactions:

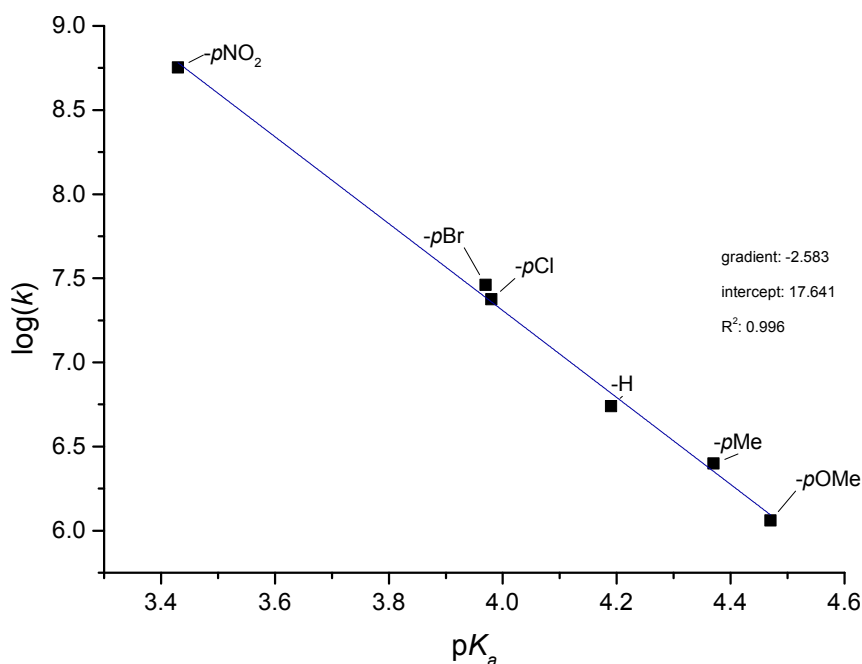


Figure 3.2.3 – Correlation of $\log(k)$ for base catalysed hydrolysis of ethyl benzoate derivatives against pK_a of benzoic acid derivatives

This leads to the equation:

$$\log k = \rho \log K + C \quad (3.2.3)$$

whereby ρ is the gradient (here given as -2.583) and C is the intercept (given as 17.641).

In order to identify the electronic effect of each substituent in both reactions relative to the unfunctionalised (hereby referred to as -H) substrates, subtraction of this value from both sides of the equation leaves equation 3.2.4 :

$$\log k_x - \log k_H = \rho (\log K_x - \log K_H) \quad (3.2.4)$$

Where x is the substrate with the substituent in question and H is the unfunctionalised substrate. As the equilibrium constant for the deprotonation of benzoic acid in water is the pK_a of

the benzoic acid, Hammett took the pK_a of carboxylic acid in water at 25 °C and 1 atm as a reference point. This was based on the premise that with the addition of meta/para positioned electron withdrawing substituents, the pK_a would decrease due to the increased stabilisation of the dissociated anion whereas the addition of the meta/para electron donating substituents would have the opposing effect.

Therefore Hammett used the following equation:

$$\sigma = pK_{a_X} - pK_{a_H} \quad (3.2.5)$$

And by applying equation 3.2.4:

$$\log \left(\frac{k_X}{k_H} \right) = \rho \left(pK_{a(X)} - pK_{a(H)} \right) \quad (3.2.6)$$

Which then leads to equation 3.2.7, currently known as the Hammett equation:

$$\log \left(\frac{k_x}{k_H} \right) = \rho \sigma \quad (3.2.7)$$

Here σ represents the electronic effects of the substituent and ρ the overall calculated Hammett reaction constant once σ and the reaction rates of each functionalised substrate are known. Applying this formula to the data from Figure 3.2.3 a full Hammett plot can be obtained.

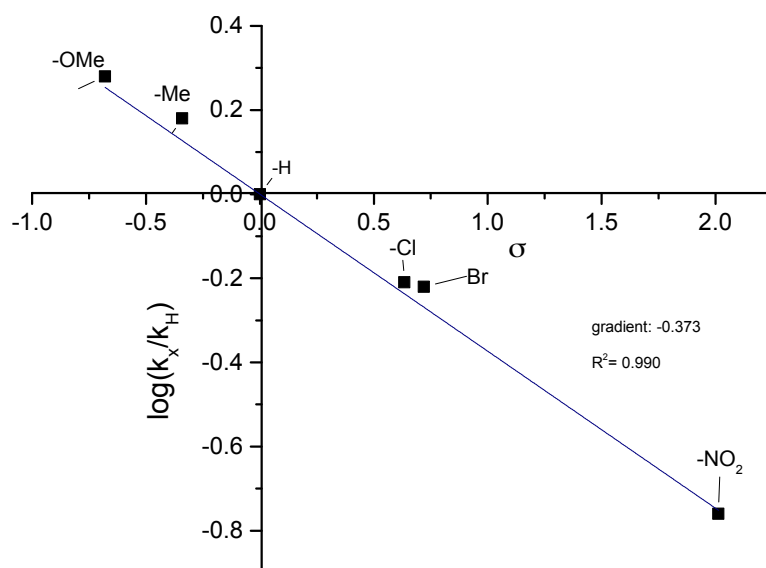


Figure 3.2.4 – Correlation of $\log(k_x/k_H)$ for base catalysed hydrolysis of ethyl benzoate derivatives against σ values (substituents all located on the para position).

3.2.2 Definition of σ and its physical meaning

The electronic effects of the substituents (hereby referred to as σ) is a measure of the total polar effect exerted by substituent X relative to having H as a substituent on the reaction centre. These measurements show how electron-donating or withdrawing a group is relative to -H as the difference in pK_a between the substituted benzoic acid and benzoic acid itself, where electron withdrawing substituents lead to positive σ values and electron donating substituents having negative values. These effects are composed of two parts which are additive in determining the overall σ value:

1. Field/inductive effects (I)

This is the effect of the intervening σ bonds between the reaction site and the substituent itself. This is known as an inductive effect and can be seen with substituents such as $-\text{CH}_3$. As inductive effects are stronger in closer proximity to the reaction centre, substituents at the meta position exert stronger inductive effects than at the para position.

2. Resonance effects (R)

In instances where the substituents act as π donors or π acceptors, the reaction site is affected *via* the conjugation of the electrons into the aromatic system. Examples of such electron donating substituents include $-\text{OH}$ and NH_2 , where the lone pair can donate into the conjugated system (+R), therefore having negative σ values. Alkyl groups can also donate electrons through resonance effects by $\sigma - \pi^*$ hyperconjugation therefore exerting both resonance and inductive properties. Equally, electron-withdrawing groups such as $-\text{NO}_2$ can withdraw electrons through conjugation (-R) by electron delocalisation with the benzene ring and therefore have large positive σ values. Similarly, $-\text{CF}_3$ can act as an electron withdrawing group, both by induction (-I) and $\sigma^* - \pi$ hyperconjugation (-R).

In general, the σ values of each substituent indicate the acid strength if that substituent was incorporated into benzoic acid. A positive σ value means a stronger acid, therefore being electron-withdrawing with respect to $-\text{H}$. Conversely, a negative σ value means a weaker acid therefore being electron donating. In addition to the original values obtained from substituted benzoic acids, further values were obtained for modern Hammett studies *via* the correlation with other reactions and are accessible in Hansch *et al*'s 1991 review.^[132] As each substituent's effects depend on its position on the ring, a different σ value was determined for substituents on the para (σ_p) or meta position (σ_m). It must be noted however that Hammett's Linear Free Energy Relationships solely look at understanding how the electronic effects of a substituent transmit through a molecule and do not take into account the steric effects of these substituents. For this reason, σ values can only be reported for substituents sitting at the para and meta positions, as functionalisation at the ortho positions will directly affect the reactivity by providing steric bulk at the site of reactivity.

3.2.3 The Hammett Reaction Constant ρ

Equation 3.2.7 identifies the Hammett equation, where k_x is the rate constant for the reaction with the substituted substrate, k_H is that for the unsubstituted substrate, σ is the substituent constant and ρ the reaction constant. In essence, a Hammett study looks at the effect of varying the substituent against the rate constant of a reaction with ρ value providing a summary of the overall correlation. In the case of the hydrolysis of ethyl benzoate, a good correlation is observed whereby all the points lie on a straight line, passing through the origin (as shown in Figure 3.2.4). The sign and gradient of this line tells us how sensitive the reaction is to the varying electronic effects compared to the ionisation of benzoic acid.

Generally speaking:

- A positive ρ value indicates the generation of negative charge through increased electron density on or near to the aromatic ring in the transition state compared to the starting material

- A negative ρ value indicates the generation of a positive charge through the decreased electron density on or near to the aromatic ring in the transition state compared to the starting material.

It must be emphasized that the ρ value encompasses all steps in a reaction up to and including the rate determining step. The magnitude of ρ shows how sensitive the reaction is to the electronic effects of the substituents but also gives an indication of the distance between the aromatic system bearing the substituent and the site of reactivity. A summary of these values can be found in Table 3.2.1 as described in Clayden *et al's* textbook of Organic Chemistry.^[74]

Table 3.2.1 – The meaning of Hammett ρ values

ρ value	Significance
-6, -5	Positive charge on ring or delocalised around aromatic ring
-4, -3, -2	Electrons flow out of the transition state, positive charge near ring
-1, 0, +1	Site of reaction too far from substituents/ No change in electron density/ Opposing charge developments before RDS cancel each other out
+2, +3, +4	Electrons flow into the transition state, negative charge near ring
+5, +6	Negative charge on ring, or delocalised around the aromatic ring

3.2.4 Deviations from Linearity

If all substrates with varying substituents show linearity in a Hammett plot for a specific reaction, a consistent mechanism can be inferred. However, in some cases a break in linearity can occur and these are referred to as non-linear Hammett plots, providing further mechanistic information on the reaction. As an example, when two intersecting straight lines are observed, usually at the point where the electron density of the ring system is reversed, this indicates either a change in mechanism or a change in rate determining step. One example of a non-linear Hammett plot is the alkaline hydrolysis of N-phenyl carbamates.^[133] This gives a concave upwards Hammett plot when electron donating groups are included, giving two contrasting ρ values as shown in Figure 3.2.5.

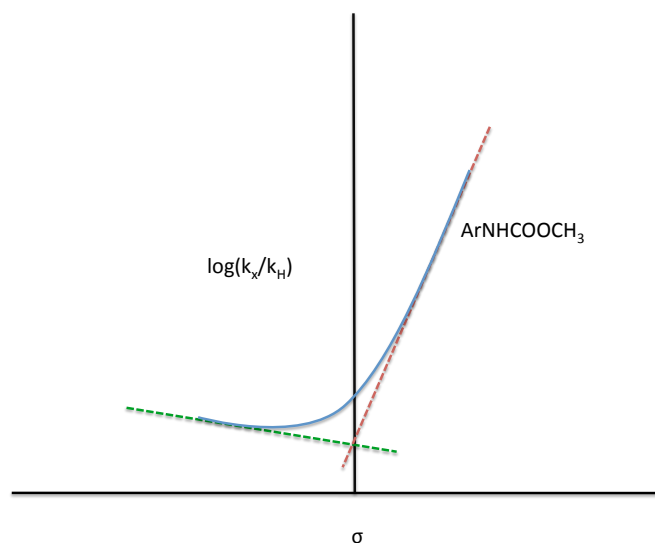


Figure 3.2.5 – Hammett plot of alkaline hydrolysis of N-phenyl carbamates

This switch in ρ value is due to a change in mechanism. The negative ρ value with low σ values shows that positive charge develops in the rate determining step and is accelerated by electron donating substituents, stabilising the acylium ion formed in step three of the reaction scheme shown in Figure 3.2.6. This is then attacked by the hydroxide nucleophile, liberating the carbamic acid. However with electron withdrawing substituents, the acylium ion cannot be stabilised, therefore the hydroxide ion directly attacks the electrophilic carbon, liberating ethanol

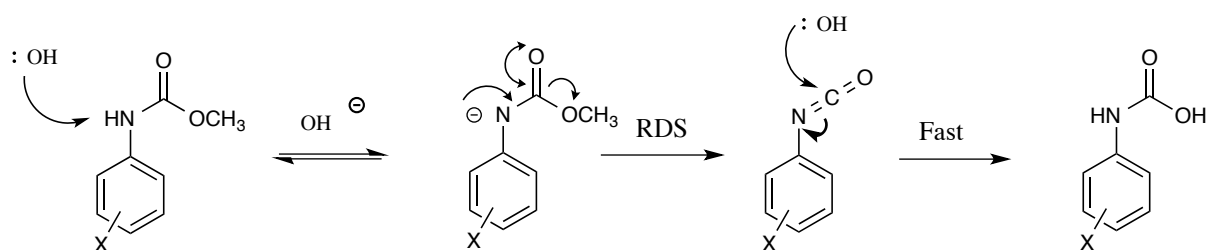


Figure 3.2.6 – Mechanism for the Alkaline hydrolysis of methyl N-phenyl carbamates where X are electron donating groups

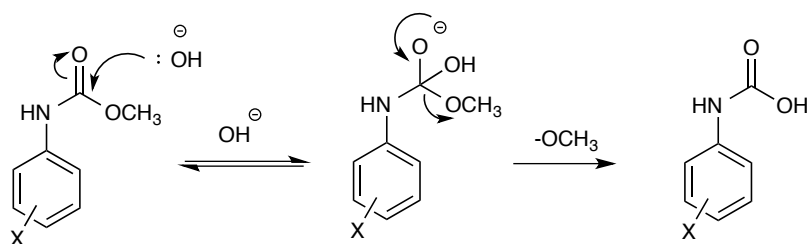


Figure 3.2.7 – Mechanism for the Alkaline hydrolysis of methyl N-phenyl carbamates where X are electron withdrawing groups.

A second deviation from linearity occurs when the opposite trend is seen, i.e. a concave downwards Hammett plot as shown in Figure 3.2.8. This infers that a single mechanism holds with all substituents but a change in rate determining step occurs when the electron density of the ring reaches a specific threshold. An example of this is the intramolecular Friedel-Crafts alkylation of a diphenyl derivative in an acidic medium (Figure 3.2.9).

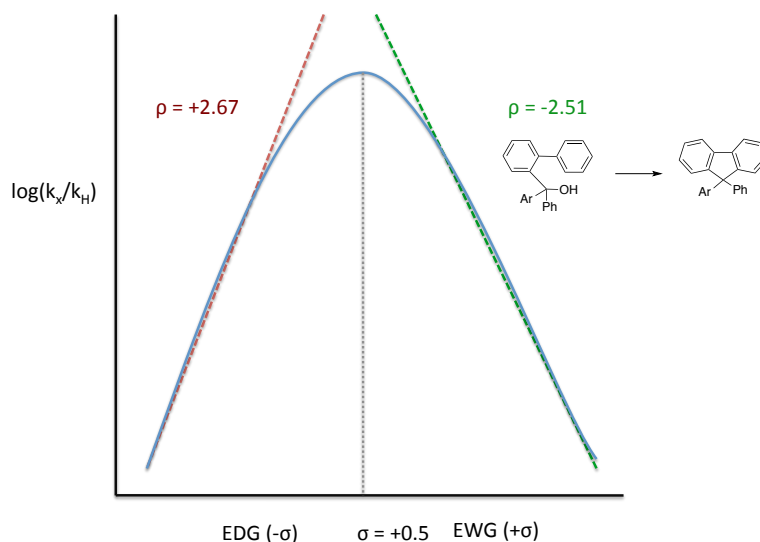


Figure 3.2.8 – Hammett plot of an intramolecular Friedel-Crafts alkylation

Here, the alkylating agent is diarylmethanol which is attached at the ortho position of one of the phenyl rings. The mechanism proceeds *via* the initial protonation of the alcohol liberating water to form a carbocation which then undergoes intramolecular ring cyclisation. In cases where the

substituent is electron withdrawing, the rate determining step is the initial hydrolysis of the alcohol. Although benzylic and tertiary, reduced electron density reduces the stability of the carbocation, rendering it the slowest step in the mechanism, giving a negative ρ value. Upon increasing electron density of the ring with electron donating substituents, the rate of hydrolysis increases until this is no longer the rate determining step. Ring cyclisation then becomes the slowest step as it involves re-establishing the electron density of the ring, giving a positive ρ value. As both steps have more or less the same flow of electron density to and from the reaction site, this accounts for the similarity in magnitude, but difference in sign of the ρ value.

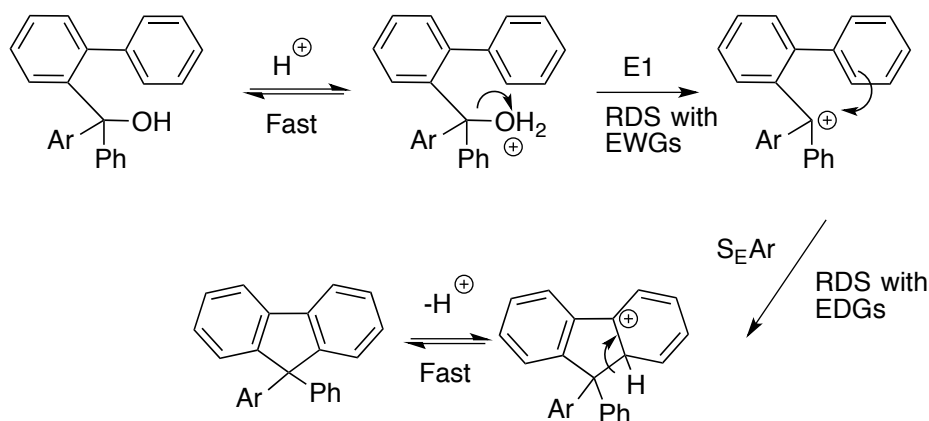


Figure 3.2.9 – Mechanism for intramolecular Friedel-Crafts alkylation of a diphenyl derivative

Whilst these two are specific acid catalysed reactions, the same observations have been made with a range of reactions where subtle changes in electron density can significantly change the kinetics and mechanistic pathway of the reactions.

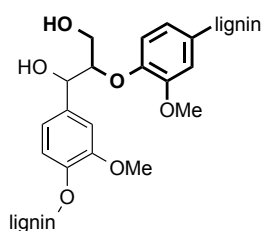
3.3 Using Hammett plots to investigate acid catalysed ether cleavage of simple ethers

3.3.1 Scope of study

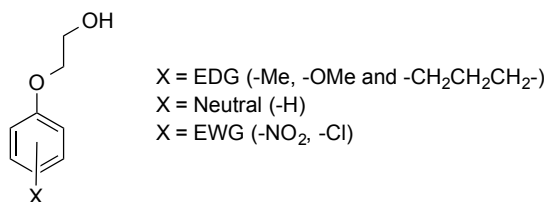
This study investigated the use of acidic ILs systems for the cleavage of simple ethers based on the substrate 2-phenoxyethanol, an ether of simple functionality bearing a primary alcohol that aids solubility in ionic media. This selection of model compound was also to reflect the backbone of the lignin macropolymer, focusing purely on the ether bond in the β -O-4 linkage and the γ -methyl hydroxyl group as shown in Figure 3.3.1.

Table 3.3.1 – Substrates studied in this investigation

Substrate	Substituent (para)	σ value	Preparation
2-phenoxyethanol	-H	0	Commercial
2-(4-methoxyphenoxy)ethan-1-ol	-OMe	-0.27	Synthesised
2-(4-methylphenoxy)ethanol-1-ol	-Me	-0.17	Synthesised
2-((5,6,7,8-tetrahydro-2-naphthalenyl)oxy)ethan-1-ol	(p)-CH ₂ CH ₂ CH ₂ -(m)	-0.26	Synthesised
2-(4-nitrophenoxy)ethan-1-ol	-NO ₂	+0.78	Commercial
2-(4-chlorophenoxy)ethan-1-ol	-Cl	+0.23	Commercial

**Figure 3.3.1** – 2-phenoxyethanol substrate within the lignin macropolymer

A series of substrates were prepared or acquired commercially with a range of electron withdrawing and donating substituents sitting para to the ether as shown in Table 3.3.1, altering the electronic properties of the ring and consequently the ether.

**Figure 3.3.2** – Analogues of 2-phenoxyethanol selected for the study

As the site of cleavage occurs at the ether, directly connected to the ring system, 2-phenoxyethanol and its functionalised analogues were all deemed as substrates suitable for participation in a Hammett study.

3.3.2 Kinetic model for reaction mechanism

It was envisaged that in cases where the ether substrate cleaves, the reaction would proceed *via* an A2 mechanism, involving the initial protonation of the ether by the acid followed by nucle-

ophilic attack at the α carbon. This would yield the substituted phenol and ethylalcohol as the cleaved products:

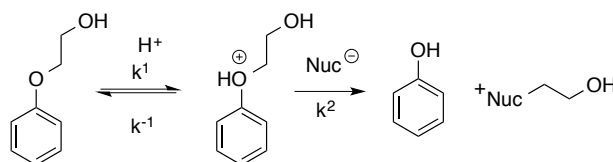


Figure 3.3.3 – Mechanism for cleavage of 2-phenoxyethanol where Nuc is the nucleophile

As the ρ value takes into account all steps up to and including the rate determining step, the equilibrium constant for the initial protonation of the ether to the oxonium must be considered in the overall rate expression. This constant, labelled K_{eq} is dependent on the concentration of the acid and the ether starting material and can be described as follows:

$$K_{eq} = \frac{[X-Ph(OH)^+CH_2CH_2OH]}{[X-PhOCH_2CH_2OH][H^+]} \quad (3.3.1)$$

The subsequent step involves the attack of the nucleophile onto the carbon adjacent to the oxonium, therefore both the protonated intermediate and the nucleophile will appear in the rate expression for this step, where [P] is the concentration of cleaved products:

$$\frac{d[P]}{dt} = k_2[Nuc][X-Ph(OH)^+CH_2CH_2OH] \quad (3.3.2)$$

Combining equations 3.3.1 and 3.3.2 gives the overall rate expression as:

$$\frac{d[P]}{dt} = K_{eq}k_2[H^+][Anion][X-PhOCH_2CH_2OH] \quad (3.3.3)$$

In our system, as the IL bearing the acid and the nucleophilic anion acts also as the solvent, it would be difficult to monitor both the formation of the product and the changing concentration of the IL components that feature in the rate expression. To simplify this, pseudo-first order reaction conditions are used where the IL is added in large excess compared to the substrate. This excess allows the concentration of the nucleophile and acid to remain approximately constant during the reaction therefore giving the following rate expression for the reaction:

$$rate = \frac{d[P]}{dt} = k_{obs}[X-PhOCH_2CH_2OH] \quad (3.3.4)$$

This differential form of the rate law can then be integrated in order to find the rate constant labelled k_{obs} of the reaction (its derivation can be found in the appendix). For the rate of consumption of the ether, if we label concentration of the initial substrate as $[A]_0$ and the concentration of the substrate at any particular time as $[A]$ with t denoting time, the following equation can be obtained:

$$\ln \left(\frac{[A]}{[A]_0} \right) = -kt \quad (3.3.5)$$

As this now represents a linear relationship between $\ln([A]/[A]_0)$ and time, the negative value of the gradient provides the observed rate constant k . The observed rate expression, which can be described as:

$$k_{\text{obs}} = k_2 K_{\text{eq}} [\text{H}^+] [\text{Anion}] \quad (3.3.6)$$

involves all the steps incorporating the acid and nucleophilic anion that participate in the reaction leading up to the rate determining step.

3.4 Results and Discussion

3.4.1 Kinetic measurements using $[\text{HC}_4\text{im}][\text{HSO}_4]$

The initial study assessed the reactivity of the ether substrates in $[\text{HC}_4\text{im}][\text{HSO}_4] \cdot (\text{H}_2\text{SO}_4)_x$, where x specifies the added molar equivalents of sulfuric acid with respect to the IL. *In-situ* ^1H NMR was used to track the reaction in the aromatic region by periodically analysing the substrate-product composition in the reaction mixture. When the substrate 2-phenoxyethanol was left in the IL for 6 hours at 100 °C no change was observed with the ether remaining intact. Upon addition of 1 molar equivalent of sulfuric acid to a fresh sample of the IL and leaving the system to dry under vacuum overnight, the NMR spectrum of the product showed two new sets of doublets in the aromatic region with similar integrations. This implies that aromatic substitution occurs at the para position of the ring with no consequential ether cleavage, as shown in the ^1H NMR spectrum (Figure 3.4.2). Due to the anhydrous nature of the IL and therefore the potential presence of the electrophilic SO_3 in the anion, it was concluded that the substrate underwent ring sulfonation.

In addition to the splitting pattern and the integration values of the newly formed aromatic signals, a selective NOESY experiment was conducted to confirm that the reaction occurring was not

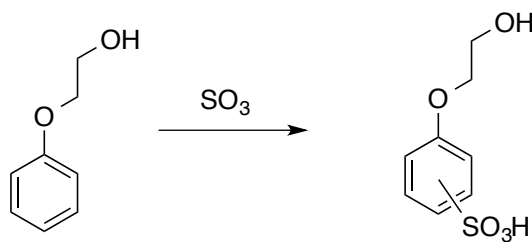
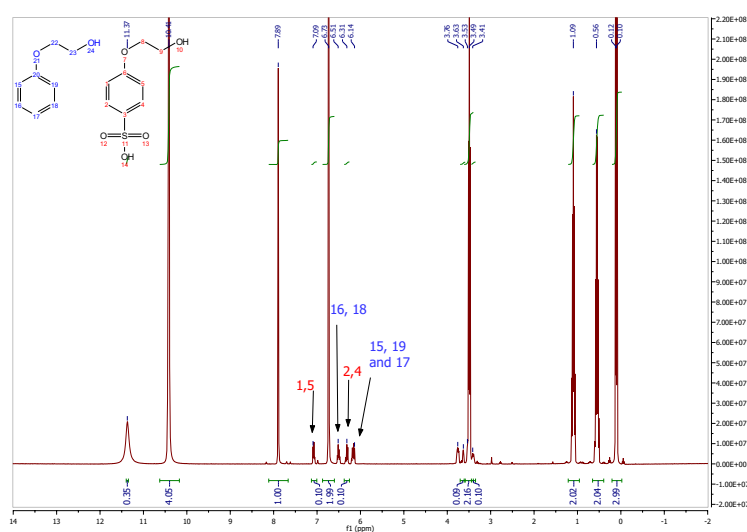


Figure 3.4.1 – Sulfonation of 2-phenoxyethanol

Figure 3.4.2 – ^1H NMR spectrum of the sulfonation of 2-phenoxyethanol in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100°C

ether cleavage (see Figure 3.4.3). After leaving 2-phenoxyethanol in dry $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100°C for 3 hours, a proton at the ortho position of the aromatic ring was selectively excited which, through spin-lattice relaxation, excited the aliphatic α protons adjacent to the ether, confirming the ether remaining intact.

Initial quantitative tests showed that sulfonation of 2-phenoxyethanol occurred relatively quickly in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100°C with 56% of the sulfonated product observed after one hour. Kinetic data under pseudo first order conditions with regards to the concentration of the 2-phenoxyethanol were collected at different temperatures with different concentrations of sulfuric acid by tracking the integration of the aromatic ortho proton in the starting material and product. Each reaction was monitored over a one hour period with readings taken at 2 minute intervals. When plotting $\ln[A]/[A_0]$ against time, a linear response was observed. The rate constant k_{obs} for each reaction was obtained from the gradients of the initial linear part of each graph. An example of this is shown in Figure 3.4.4. The rate of ring sulfonation was shown to

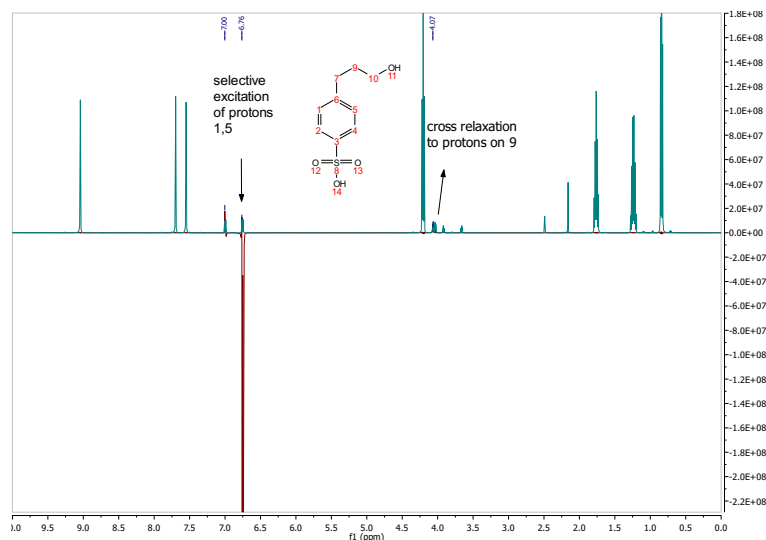


Figure 3.4.3 – 1D selective NOESY of sulfonated 2-phenoxyethanol in $[\text{HC}_4\text{im}][\text{HSO}_4] \cdot (\text{H}_2\text{SO}_4)_1$ at 100°C

increase with both an increase in temperature and concentration of the acid, however no further sulfonation of the ring occurred beyond the initial reaction. This was presumed to be due to the electron withdrawing capabilities of the sulfonate group, deactivating the substrate to further electrophilic aromatic substitution and the increase in water that quenches the electrophile.

The NMR spectra all confirm the inability of simple aryl alkyl ethers to cleave even with a high loading of sulfuric acid. It was hoped that the efficient drying of the IL would increase the nucleophilicity of the hydrogensulfate due to the decrease in hydrogen bonding with water which would impact nucleophilic strength. However this only increased the ability of the IL to act as a sulfonation source as observed in Table 3.4.1 where an increase in acid content increased rate of sulfonation. The study was then extended to the substrates described in Table 3.3.1. Through blocking the para position and altering the electron density of the ring it was hoped that the substrates' susceptibility to ether cleavage would be promoted. Using $[\text{HC}_4\text{im}][\text{HSO}_4] \cdot (\text{H}_2\text{SO}_4)_1$ at 100 °C as the selected conditions for this part of the study, only substrates with electron donating substituents reacted after one hour, showing sulfonation occurring at the ortho position of the aromatic ring with no ether cleavage as shown in Figures 3.4.5, 3.4.6 and 3.4.7. Their respective rates of consumption can be found in Figures 3.4.8, 3.4.9 and 3.4.10.

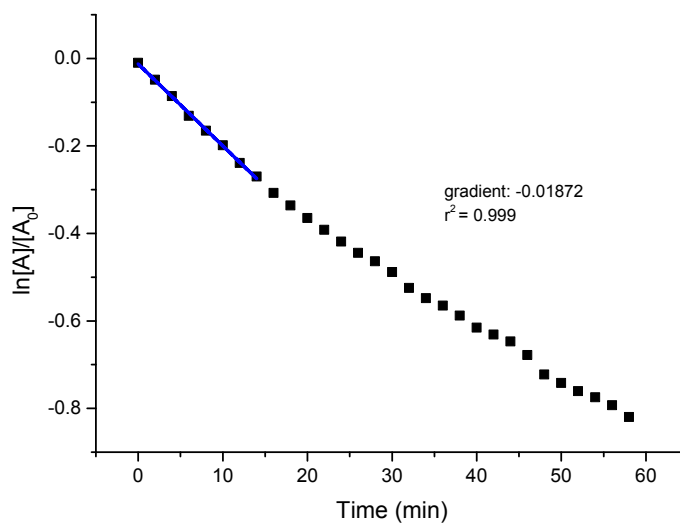


Figure 3.4.4 – Plot of $\ln[A]/[A_0]$ against time of 2-phenoxyethanol sulfonation in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$

Table 3.4.1 – Kinetic data for sulfonation of 2-phenoxyethanol in PIL.

molar quantity of x in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_x$	Temp °C	$k_{\text{obs}}/\text{s}^{-1} \times 10^{-4}$	r^2 value	% consumption after one hour
0.6	45	n/a	n/a	No reaction
0.8	45	n/a	n/a	No reaction
1.08	45	n/a	n/a	No reaction
1.2	45	n/a	n/a	No reaction
1.4	45	n/a	n/a	No reaction
1.0	100	3.12	> 0.99	56
1.2	100	5.09	> 0.99	65
1.4	100	7.27	> 0.99	85
1.6	35	3.73	> 0.99	88
1.6	65	11.66	> 0.99	82

^a Conditions: substrate dissolved in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_x$ and left to react at indicated temperature. Rate constants obtained by monitoring product increase *via* ^1H NMR.

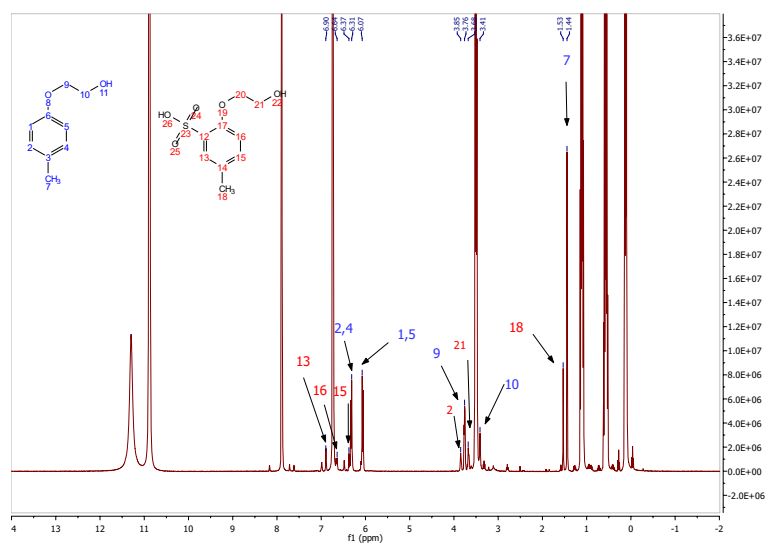


Figure 3.4.5 – Sulfonation of 4-methylphenoxyethan-1-ol in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100 °C

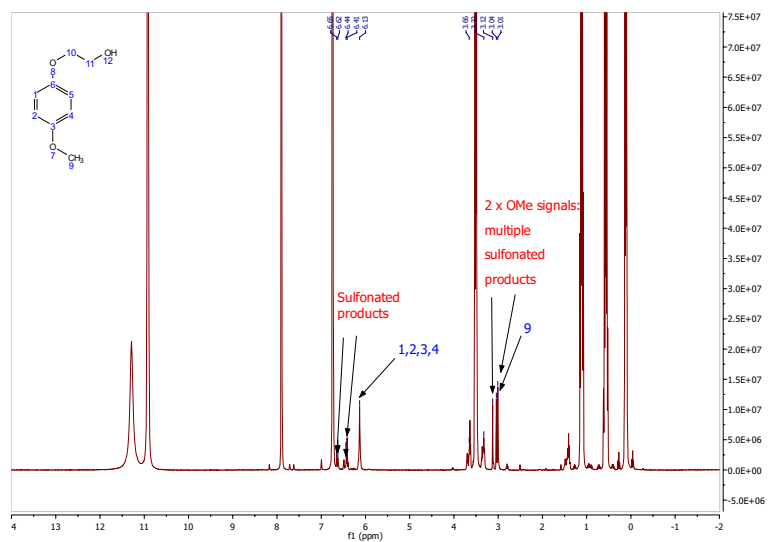


Figure 3.4.6 – Sulfonation of 4-methoxyphenoxyethan-1-ol in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100 °C

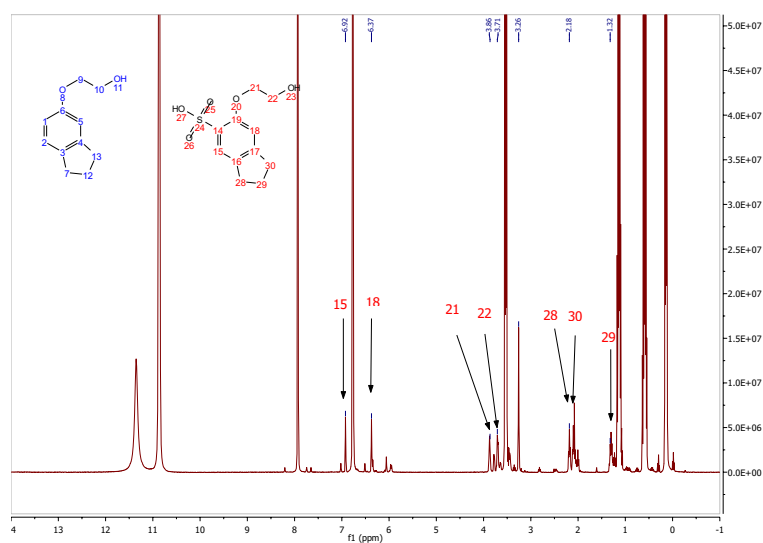


Figure 3.4.7 – Sulfonation of 2-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]ethan-1-ol in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100 °C

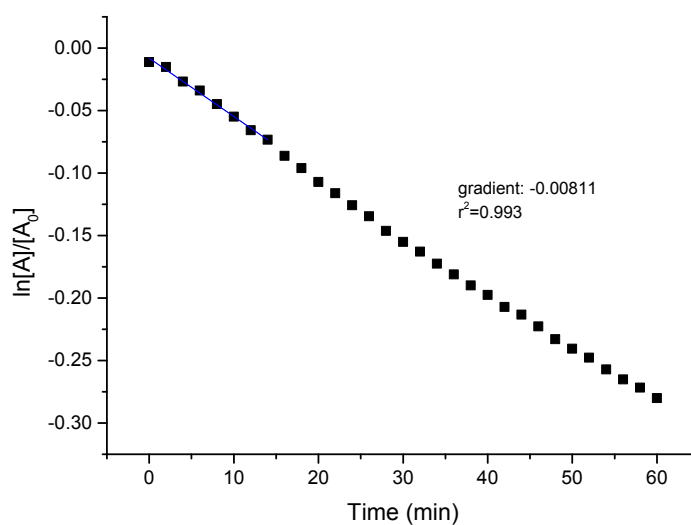


Figure 3.4.8 – Plot of $\ln[A]/[A_0]$ against time for sulfonation of 2-(4-methylphenoxy)ethan-1-ol in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100 °C

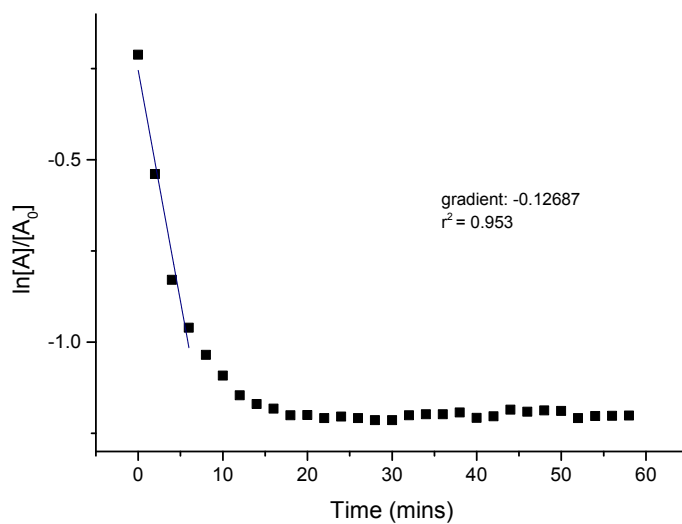


Figure 3.4.9 – Plot of $\ln[A]/[A_0]$ against time for sulfonation of 2-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]ethan-1-ol in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100 °C

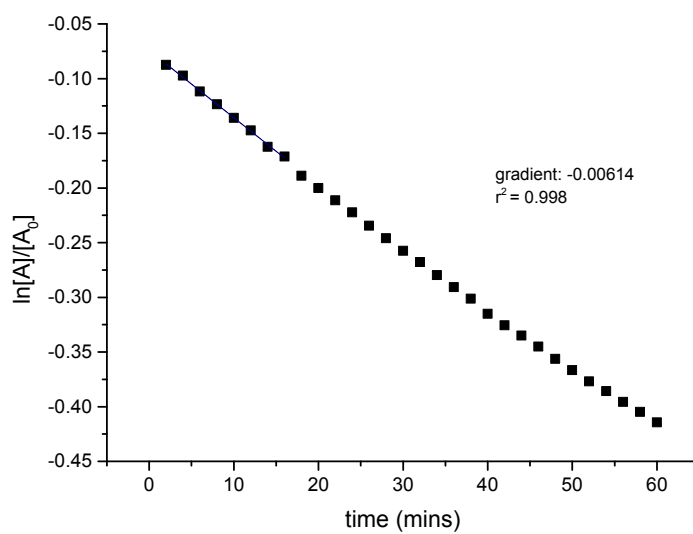


Figure 3.4.10 – Plot of $\ln[A]/[A_0]$ against time for sulfonation of 2-(4-methoxyphenoxy)ethan-1-ol in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100 °C

Table 3.4.2 – Relative rates of sulfonation of 2-phenoxyethanol analogues in PIL

Substituent	$k_{\text{obs}}/\text{s}^{-1} \times 10^{-4}$	r^2	% consumption after one hour	Sulfonation position
-H	3.12	> 0.99	56	para
-Me	7.97	> 0.99	25	ortho
-OMe	6.14	> 0.99	49	multiple
-CH ₂ CH ₂ CH ₂ -	21.15	0.95	70	ortho
-Cl	n/a	n/a	No observable reaction	n/a
-NO ₂	n/a	n/a	No observable reaction	n/a

^a Conditions: substrate dissolved in [HC₄im][HSO₄].(H₂SO₄)₁ and left to react at 100 °C. Rate constants obtained by monitoring product increase *via* ¹H NMR.

Figures 3.4.8 and 3.4.10 both show linearity in the rate of sulfonation at low consumption. The high rate of sulfonation displayed by 2-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]ethan-1-ol only allowed the first four points to be used in order to obtain the k_{obs} , where a plateau was reached at 70% conversion, presumably due to the presence of water, reducing the electrophilicity of SO₃. This is due to the high electron donating capability of the substituent bearing a σ value of -0.26. These results confirm the need for high electron density within the aromatic system to render the substrate susceptible to electrophilic aromatic substitution. This is further supported by the results obtained with 2-(4-methoxyphenoxy)ethanol where instead of displaying a high rate of sulfonation, sulfonation is observed to occur more than once, indicating that the electron density of the aromatic system is sufficiently high to overcome the deactivating properties of the initial sulfonation.

All the above kinetic results highlight that regardless of the electron density of the aromatic system adjacent to the ether, ether cleavage in [HC₄im][HSO₄] does not occur. However, under anhydrous conditions where the IL is thoroughly dried, the anion becomes a richer source of SO₃, promoting ring sulfonation *via* an electrophilic substitution mechanism. This conclusion is further supported by the speciation observed in the obtained mass spectra of the IL with different concentrations of sulfuric acid, conducted by previous members of the Welton group. In [HC₄im][HSO₄] with no additional acid, the negative mode of LSIMS shows the simple [HSO₄]⁻ entity with a mass of 97. When 1 molar equivalent of sulfuric acid is added to the IL, a signal of mass 196 in the negative mode is observed, suggesting the presence of the speciated anion with structure [H₃S₂O₈]⁻ and a signal of mass of 294 m/z, indicating the presence of the dimer.

Table 3.4.3 – Clustering of anion with change in concentration of sulfuric acid

x in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_x$	$[\text{HSO}_4]$ ion clusters in		
	$[\text{HSO}_4]^-$	$[\text{H}_3\text{S}_2\text{O}_8]^-$	$[\text{H}_5\text{S}_3\text{O}_{12}]^-$
0	100		
0.33	100		
0.50	100	50	
0.8	80	100	
1.0	35	100	55
1.6	45	100	20
^a $[\text{HSO}_4]^-$ ion clusters in negative mass spectra of $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_x$			

Selective ROESY and NOESY experiments were conducted on 2-(4-methylphenoxy)ethan-1-ol and 2-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]ethan-1-ol to determine the site of sulfonation which were concluded in both cases to occur at the ortho position of the ring relative to the ether (spectra available in appendix). The complex ^1H NMR of the 2-(4-methoxyphenoxy)ethan-1-ol sulfonation showed at least two sulfonated products at various positions on the ring. Due to the inability to distinguish between signals in the aromatic region, no attempt at determining regioselectivity of sulfonation was carried out but it can be concluded that multiple sulfonations occurred. Taking all the above data into account, the overall mechanism can be assumed to follow a standard electrophilic aromatic substitution, described as follows:

1. Formation of a dimer cluster with the anion of IL by the condensation of two moles of sulfuric acid, liberating sulfur trioxide.
2. Electrophilic aromatic substitution of 2-phenoxyethanol *via* sulfur trioxide forming an arenium ion, where a C-S bond is formed forming a highly unstable carbocation as ring aromaticity is broken.
3. Loss of a labile aromatic proton at the site of sulfonation by the hydrogensulfate anion, re-establishing aromaticity.
4. Protonation of the sulfonate with sulfuric acid giving a sulfonic acid.

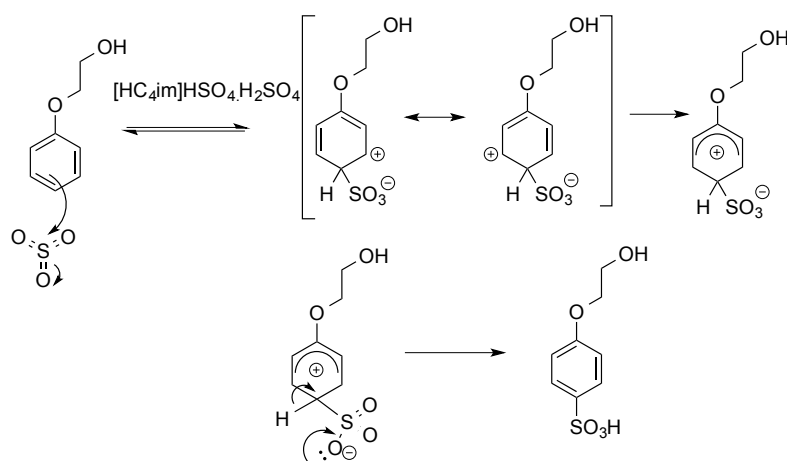


Figure 3.4.11 – Mechanism for ring sulfonation of 2-phenoxyethanol

The rate expression for the above reaction has been universally accepted to be as follows:^[134]

$$\frac{-d[\text{Ar}]}{dt} = \frac{k[\text{Ar}]A_{\text{H}_2\text{SO}_4}^2}{A_{\text{water}}} \quad (3.4.1)$$

Where $[\text{Ar}]$ is the concentration of the aromatic substrate, $A_{\text{H}_2\text{SO}_4}$ is the activity of sulfuric acid, proportional to the concentration of sulfuric acid and A_{water} is the activity of water which is proportional to the concentration of water present in the system. As one substrate undergoes sulfonation at a time, the reaction is first order with respect to the substrate and second order with respect to the sulfuric acid as two sulfuric acid molecules are required to liberate the electrophile. The negative effect of water is included as an inverse term as water slows the rate of sulfonation by hydrating SO_3 , removing its ability to act as an electrophile. The lack of reactivity without the addition of sulfuric acid to the IL confirms that successful sulfonation only occurs when an excess of acid is present whereby speciation of the hydrogensulfate to $[\text{H}_3\text{S}_2\text{O}_8]^-$ can occur. Furthermore, the need for the IL to be dry is in further agreement with sulfonation occurring *via* the above mechanism.

The above study concludes that whilst $[\text{HC}_4\text{im}][\text{HSO}_4]$ is useful in biomass pretreatment for the successful hydrolysis of the β -O-4 linkage in lignin, simple aromatic ethers do not cleave when submitted to similar conditions in this IL, leading only to ring sulfonation. Overall, the resilience of the ether substrates to cleavage can be the result of the poor nucleophilicity of the anion which has actually proven to be a stronger electrophile in the presence of sulfuric acid and under anhydrous conditions. This part of the study concludes that other functional groups present in lignin must be responsible for aiding the cleavage of the β -O-4 linkage.

3.4.2 Kinetic measurements using $[C_2C_1im]Br$

As outlined in chapter 2, acid catalysed ether cleavage requires the presence of a strong acid and strong nucleophile to promote successful cleavage. Applying this to ILs, 1-ethyl-3-methylimidazolium bromide ($[C_2C_1im]Br$) was selected as a suitable IL, prepared by the alkylation of 1-methylimidazole with ethyl bromide. Together with the addition of hydrobromic acid (diluted 47 wt/wt% in water), an IL-acid system was prepared bearing a strong acid and an increased concentration of bromide, renowned for being a strong nucleophile even in aqueous conditions. This system will be notated as $[C_2C_1im]Br.(HBr)_{(aq)X}$ where x refers to the added mole equivalent of hydrobromic acid.

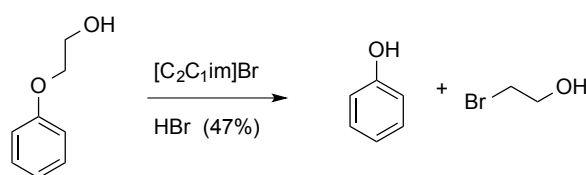


Figure 3.4.12 – Ether cleavage using $[C_2C_1im]Br$

An initial test with 2-phenoxyethanol was carried out to see whether ether cleavage could occur. Phenol and 2-bromoethanol were expected to be the major products upon successful cleavage of the ether. 70 mg of 2-phenoxyethanol was added to 10 molar equivalents of $[C_2C_1im]Br.(HBr)_{(aq)0.5}$.

The spectrum presented in Figure 3.4.13 shows successful cleavage of the unsubstituted model compound. The aromatic region of the spectrum shows the presence of the newly formed phenol protons at 7.11 ppm and 6.75 ppm with 22% consumption based on the starting material. The aliphatic region of the spectrum shows the presence of two triplets of equal integration at 3.63 ppm and 3.44 ppm which was postulated to be the 2-bromoethanol product. The integration ratio between the phenol and the 2-bromoethanol product shows that roughly 60% of the cleaved 2-bromoethanol was present post cleavage, with the difference potentially dehydrating to form vinylbromide or forming ethylene oxide which is probable under acidic conditions.^[135]

In-situ proton NMR was used once again to track reaction kinetics with the reaction monitored over a six hour period with readings taken at 5 minute intervals. Figure 3.4.14 shows conversion of 27% of the starting material after the 6 hour reaction period. $\ln[A]/[A_0]$ was then plotted against time, and the initial rate of reaction was measured. Due to the slow reaction rates, all measurements were used to obtain the k_{obs} as shown in Figure 3.4.15.

Despite evidence of reaction progression to almost 30 % yield of phenol, the graph showing %

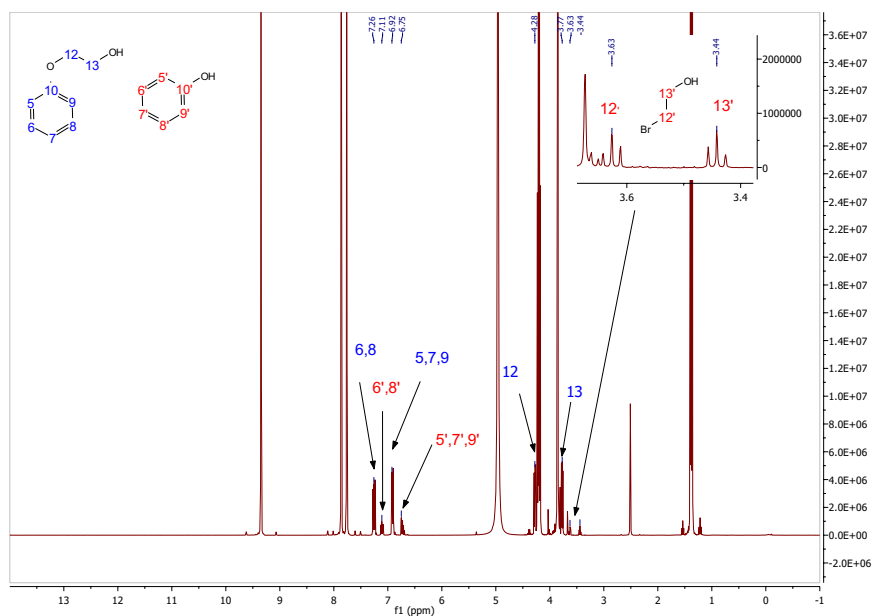


Figure 3.4.13 – ^1H NMR reaction profile for cleavage of 2-phenoxyethanol in $[\text{C}_2\text{C}_1\text{im}]\text{Br} \cdot (\text{HBr})_{(\text{aq})0.5}$

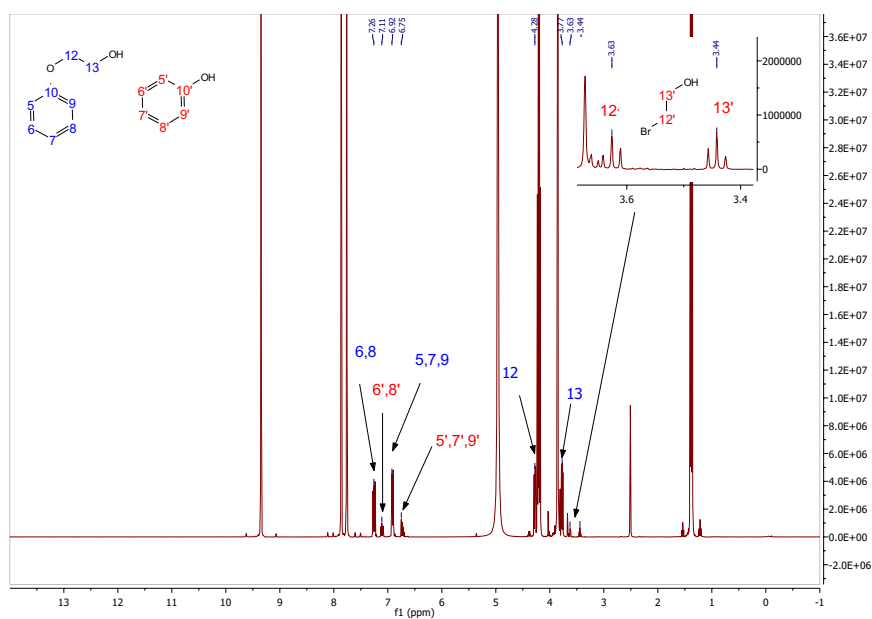


Figure 3.4.14 – Conversion to cleavage of 2-phenoxyethanol in $[\text{C}_2\text{C}_1\text{im}]\text{Br} \cdot (\text{HBr})_{(\text{aq})0.5}$ at 110°C using *in-situ* ^1H NMR

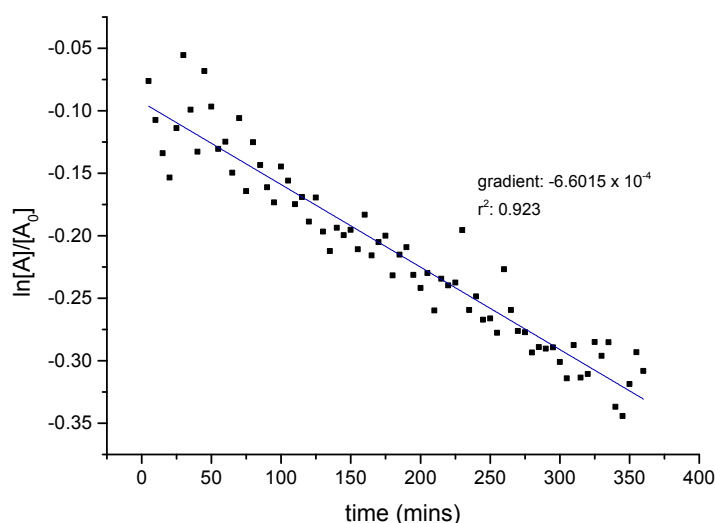


Figure 3.4.15 – Plot of $\ln[A]/[A_0]$ against time for cleavage of 2-phenoxyethanol in $[C_2C_{1im}]Br.(HBr)_{(aq)0.5}$ at $110\text{ }^{\circ}C$, monitored via in-situ 1H NMR

conversion of 2-phenoxyethanol to cleaved products and hence the $\ln[A]/[A_0]$ plot gave a lot of scatter between readings. This was assumed to be due to the constant evaporation and recondensation of water in the NMR tube which consequently caused fluctuations in the NMR signal. In order to avoid this, the reaction was carried out in a closed system over the period of 8 hours, heated to $110\text{ }^{\circ}C$ with small aliquots removed at one hour time intervals, diluted in DMSO- d_6 and analysed by 1H NMR. Performing the reaction in duplicate gave comparable k_{obs} values with linear kinetic plots. One example of such a $\ln[A]/[A_0]$ plot is given in Figure 3.4.16. Although fewer points were taken to obtain the k_{obs} , significantly less scatter and improved linearity was obtained relative to the *in-situ* NMR with an r^2 value of 0.993. As cleavage was deemed successful with quantifiable kinetics, a full Hammett study was conducted using the model compounds described in Table 3.3.1. Due to the presence of both phenol and bromoethanol, a simple mechanism was postulated involving an initial protonation of the oxygen, polarising the C-O bond, followed by nucleophilic attack of the alpha carbon *via* an S_N2 mechanism as shown in Figure 3.4.17.

Using the same method of measuring k_{obs} , the investigation was extended to all the model compounds in Table 3.3.1 for a Hammett study. All the model compounds were shown to cleave in $[C_2C_{1im}]Br.(HBr)_{(aq)0.5}$, however 2-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]ethan-1-ol formed a biphasic mixture when added to the IL and 2-(4-methoxyphenoxy)ethan-1-ol underwent cleavage both at the ether as well as the methoxy substituent. Due to the inability to record kinetic

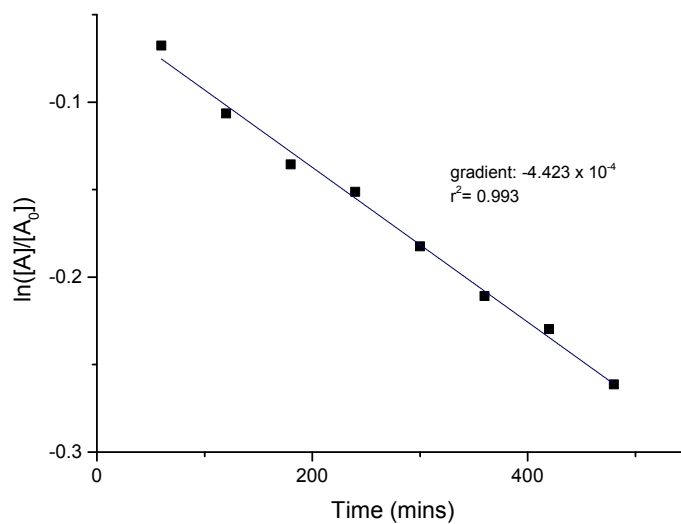


Figure 3.4.16 – Plot of $\ln[A]/[A_0]$ against time of cleavage of 2-phenoxyethanol in $[C_2C_{1im}]Br.(HBr)_{(aq)0.5}$ at $110^\circ C$ monitored by 1H NMR in aliquots

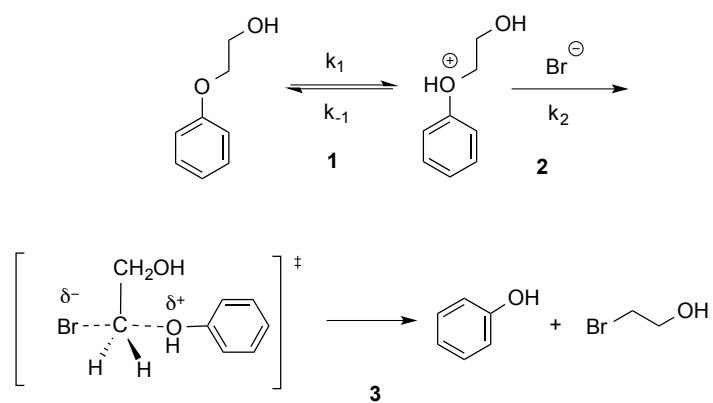


Figure 3.4.17 – Mechanism and transition state for the cleavage of 2-phenoxyethanol

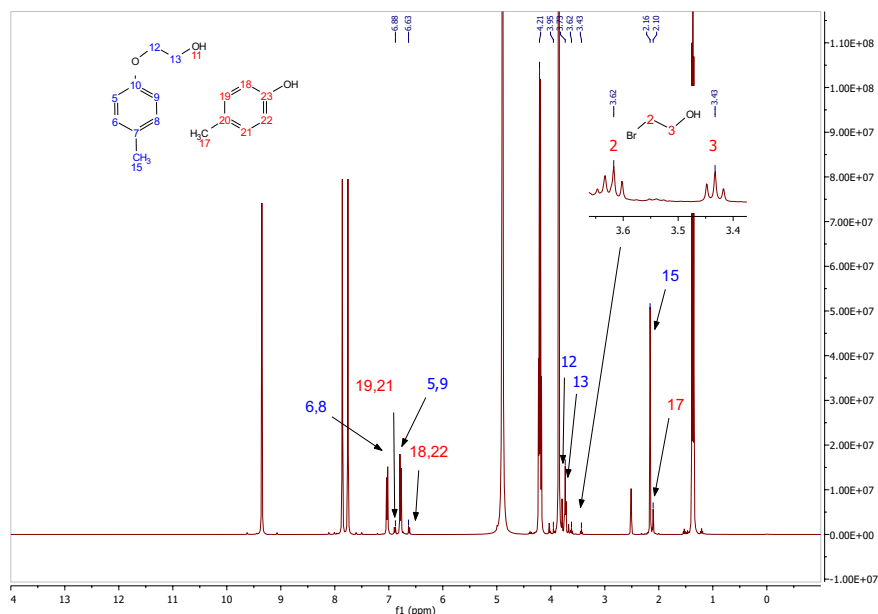


Figure 3.4.18 – ^1H NMR reaction profile for cleavage of 2-(4-methylphenoxy)ethan-1-ol in $[\text{C}_2\text{C}_1\text{im}]\text{Br} \cdot (\text{HBr})_{(\text{aq})0.5}$

measurements, these two model compounds were dismissed from the study. The ^1H NMR spectra for 2-(4-nitrophenoxy)ethan-1-ol, 2-(4-methylphenoxy)ethan-1-ol and 2-(4-chlorophenoxy)ethan-1-ol all showed formation of the cleaved phenolic product and 2-bromoethanol when left for 8 hours at 110°C and are shown in Figures 3.4.18, 3.4.19 and 3.4.20.

Using the integrations of the ortho protons of the starting material and the product, kinetic measurements were taken over the 8 hour reaction period for all three substituents and their pseudo-first order kinetic plots are available in the appendix .

All three kinetic plots gave good linear fits with r^2 values above 0.95 and were conducted in duplicate. Results show that 2-(4-methylphenoxy)ethan-1-ol proceeded the fastest, followed by the unsubstituted substrate 2-phenoxyethanol with 2-(4-chlorophenoxy)ethan-1-ol and 2-(4-nitrophenoxy)ethan-1-ol showing the slowest reaction rates. The results, together with the σ values of each substituent and the standard deviation are listed in Table 3.4.4.

It is clear that through increasing the electron density of the aromatic system, the rate of ether cleavage increases. A difference of almost one order of magnitude was observed between the 2-(4-nitrophenoxy)ethan-1-ol and 2-(methylphenoxy)ethan-1-ol. Applying the measured kinetic data into the Hammett equation expressed in 3.2.7, a set of Hammett parameters can be calculated.

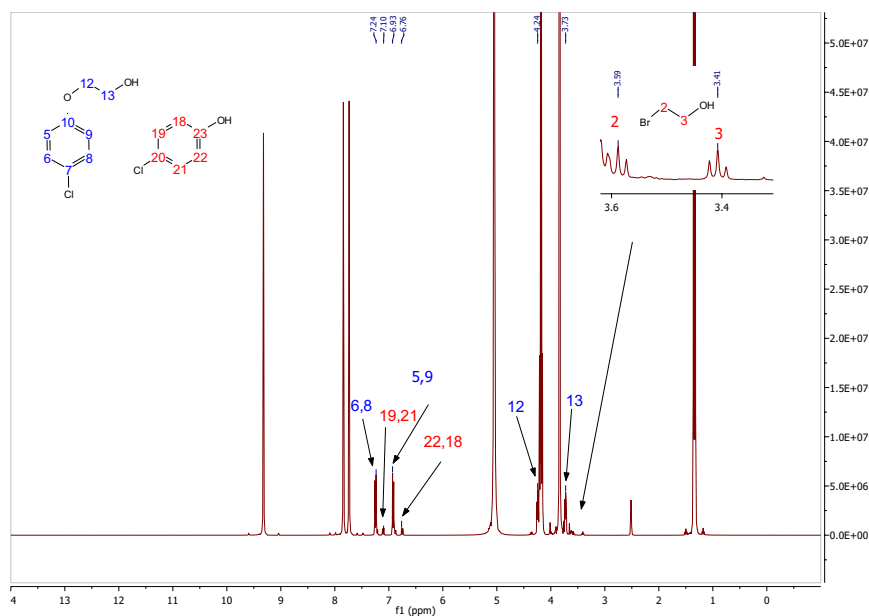


Figure 3.4.19 – ^1H NMR reaction profile for cleavage of 2-(4-chlorophenoxy)ethan-1-ol in $[\text{C}_2\text{C}_1\text{im}]\text{Br} \cdot (\text{HBr})_{(\text{aq})0.5}$

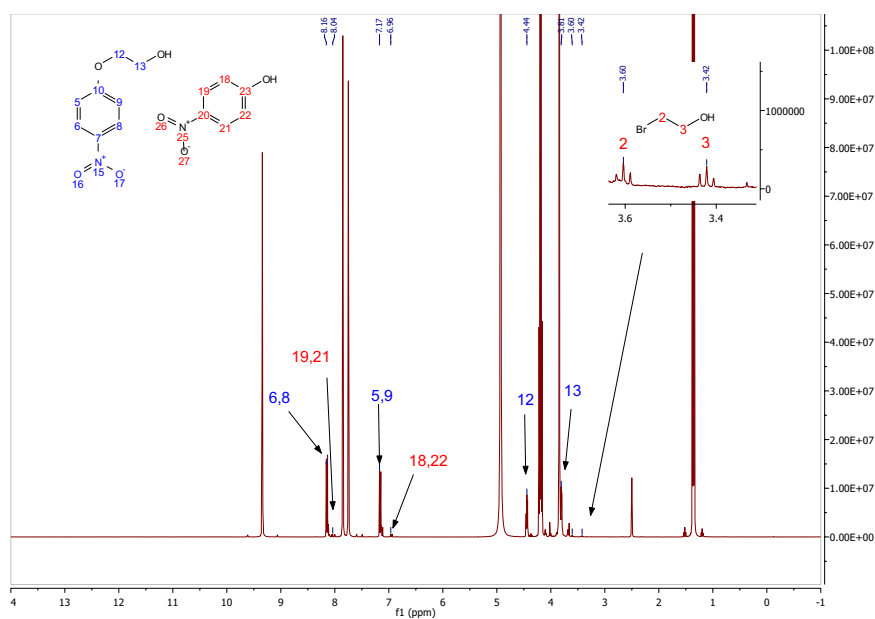


Figure 3.4.20 – ^1H NMR reaction profile for cleavage of 2-(4-nitrophenoxy)ethan-1-ol in $[\text{C}_2\text{C}_1\text{im}]\text{Br} \cdot (\text{HBr})_{(\text{aq})0.5}$

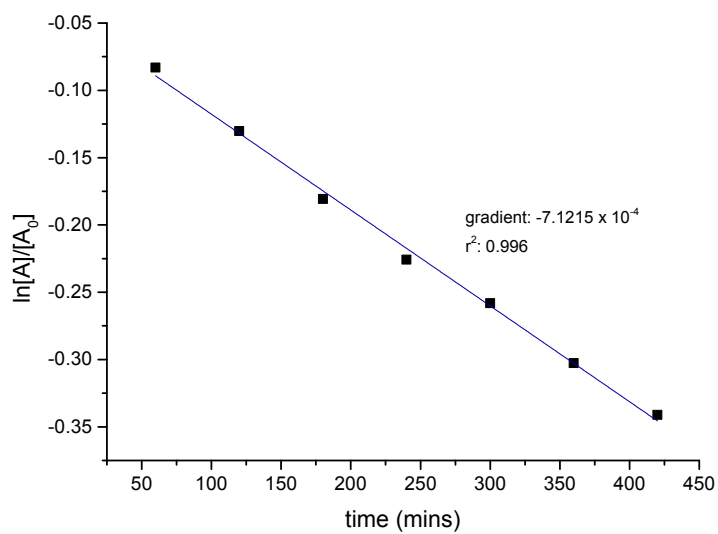


Figure 3.4.21 – Plot of $\ln[A]/[A_0]$ against time for the cleavage of 2-(4-methylphenoxy)ethan-1-ol in $[C_2C_1im]Br.(HBr)_{(aq)0.5}$ at 110 °C

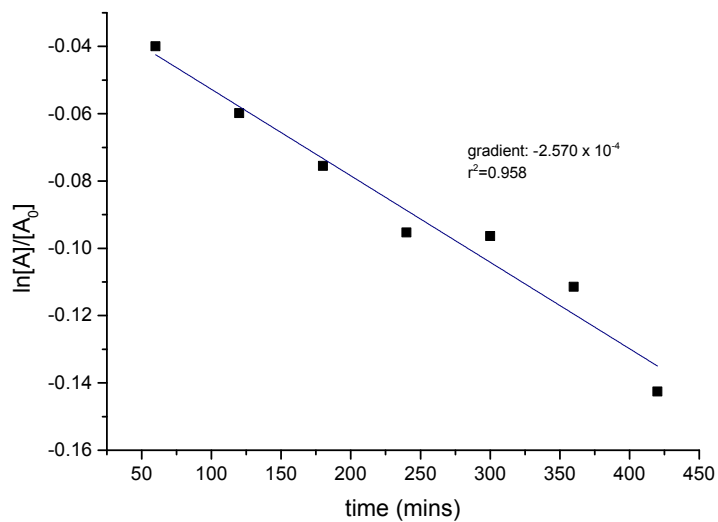


Figure 3.4.22 – Plot of $\ln[A]/[A_0]$ against time for the cleavage of 2-(4-chlorophenoxy)ethan-1-ol in $[C_2C_1im]Br.(HBr)_{(aq)0.5}$ at 110 °C

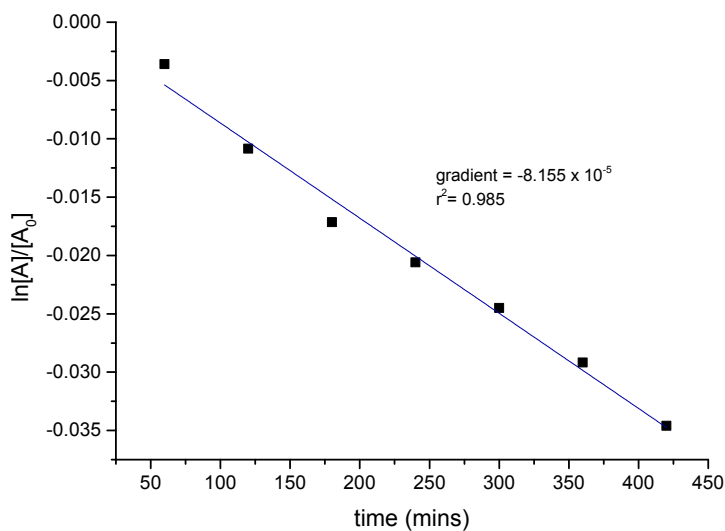


Figure 3.4.23 – Plot of $\ln[A]/[A_0]$ against time for the cleavage of 2-(4-nitrophenoxy)ethan-1-ol in $[C_2C_{1im}]Br.(HBr)_{(aq)0.5}$ at 110 °C

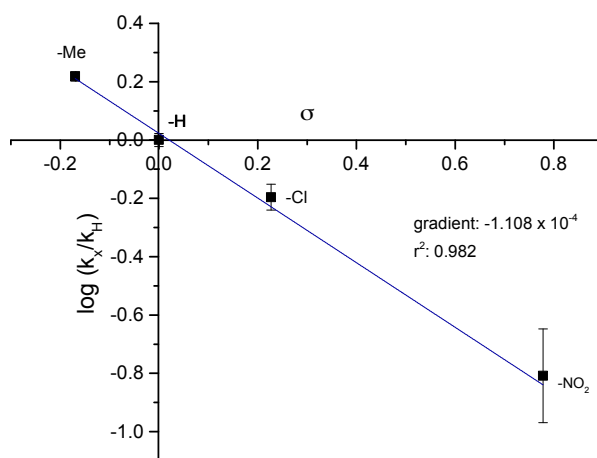
Table 3.4.4 – Summary of kinetic data for cleavage of 2-phenoxyethanol substrates

Substituent (para)	σ value	$k_{obs} \times 10^{-6} s^{-1}$			$\times 10^{-7}$
		$k_{obs}(1)$	$k_{obs}(2)$	mean k_{obs}	
-OMe	-0.27	n/a	n/a	n/a	n/a
-CH ₂ CH ₂ CH ₂ -	-0.26	n/a	n/a	n/a	n/a
-Me	-0.17	11.87	10.54	11.21	9.4
-H	0	7.01	7.37	7.19	2.5
-Cl	+0.23	4.28	4.87	4.58	4.1
-NO ₂	+0.78	1.36	0.874	1.12	3.4

^a Conditions: substrate dissolved in $[C_2C_{1im}]Br.(HBr)_{(aq)0.5}$ and left to react at 110 °C. Rate constants obtained by monitoring product increase *via* 1H NMR.

Table 3.4.5 – $\log(k_x/k_H)$ of all substituents used in ether cleavage in $[C_2C_{1im}]Br.(HBr)_{(aq)0.5}$ at 110 °C

Substituent	σ value	mean k_{obs} $s^{-1} \times 10^{-6}$	$\log(k_x/k_H)$
-Me	-0.17	11.21	0.22
-H	0	6.74	0
-Cl	+0.23	4.58	-0.17
-NO ₂	+0.78	1.12	-0.78

**Figure 3.4.24** – Hammett plot for the cleavage of 2-phenoxyethanol analogues in $[C_2C_{1im}]Br.(HBr)_{(aq)0.5}$ at 110 °C

When the $\log(k_x/k_H)$ values were plotted against the σ values, a clear correlation is seen with the ρ value given by the gradient of -1.108 as presented in Figure 3.4.24. The negative sign of the gradient indicates the development of positive charge on approach to the transition state, which would be expected from the postulated mechanism.

The Hammett plot implies that all the substrates that participated in the reaction proceed *via* the same mechanism regardless of electron density, involving initial protonation (as indicated by the negative value of the gradient) and cleavage by the nucleophile. The low ρ value can be explained by a number of interpretations as listed in Table 3.2.1. As the ρ value incorporates all

steps up to and including the rate determining step, both the initial protonation and nucleophilic attack of the bromide must be considered in order to reach a sensible hypothesis regarding the reaction mechanism. As previously discussed, Hammett plots with small ρ values can mean one of two things:

1. The site of reaction is too far from the substituents, therefore being insensitive to electronic effects
2. There is no net change in electron density as the two opposing charge developments cancel each other out.

One postulated mechanism for the acid catalysed hydrolysis of 2-phenoxyethanol that supports the first hypothesis has been suggested in a computational study whereby 2-phenoxyethanol is submitted to hydrolysis in H_3O^+ .^[135] In this mechanism, protonation would occur at the terminal alcohol followed by dehydration *via* an E2 mechanism, yielding a vinyl phenyl ether which then undergoes acid catalysed hydrolysis. Whilst the above mechanism is a plausible explanation for the low ρ value, the presence of bromoethanol in the proton NMR spectra at almost stoichiometric quantities proves that dehydration of the terminal alcohol does not occur and the cleaved products remain mostly sp^3 hybridised.

The second more plausible explanation that supports the second hypothesis encompasses the reaction occurring *via* the mechanism presented in 3.4.17. This involves an initial protonation followed by the nucleophilic attack of the ethereal carbon through an $\text{S}_{\text{N}}2$ mechanism which is the rate determining step. This would display a strongly negative ρ value for the protonation as an increase in electron density renders the oxygen more basic, therefore shifting the equilibrium towards the oxonium ion, followed by a positive ρ value for the nucleophilic substitution. If cleavage were to occur directly after the formation of the protonated species, releasing the ethanol carbocation in the rate determining step, a far more pronounced ρ value would be seen. However the low ρ value originates from the following sequence:

1. The initial decrease in electron density at the reaction centre due to the protonation of the oxygen, promoted by highly electron donating substituents that stabilise the oxonium carbocation. This leads to charge development as well as polarisation of the C-O bond (which would be manifested as a negative ρ value).
2. This is then followed by the flow of electrons to the reaction centre by the bromide nucleophile upon attack of the electron deficient ethereal carbon, cleaving the ether, consequently re-establishing electron density in the phenol moiety and the bromoethanol product. The electron withdrawing groups therefore render the oxonium more electrophilic, reducing charge development (which would be manifested as a positive ρ value).

As the rate determining step involving the nucleophilic attack occurring at the ethereal carbon is located further from the ring substituents to the oxygen, the ρ value for this step would not be

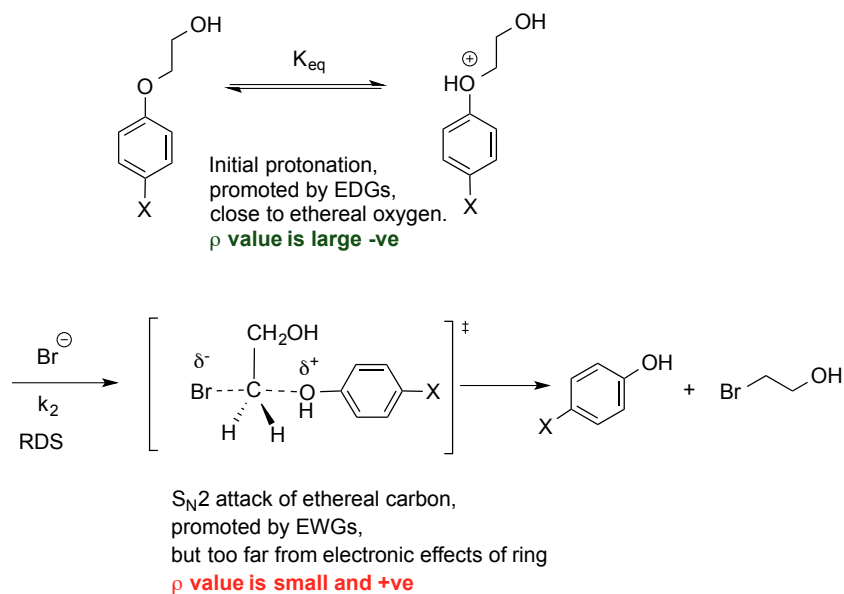


Figure 3.4.25 – Mechanism for ether cleavage using Hammett's ρ values

expected to be as high as the initial protonation. This therefore leads to the two independent ρ values cancelling each other out. However as the initial protonation is more sensitive to electronic effects, an overall slightly negative ρ value is seen. This can be visualised in Figure 3.4.25 and is further supported by the slow overall rates.

3.5 Conclusions

In this chapter, the difference in reactivity of simple ethers in two different IL-acid systems was demonstrated. Although $[\text{HC}_4\text{im}][\text{HSO}_4]$ is a useful IL for the successful hydrolysis of the β -O-4 linkage in lignin, simple aromatic ethers were shown not to cleave when submitted to similar conditions in this IL. When additional sulfuric acid is added, sulfonation was seen to occur preferentially at the para position of the substrate 2-phenoxyethanol. The incorporation of electron withdrawing groups para to the ether deactivates the ring to any electrophilic aromatic substitution whilst the addition of electron donating groups promote sulfonation at the ortho position. Generally speaking, the magnitude of the σ value gives an increase in rate when the σ value < 0 . With the para-methoxy substituent, the strong electron donating capability of the substituent promotes further sulfonation of the ring with no observed regioselectivity. Overall, the high resilience of the ether substrates to cleavage in this IL can be assumed to be due to the poor nucleophilicity of the anion and increased electrophilicity when dried, indicating that the complex functionality present in lignin is responsible for weakening the highly abundant β -O-4

linkage, rendering the ether more susceptible to cleavage as will be discussed in Chapter 3. These findings are coherent with the inability of sulfuric acid to cleave aryl-alkyl ethers, showing no overall difference in activity.

When the same study was conducted in $[\text{C}_2\text{C}_1\text{im}]\text{Br}$ with 0.5 molar equivalents of hydrobromic acid, all the model compounds cleaved, yielding 2-bromoethanol and the corresponding phenol as the only identifiable products. A full Hammett study was carried out on four substrates where measurable kinetics could be obtained using the IL - acid system: $[\text{C}_2\text{C}_1\text{im}]\text{Br}_{0.5 \text{ mol eq acid}}$ at 110 °C. An increase in σ value gave a decrease in the rate of cleavage and a ρ value of -1.1 was obtained. This indicated a consistent A_2 mechanism across the series, involving the initial protonation of the ethereal oxygen, followed by an $\text{S}_{\text{N}}2$ attack of the ethereal carbon by the bromide nucleophile. This proves the ability of ILs to act as both a solvent and efficient reaction medium for the cleavage of ethers when a strong nucleophile and acid are incorporated into the IL system, akin to many systems used in traditional organic chemistry, notably that of aqueous hydrobromic acid, for the cleavage of ethers.

3.6 Experimental

In order to ensure consistency across all data sets, ^1H NMR was selected as the technique of kinetic analysis due to its ability to detect impurities, side reactions and to confirm identity of products. All reactions were run on a 400 MHz spectrometer using ^1H NMR spectroscopy for proton detection with a scan range of -1 ppm to 14 ppm at 16 scans per minute. The temperature of each reaction was varied according to the study.

3.6.1 Kinetic measurements using $[\text{HC}_4\text{im}][\text{HSO}_4]$

The procedure was carried out by dissolving small quantities (*ca* 10 mg) of the starting material in 0.5 g of the $[\text{HC}_4\text{im}][\text{HSO}_4]$ with sulfuric acid system. The reaction mixture was then loaded in an NMR tube with a capillary containing DMSO- d_6 . A ^1H NMR spectrum was recorded every 2 minutes at a given temperature over 2 hours. Rate of conversion for 2-phenoxyethanol was measured by analysing the integration decrease of the ortho-proton of the starting material and the integration increase of the ortho-proton of the sulfonated product. The rates of conversion for the other substrates were measured by analysing the integration decrease of the substituent protons of the starting material and the integration increase of the substituent protons of the sulfonated product.

3.6.2 Kinetic measurements using $[\text{C}_2\text{C}_1\text{im}]\text{Br}$

The procedure was carried out by dissolving the starting material (*ca* 70 mg) to 10 molar equivalents of $[\text{C}_2\text{C}_1\text{im}]\text{Br}$ with 0.5 molar equivalents of hydrobromic acid relative to the IL (diluted

in 47 wt/wt % water) in a 2 mL glass vial. The reaction mixture was then put in a closed system over the period of 8 hours, heated to 110 °C using a VWR heating block with small aliquots (*ca* 100 mg) removed at one hour time intervals, diluted in DMSO- d_6 and analysed by ^1H NMR. The rates of conversion were measured by analysing the integration decrease of the ortho-proton of the starting material and the integration increase of the ortho-proton of the cleaved phenolic product.

3.6.3 Characterisation of ^1H NMR spectra for ring sulfonation of substrates in $[\text{HC}_4\text{im}][\text{HSO}_4]$

Ionic Liquid: $[\text{HC}_4\text{im}][\text{HSO}_4]$: ^1H : (400MHz, DMSO- d_6)/ppm δ 7.89 (1H, s, NCHN), 6.73 (2H, br, NCHCHN), 3.53 (2H, t, $J = 7.2$ Hz, NCH_2-), 1.09 (2H, sextet, $J = 7.2$ Hz, NCH_2CH_2-) and 0.104 (3H, t, $J = 7.2$ Hz, $-\text{CH}_2\text{CH}_3$).

NMR assignments of 2-phenoxyethanol substrate in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100 °C (Figure 3.4.2):

Starting material: ^1H : (400MHz, DMSO- d_6)/ppm δ 6.53 (2H, m, $\text{ArH}_{16,18}$), 6.15 (3H, m, $\text{ArH}_{15,17,19}$), 3.75 (2H, m, $\text{CH}_2\text{CH}_2\text{OH}$) and 3.56 (2H, m, $\text{CH}_2\text{CH}_2\text{OH}$).

Product: ^1H : (400MHz, DMSO- d_6)/ppm δ 7.09 (2H, d, $J = 8.4$ Hz, $\text{ArH}_{1,5}$), 6.31 (2H, d, $J = 8.8$ Hz, $\text{ArH}_{2,4}$), 3.63 (m, $\text{CH}_2\text{CH}_2\text{OH}$) and 3.41 (m, $\text{CH}_2\text{CH}_2\text{OH}$).

NMR assignments of 2-(4-methylphenoxy)ethan-1-ol substrate in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100 °C (Figure 3.4.5):

Starting material: ^1H : (400MHz, DMSO- d_6)/ppm δ 6.32 (2H, d, $J = 7.6$ Hz, $\text{ArH}_{2,4}$) 6.08 (2H, d, $J = 8.4$ Hz, $\text{ArH}_{1,5}$), 3.77 (br, $-\text{OCH}_2\text{CH}_2\text{OH}$) and 3.42 (br, $-\text{OCH}_2\text{CH}_2\text{OH}$) and 1.45 (s, $-\text{CH}_3$).

Product: ^1H : (400MHz, DMSO- d_6)/ppm δ 6.90 (1H, s, ArH_{13}) 6.64 (1H, d, $J = 10$ Hz, ArH_{16}), 6.37 (1H, d, $J = 8.4$ Hz, ArH_{15}), 3.74 (br, $-\text{OCH}_2\text{CH}_2\text{OH}$) and 3.68 (br, $-\text{OCH}_2\text{CH}_2\text{OH}$) and 1.53 (s, $-\text{CH}_3$).

NMR assignments of 2-(4-methoxyphenoxy)ethan-1-ol substrate in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100 °C (Figure 3.4.6):

Starting material: ^1H : (400MHz, DMSO- d_6)/ppm δ 6.14 (4H, s, $\text{ArH}_{1,2,4,5}$) 3.65 (2H, t, $J = 5.6$ Hz, $-\text{OCH}_2\text{CH}_2\text{OH}$), and 3.33 (2H, br, $-\text{OCH}_2\text{CH}_2\text{OH}$) and 3.02 (3H, s, $-\text{OCH}_3$).

Product: Due to the presence of a number of sulfonated products, the new peaks observed are labelled in the spectrum.

NMR assignments of 2-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]ethan-1-ol substrate in $[\text{HC}_4\text{im}][\text{HSO}_4].(\text{H}_2\text{SO}_4)_1$ at 100 °C (Figure 3.4.7):

Starting material: ^1H : (400MHz, DMSO- d^6)/ppm δ 6.36 (1H, d, $J = 7.2$ Hz, ArH_2), 6.07 (1H, s, ArH_5), 5.96 (1H, d, $J = 8$ Hz, ArH_1), 3.80 (2H, br, $-\text{OCH}_2\text{CH}_2\text{OH}$), 3.25 (2H, br, $-\text{OCH}_2\text{CH}_2\text{OH}$), 2.08 (2H, br, $-\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.02 (2H, t, $J = 7.2$ Hz, $-\text{CH}_2\text{CH}_2\text{CH}_2-$) and 1.24 (2H, m, $-\text{CH}_2\text{CH}_2\text{CH}_2-$).

Product: ^1H : (400MHz, DMSO- d^6)/ppm δ 6.92 (1H, s, ArH_{15}), 6.37 (1H, s, ArH_{18}), 3.86 (2H, br, $-\text{OCH}_2\text{CH}_2\text{OH}$), 3.71 (2H, br, $-\text{OCH}_2\text{CH}_2\text{OH}$), 2.18 (2H, t, $J = 7.2$ Hz, $-\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.08 (2H, t, $J = 7.2$ Hz, $-\text{CH}_2\text{CH}_2\text{CH}_2-$) and 1.32 (2H, quintet, $J = 8$ Hz, $-\text{CH}_2\text{CH}_2\text{CH}_2-$).

3.6.4 Characterisation ^1H NMR spectra for cleavage of substrates in $[\text{C}_2\text{C}_1\text{im}]\text{Br}$

Ionic Liquid: $[\text{C}_2\text{C}_1\text{im}]\text{Br}$: ^1H : (400MHz, DMSO- d^6)/ppm δ 9.35 (1H, s, NCHN), 7.86 (1H, s, NCHCHN), 7.76 (1H, s, NCHCHN), 4.21 (2H, t, $J = 7.2$ Hz, NCH_2-), 3.86 (s, NCH_3) and 1.38 (3H, t, $J = 7.6$ Hz, NCH_2CH_3).

NMR assignments of 2-phenoxyethanol substrate in $[\text{C}_2\text{C}_1\text{im}]\text{Br}.\text{(HBr)}_{(\text{aq})0.5}$ at 110 °C (Figure 3.4.13):

Starting material: 2-phenoxyethanol: ^1H : (400MHz, DMSO- d^6)/ppm δ 7.26 (2H, t, $J = 7.6$ Hz, ArH_{meta}), 6.92 (3H, m, $\text{ArH}_{1,3}$ and 5), 4.29 (2H, t, $J = 5.1$ Hz, $\text{CH}_2\text{CH}_2\text{OH}$) and 3.76 (2H, t, $J = 5.2$ Hz, $\text{CH}_2\text{CH}_2\text{OH}$).

Product: phenol ^1H : (400MHz, DMSO- d^6)/ppm δ 7.11 (t, $J = 7.2$ Hz, $\text{ArH}_{1,5}$), 6.75 (m, $\text{ArH}_{2,4}$).

2-bromoethanol ^1H : (400MHz, DMSO- d^6)/ppm δ 3.63 (t, $J = 6.4$ Hz, $\text{BrCH}_2\text{CH}_2\text{OH}$) and 3.44 (t, $J = 6$ Hz, $\text{BrCH}_2\text{CH}_2\text{OH}$).

NMR assignments of 2-(4-methylphenoxy)ethan-1-ol substrate in $[\text{C}_2\text{C}_1\text{im}]\text{Br}.\text{(HBr)}_{(\text{aq})0.5}$ at 110 °C (Figure 3.4.18):

Starting material: 2-(4-methylphenoxy)ethan-1-ol ^1H : (400MHz, DMSO- d^6)/ppm δ 7.04 (2H, d, $J = 8.8$ Hz, ArH_{meta}), 6.79 (2H, d, $J = 9.2$ Hz, $\text{ArH}_{\text{ortho}}$), 3.73 (2H, t, $J = 5.2$ Hz, $\text{CH}_2\text{CH}_2\text{OH}$), 2.16 (3H, s, $-\text{CH}_3$).

Product: para-cresol ^1H : (400MHz, DMSO- d^6)/ppm 6.88 (2H, d, $J = 8.4$ Hz, ArH_{meta}), 6.63 (2H, d, $J = 8.4$ Hz, $\text{ArH}_{\text{ortho}}$).

2-bromoethanol ^1H : (400MHz, DMSO- d^6)/ppm 3.62 (2H, t, $J = 6$ Hz, $\text{BrCH}_2\text{CH}_2\text{OH}$) and 3.43 (2H, t, $J = 6$ Hz, $\text{BrCH}_2\text{CH}_2\text{OH}$).

NMR assignments of 2-(4-chlorophenoxy)ethan-1-ol substrate in $[\text{C}_2\text{C}_1\text{im}]\text{Br}(\text{HBr})_{(\text{aq})0.5}$ at 110 °C (Figure 3.4.19).

Starting material: 2-(4-chlorophenoxy)ethan-1-ol ^1H : (400MHz, DMSO- d^6)/ppm 7.24 (2H, d, $J = 8.8$ Hz, ArH_{meta}), 6.93 (2H, d, $J = 9.2$ Hz, $\text{ArH}_{\text{ortho}}$), 4.24 (2H, t, $J = 5.2$ Hz, $\text{CH}_2\text{CH}_2\text{OH}$), 3.73 (2H, t, $J = 5.2$ Hz, $\text{CH}_2\text{CH}_2\text{OH}$).

Product: 4-chlorophenol ^1H : (400MHz, DMSO- d^6)/ppm 7.10 (2H, d, $J = 8.8$ Hz, ArH_{meta}), 6.76 (d, $J = 8.8$ Hz, $\text{ArH}_{\text{ortho}}$).

2-bromoethanol ^1H : (400MHz, DMSO- d^6)/ppm 3.59 (2H, t, $J = 6$ Hz, $\text{BrCH}_2\text{CH}_2\text{OH}$) and 3.41 (2H, t, $J = 6.4$ Hz, $\text{BrCH}_2\text{CH}_2\text{OH}$).

NMR assignments of 2-(4-nitrophenoxy)ethan-1-ol substrate in $[\text{C}_2\text{C}_1\text{im}]\text{Br}(\text{HBr})_{(\text{aq})0.5}$ at 110 °C (Figure 3.4.20):

Starting material: 2-(4-nitrophenoxy)ethan-1-ol ^1H : (400MHz, DMSO- d^6)/ppm 8.16 (2H, d, $J = 9.6$ Hz, ArH_{meta}), 7.17 (2H, d, $J = 9.2$ Hz, $\text{ArH}_{\text{ortho}}$), 4.44 (2H, t, $J = 5.2$ Hz, $\text{CH}_2\text{CH}_2\text{OH}$), 3.81 (2H, t, $J = 5.2$ Hz, $\text{CH}_2\text{CH}_2\text{OH}$).

Product: 4-nitrophenol ^1H : (400MHz, DMSO- d^6)/ppm 8.04 (2H, d, $J = 9.2$ Hz, ArH_{meta}), 6.95 (d, $J = 9.2$ Hz, $\text{ArH}_{\text{ortho}}$).

2-bromoethanol ^1H : (400MHz, DMSO- d^6)/ppm 3.60 (2H, t, $J = 6.4$ Hz, $\text{BrCH}_2\text{CH}_2\text{OH}$) and 3.4 (2H, t, $J = 6$ Hz, $\text{BrCH}_2\text{CH}_2\text{OH}$).

Chapter 4

Ether Cleavage in Lignin Model Compounds

4.1 Aims and Objectives

This chapter presents a novel and complete mechanistic study on the hydrolysis of lignin's prevalent β -*O*-4 linkage in acidic ILs where the roles of acid and water concentration as well as substrate functionality were studied to model lignin depolymerisation. Previous studies on ether cleavage in ILs, summarised in chapter 2, along with recent studies on lignin model compounds in aqueous or organic media^[68, 136] suggest that the cleavage of the β -*O*-4 linkage occurs *via* complex mechanistic pathways where the degree of functionality around the ether has a pronounced effect on reactivity and product distribution. The Hammett study presented in chapter 3 confirms the robust nature of simple aryl alkyl ethers to cleavage in $[\text{HSO}_4]^-$ ILs, further highlighting the importance of compound functionalisation in order to render the β -*O*-4 linkage susceptible to hydrolysis. This investigation aims to better represent the reactivity of real lignin in acidic ILs.

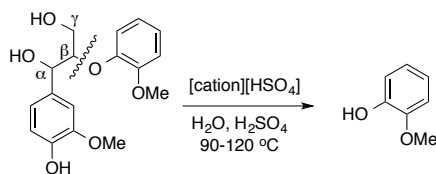


Figure 4.1.1 – Cleavage of lignin model compound guaiacylglycerol- β -guaiacyl ether in $[\text{HSO}_4]^-$ ILs

In order to study the effects of each functional group, a range of model compounds mimicking the β -*O*-4 linkage were prepared, including the archetypal guaiacylglycerol- β -guaiacyl ether (GG Figure 4.1.1), encompassing full functionality around a complete β -*O*-4 subunit in softwood lignin

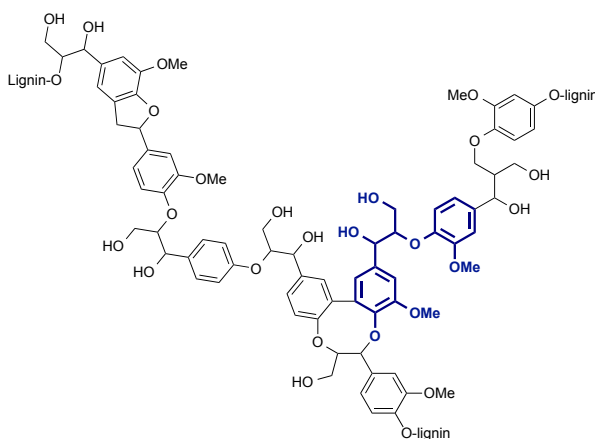


Figure 4.1.2 – GG in softwood lignin

(Figure 4.1.2). Other model compounds prepared maintain the diaryl β -O-4 backbone but vary in functionality and are presented later in Figure 4.2.8. Through monitoring reaction kinetics and the use of a number of qualitative analytical techniques, the rate determining step for the hydrolysis of the ether in $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ can be identified.

Upon determining the reaction pathway of GG hydrolysis to the cleaved products, a more in-depth investigation on the influence of the IL cation on the activation parameters of the reaction was conducted. This provides detailed information on the solvent-solute interactions between the IL and the substrate, determined by the specific properties of the IL cation. This chapter aims to answer the fundamental questions regarding the mechanism of lignin depolymerisation in acidic ILs described in this thesis' introduction, evaluating both the importance of the substrate as well as all aspects of the reaction medium. Such information will therefore provide a basis for understanding and optimising biomass deconstruction in addition to downstream lignin processing at large scale within acidic ILs.

4.2 Synthesis of Lignin model compounds

The full experimental procedure for each model compound is available in the Synthesis and Properties section of this thesis (chapter 7). All spectra regarding the identification of synthetic intermediates and products are accessible in the appendix.

4.2.1 Synthesis of Guaiacylglycerol- β -guaiacol: the Adler Route

GG has featured in many investigations mimicking the β -O-4 linkage prevalent in most lignins. Several strategies to prepare this compound exist in the literature. Initial attempts at its synthesis were first reported in 1952 by Adler et al.^[137, 138] and most recent protocols largely follow

the same synthetic strategy, as described in Figure 4.2.1. The general procedure involves four fundamental steps to form the β -O-4 dimer using simple aromatic building blocks. This involves the initial bromination of acetophenone, followed by coupling with phenol *via* a Williamson ether synthesis reaction, the incorporation of a γ -methylhydroxy group *via* a base catalysed aldol addition with formaldehyde and finally the reduction of the α -ketone to a secondary alcohol. Whilst the synthetic transformation in each step is largely retained in most synthetic protocols of related compounds, changing the degree of functionalisation around the acetophenone starting material may warrant slight modifications of both the conditions and reagents, and in cases where a hydroxy group is present, protection of the alcohol is required. Furthermore, as lignin has no preference for specific diastereomers, the lack of selectivity in this protocol allows the *erythro* and *threo* diastereoisomers to be obtained in equal amounts.

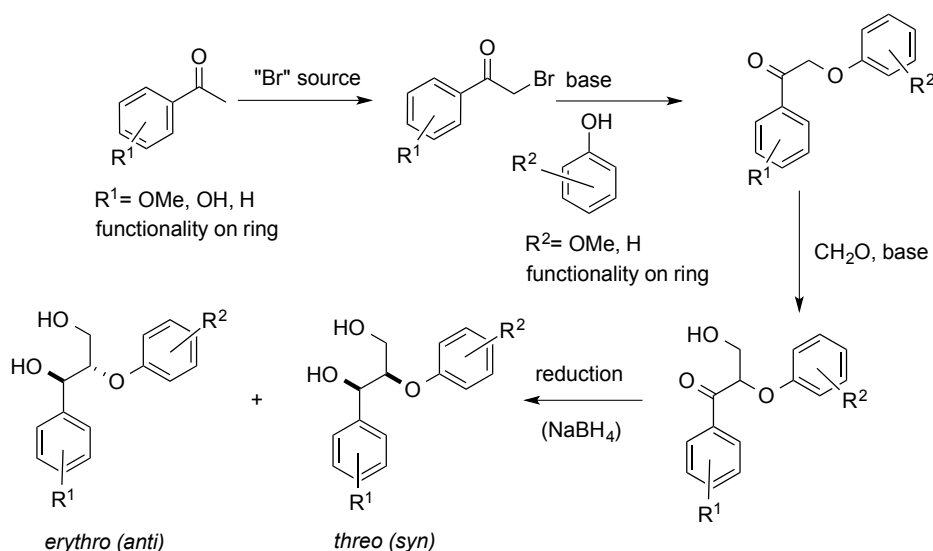


Figure 4.2.1 – Alder's original synthetic route to form a mix of GG diastereoisomers

A detailed description of the full preparation of GG along with other similar model compounds is reported by Crestini *et al*^[139] and is presented in Figure 4.2.2. The required conditions and purification techniques are reported and were found to be easily replicated by other research groups.^[140, 141, 142] The acetophenone analogue in this procedure bears a para hydroxy group and a meta methoxy group; functionality that appears on the native coniferyl alcohol monomer in lignin biosynthesis, forming guaiacyl units once incorporated in the lignin superstructure. In order to prevent the self polymerisation of bromoacetovanillone, the para hydroxy group is protected by the addition of benzoyl chloride, preventing ether formation between two bromoacetovanillone reagents. Bromination was then carried out using molecular bromine in chloroform at room temperature, followed by ether formation under basic conditions. Aldol addition of formaldehyde under basic conditions yielded both the γ -methylhydroxy group as well as deprotecting the para hydroxy group. This was then followed by reduction using sodium borohydride.

Reported yields were high and ranged from 69% for the bromination step to 99% for the initial protection of the acetovanillone.

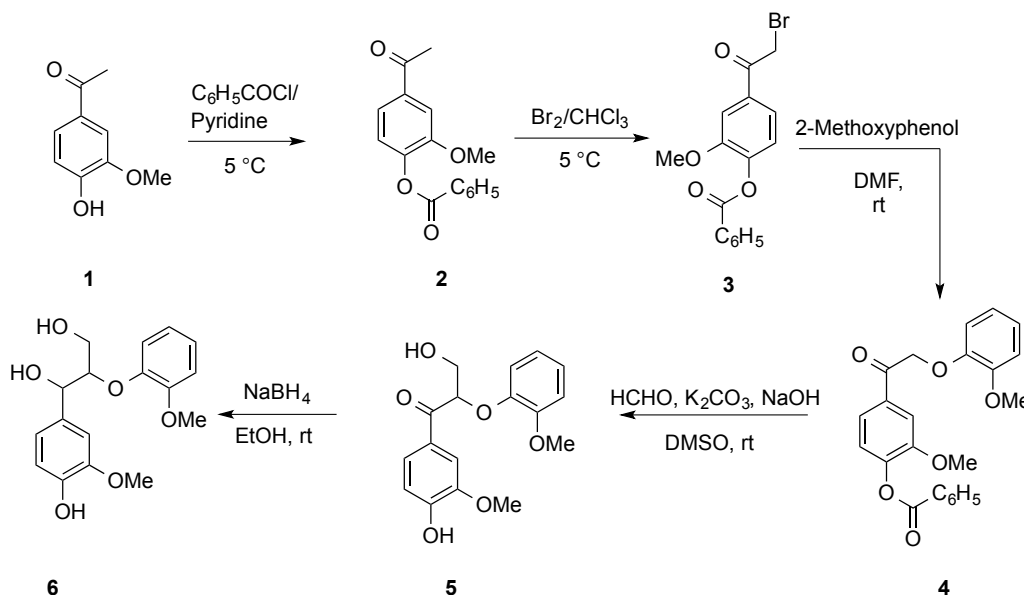


Figure 4.2.2 – Crestini's synthesis route for the preparation of GG

Using Crestini *et al.*'s protocol as the basis for GG preparation, a literature search was conducted to find optimised synthetic routes for each step to provide an easy, gram-scale synthetic strategy to prepare the model compound.

4.2.2 Attempts preparing GG using the Adler route

As aforementioned, protection of the para hydroxy group on acetovanillone (**1**) was required in order to prevent self-polymerisation. Esterification of the hydroxy group using benzoyl chloride in pyridine was carried out producing a white crystalline powder containing the product 4-benzyloxy-3-methoxyacetophenone (**2**) in 47% yield. As the repeated reaction was carried out on a 20 g scale which was sufficient for the further steps, no attempt was made to optimise this step.

Bromination of 4-benzyloxyacetovanillone (**2**) was attempted using both molecular bromine and copper bromide as the latter was carried out by Song *et al.*^[143] Both reactions were monitored *via* TLC and the crude mixtures analysed *via* NMR. Bromination was shown to be complete within 2 hours at room temperature when 1 molar equivalent of molecular bromine was used. However NMR analysis showed dibromination at the acetyl group. Repeating the reaction with 1.2 molar equivalents of copper bromide, heated to reflux over 24 hours in ethyl acetate and

chloroform, gave 45 % yield of the pure product. NMR analysis showed that by using the weaker copper brominating agent only the mono brominated product 4-benzyloxy-3-methoxy-bromoacetylbenzene (**3**) could be observed.

Once the monobrominated product was dried, coupling of 4-benzyloxy-3-methoxy-bromoacetylbenzene (**3**) with 2-methoxyphenol was carried out in acetone with potassium carbonate. TLC analysis showed complete consumption of the starting material after 16 hours and purification by column chromatography yielded the product **4** as a white solid in 80 % yield. ^1H NMR analysis showed that aside from residual solvent, the product was pure with the NMR in agreement with the literature.

The penultimate step of the reaction was to incorporate the γ -methylhydroxy group on the β carbon of **4** *via* a base catalysed-aldol condensation reaction with formaldehyde to form **5**. Potassium carbonate was used as the base and initial attempts were carried out in ethanol, allowing the reaction to stir for 2 hours at 50 °C as proposed by Zhang and Song.^[143, 144] TLC analysis showed consumption of the starting material but a number of different products were present in the reaction mixture. NMR analysis of the crude product also showed a mix of products but the characteristic proton located at the β -O-4 linkage at 5.05 ppm was not present. Repeating this reaction at different temperatures and reaction times in DMSO with a fresh batch of formaldehyde was also unsuccessful, with no indication of the formation of the desired product.

Due to the lack of success incorporating the γ -methylhydroxy group onto the product, no further attempts to synthesise GG using this route were pursued. However, the success in preparing the brominated starting material and forming the ether allowed a similar protocol to be employed for the preparation of other model compounds. Alternative synthetic methods were then pursued in order to circumvent the problematic addition of formaldehyde onto the readily-formed ether *via* having the γ -methylhydroxy already incorporated onto the starting material prior to ether coupling.

4.2.3 Synthesis of Guaiacylglycerol- β -guaiacol: The Nakatsubo route

An alternative approach to preparing lignin model dimers was proposed in 1975 by Nakatsubo and co-workers.^[145] The successful inclusion of the unsaturated aliphatic chain present in the native coniferyl alcohol monomer on the guaiacol unit was also reported, increasing the similarity of the model compound to lignin.^[146] Nakatsubo's route involves the formation of the ether with the γ -methylhydroxy group present within an ethylester precursor. After addition of the readily available lithium enolate esters to an aldehyde, β -hydroxy esters can be obtained which can subsequently be reduced to form the final 1,3-diol dilignol model compound.

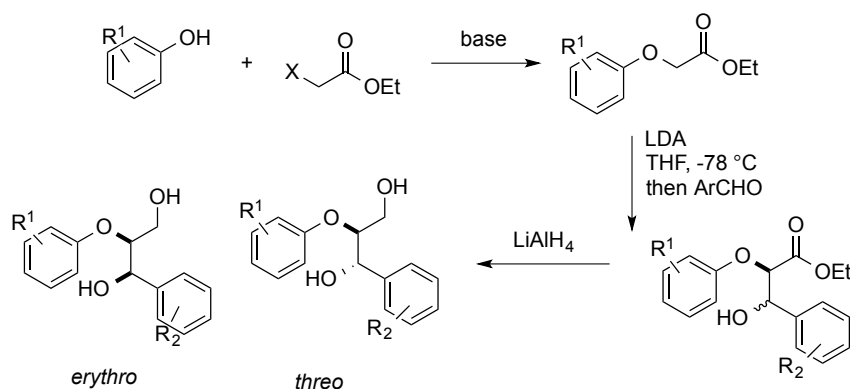


Figure 4.2.3 – Nakatsubo approach for dilignol model compound preparation

One feature of this protocol is the ability to access stereochemically well-defined lignin model compounds contrary to the final GG product in the Adler route which is obtained as a diastereomeric mixture. Using this three-step procedure as a basis for the multigram preparation of GG, Buendia and co-workers developed an optimised synthetic route for the preparation of a range of diastereomerically enriched model compounds:^[147]

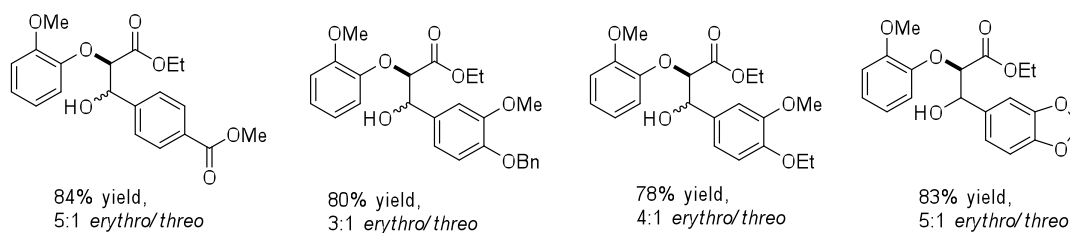
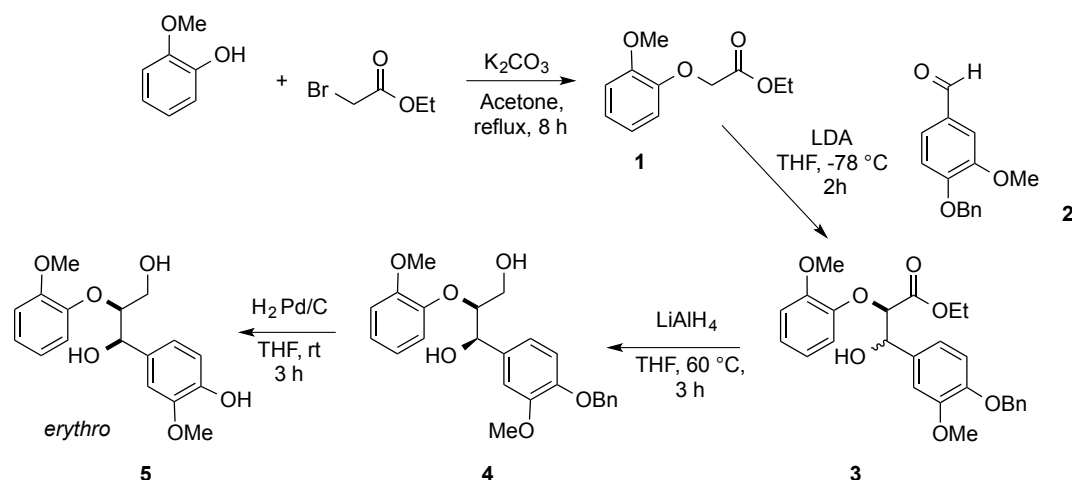


Figure 4.2.4 – Diastereoisomers of condensation products as reported by Buendia *et al.*

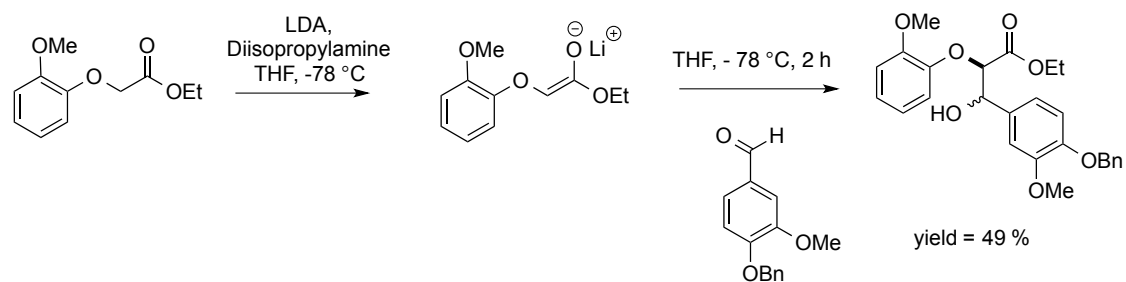
In all cases, high yields were obtained with preference towards the *erythro* diastereoisomer. Buendia *et al* also suggested that the relative ratio between both diastereoisomers can be controlled by increasing the steric bulk of the ester e.g. through replacing the ethyl group by a *tert*-butyl group. This was shown to give an increase in the relative amount of the *threo* isomer and an overall 1:1 mixture of both the *erythro* and *threo tert*-butyl β -hydroxy esters was obtained, separable *via* column chromatography. These compounds can then be reduced using lithium aluminium hydride to provide the required diastereomeric diols in high yields, with the stereochemistry of the starting material being retained.

4.2.4 Attempts to prepare GG using the Nakatsubo route

Figure 4.2.5 – Preparation of GG *via* Nakatsubo method

The strategy for the preparation of the GG model using the Nakatsubo method follows the procedure reported by Buendia *et al* and has been repeated by other research groups.^[148] The para hydroxy group present on the benzaldehyde derivative added during the condensation reaction is protected by a benzyl group to avoid any activity of the labile proton. The protecting group is then removed using hydrogen and palladium on carbon.

The formation of the ether starting material **1** was carried out in basic conditions using guaiacol and bromoethylacetate *via* a standard Williamson ether reaction. The reaction was monitored *via* TLC and was successful on initial attempt. The reaction was then repeated on an 8 g scale yielding 78 % of the ether **1** as a clear oil.

Figure 4.2.6 – Preparation of β -hydroxyester (**3**)

The β -hydroxyester **3** was prepared using LDA formed *in situ* from *n*-butyllithium and diisopropylamine, resulting in the formation of an enolate as shown in Figure 4.2.6. Addition of 4-benzyloxy-3-methoxy-benzaldehyde (**2**) gave the product ethyl-3-(3-methoxy-4-*O*-benzylphenyl)-

3-hydroxy-2-(2-methoxyphenoxy)-propanoate (**3**) which was easily isolated *via* recrystallisation from ethyl acetate. Characterisation of the product *via* mass spectrometry and proton NMR confirmed the successful addition of the aldehyde onto the ether starting material. The reaction was then repeated on an 8 g scale and yielded **3** as white crystals in 49 % yield. Direct recrystallisation of the crude product resulted in the stereoselective isolation of the *erythro* isomer with no indication of the presence of the *threo* isomer observable in the proton NMR spectrum. The presence of only one diastereomer was confirmed and the integrations of the α and β protons of the ethyl ester were consistent with those of the other chemical environments.

Attempts at reducing **3** on a 100 mg scale involved sodium borohydride and lithium aluminium hydride to produce the diol. Sodium borohydride was initially added at 5 molar equivalents relative to the substrate. After leaving the reaction for 6 hours at room temperature in a THF:water solvent system the reduction was unsuccessful. The use of lithium aluminium hydride as a reducing agent was then attempted in THF with the temperature increased to 60 °C, stirring over 3 hours. TLC showed complete consumption of the starting material **3** and work up of the reaction using the Fieser method (1:1:3, water, NaOH (aq), water) gave a 77 % crude yield of **4**. When the same reaction was worked up with a saturated solution of sodium potassium tartrate, **4** was obtained as a thick yellow oil at 48 % yield which was determined to be of higher purity according to its ^1H NMR spectrum. The reaction was then scaled up to 2 g using lithium aluminium hydride and quenched using a sodium potassium tartrate solution resulting in a yellow oil. This was then further purified using column chromatography, affording 1-(3-methoxy-4-*O*-benzylphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol (**4**) as a colourless, viscous, glue-like substance.

After analysis by ^1H NMR, the characteristic α and β protons were observed to be free from overlapping signals and showed a 1:1 integration. The α proton at 4.96 ppm gave a doublet, coupling with the adjacent β proton with a J value of 4.8 Hz. This doublet, together with the newly formed diastereotopic protons (showing two sets of doublets of doublets of equal integration) confirmed that the product **4** was diastereomerically pure. Comparison with literature showed the product retained *erythro* stereochemistry.^[149, 150]

The final step in the preparation of GG (**5**) was the removal of the benzyl protecting group *via* catalytic hydrogenation. **4** was submitted to hydrogenation using palladium on carbon. After leaving the reaction to stir for three hours at room temperature, TLC showed the reaction went to completion. After filtration and purification *via* column chromatography, the reaction afforded **5** as a yellow solid in 67% yield.

NMR analysis showed the successful removal of the benzyl protecting group and the splitting pattern of the α , β and γ protons indicated no change in stereochemistry of the product. The same ^1H NMR spectrum was then compared to that of commercially acquired GG from TCI

chemicals which confirmed the synthesis of the final *erythro*-1-(3-methoxy-4-hydroxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol product (**5**). Its mass spectrum further confirmed its successful preparation with the mother peak appearing as a mass of 343 m/z, a mass composed of the deprotonated GG model compound coupled with a Na⁺ cation.

4.2.5 Synthesis of other lignin model compounds

Model compounds with reduced functionality were prepared using a similar synthetic protocol as the Adler route described earlier in this section. The three model compounds prepared shown in Figure 4.2.7 were:

1. 2-phenoxy-1-phenylethanol (model compound **II**) bearing no methoxy groups, (R^1 , R^2 , $R^3 = H$),
2. 2-(2-methoxyphenoxy)-1-phenylethanol (model compound **III**) with an ortho methoxyl group on the phenyl group directly attached to the ether (R^1 , $R^2 = H$ and $R^3 = OMe$)
3. 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanol (model compound **IV**) with methoxyl groups on both phenyl groups (R^1 , R^2 and $R^3 = OMe$).

These model compounds were selected to single out the effects of specific functional groups that may influence the susceptibility of the β -O-4 ether linkage to cleavage and also to illustrate the difference in reactivity between the S-S and G-G linkages. Model compound **II** has the ability to dehydrate and cleave but no functional groups are added to either aryl group. Model compound **III** has an ortho methoxy group attached to the aryl ring adjacent to the ether, therefore increasing the basicity of the ether, promoting cleavage. Model compound **IV** has two methoxy groups attached to the aryl ring adjacent to the hydroxyl group. These were incorporated to study the effects of high electron density on the dehydration reaction.

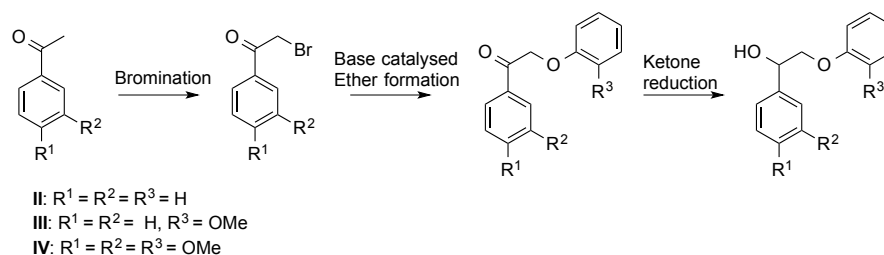


Figure 4.2.7 – Preparation of other lignin model compounds

As the brominated starting material 2-bromoacetophenone was commercially available, model compound **II** was prepared *via* the base-catalysed Williamson ether reaction using phenol, potassium carbonate in acetone. Once the reaction went to completion the product was isolated and

recrystallised from ethanol affording the ketone at 98 % yield. After reduction with sodium borohydride, isolation and purification, model compound **II** was obtained in 81 % yield. A similar synthetic route was then employed for the preparation of model compound **III**, with the sole difference of replacing phenol with guaiacol. The initial coupling reaction yielded a yellow crystalline solid at 35 % yield which then reduced to form **III** as a white solid in 93 % yield.

Model compound **IV** involved the initial bromination of a functionalised benzylketone to form 2-bromo-(3,4-dimethoxy)acetophenone, which was then coupled to guaiacol under the same conditions as stated previously to form the ketone at 45 % yield. Reduction with sodium borohydride in THF yielded the model compound **IV** as a white solid in 55 % yield. Due to the lack of enantioselectivity in the reduction of all the ketones, model compounds **II**, **III** and **IV** were obtained as a racemate. These three model compounds with varying degrees of methoxylation around the two phenyl groups and the absence of the γ -methylhydroxy group are present in Figure 4.2.8 and model compounds **II**, **III** and **IV** are displayed in Figure 4.2.9.

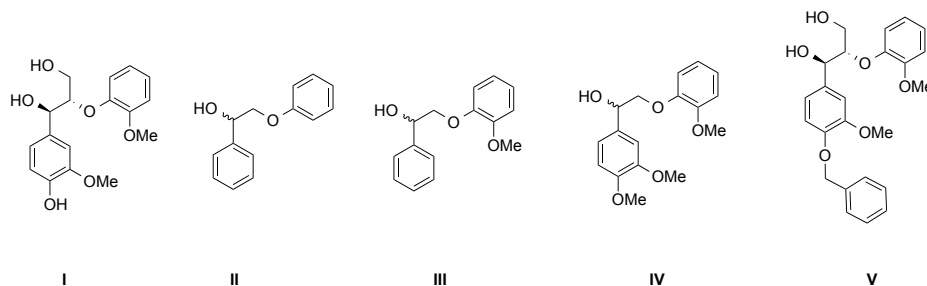


Figure 4.2.8 – Model compounds synthesised and studied

As the GG model compound (model compound **I**) embodies an end group where the terminal hydroxy group remains unattached, the model compound 1-(3-methoxy-4-*O*-benzylphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol (model compound **V**) prepared in section 5.2.4.4 was also used as a model compound, representing the full functionality of a β -*O*-4 unit where the terminal hydroxy group is etherified.



Figure 4.2.9 – Model compounds **II**, **III** and **IV** after synthesis and purification

4.3 Studies on the cleavage of the β -O-4 linkage in $[C_4C_1im][HSO_4]$

4.3.1 Kinetic studies of GG hydrolysis in $[C_4C_1im][HSO_4]$ with varying acid and water content

In this study, the archetypal GG model compound (**I**) was selected to realistically represent the β -O-4 linkage in softwood lignin and $[C_4C_1im][HSO_4]$ was selected as the IL. In order to elucidate the mechanism for the hydrolysis of the β -O-4 linkage and to identify the rate-determining step of the reaction, kinetic data were obtained, exploring the effects of both acidity and water. Through the use of HPLC as the analytical technique, the concentration of the hydrolysed guaiacol product was used as an indicator of the degree of ether cleavage due to its inertness post reaction and being a direct product of the hydrolysis reaction.

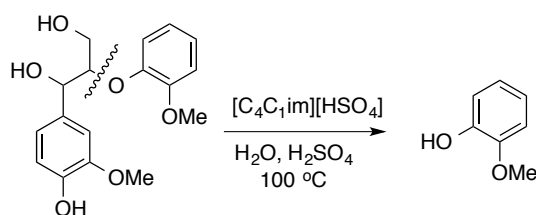


Figure 4.3.1 – Hydrolysis of GG to guaiacol using $[C_4C_1im][HSO_4]$

Calibration of guaiacol response to concentration allowed quantitative measurement of the product concentration *via* HPLC (calibration details available in the appendix). A typical HPLC trace showing the progression of the reaction is presented in Figure 4.3.2 where the IL cation and anion, the GG starting material, the guaiacol product and the 3,4,5-trimethoxybenzaldehyde internal standard are visible using a UV detector set at 280 nm along with other products.

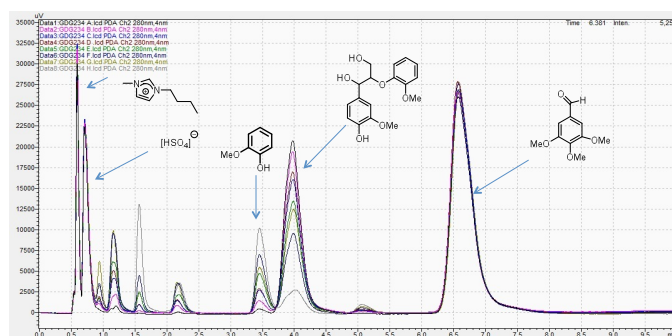


Figure 4.3.2 – HPLC chromatogram showing reaction progression using a UV detector set at 280 nm

Rate constants for each IL system were obtained using pseudo-first order reaction conditions with respect to the ether substrate, with the IL in large excess. As the IL, acid and water are in large excess with respect to the ether, the apparent rate expression for the hydrolysis of the β -O-4 linkage in GG is dependent explicitly only on the concentration of the substrate and can be expressed as follows:

$$\frac{d[\text{Guaiacol}]}{dt} = k_{\text{obs}}[\text{GG}] \quad (4.3.1)$$

And the rate law for the pseudo first order reaction being:

$$\ln\left(\frac{[\text{GG}]}{[\text{GG}_0]}\right) = kt \quad (4.3.2)$$

Where k_{obs} is the pseudo-first order rate constant, $[\text{GG}]$ the concentration of starting material (calculated from the concentration of the initial GG concentration minus the concentration of guaiacol formed) and $[\text{GG}_0]$ the initial concentration of the GG starting material. An example showing the integrated plot for GG hydrolysis to guaiacol is presented in Figure 4.3.3.

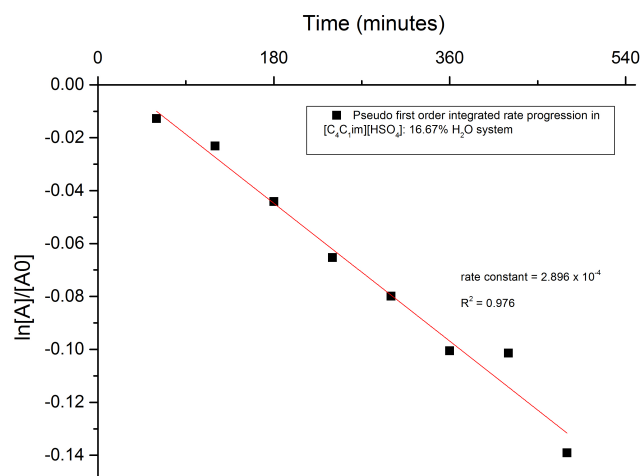


Figure 4.3.3 – Integrated rate plot for GG to guaiacol hydrolysis after 8 hours in $[C_4C_1im][HSO_4]$ with 16.67 % (wt/wt) water at 100 °C

The effects of water and acid on the rate of GG hydrolysis to guaiacol were studied at 100 °C. Mixtures of IL with varying acid and water content were prepared as outlined in the experimental procedure with excess acid quantities studied included 0, 10 and 20 mol eq % sulfuric acid relative to the IL (herein labelled as $[C_4C_1im][HSO_4] \times \text{mol}\%$ where x denotes the amount of acid added to the IL as % molar equivalent). The acid concentration at 10 mol % was calculated to be circa 30 molar equivalents with respect to the GG substrate and at 20 mol % was calculated to be circa 60 molar equivalents. The water content in each system however ranged from 0 to 50 (wt/wt) % with respect to the reaction medium where, for example, 50 (wt/wt) % signifies a 1:1 ratio of water to IL in mass. Each reaction was repeated at least twice and the measured k_{obs} values are available in the appendix

4 rate constants between 0 and 23 (wt/wt) % were obtained for the reaction of GG in $[C_4C_1im][HSO_4]$ water to IL (Figure 4.3.5). No further points could be obtained accurately due to the slow reaction progress at higher water concentrations which led to the guaiacol product being almost undetectable *via* HPLC. In ILs with added acid, 9 rate constants with water content ranging from 9.09 to 50 (wt/wt) % were measured for each system (Figures 4.3.6 and 4.3.7). Comparing the rate constants between ILs with varying acid concentration with low water content, an increase in rate is observed with an increase in acid concentration across all systems, confirming the reaction progresses *via* acid catalysis, involving at least one protonation step in its mechanism (Figure 4.3.4). Comparing the rate constants in systems where the acid concentration is kept the same with varying water content, different trends are observed depending on acid concentration. In the IL system with no added acid, the addition of water appears to have very minimal influence

on the rate of reaction. With both the 10 and 20 mol eq % acid-IL systems, no significant change in rate is observed for low concentrations of added water although a significant decrease in rate by over half an order of magnitude is observed when reaction media with over 35 (wt/wt) % of water: IL are employed. As the reaction is acid catalysed, the higher rates with lower quantities of water are presumably due to improved proton transfer of the acid, rather than dilution of the acid in the reaction system. Conversely, at larger concentrations of water, the decrease in rate may be due to the reduction of acidity due to its dilution.

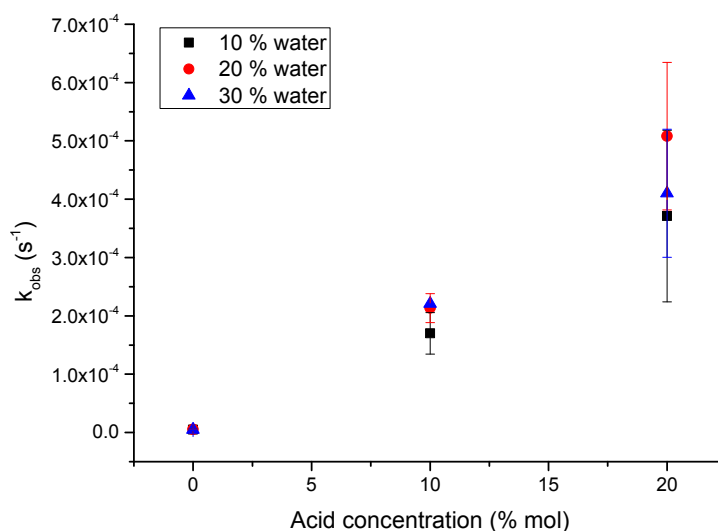


Figure 4.3.4 – Effect of acid concentration on rate of reaction of GG hydrolysis at low water content, when taken at 100 °C

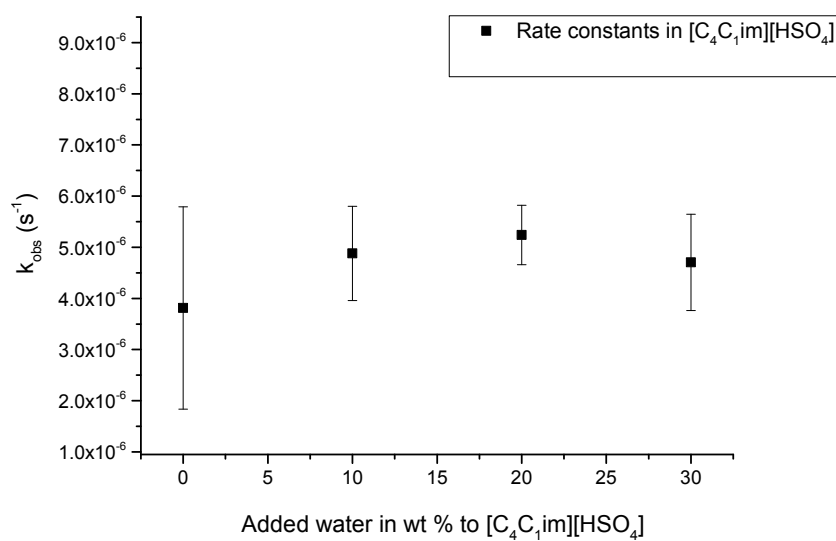


Figure 4.3.5 – Effect of water in $[C_4C_1im][HSO_4]$ on rate of reaction of GG hydrolysis with no added acid, taken at 100 °C

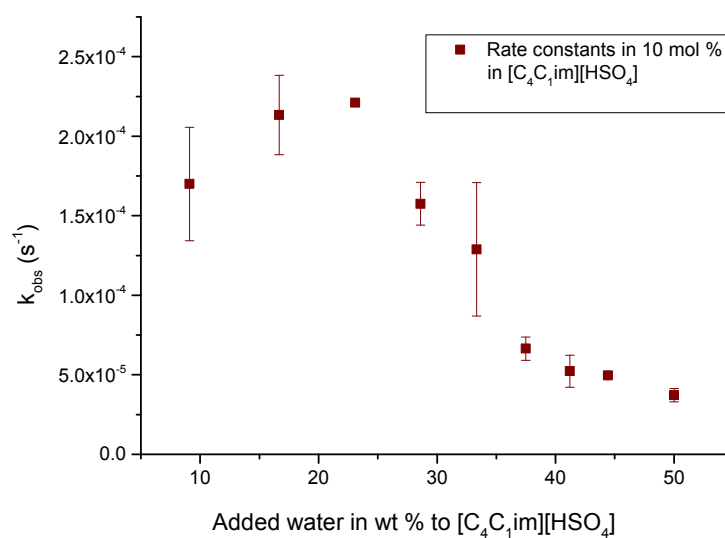


Figure 4.3.6 – Effect of water in $[C_4C_1im][HSO_4]$ on rate of reaction of GG hydrolysis with 10 mol eq % acid added, taken at 100 °C

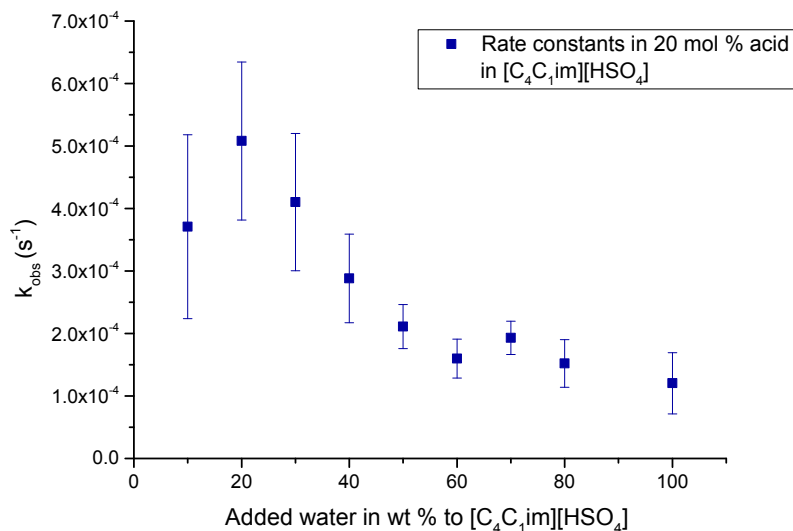


Figure 4.3.7 – Effect of water in [C₄C₁im][HSO₄] on rate of reaction of GG hydrolysis with 20 mol eq % added acid, taken at 100 °C

To scrutinise the effects of water on the acidity of the IL system, the acidity of each IL, acid and water system was measured with the help of Dr John Grasvik from the Welton group. Hammett acidity is a measurement of acidity (analogous to pH) in non-aqueous solutions^[151] and is expressed in the equation 4.3.3 where $\text{p}K_{\text{BH}^+}$ is the $\text{p}K_{\text{a}}$ of the conjugate acid of the probe base used to measure the acidity of the IL and $[\text{BH}^+]$ and $[\text{B}]$ are the concentrations of the base in its protonated and unprotonated forms.

$$H_0 = \text{p}K_{\text{BH}^+} + \log \frac{[\text{B}]}{[\text{BH}^+]} \quad (4.3.3)$$

Hammett acidity values (H_0) are depicted in Figure 4.3.8, showing the trend in acidity for each IL-acid-water system. By analogy with pH, a smaller H_0 value implies increased acidity and vice versa.

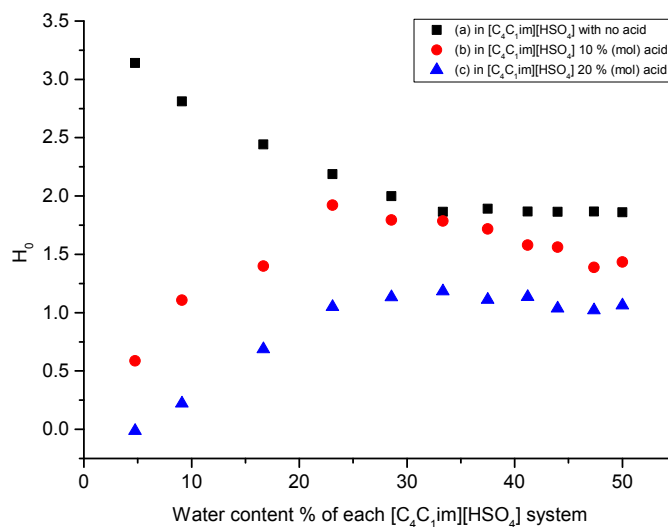


Figure 4.3.8 – H_0 values of water: $[C_4C_1im][HSO_4]$ systems (wt/wt %) a. no added acid (black squares), b. 10 mol % acid (red circles) c. 20 mol % acid (blue triangles)

When water was added to systems with 10 and 20 mol % acid, a relative decrease in acidity was observed. The H_0 values reach a maximum between 20 and 30 (wt/wt) % water, with no further decrease in acidity observed with further increases in water content. Where one would expect dilution of the acidic medium from the addition of water to the acidic IL, acidity is actually seen to plateau, showing high quantities of water maintaining the same proton activity within the reaction medium. As an increase in water was seen to significantly decrease the reaction rate of GG hydrolysis, this implies a competing effect of water, whereby its presence impedes reaction progress by a mechanism other than reduced acidity by dilution. This can be further observed when the rate constants are correlated with the Hammett acidity of each IL-acid-water system, as shown in Figure 4.3.9.

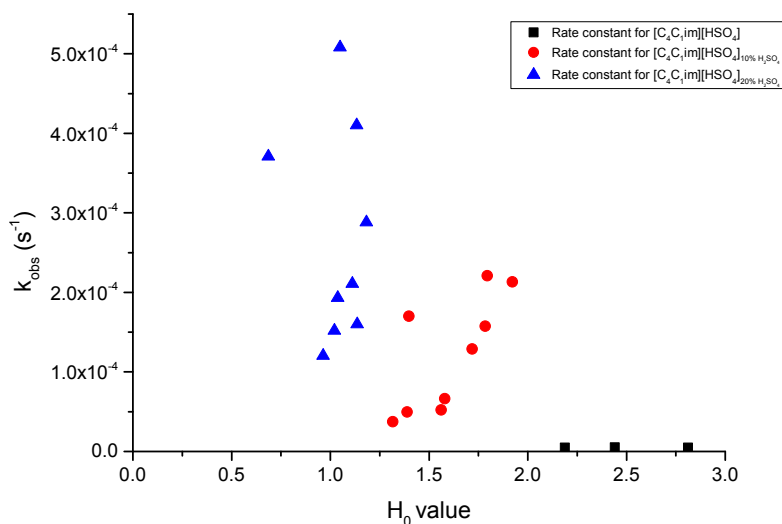


Figure 4.3.9 – Attempted correlation of rate constant with Hammett acidity

If water had the sole effect of increasing acidity as a proton transfer medium or reducing the acidity by diluting the acid, a direct correlation between Hammett acidity and rate would be observed. It is clear that poorly acidic systems in general exhibit slower rates, as shown by the three coloured regions in Figure 4.3.9 whereby the $[C_4C_1im][HSO_4]_{20mol\% \text{ acid}}$ displays the highest reaction rates and $[C_4C_1im][HSO_4]_{0 \text{ mol}\% \text{ acid}}$ the lowest. The lack of trend within each IL-acid medium infers a mechanism in which water affects reactivity beyond its role in proton transport. Further evidence of the competing effect of water is presented when examining the trend in Figure 4.3.5 where the addition of water, interestingly, increases acidity. Despite the increased acidity, there is no rate enhancement, suggesting that water has an inhibitory effect that counteracts any enhancement due to increased acidity. The inhibition observed with increasing water content suggests that a dehydration process may be rate determining. To summarise, the lack of direct correlation between Hammett acidity and rate constant implies water has multiple roles, by both influencing acidity but also in impeding reactivity through direct participation.

Through this investigation, it is clear that the hydrolysis of GG requires the initial protonation of the substrate, followed by a dehydration step where the presence of water retards reaction progress. Comparing this hypothesis with mechanisms currently proposed in the literature in both ionic and aqueous media,^[68, 69, 127, 130] GG dehydration prior to ether cleavage appears to be consistent with our results. Furthermore, this dehydration appears to be the rate determining step for the cleavage.

4.3.2 Establishing a kinetic model

The key findings from Cox^[70, 152] and Binder^[128] on the reactivity of GG in a range of Brønsted acidic and Lewis acidic ILs show the importance of acidity in catalysing ether cleavage in lignin, supporting the findings made in the kinetic study. It has been postulated that ether cleavage occurs as a consequence of a dehydration reaction after protonation of the hydroxy group located on the α carbon, yielding a stabilised carbocation. This can then form an unsaturated enol-ether which can subsequently undergo acid hydrolysis to form guaiacol and a “Hibbert ketone”, as shown in Figure 4.3.10. The overall rate expression depends on the rate determining step of the reaction. The two distinct steps in the cleavage of the linkage can be summarised as dehydration, involving protonation and loss of water, followed by hydrolysis, involving tautomerisation of the enol-ether to a keto-ether and nucleophilic attack of water at the β carbon to liberate guaiacol.

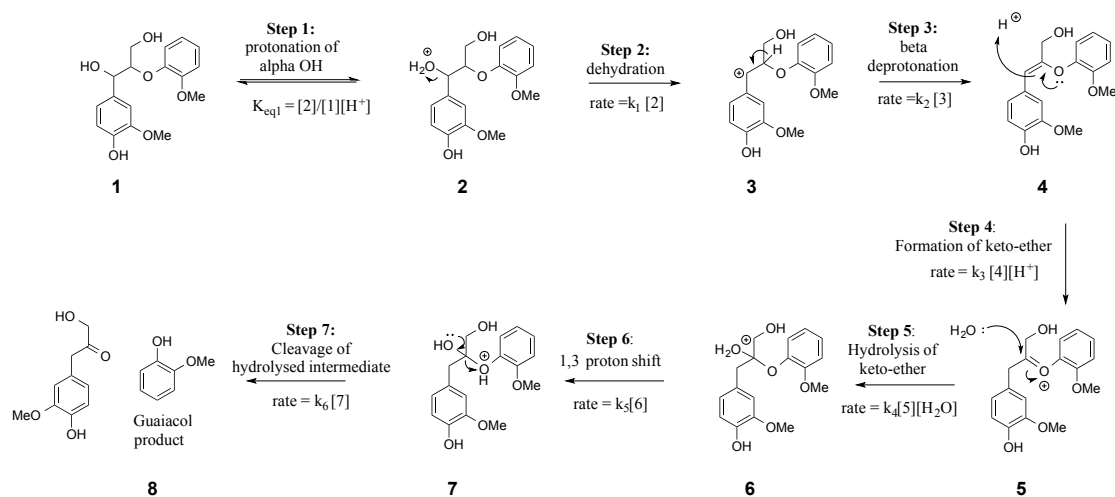


Figure 4.3.10 – Acid catalysed mechanism of GG ether cleavage

The mechanism for acid-catalysed GG hydrolysis can be described as follows:

1. The protonation of the hydroxy group at the α -carbon
2. The dehydration of the protonated hydroxy group yielding a carbocation
3. Deprotonation at the β position forming an enol-ether
4. Isomerisation to form a keto-ether
5. Hydrolysis of the keto ether by water
6. 1,3 proton shift after nucleophilic attack of water to form an ether oxonium intermediate
7. Cleavage of the ether, yielding guaiacol and the Hibbert ketone.

The rate expression for each step can be described as follows. The dehydration of GG to intermediate **3**, involves the initial protonation of the hydroxy group on the α -carbon of **1**, forming a concentration of intermediate denoted by the equilibrium constant K_{eq1} :

$$K_{eq1} = \frac{[2]}{[1][H^+]} \quad (4.3.4)$$

The protonated intermediate then undergoes dehydration, involving the loss of water from **2**:

$$\text{rate} = \frac{d[3]}{dt} = k_1[2] \quad (4.3.5)$$

Applying equation 4.3.4 to 4.3.5 gives the full rate expression for dehydration of GG as:

$$\frac{d[3]}{dt} = K_{eq1}k_1[1][H^+] \quad (4.3.6)$$

The rate expression for the subsequent hydrolysis involves the formation of the enol-ether substrate denoted as **4** by deprotonation at the β carbon:

$$\text{rate} = \frac{d[4]}{dt} = k_1[3] \quad (4.3.7)$$

This is then followed by the formation of the keto-ether **5**:

$$\text{rate} = \frac{d[5]}{dt} = k_2[4][H^+] \quad (4.3.8)$$

Which then undergoes nucleophilic attack of water:

$$\text{rate} = \frac{d[6]}{dt} = k_3[5][H_2O] \quad (4.3.9)$$

This is then followed by an intramolecular 1,3 proton shift to the basic ethereal oxygen to form an oxonium intermediate:

$$\text{rate} = \frac{d[7]}{dt} = k_4[6] \quad (4.3.10)$$

Which readily cleaves to give the guaiacol product:

$$\text{rate} = \frac{d[\text{Guaiacol}]}{dt} = k_5[6] \quad (4.3.11)$$

Combining equations 4.3.8, 4.3.9, 4.3.10 and 4.3.11 gives the rate expression for hydrolysis as:

$$\frac{d[\text{Guaiacol}]}{dt} = k_2k_3k_4k_5k_6[3][H_2O][H^+] \quad (4.3.12)$$

The fundamental difference in the dehydration and hydrolysis steps encompasses the opposite roles of water. For dehydration, on the assumption that solvent effects are negligible, the increased concentration of water would decrease the rate. If the rate determining step occurs after dehydration, the rate would have a positive dependence on water. One example of this is during the hydrolysis of intermediate **4**, water is the active nucleophile therefore an increase in its concentration would increase rate. From the kinetic data, it can be empirically concluded that GG cleaves following the initial rate expression, i.e. an initial protonation followed by dehydration.

4.3.3 HSQC studies of hydrolysis of the β -O-4 linkage in GG

In order to further confirm the hydrolysis of the GG model compound (**I**) in $[C_4C_{1im}][HSO_4]$, HSQC spectroscopy was used to track the cleavage and identify any possible intermediates present during hydrolysis with the hope to observe the dehydrated intermediate. Two reaction systems were employed, one with $[C_4C_{1im}][HSO_4]$ with 16.67 (wt/wt) % added water and the second with $[C_4C_{1im}][HSO_4]$, 10 mol eq % of sulfuric acid also with 16.67 (wt/wt) % added water. Each reaction was left to react for a set amount of time, extracted with chloroform, dried and analysed by HSQC in $CDCl_3$ (full experimental protocol available in experimental section). HSQC spectra for commercial GG and GG in $[C_4C_{1im}][HSO_4]$ with 16.67 % (wt/wt) water after one hour at 100 °C are shown in in Figures 4.3.11 and 4.3.12, with the most important signals labelled.

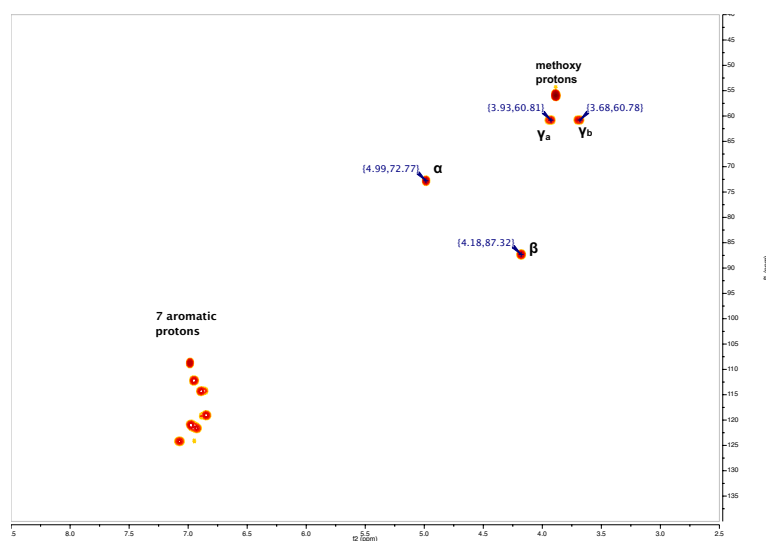


Figure 4.3.11 – HSQC spectrum of commercial GG

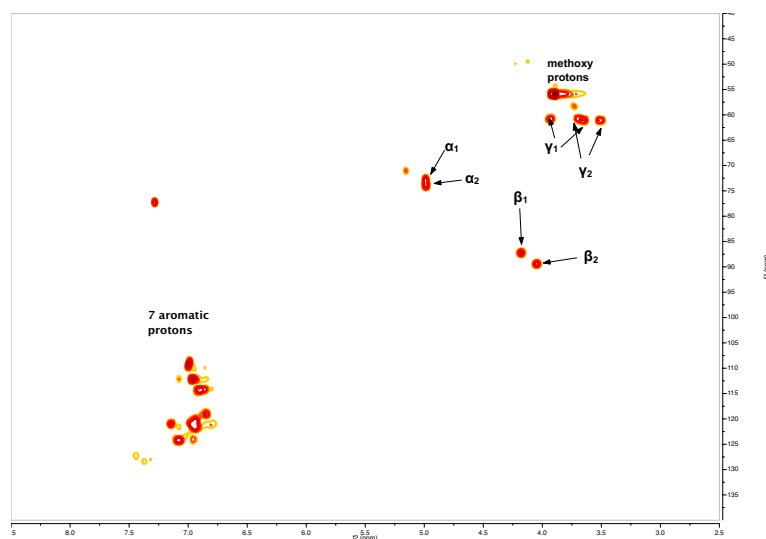


Figure 4.3.12 – HSQC spectrum of GG in $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ with 16.67 % (wt/wt) water after one hour at 100 °C

The HSQC spectrum of commercial GG clearly shows the α , β and γ protons with ^1H shifts at 4.99, 4.18 and 3.93/3.86 ppm respectively. Due to the diastereotopic nature of the protons on the γ -methylhydroxy group, two separate signals were observed of equal intensity. Integration of all of these signals were in agreement with the assigned structure and were therefore used to track any dehydration, cleavage or loss of the γ -methylhydroxy group during the reaction as formalde-

hyde, an observation made in many previous mechanistic studies.^[63, 136, 138, 153, 154] An attempt to fully identify and quantify the products was initially conducted by analysing the extracted products when GG was left to react in $[C_4C_1im][HSO_4]$ with 16.67 wt % water for one hour at 100 °C. The obtained HSQC showed no evidence of cleavage as the β proton was still present, however a new set of α , β , and γ protons was observed, as shown in Figure 4.3.12. The relative integrations of the new set of protons gave 1:1 integrals with respect to the original set, with the difference in shifts in the 1H spectra being most apparent with the γ protons (0.22 ppm), followed by the β protons (0.13 ppm) and finally the α protons where the signals largely overlap. These differences in shifts indicate preferential interaction of the IL at the γ -methylhydroxy group, where the acidic anion protonates the primary alcohol and subsequently displaces it *via* a nucleophilic substitution reaction. This hypothesis is supported when model compounds **II**, **III** and **IV** (not bearing the γ -methylhydroxy group) were placed in $[C_4C_1im][HSO_4]$ where solubility was seen only at high temperatures. This can be compared to model compounds **I** and **V** which were both soluble and homogeneous in $[C_4C_1im][HSO_4]$ at room temperature. These results suggest that the high solubility of lignin in ILs bearing $[HSO_4]^-$ anions may be due to hydrogen bonding interactions as well as sulfation of the substrate by the hydrogensulfate anion through the mechanism depicted in Figure 4.3.13.

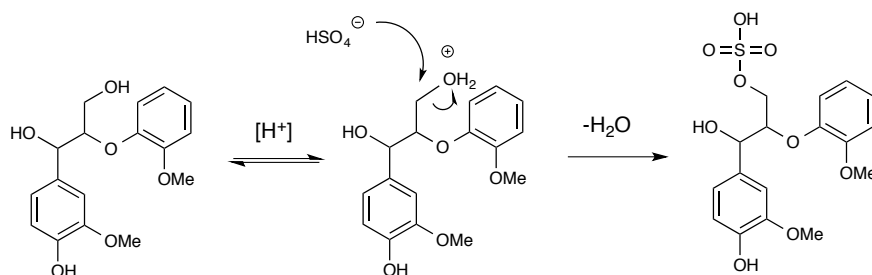


Figure 4.3.13 – Sulfation of GG by $[HSO_4]^-$

Attempts to quantify the degree of sulfation were then carried out. The reaction was repeated with fresh IL for 1, 5 and 12 hours at 100 °C with the extracted products submitted to CHNS elemental analysis to quantify the amount of sulfur remaining. Table 4.3.1 presents the results.

Table 4.3.1 – CHNS analysis of GG sulfation

Entry	Conditions	wt % of whole sample				Ratio of [HSO ₄] ⁻ to GG
		C	H	N	S	
1	Commercial	63.74	6.29	0	0	n/a
2	[C ₄ C ₁ im][HSO ₄], 16.67 wt % water, 1 hr, 100 °C	64.41	6.52	0.85	0.58	1: 17.4
3	[C ₄ C ₁ im][HSO ₄], 16.67 wt % water, 5 hr, 100 °C	62.26	6.62	1.0	0.59	1: 16.6
4	[C ₄ C ₁ im][HSO ₄], 16.67 wt % water, 12 hr, 100 °C	61.07	6.58	1.48	0.80	1: 12

The elemental analyses show a general increase in both nitrogen and sulfur content with increased reaction time. However, the relative ratios between the N and S content show that both the cation and anion have been extracted from the ionic liquid. Additionally, the low sulfur quantities observed gave little indication that the intact sulfated product is present. This large discrepancy in the degree of sulfation between the HSQC integrals and the results from the elemental analysis was not able to be reconciled with the only explanation for the presence of N and S in such quantities being due to residual IL extracted from the aqueous IL phase .

Further studies were conducted on the GG model compound with [C₄C₁im][HSO₄]_{10 mol % acid} in order to identify cleavage intermediates as well as the cleaved products. The reactions were left to react for one hour and five hours at 100 °C and the HSQC spectra of the extracted products are presented in Figures 4.3.14 and 4.3.15.

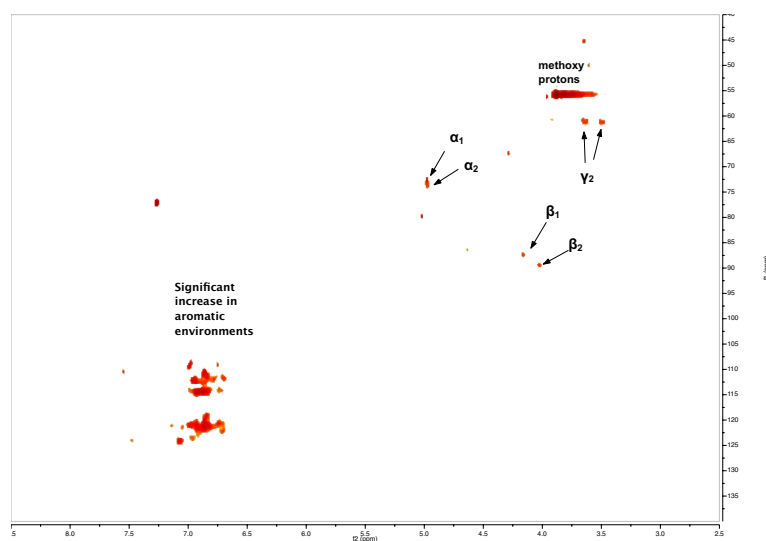


Figure 4.3.14 – HSQC spectrum of GG in $[C_4C_1im][HSO_4]_{10}$ mol% acid with 16.67 % (wt/wt) water after one hour at 100 °C

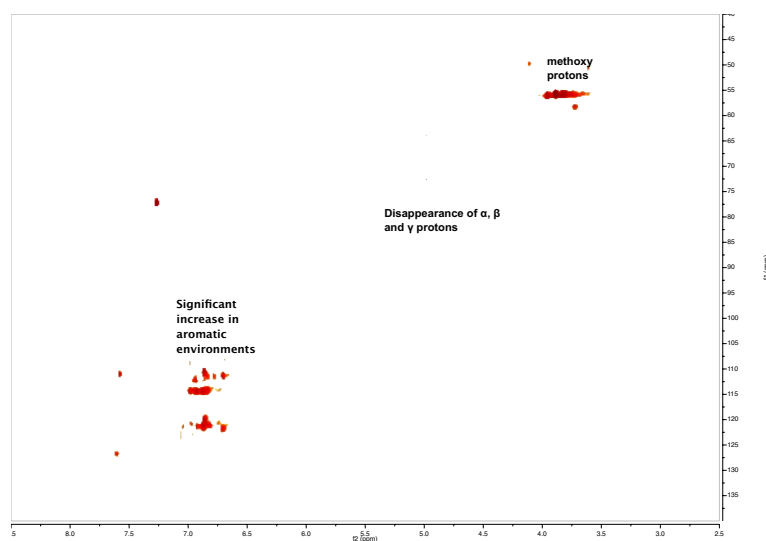


Figure 4.3.15 – HSQC spectrum of GG in $[C_4C_1im][HSO_4]_{10}$ mol% acid with 16.67 % (wt/wt) water after 5 hours at 100 °C

In both cases, the reaction medium significantly darkened compared to the previous two reactions, indicating greater reactivity of the GG substrate. After a one hour reaction time, the signal intensities of the α and β protons compared to the methoxy protons at around 3.90 ppm significantly decrease, showing substantial dehydration at the α carbon and hydrolysis of the β -O-4 linkage. The γ proton signals also show a decrease in intensity compared to the methoxy

proton signals, however only the γ_2 protons remain, implying that whilst the ether cleaves, some of the sulfated γ -methylhydroxy group remains which has been postulated in a number of studies to form the Hibbert ketone.^[50, 70, 127, 128] After a 12 hour reaction time, the HSQC spectrum shows complete disappearance of the α , β and γ proton signals, indicating complete dehydration and cleavage occurring. The loss of all the γ proton signals indicates that whilst Hibbert ketones may form during cleavage, they could not be identified by HSQC and deformylation may have occurred. This is further supported by the lack of signals in the aliphatic regions of the HSQC spectrum, with only a large methoxy smear between 3.95 ppm and 3.66 ppm and an increase in number of signals in the aromatic region due to new condensed products and the formation of guaiacol. The inability to identify GG intermediates in $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ is consistent with the hydrolysis of the β -O-4 linkage occurring directly after dehydration at the α position, and that this is the rate determining step. The major observations of the changes in α , β and γ signals are summarised in Table 4.3.2.

Table 4.3.2 – α , β and γ proton signals in GG during hydrolysis in $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$

Entry	HSQC Figure number	Reaction conditions	α signal of substrate (^1H , ^{13}C in ppm)	β signal of substrate (^1H , ^{13}C in ppm)	γ signal of substrate (^1H , ^{13}C in ppm)
1	4.3.11	unreacted starting material	4.99, 72.77	4.18, 87.32	3.93, 60.81 and 3.68, 60.78
2	4.3.12	$[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$, 16.67 % water, 1 hour, 100 °C	4.99, 72.91 and 4.99, 72.83	4.18, 87.25 and 4.05, 89.41	3.93, 60.86; 3.70, 60.64; 3.64, 61.05 and 3.52, 61.07
3	4.3.14	$[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]_{10 \text{ mol\% acid}}$, 16.67 % water, 1 hour, 100 °C	5.02, 79.93 and 4.97, 72.90	4.16, 87.49 and 4.02, 89.48	3.50, 61.37 and 3.64, 61.30
4	4.3.15	$[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]_{10 \text{ mol\% acid}}$, 16.67 % water, 5 hours, 100 °C	n/a	n/a	n/a

4.3.4 Studies towards the importance of lignin functionality

The model compounds (**II**, **III**, **IV** and **V**) presented in Figure 4.2.8 were used for investigations to identify which substituents around the ether as well as around the aromatic ring attached to the α carbon, are responsible for successful cleavage of the β -O-4 linkage. The model compounds were all placed in fresh samples of $[C_4C_1im][HSO_4]_{10 \text{ mol\% acid}}$ with 16.67 (wt/wt) % water and left to react at 100 °C for 5 hours. The organic products were then isolated by extraction with chloroform and analysed *via* HSQC spectroscopy. When all functionality was removed apart from the ether and the ability to dehydrate (as in compound **II**), the β -O-4 linkage remained intact. The addition of an electron donating methoxy group ortho to the ring adjacent to the ether, as in compound **III**, also failed to lead to ether cleavage. However, new sets of α , β and aromatic and methoxy protons were observed after the reaction of compounds **II** and **III**, with the largest proton shifts in both compounds observed between the two α signals (0.57 ppm and 0.62 ppm respectively, compared to 0.38 and 0.31 for the β protons). This was presumed to be due to sulfation occurring at the α -hydroxy group, where the absence of electron donating groups would most likely lead to the reaction proceeding *via* an A2 mechanism.

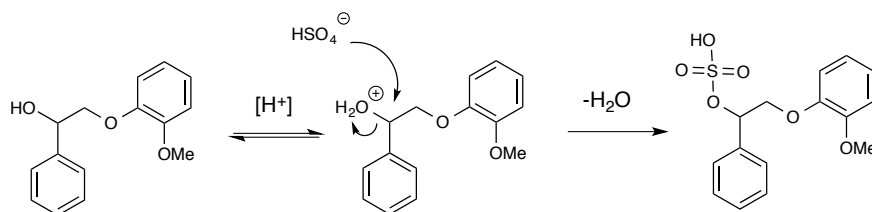


Figure 4.3.16 – Sulfation of model compound **III** at α -hydroxy position

On incorporating two further methoxy groups on the aromatic ring adjacent to the α carbon, full cleavage of the ether was observed as is the case with substrate **IV**. Similarly compound **V**, bearing the same functionality as GG with the sole difference being a benzylether group in place of the para hydroxy group was also shown to cleave. The increased intensity in the signal of the methoxy groups in 3.5 – 4 ppm region as well as the disappearance of the α and β protons indicate successful hydrolysis of the β -O-4 linkage and the formation of the guaiacol product.

The ability of compounds **IV** and **V** to completely hydrolyse suggests that the electron donating methoxy groups on the aromatic ring adjacent to the site of dehydration are required to stabilise the carbocation produced on the loss of water. A summary of the HSQC signals and their implications on the sensitivity of the β -O-4 linkage is presented in Table ??, which also includes the results of the GG model compound from the previous investigation for comparison. Full HSQC spectra of the original model compounds and the extracted products post reaction are available in the appendix.

Table 4.3.3 – HSQC shifts for hydrolysis of β -O-4 linkage in lignin model compounds **I-V**

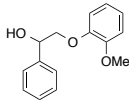
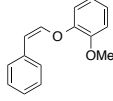
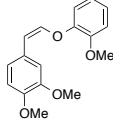
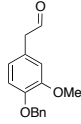
Substrate	α signal before reaction (^1H , ^{13}C in ppm)	β signal before reaction (^1H , ^{13}C in ppm)	α signal after reaction (^1H , ^{13}C in ppm)	β signal after reaction (^1H , ^{13}C in ppm)	β -O-4 linkage
I	4.99, 72.77	4.18, 87.32	not visible	not visible	full cleavage occurs
II	5.16, 72.64	4.14, 73.39 and 4.05, 73.29	5.13, 72.59 and 5.70, 76.74	4.11, 73.40; 4.03, 73.32; 4.49, 70.59 and 4.28, 70.54	no cleavage occurs
III	5.14, 72.34	4.21, 76.38 and 4.01, 76.37	5.14, 72.33 and 5.76, 76.71	4.20, 76.31; 4.02, 76.32; 4.32, 71.94 and 4.51, 72.04	no cleavage occurs
IV	5.07, 72.21	4.18, 76.51 and 3.99, 76.42	not visible	not visible	full cleavage occurs
V	4.99, 72.72	4.18, 87.43	not visible	not visible	full cleavage occurs

^aConditions: substrates dissolved in $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]_{10\% \text{ acid}}$ with 16.67 wt % water left to react for 5 hours at 100 °C

Deuss *et al* investigated the products and intermediates obtained using lignin model compounds similar to these reported investigations, but without the γ -methylhydroxy group, a significant reduction in concentration of sulfuric acid and in organic solvents.^[136] Using a similar strategy, final studies on the lignin model compounds were conducted in order to see whether the mechanism and requirement for functionalisation still hold. In order to circumvent possible issues with selective extraction, toluene was used as the solvent and the intermediates and products were identified *in situ*. Compounds **I**, **III**, **IV** and **V** were all submitted to acidolysis in toluene with 10 mol % sulfuric acid with respect to the substrate, heated to 120 °C for two hours in a closed system and analysed by GC-MS. It was hoped that the significant decrease in acid concentration, along with the absence of water in an organic solvent would allow substantial amounts of the intermediate to be identified without being hydrolysed. The unreacted starting materials, reaction intermediates and products were all identified by their molecular masses and are listed in Table 4.3.4.

The catalytic amounts of sulfuric acid in toluene successfully slowed reactivity of the model

Table 4.3.4 – GC-MS analysis of acidolysis of model compounds

Model Compound	Retention time (mins)	Mass (m/z)	Compound	Identity
I	8.53	124		product
	9.11	134	unable to identify	n/a
	22.11	262	unable to identify	n/a
III	7.60	120		product
	8.53	124		product
	20.79	242		starting material
	20.91	226		dehydrated intermediate
IV	8.53	124		product
	20.79	281	unable to identify	n/a
	23.89	286		dehydrated intermediate
V	8.54	124		product
	13.80	178	unable to identify	n/a
	15.59	182	unable to identify	n/a
	17.68	210	unable to identify	n/a
	21.89	256		product

^aConditions: substrates dissolved in toluene with 10 mol % sulfuric acid, left at 120 °C for 2 hours

compounds, allowing a range of intermediates and products to form, with low molecular weight compounds identified by GC-MS. Reaction media containing model compounds of substantial functionalisation were shown to significantly darken over the reaction period and apart from GG, where guaiacol was the only identifiable compound, dehydration intermediates and aldehyde products were identified. Model compound **III** enabled the identification of an array of compounds including the starting material, dehydrated intermediate as well as the guaiacol and aldehyde products, thus suggesting a mechanism analogous to GG hydrolysis in $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$, as shown in Figure 4.3.10. The inability to identify dehydrated intermediates and any aldehyde/Hibbert ketone products in the GG model compound suggests the possibility of competing reactions occurring. Such reactions can occur either after the formation the dehydrated intermediate or directly after cleavage. These products have been consistently referred to as condensation products in literature, mostly because the reaction mechanism involves the loss of water.^[66, 70, 136, 155, 156] However, the comparative functional simplicity of these model compounds make it difficult to replicate the condensation reactions that are known to occur in lignin itself. In order to confirm the formation of an aldehyde as a cleaved product, all of the reactions were repeated with the inclusion of 2 molar equivalents of ethylene glycol to the model compound, as was carried out by Deuss *et al.*^[136] This would protect any aldehyde products forming during the reaction as acetals, therefore preventing any reactivity of the aldehyde formed post cleavage in condensation reactions.

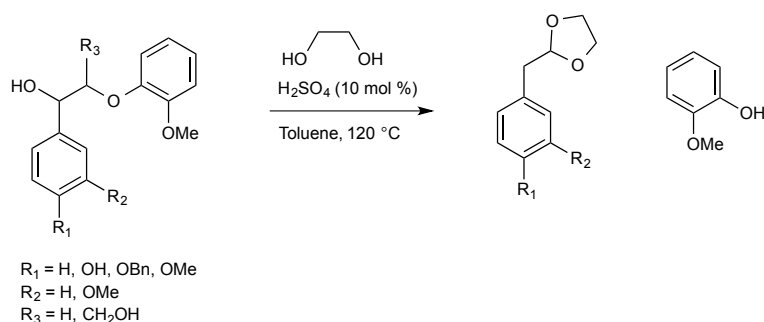
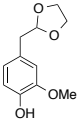
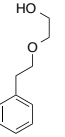
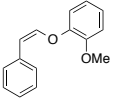
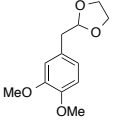
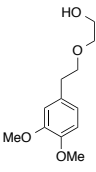
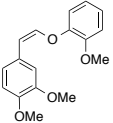
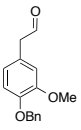


Figure 4.3.17 – Aldehyde protection *via* the formation of the acetal with ethylene glycol

The addition of ethylene glycol allowed the formation of acetals and hemiacetals in all model compounds except compound **V** where only the aldehyde was observed. This proved the formation of aromatic aldehydes occurring upon hydrolysis of the β -O-4 linkage once the γ -methylhydroxy group departs as formaldehyde. However, the observation of the fully protected acetal product with GG in significant quantities indicates that fewer condensation reactions occur once the starting material dehydrates when the aldehyde group is protected, contrary to what was proposed by Binder and Shimada.^[128, 155] Such condensation reactions take place due to the high reactivity of the aldehyde products formed post ether cleavage, which is once again promoted by

Table 4.3.5 – GC-MS analysis of acidolysis of model compounds **I-V**

Model compound	Retention time (mins)	mass (m/z)	Compound	Identity
I	8.54	124		product
	17.68	210		acetal product
III	15.37	166		hemiacetal product
	20.92	226		dehydrated intermediate
IV	8.54	124		product
	18.15	224		acetal product
	20.91	226		hemiacetal product
	23.91	286		dehydrated intermediate
V	8.54	124		product
	15.59	182	unable to identify	n/a
	21.89	256		unprotected product

Conditions: substrates dissolved in toluene with 10 mol % sulfuric acid and 2 molar equivalents of ethylene glycol, left for 2 hours at 120 °C

the highly electron donating para hydroxy group on the aromatic ring attached to the α hydroxy group. One hypothesis involves the reaction of the aldehyde group with free hydroxy groups, forming trimeric acetal compounds of large mass as well as aldol condensation reactions.

This part of the study highlights three important features of model compound functionality for the successful hydrolysis of the β -O-4 linkage in [C₄C₁im][HSO₄]. Most importantly, high electron donating substituents on the aryl group adjacent to the α hydroxy group are required to promote dehydration and without their presence, the model compounds fail to react. Secondly, the hydroxy group attached to γ protons is shown to aid solubility of the model compounds, where sulfation is seen to occur. Finally, when examining the reactivity of the model compounds in toluene, aldehyde products form which may undergo condensation reactions post ether cleavage, where the high electron density of the benzyl aldehyde cleaved products make these species prone to engage in further reactions.

4.4 Eyring activation parameters for GG dehydration

4.4.1 Transition state theory and the Eyring-Polanyi equation

The final investigation on GG hydrolysis focuses on the effects of cation selection in $[\text{HSO}_4]^-$ ILs, in order to assess any differences in solvent effects. In this part of the study, ILs with a range of protic, aprotic, aromatic and aliphatic ammonium cations were explored. One approach used to probe the differential solvation of reactants and the activated complex is transition-state theory, developed in 1935 by Henry Eyring.^[157]

The “transition state” of an elementary reaction is defined as the set of states of highest energy along the reaction coordinate.^[158] This assembly of atoms and their configurations between the reactants and products is referred to as an activated complex and is defined by IUPAC as the “the assembly of atoms which corresponds to an arbitrary infinitesimally small region at or near the col (saddle point) of a potential energy surface.”^[159] This is the thermodynamic approach of Arrhenius’s classical theory of reaction kinetics, based on the assumption that reactants have to overcome an energy barrier before forming their respective products. This can be visualised *via* a reaction coordinate diagram (Figure 4.4.1) for the simple elementary reaction shown in Equation 4.4.1 where $A + B$ are the reactants, $(AB)^\ddagger$ is the activated complex and $C + D$ are products.



However, a number of assumptions must be made to apply conventional kinetic theory to transition state theory:^[158]

- The reactants are envisaged to be in quasi-equilibrium with the activated complex with this equilibrium constant given by Equation 4.4.2. (a = activities and γ = activity coefficients).

$$K^\ddagger = \frac{a_{(AB)^\ddagger}}{a_A \cdot a_B} = \frac{[(AB)^\ddagger]}{[A] \cdot [B]} \cdot \frac{\gamma^\ddagger}{\gamma_A \cdot \gamma_B} \quad (4.4.2)$$

- The formation of products $C + D$ do not affect the equilibrium between the reactants and the activated complex.
- The activated complex has all the properties of a normal molecule (with N atoms) except that one vibrational degree of the $3N-6$ vibration degrees of freedom is transformed into a translation degree of freedom, which leads to the decomposition of the activated complex.
- The activated complex exists at the saddle point of an energy barrier and the region around this area is known as the transition state.

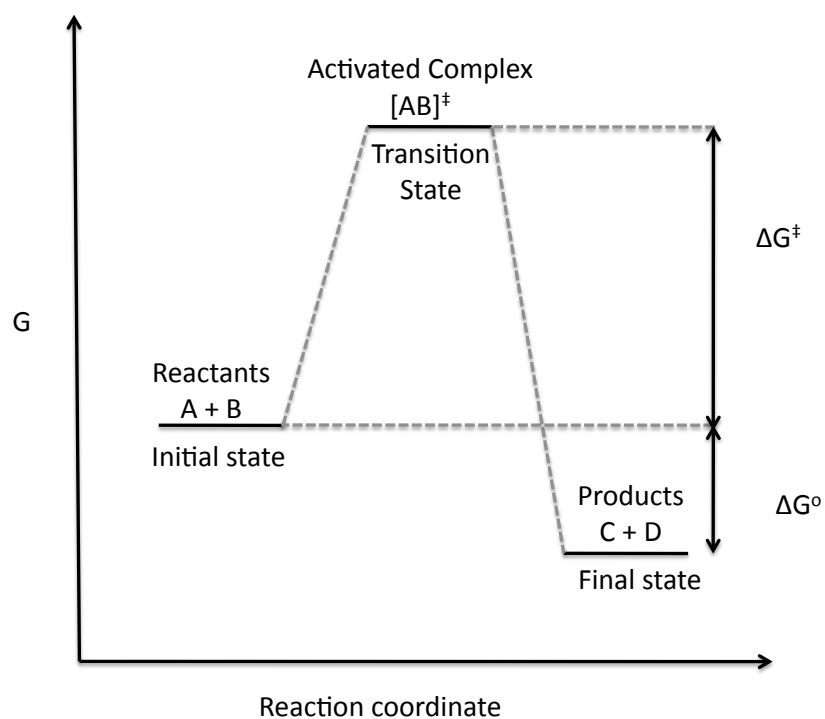


Figure 4.4.1 – One-dimensional Gibbs energy diagram for reaction 4.4.1 showing the relative standard molar Gibbs energies of reactants, activated complex and products where $\Delta G^\ddagger$ is the standard molar Gibbs energy of activation and ΔG° is the standard molar Gibbs energy of the reaction.

- The net reaction rate is determined by the rate at which the activated complex passes over the energy barrier in order to form products.
- This hypothesis is only valid for systems with solvents that undergo rapid reorientational relaxation. This allows differences in Gibbs free energy of activation for the reaction in each solvent to be evaluated as the relative modification of the solvation of the reactants and the activated complex.

In order to apply the kinetic model of reaction rates to the thermodynamic equilibrium between the reactants and activated complex, a universal frequency factor that varies with temperature must be applied. If the assumption is made that each activated complex passing through the transition state transforms into product, the frequency factor is estimated to be $k_B \cdot T/h$. Therefore the relationship between the absolute rate of reaction and the equilibrium constant can be described as follows:

$$k = \frac{k_B \cdot T}{h} \cdot K^\ddagger \cdot (1\text{mol} \cdot \text{L}^{-1})^{1-n} = \frac{R \cdot T}{N_A \cdot h} \cdot K^\ddagger \cdot (1\text{mol} \cdot \text{L}^{-1})^{1-n} \quad (4.4.3)$$

where k is the rate constant, k_B is the Boltzmann constant, h the Planck constant, T the absolute temperature, R the gas constant N_A the Avogadro constant, $K^\ddagger$ the quasi-thermodynamic equilibrium constant relating to the equilibrium between reactants and activated complex and n the kinetic order of the reaction. As the term K represents an equilibrium constant, it can be defined in terms of Gibbs free energy as well as enthalpy and entropy. Taking the frequency factor in Equation 4.4.3 and making the assumption that $\Delta H^\ddagger$ and $\Delta S^\ddagger$ do not vary with temperature, the Eyring equation provides a feasible theoretical construct to describe the dependence of reactions on temperature (full derivation of the equation can be found in the appendix):

$$k = \frac{k_B T}{h} e^{\frac{\Delta H^\ddagger}{RT}} e^{\frac{\Delta S^\ddagger}{R}} \cdot (1\text{mol} \cdot \text{L}^{-1})^{1-n} \quad (4.4.4)$$

The Eyring equation offers a suitable method for deconvoluting the value of $\Delta G^\ddagger$ into $\Delta H^\ddagger$ and $\Delta S^\ddagger$ for any specific reaction. The magnitudes of both $\Delta H^\ddagger$ and $\Delta S^\ddagger$ provide information regarding how the transition state differs from reactants and can be meaningfully compared across a series of reactions where small modifications are made (e.g. solvent change or small changes to the substrate). Through the systematic measuring of kinetic data at different temperatures, insights into the balance of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ and consequently $\Delta G^\ddagger$ can be gained.

4.4.2 Hughes Ingold Principles

It is well understood that homogeneous chemical reactions can undergo significant changes in rate when changing from one solvent to another. Reactions involving charge separation or charge dispersion such as proton transfer or nucleophilic substitution reactions have been exhaustively investigated. The role of solvation is understood to affect the differential solvation of reactants and the transition state leading to an alteration in the Gibbs energy of activation.^[160, 161] In cases where the influence of frictional/dynamic effects of solvents are negligible, the effect of the solvent on the reaction rate is dictated largely by the static solvent-solute interactions as mentioned above. Transition state theory is essential for any understanding of solvent effects on reaction rates. The following is a summary of solvent effects on reactions of different charge types as postulated by Hughes and Ingold:^[158]

- An increase in solvent polarity results in an increase in rate when the charge density in the activated complex is greater than in the initial reactant molecule(s)
- An increase in solvent polarity results in a decrease in rate when the charge density of the activated complex is lower than in the initial reactant molecule(s)
- A change in solvent polarity will have negligible effect on the rates of reactions that exhibit little or no change in charge density on going from reactant to activated complex.

For instance, when a reaction involves two equally charged ions combining in the activated complex, the increase in charge density would require polar solvents to increase rate. Equally, when a reaction involves two oppositely charged ions combining, the destruction of charge on approach to the activated complex would be favoured in less polar solvents. The effect of solvation of either the activated complex or initial reactants will consequently affect $\Delta H^\ddagger$ and $\Delta S^\ddagger$ thus providing qualitative predictions about the effect of solvent polarity on reaction rate.

$\Delta H^\ddagger$, or enthalpy of activation can be viewed as the thermodynamic analogue to Arrhenius's activation energy. When preferential interaction of the transition state occurs, $\Delta H^\ddagger$ is lowered. Equally, when preferential interaction of the reactant molecules occurs, $\Delta H^\ddagger$ increases as the energy barrier becomes greater.

$\Delta S^\ddagger$ is more complex to interpret but can generally be described as the measure of the degree of order lost or gained of a reactant in the gas phase on approach to the transition state compared to the reactant at the ground state. The value of $\Delta S^\ddagger$ is dependent on the loss or gain of translational, rotational or vibrational degrees of freedom and can be easily envisaged with elementary reactions where the sign and value of $\Delta S^\ddagger$ indicates the arrangement of atoms at the activated complex. When two molecules combine as is the case in an S_N2 reaction, the increase in order would produce a large negative $\Delta S^\ddagger$. However, with reactions involving bond cleavage creating two molecules, the decrease in order on approach to the transition state would

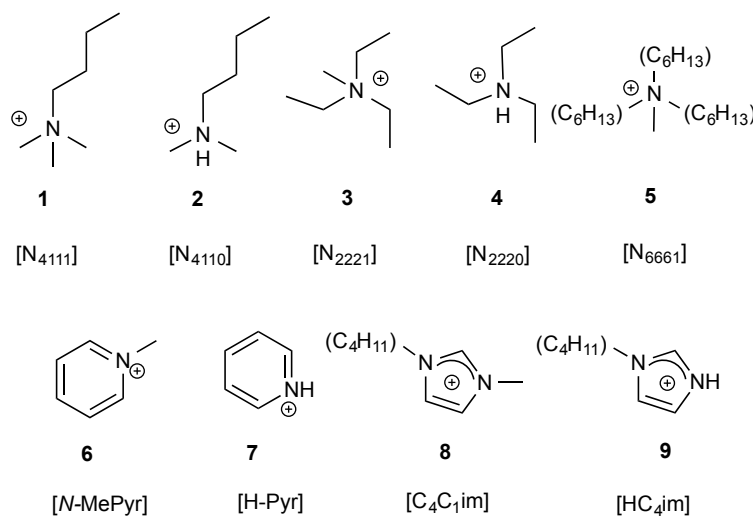


Figure 4.4.2 – ILs used in this study and their abbreviations

produce a large positive $\Delta S^\ddagger$ value. It must be noted however that in the condensed phase, the meaning of $\Delta S^\ddagger$ has been subject to much debate and is a somewhat nebulous concept. This is largely due to the myriad of physical properties that exist in the solvent and can therefore be generally referred to as the solvent's non-thermal response to a reaction. For instance, if favourable enthalpy interactions occur with the transition state, the $\Delta S^\ddagger$ value compensates by becoming more negative than expected.

The effects of solvation and its implications for the Eyring activation parameters $\Delta H^\ddagger$, $\Delta S^\ddagger$ and $\Delta G^\ddagger$ will be explored in greater detail on the hydrolysis of the ether group in GG within [HSO₄]⁻ ILs.

4.4.3 Kinetic data and Eyring activation parameters

The cleavage of GG with [C₄C₁im][HSO₄] and other acidic ILs was studied to determine the effect of varying the IL cation on the reaction activation parameters. Aromatic and alkyl-ammonium ILs (Figure 4.4.2) were prepared *via* alkylation for the aprotic set of ILs and direct acid-base neutralisation for the protic set and their full experimental protocols are detailed in chapter 7.

These ILs were selected to explore a range of cation structures that could affect the reactivity of GG, including the effects of aromaticity, steric bulk, the ability to form polar and non polar domains and most importantly, the ability to act as hydrogen bond donors. With a system of 16.67 (wt/wt) % water to IL, all the ILs employed gave faster cleavage of the substrate at 100 °C compared to [C₄C₁im][HSO₄] with yields reaching a maximum value of 36 % after a one-hour reaction time compared to 1.4 % in [C₄C₁im][HSO₄]. Kinetic data for each IL fit well to a

Table 4.4.1 – Pseudo-first order rate constants for GG hydrolysis with a range of [HSO₄][−] ILs.

Entry	IL cation	Cation type	k _{obs} (s ^{−1} × 10 ^{−6})	
1	[C ₄ C ₁ im]	Aprotic, aromatic	5.24	
2	[HC ₄ im]	Protic, aromatic	64.6	
3	[N-Mepy]	Aprotic, aromatic	54.8	
4	[Hpy]	Protic, aromatic	50.1	^a Reactions
5	[N ₄₁₁₁]	Aprotic, aliphatic, polar	92.0	
6	[N ₄₁₁₀]	Protic, aliphatic, polar	146	
7	[N ₂₂₂₁]	Aprotic, aliphatic, some steric hindrance	23.7	
8	[N ₂₂₂₀]	Protic, aliphatic, some steric hindrance	11.7	
9	[N ₆₆₆₁]	Aprotic, aliphatic, large steric hindrance	18.8	
carried out with 16.67 (wt/wt) % water at 100 °C				

pseudo-first order model and the rates of reaction were measured for each IL-water system. The ammonium ionic liquids [N₄₁₁₀][HSO₄] and [N₄₁₁₁][HSO₄] provided the fastest hydrolysis of GG with rate constants of 1.46 × 10^{−4} s^{−1} and 9.20 × 10^{−5} s^{−1} respectively and are listed in Table 4.4.1.

The kinetic data reported in Table 4.4.1 show no discernible trend regarding choice of cation, apart from the reaction in [C₄C₁im][HSO₄] being significantly slower compared to the other ILs, followed by the triethylammonium ionic liquids. Furthermore, the dimethylbutyl ammonium and trimethylbutylammonium cations show a substantial increase in rate by around half an order of magnitude compared to all the other ILs. In order to gain more insight into the microscopic role of solvent-solute interactions with acidic ILs and whether there is any break from the mechanism proposed in Figure 4.3.10, kinetic data from multiple temperatures between 90-120 °C were obtained and Eyring plots were generated for each IL. This was carried out using the linear form of the Eyring equation described in Equation 4.4.4 and is presented as follows:

$$\ln \frac{k}{T} = \frac{-\Delta H^\ddagger}{R} \cdot \frac{1}{T} + \ln \frac{k_B}{h} + \frac{\Delta S^\ddagger}{R} \quad (4.4.5)$$

Through plotting ln(k/T) (where k is the pseudo first order rate constant of the reaction and T the absolute temperature in Kelvin) against the inverse of temperature in Kelvin, an Eyring plot can be produced, giving a straight line. From the gradient and the intercept, both ΔH[‡] and ΔS[‡] can be obtained and consequently the ΔG[‡]. Figures 4.4.3 and 4.4.4 are examples of raw kinetic data for GG hydrolysis in [HC₄im][HSO₄] and the Eyring plot using the obtained pseudo first order rate constants.

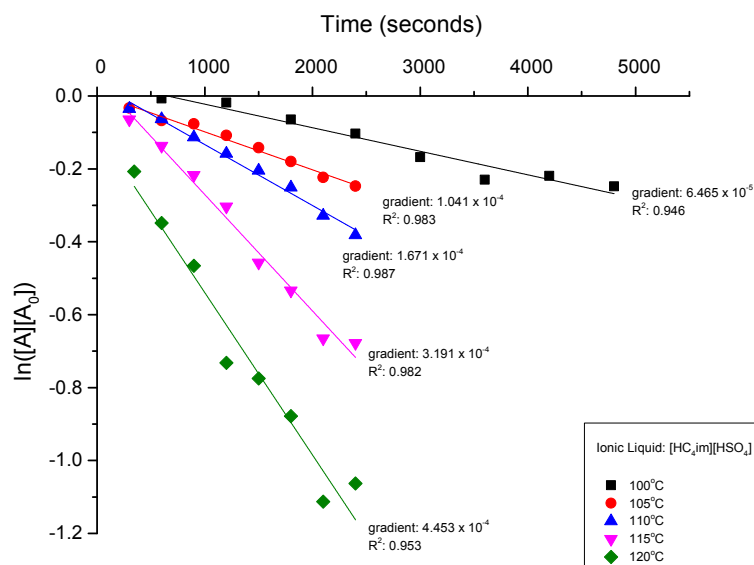


Figure 4.4.3 – Kinetic data for $[\text{HC}_4\text{im}][\text{HSO}_4]$ at five different temperatures

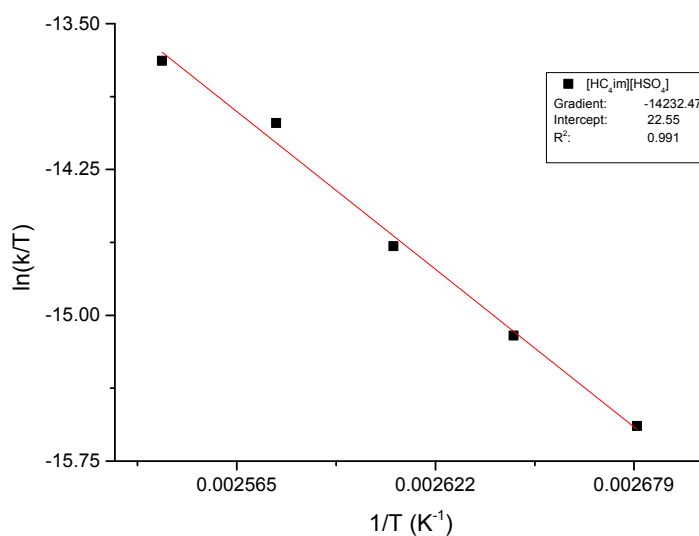


Figure 4.4.4 – Eyring plot for $[\text{HC}_4\text{im}][\text{HSO}_4]$

The values of $\Delta H^\ddagger$ can be obtained by dividing the gradient by the gas constant ($8.314 \text{ JK}^{-1}\text{mol}^{-1}$) providing the value of enthalpy of activation in units of kJ mol^{-1} . $\Delta S^\ddagger$ can be obtained by deducting the frequency factor ($\ln(k_B/h)$ which has a value of 23.7602) from the gradient followed

Table 4.4.2 – Eyring activation parameters for the hydrolysis of GG in a range of $[\text{HSO}_4]^-$ ILs.

Entry	IL cation	$\Delta H^\ddagger$ (kJ mol ⁻¹)	$\Delta S^\ddagger$ (JK ⁻¹ mol ⁻¹)	$T\Delta S_{373\text{K}}^\ddagger$ (kJ mol ⁻¹)	$\Delta G_{373\text{K}}^\ddagger$ (kJ mol ⁻¹)	^a Rate
1	[C ₄ C ₁ im]	104 ± 6	-70 ± 19	-26 ± 7	130 ± 9	
2	[HC ₄ im]	118 ± 6	-10 ± 15	-4 ± 6	122 ± 8	
3	[HPy]	84 ± 11	-99 ± 30	-37 ± 11	121 ± 16	
4	[N-Mepy]	103 ± 6	-52 ± 16	-13 ± 6	122 ± 8	
5	[N ₄₁₁₁]	121 ± 9	0 ± 23	0 ± 9	121 ± 12	
6	[N ₄₁₁₀]	75 ± 11	-121 ± 28	-45 ± 10	120 ± 15	
7	[N ₂₂₂₀]	109 ± 2	-50 ± 6	-19 ± 2	127 ± 3	
8	[N ₂₂₂₁]	126 ± 13	4 ± 34	0 ± 13	125 ± 18	
9	[N ₆₆₆₁]	132 ± 11	16 ± 28	6 ± 11	126 ± 15	

constants obtained between 90°C and 120 °C. Uncertainties are derived from the standard errors of the parameters extracted from the linear fits obtained from the Eyring plots (see ESI)

by dividing by the gas constant, providing the value of entropy of activation in units of J K⁻¹mol⁻¹. Pseudo-first order rate constants for GG hydrolysis were obtained for all ILs along with their Eyring plots (available in the appendix). The values of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ are reported in Table 4.4.2.

4.4.4 Discussion

The rate-determining step for the hydrolysis of GG is dehydration, therefore the $[\text{HSO}_4]^-$ anion is envisaged to stabilise the starting material and activated complex during dissociation of water from the protonated intermediate. According to the Hughes-Ingold rules,^[158] an increase in the dispersal of charge from the initial state would decrease the effect of solvation on the activated complex. This therefore leads to preferential solvation of the initial molecule whereby charge density in the activated complex is lower than that of the initial substrate. As the substrate has the cationic character concentrated on the α -hydroxy moiety, organization of the anion around the positively charged solute occurs, reducing the initial energy of the reactant through electrostatic stabilisation. This therefore implies an increase in reaction rate when an IL has a higher cation-anion association and a decrease in rate when the anion is less associated with the cation. This is reflected in the values in Table 4.4.1. Leffler and Jasinski postulated that if a full isokinetic compensation is observed with a set of reactions that differ subtly (either by the systematic changing of solvents or small modifications of substrate functionality) then a consistent mechanism for that particular reaction holds across the series. An entropy-enthalpy compensation can be observed when all the activation parameters ($\Delta H^\ddagger$, $T\Delta S^\ddagger$ and $\Delta G^\ddagger$) are plotted together for each IL as is shown in Figure 4.4.5. The pattern between entropy and enthalpy is consistent

across the series where the changes in entropy of activation are fully compensated by the enthalpy of activation with small differences in the overall Gibbs free energy of activation. A full isokinetic plot can be produced by plotting the values of $\Delta H^\ddagger$ against $\Delta S^\ddagger$ as shown in Figure 4.4.6.

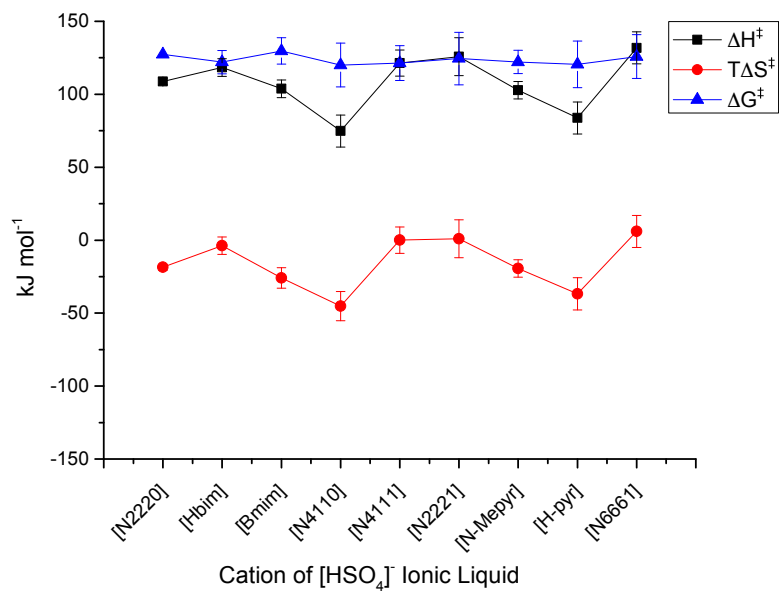


Figure 4.4.5 – Entropy-enthalpy compensation between ILs

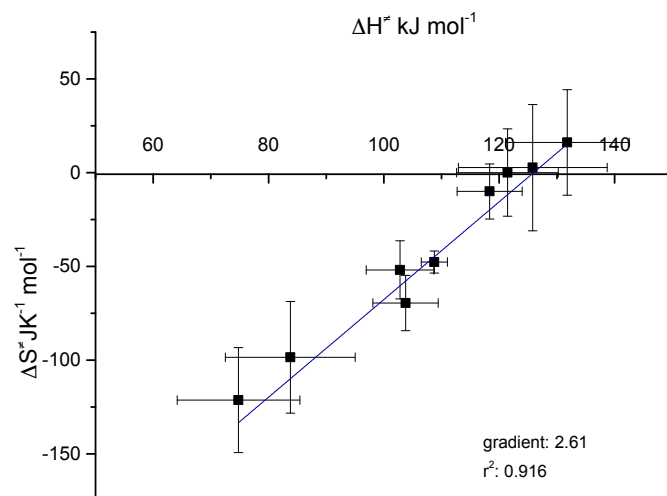


Figure 4.4.6 – Isokinetic plot for all $[\text{HSO}_4]^-$ ILs

Grouping the protic and aprotic ILs together, the isokinetic plot is more pronounced with the protic set of cations, confirming no change in mechanism. However some deviation from linearity is observed when $[\text{C}_4\text{C}_{1\text{im}}][\text{HSO}_4]$ is included with the aprotic cation set. The similar gradients of 2.4 and 2.8 confirm a consistent mechanism regardless of cation choice, with the differences in reaction rate (and therefore $\Delta G^\ddagger$) owing to the subtly different solvent-solute interactions, reflected in the large differences in $\Delta H^\ddagger$ and $\Delta S^\ddagger$. In order to identify these differences, activation parameters of each IL were ranked (Figures 4.4.9 and 4.4.10).

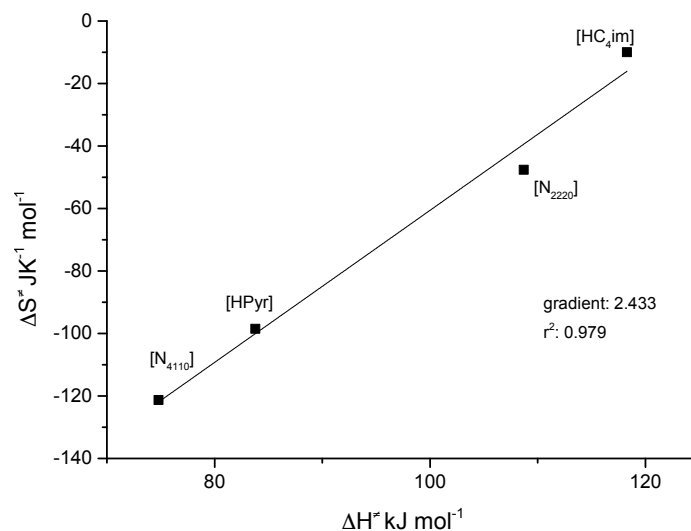


Figure 4.4.7 – Isokinetic plot for all protic $[\text{HSO}_4]^-$ ILs

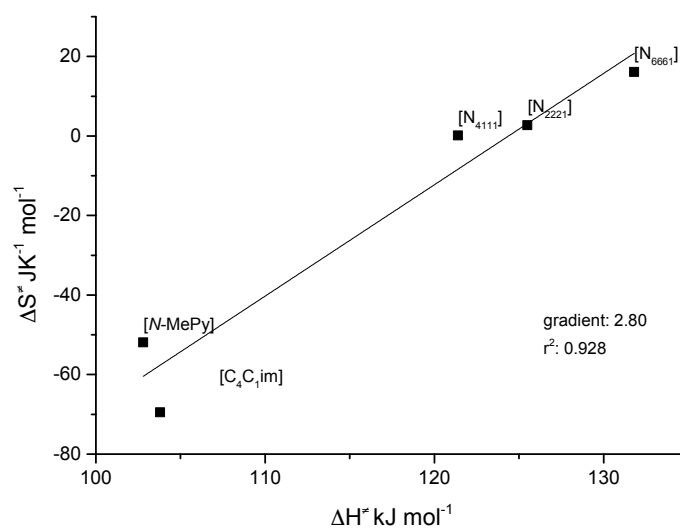


Figure 4.4.8 – Isokinetic plot for all aprotic $[\text{HSO}_4]^-$ ILs

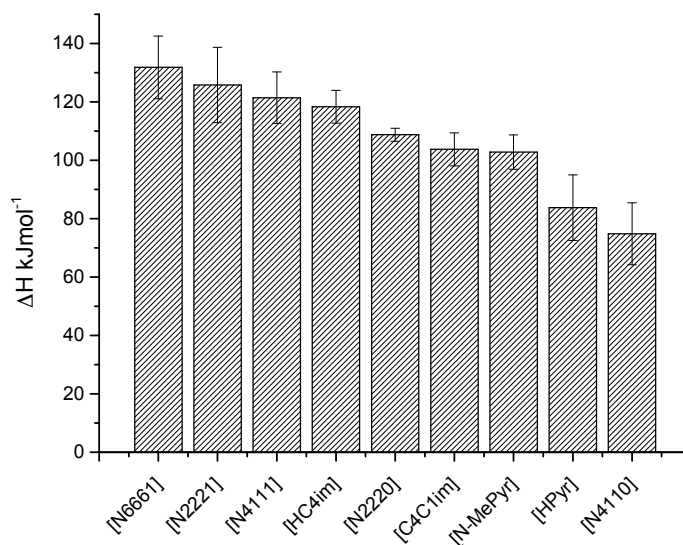


Figure 4.4.9 – Ranking of ILs in terms of enthalpy of activation

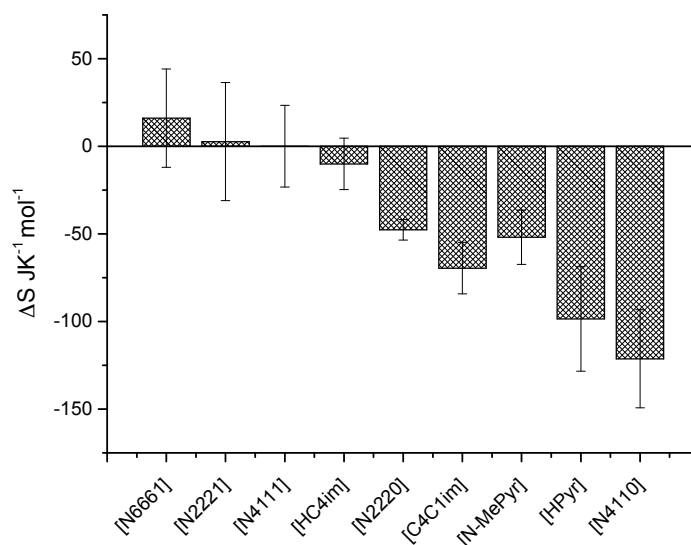


Figure 4.4.10 – Ranking of ILs in terms of entropy of activation

The effects of enthalpy are shown to dominate $\Delta G^\ddagger$ and all protic ILs (apart from those containing butylimidazolium cations) exhibit lower $\Delta H^\ddagger$ compared to their aprotic counterpart. This is compensated by a decreased $\Delta S^\ddagger$ in each case (Figure 4.4.10). An interpretation of these values

of $\Delta H^\ddagger$ can be rationalised simply by the stronger cation-anion association due to a number of factors of which hydrogen bonding between the cation and anion is the most apparent. With stronger cation-anion association, the anion weakens its interaction with the cationic oxonium solute leading to a significant decrease in the value of $\Delta H^\ddagger$. This can be conceptualised as in Figure 4.4.11.

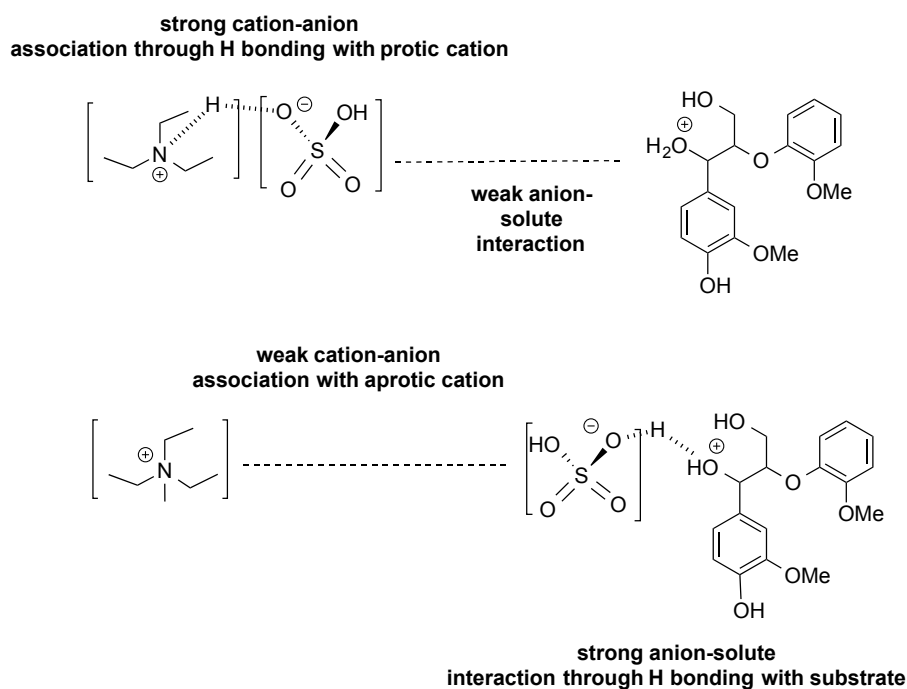


Figure 4.4.11 – Effect of hydrogen bonding on associative forces between cation, anion and substrate

Solvent interaction with the solute decreases the solute's initial energy, subsequently showing a lower difference in $\Delta H^\ddagger$ between the starting material and the activated complex. This trend is maintained with the trend in the aliphatic ammonium cations where sterics and charge density alter cation-anion association. Asymmetric cations bearing one single long alkyl chain, such as [N₄₁₁₀] and [N₄₁₁₁], possess a high charge density on the easily accessible cationic headgroup around the nitrogen, leading to stronger cation-anion association and therefore giving lower values of $\Delta H^\ddagger$. This can be compared to their isomers with greater steric bulk around the nitrogen centre: [N₂₂₂₁] and [N₂₂₂₀], whereby the presence of three ethyl chains on the cation increases the steric shielding between cation and anion, reducing the strength of cation-anion association. In these cases, the anion is more free to interact with the solute, leading to an increase in the value of $\Delta H^\ddagger$ by 33.9 kJ mol⁻¹ for the protic set and 4.1 kJ mol⁻¹ for the aprotic set relative to the [N_{411x}] ILs. The heavily hindered cationic centre in [N₆₆₆₁] further supports this rationale. The

large size of the three hexyl groups around the nitrogen providing both steric bulk, in addition to the lack of hydrogen bonding, significantly reduces the associative forces between the cation and anion. This consequently allows the free anion to solvate the solute and as a result, shows the highest enthalpy of activation at $131.8 \text{ kJ mol}^{-1}$ (Figure 4.4.12).

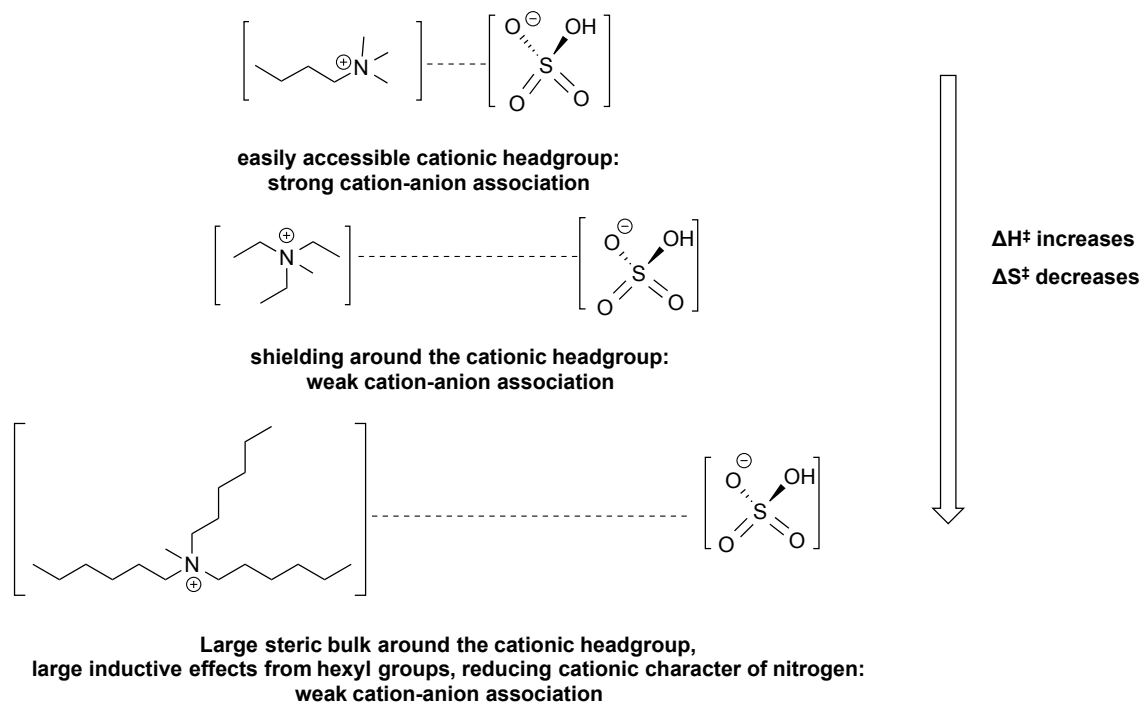


Figure 4.4.12 – Effect of alkyl groups on associative forces between cation and anion

An attempt to explain the anomalous result with the $[\text{C}_4\text{C}_1\text{im}]$ cation was carried out by exploring whether the aromaticity of the imidazolium cation had any effect on the values $\Delta H^\ddagger$ and $\Delta S^\ddagger$. Pyridinium cations were therefore selected and the aromatic $[\text{HPy}]$ cation was shown to be more associated to its anion compared to its aprotic counterpart, with a difference of 18 kJ mol^{-1} in $\Delta H^\ddagger$, as would be expected. The lack of deviation from the trend observed with aliphatic sets of ILs rendered the anomalous results of the imidazolium cations inconclusive.

Comparing the absolute values of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ to those in literature, it is clear the large positive values of $\Delta H^\ddagger$ and the smaller values of $\Delta S^\ddagger$ indicate a unimolecular E1 mechanism in which the protonated substrate dehydrates with the loss of water being rate limiting. The alternative bimolecular E2 mechanism would proceed directly through an enol-ether with the concerted abstraction of the β proton and water. Such a pathway would have a significantly lower $\Delta H^\ddagger$ than was observed here. This is supported by the activation parameters obtained from the bimolecular Menshutkin reaction between triethylamine and iodoethane where such a trend is

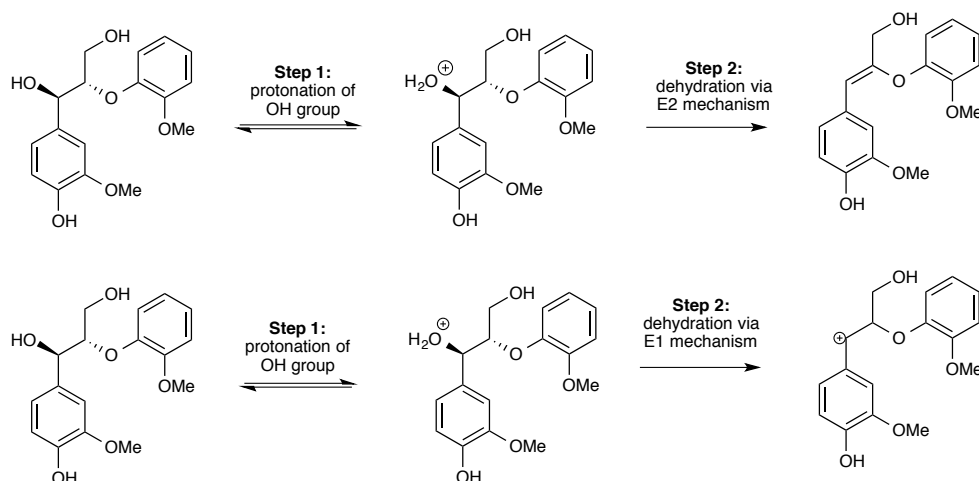


Figure 4.4.13 – E1 and E2 mechanisms for GG dehydration

observed.^[162] A similar example of unimolecular reactions in ILs with $\Delta H^\ddagger$ values has also been reported by Yau *et al.*^[163]

These findings conclude that whilst the selection of cation does not affect the mechanism of the hydrolysis of the β -*O*-4 linkage, significant differences in reaction rate arise depending on the degree of cation-anion association. The protic set of ILs generally show better performance for GG hydrolysis and should therefore be the point of reference for efficient ionic liquid design in biomass processing at lower temperatures.

4.5 Comparison of results with aqueous media

These results illustrate that hydrolysis of model compounds bearing the β -*O*-4 linkage within $[\text{HSO}_4]^-$ ILs, proceed through similar mechanisms as those reported in aqueous acidic systems.^[68, 69] The strong interaction of the anion with the γ -methylhydroxyl group has been postulated to prevent deformylation however it appears that while the $[\text{HSO}_4]^-$ is strongly interacting, deformylation still occurs.^[69, 70] The HSQC results illustrate that while there is evidence of strong interaction of the anion, with new additional γ -methyl ^1H signals, formaldehyde is lost. This is consistent with reported findings in organic/aqueous systems where sulfuric acid was found to promote deformylation whereas acids with more coordinating anions such as HCl or HBr yield fewer deformylated products.^{[69],[164]}

Quantitative comparisons can also be made between the rates of ether cleavage in IL media against other solvent environments. The activation parameters obtained from the Eyring study allow easy extrapolation of the rate constants at different temperatures, however the lack of

straightforward correlation between rates and acid concentrations may complicate the comparison of reaction rates between systems. Nonetheless, the standard aqueous or aqueous/organic systems generally feature acid concentrations in the order of 0.1 M which would have a H_0 value of < 1 due to the convergence of the Hammett acidity and pH scales in dilute aqueous solutions as shown by Grasvik *et al.*^[151] The IL systems used here with H_0 values > 2 are likely to be less acidic than the reactions reported in aqueous environments so general comparisons can be drawn regarding the rate of hydrolysis between these two systems. Table 4.5.1 shows the extrapolated rate constants of the ILs used in this study at 150 °C based on the results in Table 4.4.2.

Table 4.5.1 – Eyring activation parameters for the hydrolysis of GG in a range of $[\text{HSO}_4]^-$ ILs extrapolated at 150 °C.

Ionic Liquid	$\Delta H^\ddagger$ (kJ mol ⁻¹)	$\Delta S^\ddagger$ (JK ⁻¹ mol ⁻¹)	k_{obs} (s ⁻¹ × 10 ⁻³) at 150 °C	k_{obs} (s ⁻¹ × 10 ⁻⁶) at 85 °C
[C ₄ C ₁ im]	104 ± 6	-70 ± 19	0.28	1.12
[HC ₄ im]	118 ± 6	-10 ± 15	7.20	13.8
[HPy]	84 ± 11	-99 ± 30	2.54	28.3
[N-Mepy]	103 ± 6	-52 ± 16	3.27	13.6
[N ₄₁₁₁]	121 ± 9	0 ± 23	10.2	16.8
[N ₄₁₁₀]	75 ± 11	-121 ± 28	2.33	41.2
[N ₂₂₂₀]	109 ± 2	-50 ± 6	0.77	2.31
[N ₂₂₂₁]	126 ± 13	4 ± 34	3.99	5.08
[N ₆₆₆₁]	132 ± 11	16 ± 28	3.07	2.87

^aRate constants originate from Table 4.4.2. Uncertainties are derived from the standard errors of the extrapolated parameters extracted from the linear fits obtained from the Eyring plots (see ESI)

The reported rate constants by Sturgeon *et al.* found that acidolysis of GG proceeded with a pseudo-first order rate constant of $4.2 \times 10^{-4} \text{ s}^{-1}$ at 150 °C in 0.2 M sulfuric acid. The rate of cleavage of GG in [N₄₁₁₁][HSO₄], from extrapolation provided the fastest rate at this temperature at $1.02 \times 10^{-2} \text{ s}^{-1}$. This shows that the rate of ether cleavage in this IL would proceed 25 times faster despite being of lower acidity. Even [N₂₂₂₀][HSO₄], being the slowest performing IL would yield a rate that is almost a two-fold increase over the aqueous reaction.

Comparisons of these results with those reported by Imai *et al* can also be made.^[164] In their study, VG was used as the model compound and the reactions were performed at 85 °C in an 82:18 1,4-dioxane:water mixture with 0.1M H₂SO₄. The rate reported was $2.2 \times 10^{-6} \text{ s}^{-1}$, so when extrapolating the rate constants in Table 4.4.2 to 85 °C, the [N₄₁₁₁][HSO₄] IL would pro-

ceed at a rate 20 times faster than the aqueous/organic system at $4.1 \times 10^{-5} \text{ s}^{-1}$. Furthermore $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$, being the slowest performing IL would provide comparable rates of reaction at $1.1 \times 10^{-6} \text{ s}^{-1}$ despite being of a lower acidity. These findings show that ILs based on the $[\text{HSO}_4]$ anion are effective media for facilitating the cleavage of β -O-4 linkages even in the absence of added acid and reinforces the notion that ether cleavage can be promoted at lower temperatures by this class of ILs through correct selection of cation.

4.6 Conclusions

In this study, it was found that the mechanism of lignin's β -O-4 linkage hydrolysis in $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ proceeded *via* an acid catalysed reaction, whereby the rate determining step involves initial protonation of the α hydroxyl group followed by dehydration, analogous to the mechanism reported in aqueous acidic media. The rate of hydrolysis increased with increased acidity. This conclusion was supported by kinetic studies where water and acid concentration were varied and correlated against the rate constant of each reaction. The lack of correlation between the Hammett acidity of different IL-water-acid systems and reaction rate confirms multiple roles of water in the reaction medium, including acting as a proton transfer agent as well as impeding the dehydration reaction.

In addition to the results obtained from the initial kinetic data, 5 lignin model compounds mimicking the prevalent β -O-4 linkage found in lignin were successfully prepared and characterised using synthetic protocols found in literature. These model compounds emphasise the importance of functionalisation both in solubility and reactivity. HSQC confirms that the γ -methylhydroxy group aids solubility of the model compound through interaction of the hydroxyl group with the $[\text{HSO}_4]^-$ anion, however whilst sulfation is identified, this is followed by deformylation during hydrolysis. The incorporation of highly electron donating substituents on the aryl ring attached to the α -hydroxy group were observed to be of significant importance for the stabilisation of the carbocation formed upon dehydration of the starting material in acidic media. Whilst such substituents promote reactivity, studies in non-ionic media show they also promote condensation reactions post ether cleavage.

Finally, through the use of an Eyring plot, insight into the effects of cation choice on the hydrolysis of the β -O-4 linkage in $[\text{HSO}_4]^-$ ILs was also gained. The Gibbs free energy of activation remained approximately consistent in each IL system with an average value of 124 kJ mol^{-1} . The high enthalpies of activation observed indicated that dehydration occurs *via* an E1 mechanism and the differences in these values across the IL solvents examined were almost fully compensated by the entropic component. These variations in the enthalpy and entropy of activation can be attributed to the associative forces between the cation and anion, influenced primarily by hydrogen bonding and steric effects, determining the degree of solvation of the protonated solute. It can be concluded that whilst the $[\text{HSO}_4]^-$ anion is effective at cleaving the β -O-4 ether linkage,

anion-cation association plays a significant role in determining the solvation of the solute and therefore the rate of reaction. Comparison of these results with rate constants reported in acidic or aqueous media, shows the superior performance of ILs even with reduced acidity, where up to a 25 fold increase in rate can be expected with the best performing ILs compared to an aqueous system with 0.2 M sulfuric acid. This therefore provides scope for rationale design and selection of IL cations for successful lignin depolymerisation and processing at lower temperatures, with these results suggesting that this would be favoured by ILs with increased cation-anion association.

4.7 Experimental

4.7.1 Synthesis of lignin model compounds

Full details on the experimental protocol for the synthesis and characterisation of lignin model compounds are available in Chapter 7 with annotated ^1H NMR spectra available in the appendix.

4.7.2 Reaction procedure for kinetic studies in acidic ionic liquids

Guaiacylglycerol- β -guaiacol ether (GG 99%) was purchased from Tokyo Chemical Industry (Japan) for initial studies until sufficient quantities of synthesised GG were prepared.

3,4,5-trimethoxybenzaldehyde (98%) was purchased from Sigma Aldrich and guaiacol purchased from VWR and these were both used as received. The ILs included in this investigation were prepared following standard protocols involving either the acid-base neutralisation or alkylation of the amine with dimethylsulfate followed by acid-catalysed hydrolysis. The full synthetic procedure and characterisation is available in chapter 7. 95-98% sulfuric acid was purchased from VWR and titrated before use using a Titroline device and deionized water was purchased from VWR and used as received.

The GG substrate was initially dissolved in ethyl acetate and made up to 10 mL using a volumetric flask. Aliquots of this solution containing circa. 0.5 mg of the GG were placed in 8 x 2 mL glass vials and the solvent was left to evaporate overnight leaving the dry substrate. The ILs were vacuum dried overnight at 80 °C before use and 100 mg of the IL was then added, followed by the required amount of water. The vials were sealed and inserted into a heating module (VWR digital heating block) for the allotted amount of time at the required temperature and subsequently cooled in a dry ice-ethanol mixture. 500 μL of an acetonitrile solution containing the internal standard 3,4,5-trimethoxybenzaldehyde was then added with the vial made up to 1 mL through further addition of deionized water. The contents of the vial were then analysed by High Performance Liquid Chromatography (HPLC). HPLC analysis was performed on a Shimadzu Prominence HPLC with a Photodiode array (PDA) detector. Detection was carried

out at 280 nm and using a Purospher STAR RP-18 end-capped column using an isocratic 20% acetonitrile, 80% deionized water method lasting 10 minutes, at a flow rate of 2 mL min⁻¹ and a 2 µL injection volume. 3,4,5-trimethoxybenzaldehyde was used as an internal standard for quantitative calculations of guaiacol yield after calibration and conversion is defined as the molar ratio of guaiacol obtained to the molar amount of GG added initially.

4.7.3 Procedure for the reactivity of model compounds in [C₄C₁im][HSO₄]

A round bottom flask was charged with 25 mg of the model compound (I-V) along with a stirring flea, 1 g of [C₄C₁im][HSO₄] with the required amount of acid and 200 µL of distilled water. The reaction mixture was left to stir for the required amount of time at 100 °C under a steady flow of nitrogen gas. The reaction was then quenched with 1 mL of distilled water and the products extracted with chloroform (3 × 1 mL). The organic washings were then combined and the solvent removed under reduced pressure to yield the dry products, which were then analysed by HSQC spectroscopy.

4.7.4 Procedure for the reactivity of model compounds in toluene

A 2 mL glass vial was charged with 25 mg of the compound (I, III, IV or V), 1 mL of dry toluene and 10 mol % sulfuric acid with respect to the substrate. The glass vial was then capped, placed in a VWR digital heating block, heated to 120 °C for two hours in a closed system, left to cool to room temperature and analysed directly by a Shimadzu GC-MS. The same protocol was repeated for reactions studying acetal formation with the addition of 2 molar equivalents of ethylene glycol with respect to the substrate.

Chapter 5

Oxidative Depolymerisation of Lignin

5.1 Introduction

Lignin is a unique and highly abundant natural source of aromatic compounds, representing roughly 20% of the total mass of the planet's biosphere^[165] and could potentially be a suitable alternative to petroleum feedstocks for the production of plastics, materials and synthetic intermediates. Due to its heterogeneity and high chemical stability, most lignin is currently used as a feedstock for combustion, however, few markets currently exist where lignin is valorized beyond its application as a combustible fuel, including its use as dispersants and emulsifying agents, low grade fuel, phenolic resins and polyurethane foams.^[166, 167, 168, 169, 170] A number of reviews have explored the different catalytic processes and the applications of lignin in obtaining high value, aromatic chemicals.^[156, 170, 171, 172] The main catalytic lignin transformations studied as well as the most commonly identified are summarised in Figure 5.1.1.

Amongst all the catalytic transformations, oxidative technologies offer a large variety of valuable, functionalised aromatics, particularly functionalised benzaldehydes such as vanillin and syringaldehyde. The high abundance of extracted lignin, obtained as a by-product from the pulp and paper industry and from the production of bioethanol, demonstrates its exceptional importance as a suitable future renewable feedstock for a variety of platform chemicals.

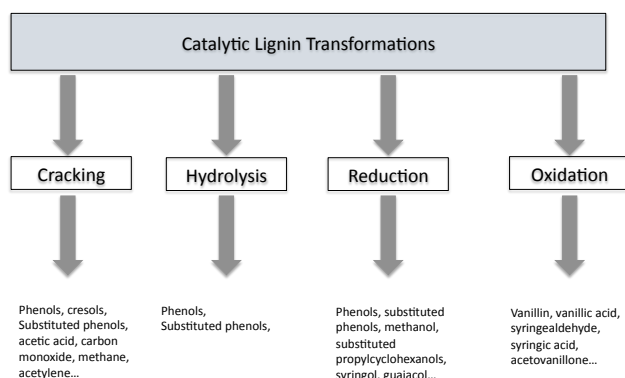


Figure 5.1.1 – Main catalytic lignin transformations studied with some examples of the products obtained, taken from reference [165]

5.1.1 Oxidative depolymerisation of lignin

A recent review by Rogers *et al* describes the current state of the art in lignin valorisation, summarising fundamental mechanistic studies conducted using model compounds followed by studies on lignin itself.^[165] The use of organometallic compounds is commonplace in most oxidative strategies with a range of metals tested to obtain benzaldehyde products from lignin model compounds. Vanadium complexes have seen a multitude of uses when coupled with either molecular oxygen or compressed air to convert aromatic alcohols such as veratryl alcohol, 4-methoxybenzylalcohol and GG to their aldehyde products.^[173, 174, 175, 176] Copper and cobalt complexes have equally been explored with their activity compared to the activity of vanadium catalysts,^[177] where copper(I) chloride and TEMPO were shown to convert lignin model compounds to benzaldehyde in up to 84 % yield. Regardless of oxidant type and the use of ILs as a reaction medium, pH is critical to ensure successful catalytic activity,^[178, 179] with reports from Korpi *et al* documenting the importance of high pH to aid solubility of the salen complex.^[180] For these reasons, basic reagents such as DABCO, triethylamine and inorganic bases such as sodium hydroxide are required to promote catalytic activity in such systems. While such strategies offer feasible routes for selective oxidation of lignin model compounds, these systems suffer from lengthy reaction times and high temperatures.

One study of interest that exploits particular chemical properties of ILs for the selective oxidation of lignin include the use of [C₂C₁im][OTf] on beech lignin using a range of common transition

metal catalysts in compressed air.^[181] Initial screening studies concluded that $\text{Mn}(\text{NO}_3)_2$ was the most effective catalyst, where up to 55 % of the original lignin was converted into depolymerised products. The stoichiometry of the catalyst was also observed to have a large effect on reaction selectivity, where a 20 wt % catalyst loading offered a higher amount of 2,6-dimethoxybenzoquinone (DMBQ) as the major product, whereas a 2 wt % catalyst loading afforded a mix of vanillin and syringaldehyde in addition to DMBQ.

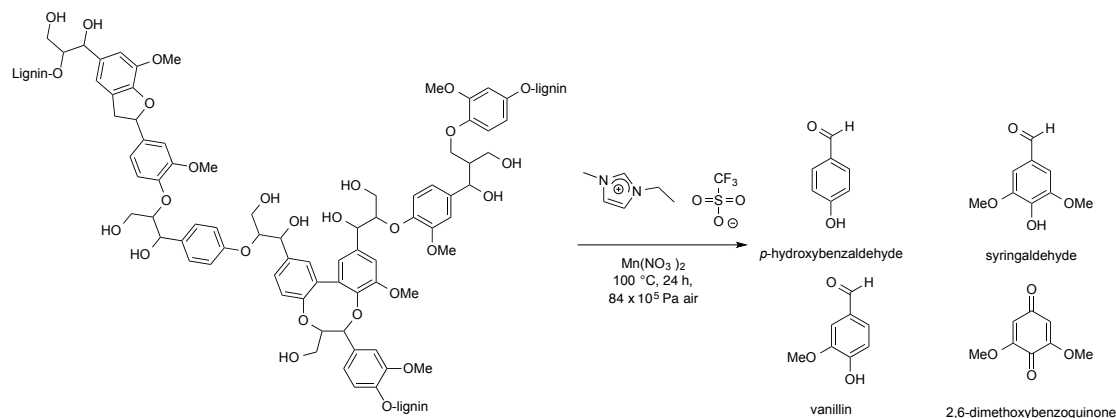


Figure 5.1.2 – Aromatic products obtained through oxidative depolymerisation using $\text{Mn}(\text{NO}_3)_2$

Additional studies using simple catalysts in ILs include employing $[\text{C}_1\text{C}_1\text{im}][\text{MeSO}_4]$ for the catalytic oxidation of rubber wood to vanillin.^[182] Shiwei *et al* reported a novel method of using $[\text{C}_1\text{C}_1\text{im}][\text{MeSO}_4]$, molecular oxygen and CuSO_4 for the oxidation of organosolv lignin. Coupling the reaction medium with an organic extraction phase containing methylisobutylketone, the aromatic aldehydes could be easily removed from the lower IL system with lignin consumption yields reaching 100 % and aromatic aldehydes containing vanillin, syringaldehyde and p-hydroxybenzaldehyde reaching yields as high as 29.7 %.^[183]

5.1.2 Vanillin and its applications

In most oxidative depolymerisation strategies, vanillin has been identified as one of the major bio-based aromatic products that can be obtained. Along with syringaldehyde and p-hydroxybenzaldehyde, vanillin originates from a single sub-unit in lignin and is more abundant in softwoods due to the low Syringyl:Guaiacyl (S:G) unit ratio. The functionality around the aromatic ring allows it to be a versatile platform chemical where through simple synthetic transformations, a number of monomers can be obtained to form useful polymers.^[172] Examples of such monomers are illustrated in Figure 5.1.3.

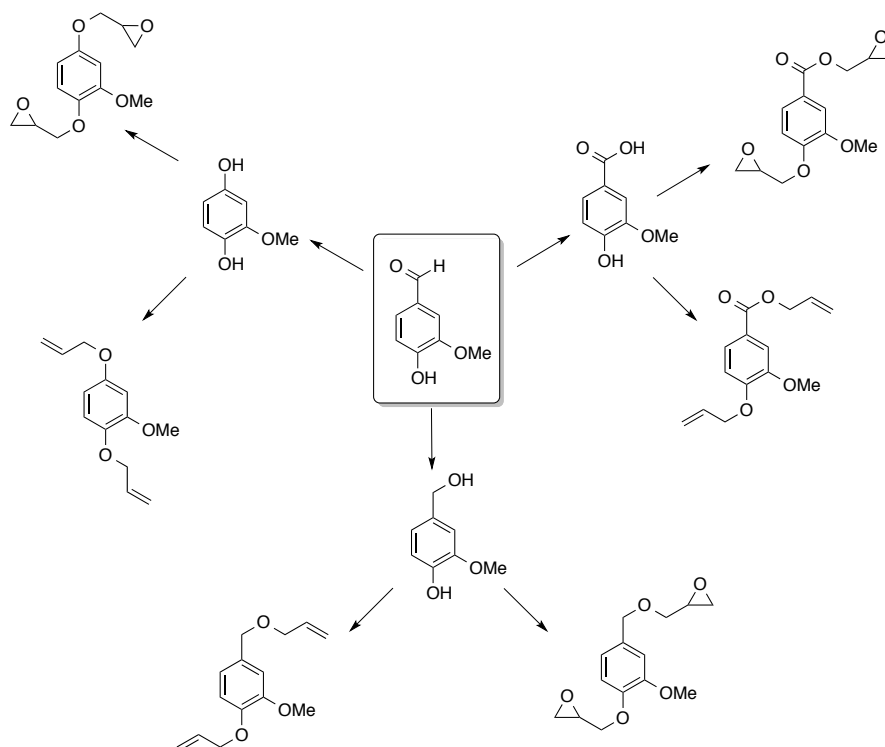


Figure 5.1.3 – Monomers originating from Vanillin taken from reference [172]

The carboxylic, epoxy and vinyl functional moieties in the monomers allow the potential of using vanillin as a renewable building block for the preparation of a range of polymers with high thermo-mechanical strength. Such polymers include epoxy resins, polyesters and polyurethanes with their applications spanning many fields, including uses as adhesives, coatings, plastics, fibers and foams.

5.2 Polyoxometalates

5.2.1 Introduction to Polyoxometalates

Polyoxometalates (POMs) are a class of oligomeric, metal oxide clusters that contain d^0 cations, with $W^{(VI)}$, $Mo^{(VI)}$, $V^{(V)}$ and $Nb^{(V)}$ being amongst the most common. POMs are renowned for exhibiting a number of interesting properties, including synthetic tractability where thermal stability, acidity and varying redox potentials can all be easily modified.^[184] Keggin structures are a family of POMs that adopt spherical conformations during self assembly in aqueous media. The anions typically include 12 structural transition metal atoms known as “addenda atoms”^[185] such as tungsten or molybdenum, surrounding a main group atom such as phosphorus, silicon or aluminium. The Keggin structure is arranged in such a way that the 12 MO_6 octahedra assemble

around the heteroatom which sits in the centre of the structure as depicted in Figure 5.2.1.

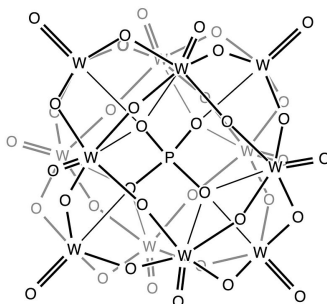


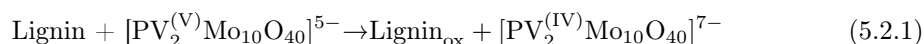
Figure 5.2.1 – Keggin structure POM with formula $[\text{PW}_{12}\text{O}_{40}]^{3+}$

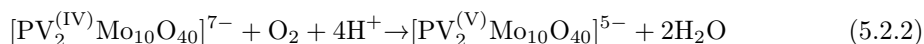
One further important attribute regarding the preparation of POMs is the facile incorporation of catalytically active d-block metals which can substitute d^0 metals, thereby forming heteropolyanionic POMs. Once this occurs, the general formula for the Keggin structure can be presented as $\text{XM}'_a\text{M}''_{12-a}\text{O}^{m-}_b$ where X is a d or p-block heteroatom and M' and M'' are the d^n and d^0 metal centres. The ability to easily incorporate specific metals into the structural framework allows a multitude of POMs to be prepared, displaying a wide range of physical and chemical properties, further increasing the number of its applications.^[186]

5.2.2 Polyoxometalates in delignification chemistry

The high flexibility in the modification of the redox properties of POMs, together with their ease of handling, preparation, robust oxidative stability, low cost and low toxicity have allowed POMs to flourish in their use as oxidation catalysts. A further subclass of the Keggin structures are the mixed vanadium(V) substituted POMs and a series of studies have been reported, using molybdovanadophosphate POMs, for the oxidation of starch and lignin.^[184, 185, 187, 188]

One particular study which aimed to simultaneously delignify pine and oxidise lignin was achieved in a one-pot process, as reported by Rogers *et al.*^[189] $[\text{C}_2\text{C}_1\text{im}][\text{OAc}]$ typically used in the dissolution process was coupled with the POM $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in an oxygen rich environment. Results showed that this system facilitated the dissolution of the biomass substrate, delignification, separation of the hemicellulose component and the oxidation of lignin into a range of small aromatics. Extraction with benzene and THF yielded methyl vanillate as the major lignin oxidation product, as well as smaller quantities of other oxidised aromatics. The role of the POM has been hypothesised to undergo reduction during lignin oxidation, with vanadium reducing from $\text{V}(\text{V})$ to $\text{V}(\text{IV})$ and no reported structural change of the POM:^[188]





5.2.3 Preparation and characterisation of Molybdovanadophosphoric acid

The POM $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ was prepared following the original report by Tsigdinos and Hallada.^[190] The preparation involved sodium metavanadate as the source of vanadium(V), sodium molybdate as the source of molybdenum, with sodium hydrogen phosphate offering phosphorus as the central heteroatom. Dissolving all the starting materials in an acidic solution afforded a red colour. However, after extraction with diethyl ether and concentration of the aqueous phase containing the POM product, a thick viscous solution was obtained that was unable to crystallise. As the POM was intended for use as a catalyst in an IL medium, butylimidazole was added as a base in an attempt to neutralise the acidic POM and therefore crystallise the product in sulfuric acid. Through the addition of excess butylimidazole, a bright orange solid formed which was then filtered off and analysed by Energy dispersive X-ray spectroscopy (EDX) for elemental analysis. The ability of the POM product to effloresce at room temperature meant the product was stored in the fridge and kept in the dark until used. Figure 5.2.2 shows Scanning Electron Microscopy (SEM) images of the POM product at different magnifications. Figure 5.2.3 is the EDX spectrum of the surface of the POM at position 1. Due to the ability of the POM to hydrate, atomic ratios between P, V and Mo were recorded at different positions of the surface of the POM and were used to confirm successful preparation of the POM.

Table 5.2.1 – Abundance of P,V and Mo in weight % without carbon, chromium and oxygen taken at different locations of the surface of the POM

Spectrum Area	P	V	Mo
1	1.58	10.19	63.58
2	2.14	14.4	82.56
3	2.04	13.66	84.3
4	2.14	13.48	84.38
5	1.38	5.72	0
6	1.78	16.27	81.95
7	2.28	15.69	82.03
8	2.13	13.18	84.69
Average	2.01	13.84	80.50

The weight % of each element in the POM was shown to be mostly consistent amongst the

different spectrum areas, however the absence of molybdenum in spectrum 5 was an obvious anomaly that was omitted from further calculations. Average calculated molar ratios between P, Mo and V were as follows: Mo:P, 12.99:1.00 and V:P, 4.21:1.00, showing some variation from the anticipated ratios of Mo:P 10:1 and V:P of 2:1. Results showed that whilst the POM mostly consisted of Molybdenum, a reduced amount of phosphorus than anticipated was present. The overall orange colour of the precipitated product suggests that the catalytically active vanadium species did not undergo any changes in oxidation state and remained Vanadium (V), therefore being able to participate in oxidation reactions. The obtained POM product was then employed directly in scouting tests to identify its catalytic properties.

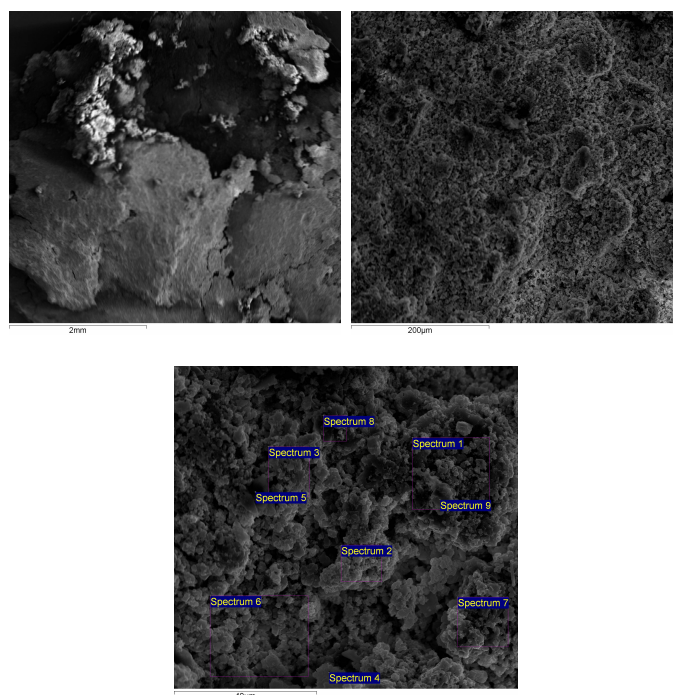


Figure 5.2.2 – SEM images of the POM taken at x 20, x 200 and x 1000 resolutions

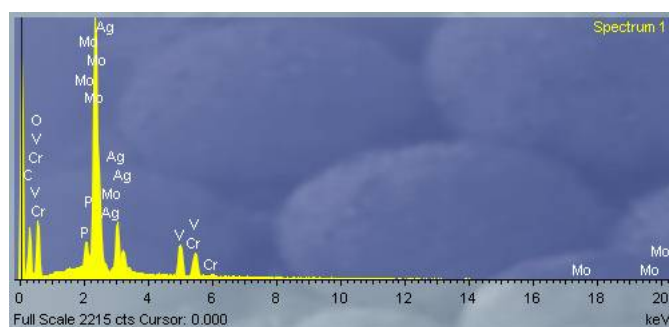


Figure 5.2.3 – EDX spectrum of POM taken at position 1

5.3 Aims and Objectives

Building on strategies that have been highlighted in literature, this study aims to explore the attractive properties of heteropolyanionic POMs in PILs for the oxidative depolymerisation of ionosolv lignin samples, obtained using standard protocols in Dr Jason Hallett’s research group. The POM, $H_5[PV_2Mo_{10}O_{40}]$ was selected to be the catalyst of choice and $[HC_4im][HSO_4]$ as the IL due to its efficiency in hydrolysing the β -O-4 linkage as explored in chapter 4.

The investigation focuses on the importance of oxidant type, comparing and contrasting the oxidative activity of lignin under molecular oxygen, hydrogen peroxide and compressed air, as well as scouting suitable reaction conditions and catalyst loadings that can target vanillin as the main product. Furthermore, different lignin substrates and the influence of pretreatment times are also explored.

5.4 Results and discussion

5.4.1 Pretreatment of Willow and Pine

Two different lignocellulosic feedstocks were selected for oxidative depolymerisation studies, Pine for softwood lignin and Willow for hardwood lignin. These two substrates were selected in order to assess the importance of lignin source on the array of products potentially released upon oxidative depolymerisation. The pretreatment experiments were performed by Dr Somnath Shinde and Dr Charles Vriamont of the Hallett group following established protocols using $[N_{2220}][HSO_4]$ as the IL.^[54, 62] The feedstocks obtained and submitted to oxidative studies were as follows:

- Ionosolv lignin from Willow obtained after a 4 hour pretreatment time (4HW)
- Ionosolv lignin from Willow obtained after a 8 hour pretreatment time (8HW)
- Ionosolv lignin from Willow obtained after a 12 hour pretreatment time (12HW)

- Ionosolv lignin from Pine obtained after a 30 minute pretreatment time (30MP)

The lignin samples from Willow also assess the effects of pretreatment time on the performance of oxidative depolymerisation. The shorter pretreatment time for Pine was selected to ensure the majority of the β -O-4 linkages were still intact with minimal formation of C-C bonds due to condensation reactions.

5.4.2 Lignin characterisation

In order to determine accurate yields of the oxidation products from each lignin sample, part of a compositional analysis protocol known as a Klason test was used to determine lignin content as outlined by the laboratory analytical procedure established by the National Renewable Energy Laboratory.^[191] ^{31}P NMR was used to identify the different hydroxyl groups present within lignin, providing insight into the structural features that could affect the yield and selectivity towards certain oxidation productions. It has been well established that softwood lignins contain low S:G ratios, with a higher abundance of guaiacyl units than syringyl, whereas hardwood lignins contain high S:G ratios. ^{31}P NMR also helped identify the relative abundances of each unit in each lignin sample and is explained below.

5.4.2.1 Klason test

In any deconstruction process, efficient fractionation of the components is necessary in order to ensure complete delignification from the carbohydrate rich pulp. Equally, in order to obtain high purity lignin in the liquor, all remaining hemicellulose has to be removed during the pretreatment process. One way to determine the lignin content of the precipitate is to quantify the lignin, carbohydrate and inorganic components in the sample.^[191] The procedure used to determine lignin content has been commonly referred to as the “Klason test” and involves the acid hydrolysis of any carbohydrate residues remaining on the precipitated lignin post pretreatment, therefore leaving the lignin fraction with some inorganics. Once the carbohydrate sugars have been hydrolysed, the acid insoluble lignin (AIL), acid soluble lignin (ASL) and ash content containing the inorganic compounds can be determined. The complete protocol can be found in the experimental section of this chapter.

Table 5.4.1 – Results from the Klason test of the different lignins obtained post pretreatment showing the total lignin content

Lignin Sample	Feedstock	Pretreatment time	Average AIL %	Average ASL %	Average ash content %	Total lignin content %
30MP	Pine	30 mins	89.4	4.5	0.9	84.4
4HW	Willow	4 h	87.2	2.8	1.8	91.2
8HW	Willow	8 h	76.1	2.8	0.2	77.9
12HW	Willow	12 h	89.9	3.0	1.1	93.6

Results show that all samples were rich in lignin and the 12HW lignin sample had the highest lignin content. The total lignin content can be used to provide a more accurate measure of oxidation product yields and will be used in such calculations to determine the yield of vanillin and syringaldehyde from the lignin substrate.

5.4.2.2 ^{31}P NMR characterisation of lignin hydroxyl groups

Through the use of a phosphitylating agent, ^{31}P NMR is a powerful technique that determines the overall distribution of OH groups present in lignin, including carboxylic groups, phenolic hydroxyls as well as aliphatic groups.^[139, 192, 193] Argyropoulos and Granata identified TMDP as a useful probe, providing sufficient resolution between hydroxyl groups once phosphitylated and is therefore used in this study for characterisation. Pyridine is used to capture the liberated HCl and total conversion of the lignin hydroxyl groups is assumed, with cyclohexanol used as the internal standard. The phosphitylation reaction of the different hydroxyl groups is presented in Figure 5.4.1 and the typical chemical shift regions for each hydroxyl group taken from Pu *et al*^[193] is summarised in Table 5.4.2.

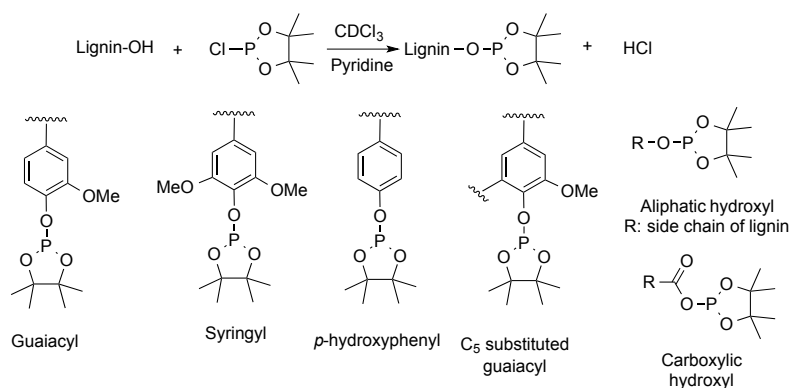


Figure 5.4.1 – Phosphitylation of hydroxyl groups in lignin structural units with 2-chloro-4,4,5,5-tetramethyl-1,3,2-dioxaphospholane (TMDP)^[193]

Table 5.4.2 – Typical chemical shifts and integration regions for lignin samples in a ³¹P NMR spectrum^[193]

Structure	δ (ppm)
Aliphatic OH	154.4-150.0
Phenols	137.6-144.0
C ₅ substituted	140.0-144.5
β-5	~143.5
Syringyl	~142.7
4-O-5	~142.3
5-5	~141.2
Guaiacyl	139.0-140.2
Catechol	~138.9
<i>p</i> -hydroxyphenyl	~137.8
Carboxylic acid OH	133.6-136.0

The four lignin samples obtained through pretreatment with [N₂₂₂₀][HSO₄] and characterised *via* Klason tests were further characterised using the above technique. The objectives of using a ³¹P NMR probe were to determine the relative syringyl and guaiacyl ratios between the lignin samples obtained from Pine and Willow, to assess whether the concentrations of the phenolic hydroxyl groups vary in lignin obtained from Willow at different pretreatment times and to also track the change in concentration of the aliphatic hydroxyl groups. The results are summarised graphically in Figure 5.4.3 and an example of a ³¹P spectrum is presented in Figure 5.4.2, showing the integrations between each hydroxyl group in the NMR region of interest for ionosolv lignin

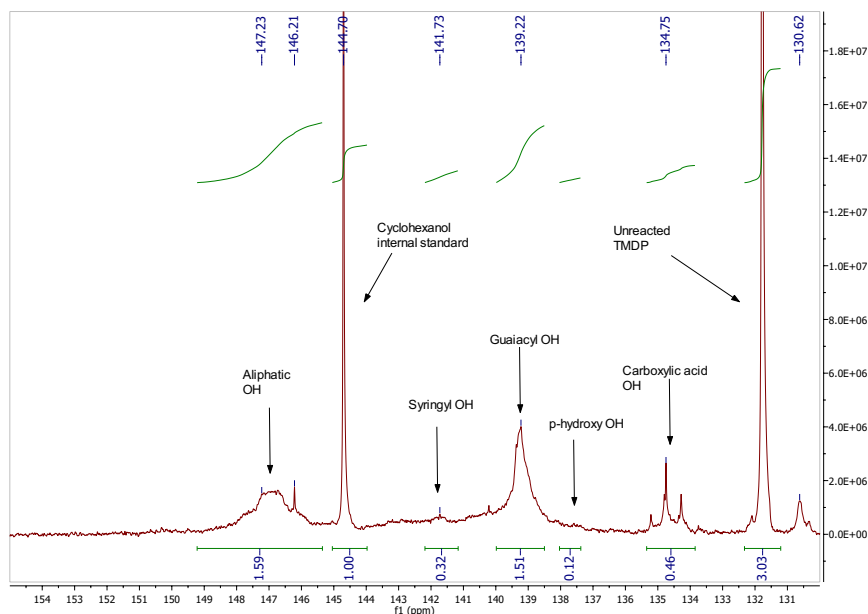


Figure 5.4.2 – ^{31}P NMR of phosphitylated ionosolv lignin from pretreated Pine

obtained from 30MP. All ^{31}P NMR spectra can be accessed in the appendix.

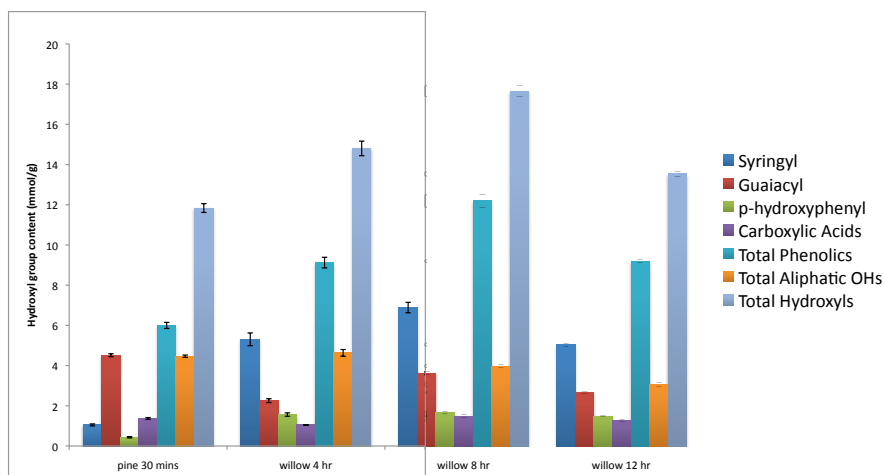


Figure 5.4.3 – Concentration of different hydroxyl groups in pretreated biomass in $[\text{N}_{2220}][\text{HSO}_4]$. Error bars originate from standard deviation from triplicate manual integration of signals.

A low S:G ratio was identified in the lignin sample obtained from 30MP, with an overall ratio of *circa* 1:5, indicating oxidative depolymerisation would yield a higher amount of vanillin to syringaldehyde. Equally, the p-hydroxyphenyl hydroxyl group was comparatively low in abun-

dance, accounting for only 6 % of the total amount of phenolic hydroxyl groups. In all willow samples pretreated at different times, the S:G ratio was higher, with the maximum ratio identified after a 4 hour pretreatment time where the overall ratio was calculated to be *circa* 3:1. The S:G ratio was observed to decrease with time to *circa* 2:1 after a 12 hour pretreatment time. In all cases, the overall abundance of phenolic hydroxyl groups exceeded the abundance of aliphatic hydroxyl groups. In the case of Willow, with an increase in pretreatment time, the abundance of aliphatic hydroxyl groups decreased with the simultaneous increase in phenolic hydroxyl groups. This has been suggested by Brandt *et al* to be due to the increased cleavage of the β -O-4 linkages,^[63] yielding phenolic alcohols which remain inert post cleavage. The decrease in the abundance of aliphatic hydroxyl groups was assumed to be due to the dehydration reactions occurring prior to the hydrolysis of the β -O-4 linkages and the reduction of hemicelluloses attached to the lignin. The similar abundance of total phenolic alcohols to aliphatic alcohols seen in the Pine sample, suggests that after a 30 minute pretreatment, most of the β -O-4 linkages are intact and that the lignin is still able to undergo further depolymerisation.

A comparison between the Pine and Willow lignin samples shows an overall higher hydroxyl group content with Willow which is further reflected by the higher lignin content calculated after the Klason tests. This is also consistent with the difference in pretreatment times. Whilst clear trends are observed in the ^{31}P NMR results of the Willow lignin samples pretreated at different times, the overall lignin content calculated in the Klason tests for lignin obtained from 8HW do not correlate with the observations made with the results from the ^{31}P NMR spectra. The lower lignin content of 77.94 % calculated for lignin obtained from 8HW compared to the 91.2 % calculated for lignin obtained from 4HW suggests that a higher lignin yield is obtained with shorter pretreatment time, contradicting the results obtained by ^{31}P NMR. As Klason tests were repeated in triplicate with the average lignin content reported in Table 5.4.1, no explanation for this disparity was able to be given and will require further analysis.

5.4.3 Oxidative Depolymerisation using POMs in $[\text{HC}_4\text{im}][\text{HSO}_4]$

The lignin samples obtained *via* pretreatment at different times were submitted to catalytic oxidation reactions using the POM in $[\text{HC}_4\text{im}][\text{HSO}_4]$, which will be referred to henceforth as POM-PIL, following a similar protocol as described by Prado *et al.*^[194] Molecular oxygen and hydrogen peroxide were selected as oxidants. Prado *et al* highlighted that the best phenolic yields were obtained when 5 wt% hydrogen peroxide was employed, this prevented over-oxidation of vanillin to vanillic acid. For this reason, the loading of hydrogen peroxide was fixed at 5 wt % for all studies. Due to the unprecedented nature of the investigations involving POMs as oxidation catalysts in acidic ILs, scouting studies of different catalyst loadings and oxidant type were carried out. In all cases, once the reaction went to completion, water was added to precipitate out the catalyst and any unreacted lignin. The suspensions were centrifuged to remove the aqueous phase and ethyl acetate was used to extract the aromatic products from the re-

action mixture as studies showed it was most selective for vanillin extraction (see appendix). As some of the catalyst was seen to precipitate out along with the lignin, no studies on the precipitated solids were carried out. Once the ethyl acetate was removed, an oil was obtained usually being of a weight between 5 -15 wt % of the original lignin loading. GC-MS was used as the characterization technique to analyse the extracted oils. Through the use of a calibrated library of compounds, the abundance of 17 aromatic compounds, previously identified as common oxidation products from lignin, could be determined. These compounds include phenol, o-cresol, m-p-cresols, guaiacol, catechol, 3-methylcatechol, 3-methoxycatechol, 4-methylcatechol, syringol, 4-hydroxybenzaldehyde, 4-ethylcatechol, vanillin, acetovanillone, varatrol, 4-hydroxy-3-methoxyphenol, syringaldehyde and acetosyringone.

The effects of catalyst loading and oxidant type were first assessed on lignin obtained from 4HW. A series of GC chromatograms is presented in Figure 5.4.4, showing the effect of POM loading on the oxidation of 4HW lignin in molecular oxygen. The absence of detectable compounds when no catalyst is present indicates the requirement of a catalyst to allow the reaction to proceed, however the relatively low abundance of products present when 20.6 wt % catalyst is incorporated indicates that catalyst loading also affects the oxidative degradation of the lignin. All oils contained a complex mixture of compounds which originated from lignin, carbohydrates and the IL. As this study focuses on vanillin as the platform chemical of interest, the yields of vanillin and the hardwood equivalent syringaldehyde were used to evaluate the effects of different reaction systems, oxidants and lignin substrates. The largest peak identified in each chromatogram was assigned to be the IL derived product, 1-butyl-2,4,5-trioxoimidazolidine with a retention time of 17.66 minutes, with small quantities of other IL oxidised products. In these studies, selectivity towards the aldehyde was observed, with very small quantities of the carboxylic acid detected.

The array of calibrated compounds identified in the oil extracted from oxidised lignin obtained from 4HW at different catalyst loadings is presented in Table 5.4.3. Syringaldehyde was observed to be the compound present in highest abundance at *circa* 200 ppm at 5 wt % POM loading, constituting 3.7 % of the detected products in the oil. This confirmed the successful activity of the reaction to oxidise the syringyl units in hardwood. In all reactions, aside from the oxidised IL, syringaldehyde was identified as being the most abundant product present in the oils.

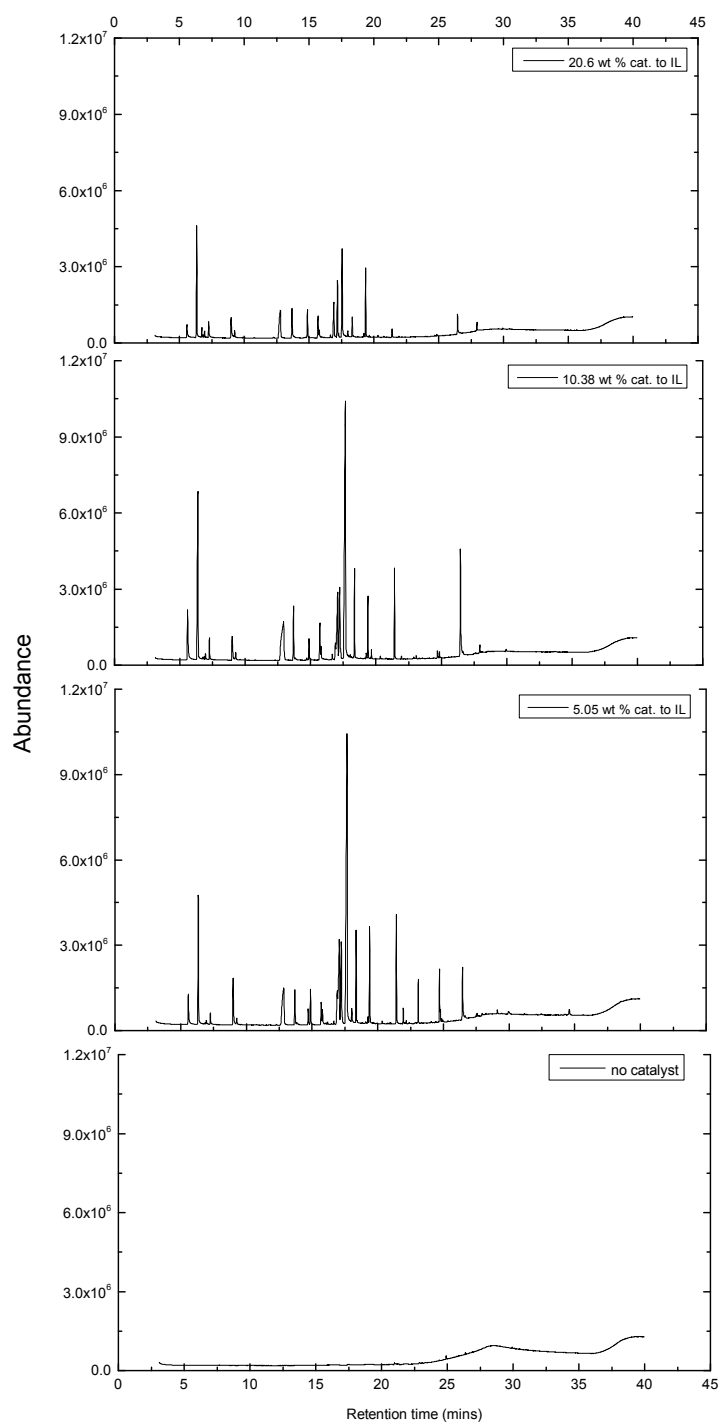


Figure 5.4.4 – GC chromatograms of lignin products obtained from 4HW, oxidised by molecular oxygen for 5 hours with different loadings of the POM catalyst at 100 °C

Table 5.4.3 – Calibrated aromatic products found in obtained oils post oxidative depolymerisation of 4HW lignin

Compound	Retention time	1 wt % POM to IL (ppm)	5 wt % POM to IL (ppm)	10 wt % POM to IL (ppm)	20 wt % POM to IL (ppm)
Phenol	5.57	12.6	69.3	141	37.8
Guaiacol	7.26	4.0	15.4	30.7	29.2
Syringol	13.69	7.0	53.2	91.4	58.5
Vanillin	14.88	24.5	65.3	44.3	56.0
Acetovanillone	16.66	1.2	3.0	4.4	3.85
Syringaldehyde	19.38	56.1	201	141	153
Acetosyringone	20.33	1.6	4.4	5.60	3.82

^aConditions: oxidised by molecular oxygen for 5 hours with 5 wt % of the POM catalyst to the IL at 100 °C

Figure 5.4.5 presents a comparison of the vanillin and syringaldehyde yields when molecular oxygen and hydrogen peroxide are employed as oxidants. When comparing product yields to the initial loading of lignin, guaiacol was observed to increase with an increase in catalyst loading when both hydrogen peroxide and molecular oxygen were employed as oxidants. The highest yields of both vanillin and syringaldehyde were obtained when 5 wt % of the catalyst to the IL was employed using molecular oxygen as the oxidant. In all reactions, the calculated yield of syringaldehyde greatly exceeded the yield of vanillin. This supports the results obtained from the ³¹P NMR data for hydroxyl group characterisation in lignin, whereby a higher S:G ratio is observed. Furthermore, when the catalyst is present in the reaction medium, molecular oxygen generally showed improved performance compared to hydrogen peroxide as an oxidant, however in all samples significant amounts of 1-butyl-2,4,5-trioximidazolidine was detected, showing the preferential oxidation of the IL over the lignin fragments.

A similar study was then carried out on lignin obtained from 30MP to obtain higher quantities of vanillin using hydrogen peroxide as presented in Figure 5.4.6. Once again, oxidation is favoured with the presence of the POM catalyst where more than a 20 fold increase in the quantity of vanillin is observed when 20 wt % of the catalyst is employed compared to the system with no catalyst. Furthermore, when no catalyst is present, a considerable amount of vanillic acid is detected, therefore demonstrating the importance of the POM to also mitigate the potent oxidising ability of hydrogen peroxide. The absence of syringaldehyde as a product also supports the results obtained from the ³¹P NMR data, where a lower S:G ratio provided increased yields of vanillin.

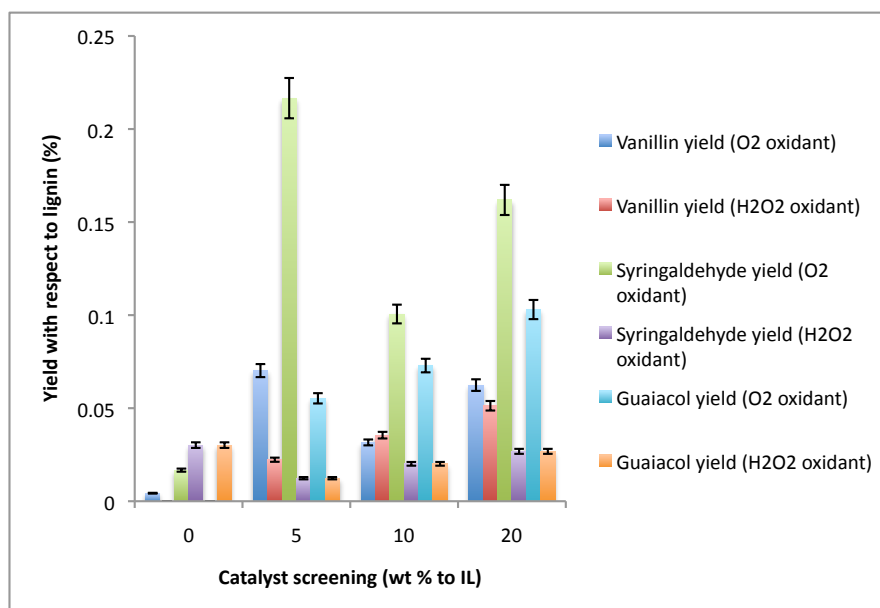


Figure 5.4.5 – Initial screening tests for the oxidative depolymerisation of 4HW with different POM loadings in $[\text{HC}_4\text{im}][\text{HSO}_4]$, stirring at 500 rpm, at 100 °C left for 5 hours, using molecular oxygen and hydrogen peroxide as the oxidants. Error bars originate from the error in GC-MS calibration of platform chemicals

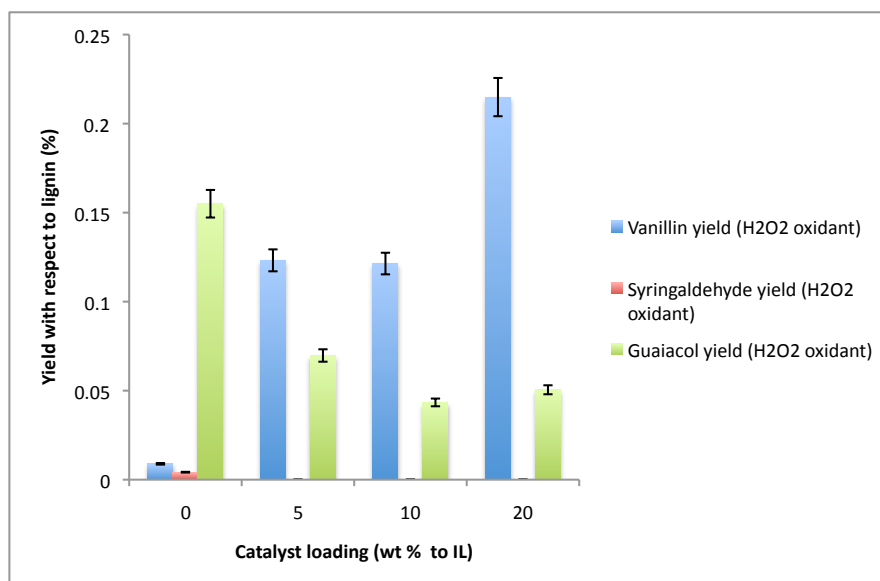


Figure 5.4.6 – Initial screening tests for the oxidative depolymerisation of lignin obtained from 30MP with different POM loadings in $[\text{HC}_4\text{im}][\text{HSO}_4]$, stirring at 500 rpm, at 100 °C left for 5 hours, using hydrogen peroxide as the oxidants. Error bars originate from the error in GC-MS calibration of platform chemicals

The organic extracts from the IL of lignin samples from 4HW and 30MP oxidised using hydrogen peroxide with and without catalyst are displayed in Figure 5.4.7. When a catalyst has been employed, the organic extracts adopt either a green or blue colour. This indicates leeching of the catalyst and reduction of the vanadium in the POM from vanadium (V) to vanadium (IV) for sample D with the green colour showing a mix of the two in sample B.

Attempts to optimise the reaction in order to obtain higher yields of vanillin were carried out

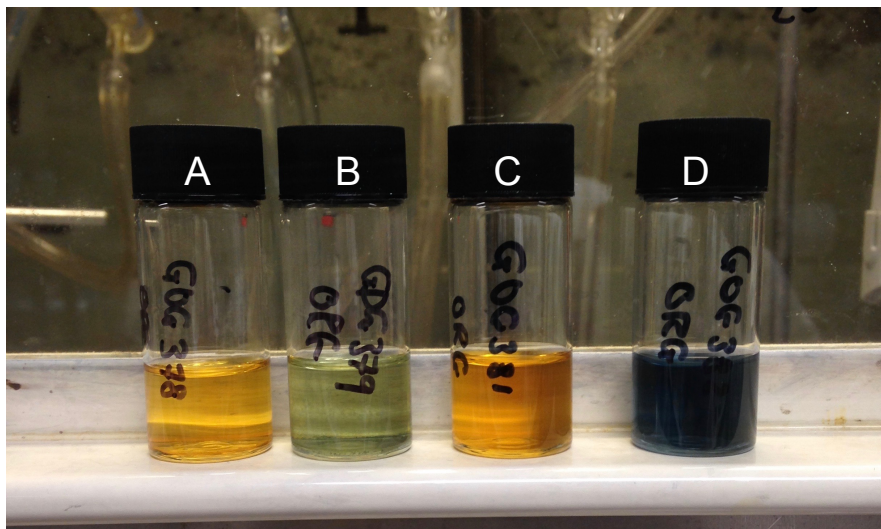


Figure 5.4.7 – Extracted oils from POM-PIL aqueous phase with A from lignin obtained from 4HW with no catalyst employed, B from lignin obtained from 4HW with 5 wt % POM employed, C from lignin obtained from 30MP with no catalyst employed and D from lignin obtained from 30MP with 5 wt % POM employed.

by increasing the reaction temperature to 150 °C. Lignin obtained from both 30MP and 4HW were used as substrates and neither showed any detectable amounts of aromatic products. The effect of shorter reaction time at 100 °C was then explored, as the lack of detectable products at prolonged reaction times and temperatures may have caused the aldehyde products to engage in further reactions after oxidation, potentially yielding water and CO₂ and involatile solids. The reaction was repeated for all four lignin samples over the course of an hour at 100 °C to assess whether such conditions favour higher yields of aldehyde products, as well as comparing the importance of lignin substrate. Figure 5.4.8 presents these results.

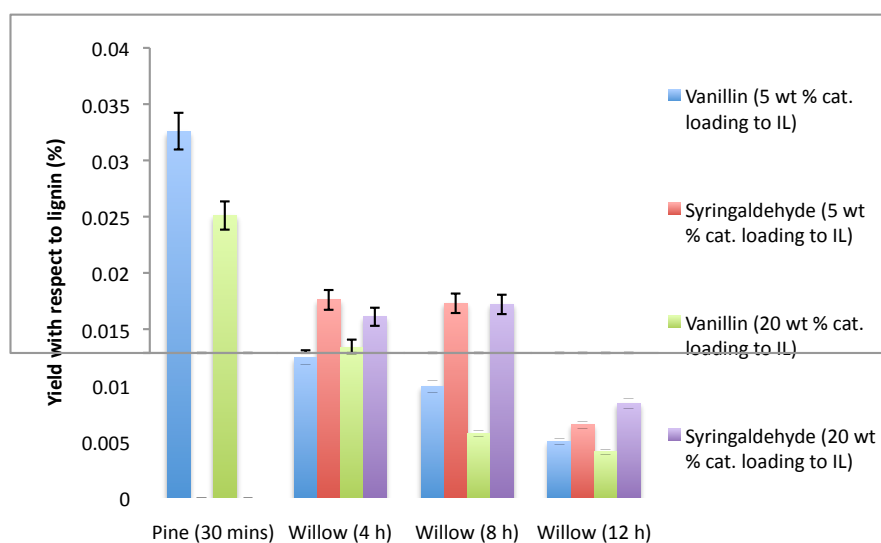


Figure 5.4.8 – Oxidative depolymerisation of all lignin samples with different POM loadings in $[\text{HC}_4\text{im}][\text{HSO}_4]$, stirring at 500 rpm, at 100 °C left for 1 hour, using hydrogen peroxide as the oxidant. Error bars originate from the error in GC-MS calibration of platform chemicals.

Lignin from 30MP was shown to provide the highest yields of aldehyde products and amongst all the lignin samples obtained from Willow, lignin from 12HW afforded the lowest yields of aldehydes. This was presumed to be due to the increased amount of condensation products precipitated from the liquor, where there is a decrease in abundance of β -O-4 linkages and an increase in the abundance of the more robust C-C bonds. Once again, 1-butyl-2,4,5-trioxoimidazolidine was present in all samples and constituted between 15 and 30 % of detectable products in the extracted oils. In terms of the overall quantities of vanillin and syringaldehyde produced and extracted, the yields were calculated to be an order of magnitude lower than when the reaction is left over a 5 hour period, showing that both shorter reaction times and higher temperatures are detrimental to oxidation activity and that a balance must be found between the two.

While some insight into preferable conditions for oxidative depolymerisation was identified, the overall yields of all the oxidised aromatic compounds were low, with the highest yields of vanillin reaching around 0.2 % of the original lignin when hydrogen peroxide was used as the oxidant and 20 wt % of POM to IL was employed. Nevertheless, comparing this to previously reported studies, results from Prado *et al* showed that the oxidised Miscanthus lignin pretreated for 8 hours gave significantly lower yields of vanillin and syringaldehyde. In these reported studies, with 5 wt % hydrogen peroxide, no vanillin or syringaldehyde was detected at all in the oil and when 10 wt % hydrogen peroxide was added, vanillin and syringaldehyde only accounted for 0.019 % and 0.007 % of the detectable products present in the oil respectively, representing trace amounts

compared to lignin sample itself.^[194] In the POM-PIL system studied in this investigation, the oil obtained from 30MP lignin with 5 wt % POM loading and 5 wt % hydrogen peroxide contained 0.32 % vanillin, a marked increase compared to the system employed by Prado *et al.*

The choice of oxidant was also shown to be important as results with 4HW lignin indicate that higher yields of syringaldehyde can be obtained with molecular oxygen compared to hydrogen peroxide. This was shown not to be the case with 30MP lignin, where hydrogen peroxide provided similar yields of aldehyde products as when molecular oxygen was used on 4HW lignin. Finally, lignin obtained from willow after different pretreatment times highlights the impact of pretreatment time on syringaldehyde yield. The Klason tests show that the purest lignin was obtained after a 12 hour reaction period, however once subjected to oxidation, the yields of aldehyde products were significantly lower than the lignins obtained after shorter pretreatment times due to the decrease in β -O-4 linkages and increase in C-C bonds from condensation reactions.

5.4.4 Oxidative Depolymerisation with $\text{Mn}(\text{NO}_3)_2$ in $[\text{C}_4\text{C}_1\text{im}][\text{OTf}]$

Stark *et al.*'s recent report employing $\text{Mn}(\text{NO}_3)_2$ as a catalyst in triflate ILs using compressed air as the oxidant was shown to yield up to 11.5 wt % 2,6-dimethoxybenzoquinone as well as vanillin and syringaldehyde. Similar reaction conditions were carried out on 30MP and were also repeated using molecular oxygen and 5 wt % hydrogen peroxide to assess whether such systems could provide higher yields of the aldehyde products. 2 wt % and 20 wt % loading of the catalyst to the lignin were employed to replicate Stark's system. The results showing the overall vanillin yield are presented in graphical form in Figure 5.4.9.

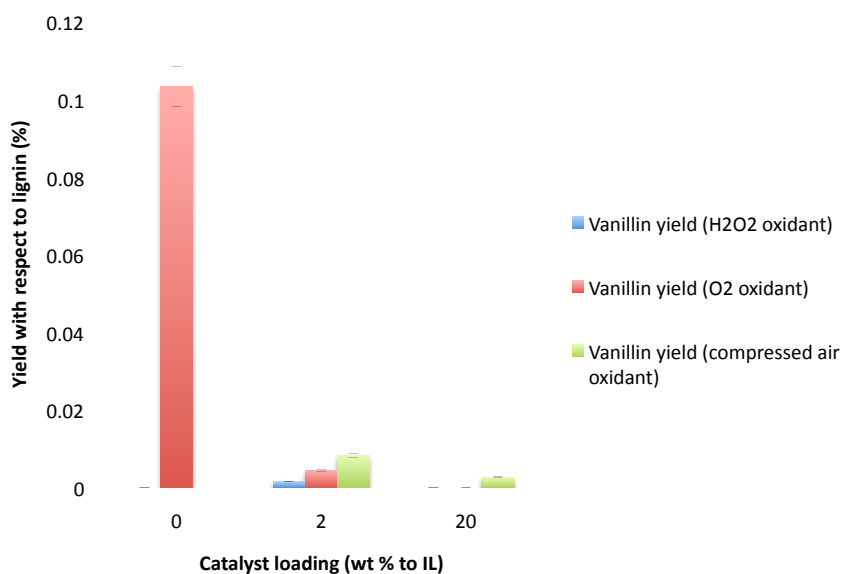


Figure 5.4.9 – Oxidative depolymerisation of lignin obtained from 30MP with different loadings of $\text{Mn}(\text{NO}_3)_2$ in $[\text{C}_4\text{C}_1\text{im}][\text{OTf}]$, stirring at 500 rpm, at 100 °C left for 5 hours using different oxidants. Error bars originate from the error in GC-MS calibration of platform chemicals.

Results show no substantial increase in vanillin yield when the catalyst $\text{Mn}(\text{NO}_3)_2$ was employed with its activity only promoting the oxidising ability of compressed air. Interestingly, the highest yield of vanillin was obtained when no catalyst was present at all and when molecular oxygen was used. In this reaction, vanillin constituted 12.4 % of the total detectable products in the oil, the highest amount of vanillin observed in all of the extracted oils. However, this only represented a yield of 0.10 % compared to the original lignin. When hydrogen peroxide was used as the oxidant, no vanillin was observed at all, however vanillic acid constituted over 10% of the total detectable products in the oil and the oxidised IL cation, 1-butyl-2,4,5-trioxoimidazolidine constituted over 20 %. This showed the overly potent oxidising ability of hydrogen peroxide in $[\text{C}_4\text{C}_1\text{im}][\text{OTf}]$ and that optimal activity can be achieved with molecular oxygen that will both reduce the amount of the IL oxidised whilst selectively oxidising the lignin fragments to vanillin rather than vanillic acid. Comparing these results to those obtained with POM and hydrogen peroxide oxidant, double the amount of vanillin can be obtained when 20 wt % of the POM is employed as the catalyst after a 5 hour reaction time, therefore showing the superior activity of POMs in oxidation reactions.

5.5 Conclusions and future work

Oxidative depolymerisation studies for lignin have previously been investigated using a wide range of catalysts, of which the POM catalyst $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ has shown promise in success-

fully oxidising lignin fragments. The POM catalyst containing butylimidazolium cations was prepared and the atomic ratios of P, V and Mo were calculated. A novel system encompassing the POM catalyst and $[\text{HC}_4\text{im}][\text{HSO}_4]$ was employed with a range of oxidants to depolymerise characterised lignin samples extracted from Pine and Willow, exploiting the ability of the IL to hydrolyse the β -O-4 linkages and the oxidation properties of the POM.

In summary, characterisation of the lignin samples showed a higher S:G ratio for lignin samples obtained from Willow and a lower S:G ratio for the lignin sample obtained from Pine. This confirms the difference in initial lignin composition of both the Willow and Pine substrates. In all oxidation studies, syringaldehyde was identified as the main product from willow lignin samples and vanillin the main product from lignin obtained from Pine. The effect of pretreatment time showed that although purer lignin was extracted after longer pretreatment times, the aldehyde yields decreased, presumably due to increased C-C linkages that form *via* condensation reactions which remain resilient to oxidative depolymerisation. In terms of the activity of the POM, it was shown that in the presence of molecular oxygen, the POM is required in order to initiate oxidation. The highest yields of aldehyde products was obtained when 5 wt % of the POM to IL was employed. Hydrogen peroxide showed successful oxidation however, the POM is required in this instance to mitigate the high oxidative capability of the oxidant, reducing any further oxidation of vanillin to vanillic acid. The overall yields of syringaldehyde and vanillin were low, and did not exceed 0.22 % of the original lignin sample, even though they represented a large proportion of the detectable products in the extracted oil. Attempts at optimising the reaction in order to obtain more vanillin were conducted both by increasing temperature and shortening the reaction time, both of which did not show improved performance. It was concluded that in this investigation, the best yields were obtained after a 5 hour reaction time at 100 °C using either molecular oxygen or hydrogen peroxide. Comparing the vanillin yields obtained with the POM and with the system proposed by Stark *et al*, our system showed overall improved activity, with double the amount of vanillin being obtained.

The major drawbacks of the POM-PIL system employed in this investigation include the overall poor yields of aldehyde product obtained from the lignin samples and the oxidation of the IL cation which extracts into the oil. This has been highlighted in previous investigations and will remain a significant challenge in order to make this process economically feasible. Further studies in finding suitable reaction conditions will be required, including evaluating the effects of increasing the partial pressure of molecular oxygen and exploring other catalysts that may promote oxidative depolymerisation. As the results reported in this chapter are initial scouting studies, once optimum conditions have been selected, the reactions must be repeated to see the reproducibility of the system and to discern whether the POM-PIL system is recyclable. Furthermore, studies into the structural changes of the remaining lignin will need to be conducted in order to identify whether the low yields of aromatic products were due to incomplete reactivity

of the lignin or due to competitive condensation reactions. Lastly, no attempts at selectively extracting vanillin were conducted, which will be the predominant challenge due to the complex mixtures of products obtained in each oil.

5.6 Experimental

5.6.1 Klason analysis of recovered ionosolv Lignin

200-300 mg of the sample was weighed out into a pressure tube and the weight was recorded (sartorium CPA 1003 S balance, +/- 0.0001 g). 3.00 mL of 72 % sulfuric acid was added to each pressure tube and stirred with a Teflon stir rod until thoroughly mixed. The pressure tubes were placed in a water bath set at 30 °C and were left 60 minutes, with the mixture stirred every 15 minutes. 84 mL of deionized water was then added. The pressure tubes were then closed with Teflon caps and the samples were mixed by inverting the tube several times to eliminate any phase separation. The tubes were then placed in an autoclave (Sanyo Labo Autoclave ML5 3020 U) for one hour set at 121 °C and then left to cool to room temperature. The contents of each autoclaved solution were then filtered through preweighed ceramic crucibles with the filtrate recovered for further analysis. The solid residue was then washed with copious amounts of deionized water. The crucibles containing the residue were placed in a convection oven at 105 °C for 24 hours, placed in a desiccator for 15 minutes and weighed to determine the amount of acid insoluble lignin (AIR) present. Once consistent weights were recorded, the crucibles and residues were placed in a muffle furnace at 575 °C for 4 hours, removed and cooled in a desiccator with the weights of the crucibles recorded in order to determine the ash content. The following equations were used to determine the AIR and AIL content:

$$\% \text{ AIR} = \frac{\text{Weight}_{\text{crucible plus AIR}} - \text{Weight}_{\text{crucible}}}{\text{ODW}_{\text{sample}}} \times 100 \quad (5.6.1)$$

$$\% \text{ AIL} = \frac{(\text{Weight}_{\text{crucible plus AIR}} - \text{Weight}_{\text{crucible}}) - (\text{Weight}_{\text{crucible plus ash}} - \text{Weight}_{\text{crucible}})}{\text{ODW}_{\text{sample}}} \times 100 \quad (5.6.2)$$

The acid soluble lignin in the filtrate was analysed by UV analysis at 240 nm using a Perkin Elmer Lambda 650 UV/Vis spectrometer using the equation below.

$$\% \text{ ASL} = \frac{\text{UV}_{\text{abs}} \times \text{Volume}_{\text{filtrate}} \times \text{Dilution}}{\epsilon \times \text{ODW}_{\text{sample}} \times \text{Pathlength}} \times 100 \quad (5.6.3)$$

Where UV_{abs} is the average UV-Vis absorbance for the sample at the appropriate wavelength, ϵ is the absorptivity of biomass at specific wavelength, $\text{ODW}_{\text{sample}}$ = weight of sample in milligrams

and Pathlength is the pathlength of the UV-Vis cell in cm.

5.6.2 ^{31}P NMR analysis of ionosolv Lignin

Quantitative ^{31}P NMR spectra of all lignin preparations were obtained using published procedures. The solvent was prepared using anhydrous pyridine and deuterated chloroform solvent solution (1.6:1, v/v). A second mixture solution was prepared containing 3.6 mg of chromium (III) acetylacetonate solution (5.6 mg/mL in the pyridine/ CDCl_3 solution) as a relaxation reagent. Approximately 10 mg of previously dried Ionosolv lignin was accurately weighed into a 2 mL glass HPLC vial. An aliquot of 100 μL of anhydrous pyridine and chloroform solution was added under stirring. This was followed by the addition of 50 μL of cyclohexanol (20.5 mg/mL in pyridine/ CDCl_3 solution), as an internal standard and 50 μL of the chromium (III) acetylacetonate solution. Finally, 50 μL of the phosphitylating reagent (TMDP) was introduced and the sealed solution vortex mixed intensely for around 5 minutes or until completely dissolved. Samples were then transferred into Shigemi NMR tubes. All the above solutions were protected under nitrogen. The NMR experiments were carried out at 298 K on a Bruker Avance 500 MHz NMR spectrometer. A relaxation delay of 25 seconds was used between 30° pulses, and the number of scans was 127. An inverse gated decoupling pulse sequence was used to obtain quantitative spectra. The acquisitions were performed at room temperature. Chemical shifts were calibrated relative to the internal standard, i.e. the cyclohexanol peak signal centered at δ 144.2 ppm. Integration regions that were used to assign the signals are tabulated in Table 5.4.2. Quantitative estimates of the various hydroxyl containing functional groups were made by calibrating to the integration region of the internal standard signal (cyclohexanol) and normalising by the weight of the lignin sample to obtain a value in mmol OH/g lignin.

5.6.3 Preparation of Pentaimidazolium-10-Molybdo-2-vanadophosphate^[190]

Sodium metavanadate (12.2 g) was dissolved by boiling in 50 mL of distilled water then mixed with Na_2HPO_4 (3.55 g) in 50 mL of water. After the solution was cooled, 2.5 mL of concentrated sulfuric acid was added and the solution developed a red color. An addition of $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$ (60.5 g) dissolved in 100 mL of water was then made. While the solution was vigorously stirred, 42.5 mL of concentrated sulfuric acid was added slowly, and the hot solution was allowed to cool to room temperature. The 10-molybdo-2-vanadophosphoric acid was then extracted with 250 mL of diethyl ether. Air was passed through the heteropoly etherate (bottom layer). The aqueous solution containing the POM was cooled in an ice bath. An excess of 1-butyylimidazolium was then added to the aqueous phase to precipitate out an orange solid. The solid formed was filtered, washed with water and air dried affording a bright orange solid (65.8 g).

5.6.4 SEM/EDX characterisation of Pentaimidazolium-10-Molybdo- 2-vanadophosphate

Energy Dispersive X-ray Spectroscopy (EDX) was performed in combination with SEM imaging (JSM 6400, Jeol, 20 keV) to obtain surface elemental analysis for the POM catalyst once precipitated using butylimidazole and dried. Each sample is mounted on carbon adhesive tape prior to insertion into the imaging chamber (ultra-high vacuum pressure) and sputter coated with a 5 nm chromium deposit to ensure complete sample surface conductivity and to provide effective contrast. Therefore carbon and chromium elemental quantification has been ignored in analysis.

5.6.5 Oxidative depolymerisation of ionosolv lignin using hydrogen peroxide as an oxidant

The IL (1 g) was placed in a 10 mL pear-shaped flask loaded with a flea magnet and a suba-seal. The appropriate amount of catalyst was then loaded and the IL – catalyst mixture was left to stir at 100 °C for one hour until complete dissolution of the catalyst was observed. The solution was then left to cool to room temperature. Hydrogen peroxide was then added (166 μ L, 37 wt % in H₂O), followed by lignin (30 mg) to the pear-shaped flask. The lignin and IL-catalyst mixture was then placed in an oil bath, capped with a suba-seal with a needle outlet. The reaction was left to stir for the allotted time under stirring and then left to cool to room temperature. Distilled water was then added to the flask (3 mL) in order to precipitate out the unreacted lignin and POM catalyst. The content of the flask was then poured into a pre-weighed falcon tube and a further 2 mL of water was used to rinse out the flask. The tube was then centrifuged at 4000 rpm for 10 minutes. The aqueous layer was decanted from the solid and kept aside. A further 5 mL of water was added to the falcon tube containing the solids and the mixture was centrifuged once again. The supernatant was decanted and disposed of whilst the solids in the tube were dried in an oven at 50 °C overnight to remove the remaining water. The lignin content was then weighed to determine the amount of reacted lignin. The depolymerised products in the aqueous layer were extracted through washing with ethyl acetate (3 x 2 mL). The organic washings were then removed under reduced pressure and weighed. A small quantity of the residue was then analysed by GC-MS to determine the amount of vanillin, vanillic acid, syringaldehyde and syringic acid.

5.6.6 Oxidative depolymerisation of ionosolv lignin using molecular oxygen as an oxidant

Oxidative depolymerisation of ionosolv lignin using molecular oxygen as an oxidant followed the same protocol as 5.6.5 with the addition of oxygen replacing hydrogen peroxide. Once the lignin and POM-PILs mixture was placed in an oil bath, an oxygen inlet was inserted through the suba-seal and into the flask. The oxygen flow rate was regulated to ensure saturation of the mixture (circa 100 bubbles per minute).

5.6.7 Oxidative depolymerisation of ionosolv lignin using compressed air as an oxidant

Oxidative depolymerisation of ionosolv lignin using compressed air as an oxidant followed the same protocol as 5.6.5 with the addition of compressed air replacing hydrogen peroxide. A Parr 100 mL pressure vessel was loaded with 10 mL of the IL, followed by the required amount of catalyst and the lignin. The reactor was then sealed, heated to 100 °C and pressurized with air to 100 bar.

5.6.8 GC-MS analysis of lignin post oxidative depolymerisation

GC-MS characterisation was done *via* GC (7890A)-MS (5975C inert MSD with Triple-Axis Detector) Agilent equipped with a capillary column HP-5MS ((5%-Phenyl)-methylpolysiloxane, 60 m x 0.32 mm). The temperature program started at 50 °C then was raised to 120 °C at 10 °C min⁻¹, held for 8 minutes, raised to 280 °C at 10 °C min⁻¹, held for 5 minutes, raised to 300 °C at 10 °C min⁻¹ and held for 2 minutes. Helium was used as carrier gas.

Calibration curves were established using pure compounds (Sigma-Aldrich)- phenol, o-cresol, m-cresol, p-cresol, guaiacol, catechol, 4-methylcatechol, syringol, acetovanillone, syringaldehyde, acetosyringone and 4-hydroxy-3-methoxyphenylacetone.

Chapter 6

Overall Conclusions and Outlook

6.1 Conclusions

The mechanistic pathways for the cleavage of a range of different ethers was investigated in acidic ILs and have been explored *via* a bottom-up strategy in this thesis. The rudimentary objective of these studies was to fully understand the nature of lignin depolymerisation in ILs bearing $[\text{HSO}_4]^-$ anions and leveraging these findings through an applied study using ILs to valorize lignin. It has been regularly documented that hydrolysis of the ether bond in the β -O-4 linkage commonly found in lignin is salient to lignin depolymerisation. In order to gain a broad appreciation of the reactions occurring during depolymerisation, the reactivity of simple aryl-alkyl ethers that feature as the backbone for the β -O-4 linkage was explored, followed by assessing the reactivity of substrates bearing multiple functional groups around the ether moiety.

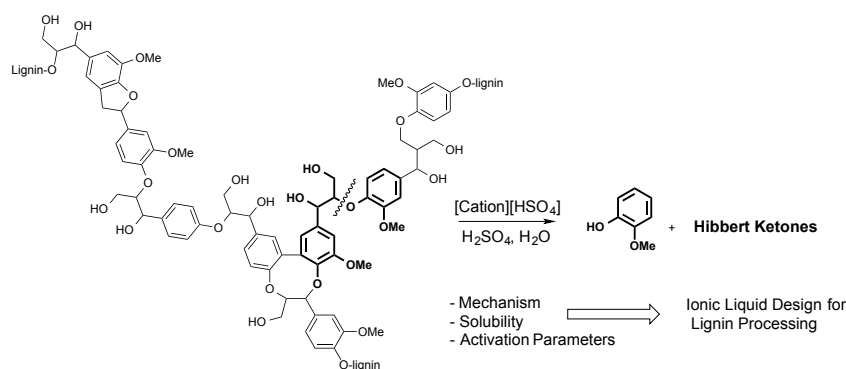


Figure 6.1.1 – Lignin depolymerisation in $[\text{HSO}_4]^-$ ILs, a focus on mechanism, solubility and activation parameters using model compounds.

Previous reported studies on the cleavage of aryl alkyl ethers by acidic reagents in organic or aqueous media have historically shown a two-step, A1 or A2 mechanism. This usually involves

an initial protonation of the oxygen, polarising the C-O bond, followed by nucleophilic attack *via* either an S_N1 or S_N2 mechanism, depending on the nature of the alkyl group attached to the ether. The general consensus for acid catalyzed ether cleavage stipulates the requirement of protic reagents with strong nucleophilic conjugate bases to successfully cleave simple ethers.

A Hammett study based on 2-phenoxyethanol concluded that reagent requirements and mechanism of the cleavage of aryl alkyl ethers in acidic ILs is synonymous with that in non-ionic media. [HC₄im][HSO₄] with various amounts of excess sulfuric acid was unsuccessful in cleaving 2-phenoxyethanol as well as other ether substrates of varying electronic density. Similar observations using sulfuric acid alone have been reported by Burwell.^[76] This concluded that the mechanism of the β-O-4 linkage hydrolysis in lignin depolymerisation catalyzed by [HC₄im][HSO₄] proceeds *via* a mechanism that renders the ether bond more susceptible to hydrolysis. Interestingly, with electron rich substrates, sulfonation was observed to occur at different locations on the aryl ring, following previously reported mechanisms, once again analogous to non-ionic media.^[134, 195] Employing [C₂C₁im]Br with hydrobromic acid showed successful ether cleavage of all substrates based on the parent 2-phenoxyethanol substrate. It was observed that with a decrease in σ value, the reaction rate increased, exhibiting a ρ value of -1.1. This indicated a consistent mechanism across the substrate series with the low ρ value indicating an A2 mechanism.

The second study encompassed investigating the effects of increased substrate functionality on reactivity. A range of compounds mirroring the structure of lignin were prepared with their relative reactivities probed. It was concluded from all the conducted studies that an initial dehydration at the α-hydroxy group was required before hydrolysis of the ether and this was also acid catalyzed. The thermodynamic parameters obtained from the Eyring study indicates two important features for the acid catalyzed hydrolysis of lignin model compounds. Firstly, the ΔH[‡] values indicated that the dehydration reaction proceeds *via* an E1 mechanism, which has also been reported to occur in non-ionic media.^[68, 69] Secondly, the enthalpy of activation for the dehydration reaction was seen to be heavily influenced by the associative forces between the cation and anion. Increased hydrogen bonding in PILs as well as reduced sterics was observed to reduce the degree of solute-solvent interactions, therefore decreasing the enthalpy of activation and increasing the rate of reaction. This part of the study succeeded in highlighting the optimal characteristics required in [HSO₄]⁻ ILs in order to promote lignin depolymerisation at lower temperatures providing faster rates. Comparing the results with studies conducted in non-ionic systems, it was shown that the same mechanism held and that deformylation occurs, even with the [HSO₄]⁻ anion interacting strongly with the γ-methylhydroxyl group. Extrapolation of the obtained rate constants to temperatures reported in literature in aqueous or aqueous/organic systems showed that ILs can hydrolyse these model compounds up to 25 times faster, displaying their superior performance as an efficient reaction medium.^{[164][68]}

The final study built on the conclusions drawn from the fundamental investigations and shifted the focus from gleaning mechanistic insights into a fully applied study. The success in identifying the reaction pathway for the hydrolysis of the β -O-4 linkages and the identification of the optimal features in the IL directed the investigation to the valorisation of ionosolv lignin. Analysis of different lignin samples obtained from different biomass feedstocks and pretreated at different times, showed marked differences in hydroxy group content. Willow samples pretreated at longer times produced lignin with a reduced aliphatic hydroxy content and an increase in phenolic hydroxy groups. Furthermore, lignin obtained from willow displayed a high S:G ratio compared to pine lignin, where G units dominate. Oxidative depolymerisation of lignin using polyoxometalate catalysts and an oxidant in $[\text{HC}_4\text{im}][\text{HSO}_4]$ was subsequently conducted. Both vanillin and syringaldehyde were obtained as the major products from lignin with small quantities of other aromatics present. Finally, a decrease in aldehyde yield was observed with increased pretreatment time with pine lignin only producing vanillin as the aldehyde product.

6.2 Further work

6.2.1 Chapter 3: Hammett study using 2-phenoxyethanol using acidic ILs

In terms of further work, it would be interesting to repeat both studies using the same ether substrates and sulfuric acid or hydrobromic acid at similar concentrations in an inert organic solvent, without the presence of an IL. This would deduce whether the inclusion of the IL is beneficial and increases the rate of sulfonation or influences the rate/change the mechanism of ether cleavage. The aromatic nature of the cation aiding substrate solubility, together with the ability of the anion to speciate with the acid may have been the reason for the high rate of ring sulfonation. Similarly, the increase in concentration of the bromide anion when hydrobromic acid is employed in $[\text{C}_2\text{C}_1\text{im}]\text{Br}$ could also show improved performance compared to a system bearing only an organic solvent and hydrobromic acid. Such a study would confirm the overall benefits of employing ILs in ring sulfonation and in ether cleavage compared to using traditional organic solvents.

Such an investigation could also be extended to other IL systems that promote ether cleavage, including those bearing Lewis acidic anions such as $[\text{C}_4\text{C}_1\text{im}][\text{AlCl}_4]$ or $[\text{C}_4\text{C}_1\text{im}][\text{BBr}_4]$. This would provide an overall review of IL's suitability to replace organic solvents in ether cleavage. For application purposes, it would be important to find a method to extract the sulfonated and cleaved products efficiently from the IL-acid medium. This would also determine whether the IL is recyclable with reproducible activity.

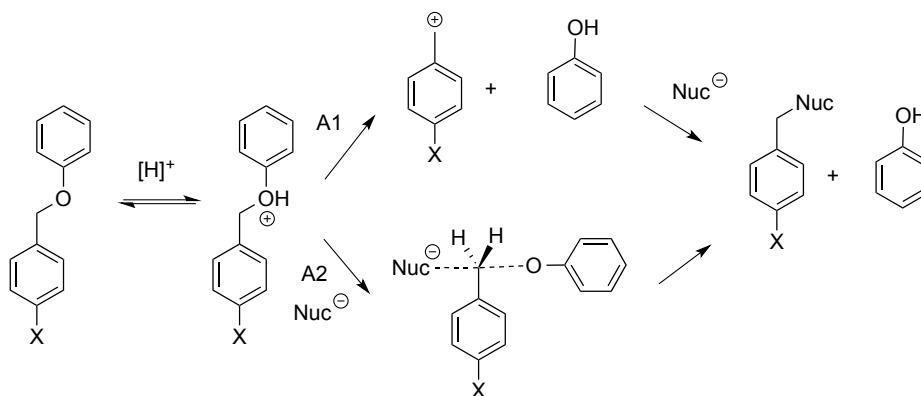


Figure 6.2.1 – Ether substrates capable of undergoing A1 and A2 cleavage mechanism

Finally, the choice of substrate used in this study examined the basicity of the ether, therefore an A2 mechanism for cleavage was expected. However, if electron density is modified at the site of nucleophilic attack, a change in mechanism could potentially be observed. An example of such a substrate is given in Figure 6.2.1, showing the possibility of both an A1 and A2 mechanism for cleavage, depending on the ability of the aryl ring to stabilise the increase in positive charge at the site of nucleophilic attack.

6.2.2 Chapter 4: Ether cleavage in lignin model compounds

An area of this investigation requiring significant further work involves developing a greater understanding of the condensation reactions which occur in parallel to lignin depolymerisation, which has proven to be a challenge in most mechanistic studies. Although the Hibbert ketones were seen with some model compounds when hydrolysed in organic media, only guaiacol was observed in IL media. Some attempts were made to determine the masses of the other peaks observed *via* HPLC, all of which were identified to have masses significantly larger than the GG starting material. This indicated the occurrence of condensation reactions, however no structural features could be assigned. Thorough analysis of the cleaved fragments will therefore need to be conducted in order to ascertain the nature of these reactions and to establish when these occur. This can be achieved by scaling up the reaction and separating out the products in large quantities in order to conduct 2D NMR analysis on both the fragments and the IL medium.

In terms of choice of model compound, it would be equally interesting to explore the relative susceptibility of other ether linkages present in lignin to hydrolysis. This can be achieved by conducting similar studies with more complex model compounds incorporating these linkages. Such model compounds would provide a better representation of lignin reactivity and would determine whether the current choices of model compounds are appropriate to simulate lignin

depolymerisation.

While the results in this chapter provide perspective in understanding the mechanism of lignin depolymerisation using the ionosolv method, a logical area of progression would be to employ other acidic ILs in order to compare differences in both reactivity and mechanism. Results from chapter 3 show that $[\text{C}_2\text{C}_1\text{im}]\text{Br}$ with hydrobromic acid is capable of cleaving simple aryl-alkyl ethers. It would therefore be interesting to reproduce the study using a similar IL-acid system. It can be assumed that reactivity, mechanism and product distribution will be significantly affected due both to the strength of the acid and the highly nucleophilic character of the anion. In the same vein, conducting an Eyring study on GG through systematically changing the cation in the IL with a range of protic, alkyl and aromatic cations and employing catalytic quantities of hydrobromic acid can confirm the importance of cation-anion interaction as observed with $[\text{HSO}_4]^-$ ILs if no deviation from mechanism is observed. These findings can then be compared to the reactivity of GG in aqueous sulfuric acid and hydrobromic acid, using previously reported strategies.^[68, 69]

The final area of further work is the mechanism elucidation of lignin depolymerisation and the changes in lignin structure during the dissolution process using $[\text{C}_2\text{C}_1\text{im}][\text{OAc}]$. It has been postulated in previous investigations that lignin can undergo depolymerisation in ILs when the anion is highly hydrogen-bond basic^[67, 196] through dehydration^[130] although no mechanistic investigations using such ILs have been reported. Successful attempts to depolymerize GG with other ILs currently employed in the dissolution process would allow comparisons to be made between the different modes of action of ILs on lignin and the preferred IL system to promote depolymerisation and prevent condensation.

6.2.3 Chapter 5: Oxidative depolymerisation of lignin

The disappointingly low yields of vanillin and syringaldehyde and the oxidation of the IL were the major drawbacks of this investigation and further scouting of reaction conditions, IL type and oxidants must be conducted in order to render the process of economic interest. Studies have reported that high yields of small aromatics can be obtained *via* oxidative depolymerisation, however based on the results presented in this chapter where similar conditions were employed, these findings could not be reproduced and oxidation of the cation was shown to dominate. The difference in lignin sources employed in this study compared to those reported in literature may be the principal reason for the poor activity observed. It would be important to replicate these studies in the POM-PIL reaction media using the same lignin samples for ease of comparison. Equally, characterization of the precipitated lignin post oxidation will have to be conducted. Identifying the structural changes in the lignin through HSQC and ^{31}P NMR analysis, determining the change in molecular weight of the polymer in addition to probing the reactivity of the IL would aid in identifying the best optimization strategy to valorize lignin in ILs.

Additionally, although vanillin and syringaldehyde were identified as the most abundant products in the extracted oils, a strategy to efficiently extract the products from the reaction mixture will be required. The most straightforward approach would be *via* crystallization if suitable purity and concentration of the products are achieved. For completion, the final area of further work would encompass a thorough mechanistic study to discern how the POM catalyst oxidises the lignin fragments post ether hydrolysis. Such an unprecedented study would aid in identifying the limitations of oxidative depolymerisation of lignin both in terms of substrate and reaction medium using ILs.

6.3 Outlook

The overall findings reported in this thesis succeed in providing detailed mechanistic information regarding acid-catalyzed ether cleavage in aryl alkyl ethers and in lignin model compounds dissolved in IL media. The use of physical organic tools and linear free energy relationships probed both the influence of substrate functionalization on reactivity and mechanism, and the solvent-solute interactions between the IL and the substrate. Model compounds appear to be a suitable starting point to understand the fundamental concepts involved in lignin depolymerisation and have succeeded in showing the superior performance of acidic ionic liquids compared to acidic aqueous systems. However, the complexity of the overall structure of the macropolymer and the inability to distinguish all the competing reactions highlight the limitations of attempting to simplify the intricate nature of lignin in order to understand the true extent of its reactivity and the associated mechanisms. In terms of lignin valorization, syringaldehyde and vanillin have been identified as the aromatic products of highest abundance when subjecting lignin to conditions where oxidative depolymerisation is promoted. However, the overall low yields of these products signify that substantial work is needed to improve our understanding of both lignin structure and its reactivity in ILs. Once sufficient appreciation of lignin reactivity and its structural modifications have been acquired, clarification on the full potential of lignin's suitability to be a renewable source of aromatic chemicals can be established.

Chapter 7

Synthesis and Characterisation

7.1 Synthesis of acidic ionic liquids

All starting materials were purchased from Sigma Aldrich and VWR. All amines were dried over potassium hydroxide for 48 hours under an inert atmosphere and distilled under reduced pressure prior to use. Dimethyl sulfate was dried over calcium hydride for 48 hours under nitrogen and distilled under reduced pressure prior to use. Ionic liquid intermediates containing methylsulfate anions were characterised *via* NMR (^1H and ^{13}C) and mass spectrometry whilst the final hydrolysed products were fully characterised *via* NMR (^1H and ^{13}C), mass spectrometry and elemental analysis (CHN).

7.1.1 1-butyl-3-methylimidazolium methylsulfate, $[\text{C}_4\text{C}_1\text{im}][\text{MeSO}_4]$

1-butylimidazole (54.24 g, 437 mmoles) was mixed with toluene (70 mL) and the mixture was cooled to 0 °C. Dimethylsulfate (55.09 g, 437 mmoles) was added drop-wise to the stirred solution. The reaction was left stirring for one hour until the reaction mixture warmed to room temperature. The organic phase was decanted off and the lower phase washed three times with toluene (3 x 50 mL). The residual toluene was removed under reduced pressure at 65 °C overnight yielding a colourless viscous liquid (106 g, 96.7 %).

$\delta_{^1\text{H}}$ (ppm)(400MHz, DMSO- d_6): 9.11 (1H, s, -N-**CH**-N-), 7.77 (1H, s, -N-**CHCH**-N-), 7.70 (1H, s, -N-**CHCH**-N-), 4.16 (2H, t, $J = 8$ Hz, **CH**₂CH₂CH₂CH₃), 3.85 (3H, s, N-**CH**₃), 3.37 (3H, s, **CH**₃OSO₄), 1.76 (2H, m, CH₂**CH**₂CH₂CH₃), 1.25 (2H, m, CH₂CH₂**CH**₂CH₃), 0.9 (3H, t, $J = 8$ Hz, CH₂CH₂CH₂**CH**₃).

$\delta_{^{13}\text{C}\{^1\text{H}\}}$ (ppm)(100MHz, DMSO- d_6): 136.73, 123.83, 122.48, 53.01, 48.69, 35.94, 31.84, 18.97 and 13.47

m/z (LSIMS⁺): 139 (100 %, $[\text{C}_4\text{C}_1\text{im}]^+$),

m/z (LSIMS⁻): 111 (100 %, [MeSO₄]⁻)

7.1.2 1-butyl-3-methylimidazolium hydrogensulfate, [C₄C₁im][HSO₄]

1-butyl-3-methylimidazolium methyl sulfate (30 g, 120 mmol) was diluted with deionized water (50 mL) in an open-topped three-necked round-bottomed flask fitted with a dropping funnel and thermometer. After the addition of 2 drops of sulfuric acid (95 - 98 %), the solution was heated to 180 °C and left for 3 h with vigorous stirring. During the reaction, deionized water was dispensed dropwise from the dropping funnel whilst the generated methanol and any unreacted water boiled off. Once ¹H NMR showed complete hydrolysis of the methylsulfate anion, the solution was allowed to cool to room temperature. The excess water was removed under reduced pressure at 65 °C overnight and when cooled to room temperature yielded a transparent yellow liquid (57.45 g, 97 %).

δ_{1H} (ppm)(400MHz, DMSO-d₆): 9.11 (1H, s, -N-CH-N-), 7.78 (1H, s, -N-CHCH-N-), 7.71 (1H, s, -N-CHCH-N-), 4.16 (2H, t, *J* = 8 Hz, CH₂CH₂CH₂CH₃), 3.85 (3H, s, N-CH₃), 1.76 (2H, m, CH₂CH₂CH₂CH₃), 1.23 (2H, m, CH₂CH₂CH₂CH₃), 0.9 (3H, t, *J* = 8 Hz, CH₂CH₂CH₂CH₃).
 δ_{13C{¹H}} (ppm)(100MHz, DMSO-d₆): 137.07, 124.06, 122.73, 48.92, 39.16, 31.82, 19.23 and 13.74.

m/z (LSIMS⁺): 139 (100 %, [C₄C₁im]⁺),

m/z (LSIMS⁻): 97 (100 %, [HSO₄]⁻).

Elemental Analysis (Predicted): % C = 40.53 (40.67); % H = 6.96 (6.83); % N = 11.94 (11.86)

7.1.3 1-butylimidazolium hydrogensulfate, [HC₄im][HSO₄]

Sulfuric acid (96 %, 65.27 g, 638 mmol) was added dropwise to 1-butylimidazole (79.33 g, 638 mmol) under stirring at 0 °C. After addition, the solution became highly viscous and the mixture was left to warm to room temperature over an hour. The light brown ionic liquid was then diluted in deionized water and passed through a C18 silica column in order to remove the colour. The water was then removed under reduced pressure at 65 °C overnight. When cooled to room temperature, the product yielded a clear viscous liquid (142 g, 96 %).

δ_{1H} (ppm)(400MHz, DMSO-d₆): 9.15 (1H, s, -N-CH-N-), 7.80 (1H, s, -N-CHCH-N-), 7.68 (1H, s, -N-CHCH-N-), 4.20 (2H, t, *J* = 7.2 Hz, NCH₂CH₂CH₂CH₃), 1.77 (2H, quintet, *J* = 7.6 Hz, NCH₂CH₂CH₂CH₃), 1.24 (2H, quintet, *J* = 7.6 Hz, NCH₂CH₂CH₂CH₃) and 0.90 (3H, t, *J* = 7.2 Hz, NCH₂CH₂CH₂CH₃).

δ_{13C{¹H}} (ppm)(100MHz, DMSO-d₆): 135.73, 122.49, 120.42, 48.68, 31.92, 19.28 and 13.75

m/z (LSIMS⁺): 139 (100 %, [HC₄im]⁺)

m/z (LSIMS⁻): 97 (100 %, [HSO₄]⁻).

Elemental Analysis (Predicted): % C = 37.77 (37.83); % H = 6.45 (6.35); % N = 12.64 (12.60)

7.1.4 Dimethylbutylammonium hydrogensulfate, [N₄₁₁₀][HSO₄]

Sulfuric acid (96 %, 29.53 g, 289 mmol) was added dropwise to a solution of *N,N*-dimethylbutylamine (29.29 g, 289 mmol) in distilled water (50 mL) under stirring at 0 °C. After addition, the mixture was left to reach room temperature over an hour. The mixture was then heated to 60 °C and dried under vacuum yielding a viscous clear liquid (55.76 g, 97 %).

δ_{1H} (ppm)(400MHz, DMSO-d⁶): 3.02 (2H, m, NCH₂CH₂CH₂CH₃), 2.76 (6H, d, *J* = 5.2 Hz, NCH₃), 1.57 (2H, m, NCH₂CH₂CH₂CH₃), 1.30 (2H, sextet, *J* = 7.4 Hz, NCH₂CH₂CH₂CH₃) and 0.89 (3H, t, *J* = 7.2 Hz, NCH₂CH₂CH₂CH₃).

$\delta_{13C\{^1H\}}$ (ppm)(100MHz, DMSO-d⁶): 56.49, 42.29, 25.77, 19.24 and 13.54

m/z (LSIMS⁺): 102 (100 %, [N₄₁₁₀]⁺)

m/z (LSIMS⁻): 97 (100 %, [HSO₄]⁻)

Elemental Analysis (Predicted): % C = 36.33 (36.17); % H = 8.46 (8.60); % N = 7.05 (7.03)

7.1.5 Trimethylbutylammonium methylsulfate, [N₄₁₁₁][MeSO₄]

N,N-Dimethylbutylamine (48.14 g, 476 mmoles) was mixed with toluene (70 mL) and the mixture cooled to 0 °C. Dimethylsulfate (50 g, 396 mmoles) was added dropwise to the stirring solution and the reaction was left for one hour until the reaction mixture warmed to room temperature. The organic phase was then decanted and the lower phase washed with toluene (3 x 50 mL) to remove excess unreacted *N,N*-Dimethylbutylamine. The residual toluene was then removed under reduced pressure at 65 °C overnight, yielding a white solid (81.2 g, 90 %).

δ_{1H} (ppm)(400MHz, DMSO-d⁶): 3.37 (3H, s, CH₃OSO₃H), 3.26 (2H, m, NCH₂CH₂CH₂CH₃), 3.03 (9H, s, -NCH₃), 1.65 (2H, quintet, *J* = 8 Hz, NCH₂CH₂CH₂CH₃), 1.31 (2H, sextet, *J* = 7.2 Hz, NCH₂CH₂CH₂CH₃) and 0.93 (3H, t, *J* = 7.2 Hz, -NCH₂CH₂CH₂CH₃).

$\delta_{13C\{^1H\}}$ (ppm)(100MHz, DMSO-d⁶): 65.10, 52.78, 52.16, 24.07, 19.17 and 13.54

m/z (LSIMS⁺): 116 (100 %, [N₄₁₁₁]⁺)

m/z (LSIMS⁻): 112 (100 %, [MeSO₄]⁻), 97 (17 %, [HSO₄]⁻)

7.1.6 Trimethylbutylammonium hydrogensulfate, $[N_{4111}][HSO_4]$

Trimethylbutylammonium methyl sulfate (76.61 g, 337 mmol) was diluted with deionized water (100 mL) in an open-topped three-necked round-bottomed flask fitted with a dropping funnel and thermometer. After the addition of 2 drops of sulfuric acid (95-98 %) the solution was heated to 180 °C and left for 5 h with vigorous stirring. During the reaction, deionized water was dispensed dropwise from the dropping funnel whilst the generated methanol and any excess unreacted water is boiled off. Once 1H NMR showed complete hydrolysis of the methylsulfate anion, the solution was allowed to cool to room temperature. The excess water was removed under reduced pressure at 65 °C overnight and when cooled to room temperature yielded a white solid (68.7 g, 96 % yield, mpt 139.2 °C).

$\delta_{^1H}$ (ppm)(400MHz, DMSO- d_6): 3.28 (2H, m, $NCH_2CH_2CH_2CH_3$), 3.04 (9H, s, $-NCH_3$), 1.65 (2H, quintet, $J = 8$ Hz, $NCH_2CH_2CH_2CH_3$), 1.28 (2H, sextet, $J = 7.2$ Hz, $NCH_2CH_2CH_2CH_3$) and 0.93 (3H, t, $J = 7.2$ Hz, $-NCH_2CH_2CH_2CH_3$).

$\delta_{^{13}C\{^1H\}}$ (ppm)(100MHz, DMSO- d_6): 65.03, 52.10, 24.07, 19.17 and 13.54

m/z (LSIMS $^+$): 116 (100 %, $[N_{4111}]^+$), 58 (45 %)

m/z (LSIMS $^-$): 97 (100 %, $[HSO_4]^-$).

Elemental Analysis (Predicted): % C = 37.21 (39.42); % H = 9.43 (8.98); % N = 6.16 (6.57)

7.1.7 Triethylammonium hydrogensulfate, $[N_{2220}][HSO_4]$

Sulfuric acid (96 %, 29.89 g, 293 mmol) was added dropwise to a solution of triethylamine (29.60 g, 293 mmol) in distilled water (50 mL) while stirring at 0 °C. After addition, the mixture was allowed to warm to room temperature over the course of an hour. The mixture was then heated to 60 °C and dried under vacuum yielding a white solid (58.7 g, 99 %).

$\delta_{^1H}$ (ppm)(400MHz, DMSO- d_6): 3.08 (6H, q, $J = 7.6$ Hz, $N(CH_2CH_3)_3$) and 1.17 (9H, t, $J = 7.6$ Hz, $N(CH_2CH_3)_3$)

$\delta_{^{13}C\{^1H\}}$ (ppm)(100MHz, DMSO- d_6): 45.87 and 8.65

m/z (LSIMS $^+$): 102 (100 %, $[N_{2220}]^+$)

m/z (LSIMS $^-$): 196 (100 %, $2[HSO_4]^-$), 97 (55 %, $[HSO_4]^-$)

Elemental Analysis (Predicted): % C = 36.02 (36.17); % H = 8.76 (8.60), % N = 6.93 (7.03)

7.1.8 Triethylmethyammonium methylsulfate, [N₂₂₂₁][MeSO₄]

Triethylamine (48.14 g, 476 mmol) was mixed with toluene (70 mL) and the mixture was cooled to 0 °C. Dimethylsulfate (50 g, 396 mmol) was then added dropwise to the stirring solution. The reaction was left stirring for one hour until the reaction mixture warmed to room temperature. The organic phase was then decanted and the lower phase washed with toluene (3 x 50 mL) to remove excess unreacted triethylamine. The residual toluene was then removed under reduced pressure at 65 °C overnight, yielding a white hygroscopic solid (89.0 g, 89 %).

δ_{1H} (ppm)(400MHz, DMSO-d₆): 3.37 (3H, s, CH₃OSO₃H), 3.25 (6H, q, $J = 8$ Hz, NCH₂CH₃), 2.88 (3H, s, NCH₃), 1.18 (9H, tt, $J = 7.2$ Hz, $J^2 = 1.6$ Hz, N(CH₂CH₃)₃).

$\delta_{13C}\{^1H\}$ (ppm)(100MHz, DMSO-d₆): 54.90, 52.78, 45.94 and 7.40

m/z (LSIMS⁺): 116 (100 %, [N₂₂₂₁]⁺)

m/z (LSIMS⁻): 111 (100 %, [MeSO₄]⁻), 97 (45%, [HSO₄]⁻).

7.1.9 Triethylmethyammonium hydrogensulfate, [N₂₂₂₁][HSO₄]

Triethylmethyammonium methyl sulfate (78.01 g, 343 mmol) was diluted with deionized water (100 mL) in an open-topped three-necked round-bottomed flask fitted with a dropping funnel and thermometer. After the addition of 2 drops of sulfuric acid (95-98 %), the solution was heated to 180 °C and left for 5 h with vigorous stirring. During the reaction, deionized water was dispensed dropwise from the dropping funnel, whilst the generated methanol and any unreacted water was boiled off. Once ¹H NMR showed complete hydrolysis of the methylsulfate anion, the solution was allowed to cool to room temperature. The excess water was then removed under reduced pressure at 65 °C overnight and when cooled to room temperature yielded a white hygroscopic solid (74.01 g, 99 % yield).

δ_{1H} (ppm)(400MHz, DMSO-d₆): 3.25 (6H, q, $J = 7.2$ Hz, N(CH₂CH₃)₃), 2.88 (3H, s, -NCH₃) and 1.19 (9H, tt, N(CH₂CH₃)₃).

$\delta_{13C}\{^1H\}$ (ppm)(100MHz, DMSO-d₆): 54.90, 52.81, 45.97 and 7.42

m/z (LSIMS⁺): 116 (100 %, [N₂₁₁₁]⁺)

m/z (LSIMS⁻): 97 (100 %, [HSO₄]⁻)

Elemental Analysis (Predicted): % C = 38.23 (39.42); % H = 9.31 (8.98); % N = 6.32 (6.57)

7.1.10 Pyridinium hydrogensulfate, [HPy][HSO₄]

Sulfuric acid (97.05 %, 39.24 g, 388 mmol) was added dropwise to a solution of pyridine (30.71 g, 388 mmol) in distilled water (50 mL) under stirring at 0 °C. After addition, the solution became highly viscous and the mixture was left to warm to room temperature over an hour. The mixture was then heated to 60 °C and dried under vacuum yielding a white solid (69.42 g, 99 %).

$\delta_{1\text{H}}$ (ppm)(400MHz, DMSO-d⁶): 8.95 (2H, d, J = 5.6 Hz, Ar-**H**_{ortho}), 8.64 (1H, t, J = 8 Hz, Ar-**H**_{para}) and 8.12 (2H, t, J = 6.4 Hz, Ar-**H**_{meta}).

$\delta_{13\text{C}\{\text{H}\}}$ (ppm)(100MHz, DMSO-d⁶): 145.6, 145.08, 127.72 and 47.92

m/z (LSIMS⁺): 79 (100%, [HPy]⁺)

m/z (LSIMS⁺): 97 (100 %) ([HSO₄]⁻)

Elemental Analysis (Predicted): % C = 33.84 (33.90); % H = 4.11 (3.98); % N = 7.80 (7.91)

7.1.11 *N*-methypyridinium methysulfate, [N-MePy][MeSO₄]

Pyridine (49.56 g, 627 mmoles) was mixed with dry toluene (70 mL) and the mixture was cooled to 0 °C. Dimethylsulfate (61.85 g, 490 mmoles) was added dropwise to the stirred solution. The reaction was left stirring for one hour until the reaction mixture warmed to room temperature. The organic phase was then decanted and the lower phase washed with toluene (3 x 50 mL) to remove the excess unreacted pyridine. The residual toluene was then removed under reduced pressure at 65 °C overnight, yielding an off yellow solid (111.4 g, 100 %).

$\delta_{1\text{H}}$ (ppm)(400MHz, DMSO-d⁶): 8.99 (2H, d, J = 5.6 Hz, Ar-**H**_{ortho}), 8.58 (1H, t, J = 7.6 Hz, Ar-**H**_{para}), 8.13 (2H, t, J = 6.8 Hz, Ar-**H**_{meta}), 4.36 (3H, s, **N-CH**₃) and 3.38 (3H, s, **CH**₃OSO₃).

$\delta_{13\text{C}\{\text{H}\}}$ (ppm)(100MHz, DMSO-d⁶): 145.6, 145.08, 127.72 and 47.92

m/z (LSIMS⁺): 94 (100 %, [N-MePyr]⁺)

m/z (LSIMS⁻): 111 (100 %, [MeSO₄]⁻)

7.1.12 *N*-methylpyridinium hydrogensulfate, [N-Mepyr][HSO₄]

N-Methylpyridinium methysulfate (111.44 g, 543 mmol) was diluted with deionized water (100 mL) in an open-topped three-necked round-bottomed flask fitted with a dropping funnel and thermometer. After the addition of 2 drops of sulfuric acid (95-98 %), the solution was heated to 180 °C and left for 5 h with vigorous stirring. During the reaction, deionized water was dispensed dropwise from the dropping funnel, whilst the generated methanol and any unreacted water was boiled off. Once ¹H NMR showed complete hydrolysis of the methysulfate anion, the solution

was allowed to cool to room temperature. The excess water was then removed under reduced pressure at 65 °C overnight and when cooled to room temperature yielded a yellow solid (98.0 g, 93 %)

$\delta_{1\text{H}}$ (ppm)(400MHz, DMSO- d^6): 8.98 (2H, d, $J = 5.6$ Hz, Ar- H_{ortho}), 8.58 (1H, t, $J = 7.6$ Hz, Ar- H_{para}), 8.13 (2H, t, $J = 6.8$ Hz, Ar- H_{meta}) and 4.35 (3H, s, N- CH_3).

$\delta_{13\text{C}\{\text{H}\}}$ (ppm)(100MHz, DMSO- d^6): 145.6, 145.08, 127.72, 52.92 and 47.92

m/z (LSIMS⁺): 94 (100 %, [N-MePyr]⁺)

m/z (LSIMS⁻): 196 (100 %, 2[HSO₄]⁻) and 97 (65 %, [HSO₄]⁻)

Elemental Analysis (Predicted): % C = 33.84 (33.90); % H = 4.11 (3.98); % N = 7.80 (7.91)

7.1.13 Trihexylmethyllammonium methylsulfate, [N₆₆₆₁][MeSO₄]

Trihexylamine (34.55 g, 128 mmoles) was mixed with dry toluene (70 mL) and the mixture was cooled to 0 °C. Dimethylsulfate (14.16 g, 112 mmoles) was added dropwise to the stirring solution and the reaction was left to stir for one hour until the reaction mixture warmed to room temperature. The organic phase was then decanted and the lower phase washed with toluene (3 x 50 mL) to remove the excess unreacted pyridine. The residual toluene was then removed under reduced pressure at 65 °C overnight, yielding a white solid (44.2 g, 99 %).

$\delta_{1\text{H}}$ (ppm)(400MHz, DMSO- d^6): 3.37 (3H, s, CH_3OSO_3), 3.18 (6H, m, N(CH₂CH₂CH₂CH₂CH₂CH₃)₃), 2.94 (3H, s, NCH₃), 1.61 (6H, br, N(CH₂CH₂CH₂CH₂CH₂CH₃)₃), 1.29 (18H, br, (NCH₂CH₂CH₂CH₂CH₂CH₃)₃) and 0.88 (9H, t, $J = 6.8$ Hz, (NCH₂CH₂CH₂CH₂CH₂CH₃)₃).

$\delta_{13\text{C}\{\text{H}\}}$ (ppm)(100MHz, DMSO- d^6): 51.93, 30.72, 25.66, 22.95, 21.93 and 13.88

m/z (LSIMS⁺): 284 (100 %, [N₆₆₆₁]⁺) and 128 (22 %),

m/z (LSIMS⁻): 111 (100 %, [MeSO₄]⁻)

7.1.14 Trihexylmethyllammonium hydrogensulfate, [N₆₆₆₁][HSO₄]

Trihexylmethyllammonium methyl sulfate (42.09 g, 106.4 mmol) was diluted with deionized water (100 ml) in an open-topped three-necked round-bottomed flask fitted with a dropping funnel and thermometer. After the addition of 2 drops of sulfuric acid (95-98 %) the solution was heated at 180 °C for 5 h with vigorous stirring. During the reaction, deionized water was dispensed dropwise from the dropping funnel, whilst the generated methanol and any unreacted water was boiled off. Once ¹H NMR showed complete hydrolysis of the methylsulfate anion, the solution was allowed to cool to room temperature. The excess water was removed under reduced pressure at 65 °C. When cooled to room temperature the product yielded a clear solid (40.1 g, 99 % yield).

$\delta_{1\text{H}}$ (ppm)(400MHz, DMSO- d^6): 3.21 (6H, m, $(\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$), 2.94 (3H, s, NCH_3), 1.61 (6H, br, $(\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$), 1.29 (18H, br, $(\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$) and 0.88 (9H, t, $J = 6.8$ Hz, $(\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$).

$\delta_{13\text{C}\{^1\text{H}\}}$ (ppm)(100MHz, DMSO- d^6): 60.53, 47.47, 30.63, 25.44, 21.88, 21.31 and 13.81.

m/z (LSIMS $^+$): 284 (100 %, $[\text{N}_{6661}]^+$) and 128 (25 %),

m/z (LSIMS $^-$): 97 (100 %, $[\text{HSO}_4]^-$)

Elemental Analysis (Predicted): % C = 58.97 (59.80); % H = 11.31 (11.36); % N = 3.69 (3.67)

7.2 Synthesis of Other Ionic Liquids

All starting materials were purchased from Sigma Aldrich and VWR. 1-methylimidazole was dried over potassium hydroxide for 48 hours under an inert atmosphere and distilled under reduced pressure prior to use. The alkylating agents, 1-bromoethane and 1-chlorobutane, were dried over phosphorus pentoxide for 48 hours under nitrogen and distilled under reduced pressure prior to use. The final pure ionic liquids were fully characterised via NMR (^1H and ^{13}C), mass spectrometry and elemental analysis (CHN). The synthesis of 1-ethyl-3-methylimidazolium bromide was conducted by Dr Jeraime Griffith of the Welton group.

7.2.1 Synthesis of 1-ethyl-3-methylimidazolium bromide, $[\text{C}_2\text{C}_1\text{im}]\text{Br}$

Bromoethane (58.4 g, 536 mmol) was added dropwise to a solution of methylimidazole (40 g, 487 mmol) in ethyl acetate (40 mL). After complete addition, the mixture was stirred at room temperature overnight. A biphasic mixture with two clear phases was observed. The upper layer was removed under an inert atmosphere whilst the bottom layer was left to crystallise. The white solid was then recrystallised from a mixture of acetonitrile (60 mL) and ethyl acetate (20 mL) under cooling in an ice bath. After removing the solvent, the product was further washed with ethyl acetate (2 x 50 mL) and dried under reduced pressure at 30 °C yielding white crystals (61.9 g, 67 %).

$\delta_{1\text{H}}$ (ppm)(400MHz, DMSO- d^6): 9.43 (1H, br, NCHN), 7.91 (1H, br, NCHCHN), 7.81 (1H, br, NCHCHN), 4.23 (2H, q, $J = 7.2$ Hz, NCH_2CH_3), 3.88 (3H, s, $-\text{NCH}_3$) and 1.40 (3H, d, $J = 7.2$ Hz, NCH_2CH_3)

$\delta_{13\text{C}\{^1\text{H}\}}$ (ppm)(100MHz, DMSO- d^6): 136.76, 123.99, 122.44, 44.56, 36.22 and 15.64

m/z (LSIMS $^+$): 111 (100 %, $[\text{C}_2\text{C}_1\text{im}]^+$)

m/z (LSIMS $^-$): 79 (100 %, Br^-), 81 (95%, Br^-).

Elemental Analysis (Predicted): % C = 32.84 (37.72); % H = 6.14 (5.8), % N = 12.69 (14.66)

7.2.2 Synthesis of 1-butyl-3-methylimidazolium chloride, [C₄C₁im]Cl

1-chlorobutane (278.9 g, 3.01 moles) was added dropwise to 1-methylimidazole (225 g, 2.74 moles) in ethyl acetate (200 mL) under nitrogen. The reaction mixture was left to stir for 7 days at 75 °C after which two phases were observed. The reaction was left to cool to room temperature and left to crystallise in the freezer overnight. The solvent was then removed via cannula with the product recrystallised from dry acetonitrile and ethyl acetate (150 mL: 50 mL) and washed with ethyl acetate until all unreacted starting materials were removed. The product was then dried overnight at 40 °C under reduced pressure yielding a white solid. (413 g, 86 %).

δ_{1H} (ppm)(400MHz, DMSO-d⁶): 9.35 (1H, s, -NCHN-), 7.83 (1H, s, -NCHCHN-), 7.75 (1H, s, -NCHCHN-), 4.18 (2H, t, $J = 7.2$ Hz, NCH₂CH₂CH₂CH₃), 3.86 (3H, s, NCH₃), 1.76 (2H, quintet, $J = 7.6$ Hz, NCH₂CH₂CH₂CH₃), 1.26 (2H, quintet, $J = 7.6$ Hz, NCH₂CH₂CH₂CH₃) and 0.89 (3H, t, $J = 7.2$ Hz, $J = 7.6$ Hz, NCH₂CH₂CH₂CH₃)

$\delta_{13C\{^1H\}}$ (ppm)(100MHz, DMSO-d⁶): 136.70, 123.55, 122.25, 48.37, 35.68, 31.36, 18.74 and 13.26.

m/z (LSIMS⁺): 139 (100 %, [C₄C₁im]⁺)

m/z (LSIMS⁻): 35 (100 %, Cl⁻), 37 (32 %, Cl⁻)

Elemental Analysis (Predicted): % C = 54.59 (55.01); % H = 9.28 (8.66); % N = 15.89 (16.04)

7.2.3 Synthesis of 1-butyl-3-methylimidazolium trifluoromethanesulfonate, [C₄C₁im][OTf]

Lithium trifluoromethanesulfonate (93.70 g, 600 mmoles) was added to 1-butyl-3-methylimidazolium chloride (105.96 g, 606 mmoles) in dry dichloromethane (300 mL). The suspension was left to stir for 3 days under an inert atmosphere at room temperature. The mixture was then filtered and washed with small quantities of deionized water (20 x 5 mL) until tests on the aqueous phase with AgNO_{3(aq)} (0.1 M) showed no presence of chloride salts. Once the solution was deemed chloride free, the solvent was removed under reduced pressure and the ionic liquid was dried under vacuum at 65 °C yielding a colourless, viscous, liquid (140 g, 81 %).

δ_{1H} (ppm)(400MHz, DMSO-d⁶): 9.08 (1H, s, -NCHN-), 7.75 (1H, s, -NCHCHN-), 7.68 (1H, s, -NCHCHN-), 4.16 (2H, t, $J = 7.2$ Hz, NCH₂CH₂CH₂CH₃), 3.85 (3H, s, NCH₃), 1.76 (2H, quintet, $J = 7.6$ Hz, NCH₂CH₂CH₂CH₃), 1.27 (2H, quintet, $J = 7.6$ Hz, NCH₂CH₂CH₂CH₃) and 0.89 (3H, t, $J = 7.2$ Hz, $J = 7.6$ Hz, NCH₂CH₂CH₂CH₃)

$\delta_{13C\{^1H\}}$ (ppm)(100MHz, DMSO-d⁶): 136.51, 123.6, 122.26, 119.09, 48.54, 35.71, 31.36, 18.77

and 13.19.

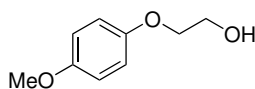
m/z (LSIMS⁺): 139 (100 %, [C₄C₁im]⁺)

m/z (LSIMS⁻): 149 (100 %, [OTf]⁻)

7.3 Synthesis of simple aryl alkyl ethers

Starting materials for the synthesis of these model compounds were acquired commercially from VWR and Sigma Aldrich and were used as received. All products were characterised via NMR (¹H and ¹³C), mass spectrometry and elemental analysis (CHN).

7.3.1 Synthesis of 2-(4-methoxyphenoxy)ethan-1-ol



4-Methoxyphenol (3.05 g, 24.5 mmol), 2-chloroethanol (1.55 g, 19.3 mmol) and aqueous sodium hydroxide (0.1 M, 50 mL) were stirred together for 64 h at room temperature. Water was added (50 mL) and the reaction mixture extracted with diethyl ether. The combined organics were washed with water, sodium hydroxide (10 wt %) solution and brine before being dried and concentrated in vacuo. The product was then recrystallised twice using acetonitrile yielding a white crystalline solid (0.32 g, 10 %).

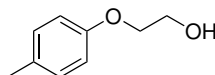
δ_{H} (ppm)(400MHz, CDCl₃): 6.89 (4H, m, ArH), 4.02 (2H, m, -OCH₂CH₂OH), 3.93 (2H, m, -OCH₂CH₂OH) and 3.77 (3H, s, OCH₃).

$\delta_{\text{C}}^{\{^1\text{H}\}}$ (ppm)(100MHz, CDCl₃): 154.12, 152.74, 115.58, 114.70, 69.88, 61.60 and 55.73

m/z (CI): 186 (100 %, M+NH₄⁺), 168 (12 %, M⁺)

Elemental Analysis (Predicted): % C = 64.17 (64.27); % H = 7.30 (7.19)

7.3.2 Synthesis of 2-(4-methylphenoxy)ethan-1-ol



p-Cresol (4.48 g, 40.7 mmol), 2-chloroethanol (2.1 g, 27.1 mmol) and potassium carbonate (10.5 g, 76 mmol) in DMF (50 mL) were refluxed for 6 hours. Water (50 mL) was added and the mixture extracted with ethyl acetate. The organic phase was washed with saturated potassium

carbonate and brine, dried over magnesium sulfate and the solvent evaporated. Purification by column chromatography (cyclohexane/ethyl acetate 7:3) yielded the desired product as an off yellow solid (0.8 g, 18 %).

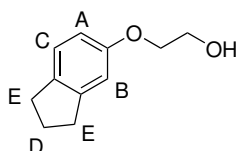
δ_{1H} (ppm)(400MHz, $CDCl_3$): 7.08 (2H, d, $J = 8$ Hz, Ar H_{ortho}), 6.84 (2H, d, $J = 8$ Hz, Ar H_{meta}), 4.05 (2H, t, $J = 4$ Hz, $-OCH_2CH_2OH$), 3.95 (2H, t, $J = 4$ Hz, $-OCH_2CH_2OH$) and 2.29 (3H, s, Ar CH_3).

$\delta_{13C}\{^1H\}$ (ppm)(100MHz, $CDCl_3$): 156.62, 130.53, 130.10, 114.56, 69.38, 61.69 and 20.60

m/z (CI): 170 (100 %, $M + H_2O$), 152 (85%)

Elemental Analysis (Predicted): % C = 71.11 (71.03); % H = 8.10 (7.95)

7.3.3 Synthesis of 2-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]ethanol



5-indanol (5 g, 37.3 mmol), 2-chloroethanol (4.5 g, 55.9 mmol) and potassium carbonate (10.3 g, 74.5 mmol) were refluxed for 9 h in DMF (50 mL). The reaction was monitored *via* TLC (cyclohexane/ethyl acetate 7:3). Once the starting material was consumed, distilled water (50 mL) was added and the mixture extracted with ethyl acetate. The organic phase was washed with saturated potassium carbonate and brine, dried over magnesium sulfate and the solvent evaporated. The crude product was purified by column chromatography (cyclohexane/ethyl acetate 7:3) yielding the desired product as a clear liquid (1.87 g, 28 %).

δ_{1H} (ppm)(400MHz, $CDCl_3$): 7.12 (1H, d, $J = 8$ Hz, H_a), 6.81 (1H, s, H_b), 6.72 (1H, dd, $J = 8$ Hz, H_c), 4.06 (2H, t, $J = 8$ Hz, $-OCH_2CH_2OH$), 3.95 (2H, t, $J = 8$ Hz, $-OCH_2CH_2OH$), 2.87 (4H, quintet, H_e), 2.22 (1H, s, OH) and 1.29 (2H, quintet, H_d).

$\delta_{13C}\{^1H\}$ (ppm)(100MHz, $CDCl_3$): 157.53, 145.85, 136.74, 124.83, 112.62, 110.73, 69.46, 61.62, 33.17, 31.99 and 25.85

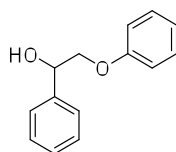
m/z (CI) 179 (100 %, M^+), 196 (92 %, $M+17$)

Elemental Analysis (Predicted): % C = 74.24 (74.13); % H = 7.85 (7.92)

7.4 Synthesis of lignin model compounds

Reagents were purchased from VWR and Sigma Aldrich, and were used as received. Synthesis of each model compound followed standard procedures as found in literature. All intermediates were characterised via NMR (^1H and ^{13}C) and mass spectrometry whilst the final hydrolysed products were analysed via NMR (^1H and ^{13}C), mass spectrometry and elemental analysis (CHN).

7.4.1 Synthesis of 2-phenoxy-1-phenylethanol (model compound II)



A 250 mL round bottom flask equipped with a reflux condenser and dropping funnel was charged with phenol (1.18 g, 12.56 mmol) and potassium carbonate (2.07 g, 15 mmol) in acetone (50 mL) and stirred at room temperature. To this solution, 2-bromoacetophenone (2 g, 10 mmol) in acetone (50 mL) was added dropwise over the course of 30 minutes. The resulting suspension was stirred under reflux for 4h during which the colour changed to yellow. Once TLC (dichloromethane: methanol 98:2) confirmed the reaction went to completion, the suspension was filtered and concentrated under reduced pressure. The crude product was purified by recrystallization from ethanol to give 2-phenoxy-1-phenylethanol as a white solid (2.09 g, 9.84 mmol, 98 %).

A 100 mL round bottom flask was charged with 2-phenoxy-1-phenylethanol (1.03 g, 4.85 mmol) along with a THF-water mixture (28 mL and 5 mL). NaBH_4 (0.36 g, 9.41 mmol) was added in one portion at room temperature. The flask was equipped with a reflux condenser and the reaction was left to stir under reflux for 2 h. After cooling to room temperature an excess of NH_4Cl was added (until the reaction mixture reached pH 5-6) and the reaction mixture was left to stir for 1 h. The crude product was extracted with diethyl ether (3×50 mL), with the combined organic extracts washed with brine (100 mL) and dried over anhydrous Na_2SO_4 . The crude product was then purified via column chromatography producing a white solid (0.84 g, 81 %, 62.4 – 63.3 °C mpt).

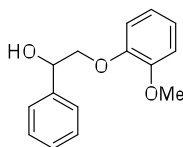
δ_{H} (ppm)(400MHz, CDCl_3): 7.48-7.30 (7H, m, ArH), 7.00-6.94 (3H, m, ArH), 5.13 (1H, dd, $J = 8.8, 3.2$ Hz, ArCH_a -), 4.12 (1H, dd, $J = 9.6, 3.2$ Hz, ArCH_b -) and 4.02 (1H, t, $J = 9.2$ Hz, OH-CH-).

δ_{C} (ppm)(100MHz, CDCl_3): 158.50, 139.78, 129.68, 128.69, 128.30, 126.41, 121.43, 114.76, 73.40 and 73.70

m/z (CI) , 232 (100 %, $M + NH_4$), 197 (48 %)

Elemental Analysis (Predicted): % C = 78.57 (78.48); % H = 6.65 (6.59)

7.4.2 Synthesis of 2-(2-methoxyphenoxy)-1-phenylethanol (model compound III)



Synthesis followed the same protocol as 2-phenoxy-1-phenylethanone with the addition of 2-methoxyphenol instead of phenol to form 2-(2-methoxyphenoxy)-1-phenylethanone as a yellow crystalline solid (6.41 g, 35 %). Reduction of 2-(2-methoxyphenoxy)-1-phenylethanone followed the same protocol as above producing the 2-(2-methoxyphenoxy)-1-phenylethanol product as white solid (1.4 g, 93 % yield, 49.2 – 50.4 °C mpt).

δ_{1H} (ppm)(400MHz, $CDCl_3$): 7.45-7.30 (5H, m, ArH), 7.02-6.88 (4H, m, ArH), 5.12 (1H, dd, $J = 9.6, 2.8$ Hz, ArCH_aH), 4.19 (1H, dd, $J = 9.6, 2.8$ Hz, ArCH_bH), 4.01 (1H, t, $J = 10$ Hz, OH-CH-) and 3.89 (3H, s, -OCH₃).

$\delta_{13C}\{^1H\}$ (ppm)(100MHz, $CDCl_3$): 150.30, 148.10, 139.63, 128.62, 128.15, 126.42, 122.73, 121.23, 116.23, 112.15, 72.46 and 55.99.

m/z (EI⁺), 244, (28 %, M^+), 202 (75 %) and 124 (100 %)

Elemental Analysis (Predicted): % C = 71.11 (71.03); % H = 8.10 (7.95)

7.4.3 Synthesis of 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanol (model compound IV)

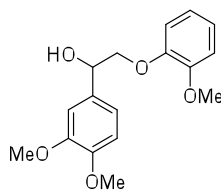


Figure 7.4.1 – 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanol

Synthesis followed the same protocol as 2-phenoxy-1-phenylethanol with the addition of 2-bromo-(3,4-dimethoxy)acetophenone replacing bromoacetophenone and 2-methoxyphenol replacing phenol to produce 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanone (0.52 g, 45 % yield).

Reduction of 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanone followed the same protocol as above producing the 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanol product as a white solid (0.16 g, 55 % yield, 131.4 – 132.8 °C mpt).

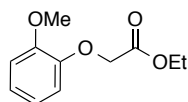
δ_{1H} (ppm)(400MHz, $CDCl_3$): 7.01-6.83 (7H, m, ArH), 5.06 (1H, dd, $J = 9.2, 2.4$ Hz, $-OCH_aH-$), 4.17 (1H, dd, $J = 9.2, 2.4$ Hz $-OCH_bH-$), 3.97 (1H, t, $J = 9.6$ Hz, OH-CH-), 3.90 (3H, s, $-OCH_3$), 3.89 (3H, s, $-OCH_3$) and 3.88 (3H, s, $-OCH_3$).

$\delta_{13C\{^1H\}}$ (ppm)(100MHz, $CDCl_3$): 132.12, 122.59, 121.12, 118.64, 116.04, 111.99, 111.03, 109.38, 76.40, 72.13, 55.96, 55.91 and 55.87.

m/z (EI^+), 368 (100 %, $M+CH_3CN+Na$) and 327 (22 %, $M+Na$).

Elemental Analysis (Predicted): % C = 66.19 (67.09); % H = 6.71 (6.62)

7.4.4 Synthesis of ethyl (2-methoxyphenoxy)acetate



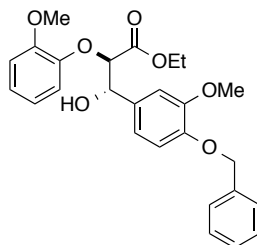
Dry potassium carboante (8.29 g, 60 mmol) was added to 2-methoxyphenol (7.45 g, 60 mmol), with stirring, in acetone (200 mL). The mixture was stirred at room temperature for 15 minutes and then cooled to 0 °C. Ethyl bromoacetate (8.35 g, 50 mmol) was added dropwise over 5 minutes and the reaction warmed to reflux and left for 8 hours. The reaction mixture was then left to cool to room temperature and filtered over a pad of celite. The solvent was then removed under reduced pressure, before diluting in diethyl ether (100 mL) and washing with NaOH solution (5 wt%, 3 x 100 mL), water (100 mL) and brine (100 mL). The organic layer was then dried with magnesium sulfate, filtered and evaporated under reduced pressure and purified by flash chromatography yielding a colourless oil (8.24 g, 78 %).

δ_{1H} (ppm)(400MHz, $CDCl_3$): 6.92-6.82 (3H, m, ArH), 4.67 (2H, s, $-CH_2-$), 4.24 (2H, q, $J = 7.3$ Hz, $-CH_2CH_3$), 3.87 (3H, s, $-OCH_3$) and 1.27 (3H, t, $J = 7.3$ Hz, $-CH_2CH_3$).

$\delta_{13C\{^1H\}}$ (ppm)(100MHz, $CDCl_3$): 169.16, 149.77, 147.40, 122.62, 120.81, 114.55, 112.21, 66.67, 61.34, 55.95 and 14.25.

m/z (EI^+), 211 (100 %, M^+), 228 (98 %, $M+H_2O$)

7.4.5 Synthesis of

erythro-1-(3-methoxy-4-*O*-benzylphenyl)-2-(2-methoxyphenoxy)-propanoate

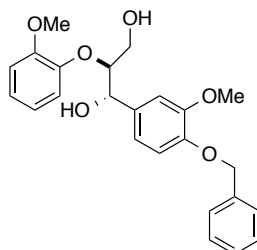
A dry and argon flushed 250 mL three-necked flask equipped with a magnetic stirrer, a low temperature thermometer, an argon inlet and an addition funnel was charged with diisopropylamine (3.64 g, 36 mmol) and THF (50 mL). The reaction mixture was cooled to 0° C and a solution of commercial *n*BuLi in hexanes (21.9 mL, 1.6 M, 34.5 mmol) was added dropwise over 15 min. After stirring for 30 min at 0 °C the reaction mixture was cooled to -78 °C, and a solution of ethyl (2-methoxyphenoxy)acetate (6.3 g, 30 mmol) in THF (60 mL) was added dropwise over a period of 1 h. After stirring for an additional 10 min, a solution of 3,4-dimethoxybenzaldehyde (7.99 g, 33 mmol) in THF (60 mL) was added in 30 min at -78 °C. At the end of the addition, stirring was continued for 90 min at -78 °C, leaving the mixture to warm to 0 °C, followed by the addition of distilled water (100 mL). The aqueous phase was extracted with ethyl acetate (3 x 100 mL). The combined organic layers were washed with aqueous HCl solution (1 M, 80 mL), water (80 mL) and brine (80 mL), dried with magnesium sulfate, filtered and concentrated under reduced pressure. The crude solid was recrystallized in ethyl acetate (2.5 mL of solvent for 4 g of crude material; diethyl ether was used to wash the recrystallized solid) to obtain *erythro*-ethyl 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-(2-methoxyphenoxy)propanoate (5.59 g, 41 %) as a white solid.

δ_{1H} (ppm)(400MHz, CDCl₃): 7.44-7.26 (5H, m, ArH), 7.06 (1H, ddd, $J = 8, 7.2, 1.6$ Hz, ArH), 6.99 – 6.83 (6H, m, ArH), 5.14 (2H, s, ArCH₂), 4.96 (1H, d, $J = 4.8$ Hz, OH-CH-), 4.17-4.13 (1H, m, O-CH-), 3.88 (3H, s, -OCH₃), 3.88 (3H, s, -OCH₃), 3.92 (1H, m, CH_aHOH), 3.65 (1H, m, CH_bHOH).

$\delta_{13C\{^1H\}}$ (ppm)(100MHz, CDCl₃): 151.68, 149.84, 147.68, 146.97, 137.22, 133.19, 128.64, 127.94, 127.39, 124.32, , 11.74, 121.06, 118.47, 114.04, 112.27, 109.88, 87.45, 72.81, 71.17, 60.8 56.15 and 55.98.

m/z (EI⁺), 433 (100 %, M+Na) and 343 (15 %).

7.4.6 Synthesis of *erythro*-1-(3-methoxy-4-*O*-benzylphenyl)-2-(2-methoxyphenoxy)-1,3-diol (model compound V)



A dry and argon flushed 250 mL three-necked flask equipped with a magnetic stirrer, a reflux condenser, an argon inlet and an addition funnel was charged with LiAlH_4 in THF (11.05 mL, 1.6 M, 11.05 mmol). The reaction mixture was cooled to 0 °C and a solution of 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-(2-methoxyphenoxy)propanoate (2 g, 4.42 mmol) in THF (20 mL) was added dropwise over 15 min. The heterogeneous reaction mixture was then stirred at 60 °C for 3 h, and cooled to 0 °C. The reaction mixture was carefully quenched *via* the addition of ethyl acetate (20 mL) and the dropwise addition of half saturated potassium sodium tartrate solution (20 mL). The reaction mixture was then stirred 30 min at ambient temperature. The filtrate was dried over magnesium sulfate and evaporated under reduced pressure. The crude residue was purified by flash chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$ 99:1 $\rightarrow$ 97:3). The resulting pure diol was dried by azeotropic distillation with toluene under reduced pressure, and then dried overnight yielding *erythro*-1-(3-methoxy-4-*O*-benzylphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol (1.0 g, 55 %) as a viscous oil.

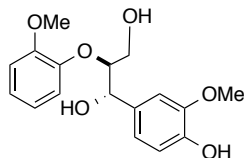
δ_{H} (ppm)(400MHz, CDCl_3): 7.44-7.26 (5H, m, ArH), 7.06 (1H, ddd, $J = 8, 7.2, 1.6$ Hz, ArH), 6.99 – 6.83 (6H, m, ArH), 5.14 (2H, s, ArCH₂), 4.96 (1H, d, $J = 4.8$ Hz, OH-CH-), 4.17-4.13 (1H, m, O-CH-), 3.88 (3H, s, -OCH₃), 3.88 (3H, s, -OCH₃), 3.92 (1H, m, CH_aHOH), 3.65 (1H, m, CH_bHOH).

$\delta_{\text{C}}\{\text{H}\}$ (ppm)(100MHz, CDCl_3): 151.68, 149.84, 147.68, 146.97, 137.22, 133.19, 128.64, 127.94, 127.39, 124.32, , 11.74, 121.06, 118.47, 114.04, 112.27, 109.88, 87.45, 72.81, 71.17, 60.8 56.15 and 55.98.

m/z (EI^+), 433 (100 %, $\text{M}+\text{Na}$) and 343 (15 %).

Elemental Analysis (Predicted): not possible to obtain

7.4.7 Synthesis of *erythro*-1-(3-methoxy-4-hydroxyphenyl)-2-(2-methoxyphenoxy)-1,3-diol, (model compound I)



erythro-1-(3-methoxy-4-*O*-benzylphenyl)-2-(2-methoxyphenoxy)-1,3-diol (85 mg, 0.2 mmol) and palladium on carbon (10 %, 15 mg, 0.014 mmol) was dissolved in dry methanol (10 mL). The reaction mixture was degassed at room temperature for 10 minutes via a nitrogen insert. After degassing, a needle insert attached to rubber balloon filled with hydrogen was fed into the reaction mixture *via* a suba-seal. The reaction was then left to stir for three hours at room temperature. After complete consumption of the starting material, the reaction mixture was filtered through a pad of celite and the filtrate evaporated under reduced pressure. The crude product was purified *via* column chromatography yielding an off-white solid (41.2 mg, 67 %).

δ_{H} (ppm)(400MHz, CDCl_3): 7.09 -6.81 (7H, m, ArH), 4.97 (1H, d, $J = 4.8$ Hz, OH-CH-), 4.16 (1H, m, O-CH-), 3.94 (1H, m, CH_aOH), 3.89 (3H, s, $-\text{OCH}_3$), 3.88 (3H, s, $-\text{OCH}_3$), 3.66 (1H, dd, $J = 12.2, 3.6$ Hz, CH_bOH)

$\delta_{\text{C}}^{\{^1\text{H}\}}$ (ppm)(100MHz, CDCl_3): 151.82, 147.05, 146.77, 145.27, 131.93, 124.43, 121.81, 121.27, 119.18, 114.41, 112.35, 108.79, 87.65, 72.91, 60.89, 56.14 and 56.05.

m/z (EI^+), 343 (100 % $\text{M}+\text{Na}$) and 338 (45 %, $\text{M}+\text{H}_2\text{O}$).

Elemental Analysis (Predicted): % C = 63.89 (63.74); % H = 6.41 (6.29)

Bibliography

- [1] Narbel, P. A.; Hansen, J. P. *Renew. Sustain. Energy Rev.* **2014**, *34*, 91–97.
- [2] Nelson, V.; *Key World Energy Statistics*; Tech. Rep.; 2013.
- [3] Ellabban, O.; Abu-Rub, H.; Blaabjerg, F. *Renew. Sustain. Energy Rev.* **2014**, *39*, 748–764.
- [4] IEA *Technol. Roadmap* **2011**, 1–56.
- [5] Mikkola, J.-p.; Sklavounos, E.; King, A. W. T.; Virtanen, P. *Chemistry*; The Royal Society of Chemistry, 2015.
- [6] Saini, J. K.; Saini, R.; Tewari, L. *3 Biotech* **2015**, *5*, 337–353.
- [7] Eisentraut, A.; *Sustainable Production of Second-Generation Biofuels*; Tech. Rep.; 2010.
- [8] Franks, C. D.; Burow, G. B.; Burke, J. J. *Crop Sci.* **2006**, *46*, 1371–1376.
- [9] Bosch, M.; Hazen, S. P. *Front. Plant Sci.* **2013**, *4*, 474.
- [10] Somerville, C.; Youngs, H.; Taylor, C.; Davis, S. C.; Long, S. P. *Science (80-.)*. **2012**, *329*, 790–793.
- [11] Cotana, F.; Cavalaglio, G.; Gelosia, M.; Nicolini, A.; Coccia, V.; Petrozzi, A. *Energy Procedia* **2014**, *45*, 42–51.
- [12] Keoleian, G.; Volk, T. *CRC. Crit. Rev. Plant Sci.* **2005**, *24*, 385–406.
- [13] https://public.ornl.gov/site/gallery/originals/Cellulose_Processed_by.jpg.
- [14] Jorgensen, H.; Kristensen, J.; Felby, C. *Biofuels, Bioprod. Biorefining* **2007**, *1*, 119–134.
- [15] Qian, X.; Ding, S.; Nimlos, M.; Johnson, D.; Himmel, M. *Macromolecules* **2005**, *38*, 10580–10589.
- [16] Brandt, A.; Gräsvik, J.; Hallett, J. P.; Welton, T. *Green Chem.* **2013**, *15*, 550.
- [17] Kolpak, F. J.; Blackwell, J. *Macromolecules* **1976**, *9*, 273–278.

- [18] Kobayashi, H.; Fukuoka, A. *Green Chem.* **2013**, *15*, 1740.
- [19] Saha, B.; Abu-Omar, M. M. *Green Chem.* **2014**, *16*, 24.
- [20] Haghighi Mood, S.; Hossein Golfeshan, A.; Tabatabaei, M.; Salehi Jouzani, G.; Najafi, G. H.; Gholami, M.; Ardjmand, M. *Renew. Sustain. Energy Rev.* **2013**, *27*, 77–93.
- [21] Timell, T. *Wood Sci. Technol.* **1967**, *1*, 45–70.
- [22] Sjostrom, E. *Wood Chemistry: Fundamentals and Applications*; Academic Press, 1993.
- [23] Whetten, R.; Sederoff, R. *Plant Physiol.* **1995**, *7*, 1001–1013.
- [24] Freudenberg, K.; Neish, A. *Constitution and Biosynthesis of Lignin*, 1st ed.; Springer-Verlag Berlin Heidelberg, 1968.
- [25] Boerjan, W.; Ralph, J.; Baucher, M. *Ann. Rev. Plant. Biol.* **2003**, *54*, 519–46.
- [26] Ralph, J.; Schatz, P.; Fachuang, L.; Hoon, K.; Akiyama, T.; Nelsen, S. *Quinone Methides*; John Wiley & Sons, Inc., 2009.
- [27] Adler, E. *Wood Sci. Technol.* **1977**, *11*, 169–218.
- [28] Ralph, J.; Grabber, J. H.; Hatfield, R. D. *Carbohydr. Res.* **1995**, *275*, 167–178.
- [29] Balakshin, M.; Capanema, E.; Gracz, H.; Chang, H. M.; Jameel, H. *Planta* **2011**, *233*, 1097–1110.
- [30] Yuan, T. Q.; Sun, S. N.; Xu, F.; Sun, R. C. *J. Agric. Food Chem.* **2011**, *59*, 10604–10614.
- [31] Wyman, C. E.; Dale, B. E.; Elander, R. T.; Holtzapple, M.; Ladisch, M. R.; Lee, Y. *Bioresour. Technol.* **2005**, *96*, 1959–1966.
- [32] Yang, B.; Wyman, C. E. *Biofuels, Bioprod. Bioref.* **2008**, *2*, 26–40.
- [33] *Breaking the Biological Barriers to Cellulosic Ethanol*; Tech. Rep.; 2006.
- [34] Grace, T.; Malcolm, E. *Alkaline Pulping (Pulp and Paper Manufacture Series)*, 3rd ed.; Tappi Press, 1989.
- [35] Chakar, F. S.; Ragauskas, A. J. *Ind. Crops Prod.* **2004**, *20*, 131–141.
- [36] Zhao, X.; Cheng, K.; Liu, D. *Appl. Microbiol. Biotechnol.* **2009**, *82*, 815–827.
- [37] Mutjé, P.; Pélach, M. A.; Vilaseca, F.; García, J. C.; Jiménez, L. *Bioresour. Technol.* **2005**, *96*, 1125–1129.
- [38] Huijgen, W. J. J.; Smit, A. T.; de Wild, P. J.; den Uil, H. *Bioresour. Technol.* **2012**, *114*, 389–398.

- [39] Welton, T. *Chem. Rev.* **1999**, *99*, 2071–2083.
- [40] Hallett, J. P.; Welton, T. *Chem. Rev.* **2011**, *111*, 3508–76.
- [41] Welton, T. *Coord. Chem. Rev.* **2004**, *248*, 2459–2477.
- [42] Niedermeyer, H.; Ab Rani, M. A.; Lickiss, P.; Hallett, J. P.; Welton, T.; White, A.; Hunt, P. A. *Phys. Chem. Chem. Phys.* **2010**, *12*, 2018–2029.
- [43] Plechkova, N. V.; Seddon, K. R. *Chem. Soc. Rev.* **2008**, *37*, 123–50.
- [44] Weyershausen, B.; Lehmann, K. *Green Chem.* **2005**, *7*, 15.
- [45] Stärk, K.; Taccardi, N.; Bçsmann, A.; Wasserscheid, P. *ChemSusChem* **2010**, *3*, 719–723.
- [46] Ong, S. P.; Andreussi, O.; Wu, Y.; Marzari, N.; Ceder, G. *Chem. Mater.* **2011**, *23*, 2979–2986.
- [47] Walden, P. *Bull. Acad. Imper. Sci* **1914**, 1800.
- [48] Pagni, R. *Advances in Molten Salt Chemistry*, 6th ed.; Mamantov, G.; Braunstein, J., Eds.; Elsevier: New York, 1987.
- [49] Wasserscheid, P.; Welton, T. *Ionic Liquids in Synthesis*; WILEY-VCH Verlag GmbH, 2002.
- [50] Hossain, M.; Aldous, L. *Aust. J. Chem.* **2012**, 1465–1477.
- [51] Fort, D. A.; Remsing, R. C.; Swatloski, R. P.; Moyna, P.; Rogers, R. D. *Green Chem.* **2007**, *9*, 63–69.
- [52] Sun, N.; Rahman, M.; Qin, Y.; Maxim, M. L.; Rodríguez, H.; Rogers, R. D. *Green Chem.* **2009**, *11*, 646.
- [53] Zavrel, M.; Bross, D.; Funke, M.; Büchs, J.; Spiess, A. C. *Bioresour. Technol.* **2009**, *100*, 2580–2587.
- [54] Brandt, A.; Ray, M. J.; To, T. Q.; Leak, D. J.; Murphy, R. J.; Welton, T. *Green Chem.* **2011**, *13*, 2489.
- [55] Zhao, H.; Baker, G. A.; Song, Z.; Olubajo, O.; Crittle, T.; Peters, D. *Green Chem.* **2008**, *10*, 696.
- [56] Pinkert, A.; Marsh, K. N.; Pang, S. *Ind. Eng. Chem. Res.* **2010**, *49*, 11121–11130.
- [57] Mazza, M.; Catana, D.-A.; Vaca-Garcia, C.; Cecutti, C. *Cellulose* **2009**, *16*, 207–215.
- [58] Pu, Y.; Jiang, N.; Ragauskas, A. J. *J. Wood. Chem. Technol.* **2007**, *27*, 23–33.
- [59] Fu, D.; Mazza, G.; Tamaki, Y. *J. Agric. Food Chem.* **2010**, *58*, 2915–2922.

- [60] Lee, S. H.; Doherty, T. V.; Linhardt, R. J.; Dordick, J. S. *Biotechnol. Bioeng.* **2009**, *102*, 1368–1376.
- [61] Kilpeläinen, I.; Xie, H.; King, A.; Granstrom, M.; Heikkinen, S.; Argyropoulos, D. *J. Agric. Food Chem.* **2007**, *55*, 9142–9148.
- [62] Verdía, P.; Brandt, A.; Hallett, J. P.; Ray, M. J.; Welton, T. *Green Chem.* **2014**, *16*, 1617.
- [63] Brandt, A.; Chen, L.; van Dongen, B. E.; Welton, T.; Hallett, J. P. *Green Chem.* **2015**, *17*, 5019–5034.
- [64] Chen, L.; Sharifzadeh, M.; MacDowell, N.; Welton, T.; Shah, N.; Hallett, J. P. *Green Chem.* **2014**, *16*, 3098.
- [65] El Hage, R.; Brosse, N.; Chrusciel, L.; Sanchez, C.; Sannigrahi, P.; Ragauskas, A. *Polym. Degrad. Stabil.* **2009**, *94*, 1632–1638.
- [66] Wen, J.-L.; Yuan, T.-Q.; Sun, S.-L.; Xu, F.; Sun, R.-C. *Green Chem.* **2014**, 181–190.
- [67] Sathitsuksanoh, N.; Holtman, K. M.; Yelle, D. J.; Morgan, T.; Stavila, V.; Pelton, J.; Blanch, H.; Simmons, B. A.; George, A. *Green Chem.* **2014**, *16*, 1236.
- [68] Sturgeon, M. R.; Kim, S.; Lawrence, K.; Paton, R. S.; Chmely, S. C.; Nimlos, M.; Foust, T. D.; Beckham, G. T. *ACS Sustain. Chem. Eng.* **2014**, *2*, 472–485.
- [69] Yokoyama, T. *J. Wood Chem. Technol.* **2014**, *35*, 27–42.
- [70] Cox, B. J.; Jia, S.; Zhang, Z. C.; Ekerdt, J. G. *Polym. Degrad. Stabil.* **2011**, *96*, 426–431.
- [71] *IUPAC Nomenclature of Organic Chemistry.*
- [72] van Scheppingen, W.; Dorrestijn, E.; Arends, I.; Mulder, P.; Korth, H.-G. *J. Phys. Chem. A* **1997**, *101*, 5405–5411.
- [73] Williamson, A. *Philos. Mag.* **1850**, *37*, 350–356.
- [74] Hemming, K. *Chem. Educ.* **2001**, *6*, 396–398.
- [75] Sala, T.; Sargent, M. V. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2593–2598.
- [76] Burwell, R. L. *Chem. Rev.* **1954**, *54*, 615–686.
- [77] Vivekananda Bhatt, M. Kulkarni, S. U. *Synthesis (Stuttg.)* **1983**, *4*, 249–282.
- [78] Ranu, B.; Bhar, S. *Org. Prep. Proced. Int.* **1996**, *28*, 371.
- [79] Weissman, S. A.; Zewge, D. *Tetrahedron* **2005**, *61*, 7833–7863.
- [80] Butlerow, A. *Justus Liebigs Ann. Chem.* **1861**, *120*, 295–298.

- [81] Dario, L.; Montanari, F.; Rolla, F. *Synthesis (Stuttg)*. **1978**, 771–773.
- [82] Craig, P. N.; Abenhauek, F. N.; Williams, P. M.; Macko, E.; Toner, J. *J. Am. Chem. Soc.* **1952**, *74*, 1316.
- [83] Sintenis, F. *Justus Liebigs Ann. Chem.* **1872**, *161*, 329–346.
- [84] Bachmann, W. E.; Cole, W.; Wilds, A. L. *J. Am. Chem. Soc.* **1940**, *62*, 824–839.
- [85] Silva, R. *Ann. Chim. Phys.* **1876**, *7*, 429.
- [86] Lippert, W. *Ann.* **1893**, *276*, 148.
- [87] Bonhoeffer, K.; Reitz, O. *Z. Phys. Chem* **1937**, *179A*, 143.
- [88] Hughes, E. D.; Ingold, C. K. *J. Chem. Soc* **1935**, 251.
- [89] Svanholm, U.; Parker, V. *J. Chem. Soc., Perkin Trans.* **1966**, 1966–1969.
- [90] Kogl, F.; Postowsky, J. *J. Ann.* **1925**, *6*, 444.
- [91] Hughes, G.; Thompson, E. *Nature* **1949**, *164*, 365.
- [92] Zoltewicz, J. A.; Sale, A. A. *J. Org. Chem.* **1970**, *35*, 3462–3467.
- [93] Shelton, R. S.; Campen, M. G. V.; Meisner, D. F.; Parmarter, S. M.; Andrews, E. R.; Allen, R. E.; Wyckoff, K. K. *J. Am. Chem. Soc.* **1953**, *75*, 5491–5495.
- [94] De Lange, P. W. *Rec. Trav. Chim* **1919**, *38*, 101.
- [95] Kolhatkar, G. B.; Bapat, V. V. *Chem. Abstr.* **1939**, *33*, 5268.
- [96] Sainsbury, M.; Dyke, S. F.; Moon, B. J. *J. Chem. Soc* **1970**, 1797.
- [97] Roberts, V.; Fendt, S.; Lemonidou, A. A.; Li, X.; Lercher, J. A. *Appl. Catal. B Environ.* **2010**, *95*, 71–77.
- [98] Hwu, J. R.; Wong, F. F.; Huang, J.-J.; Tsay, S.-C. *J. Org. Chem.* **1997**, *62*, 4097–4104.
- [99] Maercker, A. *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 972–989.
- [100] Schnizer, A. W.; Robert, I.; Letsikger, L. *J. Am. Chem. Soc.* **1951**, *73*, 5708.
- [101] Ziegler, K.; Gellert, H.-G. *Justus Liebigs Ann. Chem.* **1950**, *567*, 185–195.
- [102] Maercker, A.; Stumpe, R. W. *Tetrahedron Lett.* **1979**, 3843–3846.
- [103] Hartmann, C.; Gattermann, L. *Berichte der Dtsch. Chem. Gesellschaft* **1892**, *25*, 3531–3534.
- [104] Pfeiffer, P.; Loewe, W. *J. für Prakt. Chemie* **1937**, *147*, 293–310.

- [105] Menzel, W. *Berichte der Dtsch. Chem. Gesellschaft* **1942**, *75*, 1055–1061.
- [106] Horie, T.; Shibata, K.; Yamashita, K.; Kawamura, Y.; Tsukayama, M. *Chem. Pharm. Bull* **1997**, *45*, 446.
- [107] Dillon, E.; Benton, F. *J. Am. Chem. Soc.* **1942**, *64*, 1128–1129.
- [108] Punna, S.; Meunier, S.; Finn, M. G. *Org. Lett.* **2004**, *6*, 2777–9.
- [109] Fujita, M.; Qi, G.; Verkerk, U. H.; Dzwiniel, T. L.; McDonald, R.; Stryker, J. M. *Org. Lett.* **2004**, *6*, 2653–2656.
- [110] Taub, D.; Girotra, N. N.; Hoffsommer, R. D.; Kuo, C. H.; Slates, H. L.; Weber, S.; Wendler, N. L. *Tetrahedron* **1968**, *24*, 2443–2461.
- [111] Brooks, P. R.; Wirtz, M. C.; Vetelino, M. G.; Rescek, D. M.; Woodworth, G. F.; Morgan, B. P.; Coe, J. W. *J. Org. Chem.* **1999**, *64*, 9719–9721.
- [112] Morgan, B. P.; Swick, A. G.; Hargrove, D. M.; LaFlamme, J. A.; Moynihan, M. S.; Carroll, R. S.; Martin, K. a.; Lee, E.; Decosta, D.; Bordner, J. *J. Med. Chem.* **2002**, *45*, 2417–2424.
- [113] Min, J.; Kim, J.; Park, O. *Synth. Commun.* **2004**, *34*, 383–390.
- [114] Maeyama, K.; Kobayashi, M.; Yonezawa, N. *Synth. Commun.* **2001**, *31*, 869–875.
- [115] Wu, Y. Q.; Limburg, D. C.; Wilkinson, D. E.; Vaal, M. J.; Hamilton, G. S. *Tetrahedron Lett.* **2000**, *41*, 2847–2849.
- [116] Sharghi, H.; Tamaddon, F. *Tetrahedron* **1996**, *52*, 13623–13640.
- [117] Ford, W. T.; Hauri, R. J.; Smith, S. G. *J. Am. Chem. Soc.* **1974**, *96*, 4316–4318.
- [118] Driver, G.; Johnson, K. E. *Green Chem.* **2003**, *5*, 163–169.
- [119] Boovanahalli, S. K.; Kim, D. W.; Chi, D. Y. *J. Org. Chem.* **2004**, 3340–3344.
- [120] Schmid, C. R.; Beck, C. A.; Cronin, J. S.; Staszak, M. A. *Org. Process Res. Dev.* **2004**, 670–673.
- [121] Kulkarni, P.; Kadam, A.; Mane, R.; V., U.; Wadgaonkar, P. *J. Chem. Res.* **1999**, 394.
- [122] Oye, H.; Jagtoyen, M.; Oksefjell, T.; Wilkes, J. *Mater. Sci. Forum* **1991**, *73*, 183–189.
- [123] Green, L.; Hemeon, I.; Singer, R. D. *Tetrahedron Lett.* **2000**, *41*, 1343–1346.
- [124] Kemperman, G. J.; Roeters, T. A.; Hilberink, P. W. *Eur. J. Org. Chem.* **2003**, 1681–1686.
- [125] Sun, N.; Rodríguez, H.; Rahman, M.; Rogers, R. D. *Chem. Commun.* **2011**, *47*, 1405–21.
- [126] Jia, S.; Cox, B. J.; Guo, X.; Zhang, Z. C.; Ekerdt, J. G. *ChemSusChem* **2010**, *3*, 1078–84.

- [127] Jia, S.; Cox, B. J.; Guo, X.; Zhang, Z. C.; Ekerdt, J. G. *Ind. Eng. Chem. Res* **2011**, *50*, 849–855.
- [128] Binder, J. B.; Gray, M. J.; White, J. F.; Zhang, Z. C.; Holladay, J. E. *Biomass and Bioenergy* **2009**, *33*, 1122–1130.
- [129] Mäki-Arvela, P.; Anugwom, I.; Virtanen, P.; Sjöholm, R.; Mikkola, J. P. *Ind. Crop. Prod.* **2010**, *32*, 175–201.
- [130] Kubo, S.; Hashida, K.; Yamada, T. *J. Wood Chem. Technol.* **2008**, *28*, 84–96.
- [131] Hammett, L. P. *Chem. Rev.* **1956**, *17*, 125–136.
- [132] Hansch, C.; Leo, A.; Taft, R. *Chem. Rev.* **1991**, *91*, 165–195.
- [133] Bergon, M.; Calmon, J.-p. *Tetrahedron Lett.* **1981**, *22*, 937–940.
- [134] Katritzky, A. R.; Kim, M. S.; Fedoseyenko, D.; Widyan, K.; Siskin, M.; Francisco, M. *Tetrahedron* **2009**, *65*, 1111–1114.
- [135] Janesko, B. G. *Phys. Chem. Chem. Phys.* **2014**, 1–11.
- [136] Deuss, P. J.; Scott, M.; Tran, F.; Westwood, N. J.; de Vries, J. G.; Barta, K. *J. Am. Chem. Soc.* **2015**, *137*, 7456–7467.
- [137] Alder, E.; Lindgren, B.; Saedlén, U. *Sven. Papperstidning* **1952**, *55*, 245–254.
- [138] Adler, E.; Eriksoo, E. *Acta. Chem. Scand.* **1955**, *9*, 341–342.
- [139] Crestini, C.; Argyropoulos, D. S. *J. Agric. Food Chem.* **1997**, *45*, 1212–1219.
- [140] Pardini, V. L.; Smith, C. Z.; Utley, J. H. P.; Vargas, R. R.; Viertler, H. *J. Org. Chem.* **1991**, *56*, 7305–7313.
- [141] Kawai, S.; Okita, K.; Sugishita, K.; Tamaka, A.; Ohashi, H. *J. Wood. Sci* **1999**, 440–443.
- [142] Badamali, S. K.; Luque, R.; Clark, J. H.; Breeden, S. W. *Catal. Commun.* **2011**, *12*, 993–995.
- [143] Song, Q.; Wang, F.; Xu, J. *Chem. Commun.* **2012**, *48*, 7019.
- [144] Zhang, J.; Liu, Y.; Chiba, S.; Loh, T.-P. *Chem. Commun.* **2013**, *49*, 11439–41.
- [145] Nakatsubo, F.; Sato, K.; Higuchi, T. *Holzforschung* **1975**, *62*, 165–168.
- [146] Nakatsubo, F.; Higuchi, T. *Wood Res.* **1980**, *66*, 23–29.
- [147] Buendia, J.; Mottweiler, J.; Bolm, C. *Chem. Eur. J.* **2011**, *17*, 13877–82.

- [148] Rahimi, A.; Azarpira, A.; Kim, H.; Ralph, J.; Stahl, S. S. *J. Am. Chem. Soc.* **2013**, *135*, 6415–8.
- [149] Besombes, S.; Utille, J.-P.; Mazeau, K.; Robert, D.; Taravel, F. R. *Magn. Reson. Chem.* **2004**, *42*, 337–347.
- [150] Galkin, M. V.; Sawadjoon, S.; Rohde, V.; Dawange, M. *ChemCatChem* **2014**, *6*, 179–184.
- [151] Gräsvik, J.; Hallett, J. P.; To, T. Q.; Welton, T. *Chem. Commun.* **2014**, *50*, 7258–61.
- [152] Cox, R. A. *Can. J. Chem.* **2012**, *90*, 811–818.
- [153] Gierer, J. *Wood Sci. Technol.* **1985**, *19*, 289–312.
- [154] Beauchet, R.; Monteil-Rivera, F.; Lavoie, J. M. *Bioresour. Technol.* **2012**, *121*, 328–34.
- [155] Shimada, K.; Hosoya, S.; Ikeda, T. *J. Wood Chem. Technol.* **1997**, *17*, 57–72.
- [156] Zakzeski, J.; Bruijninx, P. C. A.; Jongerius, A. L.; Weckhuysen, B. M. *Chem. Rev.* **2010**, *110*, 3552–3599.
- [157] Eyring, H. *J. Chem. Phys.* **1935**, *3*, 107.
- [158] Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 3rd ed.; WILEY-VCH Verlag, 2003.
- [159] McNaught, A.; Wilkinson, A. *Compendium of Chemical Terminology*, 2nd ed.; Blackwell Scientific Publications, Oxford, 1997.
- [160] Hughes, E. D.; Ingold, C. K. *Trans. Faraday Soc.* **1935**, *37*, 657.
- [161] Ingold, C. *Structure and Mechanism in Organic Chemistry*; Cornell University Press, 1969.
- [162] Hartmann, H.; Schmidt, A. *Z. Phys. Chem* **1969**, *66*, 183.
- [163] Yau, H. M.; Barnes, S. A.; Hook, J. M.; Youngs, T. G. A.; Croft, A. K.; Harper, J. B. *Chem. Commun.* **2008**, 3576–8.
- [164] Imai, T.; Yokoyama, T.; Matsumoto, Y. *J. Wood Sci.* **2011**, *57*, 219–225.
- [165] Chatel, G.; Rogers, R. D. *ACS Sustain. Chem. Eng.* **2014**, *2*, 322–339.
- [166] Ge, X.; Ji-he, Y.; Hui-hui, M.; Zhi, Y. *Chem. Technol. Fuels Oils* **2011**, *47*, 283–291.
- [167] Piskorz, J.; Majerski, P.; Radlein, D.; Scott, D. S. *Energy Fuels* **1989**, *3*, 723–726.
- [168] Thring, R. W.; Katikaneni, S. P. R.; Bakhshi, N. N. *Fuel Process. Technol.* **2000**, *62*, 17–30.
- [169] Çetin, N. S.; Özmen, N. *Int. J. Adhes. Adhes.* **2002**, *22*, 477–480.

- [170] Hatakeyama, H.; Kosugi, R.; Hatakeyama, T. *J. Therm. Anal.* **2008**, *92*, 419–424.
- [171] Varanasi, P.; Singh, P.; Auer, M.; Adams, P. D.; Simmons, B. a.; Singh, S. *Biotechnol. Biofuels* **2013**, *6*, 14.
- [172] Fache, M.; Darroman, E.; Besse, V.; Auvergne, R.; Caillol, S.; Boutevin, B. *Green Chem.* **2014**, *16*, 1987.
- [173] Hanson, S. K.; Baker, R. T.; Gordon, J. C.; Scott, B. L.; Thorn, D. L. *Inorg. Chem.* **2010**, *49*, 5611–8.
- [174] Hanson, S. K.; Wu, R.; Silks, L. a. P. *Angew. Chem. Int. Ed. Engl.* **2012**, *51*, 3410–3.
- [175] Jiang, N.; Ragauskas, A. J. *Tetrahedron Lett.* **2007**, *48*, 273–276.
- [176] Jiang, N.; Ragauskas, A. J. *J. Org. Chem.* **2007**, *72*, 7030–7033.
- [177] Sedai, B.; Díaz-urruia, C.; Baker, T. R.; Wu, R.; Silks, L. A. P.; Hanson, S. K. *ACS Catal.* **2011**, *1*, 794–804.
- [178] Sun, R.; Lawther, J. M.; Banks, W. B. *Ind. Crop. Prod.* **1995**, *4*, 241–254.
- [179] Korpi, H. *Appl. Catal. A Gen.* **2004**, *268*, 199–206.
- [180] Kervinen, K.; Korpi, H.; Leskelä, M.; Repo, T. *J. Mol. Catal. A Chem.* **2003**, *203*, 9–19.
- [181] Stärk, K.; Taccardi, N.; Bösmann, A.; Wasserscheid, P. *ChemSusChem* **2010**, *3*, 719–23.
- [182] Shamsuri, A. A.; Abdullah, D. K. *Oxid. Commun.* **2012**, *775*, 767–775.
- [183] Liu, S.; Shi, Z.; Li, L.; Yu, S.; Xie, C.; Song, Z. *RSC Adv.* **2013**, *3*, 5789.
- [184] Grigoriev, V.; Hill, C. L.; Weinstock, I. A. *Oxid. Delignification Chem.* **2001**, 297–312.
- [185] Evtuguin, D. V.; Neto, C. P. *Am. Chem. Soc.* **2001**, 327–341.
- [186] Wemple, M. W.; Geletii, Y. V.; Barbuzzi, E. M. G. *Am. Chem. Soc.* **2001**, 313–326.
- [187] Chen, X.; Souvanhthong, B.; Wang, H.; Zheng, H.; Wang, X.; Huo, M. *Appl. Catal. B Environ.* **2013**, *138-139*, 161–166.
- [188] Evtuguin, D. V.; Neto, C. P. *Oxidative delignification Chem.* **2001**, 342–355.
- [189] Cheng, F.; Wang, H.; Rogers, R. D. *ACS Sustain. Chem. Eng.* **2014**, *2*, 2859–2865.
- [190] Tsigdinos, G.; Hallada, C. *Inorg. Chem.* **1968**, *7*, 437–441.
- [191] Sluiter, A.; Hames, B.; Ruiz, R.; Scarlata, C.; Sluiter, J.; Templeton, D.; Crocker, D. *Lab. Anal. Proced.* **2012**, 17.

- [192] Granata, A.; Argyropoulos, D. S. *J. Agric. Food Chem.* **1995**, *43*, 1538–1544.
- [193] Pu, Y.; Cao, S.; Ragauskas, A. J. *Energy Environ. Sci.* **2011**, *4*, 3154.
- [194] Prado, R.; Brandt, A.; Erdocia, X.; Hallet, J.; Welton, T.; Labidi, J. *Green Chem.* **2016**, *18*, 834–841.
- [195] Koeberg-Telder, A.; Cerfontain, H. *J.C.S Perkin II* **1973**, 633–637.
- [196] George, A.; Tran, K.; Morgan, T. J.; Benke, P. I.; Berrueco, C.; Lorente, E.; Wu, B. C.; Keasling, J. D.; Simmons, B. a.; Holmes, B. M. *Green Chem.* **2011**, *13*, 3375.

Appendix A

Supplementary Information

A.1 Mathematical transformations

A.1.1 To obtain equation 3.3.5:

For the rate of consumption of the ether identified in 3.3.3, if we label concentration of the initial substrate as $[A]_0$ and the concentration of the substrate at any particular time as $[A]$ with t denoting time, the following rearrangements of 3.3.4 can be obtained:

$$\frac{d[A]}{[A]_0} = -kdt$$

integrating both sides of the equation gives:

$$\int \frac{d[A]}{[A]_0} = - \int kdt$$

$$\int \frac{1}{[A]} d[A]_0 = - \int kdt$$

As:

$$\int \frac{1}{x} = \ln(x)$$

Then upon integration:

$$\ln[A] - \ln[A]_0 = -kt$$

Make $\ln[A]$ the subject:

$$\ln[A] = -kt + \ln[A]_0$$

Which can be further rearranged to appear in the linear $y = mx + c$ form:

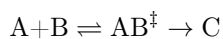
$$\ln \left(\frac{[A]}{[A]_0} \right) = -kt$$

A.1.2 Derivation of Eyring Equation 4.4.4.

Consider the bimolecular reaction:



In transition state theory, the activated complex $[AB]^\ddagger$ is formed:



As transition state theory assumes the activated complex forms in equilibrium, the constant K is used to denote the position of the equilibrium:

$$K^\ddagger = \frac{[AB]^\ddagger}{[A][B]}$$

The rate of a reaction is equal to the number of activated complexes surpassing the activation energy in order to form products. This can be expressed kinetically by the concentration of the activated complex multiplied by the frequency factor, i.e. the frequency of the complex overcom-

ing this energy barrier:

$$\text{rate} = v[\text{AB}]^\ddagger \quad (\text{A.1.1})$$

$$\text{rate} = v[\text{A}][\text{B}]\text{K}^\ddagger \quad (\text{A.1.2})$$

Therefore:

$$\text{rate} = k[\text{A}][\text{B}] \quad (\text{A.1.3})$$

Combining equations A.1.2 and A.1.3 gives a Linear Free Energy Relationship between the rate of reaction and formation of the activated complex:

$$k[\text{A}][\text{B}] = v[\text{A}][\text{B}]\text{K}^\ddagger$$

$$k = v\text{K}^\ddagger \quad (\text{A.1.4})$$

v denotes the frequency of vibration, k is the rate of the reaction and $\text{K}^\ddagger$ the equilibrium constant. The frequency of vibration can be expressed as follows:

$$v = \frac{k_B T}{h}$$

Where k_B is the Boltzmann's constant ($1.381 \times 10^{-23} \text{ J/K}$), T the absolute temperature in Kelvin (K) and h is Planck's constant ($6.626 \times 10^{-34} \text{ Js}$). This can then be substituted into equation A.1.4 giving:

$$k = \frac{k_B T}{h} \text{K}^\ddagger \quad (\text{A.1.5})$$

The equilibrium constant can be expressed in terms of Gibbs energy of activation ($\Delta G^\ddagger$) and which is described as follows:

$$\Delta G^\ddagger = -RT \ln \text{K}^\ddagger \quad (\text{A.1.6})$$

$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger \quad (\text{A.1.7})$$

Combining Equations A.1.6 and A.1.7, where $\Delta H^\ddagger$ is the enthalpy of activation and $\Delta S^\ddagger$ is the entropy of activation the following can be obtained:

$$\ln K^\ddagger = -\frac{\Delta H^\ddagger}{RT} + \frac{\Delta S^\ddagger}{R}$$

Substituting the frequency factor expressed in A.1.5 in order to make k the subject gives the Eyring equation as follows:

$$k = \frac{k_B T}{h} e^{\frac{\Delta H^\ddagger}{RT}} e^{\frac{\Delta S^\ddagger}{R}}$$

Which can be further rearranged to appear in the linear $y = mx + c$ form:

$$\ln \frac{k}{T} = \frac{-\Delta H^\ddagger}{R} \cdot \frac{1}{T} + \ln \frac{k_B}{h} + \frac{\Delta S^\ddagger}{R} \quad (\text{A.1.8})$$

A.2 Chapter 3: Hammett study on 2-phenoxyethanol using acidic ionic liquids

A.2.1 ROESY and NOESY spectra

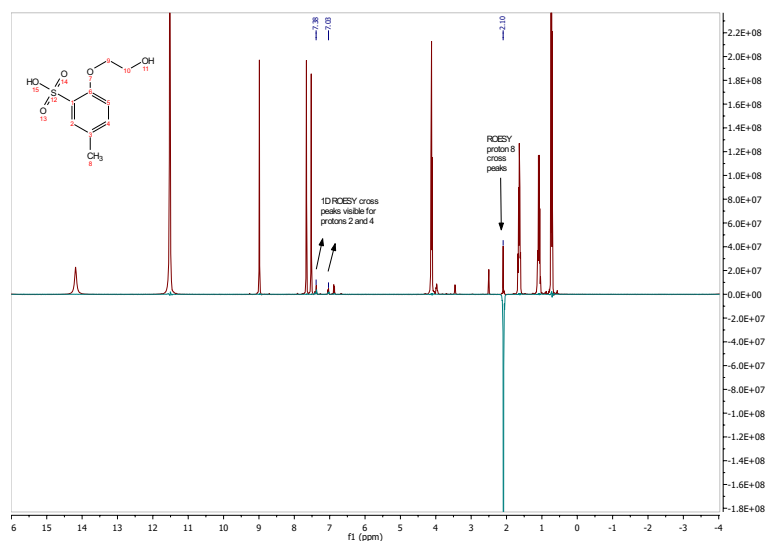


Figure A.2.1 – 1D selective ROESY spectra for 2-(4-methylphenoxy)ethanol: methyl group

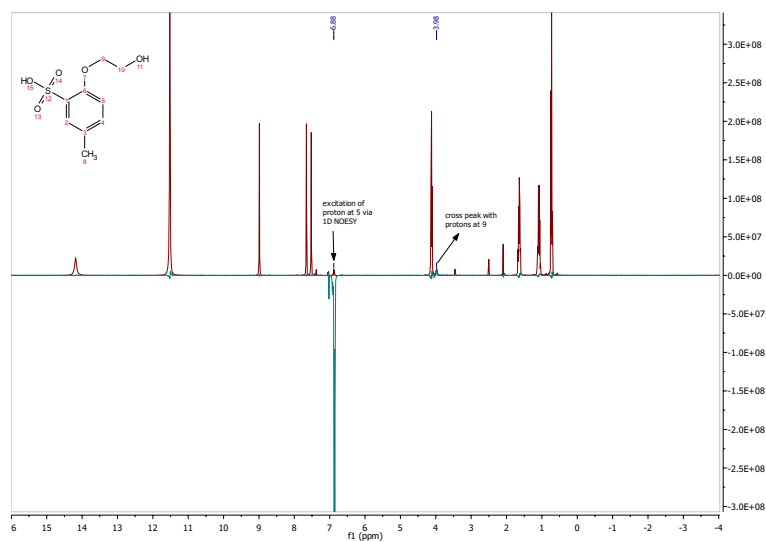


Figure A.2.2 – 1D selective NOESY spectra for 2-(4-methylphenoxy)ethanol: aromatic proton at 5 position

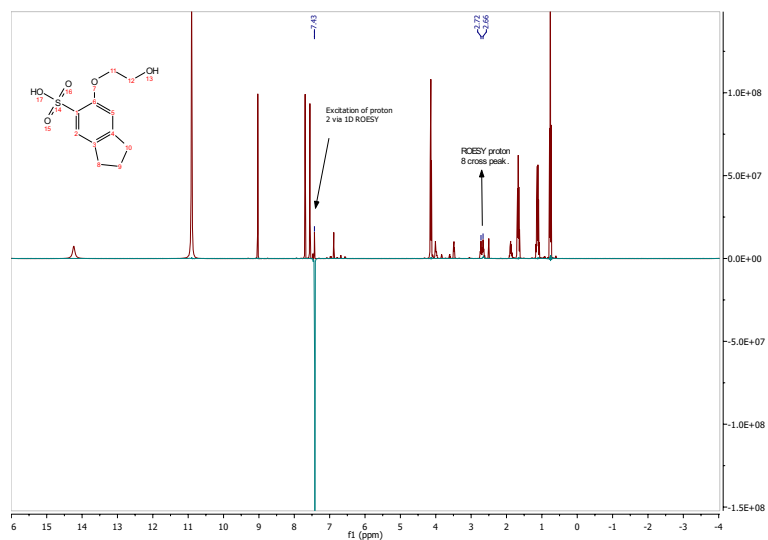


Figure A.2.3 – 1D selective ROESY spectra for 2-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]ethanol: proton at 2 position

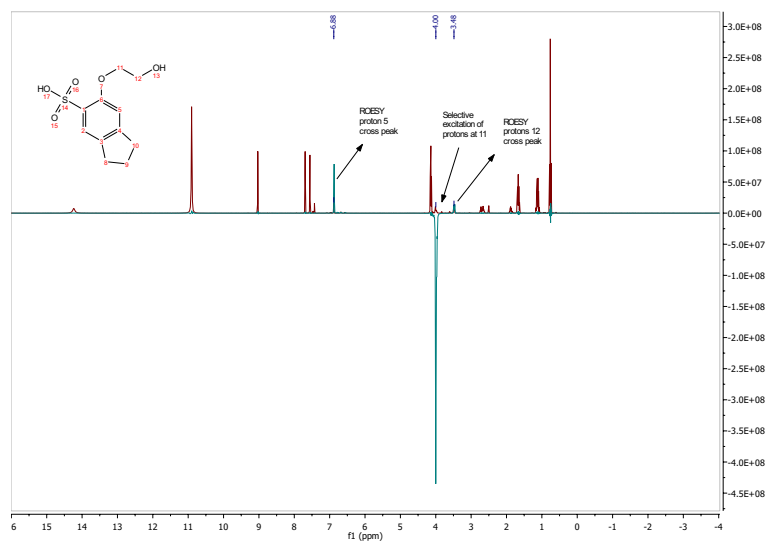


Figure A.2.4 – 1D selective NOESY spectra for 2-[(5,6,7,8-tetrahydro-2-naphthalenyl)oxy]ethanol: proton at 11 position

A.3 Chapter 4: Ether cleavage in lignin model compounds

A.3.1 ^1H NMR spectra for synthesis of lignin model compounds

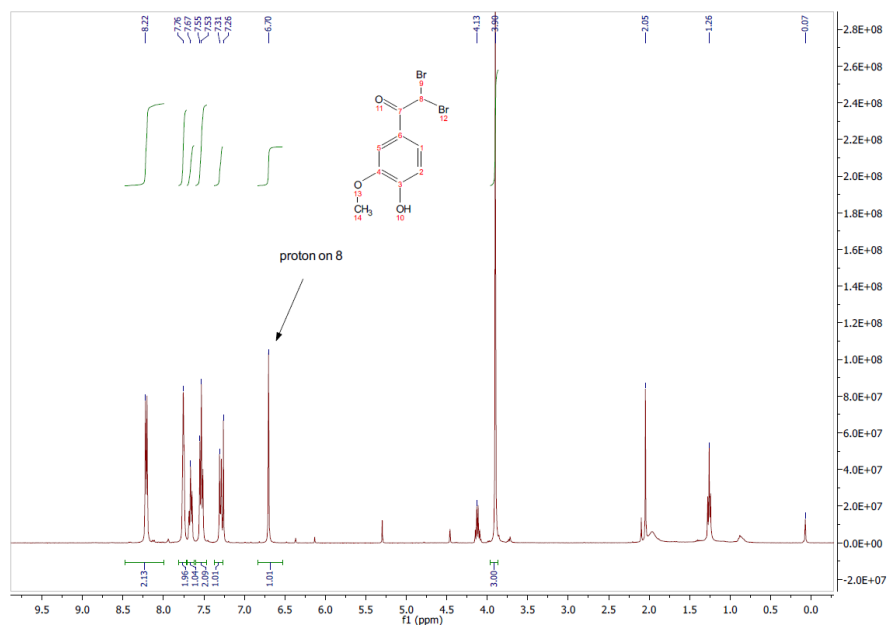


Figure A.3.1 – Bromination of 4-benzloxyacetovanillone using molecular bromine

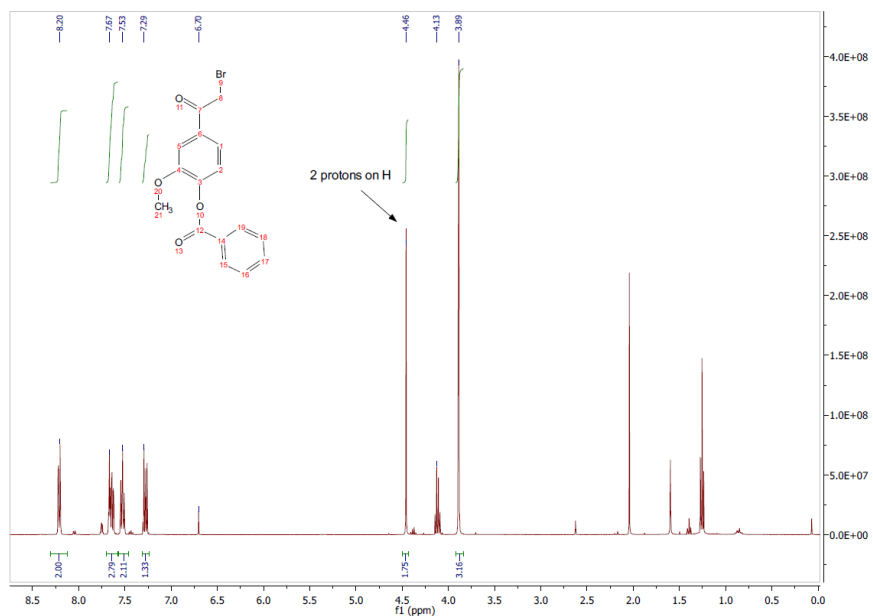


Figure A.3.2 – Bromination of 4-benzloxyacetovanillone using copper bromide

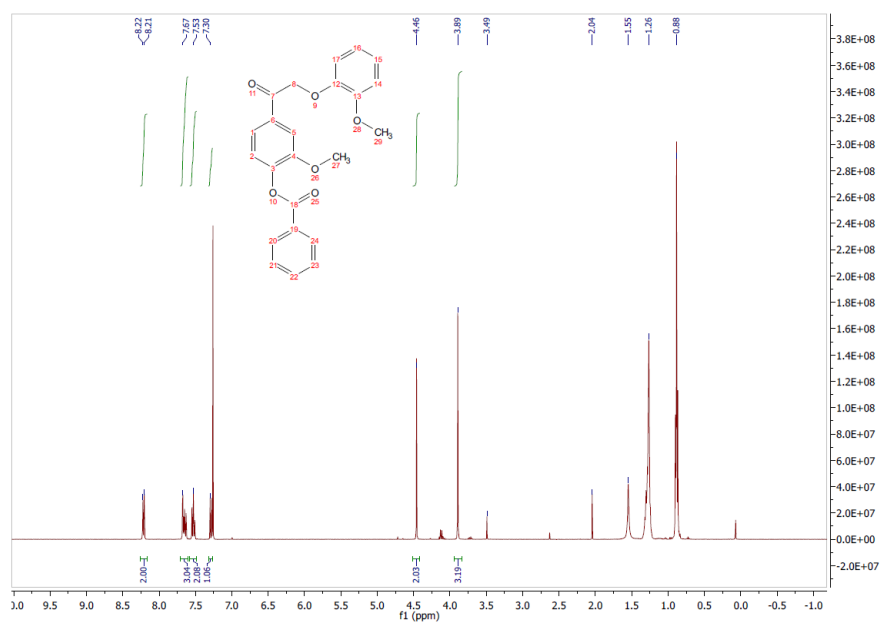


Figure A.3.3 – 4-benzyloxy-3-methoxy-2-(2-methoxyphenoxy)-acetophenone

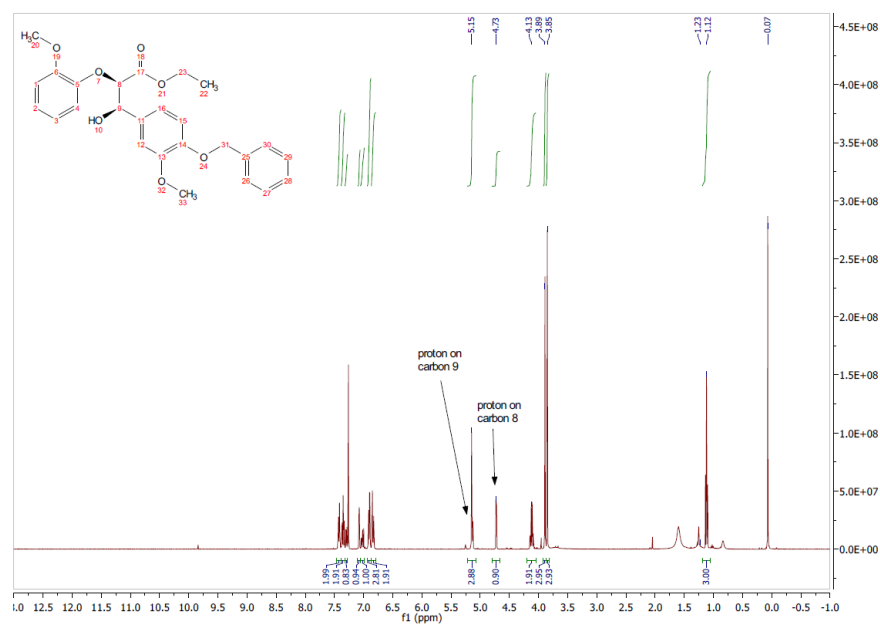
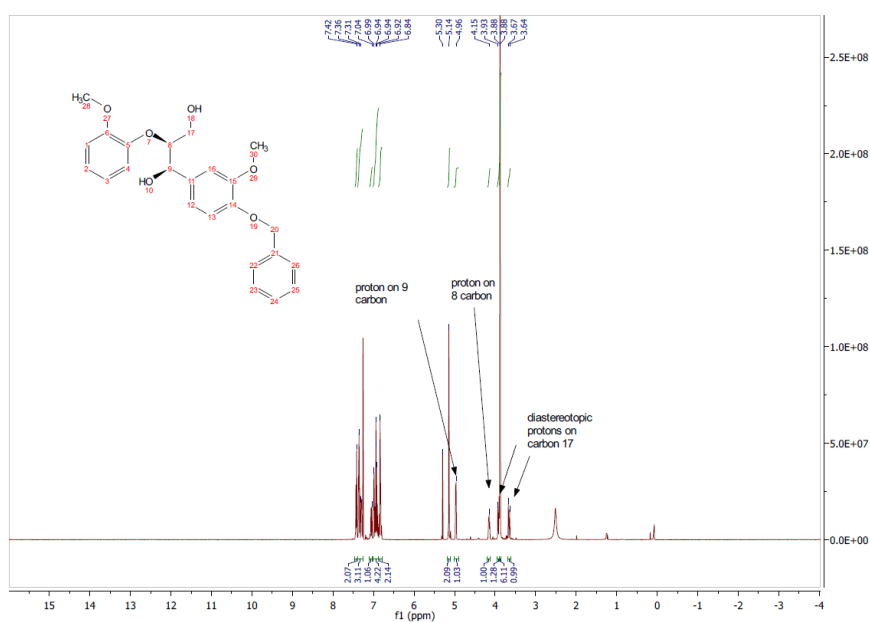
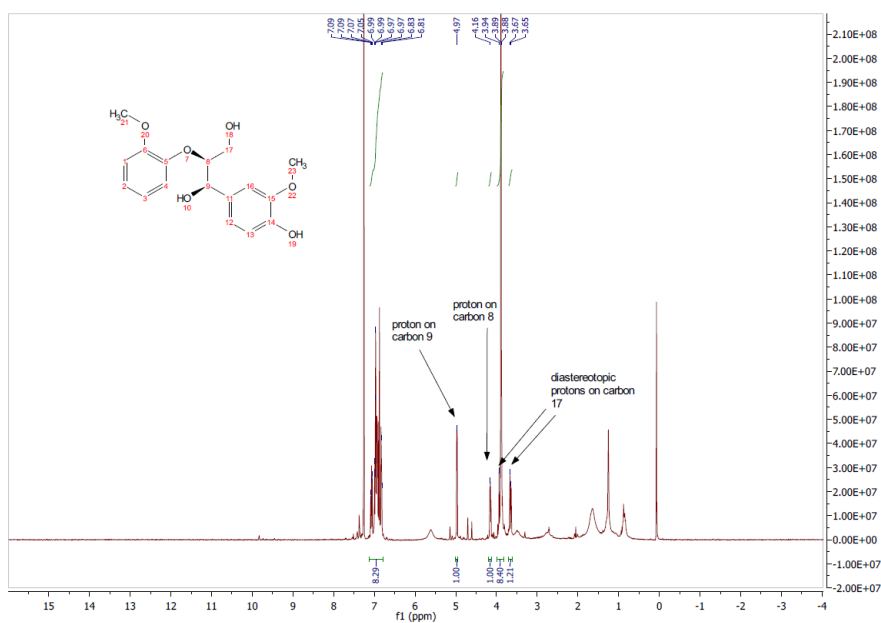


Figure A.3.4 – β -hydroxyester product

**Figure A.3.5** – Reduced β -hydroxyester product**Figure A.3.6** – Deprotected product, final GG model compound

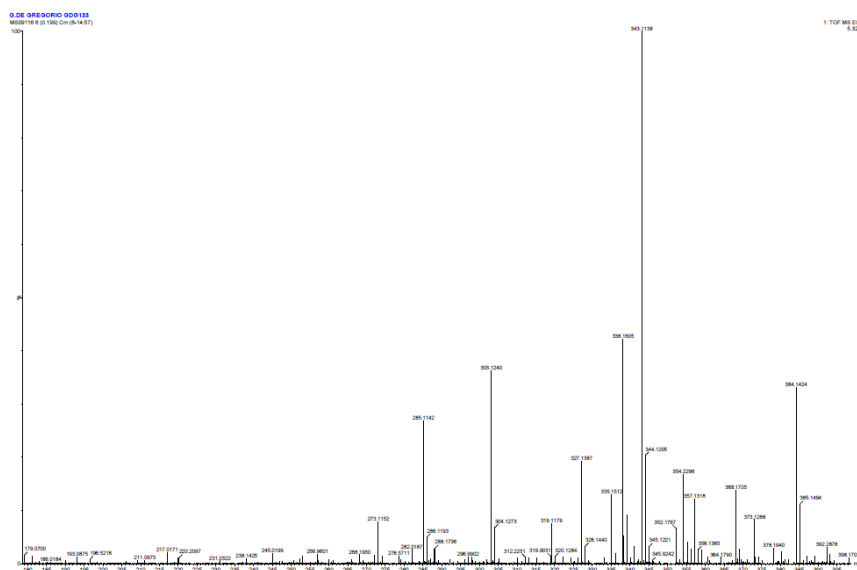


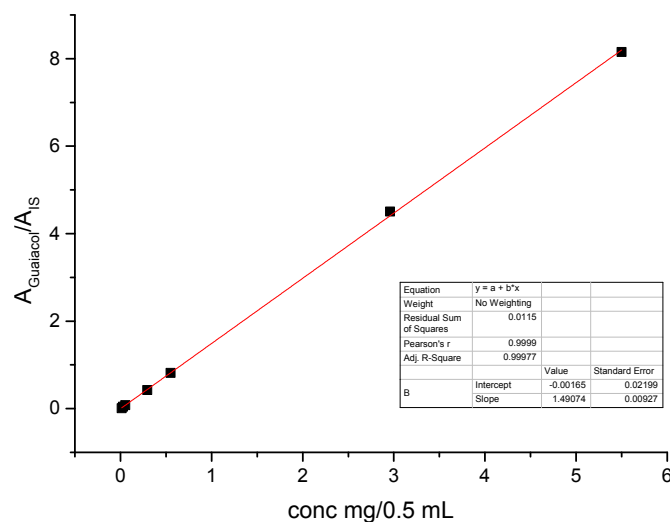
Figure A.3.7 – Mass spectrum of final GG model compound

A.3.2 Calibration and analysis of product

In order to quantify the amount of guaiacol produced in each reaction, calibration of the guaiacol product was carried out against a set concentration of 3,4,5-trimethoxybenzaldehyde internal standard in acetonitrile. Two dilution series with varying guaiacol concentration were prepared whereby a measured quantity of guaiacol was dissolved in acetonitrile and made up to 5 mL in a volumetric flask. A 0.5 mL aliquot of this original solution was then diluted in a further 5 mL of acetonitrile and repeated until 4 dilution samples were obtained. A second dilution series was also prepared using a fresh guaiacol solution in order to compensate for any systematic experimental error. As matrix effects of the IL during HPLC analysis can affect the PDA response, vials were prepared with 0.5 mL of the diluted guaiacol, 400 μ L of the internal standard of set concentration in acetonitrile and 100 mg of vacuum dried $[C_4C_{1im}][HSO_4]$. HPLC analysis of each guaiacol - IL - internal standard was then carried out with the relative areas of both guaiacol and internal standard recorded as shown in table A.3.1. The ratio in guaiacol: Internal standard area (denoted in table as $A_{Guaiacol}/A_{IS}$) was then plotted against conc guaiacol mg/0.5 mL to give a gradient that describes the linear relationship between concentration and response.

Table A.3.1 – Guaiacol calibration using HPLC

Set	conc mg/ mL	conc mg/0.5 mL	Area of Guaiacol	Area of IS	A_{GG}/A_{IS}
1	11	5.5	6340030	778008	8.149055023
1	1.1	0.55	629355	773916	0.81320841
1	0.11	0.055	60028	791867	0.075805659
2	5.92	2.96	3635325	807213	4.503551107
2	0.592	0.296	333510	788482	0.422977316
2	0.0592	0.0296	31216	772471	0.040410579
2	0.0296	0.0148	3519	798161	0.004408885

**Figure A.3.8** – Guaiacol calibration curve using HPLC

The high r^2 value of >0.999 shows a strong linear correlation between concentration and PDA response with the intercept passing closely through the origin. Consequently, any unknown concentration of guaiacol can be calculated once HPLC response is known through the applying the following equation if we assume the calibration intercept passes through the origin:

$$[\text{guaiacol}] = \left(\frac{A_{\text{Guaiacol}}}{A_{\text{IS}}} \right) / \text{Calibration Coefficient} \quad (\text{A.3.1})$$

A.3.3 Pseudo first order rate constants for GG hydrolysis

Figure A.3.9 – Rate constants for GG hydrolysis in $[\text{C}_4\text{C}_{1\text{im}}][\text{HSO}_4]$ with varying acid concentration and water content at 100 °C

Entry	Added Acid content (mol eq %)	Added Water content (in wt %)	Water content of overall system (wt/wt %)	mean k_{obs} (s^{-1})	Standard deviation
1	0	0	0	4.94×10^{-6}	1.98×10^{-6}
2	0	10	9.09	4.88×10^{-6}	9.19×10^{-7}
3	0	20	16.67	5.24×10^{-6}	5.80×10^{-7}
4	0	30	23.07	4.71×10^{-6}	9.40×10^{-7}
5	10	10	9.09	1.7×10^{-4}	3.57×10^{-5}
6	10	20	16.67	2.13×10^{-4}	2.49×10^{-5}
7	10	30	23.07	2.21×10^{-4}	n/a
8	10	40	28.57	1.58×10^{-4}	1.34×10^{-5}
9	10	50	33.33	1.29×10^{-4}	4.19×10^{-5}
10	10	60	37.5	6.64×10^{-5}	7.38×10^{-6}
11	10	70	41.17	5.23×10^{-5}	1.00×10^{-5}
12	10	80	44.44	4.97×10^{-5}	7.07×10^{-8}
13	10	100	50	3.73×10^{-5}	4.17×10^{-6}
14	20	10	9.09	3.71×10^{-4}	1.47×10^{-4}
15	20	20	16.67	5.08×10^{-4}	1.27×10^{-4}
16	20	30	23.07	4.10×10^{-4}	1.10×10^{-4}
17	20	40	28.57	2.88×10^{-4}	7.09×10^{-5}
18	20	50	33.33	2.11×10^{-4}	3.54×10^{-5}
19	20	60	37.5	1.60×10^{-4}	3.11×10^{-5}
20	20	70	41.17	1.93×10^{-4}	2.67×10^{-5}
21	20	80	44.44	1.52×10^{-4}	3.82×10^{-5}
22	20	100	50	1.20×10^{-4}	4.89×10^{-5}

A.3.4 HSQC spectra of lignin model compounds

a) HSQC spectra for model compound **II**: 2-phenoxy-1-phenylethanol

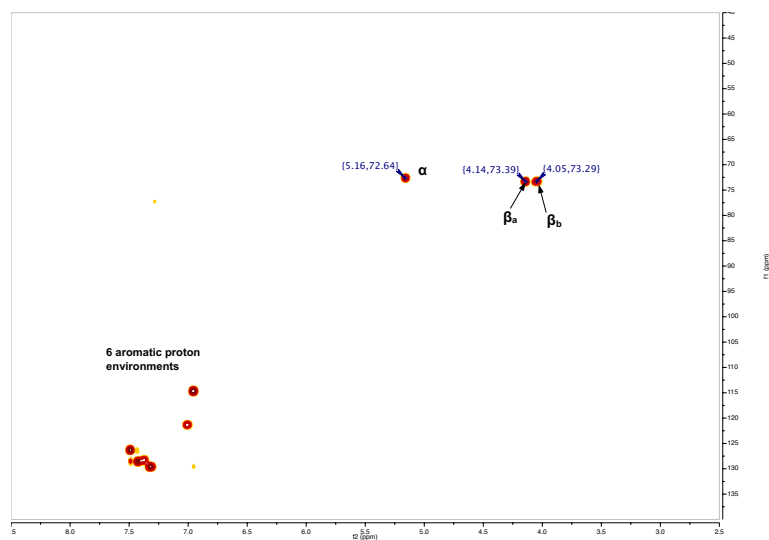


Figure A.3.10 – HSQC of model compound **II** before reaction

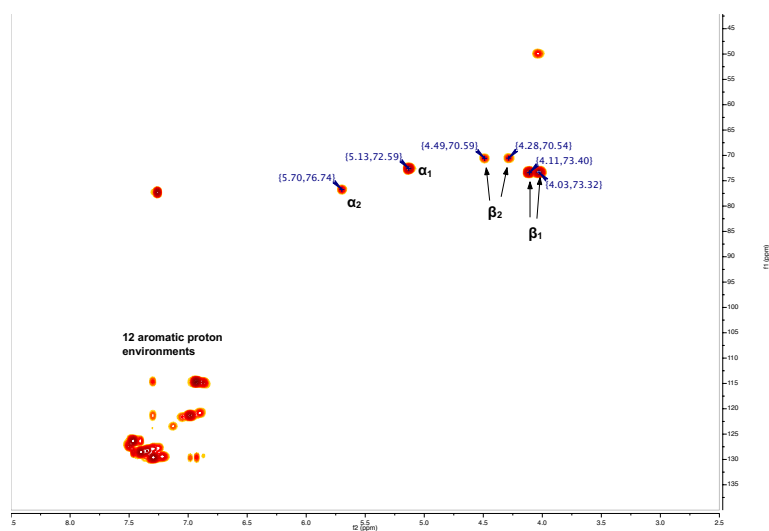


Figure A.3.11 – HSQC of model compound **II** in $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]_{10\%}$ acid with 16.67 wt % water left to react for 5 hours at 100 °C

b) HSQC spectra for model compound **III**: 2-(2-methoxyphenoxy)-1-phenylethanol

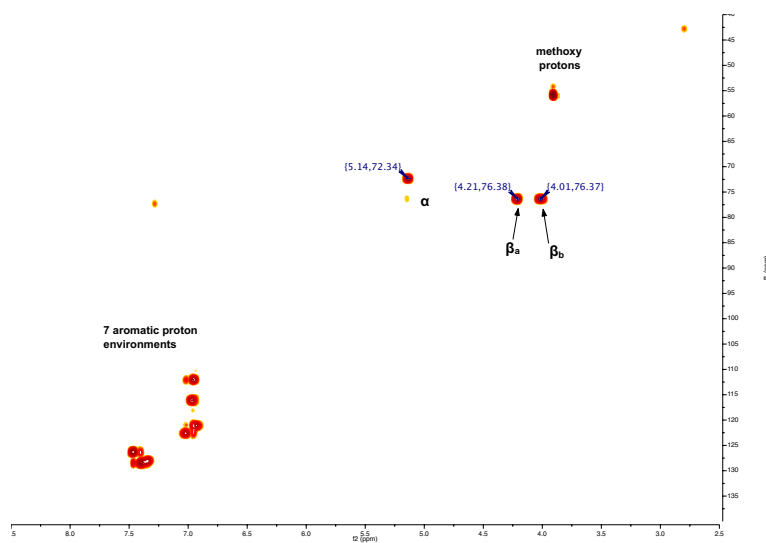


Figure A.3.12 – HSQC of model compound **III** before reaction

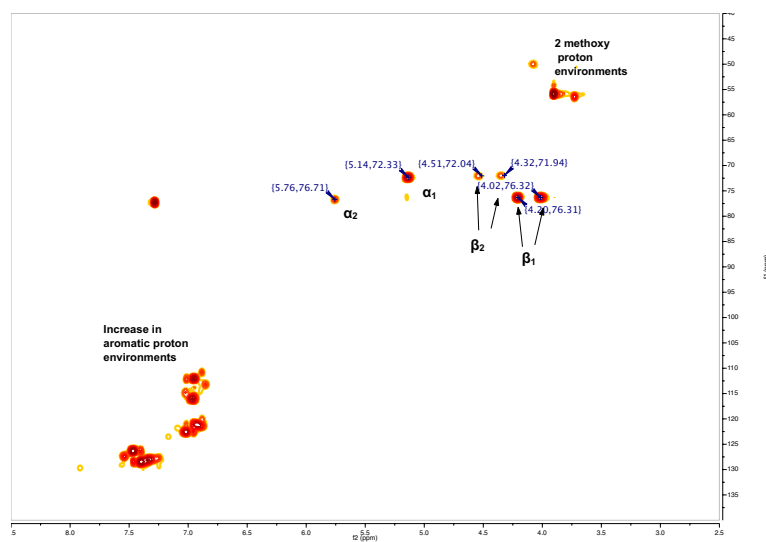


Figure A.3.13 – HSQC of model compound **III** in $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]_{10\%}$ acid with 16.67 wt % water left to react for 5 hours at 100 °C

c) HSQC spectra for model compound **IV**: 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanol

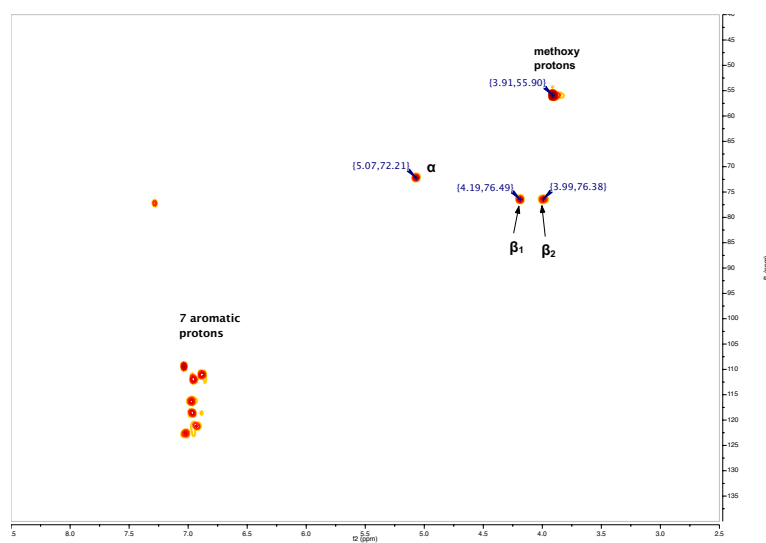


Figure A.3.14 – HSQC of model compound **IV** before reaction

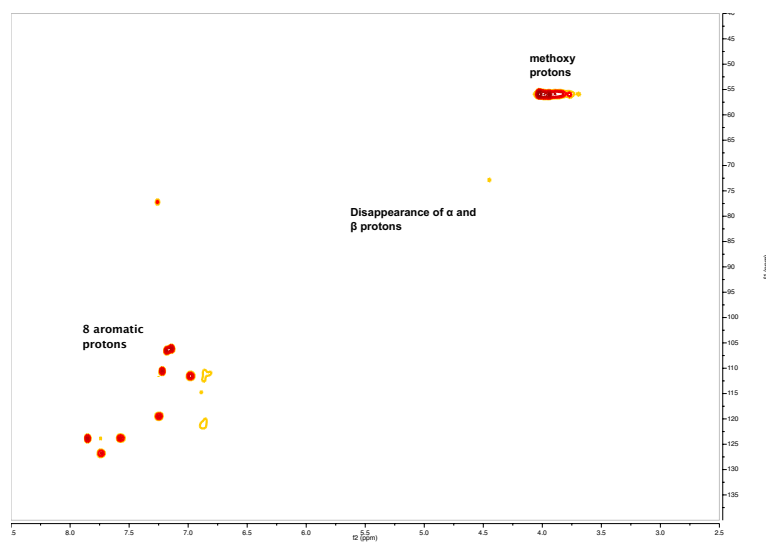


Figure A.3.15 – HSQC of model compound **IV** in $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]_{10\%}$ acid with 16.67 wt % water left to react for 5 hours at 100 °C

d) HSQC spectra for model compound **V**: *erythro*-1-(3-methoxy-4-*O*-benzylphenyl)-2-(2-methoxyphenoxy)-1,3-diol:

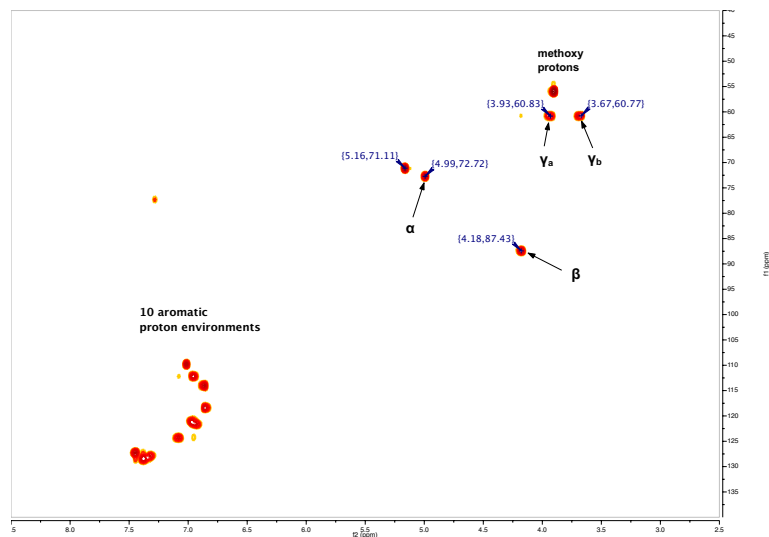


Figure A.3.16 – HSQC of model compound **V** before reaction

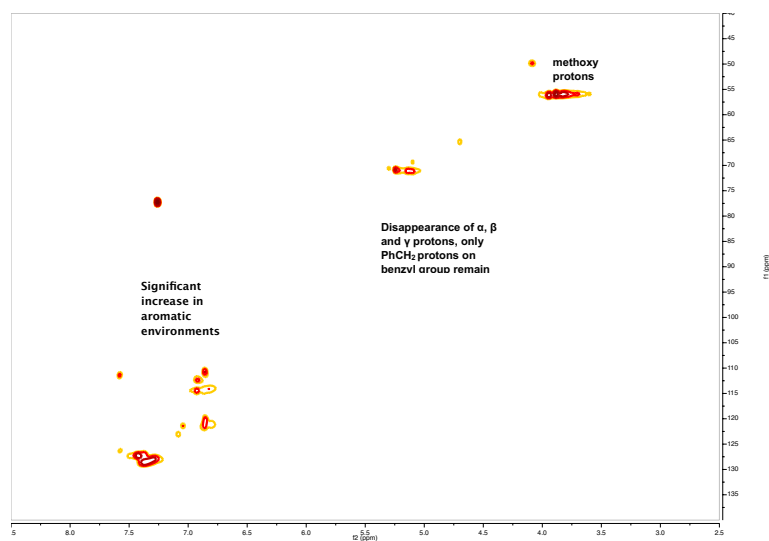
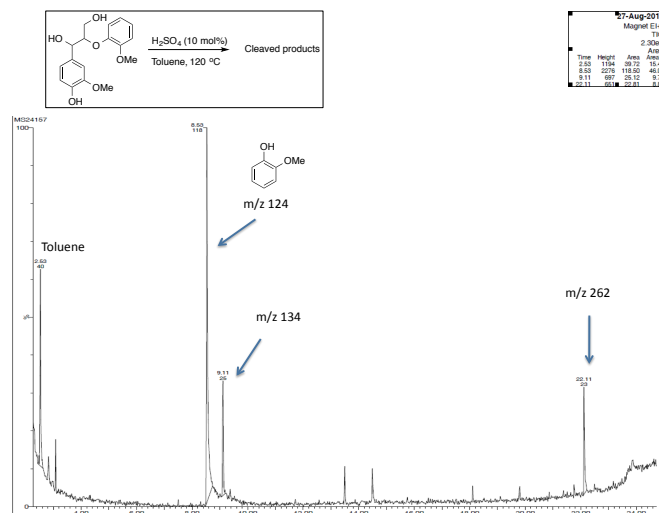
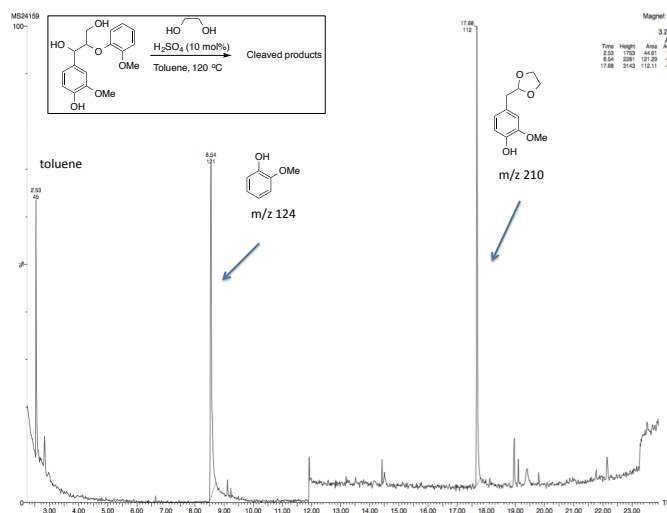
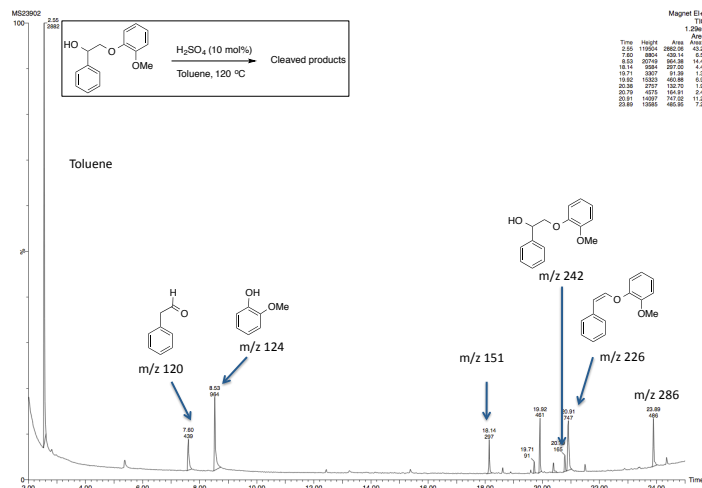
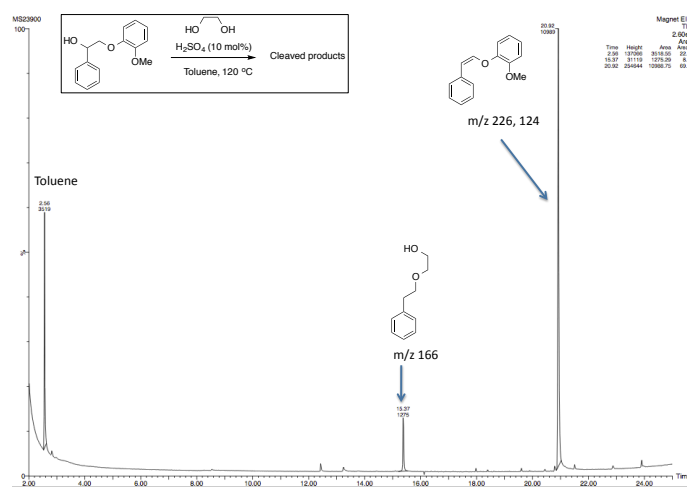
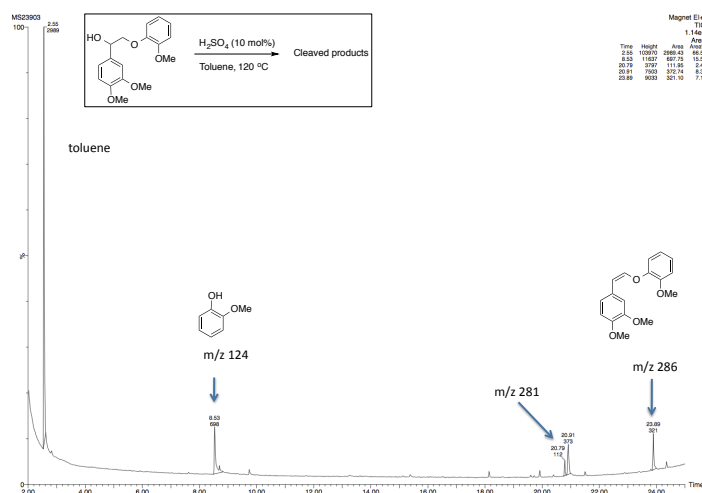
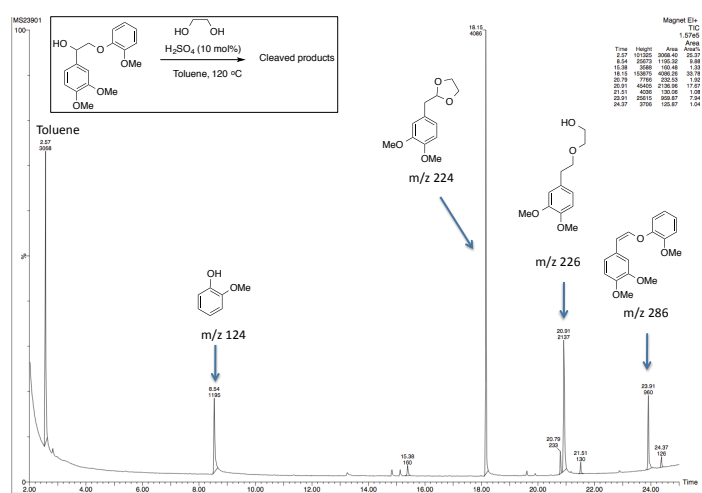


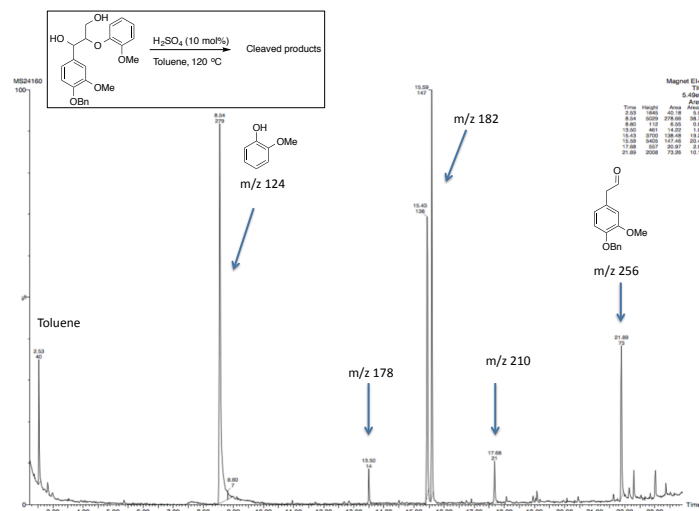
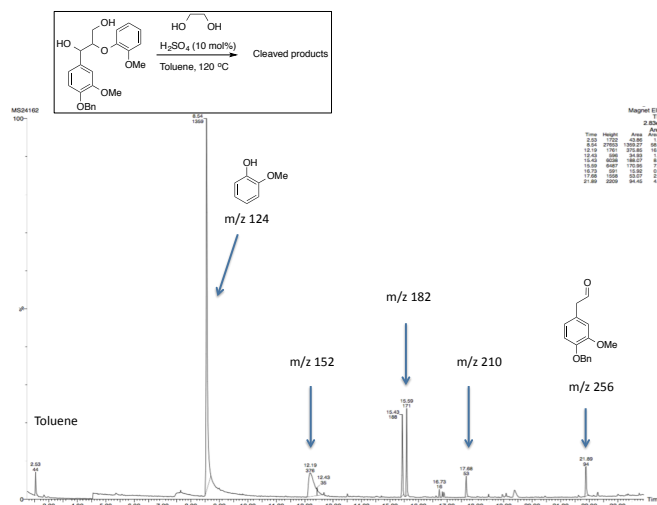
Figure A.3.17 – HSQC of model compound **V** in $[C_4C_{1im}][HSO_4]_{10\%}$ acid with 16.67 wt % water left to react for 5 hours at 100 °C

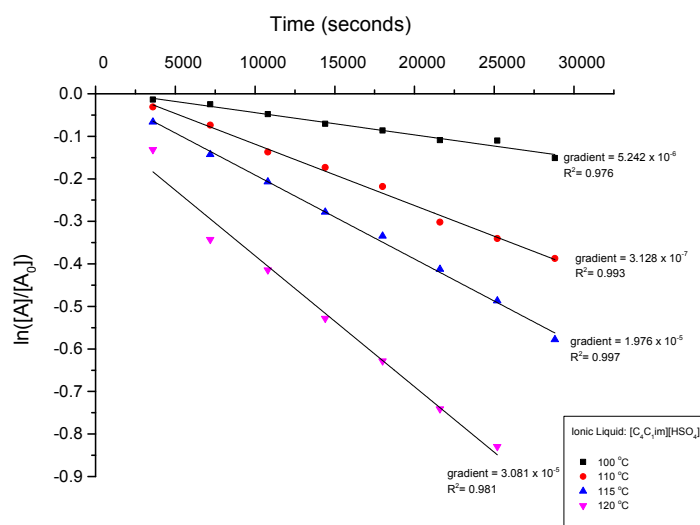
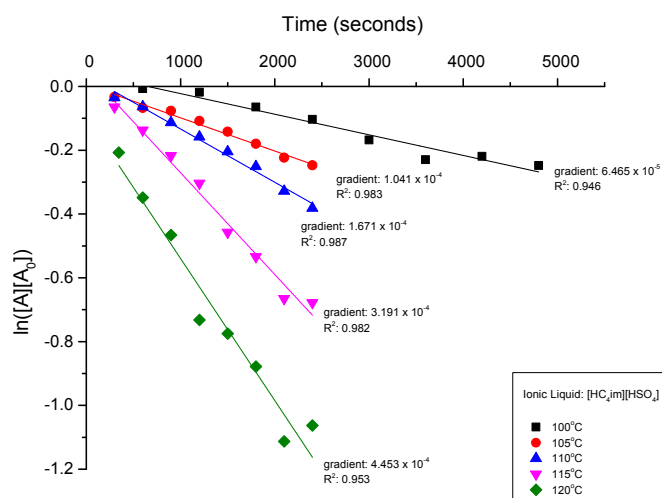
A.3.5 GC-MS chromatograms of lignin model compounds

a) Chromatograms for model compound **I**Figure A.3.18 – Acidolysis of **I** in toluene with 10 mol % sulfuric acidFigure A.3.19 – Acidolysis of **I** in toluene with 10 mol % sulfuric acid and 2 molar equivalents of ethylene glycol

b) Chromatograms for model compound **III**Figure A.3.20 – Acidolysis of **III** in toluene with 10 mol % sulfuric acidFigure A.3.21 – Acidolysis of **III** in toluene with 10 mol % sulfuric acid and 2 molar equivalents of ethylene glycol

c) Chromatograms for model compound **IV**Figure A.3.22 – Acidolysis of **IV** in toluene with 10 mol % sulfuric acidFigure A.3.23 – Acidolysis of **IV** in toluene with 10 mol % sulfuric acid and 2 molar equivalents of ethylene glycol

d) Chromatograms for model compound **V**Figure A.3.24 – Acidolysis of **V** in toluene with 10 mol % sulfuric acidFigure A.3.25 – Acidolysis of **V** in toluene with 10 mol % sulfuric acid and 2 molar equivalents of ethylene glycol

A.3.6 Raw kinetic data for Eyring plots for $[\text{HSO}_4]^-$ ionic liquidsFigure A.3.26 – Kinetic data for $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ Figure A.3.27 – Kinetic data for $[\text{HC}_4\text{im}][\text{HSO}_4]$

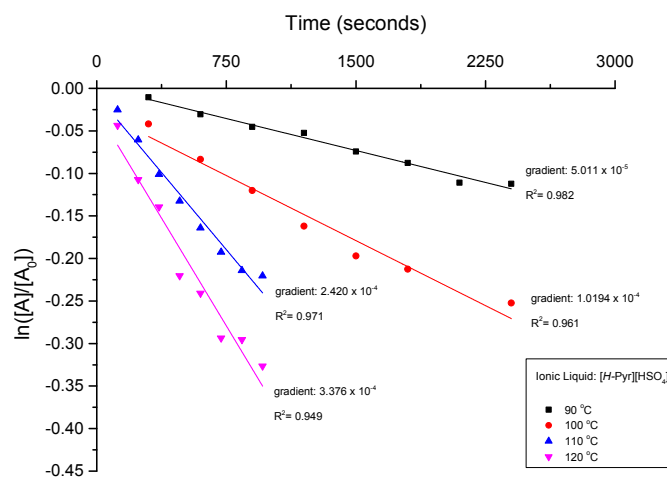


Figure A.3.28 – Kinetic data for [HPy][HSO₄]

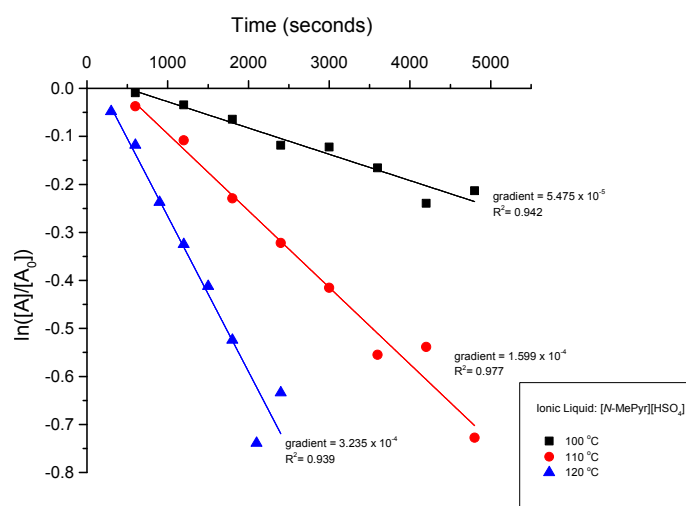
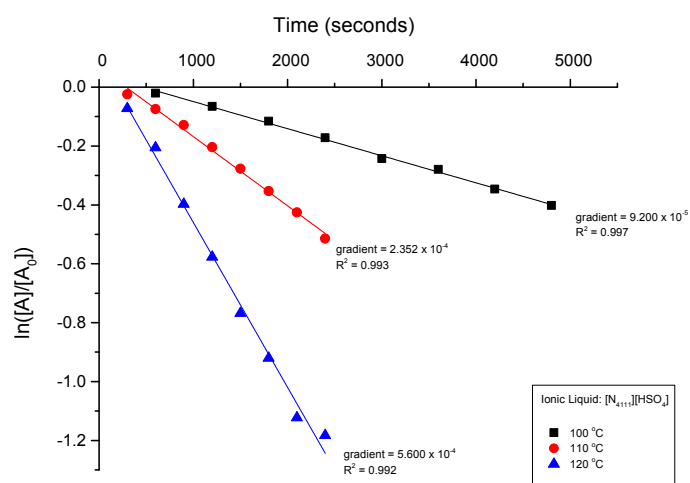
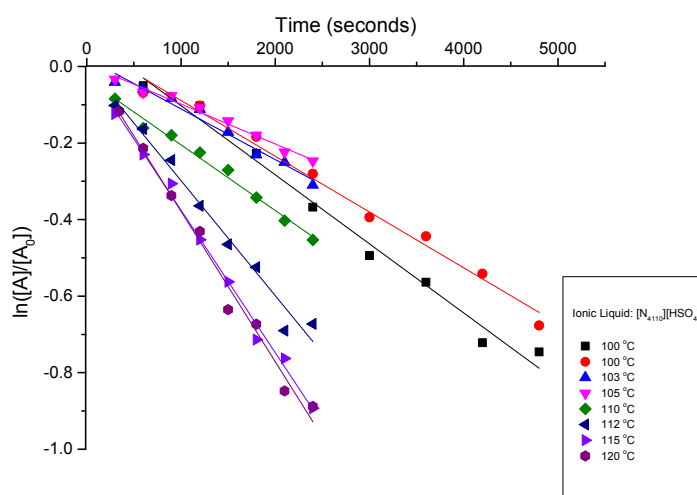


Figure A.3.29 – Kinetic data for [N-Mepy][HSO₄]

Figure A.3.30 – Kinetic data for $[N_{4111}][HSO_4]$ Figure A.3.31 – Kinetic data for $[N_{4110}][HSO_4]$

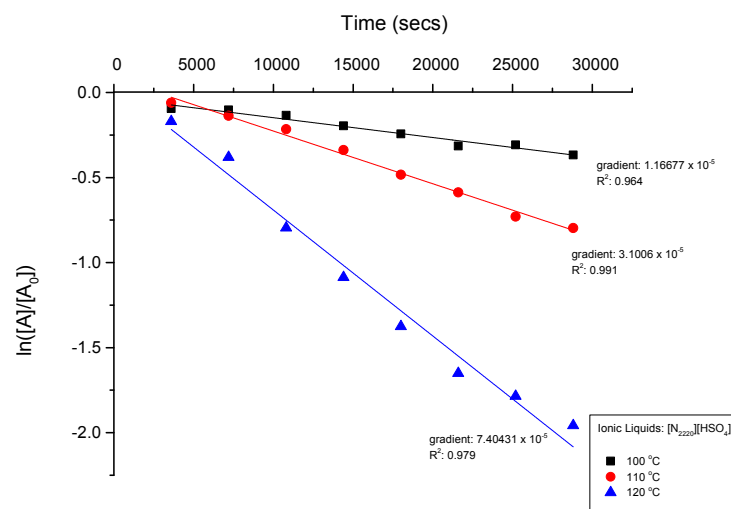


Figure A.3.32 – Kinetic data for $[N_{2220}][HSO_4]$

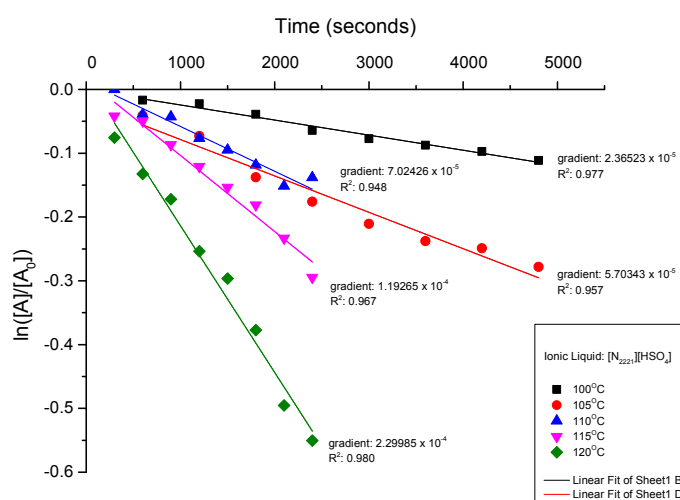
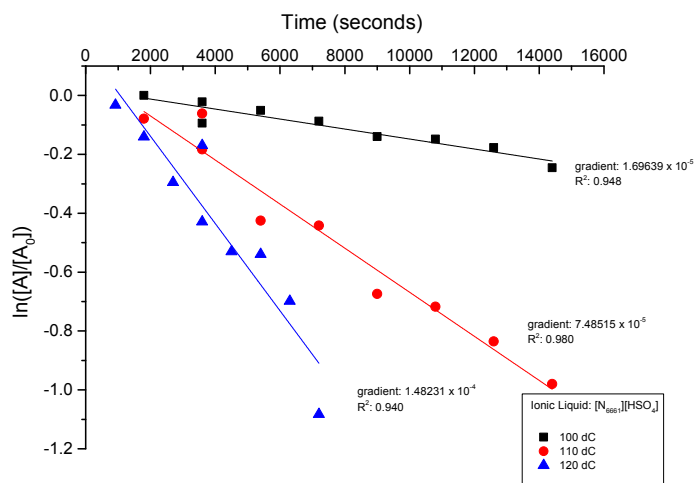
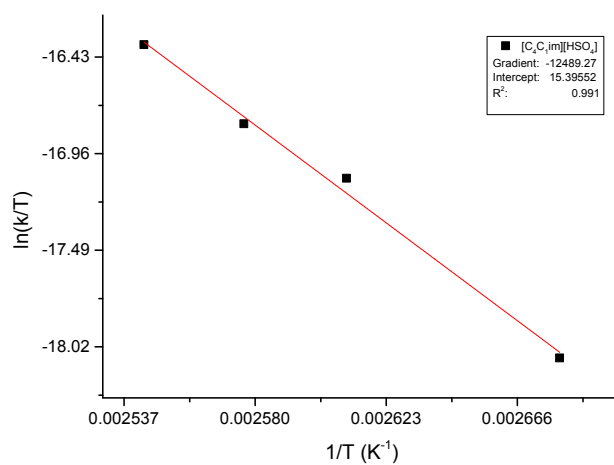


Figure A.3.33 – Kinetic data for $[N_{2221}][HSO_4]$

Figure A.3.34 – Kinetic data for $[N_{6661}][HSO_4]$

A.3.7 Full Eyring plots for $[HSO_4]^-$ ionic liquids

Figure A.3.35 – Eyring plot for $[C_4C_{1im}][HSO_4]$

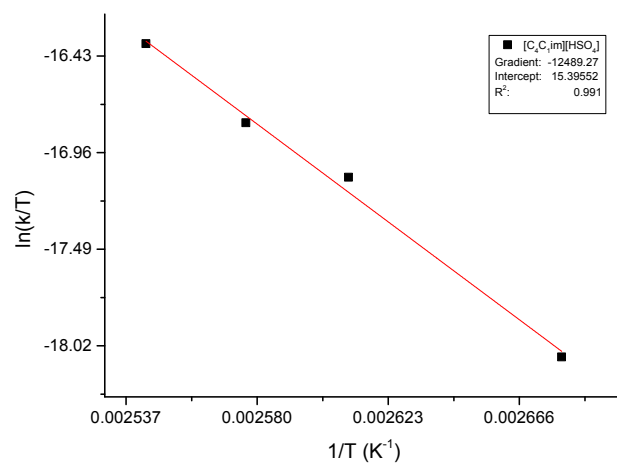


Figure A.3.36 – Eyring plot for [HC₄im][HSO₄]

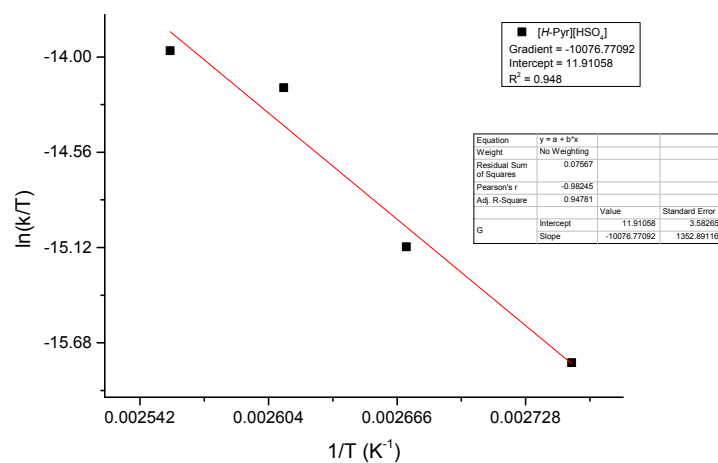


Figure A.3.37 – Eyring plot for [HPy][HSO₄]

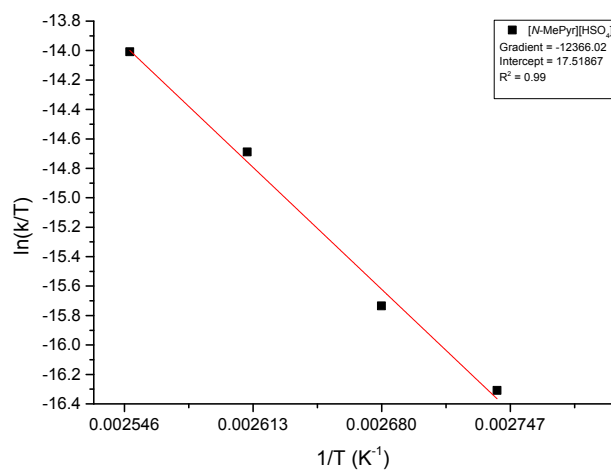


Figure A.3.38 – Eyring plot for [N-Mepy][HSO₄]

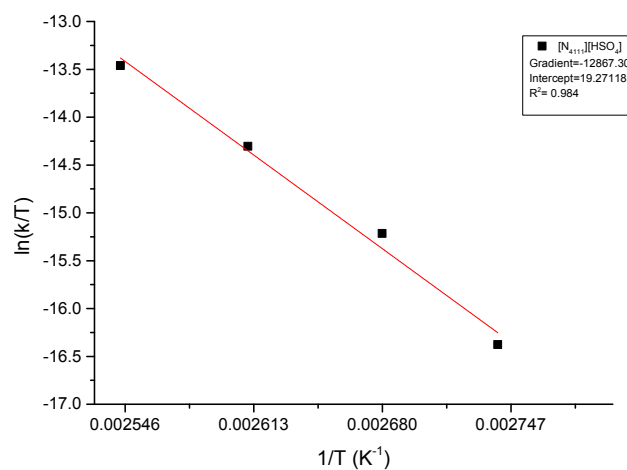


Figure A.3.39 – Eyring plot for [N₄₁₁₁][HSO₄]

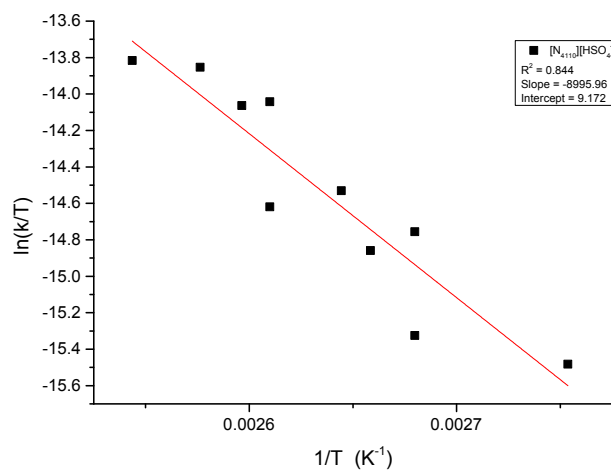


Figure A.3.40 – Eyring plot for $[N_{4110}][HSO_4]$

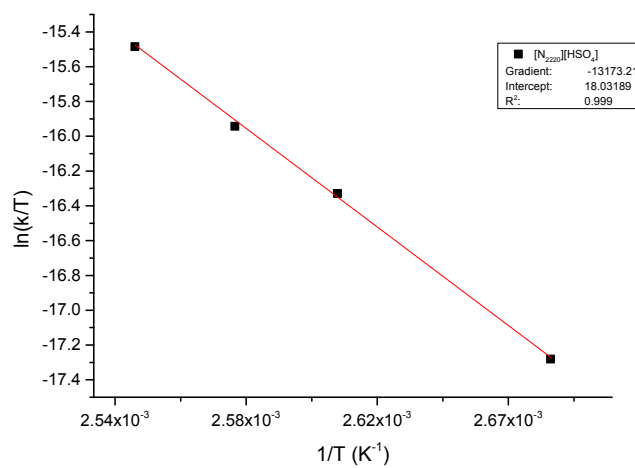
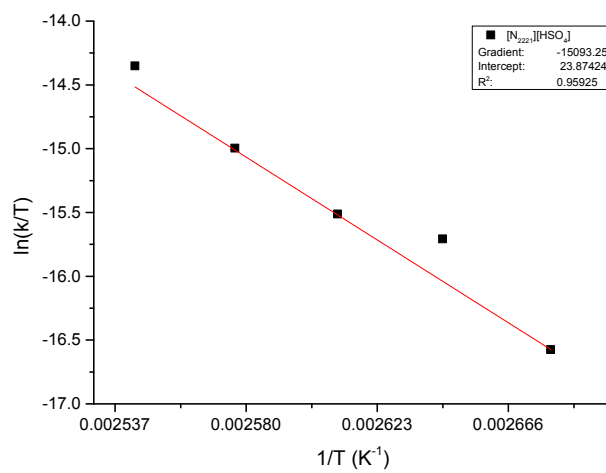
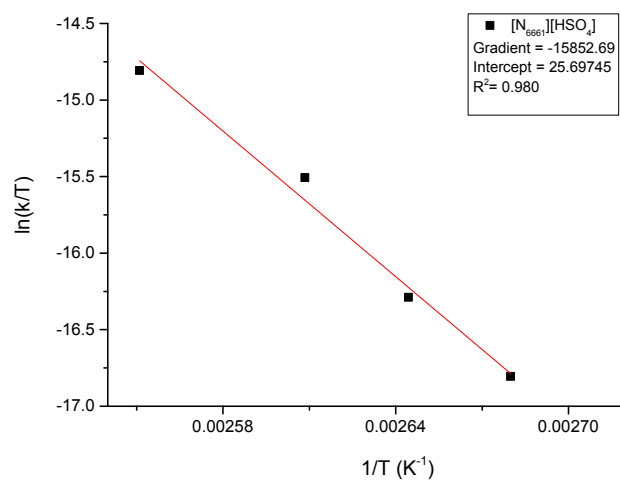


Figure A.3.41 – Eyring plot for $[N_{2220}][HSO_4]$

**Figure A.3.42** – Eyring plot for $[N_{2221}][HSO_4]$ **Figure A.3.43** – Eyring plot for $[N_{6661}][HSO_4]$

A.4 Chapter 5: Oxidative depolymerisation

A.4.1 ^{31}P NMR of Lignin samples

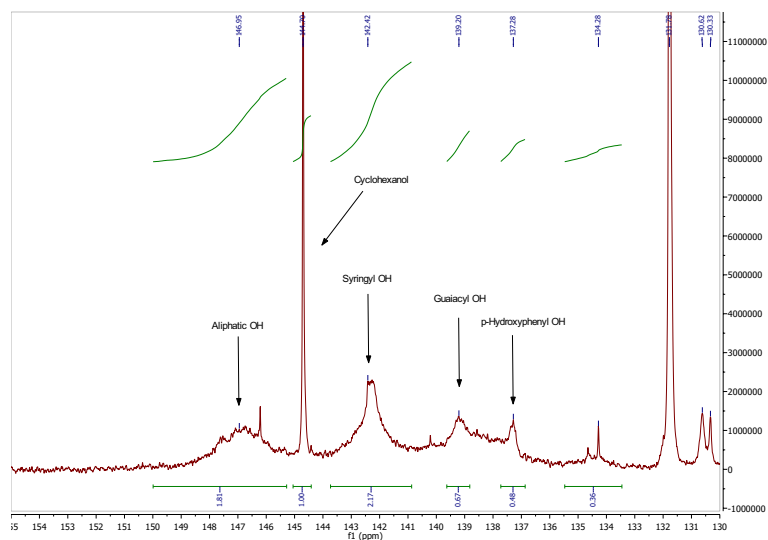


Figure A.4.1 – ^{31}P NMR of phosphitylated ionosolv lignin from pretreated 4HW

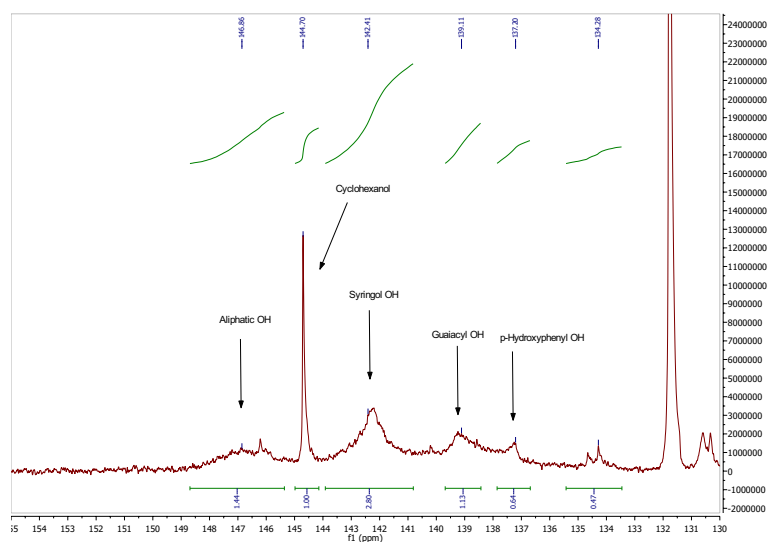


Figure A.4.2 – ^{31}P NMR of phosphitylated ionosolv lignin from pretreated 8HW

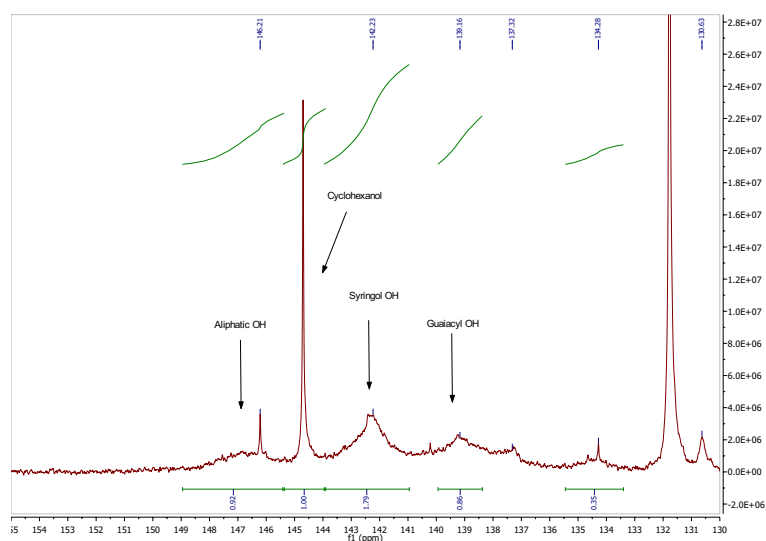


Figure A.4.3 – ^{31}P NMR of phosphitylated ionosolv lignin from pretreated 12HW

A.4.2 Vanillin extraction from $[\text{HC}_4\text{im}][\text{HSO}_4]$ by organic solvents

Table A.4.1 – Efficiency of organic solvents to extract vanillin from $[\text{HC}_4\text{im}][\text{HSO}_4]$ and water mixture (1:1 by weight ratio IL: H_2O).

Entry	Organic Solvent	Biphasic system observed?	Extraction efficiency of Vanillin (wt %)
1	Ethyl Acetate	Yes	65
2	Toluene	Yes	19
3	THF	Yes	30
4	Diethyl ether	Yes	11
5	<i>Tert</i> -butylmethylether	Yes	27
6	Methyl-THF	Yes	20

^aVanillin quantity determined via HPLC analysis of organic solvent post extraction

A.4.3 Oxidative depolymerisation of lignin summary

Table A.4.2 – Initial screening tests for the oxidative depolymerisation of 4 h pretreated Willow with different POM loadings in $[\text{HC}_{41}\text{m}][\text{HSO}_4]$

Entry	Catalyst loading (wt % to IL)	Oxidant	Vanillin yield in oil (%)	Vanillin yield from Klason lignin content (%)	Syringaldehyde yield in oil (%)	Syringaldehyde from Klason lignin content	Guaiacol yield from Klason lignin content
1	none	none	-	-	-	-	-
2	none	O ₂	0.003	0.004	0.011	0.017	-
3	1.32	O ₂	0.668	0.026	1.53	0.060	0.015
4	5.05	O ₂	0.816	0.070	2.52	0.217	0.055
5	10.4	O ₂	0.665	0.032	2.12	0.101	0.073
6	20.6	O ₂	1.106	0.062	2.87	0.162	0.103
7	none	5 % H ₂ O ₂ (30 wt % in H ₂ O)	-	-	-	-	0.031
8	5.3	5 % H ₂ O ₂ (30 wt % in H ₂ O)	0.309	0.020	0.462	0.033	0.012
9	10.8	5 % H ₂ O ₂ (30 wt % in H ₂ O)	0.110	0.032	0.146	0.047	0.020
10	20.1	5 % H ₂ O ₂ (30 wt % in H ₂ O)	0.484	0.047	0.710	0.075	0.027

^aConditions: Stirring at 500 rpm, at 100 °C left for 5 hours. using molecular oxygen and hydrogen peroxide as the oxidants

Table A.4.3 – Initial screening tests for the oxidative depolymerisation of 30 minute pretreated Pine with different POM loadings in $[\text{HC}_{4\text{im}}][\text{HSO}_4]$.

Entry	Catalyst loading (wt % to IL)	Oxidant	Vanillin yield in oil (%)	Vanillin yield from Klason lignin content (%)	Syringaldehyde yield in oil (%)	Syringaldehyde from Klason lignin content (%)	Guaiacol yield from Klason lignin content
1	none	5 % H_2O_2 (30 wt % in H_2O)	0.308	0.008	0.002	0.015	0.014
2	5.3	5 % H_2O_2 (30 wt % in H_2O)	0.478	0.104	-	-	0.065
3	10.8	5 % H_2O_2 (30 wt % in H_2O)	1.31	0.103	-	-	0.040
4	20.0	5 % H_2O_2 (30 wt % in H_2O)	0.228	0.181	-	-	0.051
5	4.25	Compressed air, 98 bars	0.033	0.035	-	-	-
6	0.49	Compressed air, 98 bars	0.003	0.004	-	-	-

^aConditions: stirring at 500 rpm, at 100 °C left for 5 hours

Table A.4.4 – Oxidative depolymerisation of different lignin substrates with different POM loadings in $[\text{HC}_{4\text{im}}][\text{HSO}_4]$.

Entry	Substrate	Pretreatment time	Catalyst loading (wt % to IL)	Vanillin yield in oil (%)	Vanillin yield from Klason lignin content (%)	Syringaldehyde yield in oil (%)	Syringaldehyde yield from Klason lignin content (%)	Guaiacol yield from Klason lignin content
1	Pine	30 mins	20.9	0.055	0.025	-	-	-
2	Willow	4 h	19.9	0.049	0.013	0.059	0.016	-
3	Willow	8 h	19.5	0.013	0.006	0.039	0.017	-
4	Willow	12 h	20.7	0.018	0.004	0.036	0.008	-
5	Pine	30 mins	5.4	0.315	0.033	-	-	-
6	Willow	4 h	5.3	0.104	0.013	0.146	0.018	-
7	Willow	8 h	5.5	0.090	0.010	0.158	0.017	-
8	Willow	12 h	5.0	0.050	0.005	0.065	0.007	-

^aConditions: stirring at 500 rpm, at 100 °C left for 5 hours, using 5 % H_2O_2 (30 wt % in H_2O) as the oxidant

Table A.4.5 – Oxidative depolymerisation of lignin obtained from 30MP with different loadings of $\text{Mn}(\text{NO}_3)_2$ in $[\text{C}_4\text{C}_1\text{im}][\text{OTf}]$, stirring at 500 rpm, at 100 °C left for 5 hours using different oxidants.

Entry	Catalyst loading	Oxidant	Vanillin yield in oil (%)	Vanillin yield in Klason lignin (%)	Syringaldehyde yield in oil (%)	Syringaldehyde yield in Klason lignin (%)	Guaiacol yield in Klason lignin content (%)
1	2.71	5 % H_2O_2 (30 wt % in H_2O)	0.011	0.002	0.005	0.006	0.016
2	2.57	O_2	0.067	0.004	-	-	-
3	20.26	5 % H_2O_2 (30 wt % in H_2O)	-	-	-	-	-
4	19.63	O_2	-	-	-	-	-
5	-	O_2	0.215	0.103	-	-	0.001
6	-	5 % H_2O_2 (30 wt % in H_2O)	-	-	0.005	0.006	0.001
7	21.50	Compressed air, 98 bars	0.002	0.003	-	-	-
8	2.42	Compressed air, 98 bars	0.012	0.008	-	-	-

^aConditions: stirring at 500 rpm, at 100 °C left for 5 hours.

