

**CATALYTIC CONVERSION OF FRUCTROSE, GLUCOSE AND CELLULOSE TO
5-(HYDROXYMETHYL)FURFURAL (HMF)**

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ABSTRACT

The current dominant raw material for the energy and chemical sectors worldwide is crude oil. Within the last few years, petroleum prices have increased, geo-political stability has decreased, and supply has been threatened, driving a renewed interest across academic, government, and corporate centres to utilise biomass as an alternative raw material. The quest to make useful chemicals and fuels, which are potentially versatile intermediates between bio-based carbohydrate chemistry and petroleum-based organic chemistry, is among the most active research areas in chemistry. Many of the most promising alternatives for the sustainable supply of fuels and valuable chemicals are biomass resources. However, this process requires both economically and environmentally efficient methods before a biorefinery platform can be built on the basis of this route. In this research, the high-yield conversion of fructose, glucose and cellulose to the versatile intermediate 5-hydroxymethylfurfural (HMF) is described. The role of different transition metal salts in dithiocarbamate-based, hydrogensulfate-based and chloride-based ionic liquids in this process was investigated. Among all those investigated, the chromium(III) chloride catalyst system in hydrogensulfate-based ionic liquids was found to be the most effective method for conversion of fructose, giving an HMF yield of 96% whereas a chloride-based ionic liquid was found to be the most effective method for converting glucose to HMF, achieving a yield of 90%. Little or no side products (such as formic acid, levulinic acid, or humins) were observed, indicating the selectivity of the system. The activity of various catalysts for the conversion of fructose to 5-hydroxymethylfurfural (HMF) was investigated under different conditions including lower and higher temperatures and addition of co-solvents. The most challenging of the substrates investigated was cellulose, representing the closest substrate to untreated biomass. The best yield of HMF obtained from this substrate was 58% after one hour at 150 °C, which compares well with leading values in the literature. In these studies, the effects of temperature, substrate concentration, co-solvent addition and the nature of the ionic liquid were all investigated.

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LIST OF ABBREVIATIONS

MJ	Megajoule
CO ₂	Carbon dioxide
BTU	British thermal unit
EIA	Energy information administration
Mtoe	Million tonnes of oil equivalent
FFVs	Flexible Fuel Vehicles
CNG	Compressed Natural Gas
LPG	Liquefied Petroleum Gas
FAME	Fatty acid methyl ester
ETBE	Ethyl tertiarybutyl ether
CH ₄	Methane
SNG	Synthetic natural gas
DME	Dimethyl ether
HMF	5-hydroxymethylfurfural
AGU	Anhydroglucose unit
DMF	2,5-dimethylfuran
PETs	Polyethylene terephthalate
DFF	2,5-diformylfuran
FDA	2,5-furandicarboxylic acid

EPA	Environmental Protection Agency (USA)
GCI	Green Chemistry Institute
VOC	Volatile organic compounds
IL	Ionic liquid
NMMO	<i>N</i> -methylmorpholine- <i>N</i> -oxide monohydrate
DMA	<i>N,N</i> -dimethylacetamide
DMSO	Dimethylsulfoxide
TBAF	Tetrabutylammonium fluoride
MI	Microwave irradiation
h	Hours
RTILs	Room Temperature Ionic Liquids
$S_2CNR_2^-$	Dialkyldithiocarbamates
$[C_4C_1im]Cl$	1-butyl-3-methylimidazolium chloride
$[C_4C_1im][S_2CN(n-Bu)_2]$	1-butyl-3-methylimidazolium di- <i>n</i> -butyldithiocarbamate
NMR	Nuclear magnetic resonance
ppm	Parts per million
$[C_4C_1im][MeSO_4]$	1-butyl-3-methylimidazolium methylsulfate
$[C_4C_1im][HSO_4]$	1-butyl-3-methylimidazolium hydrogensulfate
$[C_2C_1im]Cl$	1-ethyl-3-methylimidazolium chloride
$[BMIM]^+$	1-butyl-3-methylimidazole
ZSM-5	Zeolite Socony Mobil-5

Tf ₂ N ⁻	Bis(trifluoromethanesulfonyl)imide
TFA	Trifluoroacetate
Sacc ⁻	Saccharin
Trif ⁻	Trifluoromethylsulfonate
C ₄ C ₁ im ⁺	1-butyl-3-methylimidazole
mol%	Mole percent
g	Grams
<i>n</i> -Bu ₂ NCS ₂ ⁻	Di- <i>n</i> -butyldithiocarbamate
12-MPA	12-molybdophosphoric acid
HPLC	High performance liquid chromatography
v/v	Volume to volume ratio
pK _a	Acidity constant
BEA	Beta zeolite polymorph A
[C ₂ C ₁ im]Br	1-butyl-3-methylimidazolium bromide
MCM	Mobil composition of matter
MIBK	Methylisobutylketone
THF	Tetrahydrofuran
GM	Genetically modified
AC	Active carbon
mL	Millilitre

Hz	Hertz
eq.	Equivalent
δ	Chemical shift
mmol	Millimole
m/z	Mass charge ratio
s	Singlet
d	Doublet
t	Triplet
m	Multiplet

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Three chapters from this thesis have been published.

Chapter 2 (Fructose to HMF) has been published and it was selected as an **Editors' Choice Article** and it appears as a cover image of that issue of the journal.

Chapter 3 (Glucose to HMF) has been published.

Chapter 4 (Cellulose to HMF) has been published.

Publications

Eminov, S.; Wilton-Ely, J. D. E. T.; Hallett, J. P., Highly selective and near-quantitative conversion of fructose to 5-hydroxymethylfurfural using mildly acidic ionic liquids. *ACS Sustainable Chem. Eng.* **2014**, 2, 978.

Eminov, S.; Brandt, A.; Wilton-Ely, J. D. E. T.; Hallett, J. P., The highly selective and near-quantitative conversion of glucose to 5-hydroxymethylfurfural using ionic liquids. *PLoS ONE*, **2016**, 11, 10.

Eminov, S.; Filippousi, P.; Brandt, A.; Wilton-Ely, J. D. E. T.; Hallett, J. P., Direct catalytic conversion of cellulose to 5-hydroxymethylfurfural using ionic liquids. *Inorganics*, **2016**, 4, 32.

Conferences (poster and oral presentations)

8th Baku International Mamedaliyev Conference on Petrochemistry
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New Challenges in the European Area: Young Scientists' 1st International Baku Forum
Baku, Azerbaijan 20-26 May 2013 (Oral presentation)

Postgraduate Symposium, Poster Presentation
Imperial College London, UK 03-05 June 2013 (Poster presentation)

3rd Low Carbon Energy for Development Network (LCEDN) Workshop,
London 23-24 June 2013 (Oral presentation)

Postgraduate Symposium, Research Presentation
London, UK 07-10 June 2014 (Oral presentation)

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CHAPTER 1

INTRODUCTION

1.1 Energy demand

At no stage in history has the world's population been more reliant on energy and the continued socio-economic development of the world is dependent on this vital input. In order to store, convert, and amplify energy for the use of the global community, many different methods have been employed and the search continues to find the most efficient method to meet our energy needs. As a result, the production of energy from different resources (fossil and non-fossil) is a major concern for policy makers as well as researchers.

Nuclear (fissile), fossil and renewable energy sources are the three main groups used for the production of energy. Fossil fuel sources are natural gas, petroleum, coal, oil shales and bitumens which were formed in early geological periods. They are not renewable energy sources and are distributed in specific geographical locations, which are both concerns for policy makers. If the planet is to continue to function, the main source of energy for the population cannot continue to come from unsustainable resources. These resources cause greenhouse gas emissions, problems with energy security and environmental pollution. Therefore, there is a great need to replace unsustainable resources (fossil fuels) with renewable energy resources, such as solar, hydro, wind, marine, geothermal and biomass. The role of nuclear energy sources, which rely on thorium and uranium, is unclear.¹ The reserves of some of these energy sources are described in Table 1.1.

Today, the greatest consumption is of petroleum, exceeding natural gas, coal, renewable and nuclear. Just three different fossil fuels (natural gas, petroleum and coal) account for almost

80% of the energy consumed by the global community.¹ Moreover, they are consumed far more rapidly than nature can replace them.

Table 1.1. *Energy reserves of the world.*¹

Source	Amount (1x10 ⁵ MJ)
Uranium	1.2 x 10 ⁵
Coal	320.0
Shale Oil	79.0
Crude Oil	37.0
Natural Gas	19.6
Tar Sands	6.1

There is hope that carbon dioxide emissions will be reduced through the use of renewable energy and so dependence on fossil fuels. Another approach is to develop sequestering technology for the carbon dioxide emitted during the combustion of fossil fuels, however, this method is limited due to the energy and storage cost.¹ As a result, the most promising approach is to use renewable energy resources, which either consume CO₂ or produce negligible CO₂ during operation.

Another problem with the use of non-renewable resources is their uneven worldwide distribution. For example, currently the Middle East is the largest supplier of petroleum worldwide and accounts for 63% of the total reserves. Environmental, geopolitical, as well as equity issues, make these resources unsustainable in addition to the related economic concerns. In contrast to the inequity issue with petroleum prevalence, renewable energy resources are

distributed more evenly across the world compared with either nuclear or fossil fuels. Even so, effective solar, hydro, tidal or wind options have to rely on favourable geography and climate. Biomass is the most evenly and widely distributed material resource of those mentioned above.

The world will require 56% more energy in 2040 than in 2010 (Figure 1.1).² As can be seen in Figure 1.1, the current dominant energy sources are oil, coal and natural gases. However, compared with nuclear and renewables, which have both increased by 3-4%, fossil fuel resources will be further depleted by 2040 (Figure 1.1). It is estimated that the use of petroleum is 100,000 faster than the speed with which it can be replaced by nature. As a result, the development of renewable energy resources becomes a major requirement so as to supply the future global energy demand.

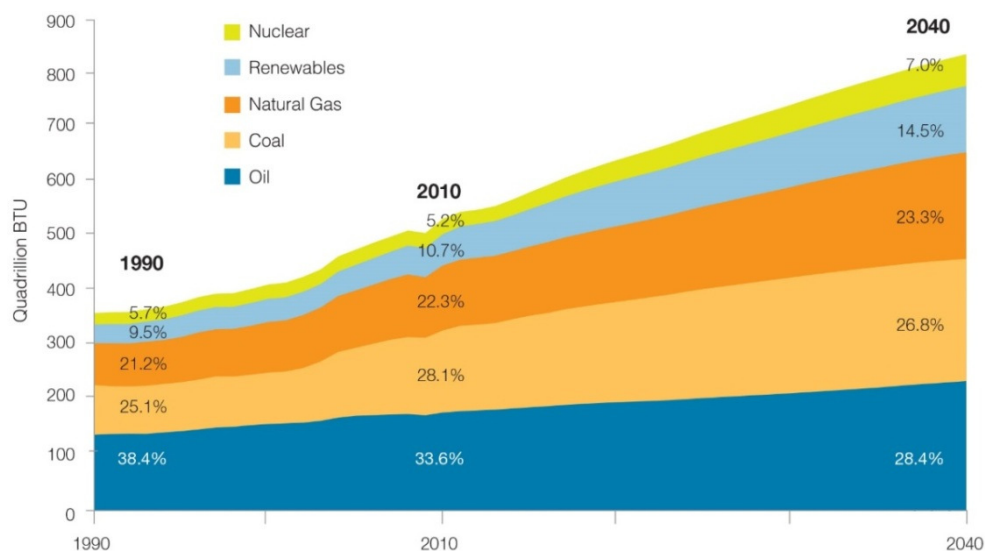


Figure 1.1. *The future global energy demand.*²

It is estimated that renewable energy resources will be used to generate around 80% of the total global electricity supply by 2040.¹ Table 1.2 illustrates the breakdown of energy from solely

renewable energy resources. Biomass accounts for the largest portion of total consumption and this has increased over time. Moreover, biomass is the only non-fossil option for the production of organic chemical compounds and aromatic hydrocarbons.

Table 1.2. *Estimated renewable global energy scenario by 2040.*

Source	2001 (Mtoe)	2010 (Mtoe)	2020 (Mtoe)	2030 (Mtoe)	2040 (Mtoe)
Total consumption	10038	10549	11425	12352	13310
Biomass	1080	1313	1791	2483	3271
Large hydroelectric	22.7	266	309	341	358
Geothermal	43.7	86	186	333	493
Small hydroelectric	9.5	19	49	106	189
Wind	4.7	44	266	542	688
Solar energy	4.1	15	66	244	480
Photovoltaic	0.2	2	24	221	784
Solar thermal electricity	0.1	0.4	3	16	68
Marine (tidal/wave/ocean)	0.05	0.1	0.4	3	20
Total renewable energy sources	1365.5	1745.5	2694.4	4289	6351
Total renewable energy contribution (%)	13.6	16.6	23.6	34.7	47.7

Mtoe = Million tonnes of oil equivalent

1.2 Biofuels

The careless use and rapid depletion of fossil fuels makes renewable energy sources the only currently viable option for the near future. The vast infrastructure based on the use of liquid fossil fuels for transportation favours their direct replacement with biofuels produced from biomass feedstock. Many different techniques exist to convert biomass into biofuels or its precursors, including, gasification,³ hydrolysis,⁴ transesterification,⁵ and pyrolysis.⁶ Additionally, the production of biofuels together with bioproducts can provide new employment and income opportunities in rural areas. A shift to alternative biofuels and green processes to make these biofuels from biomass feedstock is one of the main tasks facing the 21st century. One of the promising benefits of biomass is the cycle of capture and release of carbon dioxide, resulting in a carbon-neutral system, if the energy required for the process to be created is discounted. (Figure 1.2)

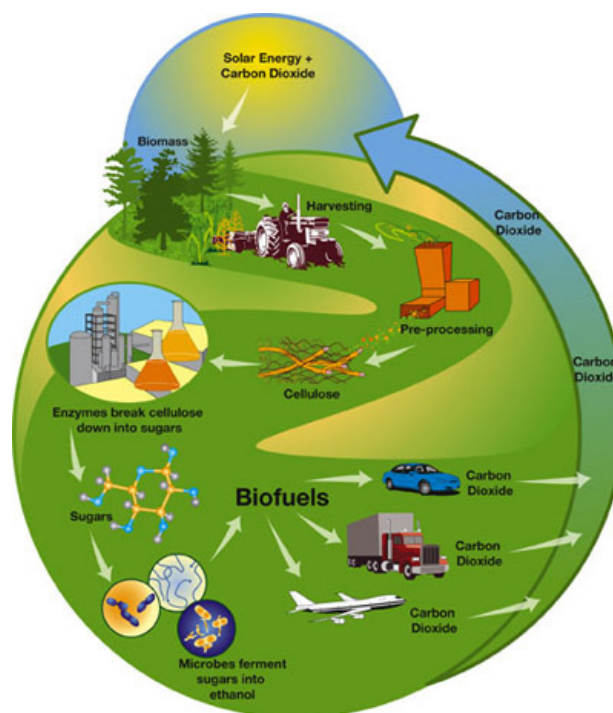


Figure 1.2. *Biomass to biofuel cycle.*⁷

First generation biofuels (e.g., bioethanol from sugarcane) are able to provide a contribution to the reduction of carbon dioxide emission and can improve domestic energy security. However, there are many concerns regarding the sourcing of feedstocks and their impact on land use, competition with food and biodiversity. Biogas, bio-diesel (bio-esters), and bio-ethanol are examples of first generation biofuels which can be blended with petroleum-based products and so can be burned in traditional combustion engines or used in alternative vehicle technologies, such as FFVs (Flexible Fuel Vehicles). Around 50 billion litres of first generation biofuels are produced worldwide, which makes them a current commercial option. Biogas, produced from the anaerobic treatment of manure and other biomass materials, has also been used but the amount of biogas used for transportation is still relatively small.⁸

The use of first generation biofuels is still a source of debate in many areas of the world, in particular, where it has impacted negatively on food prices. There are many concerns surrounding such biofuels, which limit their production on a larger scale, such as carbon balances and environmental impacts. As referred to earlier, one of the main issues is the food-versus-fuel debate, which addresses the rise in food prices due to the increase in production of first generation biofuels. Moreover, it is claimed that such biodiesels are not considered to be a cost effective emission abatement technology for transportation. Therefore, in order to replace current petroleum transportation fuels, it is important to have more efficient renewable alternatives.

Thus, lignocellulosic feedstocks which do not compete with food, have the potential to provide novel biofuels which can be termed second generation.⁹ As these feedstocks are widely

distributed throughout the world and can be grown and harvested on a billion ton scale, they are considered a suitable feedstock for future large-scale biorefineries.¹⁰ The main components of lignocellulosic biomass are hemicellulose, cellulose and lignin in which cellulose and hemicellulose are strongly bound to the lignin (Figure 1.3).

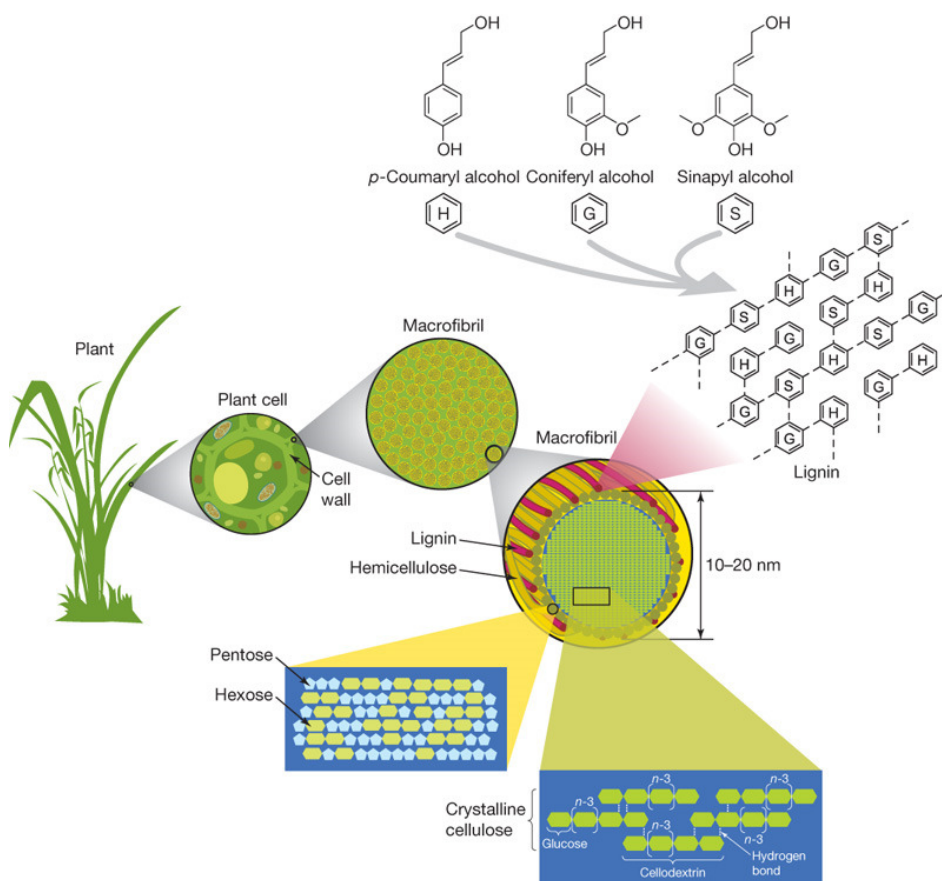


Figure 1.3. Microscopic view of lignocellulosic biomass.¹¹

Another advantage of second generation biofuels produced from lignocellulosic biomass is their high abundance in the form of non-food materials available from plants. Consequently, there is no food-versus-fuel debate with the use of second generation biofuels. However, the large-scale production of such biofuels is currently not cost-effective due to the technical barriers which need to be overcome before their potential can be recognised. Biomass from plants is the most

abundant biological resource on the earth, which makes it a promising source of compounds for both biofuels and raw materials. In their most basic form, the plants can simply be burned for heat and electricity but there is also great potential for the production of liquid biofuels from plant residues (e.g., corn stover). However, the production of biofuels from agricultural waste can satisfy only a small part of the increasing demand for biofuels. For this reason, researchers are interested in finding new sources or making use of dedicated biomass crops for liquid fuel production. Two examples of second generation liquid fuels are fuels derived from the Fischer-Tropsch process and lignocellulosic biofuels. There are already some pilot plants which have been developed for the production of second generation biofuels but they have not yet been commercialised. It is anticipated that second generation biofuels will also be able to improve engine performance as well as significantly reducing CO₂ emission without competing with food. It is likely that, given a viable commercial biorefinery process, the cost of these biofuels will be comparable with diesel and petrol, as well as possessing the benefits of being low carbon, cost effective and renewable.⁸

Due to the obvious advantages of second generation biofuels (Figure 1.4) over first generation biofuels, the approach relies on the use of the whole plant, including bark, leaves, fruits and seeds to be converted into useful products. The term 'biorefinery' was coined in the 1990s and is used for the production of biofuels and bio-products from biomass. The meaning of this term refers to a facility which relates the production of fuels and chemicals to energy production.¹² The process involves three steps: production, processing and use. It is estimated that the total production of biomass on earth is around 100 billion tons of dry matter on land and 50 billion tons of aquatic biomass per year. It can be used as animal feed, food, industrial raw material as

well as for energy. However, only 1.25% of total biomass on land is used for food with the rest being returned to the earth instead of being exploited as a potential resource for biofuel production.¹³

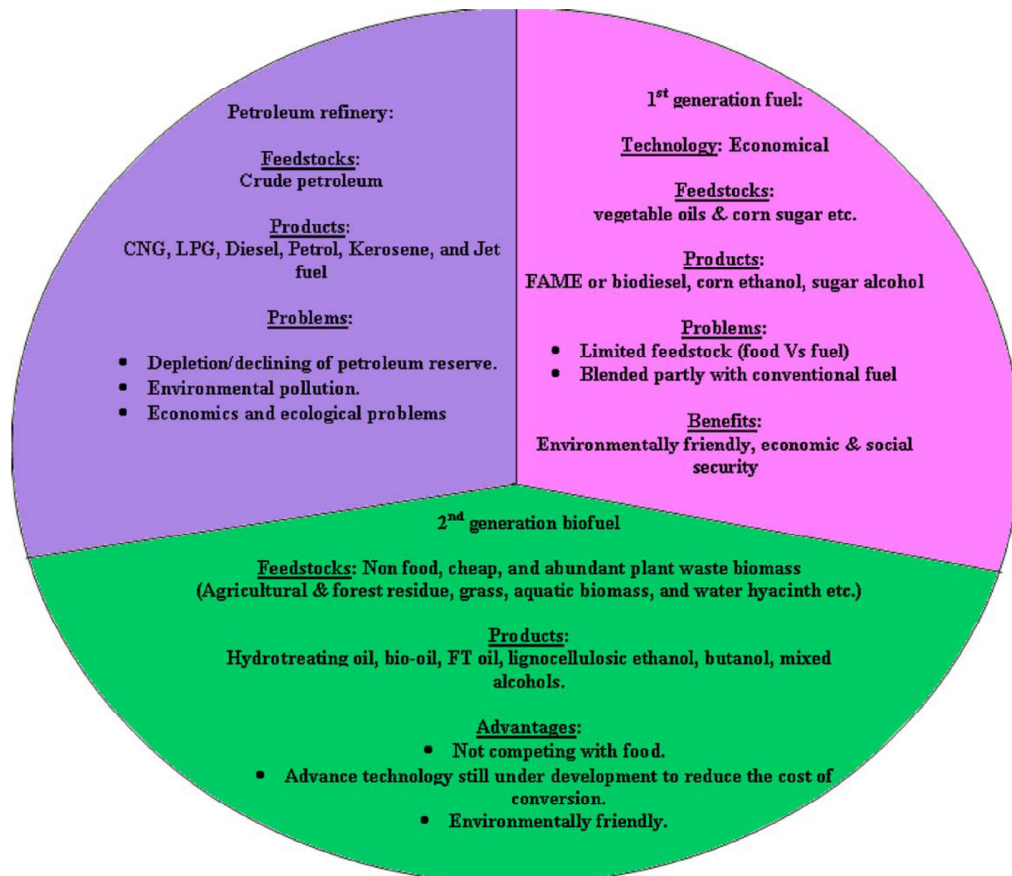


Figure 1.4. Comparison of first and second generation biofuels and petroleum-based fuels.¹⁴

Much research has been performed on the biorefinery concept with specialisation in areas such as the corn biorefinery,¹⁵ forest residue biorefinery,¹⁶ and wheat straw biorefinery.¹⁷ However, there is relatively little information on first and second generation biofuels based on non-food crops in the literature.

1.3 Disadvantages of biofuels

❖ Negative features from the perspective of the food industry

Currently, the most serious problem arising from the use of biofuels is the increase of food market prices.¹⁸ It can be explained by the fact that cultivation of land for biomass manufacturing occurs at the cost of decreasing food production. Moreover, this can lead to substantial variation in the price of both the biofuel and the food crops it substitutes.

Table 1.3. *Corn price in the U.S.A. from 2000 to 2008.*¹⁹

Period	Price (\$/bushel)
2000-2001	1.82
2001-2002	1.85
2002-2003	1.97
2003-2004	2.32
2004-2005	2.42
2005-2006	2.06
2006-2007	2.00
2007-2008	3.04

The worldwide demand for food is very large and is increasing and this need is only partially satisfied today. Therefore, the substitution of food with biofuels risks contributing to more severe food shortages and causing food prices to rise. A vivid example of this was the variation of the corn price in the U.S.A. during the periods 2000-2008 (Table 1.3) due to the fact that corn is broadly utilized in ethanol manufacturing in the U.S.A. From Table 1.3, it can be seen that the price for the corn increased from \$1.82/bushel in the period 2000-2001 to \$3.04/bushel in the years 2007-2008. It is essential to note that prices below are only those given to farmers, which means that end-users prices were actually much higher.¹⁸

Similar price rises also occurred for non-food biomass, which is used as a raw material for the production of biofuels. This happened in accordance with the mechanism of the carbon dioxide credits trading system which was formed as part of the Kyoto agreement on Climate Change, the main target of which was to reduce global carbon dioxide emissions.¹⁸

❖ **Regional and seasonal abundance of biofuel feedstocks**

Another disadvantage related to biofuel production is the regional and seasonal abundance of biomass. These two aspects play an important role in deciding whether biofuels can be prepared in a particular location or not. For instance, sugar cane, which is one of the most efficient crops from the yield per unit of land perspective, can be considered a sustainable feedstock only under rainy conditions and if there is a minimal necessity for irrigation (such as in Brazil). Another representative feedstock which poses challenges due to its availability in certain areas is soybean oil. Countries such as Argentina and Brazil also face a number of challenges associated with the expansion of soybean harvesting to become a monoculture.²⁰ There could be a fundamental problem with large monoculture over a large geographical region because it is inadvisable to rely on narrow genetics within a crop that is grown on a large scale as a single disease or change in climate could cause massive crop failure.

A second negative feature of growing biomass as a feedstock for biofuels is because of their seasonal nature. In order to illustrate how this feature affects the production of biodiesel, it is necessary to draw attention to the case of small scale biodiesel plants. These suffer when biomass cannot be produced out of season (e.g., in winter) and will spend substantial time out of

operation due to lack of raw material, preventing the production of biofuels and having an adverse effect on the local economy and employment.²¹

❖ **Other negative aspects of biofuels production**

The transesterification of vegetable oils with the help of NaOH and KOH or mineral Brønsted acids cannot be considered environmentally-friendly.²² The mixture obtained at the final stage of the process needs to be separated, neutralized and meticulously washed, causing the formation of salts, soaps, and waste water which needs further purification. The homogeneous catalysts used during this approach cannot be recycled which leads to overall increase of production cost. The issues with heterogeneous catalysis using solid acids and bases which can be recycled²³ are associated with meeting EU regulations. The technical challenges involve achieving good separation, disposal and usage of the glycerol also produced in the transesterification process.

The limitations on the use of enzymatic methods are mainly those related to high production costs, which can be addressed by means of molecular technologies.²⁴ The utilization of biofuels in the field of transport can be affected by the performance of the biofuels in diesel engines because of their large additive content. These include triacetin, MG (monoglycerides), GC (glycerol carbonate) and substances such as MG often have high melting points which can contribute to the formation of carbonaceous deposits when combusted.²⁵

❖ **Biofuels produced by biochemical conversion**

Bioethanol is the most well-known of the first generation of biofuels but has a number of disadvantages, such as the following:

- It is highly hygroscopic, causing serious issues when using it as a transportation fuel.
- Storage and distribution issues associated with the usage of blends of bioethanol with gasoline. This lead to an increase in the final product price.
- Problems associated with physical properties, requiring the modification of automobile engines in accordance with EN228 and ASTM D5798 regulations in order to utilize bioethanol as transport fuel.
- Low energy density and lower vapour pressure than gasoline.²⁴ The latter aspect causes difficulties in starting the engine during cold weather.
- Corrosive, miscible with water and comparatively toxic to ecosystems.²⁶

Biobutanol is another representative of first generation biofuels with the negative properties shown below:

- Low Reid vapour pressure (RVP)
- Low flash point meaning that it is less safe for general usage²⁷

Bio-synthetic natural gas (Bio-SNG):

- Storage issues since bio-SNG is also a gas at room temperature and needs to be liquefied or compressed in order to be used as an automotive fuel
- Catalyst development and gas cleaning are major technological challenges though selective catalysts such as Ru/C can be used²⁸

Biomethanol production requires improvements in efficiency and scale up to make it an economically viable transportation fuel

- Low vapour pressure, low volume to energy density (half of that of petrol), high toxicity, high flammability and inconsistency of behaviour across different engine types
- The traditional gasification step is a more expensive process compared to inexpensive biological conversion (for bioethanol)²⁵
- Lack of standards for consumers and producers

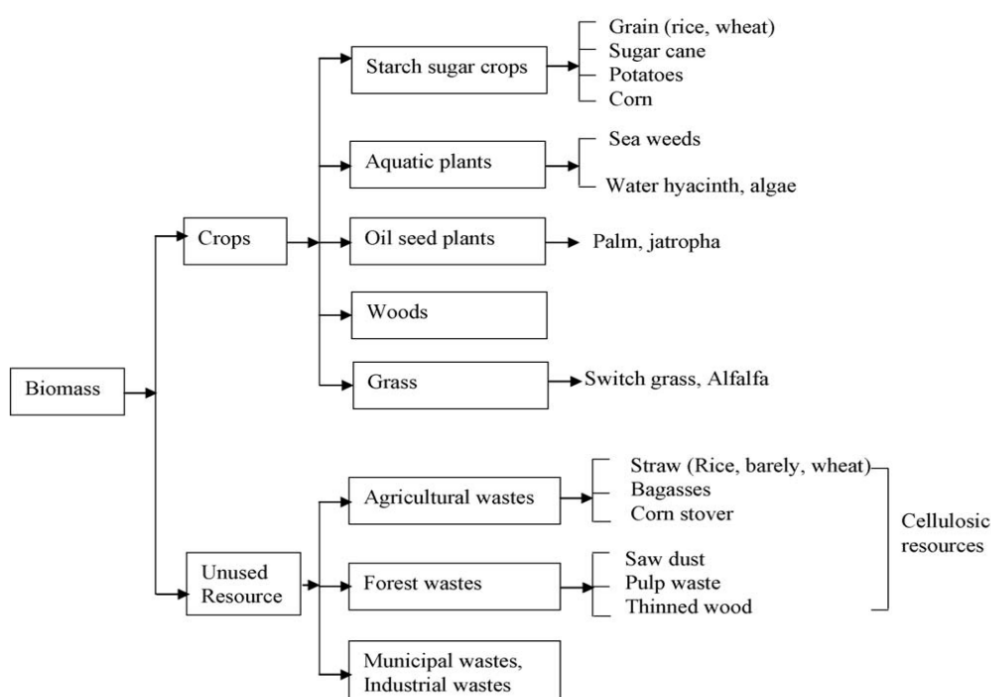
Biofuels from fast pyrolysis:

- Corrosive nature of the bio-oil produced because of its acidity, presence of additives such as salts and solids, plus formation of aromatic toxins
- They are not stable, leading to viscosity changes and precipitation by time
- High oxygen content leads to decreased energy density which is approximately 40% lower than that of fuel oil²⁹
- The cost of bio-oils is 10 to 100% more expensive than fossil fuels³⁰
- Lack of standards for usage and distribution

1.4 Biomass feedstocks

Biomass obtained from sources as diverse as agro forest residues, grasses, trees and aquatic plants are very useful and important sustainable and renewable feedstocks for the chemical industry (Scheme 1.1). During photosynthesis, plants convert carbon dioxide and water into primary and secondary metabolite biochemicals which have become industrially important chemicals. These primary metabolites are carbohydrates (starch, cellulose, hemicellulose etc.)

and lignin from lignocellulosic biomass, which account for a large volume of all biomass. Examples of secondary metabolites derived from these species are resins, rubber, terpenoids, steroids, tannins and alkaloids, which are high-value biochemicals but only present in small quantities in the plants.³¹ High-value chemicals such as food supplements, cosmetic ingredients, food flavours and pharmaceuticals can also be obtained from secondary metabolites.



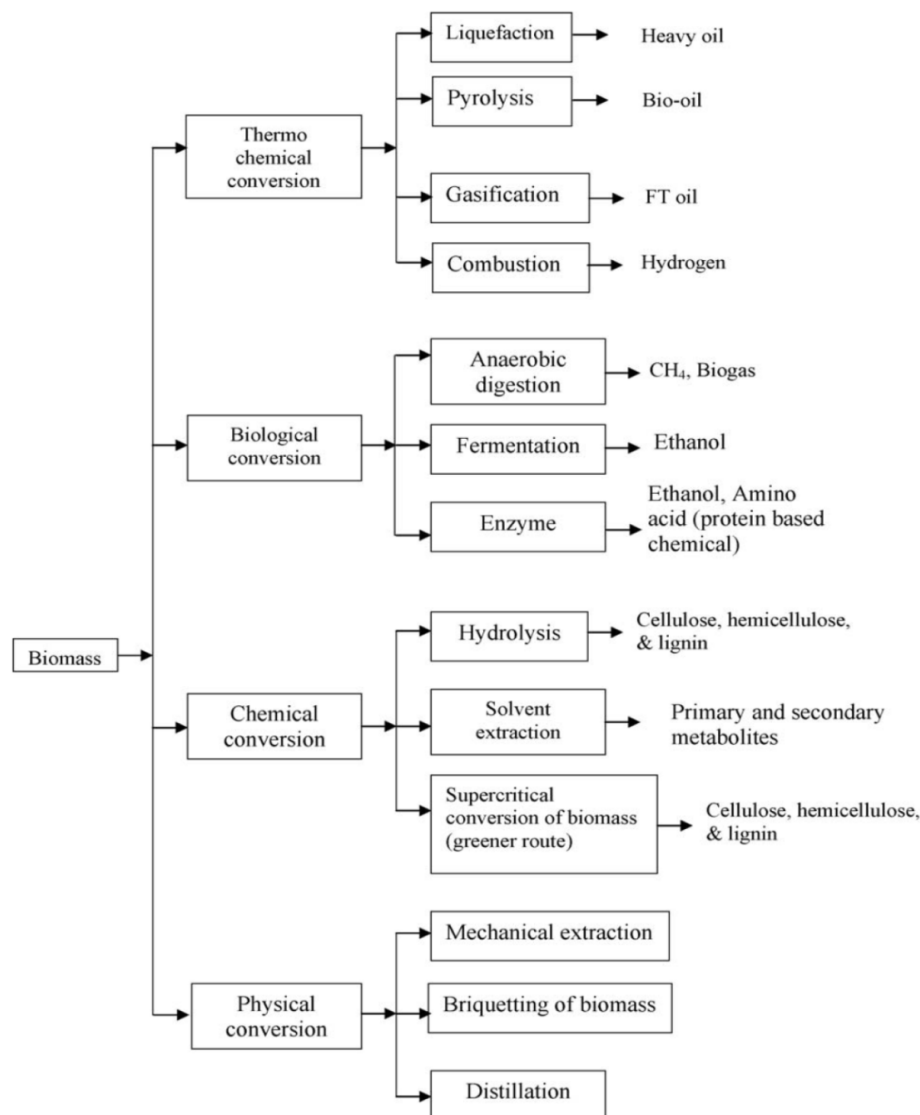
Scheme 1.1. *Biomass as a renewable feedstock.*¹⁴

The main concern is to develop a novel biomass system in which production, conversion and application are efficient and are performed in harmony with nature.¹³ For this reason, many researchers are working on new technologies so as to obtain the most efficient system for biomass conversion. For example, the different methods for production of ethanol and other products from lignocellulosic biomass have recently been reviewed.¹⁵ This addresses current

and future technologies for the production of ethanol from corn, the pre-extraction of hemicellulose and other important substances as well as the production of biofuels from lignocellulose. The conversion of low value waste biomass to important and green chemicals such as ethanol, waxes and others using green technologies has been studied by Clark *et al.*,³² while Chew *et al.* have reported a process for the production of biofuels from palm oil using different catalysts.³³ The opportunities for biorefinery implementation in specific countries (such as Canada¹⁶ and Australia³⁴) has been investigated. Using a detailed flowchart, Scheme 1.2 describes the steps of the conversion process such as chemical, physical, thermal, biological together with products obtained in each method.

1.5 First generation biofuels

The dramatic increase in petroleum prices seen during the last decade coupled with inequity issues has enabled biofuels to become cost-competitive with petroleum-based transportation fuels. This has driven research targeting the discovery of productive and cost-effective technologies for the production of biofuels from biomass. Biodiesel, ethanol and biogas are the three main types of first generation biofuels used commercially and these are considered to be ‘established technologies’ as large quantities have been produced worldwide. Diesel can be substituted with biodiesel which is obtained through transesterification of waste oil, fats and vegetable oils with only minor modifications of the engine. Petrol can also be substituted by bioethanol through the fermentation of starch and sugars (Scheme 1.2). Such complete substitution for petrol is only possible for flexi-fuel-vehicles, however, ethyl-tertiary butyl ether (ETBE), which mixes well with petrol, can be obtained from bioethanol.



Scheme 1.2. *Conversion of biomass by various different methods.*¹⁴

Biogas can also be used as a fuel in vehicles with only small modifications needed. Biogas is produced from the anaerobic digestion of liquid manure or various digestible feedstocks. However, bioethanol, biodiesel, and biogas are all obtained from commodities, which are frequently used as food. It is therefore problematic to use agricultural food crops for the

production of biofuels as there is an increasing demand for edible oils.³⁵ Although, there are some important advantages of first generation biofuels, the key disadvantage is the food-versus-fuel issue, which drives us to look for better alternatives.

1.6 Second generation biofuels

In contrast to first generation biofuels, second generation biofuels are obtained from biomass (with a wide range of options, as shown in Figure 1.5) in a more versatile and sustainable fashion, which is also carbon neutral in terms of its effect on environmental carbon dioxide concentration. In the context of second generation biofuels, plant biomass mainly refers to lignocellulosic biomass which makes up the vast majority of cheap and abundant non-food materials from plants.^{36,37}



Figure 1.5. Biomass sources for first and second generation biofuels.³⁸

At the present time, the production of second generation biofuels is not very cost-effective as there are some major technical barriers which need to be overcome before an industrial process

can be built on this method. Plants are the feedstock for the production of second generation biofuels and can be considered one of the most abundant and underutilised biological resources available on the planet. The plants can simply be burned for heat or electricity but there are clearly more promising methods for producing a liquid fuel from plants. The plant cell wall is composed of 75% polysaccharides, which is a valuable pool of potential sugars. For example, wheat, a traditional food crop, has much of its sugar content tied up in the stems compared with the starch in grains. Unfortunately, the potential of crop residues and waste, such as wood shavings, straw and stover, which could provide sugar feedstocks for biofuel production, have not yet been realised. In any case, the production of fuels from agricultural residues can only satisfy a certain proportion of the growing demand for biofuels.

Advanced biofuels can be obtained by hydrolysis (e.g., 2,5-dimethylfuran), fermentation (e.g., bioethanol) and gasification (e.g., Fischer-Tropsch bio-diesel, bio-SNG) from lignocellulosic biomass feedstock. Potential feedstocks are perennial grasses (miscanthus, reed canary grass and switch grass) short rotation forestry crops (willow, poplar) and residues from agriculture, wood and forestry. Advanced bioethanol, produced from lignocellulosic biomass, is a good replacement for petrol even as a complete substitute in flexi-fuel vehicles. This is achieved by hydrolysis of lignocellulosic biomass to produce sugars, which are then fermented into bioethanol. Fischer-Tropsch diesel is a complete substitute for conventional diesel, avoiding the need for modification of the vehicle. Also, syngas is produced from the gasification of lignocellulosic biomass which can be transformed into liquid hydrocarbons such as kerosene and diesel. Petrol vehicles can also use synthetic natural gas (bio-SNG) with only slight

adaptations. Syngas produced from lignocellulosic biomass can easily be transformed to methane and dimethyl ether (bio-DME) as well.

Liquid biofuels are produced from biomass using two main pathways: biochemical processing and thermochemical processing. A range of products can be obtained by thermochemical processing, involving simple chemical reformation and thermal decay through heating biomass in the presence of different chemicals and conditions. The main advantage of chemical processing is that all organic components of biomass are converted, while biochemical processing only focuses on polysaccharides.³⁶ Bio-routes also offer higher selectivity and fewer toxic products, though chemical routes are still faster.

As discussed previously, bioethanol production from lignocellulosic biomass has substantial potential to act as a substitute for petrol. The most important and vital step in bioethanol production is the hydrolysis of cellulose and hemicellulose to monomer sugar molecules. One of the best known methods for the conversion of cellulose to sugar monomers is the use of enzymes (such as cellulases).¹⁰ In this process, the pretreatment of the raw material is required to make it accessible for the enzymes. The main disadvantage of this approach is the high overall energy consumption and the high cost of enzymes.³⁹ Currently, cost and energy-effective, practicable, non-fermentation processes for the conversion of biomass to liquid transportation fuels remain a great challenge.¹ In the work described here, this challenge is addressed using a green, cost-effective and non-fermentation process, which has been designed for the conversion of sugars into the platform chemical and biofuel precursor, 5-hydroxymethylfurfural (HMF).

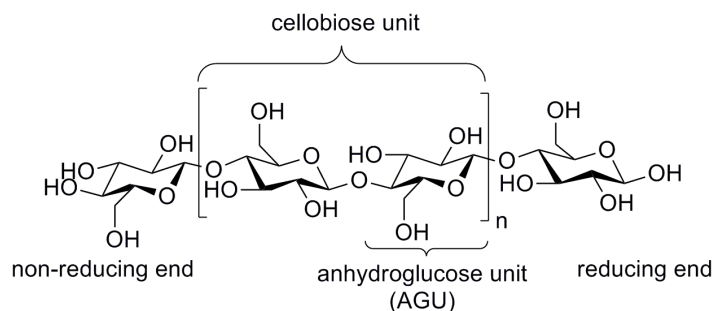
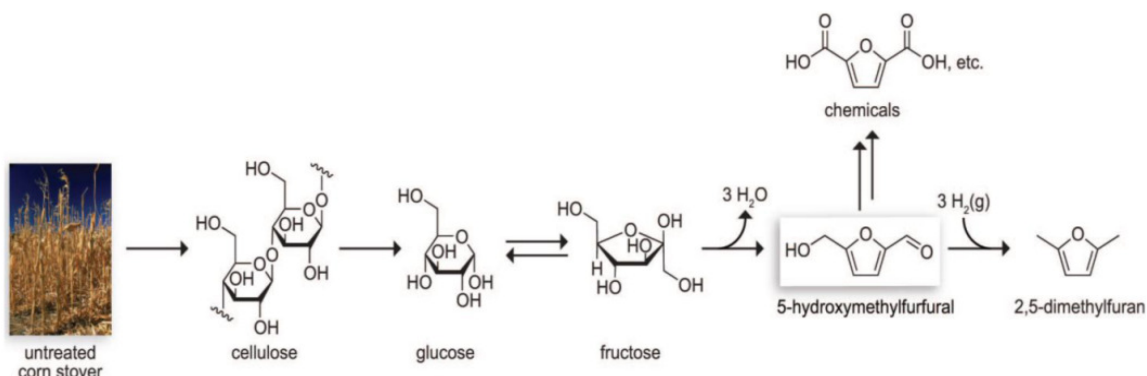


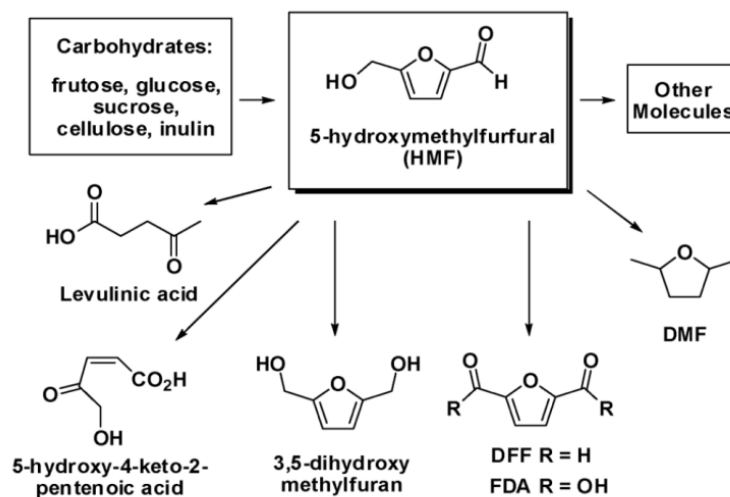
Figure 1.6. Cellulose polymer chain structure.⁴¹

Three different sugars (fructose, glucose, and cellulose) were investigated as starting points for the synthesis of HMF. Cellulose is a promising feedstock for glucose and fructose (Figure 1.6). It is well known that the most abundant component of lignocellulosic biomass is cellulose, which is considered an ideal source of raw materials to supply the increasing demand for biofuels.⁴⁰ Approximately, 40-50 % of the plant cell wall is composed of cellulose, which is the main structural component of plants. It contains two glucose sugar units linked by β -1,4-glycosidic bonds in a linear polymer of cellobiose (Figure 1.6). Currently, the conversion of cellulose into liquid transportation fuels and other useful chemicals is one of the most active and challenging areas in this area of chemistry. The main pathway is through the conversion of sugar monomers, which originate from cellulose, to HMF, a versatile intermediate between biomass-based carbohydrate chemistry and petroleum-based industrial chemistry. A general conversion scheme of biomass to useful chemicals and biofuels is described below (Scheme 1.3).



Scheme 1.3. *A pathway from biomass to useful chemicals.*⁴²

The main target of this pathway is to obtain 5-hydroxymethylfurfural (HMF), which can then be converted into biofuels and other useful chemicals. A leading biofuel candidate, 2,5-dimethylfuran (DMF) can be obtained from HMF via selective hydrogenation.⁴³ DMF is a very promising biofuel as it has an energy density comparable to petrol and boasts 40% more energy density than bioethanol. In addition, it is very stable and, being insoluble in water, does not absorb moisture, in contrast to bioethanol, for example. HMF is not only an important intermediate for the production of DMF but is also a good material for the production of important molecules such as levulinic acid, 5-hydroxy-4-keto-2-pentenoic acid, 2,5-dimethylfuran (biofuel), 3,5-dihydroxymethylfuran (diols) and 2,5-furandicarboxylic acid (FDA) (Scheme 1.4).



Scheme 1.4. *Useful Chemicals from HMF.*⁴⁴

The first step in the pathway from biomass to useful chemicals is the separation of cellulose from biomass through the deconstruction of the lignocellulosic material. Hallett and co-workers have reported low-cost, green and effective methods for the deconstruction and fractionation of lignocellulosic biomass.⁴⁵ The aim of the research described here is to follow this by adding a low-cost, environmentally-benign, high-yielding and selective method for the conversion of the resultant cellulose, glucose, and fructose to 5-hydroxymethylfurfural (HMF).

The most challenging step in this route is the dissolution of cellulose. Due to the highly ordered and rigid structure of cellulose, it is necessary to find suitable solvents for cellulose dissolution. Several aqueous and non-aqueous solvent systems (e.g., xanthate and cuprammonium processes) have been reported to dissolve cellulose but all of them suffer from insufficient

solvation power, high toxicity and cost.⁴⁰ Therefore, most of these methods have not offered an effective solvent system for cellulose dissolution. In addition to energy-intensive and harsh conditions, these processes require the use of unusual and expensive solvents, which are not environmentally benign and can prove difficult to recover after use.⁴⁶⁻⁴⁸ Considering all the drawbacks of conventional methods, there is an urgent need to design a solvent system which is environmentally-friendly, inexpensive and recyclable.

1.7 The development of green chemistry

It is clear that our planet does not have the ability to deal with much of the aquatic and land pollution which industrial sectors and billions of people generate (at least in a short timeframe).⁴⁹ There is an increasing need for the direct or indirect use of products currently based on petrochemicals, such as cleaning and personal care products, agrochemicals, pharmaceuticals, paints and coatings, as well as more innovative materials for the development of society.⁵⁰ It is a fact that all these chemical products, including the more toxic ones will be released into the environment during their manufacture, use or disposal. This will cause an inevitable ecotoxicological hazard for our planet.⁵⁰ As awareness of this grows, governments and non-governmental organisations are forcing industry to reduce pollution during the manufacture of their products and to mitigate their effects due to the consequent risk for human health and the environment.

The term 'Green Chemistry' was first used at the end of the 20th century by Paul Anastas in a special program organised by the U.S. Environmental Protection Agency (EPA) in order to

promote advanced technologies that eliminate or reduce the impact of hazardous chemicals in the manufacture, design and use of chemical products, and to encourage sustainable development of chemistry and chemical technology by government, academia and industry. The U.S. Presidential Green Chemistry Challenge was publicised in 1995 and was followed by similar awards in European countries. The Green Chemistry Institute (GCI) was formed to create contacts between industrial corporations and governmental agencies with research centres and universities to implement and design innovative, green, and effective technologies. In 1997, the first conference on the theme of green chemistry was held in Washington followed by subsequent conferences all around the world.

1.8 The idea of green chemistry

The interdisciplinary cooperation of industry, universities, research institutes, governmental agencies and scientists, which have their own programs and methods to decrease the pollution, has resulted in the formation of the ‘green’ or ‘sustainable’ concept. In adhering to the ethos of ‘Green Chemistry’, all processes, such as synthesis, processing, and application of chemical materials, must be carried out in such a manner as to reduce impact on the environment and human health (Figure 1.7). This approach mainly covers four important aspects:

1. Atom economy
2. Clean chemistry
3. Environmentally-benign chemistry
4. Design of benign chemicals

Green Chemistry reduces:

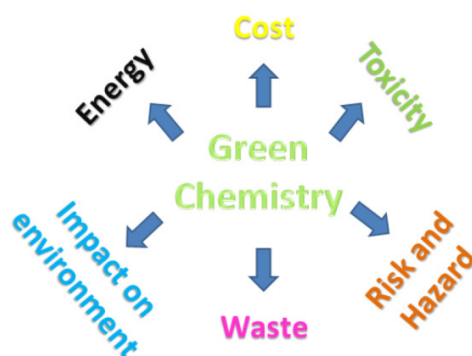


Figure 1.7. *Impact of ‘Green Chemistry’ in production, processing and application.*

1. Prevention

It is better to prevent waste than to treat or clean up waste after it has been created.

2. Atom Economy

Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.

3. Less hazardous chemical syntheses

Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment.

4. Designing safer chemicals

Chemical products should be designed to affect their desired function while minimizing their toxicity.

5. Safer solvents and auxiliaries

The use of auxiliary substances (e.g., solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used.

6. Design for energy efficiency

Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.

7. Use of renewable feedstock

A raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable.

8. Reduce derivatives

Unnecessary derivatization (use of blocking groups, protection/de-protection, and temporary modification of physical/chemical processes) should be minimized or avoided if possible, because such steps require additional reagents and can generate waste.

9. Catalysis

Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

10. Design for degradation

Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment.

11. Real-time analysis for pollution prevention

Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.

12. Inherently safer chemistry for accident prevention.

Substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions, and fires.

Figure 1.8. *The twelve principles of ‘Green Chemistry’.*

‘Green Chemistry’ is usually presented as a set of twelve principles (Figure 1.8) which have been popularised in order to establish a methodology and a culture for accomplishing sustainability. These principles instruct professional scientists in how to implement new technological processes, new syntheses and new chemical compounds, while bearing in mind the need to improve efficiency and avoid waste and environmental impact.⁴⁹

Four of the ‘Twelve Principles’ are highlighted because they are illustrated by the efficient, effective, sustainable and ‘green’ conversion of biomass to a leading platform chemical and biofuel precursor in this ionic-liquid based research project.

Principle 5: Safer solvents and auxiliaries

‘The use of auxiliary substances (e.g., solvents, separation agents etc.) should be made unnecessary wherever possible and innocuous when used.’

Almost all chemical processes require extensive use of solvent for dissolving reagents, affecting chemical reactivity and rates, and in purification.⁵⁰ Many organic solvents used in chemical processes are volatile organic compounds (VOCs), which increase the risk of fire and explosion and are easily released into the atmosphere. This causes them to act as air pollutants with an impact on ozone depletion, photochemical smog and global warming.⁵⁰ In contrast, this project employs ionic liquids as the solvent systems, which are essentially non-volatile and can be re-used, and thus conform to the fifth Principle of Green Chemistry.

Principle 6: Design for energy efficiency

‘Energy requirements of chemical processes should be recognised for their environmental and economic impacts and should be minimised. If possible, synthetic methods should be conducted at ambient temperature and pressure.’

Much research performed in this field requires high temperatures and/or long reaction times. Microwave irradiation has also been used in some of the reported research, which is rapid but requires a very high energy input.⁵¹ A conventional oil bath was used in this research project and efforts were made to minimise the reaction time and temperature.

Principle 7: Use of renewable feedstocks

‘A raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable.’

This project studied the conversion of fructose, glucose and cellulose to a platform chemical, HMF. Lignocellulosic biomass, the main source of these starting materials, is considered to be a renewable material which is supported by the seventh Principle of Green Chemistry.

Principle 9: Catalysis

‘Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.’

Ionic liquids were used for the conversion of cellulose, glucose and fructose to 5-hydroxymethylfurfural (HMF), both as solvent and as an active part of the catalytic system. The

chromium (III) chloride catalysts used have a low environmental impact and were employed using modest (7 mol%) loadings.

Finally, this research project was designed to encompass as much as possible from the Twelve Principles of Green Chemistry with the minimisation of any environmentally-harmful chemicals together with energy and time efficient reaction methods for the conversion of three different bioderived precursors to 5-hydroxymethylfurfural (HMF).

1.9 The role of catalysts in chemical reactions

Catalysts are chemical substances that accelerate the rate of a chemical reaction but which are not consumed by it and do not appear in the overall reaction equation. Moreover, they have an equal influence on the forward and reverse rates, meaning that catalysts have no effect on the equilibrium constant and thus on the composition of the equilibrium state.

Catalysts can be divided into two categories, homogeneous and heterogeneous catalysts. Homogeneous catalysts are those which exist in the same phase as reactants, while heterogeneous catalysts are in a different phase to that of the reacting species.⁵²

An example of homogeneous catalysis is the preparation of sulfuric acid in the lead chamber process. Sulfuric acid is also chosen as an example as it is considered to be one of the most crucial chemicals in industry. In order to make the sulfuric acid, sulfur is burned to produce sulfur dioxide, which is then oxidized to sulfur trioxide. Ultimately, the sulfur trioxide is dissolved in water in order to manufacture sulfuric acid (Figure 1.9).

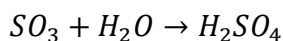
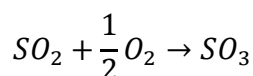
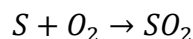


Figure 1.9. *Formation of sulphuric acid.*

In the absence of a catalyst, oxidation of SO_2 to SO_3 occurs slowly. In the lead chamber process, sulfur dioxide is brought into contact with a mixture of nitrogen oxide (NO) nitrogen dioxide NO_2 , air and steam in enormous lead-lined reaction chambers. Nitrogen dioxide readily oxidizes sulfur dioxide to give nitrogen oxide and sulfur trioxide (see first chemical equation below). Afterwards, nitrogen oxide is reoxidised to regenerate the nitrogen dioxide. In this particular case, NO_2 serves as a catalyst (Figure 1.10).

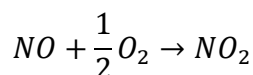
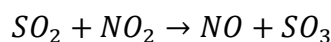


Figure 1.10. *Role of NO_2 in the oxidation of SO_2 to SO_3 .*

There are many examples of metal complexes acting as homogeneous catalysts and this has been recognised in the award of Nobel Prizes in 2005 for olefin metathesis and in 2010 for C-C coupling reactions. The latter process usually involves zerovalent palladium compounds which are able to react with polar bonds and then undergo coupling with other species to produce a new C-C bond (Figure 1.11), such as the Suzuki, Sonogashira, Heck and Stille reactions.⁵³

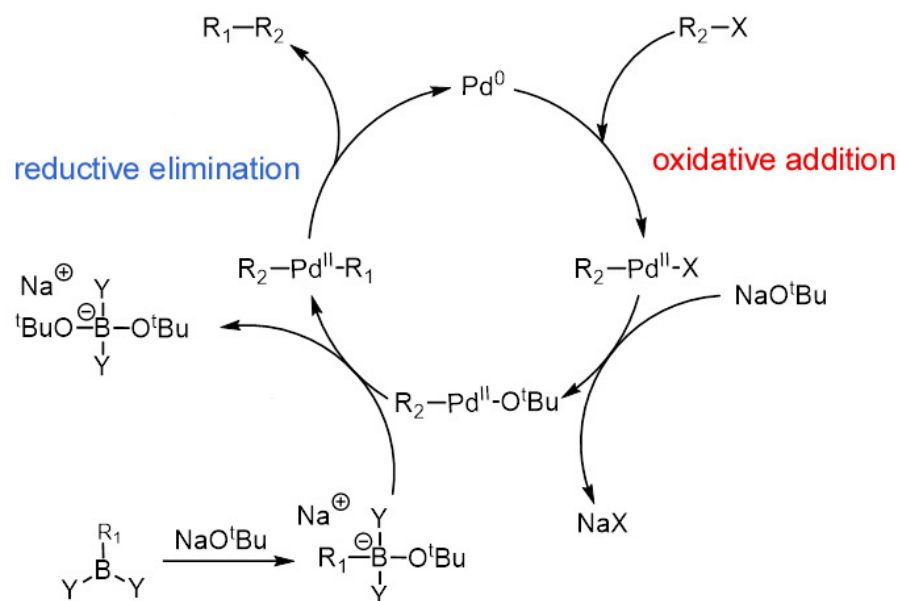


Figure 1.11. Suzuki-Miyaura coupling of boronic acids with aryl halides.

Industrial examples include the rhodium-catalysed Monsanto process for the production of acetic acid (Figure 1.12) and the Wacker process, used to make ethanal from ethane. This process has largely been superseded by the Cativa process based on iridium.⁵⁴

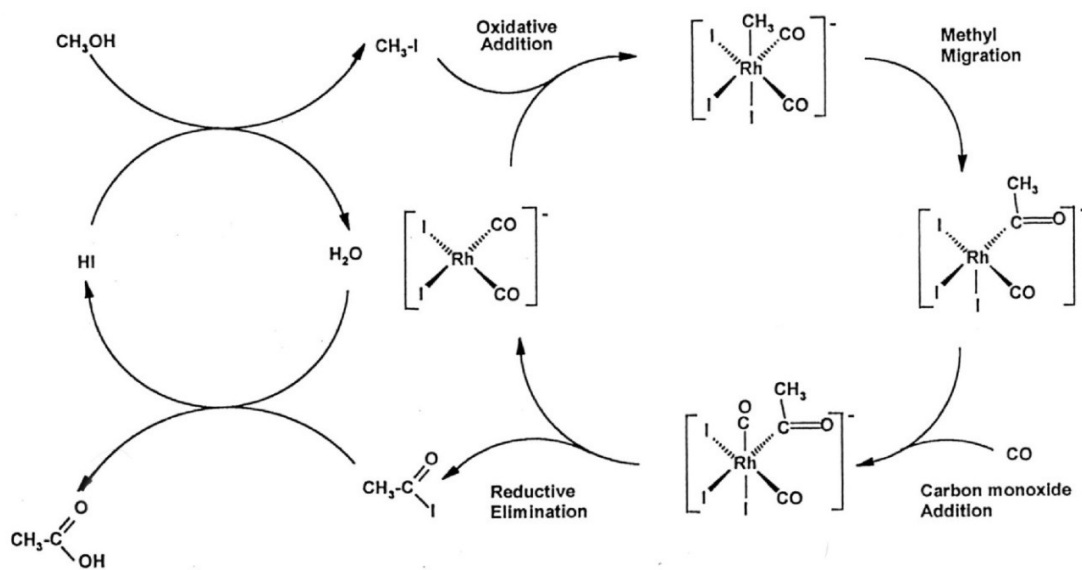


Figure 1.12. Monsanto process for the production of acetic acid.

The advantages of these processes include high activity, well-understood mechanisms and tailoring of the process through modification of the ligand set. Major drawbacks focus on the separation and recycling of the catalyst.

Another, very different type of homogeneous catalyst, is an enzyme, otherwise known as a biocatalyst. Enzymes are composed of proteins and have a specifically shaped area called an “active site” that lowers the energy of the activated complex (transition state) of the reaction being catalysed. These catalysts are extremely specific and usually have a tremendous influence on the reaction they control. Qualitatively, substrates are reversibly linked to the active sites of enzymes, creating an enzyme-substrate complex (Figure 1.13). The enzymes allow substrates to be converted into products which are then released from the enzyme-substrate complex. Moreover, these biocatalysts do not normally change form after the reaction.

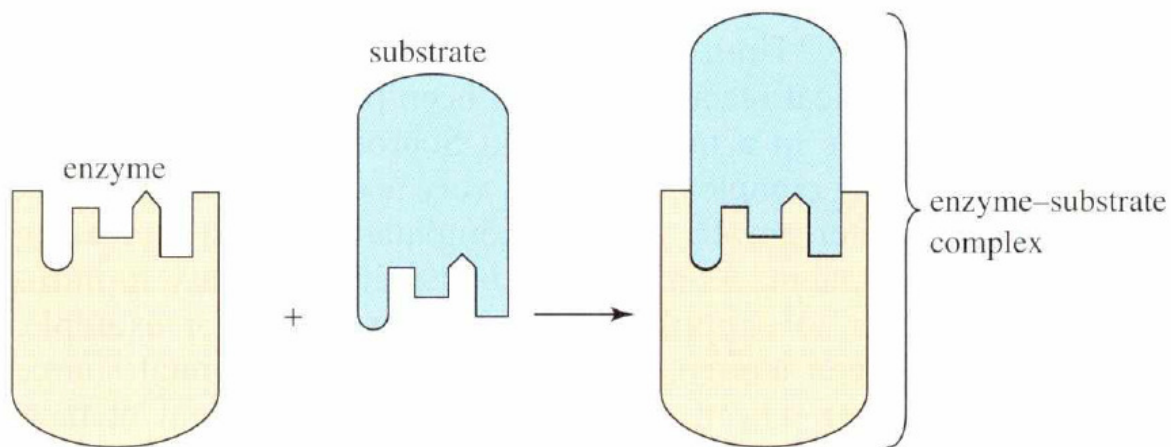


Figure 1.13. *Schematic representation of the lock-and-key model in substrate binding by an enzyme.*⁵⁵

The specific action of an enzyme with a single substrate can be explained using a lock and key analogy first postulated in 1894 by Emil Fischer.⁵⁵ In this analogy, the lock is the enzyme and the key is the substrate. Only the correctly sized key (substrate) fits into the keyhole (active site) of the lock (enzyme). Smaller keys, larger keys, or incorrectly positioned teeth on keys (incorrectly shaped or sized substrate molecules) do not fit into the lock (enzyme). Only the correctly shaped key opens a particular lock. This is illustrated in Figure 1.13.

Heterogeneous catalysts are usually solids and operate by increasing the rate of reaction on the solid surface. An example, which provides a similarly vital product to the sulfuric acid process mentioned above, is the industrial production of ammonia from hydrogen and nitrogen using the Haber-Bosch process (Figure 1.14). This process employs an iron catalyst on an aluminium oxide support.

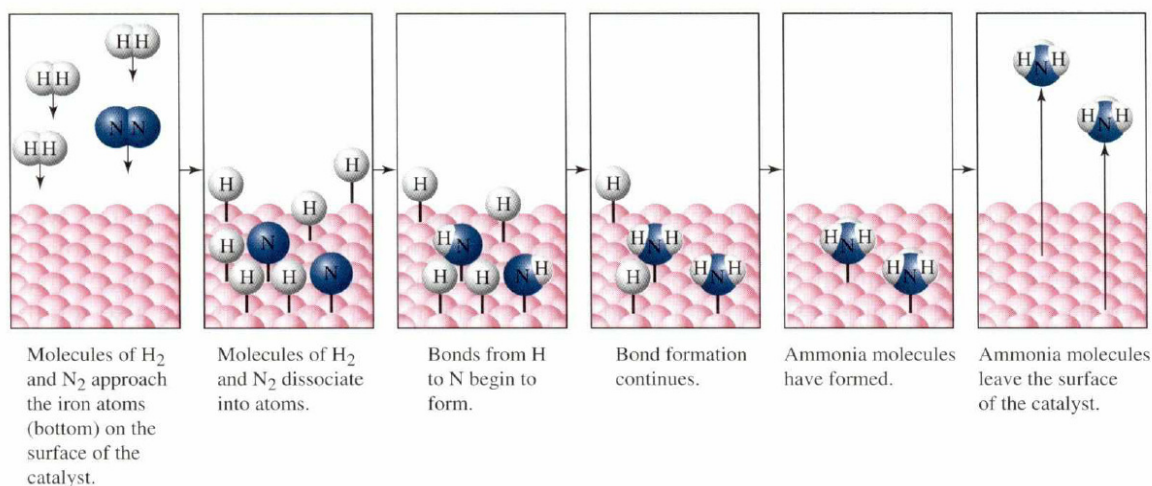


Figure 1.14. *The Haber-Bosch process. Catalytic formation of ammonia molecules from nitrogen and hydrogen on a catalyst surface.*⁵⁵

In fact, heterogeneous catalysts play a major role in many commercial processes. The petroleum industry makes use of heterogeneous catalysts in order to crack hydrocarbons into smaller fragments and then re-combine them into the constituents of petrol.⁵⁵

Fundamentally, a catalyst operates by lowering the activation energy (the energy barrier which must be overcome for a chemical reaction to occur). It can do this in a number of different ways:

- Stabilization of the transition state (lowering the transition state energy)
- Destabilization of the reactants (pushing energy of reactants up and making them move closer to the free energy of activation associated with the transition state)
- Enabling a new reaction path, illustrated by the violet colour in Figure 1.15 (a catalyst can operate using a completely new chemical pathway which possesses a lower activation energy)

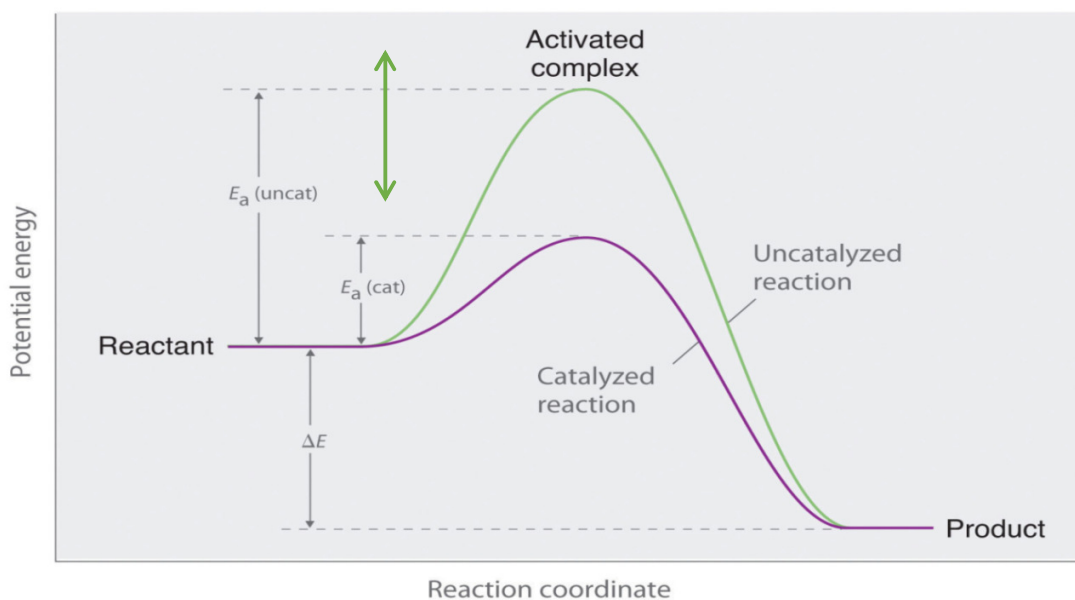


Figure 1.15. Free energy graph.⁵⁶

The key parameter that makes the catalysed reaction proceed at a fast rate relative to the uncatalysed reaction is the term on the right hand side of Equation 1.1. It is called the difference in free energy and is represented by the orange arrow in Figure 1.15.

$$\Delta G_{uncat}^{++} - \Delta G_{cat}^{++} = \Delta\Delta G^{++} \quad (1.1)$$

Where,

ΔG_{uncat}^{++} - is the free energy of uncatalyzed reaction $\left(\frac{kJ}{mol}\right)$

ΔG_{cat}^{++} -is the free energy of catalyzed reaction $\left(\frac{kJ}{mol}\right)$

$\Delta\Delta G^{++}$ -is the free energy difference $\left(\frac{kJ}{mol}\right)$

Figure 1.15 also indicates that the free energy change associated with transforming reactants into products remains the same in the presence of catalysts.

In order to understand the role of catalysts in a chemical reaction it is also necessary to refer to the Arrhenius equation.

$$k = Ae^{-\frac{E_{act}}{RT}} \quad (1.2)$$

Where,

k is the rate constant $\left(\frac{mol^{1-n}}{l^{1-n}*s}\right)$

A is the Arrhenius parameter $\left(\frac{mol^{1-n}}{l^{1-n}*s}\right)$

E_{act} is the activation energy $\left(\frac{kJ}{mol}\right)$

R is the Universal gas constant $\left(8.314\left(\frac{kJ}{kmol\ K}\right)\right)$

T is the temperature (K)

From Equation 1.2, it is apparent that the rate constant is exponentially dependent upon the activation energy. In other words, at constant temperature, a decrease of activation energy increases the rate constant, which in turn leads to an increase in the rate of reaction.

1.10 Ionic liquids

Green Chemistry, sustainability, and eco-efficiency are inspiring researchers to develop next generation materials, processes and applications. It has been mentioned above that biomass could be a viable resource for the replacement of fossil fuels. Cellulose, the main component of biomass, is the most abundant natural polymer on the earth. The annual biosphere production of cellulose is around 90×10^9 metric tons making this the most recognised renewable resource for platform chemical and biofuel production.⁵⁷ Cellulose possesses attractive mechanical and chemical properties due to its highly ordered structure but this aspect also makes it a significant challenge to find a good solvent for its dissolution.⁵⁸

The first trials to dissolve cellulose were performed in the early 1920s. Several solvents (aqueous and nonaqueous) have since been reported to dissolve sugars but all of these approaches suffer from high cost, toxicity and/or low solvation power.⁵⁹ However, in 2002 Swatloski *et al.* introduced a new class of solvents to the cellulose research community and since then ionic liquid solvent systems have been used widely in the

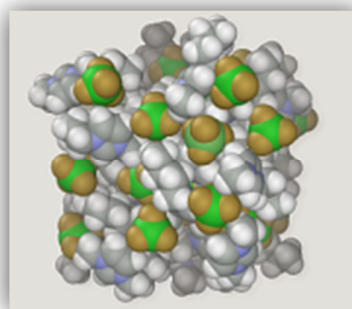


Figure 1.16. Ionic liquid model.⁶⁰

dissolution of cellulose and in the chemical modification of polysaccharides.⁶¹ Ionic liquids (ILs) are salts that exist as liquids at moderately low temperatures ($< 100\text{ }^{\circ}\text{C}$). Ones which are liquid under ambient conditions are termed room temperature ionic liquids (RTILs). They consist of anions and cations which display strong ion-ion interactions between the molecules (Figure 1.16) but are unable to pack efficiently. Their chemical and physical stability, low vapour pressure, and non-flammable nature make them very attractive solvents. While ordinary liquids such as gasoline and water are mainly made of electrically neutral molecules, ILs are predominantly composed of ions and short-lived ion pairs. These substances are variously called ionic melts, ionic fluids, liquid electrolytes, liquid salts, fused salts or ionic glasses. Ionic liquids have a variety of applications, such as electrically conducting fluids and versatile solvents. In fact, salts that are in the liquid phase at ambient temperature are essential for electric battery usage, and have been utilized as sealants because of their low vapour pressure. Commonly, any salt that fuses without vaporizing or decomposing produces an ionic liquid. For instance, sodium chloride fuses at $801\text{ }^{\circ}\text{C}$ into a liquid that is composed of sodium cations and chloride anions.⁶² In contrast, when an ionic liquid is cooled down, it forms an ionic solid which can either be crystalline or glassy. Electrostatic interactions are normally much stronger than the van der Waals forces between the molecules in liquids. For this reason, common salts are prone to fuse at higher temperatures than other solids. Several salts are liquid at or below ambient temperature. For example, substances based on the 1-ethyl-3-methylimidazolium cation and chloride or dicyanamide anions fuse at $-21\text{ }^{\circ}\text{C}$.

The discovery of ionic liquids can be traced to the middle of the 19th century, when a little “red oil” was detected in Friedel-Crafts reactions using aluminium salts.⁶³ Decades later, in 1914, the first room-temperature ionic liquid ethylammonium nitrate, $[\text{EtNH}_3][\text{NO}_3]$, was prepared by

Walden.⁶⁴ In order to find new electrolytes for batteries, the U.S. Air Force Academy developed the work on ionic liquids even further starting from 1963. In the 1980s, Hussey and Seddon began to utilize alkylpyridinium tetrahalidoaluminate, [Rpy][AlCl₃X], ionic liquids as solvents in the study of transition metal complexes.⁶⁵ In fact, the first generation of ILs that contained aluminium-based anions proved extremely hygroscopic and air-sensitive, and accordingly difficult to handle. This challenge was solved when new air- and water-stable anions, such as [BF₄]⁻, [PF₆]⁻, [CF₃CO₂]⁻ and halides were discovered by Wilkes and Zaworotko.⁶⁶ Since then, many ionic liquids of various compositions have been manufactured.

Another significant contribution to the development of this area are the books on ionic liquids (including an accessible, introductory text) on the topic by Freemantle. These books describe many important aspects of ILs such synthesis, properties, applications as well as history, popularising the area and accelerating the wider adoption of ILs.

Since these discoveries, it has become widely recognized that the physical and chemical properties of ionic liquids can be altered depending on the particular cation and anion combinations.⁶⁷ Moreover, ionic liquids can be mixed together in order to make binary or ternary ILs. The development in the field has necessitated the definition of some general properties of ionic liquids, one of which is that they possess a fusing point lower than 100 °C. Another key characteristic of ionic liquids is that they decompose at high temperatures rather than being vaporized like volatile organic compounds.

Ionic liquids are composed of large organic cations such as alkylimidazolium, alkylpyridinium, alkylpyrrolidinium, and anions such as tetrafluoroborate, hexafluorophosphate, chloride,

bromide as well as many others (Figure 1.17). Low temperature ionic liquids are composed of unsymmetrical and bulky ions with delocalised charge which decrease melting temperature.

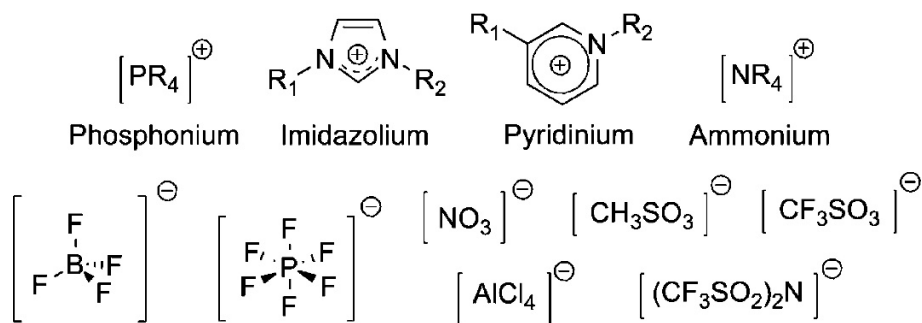


Figure 1.17. Examples of cations and anions typically found in ionic liquids.⁶⁹

To give an indication of the versatility, it has been estimated that the number of potential ion combinations amounts to around 10^{25} different ionic liquids.⁶⁸ This allows the properties of the medium (acidity, hydrophobicity, viscosity etc.) to be adjusted and tailored to a specific application.

1.11 Disadvantages of ionic liquids

❖ Toxicity

One of the most essential aspects of designing new ionic liquids is an assessment of their toxicological and ecotoxicological risks. In terms of comparing effective concentrations, ionic liquids are more toxic than organic solvents. In fact, the release of specific ionic liquids into an aqueous environment may contribute to water pollution due to their high solubility in water. A number of acute toxicity tests on saltwater bacteria and water flea species were performed in

order to evaluate acute toxicity.⁷⁰ The investigated imidazolium-based ionic liquids were the $[C_6\text{im}]^+$ cation with Cl^- , $[\text{BF}_4]^-$ and $[\text{PF}_6]^-$ anions; the $[C_4\text{im}]^+$ cation with Br^- , Cl^- , $[\text{BF}_4]^-$ and $[\text{PF}_6]^-$ anions and the $[C_8\text{im}]^+$ cation with Cl^- , $[\text{BF}_4]^-$ and $[\text{PF}_6]^-$ anions. From these studies it was deduced that imidazolium cations with long alkyl chains are more toxic than those with shorter chains. Moreover, comparison of the results obtained with corresponding data for organic solvents revealed that ionic liquids are more toxic than organic solvents in an aquatic environment. These findings were corroborated by other experiments, which showed that the toxicity of ionic liquids increases with the length of the alkyl chain.^{71,72}

❖ Recycling

Ionic liquids are reasonably expensive and the necessity of their recycling should be taken into account after their usage. Some studies have demonstrated the successful recycling of ionic liquids can be achieved after their use.⁷³ Several procedures for recycling ILs have been reported, which display a variation in efficiency of the recycling from poor to good recovery.^{74,75,76} In general, recyclability is largely dependent on the non-volatile nature of ILs and the differences in solubility between ILs, water and organic compounds. Based on these factors, it can be stated that poor ionic liquids reuse is a challenge and can incur severe impacts, both from financial and ecological perspectives.

❖ Synthetic cost and handling

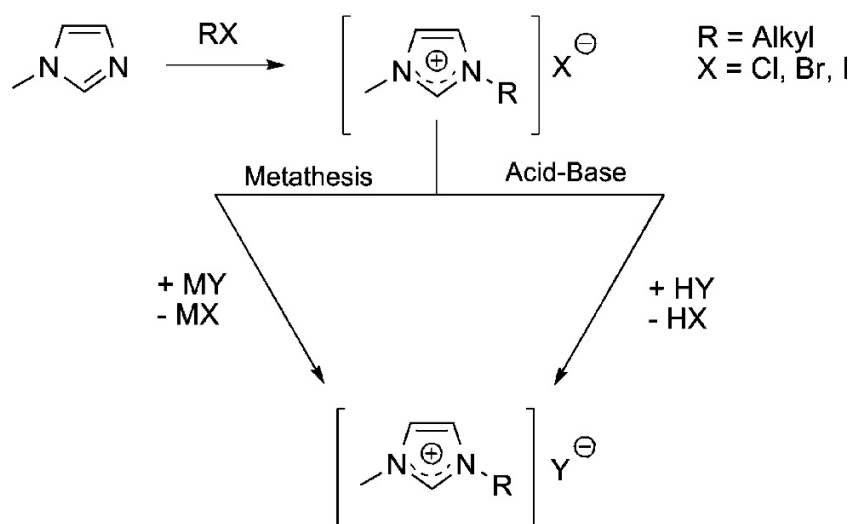
Ionic liquids can be classified into two main categories: protic ionic liquids (PILs) and aprotic ionic liquids (APILs).⁷⁷ In comparison with PILs, APILs are more expensive which is due to the

methods and raw materials used for their preparation. Ionic liquids can be synthesized from amines, sulfonates and phosphines. The first production step is usually a quaternisation reaction, where NR_3 , for example, is alkylated with a suitable alkylation reagent (R^+X^-) such as an alkyl halide, which results in the formation of ionic liquid. However, when an ionic liquid with a desired anion cannot be obtained directly by means of this reaction, an anion exchange reaction is required. It is this feature of their synthesis, which makes ionic liquids more expensive compared to corresponding organic solvents. Another key challenge related to the application of ionic liquids is their availability on a commercial scale.⁷⁸ In fact, the quality of ionic liquids also plays a significant role in determining the price of ILs. Higher purities of ILs require extensive purification steps, which inflate their synthetic cost and so raises their market price. However, two ionic liquids have recently been reported to be accessible at very low cost prices.⁷⁹ The prices of triethylammonium hydrogen sulfate and 1-methylimidazolium hydrogen sulfate are estimated to be roughly \$1.24 per kg and between \$2.96-5.88 per kg, respectively, which are comparable with organic solvents such as ethyl acetate or acetone, which cost around \$1.30-1.40 per kg.⁷⁹ If reactions using more expensive ILs can also be carried out in these less expensive IL media, then the cost barrier will become less significant. These benefits will be increased when coupled with improvements in their recycling.

1.12 Synthesis and purification of ionic liquids

There are two main steps in the synthesis of imidazolium-based ionic liquids (the most commonly used family of ILs in this field): the formation of the preferred cation followed by

exchange (metathesis) of the anion with the desired anionic partner to produce the final ionic liquid (Scheme 1.5).



Scheme 1.5. Synthesis pathway for the preparation of imidazolium ionic liquids.⁶⁷

During the anion exchange there are two possible pathways, which can be followed. One is the formation of complex anions by the direct treatment of a halide salt with a strong Lewis acid and the other is the formation of the IL through addition of a metal salt so as to precipitate the unwanted anion. There are several other methods which have been developed for the synthesis of ionic liquids, such as halide and solvent free pathways, sonochemical or microwave methods, or using very cheap industrial products (e.g., H₂SO₄) as reagents.

Depending on the methods used in the synthesis of the ionic liquids, common impurities include alkyl halides or alkylsulfates, tertiary amines or other side-reaction products and, after metathesis, residual sulfate and halide. There are several purification methods which can be employed after the synthesis of the ionic liquid, such as extraction of the aqueous solution of the

ionic liquid with an immiscible organic solvent or extraction of the ionic liquid with a polar solvent or treatment of the IL with activated charcoal. The extensive use of solvent in the purification steps is one of the main factors which tarnishes the ‘green’ credentials of ionic liquids. However, due to their low volatility compared to the dissolved species allows them to be recovered and reused, thus offsetting the negative aspects of their synthesis.

1.13 Properties and applications

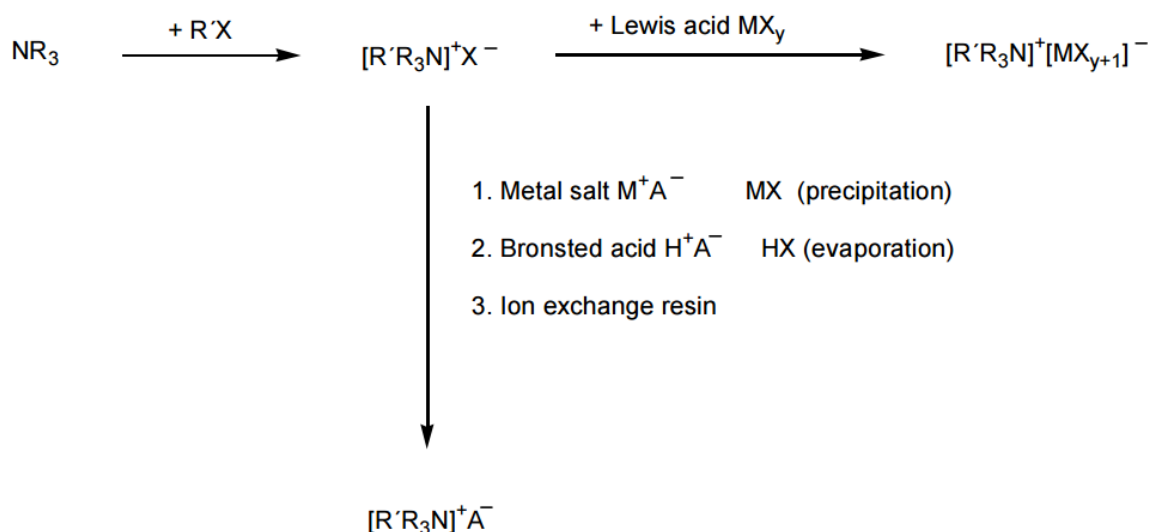
The different physical and chemical characteristics of ionic liquids make them very attractive in a broad field of applications. There are some properties which are common to many ionic liquids. For example, ionic liquids with quaternary nitrogen cations are non-flammable and considered to exhibit negligible vapour pressure. Though Earle and co-workers have shown that, under low pressure and high temperature, these ionic liquids can be distilled,⁸⁰ the extremely low vapour pressure of ILs under usual operating conditions (room temperature to 200 °C) makes them a very attractive solvent as evaporation is limited, thus reducing the need for an exhaust system or respiratory protection. The negligible vapour pressure of ILs also enhances their recycling contributing to their classification as ‘green solvents’.

Most significant properties of ionic liquids are: low (negligible) vapour pressure, thermal stability, tuneable solubility (feasibility for biphasic systems), high electroelasticity, liquid crystal structures, high heat capacity, electric conductivity and non-flammability. These properties allow ionic liquids to be utilized in a wide range of applications which are listed in Table 1.4.

Table 1.4 *Selection of applications where ionic liquids have been utilized.*⁸¹

IONIC LIQUIDS	Analytics	MALDI-TOF matrices GC headspace solvents Protein crystallization
	Separation	Gas separations Extractive distillation Extraction Membranes
	Heat storage	Thermal fluids
	Lubricants & additives	Lubricants Fuel additives
	Electroelastic materials	Artificial muscles Robotics
	Liquid crystals	Displays
	Electrolytes	Fuel cells Sensors Batteries Metal finishing Coating
	Solvents	Organic reactions & catalysis Nanoparticle synthesis Polymerization Bio-catalysis

Ionic liquids can be prepared from amines, sulfonates or phosphines. Typical synthetic paths for manufacturing ammonium-based ionic liquids are illustrated in Scheme 1.6. The initial step is a quaternisation reaction, where an amine (NR_3) is alkylated with a suitable alkylation agent (R^+X^-) such as an alkyl halide, resulting in the formation of an ionic liquid. However, when an ionic liquid with a desirable anion cannot be formed by means of this reaction, an anion exchange reaction is necessary. Consequently, a previously obtained IL is utilized as a precursor, and the anion is exchanged in a metathesis reaction with a Lewis acid (MX_y) or Brønsted acid.

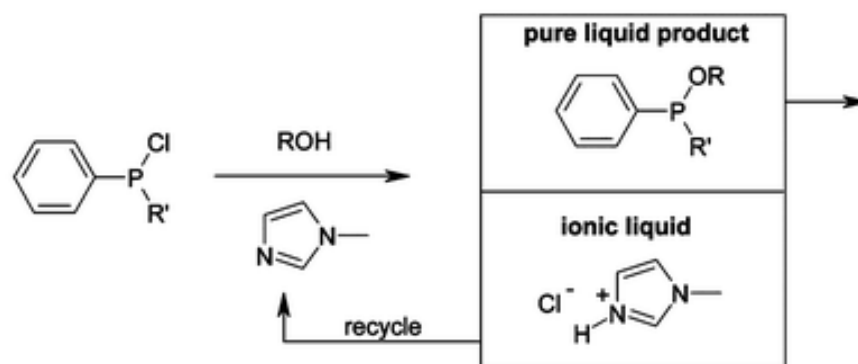


Scheme 1.6. Synthetic paths for manufacturing ammonium-based ionic liquids.⁸¹

Currently, frequently utilized ionic liquids can be purchased from various commercial sources (BASF, Sigma-Aldrich, Acros Organics, Merck, Fulka, Solvent Innovation, Covalent Associates and Waco). Of the sources mentioned above, the BASF Chemical Company has developed the Bacionics portfolio of ILs covering a variety of properties. Imidazolium-based ILs are a predominant focus in this product line.⁸² Moreover, the ionic liquid products offered by BASF are utilized in fields such as metal processing, electronic devices, chemical processing, separation processes, polymer processing and many others.

The use of the ionic liquids as reaction media for chemical processes is one of the most important applications of ILs. In 2001, BASF introduced the first commercial scale application of ILs: the BASIL process.⁸³ Many chemical reactions produce acid by-products which cause decomposition of the desired reaction products or participate in other side reactions. In the BASIL process, tertiary amines are used to produce ammonium salts and then removed by an

aqueous extraction phase. However, if the reaction mixture is sensitive to water, the process becomes complicated. This was the problem BASF faced during the production of diethoxyphenylphosphine but this was addressed by the use of 1-methylimidazole instead of triethylamine (Scheme 1.7). The ionic liquid formed during the reaction is methylimidazolium chloride which is liquid at the reaction temperature of 80 °C.. The resulting two clear liquid phases were simply separated by a phase separation. The upper phase provides the pure product while the lower phase is the IL which can be deprotonated to regenerate methylimidazole.



Scheme 1.7. *The BASIL process.*⁸³

1.14 Cellulose dissolution using conventional methods and ILs

The dissolution of cellulose is one of the most important goals in cellulose research and continues to be of great importance. The poor solubility of cellulose in water and other organic solvents is due to the highly branched hydrogen-bonding network and highly crystalline regions. The most common traditional solvents for cellulose are shown in Figure 1.18. There are two types of solvent for cellulose, termed derivatising and non-derivatising systems, depending on

the interaction of the solvent with cellulose.⁸⁴ Derivatising solvent systems such as sodium hydroxide/carbon disulfide or sodium hydroxide/urea mixtures directly interact chemically with cellulose hydroxyl groups while non-derivatising solvents do not.^{84,85} *N*-methylmorpholine-*N*-oxide monohydrate (NMMO) and *N,N*-dimethylacetamide/LiCl are two examples of non-derivatising solvent systems. There are some significant disadvantages associated with these conventional methods such as cost, toxicity and the large excess of these reagents necessary for cellulose dissolution.

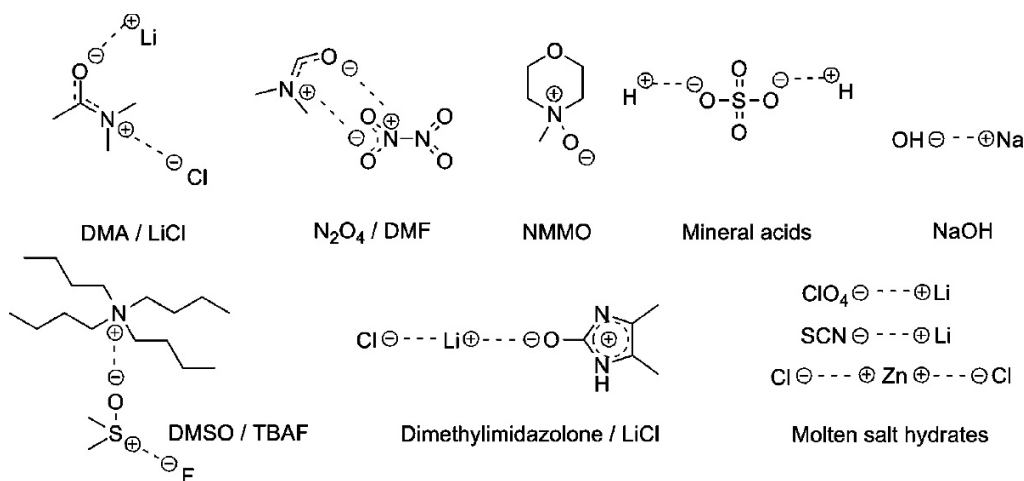


Figure 1.18. Conventional solvents for cellulose dissolution.⁶⁷

It is clear from Figure 1.18 that all these solvent systems for cellulose dissolution are very polar and offer high H-bond basicity, which is a key factor. Ionic liquids are also highly polar due to their ionic character and this plays a major role in their ability to dissolve the biopolymer. There are certain factors which affect cellulose dissolution using ILs. For example, the low viscosity of ILs promote the dissolution of cellulose but longer reaction times (> 12 h), particularly at higher

temperatures, do not always lead to favourable results due to the formation of humins (insoluble polymers).^{86,87} An approach to address this is to use microwave irradiation (MI) instead of thermal heating in order to improve the rapid dissolution due to the direct absorption of energy by the polar molecules instead of heat transfer. However, the energy requirement for this approach is significant and there are also difficulties in scaling up the process.

1.15 Room temperature ionic liquids (RTILs)

Room temperature ionic liquids (RTILs) are low melting ionic liquids which are liquid at room temperature and consist of bulky organic cations with low charge density, low symmetry and weak association of inorganic and organic anions. As there are many different ion combinations for ionic liquids, it is relatively simple to tailor ionic liquids solvents for a specific task.⁸⁸

The key properties of RTILs are listed below:

1. Negligible vapour pressure

Ionic liquids are deemed to be environmentally-friendly solvents since exposure to the environment is limited by their extremely low (negligible) vapour pressure. Separation of volatile substances is straightforward as ILs can be submitted to high vacuum.

2. Thermal stability

They are physically very stable and many processes in ionic liquids can be carried out at elevated temperatures without concerns over decomposition.

3. *Chemical stability*

Ionic liquids with imidazolium cations, in particular, are very resistant to oxidation and reduction.

4. *'Designer solvents'*

The variation of structure, substitution and symmetry of either anions or cations provides access to a huge variety of ionic liquids with different solvent properties.

The attractive properties (stability, cost, low vapour pressure and etc.) of ionic liquids represent distinct advantages over traditional solvents used in chemical processes. The reaction rate, chemo- and regioselectivity of organic reactions can also be improved by ILs. It has been shown that a significant level of polysaccharide dissolution can be achieved by alternating the anionic parts of ILs.⁸⁹ Encouraged by this observation and the many attractive advantages of ionic liquids described above, the use of this solvent system was used as the basis for the research presented here.

CHAPTER 2

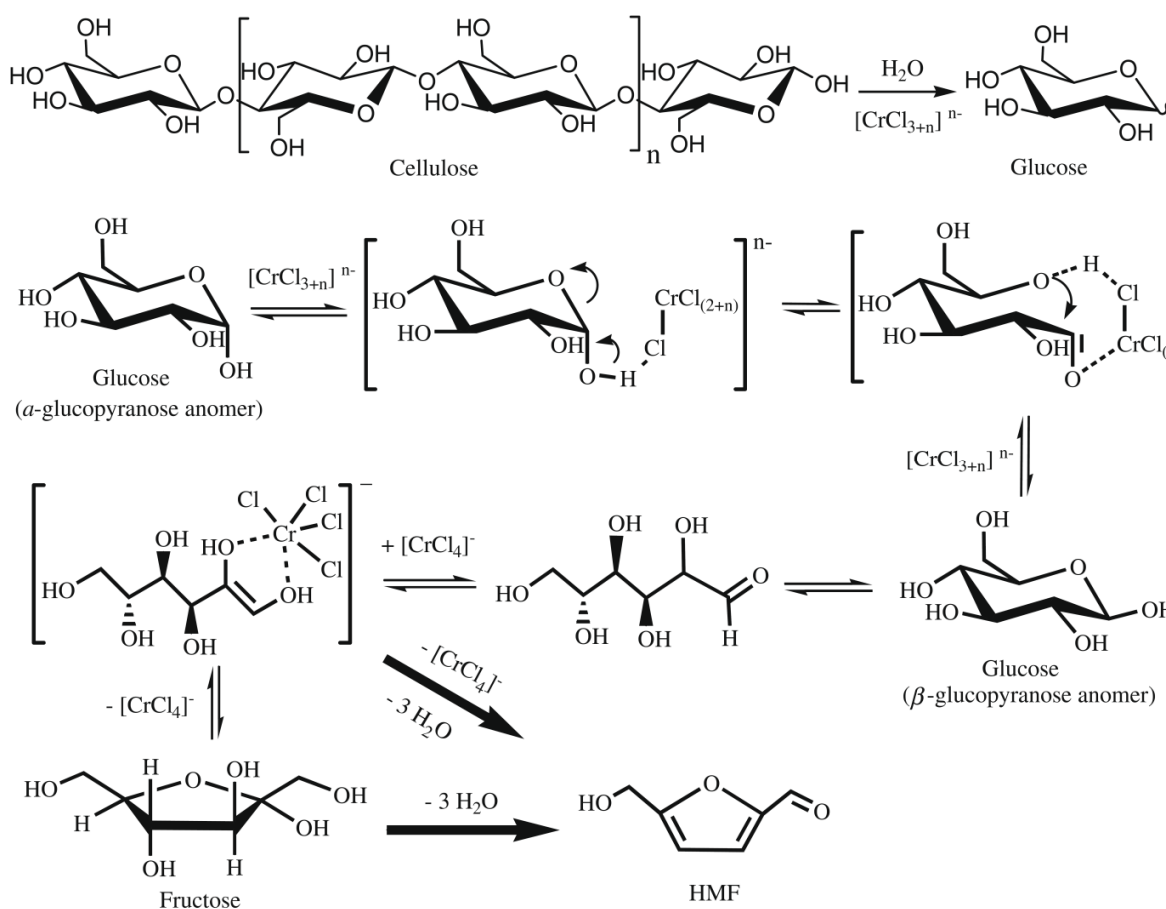
FRUCTOSE TO HMF

2.1 The role of ionic liquids in sugar conversion

Ionic liquids, containing dialkylimidazolium cations, are known to interact strongly with lignocellulosic biomass.⁶⁷ The main role of the cation is to stabilise and liquify the ionic liquids, allowing them to play the role of both solvent and catalyst. Ionic liquids, which have low symmetry cations, melt at lower temperatures than symmetrical analogues.⁹⁰ Increasing the number of carbon atoms in the side chain results in a decrease of the melting point.⁶⁷ They are often termed ‘designer solvents’, since the variation of the structure, type and symmetry of cations and/or anions can result in a wide range of ionic liquids with different solvent properties. For chemical processes, these attractive properties often represent significant advantages over traditional solvents. For example, ionic liquids can improve chemo- and regioselectivity of organic reactions and enhance reactions rates.⁹¹ By altering the anionic unit of the ionic liquid, a reasonable level of dissolutions of sugars can be achieved.⁵¹ Encouraged by these properties, five different ionic liquids were prepared with chloride, dithiocarbamate, and hydrogensulfate anions and these were investigated for the catalytic conversion of sugars to 5-hydroxymethylfrufural (HMF). Chloride-based ionic liquids were initially synthesised and then used as the starting material for the preparation of the other ionic liquids. While the other ionic liquids employed here have been reported previously, ionic liquids based on dialkyldithiocarbamates $[S_2CNR_2]^-$ have not been reported previously. This class of compounds was chosen for the anionic component of the ionic liquids because of their high coordinating

ability to transition metals. Indeed, dithiocarbamates form very stable complexes with all the transition metals in all common oxidation states.⁹² It was thought that dithiocarbamate-based ionic liquids could play the role of both solvent and ligand. In contrast, hydrogensulfate-based ionic liquids were chosen as this anion does not coordinate readily with metal centres and also introduces acidity to the system (due to the HSO_4^- anion) which will also promote the reaction. Using these ionic liquids, which possess different chemical properties, allows the investigation of a system which will not only dissolve sugars but also play a catalytic role in converting sugars to platform chemicals and ultimately providing a route to biofuels. The main purpose of using ILs in these reaction systems is to utilise them both as the solvent medium and as an additional catalyst (to promote dehydration) or co-catalyst (to provide additional halide ligands to the metal catalyst). In this study the conversion of sugars to HMF in ionic liquids without a metal catalyst was poor but the ILs did provide a suitable medium for sugar dissolution and some conversion to HMF was observed. However, in the presence of the metal catalyst, the IL plays the roles of solvent and co-catalyst with this hypothesis being supported by the NMR studies performed by Zhao and co-workers.⁴³ These investigations show that the glucose starting material, dissolved in $[\text{C}_2\text{C}_{1\text{im}}]\text{Cl}$, is mainly the α -anomer and so solvation occurs through hydrogen bonding of the carbohydrate hydroxyl groups with the chloride ions of the solvent, though this interaction is not enough to initiate mutarotation (conversion of α - to β - anomer; Scheme 2.1).⁴³ Even after several hours at 80 °C, only a little interconversion of the α - to β -anomer occurred, which leads to lower yields.⁹³ However, in the presence of the metal catalyst, mutarotation is rapid, leading to an equilibrium mixture. It is purposed that mutarotation is facilitated by the role of the CrCl_3^- anion, which mediates the isomerisation of glucose to fructose. Among tested metals, Cr was found to be the most effective and chromium enolate

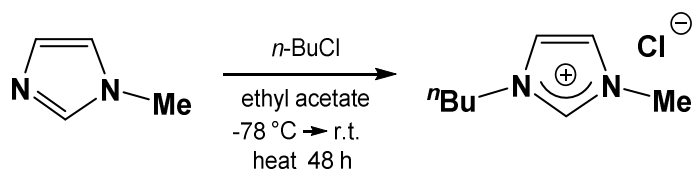
complexes may be the key intermediates (Scheme 2.1).⁴³ This previous work also supports our findings as the use of $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ led to better yields when compared with $[\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$ during glucose conversion as Cl^- anions were identified as a key factor in the stabilisation of the chromium enolate species. However, during the conversion of fructose to HMF, $[\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$ was very effective as a solvent and catalyst in our study due to the acidity of HSO_4^- , which promotes the dehydration of fructose to HMF. Finally, the use of $[\text{C}_4\text{C}_1\text{im}][\text{S}_2\text{CNEt}_2]$ was not effective at all due to the strong coordinating capacity of $[\text{S}_2\text{CNEt}_2]^-$ with the metal centre, which leads to catalyst deactivation. However, $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ and $[\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$ are known to be weakly coordinating and do not compete with the sugar for the binding to metal chlorides.⁹³



Scheme 2.1. Proposed conversion mechanism of sugar to HMF.⁴³

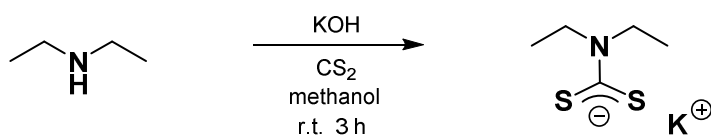
2.2 Synthesis of the ionic liquids

The formation of 1-butyl-3-methylimidazolium chloride proceeds *via* the *N*-alkylation reaction of 1-chlorobutane and 1-methylimidazole (Scheme 2.2). A mixture of distilled starting materials was stirred at 65-70 °C under reflux for 48 h in ethyl acetate under an inert atmosphere of nitrogen. The product, [C₄C₁im]Cl, was crystallised from acetonitrile, after removal of ethyl acetate to provide colourless crystals in 82% yield.



Scheme 2.2. Synthesis of 1-butyl-3-methylimidazolium chloride [C₄C₁im]Cl.

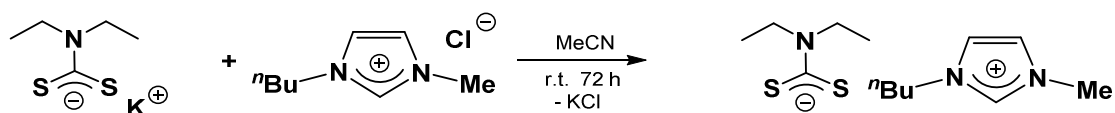
The novel ionic liquid, [C₄C₁im][S₂CN(Et)₂], was formed through a halide metathesis reaction of [C₄C₁im]Cl with potassium diethyldithiocarbamate (Scheme 2.4). Potassium-diethyldithiocarbamate is not commercially available and so was prepared from the reaction of carbon disulfide with diethylamine in the presence of the base, potassium hydroxide (Scheme 2.3). The reaction was stirred for 3 hours in methanol under standard conditions. After the recrystallisation of the yellow crude product, colourless crystals of the product were obtained with a yield of 85%.



Scheme 2.3. Synthesis of potassium diethyldithiocarbamate.

The potassium diethyldithiocarbamate needed no further purification and was thus added to 1-methyl-3-imidazolium chloride in acetonitrile and stirred for 72 hours at room temperature. The ionic liquid produced was collected by cannula filtration to separate it from the KCl formed. After removal of the solvent, a dark-brown room temperature ionic liquid was obtained with a yield of 82%. The product was characterised by ^1H NMR spectroscopy, showing additional resonances for the ethyl protons between 0.89 and 3.99 ppm in dmso-d_6 . These integrated corrected with the typical features of the imidazolium cation. Direct evidence for the dithiocarbamate unit was provided by a resonance at the typically low field value of 212 ppm for the CS_2 carbon in the $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum.

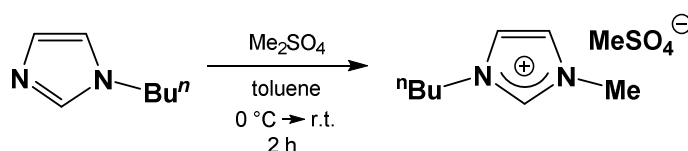
Ionic liquids containing dithiocarbamate anions have been reported by a different route, such as $[\text{RN}(\text{H})\text{C}(\text{R}')\text{NMe}_2][\text{S}_2\text{CNHR}'']$,⁹⁴ this is the first example of one based on a secondary amine. These dithiocarbamates are known to be far more robust than derivatives based on primary amines, such as the ones reportedly previously.



Scheme 2.4. *Synthesis of 1-butyl-3-methylimidazolium diethyldithiocarbamate.*

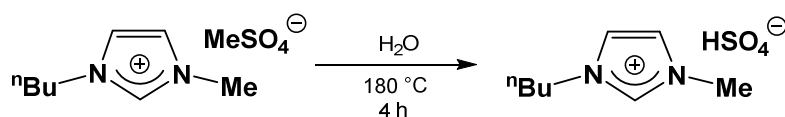
1-butylimidazole was again used as the starting point for the preparation of the methylsulfate ionic liquid, $[\text{C}_4\text{C}_1\text{im}][\text{MeSO}_4]$, which is the precursor to $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$. *N*-alkylation of 1-

butylimidazole in toluene was achieved by slow addition of dimethylsulfate (Scheme 2.5). Isolation of the lower layer provided the desired colourless ionic liquid in a yield of 82%.



Scheme 2.5. *Synthesis of 1-butyl-3-methylimidazolium methylsulfate.*

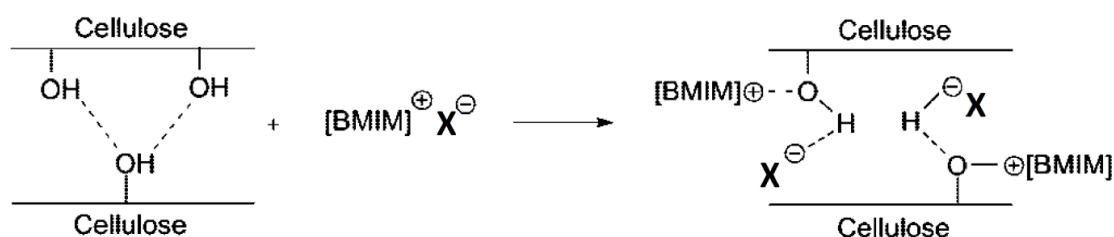
The 1-butyl-3-methylimidazolium hydrogensulfate ionic liquid, $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$, was obtained from the hydrolysis of $[\text{C}_4\text{C}_1\text{im}][\text{MeSO}_4]$ by heating in deionised water between 170 to $180\text{ }^\circ\text{C}$ for four hours (Scheme 2.6). The residual water was removed by placing the product under vacuum overnight at $65\text{ }^\circ\text{C}$, allowing the colourless liquid to be isolated in 98% yield.



Scheme 2.6. *Synthesis of 1-butyl-3-methylimidazolium hydrogensulfate.*

In many reports, enzymes and mineral acids have been used as catalysts for the hydrolysis of sugars in the aqueous phase.⁹⁵ Higher yields could be achieved at higher temperatures in acid catalysed reactions, however the formation of side products was found to be unavoidable. The selectivity was better for enzyme catalysed reactions but satisfactory rates could not be achieved as the thermal stability of enzymes is limited at higher temperatures. The best solvent system for

dissolution would combine a satisfactory rate with good selectivity in a process operable at higher temperatures. Several ionic liquids have been proposed as good examples of such model systems. Rogers and co-workers studied the solubility of sugar polymers in 1-butyl-3-methylimidazolium chloride, [BMIM] Cl ⁹⁶ and it was found that both the anion and the cation of the ionic liquid play a role in the dissolution process (Scheme 2.7).



Scheme 2.7. *The role of anion and cation in the dissolution of the sugar polymer.*

Bearing in mind that the nature of both cation and anion are likely to be important, several aspects were considered during the design and synthesis of the ionic liquids. Methylpyridinium and methylimidazolium cores with butyl-, ethyl-, and allyl- side chains are often considered to be the best cations for the dissolution of sugars.⁶⁷ Ionic liquids with 1,3-methylimidazolium cores, paired with chloride, acetate, phosphate, or phosphonate anions, were reported to dissolve lignocellulose.⁶⁷ Ionic liquids, which dissolve cellulose are also good solvents for lignocellulose.⁸⁷

2.3 Overview

Conversion of biomass to useful chemical building blocks is a vital aspect in the long-term goal of replacing petroleum-based feedstocks with sustainable alternatives.^{97, 98} It is highly probable

that lignocellulosic biomass will be a major feedstock for future large-scale biorefineries as it is distributed widely and can be grown on a billion ton scale. This offers an opportunity to reduce the carbon footprint as well as diversifying fuel and material supplies. A major driving force behind this is the fact that the fuels and materials derived from such biomass are potentially 'carbon neutral', however, the current production of lignocellulosic biomass requires extensive, costly and environmentally harmful pre-treatment.⁹⁹ In contrast, the use of ionic liquids has provided a far more benign method of separating cellulose and this process is critical in the development of the functionalisation of the resultant biopolymer.¹⁰⁰⁻¹⁰³

In 2004, the U.S. Department of Energy identified 5-hydroxymethylfurfural (HMF) as a key platform chemical, which is a precursor to many chemical feedstocks. It can also be transformed into potential fuels, such as 2,5-dimethylfuran, which possesses 40% higher energy density than ethanol.¹⁰⁵ The versatility of this synthetic building block is now widely recognised, prompting a dramatic increase in reports detailing transformations involving HMF.¹⁰⁶

In the past decade, there has been an increasing number of papers focusing on the conversion of carbohydrates to biofuels. In 2007, pioneering work by Zhao illustrated that an ionic liquid (IL), [C₄C₁im]Cl, could be used in combination with various metal salts to break down fructose to HMF in 70% yield at 120 °C over the course of 3 hours.⁴³ The main pathway from biomass to platform chemicals involves the conversion of cellulose to 5-hydroxymethylfurfural (HMF), which confirms its position as a versatile intermediate between petroleum-based industrial organic chemistry and biomass-based carbohydrate chemistry. Acid-promoted production of 5-

hydroxymethylfurfural (HMF) has also been described under conditions of high fructose concentration in ionic liquids at 80 °C with an HMF yield up to 97% catalysed by hydrochloric acid.¹⁰⁷ It was shown that zeolites (H-ZSM-5) could replace chromium catalysts, allowing a 45% yield of HMF.¹⁰⁸ Catalyst recovery in this system is straightforward and a departure from the usual chromium catalysts. Zhang *et al.* reported the conversion of fructose into 5-hydroxymethylfurfural (HMF) catalysed by germanium(IV) chloride in a mixed dimethyl sulfoxide (DMSO) and [C₄C₁im]Cl system at room temperature with HMF yield of 70 %.¹⁰⁹ More recently, it has been found that dicationic room temperature ionic liquids (RTILs), with short oligoethylene glycol linkers are highly active catalyst for the dehydration of fructose to 5-hydroxymethylfurfural with a yield of 93%.¹¹⁰ However, many of these approaches were compromised by high energy consumption, low HMF yields, high catalyst and solvent cost or formation of by-products. Thus, while many combinations have been explored, no viable route suitable for larger scale HMF production has been reported. A viable, economic route, showing high activity and selectivity for HMF production, is needed in order for a biorefinery platform to be built on the basis of these compounds.¹¹¹

Chromium salts have consistently been found to provide the highest conversions and as confirmed many studies related to the one presented here.¹¹²⁻¹¹⁴ The combination of these metal catalysts with an ionic liquid medium has also become the most actively researched system to address this transformation. While the ‘green’ credentials of ILs can be overstated¹¹⁶ they offer substantial environmental benefits, such as their reusability, negligible vapour pressure and relatively low toxicity. More importantly, they offer many significant improvements over

current industrial process, which employs highly acidic aqueous solutions with all the attendant safety, environmental and containment issues.⁶

Over the last five years, a plethora of reports has appeared in which ILs have been employed to dissolve and breakdown sugars (fructose, sucrose, cellulose etc.) derived from biomass.¹¹²⁻¹¹⁵ Most of these have adopted the media employed in the original research, principally using imidazolium chloride ionic liquids, such as [C₄C₁im]Cl and [C₂C₁im]Cl (Figure 2.1). However, an overview of the catalytic literature using ILs illustrates that the presence of chloride (an excellent ligand) as part of the solvent system (and hence in huge concentration) in many cases inhibits the ability of transition metals to generate a vacant site, compromising its ability to perform catalytically.¹¹⁷

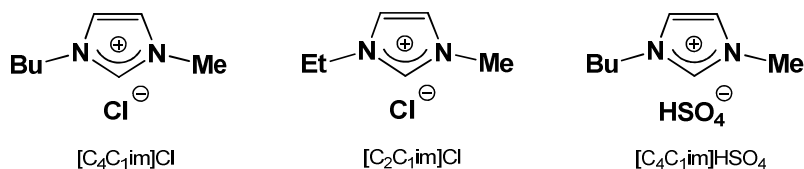


Figure 2.1. *Ionic liquids often used in the dissolution and breakdown of biomass.*

One of the many advantages of ionic liquids is the potential for tuning their physical and chemical properties in order to provide the best medium for a specific transformation. Initially, [C₄C₁im][S₂CN(*n*-Bu)₂] was chosen because of the ability of dithiocarbamates to stabilise transition metals (in many different oxidation states).⁹² It was thought that dithiocarbamate-based ILs could play both role of solvent and ligand for the metal catalyst employed in the

process as well as allowing interactions between the dithiocarbamate anion and the substrate in a similar manner to the acetate anion. The breakdown of fructose is known to be favoured by acidic conditions so the IL, [C₄C₁im][HSO₄] was also included in the study as a suitable candidate for this transformation due to the mildly acidic proton in the anion. Dilute acids have been reported to accelerate fructose conversion to HMF in both water¹¹⁸ and ILs.¹¹⁴ In addition, the absence of a chloride counter anion and the presence of only a weakly coordinating hydrogensulfate anion were also important factors in providing a spectrum of IL media with different properties, with which to probe the conditions required for the conversion of fructose to HMF.

The coordinating ability of the IL anion was demonstrated to be a significant factor by Hu and co-workers. They reported the conversion of glucose to HMF using a Lewis acid (SnCl₄) in ILs with a range of anionic species while the cation used in all cases was [C₄C₁im]⁺.¹¹² The best results were obtained when the anion was [BF₄]⁻ while lower yields were obtained with ILs bearing the following anions: Cl⁻, Tf₂N⁻, TFA⁻, Trif⁻ and Sacc⁻, all of which have the ability to coordinate (Figure 2.2).¹¹² It was suggested that coordinating anions, showing stronger interactions with the metal centre, would compete with the interaction between sugar and catalyst and thus inhibit the formation of HMF.¹¹²

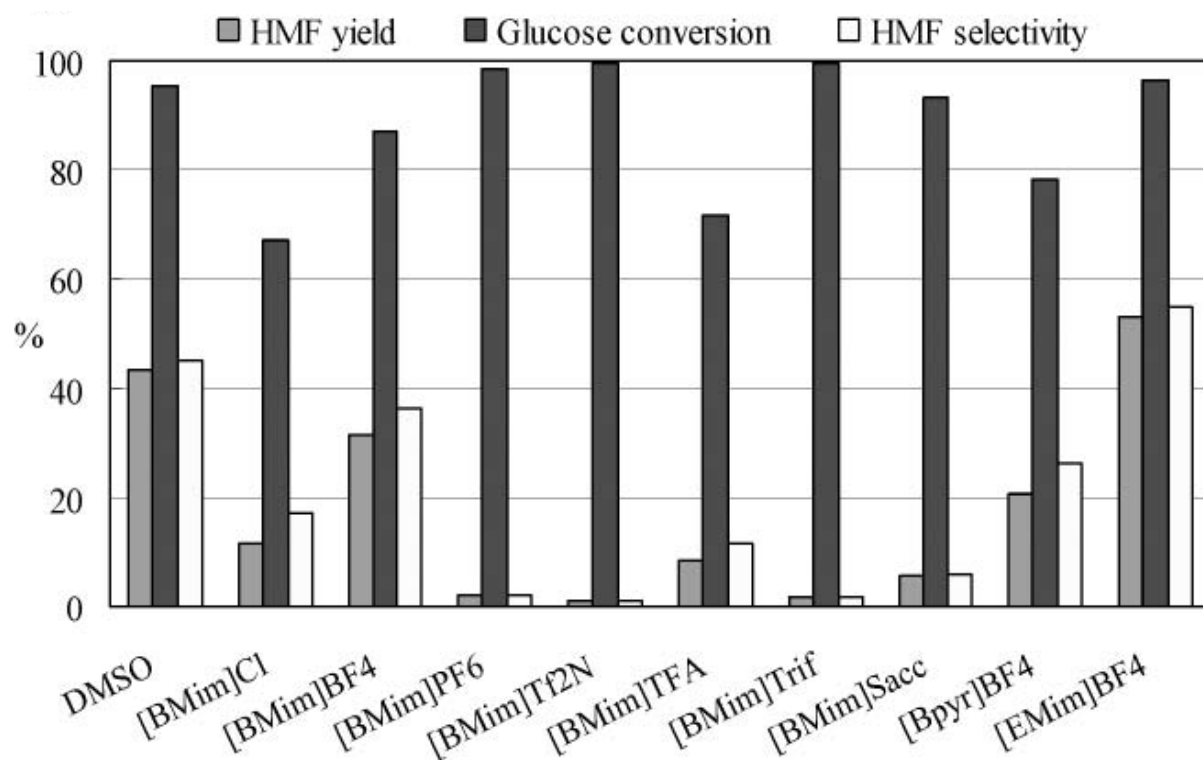


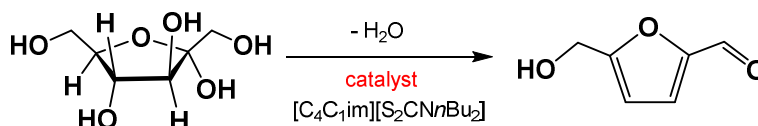
Figure 2.2. HMF yields in various ILs and DMSO.¹¹²

2.4 Results

It was proposed that a suitable medium should have strong solvent power for sugar but low coordination ability to metal centre. Using three different anions ($n\text{-Bu}_2\text{NCS}_2^-$, Cl^- and HSO_4^-) with differing coordination ability in conjunction with the same cation ($\text{C}_4\text{C}_1\text{im}^+$) permits these effects to be explored in a systematic way. The transformation of fructose to HMF proceeds via the dehydration of fructose. So far, many different reactions conditions, including acid catalysis,¹⁰⁶ zeolite catalysis,¹⁰⁸ and the use of microwave irradiation,¹¹² have been employed for the conversion of fructose to HMF. However, in each case, the use these methods was limited to lab scale production of HMF due to factors such as high energy consumption, modest HMF

yields, high catalyst loadings, prohibitive solvent cost and the formation of undesirable by-products. Considering the drawbacks of these methods, the development of a process which is economical, environmentally-friendly, allows easy separation and reuse, has a high rate and operates at low temperatures is necessary. Taking into account prior research from the literature, and with the knowledge of the sugar dissolution capacity of $[\text{C}_4\text{C}_1\text{im}][\text{S}_2\text{CN}(n\text{-Bu})_2]$, $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ and $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$,¹⁰⁶ these ILs were used as a reaction medium for conversion of fructose to HMF in this project.

Various different metal catalysts were explored for the conversion of fructose to HMF in the ionic liquid, $[\text{C}_4\text{C}_1\text{im}][\text{S}_2\text{CN}(n\text{-Bu})_2]$. The temperature was maintained at 80 °C and the duration of the reaction was 3 hours (Scheme 2.8). It was considered that the anions in $[\text{C}_4\text{C}_1\text{im}][\text{S}_2\text{CN}(n\text{-Bu})_2]$ would act as bidentate ligands for the metal compounds in addition to their role in breaking down the sugar substrate (See structure in Scheme 2.4).



Scheme 2.8. Conversion of fructose to HMF using a dithiocarbamate-based IL.

Many different metal catalysts were used in this reaction medium ($\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$, CrCl_2 , RhCl_3 , RuCl_3 , K_2PtCl_4 , $\text{RhCl}(\text{PPh}_3)_3$, $\text{PdCl}_2(\text{PPh}_3)_2$, Na_2PdCl_4) at a loading of 7 mol%, however none showed any catalytic activity in the conversion of fructose to 5-hydroxymethylfurfural. Indeed,

the fructose (0.1 g) remained undissolved in the ionic liquid (0.7 g) and no side reactions were observed (Table 2.1).

Table 2.1. *HMF yields from fructose in DTC-ILs (%)*.

Ionic Liquid	Catalyst	Temp. (°C)	Time (h)	HMF yield
[C ₄ C ₁ im][S ₂ CN(<i>n</i> -Bu) ₂]	Na ₂ PdCl ₄	80	3	0
[C ₄ C ₁ im][S ₂ CN(<i>n</i> -Bu) ₂]	CrCl ₂	80	3	0
[C ₄ C ₁ im][S ₂ CN(<i>n</i> -Bu) ₂]	RhCl ₃	80	3	0
[C ₄ C ₁ im][S ₂ CN(<i>n</i> -Bu) ₂]	RuCl ₃	80	3	0
[C ₄ C ₁ im][S ₂ CN(<i>n</i> -Bu) ₂]	K ₂ PtCl ₄	80	3	0
[C ₄ C ₁ im][S ₂ CN(<i>n</i> -Bu) ₂]	CuCl ₂	80	3	0
[C ₄ C ₁ im][S ₂ CN(<i>n</i> -Bu) ₂]	RhCl(PPh ₃) ₃	80	3	0
[C ₄ C ₁ im][S ₂ CN(<i>n</i> -Bu) ₂]	PdCl ₂ (PPh ₃) ₃	80	3	0
[C ₄ C ₁ im][S ₂ CN(<i>n</i> -Bu) ₂]	PtCl ₂ (PPh ₃) ₃	80	3	0

All experiments were replicated based on 3 runs
0.1 g fructose in 0.7 g [C₄C₁im][S₂CN(*n*-Et)₂]; 7 mol% catalyst where present. Non-isolated yields.

These experimental results were in sharp contrast to those in the literature, which report varying levels of catalytic activity with these metals in the ionic liquid [C₂C₁im]Cl. The anionic part of the IL used in these initial investigations is one of the family of dialkyldithiocarbamates [S₂CNR₂][−], which are known to be good ligands for transition metals. Dithiocarbamates and their transition metal complexes have been used in many different applications. Due to the insoluble nature of the metal complexes in aqueous solution, they are widely used in analysis of metal ions.⁹² They can also be used to remove metals from solutions (metal ion sequestration). With the use of dithiocarbamates, different metal ions can be separated by HPLC or GC. In this research dialkyldithiocarbamates, [S₂CNR₂][−], were chosen as the anionic component of the ionic

liquids due to their coordinating properties to transition metals. Dithiocarbamates form stable complexes with all transition metals in many different oxidation states, which make them very useful in a variety of applications where changes in oxidation state occur, such as catalysis (Table 2.2).⁹² Due to this high affinity of dialkyldithiocarbamates for metals, there is a possibility that the $[S_2CNR_2]^-$ ligand could bind too strongly to the metal centre. This would deactivate the catalyst by blocking the catalytically active sites of the metal complex. In the case of coordinatively-unsaturated, square planar species. $[M(S_2CNR_2)_2]$, (M = Ni, Pd, Pt), the vacant coordination sites are unable to coordinate and undergo rearrangement without loss of one of the ligands.

Table 2.2. *Range of oxidation states stabilized by dithiocarbamates.*⁹²

Ti	+4 +3?	V	+3 +4 +5	Cr	0 +2 +3 +4	Mn	+1 +2 +3 +4	Fe	+2 +3 +4	Co	+1 +2 +3 +4	Ni	+1? +3 +3 +4	Cu	+1 +2 +3	Zn	+2
Zr	+4	Nb	+3 +4 +5	Mo	0 +1 +2 +3 +4 +5 +6	Tc	+1 +2 +3 +4 +5	Ru	+2 +3 +4	Rh	+1 +2? +3	Pd	+2 +4	Ag	+1 +2?	Cd	+2
Hf	+4	Ta	+3 +4 +5	W	0 +2 +3 +4 +5 +6	Re	+1 +2 +3 +4 +5	Os	+2 +3 +4 +6?	Ir	+1 +3	Pt	+2 +3 +4	Au	+1 +2 +3	Hg	+2

The absorption bands for Cr^{3+} in pure water were measured to be at λ_{max} values of 410 and 582 nm.²¹¹ However, addition of 3 equivalents of the diethyldithiocarbamate ligand resulted in a shift of the wavelength of each band by 65-75 nm to 491 and 646 nm (Figure 2.3). Oxidation of Cr^{3+} was not observed as there are no absorption bands observed in the region of 440-340 nm,

which are typical of higher valent complexes, such as Cr^{6+} species.¹¹⁹ Therefore, the changes in wavelength observed were attributed to the addition of the DTC ligands rather than oxidation.

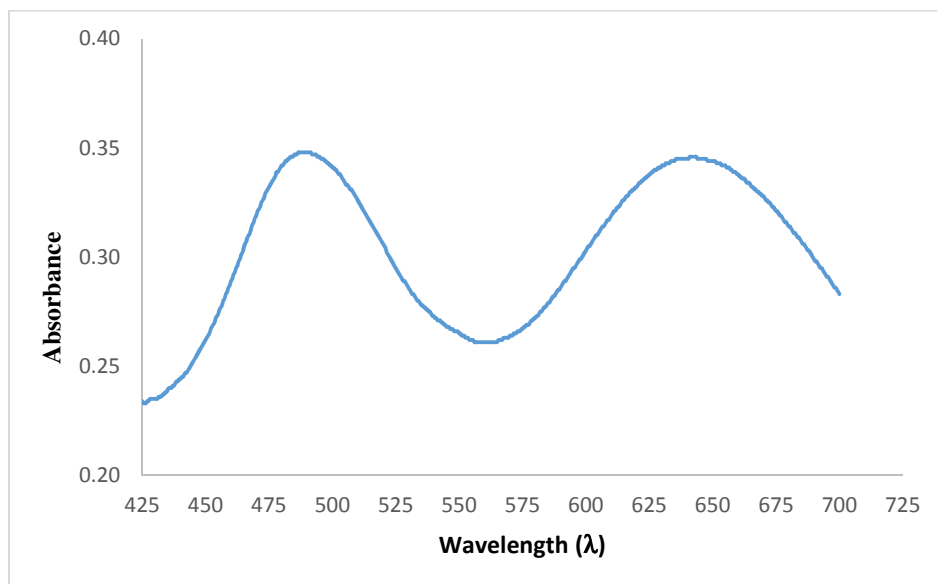
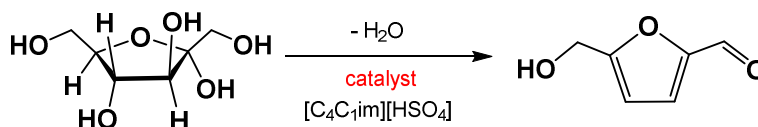


Figure 2.3. UV-vis spectrum after $[\text{Et}_2\text{NCS}_2]^-$ added to Cr^{3+} in water.

While it was expected that the $n\text{-Bu}_2\text{NCS}_2^-$ anions would coordinate to the metal centres (and displace some of the other ligands in the molecular species (e.g., $\text{RhCl}(\text{PPh}_3)_3$), it was a surprise to observe the complete deactivation of the catalytic system. This is likely to occur due to through strong binding of the dithiocarbamate chelates to the metal centres and preventing the generation of the vacant site needed to interact with the fructose substrate. This was consistent with the work of Hu *et al*, who suggested that coordinating anions could display unfavourably strong interactions with the metal centre, resulting in competition with the desirable interaction between sugar and catalyst and thus inhibit the formation of HMF (Figure 2.2).¹¹² However, the degree to which the catalysis was inhibited (i.e., completely) was unexpected.

It was thus proposed that a suitable medium should have strong solvent power for the dissolution of sugars but limited coordinating ability with metal centres. It was thus thought that $[\text{HSO}_4]^-$ would be a good candidate for anion as it has strong solvent power for sugar dissolution and is essentially a non-coordinating ion. Additionally, the acidity of hydrogensulfate-based ionic liquids was anticipated to enhance the catalytic activity of the catalyst without being acidic enough to produce by-products. High HMF yields have been reported using of sulfuric acid¹⁰⁶ and 12-molybdophosphoric acid (12-MPA)¹²⁰ as a catalyst in conversion of sugars to HMF. However, both of them failed to act as a selective catalyst as they form byproducts, mainly levulinic acid.¹⁰⁶

As described previously, the acidity of ILs enhances the conversion of sugars to HMF. In order to ascertain the conversion of fructose to HMF in this IL without any additives, the sugar was heated at 80 °C in $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ in air (Scheme 2.9) and the reaction monitored by removing aliquots after 0.5 hours, 1 hour, 3 hours and 24 hours. The yield of HMF was determined by ^1H NMR analysis (and confirmed additionally by HPLC data). This conversion is performed industrially in acidic aqueous media so it was not a surprise to observe some HMF being formed after 0.5 hours (11%), rising to 38% yield after 24 hours.



Scheme 2.9. Fructose conversion to 5-hydroxymethylfurfural (HMF).

Zhao and co-workers used 0.1 g of substrate in 0.5 g of IL and 6-7 mol% of catalyst which was used as the benchmark to compare with our methods.⁴³ Lowering the concentration of substrate had a negative effect and increasing it had a small beneficial effect on fructose conversion. At higher reaction temperatures, the viscosity of ILs decreases, which enables better diffusion of the dissolved species and mass transfer. Additionally, as this is a monophasic system, it does not suffer from diffusion control limitations as the substrate diffusion is high under these conditions.

Table 2.3. *The effect of fructose loadings on HMF yields (%).*

Ionic Liquid	Fructose (g)	Temp. (°C)	0.5 h	1 h	3 h
[C ₄ C ₁ im]HSO ₄	0.02	80	42	50	62
[C ₄ C ₁ im]HSO ₄	0.05	80	45	52	65
[C ₄ C ₁ im]HSO ₄	0.1	80	54	60	80
[C ₄ C ₁ im]HSO ₄	0.2	80	56	61	77

All experiments were replicated based on 3 runs
0.7 g [C₄C₁im][HSO₄]; 7 mol% catalyst where present. Non-isolated yields.

Different catalyst loadings were also studied in order to identify the optimal catalyst performance (Fig. 2.4). Decreasing the catalyst loading to 3 mol% had a negative effect on HMF yield, while an increase, from 7 mol% to 28 mol%, had almost no effect on fructose conversion.

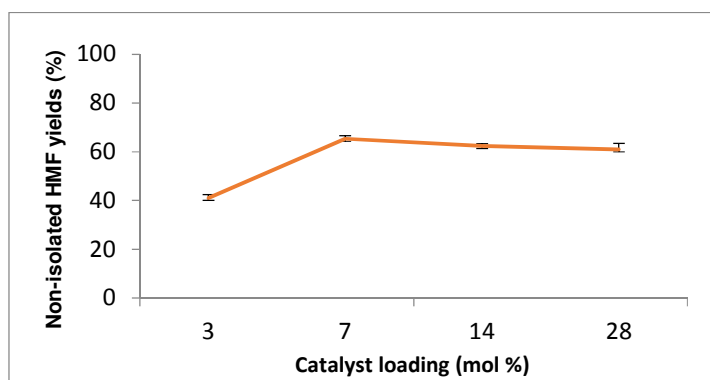


Figure 2.4. *Different catalyst loadings for conversion of fructose to HMF.*

Four different experiments were conducted at 80 °C with sampling after 0.5, 1 and 3 h; a control experiment in water, water plus catalyst, IL alone and IL plus catalyst. Initial reaction rates of fructose conversion were then calculated and compared. In water and water plus catalyst systems there was no conversion at 80 °C and so it was concluded that water is not an effective solvent system for this transformation under the conditions tested. This is consistent with the observation that this transformation is a dehydration reaction. The highest reaction rates were obtained using the ionic liquid system with catalyst.

Table 2.4. Control experiments using water and $[C_4C_1im]HSO_4$.

Entry	Solvent	Fructose (g)	Temp. (°C)	Time (h)	Cat.	k (s ⁻¹)	Rate (M/s)
1	$[C_4C_1im]HSO_4$	0.1	80	0.5	Yes	9E-05	4.18182E-05
2	$[C_4C_1im]HSO_4$	0.1	80	1	Yes	9E-05	3.63636E-05
3	$[C_4C_1im]HSO_4$	0.1	80	3	Yes	9E-05	1.81818E-05
4	$[C_4C_1im]HSO_4$	0.1	80	0.5	No	2E-05	1.79798E-05
5	$[C_4C_1im]HSO_4$	0.1	80	1	No	2E-05	1.59596E-05
6	$[C_4C_1im]HSO_4$	0.1	80	3	No	2E-05	1.47475E-05
7	Water	0.1	80	0.5	Yes	0	0
8	Water	0.1	80	1	Yes	0	0
9	Water	0.1	80	3	Yes	0	0
10	Water	0.1	80	0.5	No	0	0
11	Water	0.1	80	1	No	0	0
12	Water	0.1	80	3	No	0	0

All experiments were replicated based on 3 runs

0.7 g $[C_4C_1im][HSO_4]$; 7 mol% catalyst where present. Non-isolated yields.

According to the mass balance the missing carbon was due to the formation of humins. The picture below shows the formation of humins by darkening of the solution. (Figure 2.5).

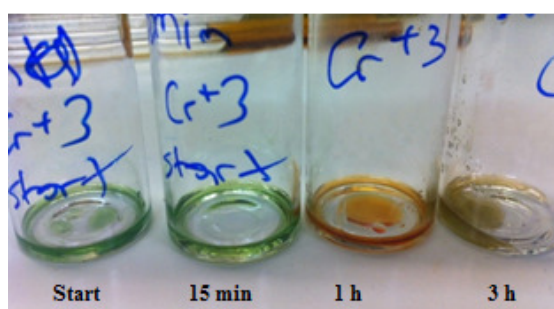
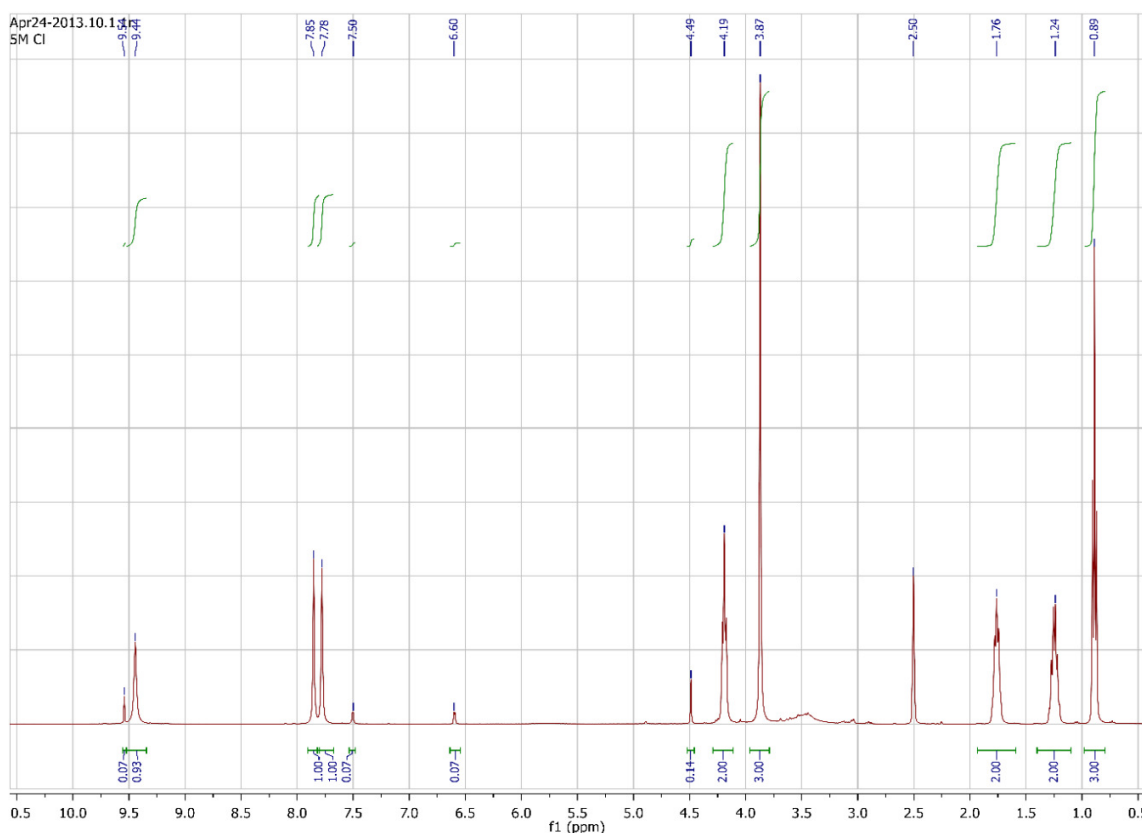


Figure 2.5. The formation of humins at different time periods.

❖ Yield calculation



[C₄C₁im]HSO₄. ¹H NMR (400 MHz, DMSO) δ 9.44 (s, 1H, N₂CH), 7.85, 7.78 (m x 2, 2 x 1H, 2 x NCH), 4.19 (t, 2H, NCH₂, *J*_{HH} = 7.2 Hz), 3.87 (s, 3H, NCH₃), 1.76, 1.24 (m x 2, 2 x 2H, CCH₂), 0.89 (t, 3H, CCH₃, *J*_{HH} = 7.3 Hz) ppm. HMF. ¹H NMR (400 MHz, DMSO) δ 9.54 (s, 1H, CHO), 7.50 (d, 1H, furan-CH, *J*_{HH} = 3.5 Hz), 6.60 (d, 1H, furan-CH, *J*_{HH} = 3.5 Hz), 5.57 (t, 1H, OH, *J*_{HH} = 6.0 Hz), 4.49 (d, 2H, CH₂O, *J*_{HH} = 6.0 Hz) ppm. [residual protons in DMSO. ¹H NMR (400 MHz) δ 2.50 (s)]

Figure 2.6. NMR spectra after reaction of fructose to form HMF in [C₄C₁im]HSO₄.

HMF yields were calculated based on the integration of HMF resonances against those of the ionic liquid [C₄C₁im]Cl itself. The ionic liquid was considered to be an internal standard, as it does not precipitate and has negligible vapour pressure. HMF peaks could be chosen for calculation of the yields either at the lowest field chemical shift value of 9.55 ppm or the highest field chemical shift value of 4.49 ppm as neither overlaps with any of the solvent resonances in

the ^1H NMR spectrum (integration values are 0.07 for 1H and 0.14 for 2H). The calculation method is shown below:

1. Calculate the molar amount of internal standard (IS), $[\text{C}_4\text{C}_{1\text{im}}]\text{Cl}$, by dividing 0.7 g of the IL with the molar mass of internal standard (174.5 g/mol).

$$n(\text{internal standard}) = \frac{0.7 \text{ g}}{174.5 \text{ g/mol}} = 4.01 \text{ mmol}$$

2. Internal standard (IS) and product (HMF) signals are integrated and then normalised to one proton equivalent values. So, if a peak of the IS at 0.89 (t, 3H, CCH_3 , $J_{\text{HH}} = 7.3 \text{ Hz}$) ppm is compared with a peak of HMF at 6.60 (d, 1H, furan-CH, $J_{\text{HH}} = 3.5 \text{ Hz}$) then the integration value of the former is divided by 3 as the methyl group has 3 hydrogens.
3. The ratio of the normalised values for the integrals of the product (HMF) and the IS will give the molar ratio of HMF to the internal standard.

$$\text{Molar ratio} = \frac{0.07}{3/3} = 0.07$$

4. Multiplying the molar ratio by the moles of IS will give the molar amount of the product.

$$n(\text{HMF}) = 0.07 \times 4.01 \text{ moles} = 0.28 \text{ mmol}$$

$$\text{Yield} = \frac{\text{mmol product(HMF)}}{\text{mmol starting material}} \times 100$$

$$\text{Selectivity} = \frac{\text{mmol product}}{\text{mmol starting material} - \text{mmol residual starting material}} \times 100$$

5. The moles of starting material (fructose) was calculated by dividing 0.1 g with the molar mass of fructose (180.2 g/mol).

$$n(\text{fructose}) = \frac{0.1 \text{ g}}{180.2 \text{ g/mol}} = 0.55 \text{ mmol}$$

6. HMF yield:

$$\text{HMF Yield} = \frac{0.28}{0.55} \times 100 = 51 \%$$

7. Selectivity could only be calculated in terms of the components dissolved in the solution.

However, in most cases, no peaks were observed either for residual starting material or byproducts with the products being only the desired HMF product or insoluble humins, undetectable by NMR spectroscopy.

Chromium salts have been shown to be particularly active in catalysing this transformation⁴³ and so 7 mol% chromium(III) chloride hexahydrate was introduced, maintaining the same conditions as before. This resulted in substantial yield after only 0.5 hours (54%), rising to 80% after 3 h, which was also the final yield after 24 h (Table 2.6, Entry 2). This represented an improvement on the results obtained using [C₄C₁im]Cl under the same conditions.⁴³ Using the hydrated salt, CrCl₃•6H₂O, introduced a small amount of water into the system so anhydrous CrCl₃ was investigated and found to result in a much slower reaction (Table 2.6, Entry 4), indicating that the presence of water was necessary. When 15% water (v/v with the IL) was used, a higher overall yield (at 80 °C) of 85% was observed (Table 2.6, Entry 1). However, the addition of 50% water slowed the process substantially, although the addition of other co-solvents, such as acetonitrile, did not lead to the same observed sluggishness. In contrast to the anhydrous trivalent salt, anhydrous chromium(II) chloride was also found to be a reasonable catalyst for the formation of HMF, resulting in 74% HMF yield after 24 h. This is significantly higher than the anhydrous chromium(III) chloride, which performed very poorly in our system (only 6% HMF yield in the first 0.5 h, though increasing to 65% after 24 h). This can be traced, at least in part, to the poor solubility of anhydrous chromium(III) chloride in the anhydrous IL.

Only after approximately an hour did the catalyst fully dissolve and so it is likely that the water produced by the dehydration reaction was necessary to hydrate the CrCl_3 sufficiently for it to become soluble, and so the catalyst performance suffered until this condition was met.

Table 2.6. *HMF yields from fructose (%)*.

Entry	Metal Salt	Temp	Substrate	0.5 h	1h	3h	24h
1	$\text{CrCl}_3 \cdot 6\text{H}_2\text{O} + 15\% \text{H}_2\text{O}$	80°C	Fructose	11	30	65	85
2	$\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$	80°C	Fructose	54	60	80	80
3	CrCl_2 (anhydrous)	80°C	Fructose	48	54	70	74
4	CrCl_3 (anhydrous)	80°C	Fructose	6	11	32	65
5	$\text{CrCl}_3 \cdot 6\text{H}_2\text{O} + 50\% \text{H}_2\text{O}$	80°C	Fructose	5	5	15	65
6	$\text{CrCl}_3 \cdot 6\text{H}_2\text{O} + 15\% \text{MeCN}$	80°C	Fructose	54	60	80	65
7	WCl_4	80°C	Fructose	49	54	60	65
8	MoCl_3	80°C	Fructose	33	49	54	60
9	$\text{Y}(\text{OTf})_3$	80°C	Fructose	27	38	49	60
10	LaCl_3	80°C	Fructose	11	30	65	85
11	RuCl_3	80°C	Fructose	27	37	48	59
12	K_2PtCl_4	80°C	Fructose	22	32	42	58
13	NiCl_2	80°C	Fructose	22	37	41	54
14	RhCl_3	80°C	Fructose	16	26	42	53
15	$\text{La}(\text{OTf})_3$	80°C	Fructose	22	33	49	49
16	$\text{Sc}(\text{OTf})_3$	80°C	Fructose	27	38	43	49
17	no catalyst + 15% water	80°C	Fructose	5	5	11	44
18	ZnCl_2	80°C	Fructose	16	21	32	38
19	no catalyst	80°C	Fructose	11	21	27	38

All experiments were replicated based on 3 runs
0.1 g fructose in 0.7 g $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$; 7 mol% catalyst where present. Non-isolated yields.

While other group 6 transition metal salts led to acceptable yields after 24 h, none tested matched the chromium salts. This has been remarked upon in many reports and has been the subject of a combined experimental and computational study.¹¹³ Metal salts from later in the

transition series fared even worse. This led us to investigate whether the activity observed was an effect of Lewis acidity.¹¹⁴ The metal compounds, which can be deemed ‘hard’ in nature, being salts of higher oxidation state metals, generally performed better compared to related ‘softer’ species (Table 2.6). However, the strongly Lewis acidic lanthanide triflate ions showed comparatively poor activity under the conditions tested (see Table 2.6). Thus, the Lewis acidity of these metal species appears to have no effect on the conversion of fructose to HMF.

The concept of soft and hard acids and bases has long been a useful concept with which to help understand the tendency of certain elements to be found in compounds with each other. The affinity of hard acids for hard bases and soft acids for soft bases is used to rationalise observed patterns in complex stability. This is explained through the concept of ‘polarising power’. The assignment of Lewis acids and bases according to their characteristics using the descriptors ‘hard’ and ‘soft’ was first proposed by Ralph Pearson in his 1963 paper.¹²¹ In this paper he introduced the general rule that “Hard acids prefer to bind with hard bases while soft acids prefer soft bases”.

Lewis bases can be separated into two categories:

- **Hard bases** contain small, non-polarizable donor atoms (examples are nitrogen, oxygen and fluoride)
- **Soft bases** contain large, polarizable donor atoms (examples are phosphorus, sulfur and chloride)

Hard acids are typically small, monocations or highly charged, leading to a high charge density. **Soft acids** are less electropositive metals with a lower charge-to-radius ratio and are more polarisable. Examples of soft and hard acids and bases can be seen in Table 2.7.

Table 2.7. *Soft, hard acids and bases.*

	ACIDS	BASES
SOFT	BF ₃ ; Al ₂ Cl ₆ ; CO ₂ ; SO ₃	
	Cu ⁺ ; Ag ⁺ ; Au ⁺ ; Tl ⁺ ; Hg ₂ ²⁺	H ⁻
	Pd ²⁺ ; Pt ²⁺ ; Hg ²⁺	CN ⁻ ; SCN ⁻ ; I ⁻ ; RS ⁻
	GaCl ₃ ; GaBr ₃ ; GaI ₃	CO; R ₂ S
HARD	H ⁺	NH ₃ ; RNH ₂ ; N ₂ H ₄
	Li ⁺ ; Na ⁺ ; K ⁺	H ₂ O; ROH; R ₂ O
	Be ²⁺ ; Mg ²⁺ ; Ca ²⁺ ; VO ²⁺	OH ⁻ ; F ⁻ ; Cl ⁻ ; CH ₃ CO ₂ ⁻
	Al ³⁺ ; Sc ³⁺ ; Cr ³⁺	CO ₃ ²⁻
	Ti ⁴⁺	PO ₄ ³⁻

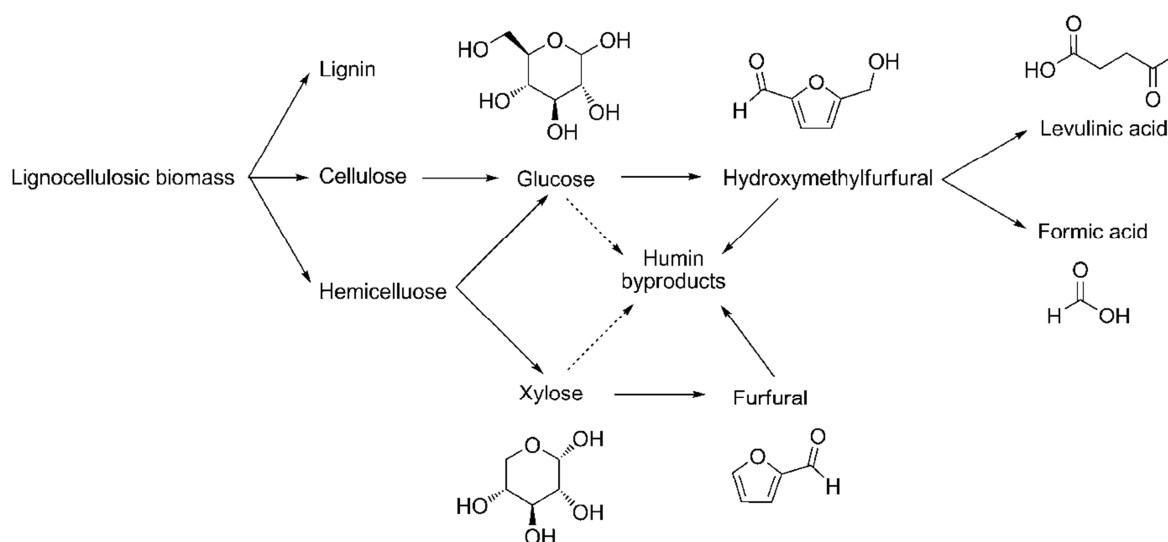
It is found that **hard cations** form more stable complexes with **hard ligands** (ionic bonding – entropy driven), while **soft cations** form more stable complexes with **soft ligands** (covalent bonds - enthalpy). **Hard-soft** mismatches are not favoured as not enough energy is released to overcome the high solvation energy of the hard species. These trends can be observed in the stability constants, such as those below:

Stability constant values (Log K ₁)	F ⁻	Cl ⁻	Br ⁻	I ⁻
Hard: Fe³⁺_(aq)	6.0	1.4	0.5	-
Soft: Hg²⁺_(aq)	1.0	6.7	8.9	12.9

The knowledge of soft and hard acids and bases concept permits scientists to comprehend why metals are found in nature in particular combinations in various types of ores.

As chromium salts were found to be particularly active in catalysing this transformation, UV-vis measurements were carried out for this catalyst in order to see the change of electronic environment of Cr^{3+} ion. It was found that addition of ligands moves the wavelength of each band by 60-70 nm however there was no oxidation observed. Once the effect of varying the duration of the reaction and the nature of the catalyst had been investigated, the effect of raising the temperature to 100 °C was probed. Maintaining the other variables as constant, this change led not only to the highest yield observed in this study (97% after 3 h) but also to over 82% after only 0.5 hours (Table 2.8, Entry 21). At higher temperatures, the formation of humins, from the reaction of HMF with the unreacted sugar,¹²² often becomes an issue, leading to darkening of the ionic liquid. The question is: “What are humins?” During the process of obtaining fuels and sustainable chemicals from monosaccharides, a key step is the depolymerisation of cellulose and hemicellulose to the individual glucose and pentose units. For example, the acid-catalysed conversion of glucose or xylose to the platform chemicals HMF and furfural followed by further dehydration of HMF yields to the important chemicals, levulinic acid (LA) and formic acid (FA) (Scheme 2.10).¹²³⁻¹²⁵ These chemicals are currently of interest to industry, especially the production of HMF and LA-based chemicals. The Dutch company Avantium has constructed a pilot plant to convert carbohydrates into various furanic substances. These furanics can subsequently be used to produce biofuels and tailored polymers.¹²⁶ The Biofine process is a well-known example of the commercial-scale production of LA.¹²⁷ However, acid-catalysed conversion of cellulose and hemi-cellulose to this platform chemical may unavoidably lead to

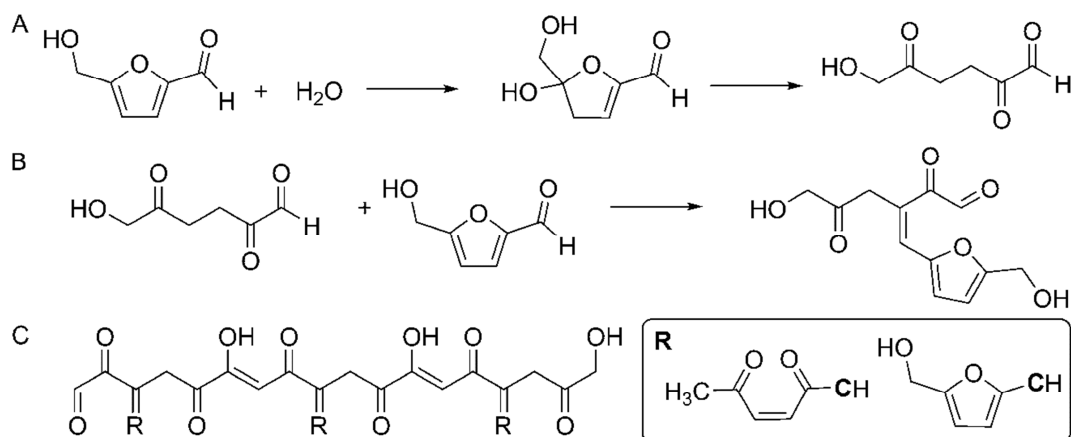
the formation of humin byproducts (Scheme 2.10).¹²⁸⁻¹³⁰ These humin byproducts are considered to be heterogeneous, carbonaceous and polydisperse materials the chemical structure of which is not precisely known. For example, the formation of humins in the Biofine process decreases the yield of LA, which poses a challenge for the reactor design.¹²⁷



Scheme 2.10. *The production of chemicals from biomass and further formation of humin byproducts by polymerization of sugars and their derivatives.*¹²⁸

While the structural elucidation of humins is lacking, and the mechanism of their formation has yet to be studied in significant detail, there have been some suggested mechanisms to explain the formation of humin byproducts. Summers et al.¹³¹ investigated the molecular structure of humins formed during acid-catalysed treatment of sugars and HMF. It was found that humin byproducts are composed of 60% furan rings and 20% aliphatic linkers were formed. The formation of humins from HMF and sugars was also investigated by Lund and co-workers.¹³² From the rehydration of HMF, it was found that a key intermediate DHH (2,5-dioxo-6-

hydroxyhexanal) was formed and this intermediate was polymerized through the subsequent aldol condensations with carbonyl groups of 5-hydroxymethylfurfural (Scheme 2.11).



Scheme 2.11 a) Rehydration of HMF to form DHH. b) Condensation of DHH with HMF. c) Idealized structure of humins

It was also suggested that these polymers could interact with hexoses and pentoses in order to form larger humin byproducts.¹²⁸⁻¹³⁰ The effect of sugar concentration on humin formation was also studied in this research project and will be discussed further elsewhere.

The addition of acetonitrile has previously been shown to limit this process.¹²⁰ Conducting the reaction with 15% acetonitrile (v/v with the IL) led to equally high, almost quantitative yields (Table 2.8, Entry 20). There are several possible explanations for this result. As these ILs are highly viscous, acetonitrile may simply be acting as a diluent, reducing the viscosity of the solution, thereby enabling faster mass transport and accelerating the reaction. Acetonitrile also has a fairly high dielectric constant (ca. 36), which could affect the dissociation ability of the

acidic IL solvent. In order to test this effect, the Hammett acidity values were measured using the technique described by Fărcașiu¹³³ for the IL with and without added acetonitrile. As Hammett acidity is intended as an extended pH scale, lower values indicate a more strongly acidic medium. It is often used to measure the acidity of very concentrated solution of strong acids, including superacids. The measured value for pure [C₄C₁im][HSO₄] ($H_0 = 1.96$) in the present study was noticeably lowered by the addition of 15% acetonitrile ($H_0 = 1.12$). This suggests that adding acetonitrile to the IL enhances the ability of the HSO₄⁻ anion to protonate the substrate, increasing the acidity of the solvent medium. This effect appears to be at least partially responsible for the higher yield in the presence of acetonitrile. It should be noted that the Cr (II) chloride system also benefited from operating at a higher temperature (conversion to HMF increased from 70% at 80 °C to 87% at 100 °C after 3 hours), though the effect of acetonitrile on this system was minimal.

Using the chromium(III) chloride system with 50% water (v/v with IL), the effect of lowering the temperature to 80 °C was investigated. This was found to decrease the final yield after 24 h substantially (Tables 2.6 and 2.8, Entries 1 and 5). This is in stark contrast to the effect of adding acetonitrile, which accelerated the reaction as described above. Water is likely to lead to dissociation of any metal-substrate complexes, and will also solvate the sugar substrates, likely retarding catalytic effects. Water could also stabilise the Cr(III) complex ions in solution, possibly inhibiting the binding of the substrate. This same principle would lead to the formation of dehydrated intermediates becoming less favourable. However, though water is eliminated during this reaction, the water byproduct (or the water content of a 'wet' IL) is not likely to form part of the ligand set at the chromium metal centre due to the solvation of the IL anion taking

precedence (indeed, it is present in much higher concentration even though it is a poorer reaction partner).

Table 2.8. Yield (%) of HMF from fructose at higher temperatures.

Entry	Metal Salt	Temp.	Substrate	0.5 h	1h	3h	24h
20	CrCl ₃ •6H ₂ O	100 °C	Fructose	69	87	96	-
21	CrCl ₃ •6H ₂ O	120 °C	Fructose	87	87	89	-
22	no catalyst	100 °C	Fructose	51	69	69	-
23	no catalyst	120 °C	Fructose	71	71	78	-
24	CrCl ₂ (anhydrous)	100 °C	Fructose	69	80	87	-
25	CrCl ₂ (anhydrous) + 15% MeCN	100 °C	Fructose	64	73	80	-
3	CrCl ₂ (anhydrous)	80 °C	Fructose	48	54	70	74
2	CrCl ₃ •6H ₂ O	80 °C	Fructose	54	60	80	80
6	CrCl ₃ •6H ₂ O + 15% MeCN	80 °C	Fructose	54	60	80	65
1	CrCl ₃ •6H ₂ O + 15% H ₂ O	80 °C	Fructose	11	30	65	85
5	CrCl ₃ •6H ₂ O + 50% H ₂ O	80 °C	Fructose	5	5	15	65

All experiments were replicated based on 3 runs

0.1 g fructose in 0.7 g [C₄C₁im][HSO₄]; 7 mol% catalyst where present. Non-isolated yields.

Entries 1,2,3,5 and 6 are reproduced from Table 2.6 to aid comparison.

There are several possible reasons for the high performance of the [C₄C₁im][HSO₄] as the ionic liquid medium for HMF formation. The mildly acidic HSO₄⁻ proton (pK_a = 1.7) is likely to be acting as a co-catalyst for this reaction as well as being the solvent (and thus present in large excess). However, most strong acids promote over-dehydration of sugars to levulinic acid and formic acid, in both water¹¹⁸ and ILs,¹¹⁴ even when present in only catalytic amounts. A large excess of a weaker acid appears to be an ideal compromise between acid strength and concentration that optimises the formation of the dehydration intermediate HMF without promoting either levulinic acid or humin formation (as observed when concentrated H₂SO₄ is

added to this system). The HSO_4^- anion itself is also a mild hydrogen bond acceptor, compared to the much more basic chloride anion.¹³⁴ It is also less likely to compete with the substrate for the coordination sites at the metal catalyst, being a weakly coordinating anion. This result is in stark contrast to the results reported by Qi *et al.*¹³⁵ where a sulfonated zirconia catalyst was much more selective in $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ (89% HMF) than $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ (43%). This observation is likely due to the overly acidic nature of the combined catalyst and solvent system.

The effective reaction medium requires elevated temperatures which rises the stability issue of HMF. The stability of HMF in various ionic liquids, including ones with chloride and hydrogensulfate ions, has been tested at elevated temperatures (up to 150 °C) in the Hallett group and no decomposition was observed.¹³⁶

Initial rates of fructose conversion and activation energies were also calculated so as to compare it with literature values (Table 2.9).

Table 2.9. *Initial rates of fructose conversion at different temperatures.*

Entry	Solvent	Temp. (°C)	Time (h)	k (s ⁻¹)	Rate (mol l ⁻¹ s ⁻¹)
1	$[\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$	80	0.5	9E-05	4.18182E-05
2	$[\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$	80	1	9E-05	3.63636E-05
3	$[\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$	80	3	9E-05	1.81818E-05
4	$[\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$	100	0.5	2E-04	6.26263E-05
5	$[\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$	100	1	2E-04	2.62626E-05
6	$[\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$	100	3	2E-04	8.08081E-06

All experiments were replicated based on 3 runs

0.1 g fructose in 0.7 g $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$; 7 mol% catalyst where present. Non-isolated yields.

$$E_a = \ln \frac{k_2}{k_1} \times \frac{R}{\left(\frac{1}{T_1} - \frac{1}{T_2}\right)} = \ln \frac{2 \times 10^{-4}}{9 \times 10^{-5}} \times \frac{8.314}{\left(\frac{1}{353} - \frac{1}{373}\right)} = 43706 \text{ J/mol}$$

k_2 = rate constant at 100 °C (373 K)

k_1 = rate constant at 80 °C (353 K)

$E_a = 43706 \text{ J/mol} = 10.45 \text{ kcal/mol}$

The acid catalysed dehydration of fructose to HMF requires an activation free energy of 31.8 kcal/mol according to Caratzoulas and co-workers.¹³⁷ Lee and co-workers studied the conversion of fructose to HMF in an IL + CrCl₂ system with and without a bi-functional mesoporous silica nanoparticle (MNS) catalyst and found that the results for the E_a of the systems with and without catalysts were 67.50 and 80.05 kcal/mol, respectively.¹³⁸ However, in our study the use of [C₄C₁im]HSO₄ with a chromium catalyst has altered the reaction route, consequently lowering the activation energy to 10.45 kcal/mol, which is lower than other systems in literature, and leading to a higher reaction rate. The increase of temperature leads to higher yields which has a positive effect on the mass balance (yield) and rate.

2.5 Conclusion

The results described above demonstrate that the room temperature ionic liquid [C₄C₁im][S₂CN(*n*-Bu)₂] fails to yield any measurable conversion of fructose to HMF. This effect can be traced to the strong coordination of metal species by the dithiocarbamate anion, inhibiting any catalytic activity possessed by the metal centre. In contrast, an IL possessing the same cation but an effectively non-coordinating anion (HSO₄⁻) provides the perfect combination of properties as a medium for almost quantitative and highly selective conversion of fructose to

5-hydroxymethylfurfural (HMF) in the presence of a low loading of chromium(III) chloride. Previous to this report, the transformation of sugars to HMF in ILs had been performed predominantly in dialkylimidazolium chloride salts. This research reveals that careful tailoring of the IL properties beyond the standard chloride salts (which represent intermediate metal coordinating ability between dithiocarbamates and hydrogensulfate) improves the performance of the system substantially. Of all the conditions investigated, optimal performance is achieved in 3 hours at 100 °C, yielding 96% HMF using a 7 mol% catalyst loading. In addition to this activity, this system demonstrates a very high selectivity for HMF, as indicated by the fact that no trace of levulinic acid or formic acid was encountered after conversion of fructose. These results illustrate well the advantages of combining the well-established advantages of ILs (negligible vapour pressure, recyclability) with a weakly acidic, weakly-coordinating medium to provide an excellent environment for selective catalysis by a low toxicity metal species in only a few hours. This is particularly important since HMF has recently become the starting point for scaled up production of 'green' beverage packaging.¹³⁹ However, the optimisation of high yielding routes to this platform chemical from even closer proxies for biomass, such as glucose (Chapter 3) or cellulose (Chapter 4), is of even greater importance.

CHAPTER 3

GLUCOSE TO HMF

3.1 Overview

The development of the biorefinery concept requires efficient routes for the conversion of biomass to useful platform chemicals.¹⁴⁰ As described earlier, lignocellulosic biomass represents the most promising renewable feedstock for commercial large-scale biorefineries as lignocellulose is distributed widely across the planet and can be grown on a billion ton scale.⁹⁹ However, Ionic liquids (ILs)¹⁴¹ have been shown to be an environmentally benign media for separating cellulose from lignin due to their unique chemical and solvent characteristics,¹⁴² and this process is critical for further functionalisation of the fractionated biopolymers.¹¹⁷ As outlined in Chapters 1 and 2, 5-hydroxymethylfurfural (HMF) is one of the leading platform chemicals accessible from lignocellulosic biomass on a large scale¹⁰⁵ However, the precursors for HMF production needs to be as close to the raw biomass feedstock as possible. While the effective and selective generation of HMF from fructose (Chapter 2) is an important process, the direct conversion of glucose (whence fructose is produced) is more significant still. An effective route to HMF from glucose will improve the chances of unlocking the potential of HMF as a synthetic building block.

The potential for making HMF using ionic liquid (ILs) media was first demonstrated by Zhao *et al.*⁴³ This study assessed the ability of various metal salts to convert glucose to HMF in [C₄C₁im]Cl and found that chromium salts were the most active, providing 70% HMF yield at 80 °C in 3 hours. The superiority of chromium salts over other metal species for this particular

transformation has subsequently been verified by other groups.¹⁴³ While the ‘green solvent’ credentials of ILs can often be overstated,¹¹⁶ they have environmental advantages, such as their reusability and negligible vapour pressure, which add potential economic and safety benefits to their use,¹²⁹ especially in contrast to the traditional option of strong aqueous acids. With this in mind, the approach described in Chapter 2^{143e} employs the mildly acidic IL, [C₄C₁im][HSO₄] (see Figure 3.1), as solvent to convert fructose to HMF in the presence of a low loading of chromium(III) chloride. This achieves a 96% yield of HMF in 3 hours at 100 °C, with no trace of levulinic acid or formic acid as byproducts.^{143e} This imidazolium ionic liquid utilises the same anion (HSO₄⁻) as the ionic liquids which have recently been demonstrated to have a similar cost to traditional organic solvents such as acetone.¹⁴⁴ It was thus decided to extend these promising results to other sugar substrates, such as glucose, which is one step closer to the original biomass feedstock than fructose.

In addition to studies on fructose conversion, there have been several reports of HMF synthesis from glucose in ILs, predominantly in imidazolium chloride ionic liquids, such as [C₄C₁im]Cl and [C₂C₁im]Cl (Figure 3.1).^{143a-d,146} Recent investigations into glucose conversion to HMF have shown strong media- and catalyst-dependent activity and selectivity. For example, a variety of zeolite catalysts has been investigated in [C₄C₁im]Cl, with an H β -zeolite consisting of a unique BEA structure and a moderate Si/Al ratio of 25 possessing the highest catalytic activity (50% HMF yield at 150 °C in only 50 min).¹⁴⁶ In order to improve the catalytic performance of β -zeolites, the effects of calcination and steam treatment on the structure of Al atoms in the framework and acid properties were examined in detail.¹⁴⁷ With sufficient Lewis acid sites available, effective bifunctional catalysts demonstrated 55% selectivity to HMF. In another

report, a tin-containing silica molecular sieve (Sn-MCM-41) was found to act as a bifunctional heterogeneous catalyst for the efficient conversion of glucose to HMF in $[\text{C}_2\text{C}_1\text{im}]\text{Br}$, with 70% yield at 110 °C after 4 h.¹⁴⁸ This is a much higher yield than reported for several mesoporous MCM-41 silicas containing ZrO_2 in biphasic water/MIBK mixtures. The most active of these catalysts was obtained after incorporation of zirconium into MCM-41 silica in the synthesis gel (Zr-MCM-550), but yielded only 23% HMF.¹⁴⁹ A similar HMF yield was obtained using mesoporous tantalum oxide.¹⁵⁰ This catalytic process was found to be selective toward HMF, which is preserved from further dehydration to levulinic acid. By using a glucose:catalyst weight ratio of 3:1, a glucose conversion of 56% and an improved HMF yield of 33% was achieved at 170 °C in only 1 h in the presence of a mesoporous tantalum phosphate, also in biphasic water/MIBK.¹⁹ Dumesic *et al.* reported¹⁵¹ slightly higher yields of 62% with a Lewis acid (AlCl_3) and Brønsted acid (HCl) combination in biphasic water/2-*sec*-butylphenol. The conversion of glucose in the presence of Lewis and Brønsted acidity proceeds through a tandem pathway involving isomerisation of glucose to fructose, followed by dehydration of fructose to HMF. This mechanism was recently elucidated using bifunctional SO_4/ZrO_2 catalysts with tuneable acid-base properties,¹⁵² whereas sulfated zirconia alone has been shown to be efficient for fructose conversion.¹³⁵ The addition of 0.1M HCl to an $\text{AlCl}_3\text{--H}_2\text{O/THF}$ biphasic system has also been reported to result in an 11% increase (to 62%) of HMF yield from glucose, further supporting the need to balance Lewis and Brønsted effects so as to improve the selectivity of glucose conversion.¹⁵³ Addition of protic solvents such as methanol and ethanol to the ionic liquid had a similar synergistic effect as adding water, promoting fructose and HMF formation. This mechanism presents an excellent opportunity to study IL solvent design, as described below.

ILs have also been explored as additives/co-solvents rather than as the sole liquid medium for the reaction. For example, addition of 1-hydroxyethyl-3-methylimidazolium tetrafluoroborate as a catalyst (rather than as a solvent) led to yields of HMF as high as 67% after 1 h at 180 °C in dimethylsulfoxide solution.¹⁵⁴ In more traditional homogeneously catalysed systems, the combination of $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ (10 mol%) and $\text{B}(\text{OH})_3$ (20 mol%) was reported to act as a double catalyst in $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ to provide an HMF yield of 79%, achieved at 120 °C in only 30 min.¹⁵⁵ In 1:1 $[\text{C}_6\text{C}_1\text{im}]\text{Cl}$ /water biphasic mixtures, HMF yields of 53% were obtained within just 10 min at 200 °C in the presence of ZrO_2 .¹⁵⁶ Clearly, both the presence and the nature of ILs (such as those shown in Figure 3.1) can serve to increase activity and limit byproduct formation in these systems.

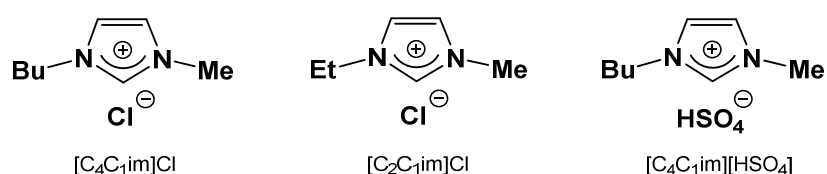
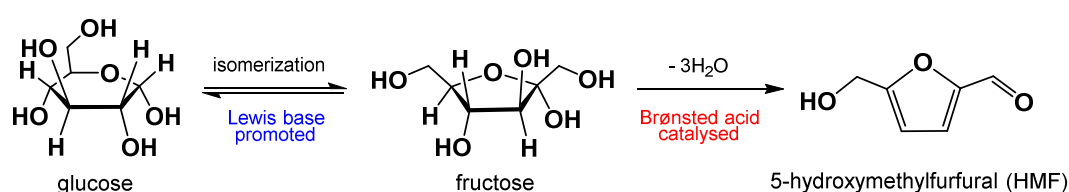


Figure 3.1. *Ionic liquids used for the dissolution of glucose in this chapter.*

In addition to the potential environmental benefits, ILs are unique media for chemical transformations as ‘designer solvents’¹⁵⁷ that can be tuned for a specific chemical effect. Since the breakdown of fructose is known to be favoured by acidic conditions,^{143c, 118} the mildly acidic IL, $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ was chosen to accelerate that transformation. However, the conversion of glucose to fructose is known to proceed through a two-step mechanism involving

isomerisation of glucose to fructose and subsequent dehydration to HMF (Scheme 3.1).¹³² The former reaction is catalysed by Lewis base functionalities, while the latter reaction is promoted by Brønsted acids.¹⁵² As such, it was initially unclear whether a Lewis basic IL (such as [C₄C₁im]Cl) or a Brønsted acidic IL (such as [C₄C₁im][HSO₄]) would favour this transformation. It was thus attempted to investigate this aspect and to provide insight into the factors involved.

In addition to acid or base concerns, the coordinating ability of the IL anion has been shown in Chapter 2 to be a significant factor when metal catalysts are used to convert glucose to HMF. Hu *et al.* used a Lewis acid catalyst (SnCl₄) in ILs with a range of [C₄C₁im]⁺ salts with different anions.^{143a} They found the highest activity with [BF₄][−] as the IL anion, while ILs with more coordinating anions (including Cl[−]) demonstrated lower yields. This is consistent with the view that coordinating anions compete with the sugar substrate for catalyst sites and thus inhibit the formation of HMF.^{143a} This provides conflicting information on which solvent type would be optimal for HMF formation from glucose, in contrast to the simple acid-catalysed mechanism for HMF production from fructose. Clearly, promoting the isomerisation reaction step is an important consideration in the solvent design for this more challenging transformation.



Scheme 3.1. Glucose conversion to 5-hydroxymethylfurfural (HMF).

3.2 Results

❖ Catalyst selection

In previous research, a yield of 96% HMF from fructose was achieved by employing hydrogensulfate-based ILs (Chapter 2).^{143e} As a starting point, the same ILs and conditions were applied with glucose as a substrate in order to compare HMF yields from glucose to those from fructose directly. This assumes that the dehydration step in Scheme 3.1 is the rate determining step – or at least controls the selectivity, as HMF can combine with monosaccharides to produce humins under acidic conditions.¹⁵⁸ Several different metal catalysts were examined in [C₄C₁im][HSO₄] and aliquots were collected after 0.5, 1, 3 and 24 h. After 0.5 h, formation of HMF was not observed under any conditions (Table 3.1). Only 5% yield was observed using CrCl₃ as catalyst after 3 h at 80 °C (Table 3.1, entries 1 and 2). In the presence of the IL without any catalyst, no HMF formation was detected after 3 h (Table 3.1, entry 6). After 24 h, under the same conditions, only 15% yield of HMF was observed for the chromium catalysts and only 3% yield for all other metals tested. These results indicate that, while the Cr(III) catalyst is a good choice for glucose conversion to HMF, the [C₄C₁im][HSO₄] IL system does not provide the optimal environment at 80 °C.

Among the catalysts tested, chromium chlorides yielded better conversion of glucose to HMF in [C₄C₁im][HSO₄], in line with the fructose results from Chapter 2.^{143e} Further catalytic studies were therefore restricted to chromium-based catalysts in [C₄C₁im][HSO₄]. Attempts were made to raise the HMF yield by increasing the temperature to 100 °C under identical catalyst and sugar loadings. However, HMF formation was not observed after 0.5 h under these conditions

(Table 3.1, entries 7-9). Very poor yield (15%) was obtained after 3 h which was only 10% more than found for the reaction at 80 °C (Table 3.1, entries 7 and 8).

Table 3.1. HMF yields in $[C_4C_{1im}][HSO_4]$ at 80°C.

Entry	Metal Salt	Temp.	Substrate	0.5 h	1h	3h	6h	24h	48h	72h
1	CrCl ₃ ·6H ₂ O	80 °C	Glucose	0	<3	<5	-	15	-	-
2	CrCl ₂	80 °C	Glucose	0	<3	<5	-	15	-	-
3	K ₂ PtCl ₄	80 °C	Glucose	0	0	0	-	<3	-	-
4	NiCl ₂	80 °C	Glucose	0	0	0	-	<3	-	-
5	ZnCl ₂	80 °C	Glucose	0	0	0	-	<3	-	-
6	no catalyst	80 °C	Glucose	0	0	0	-	<3	-	-
7	CrCl ₃ ·6H ₂ O	100 °C	Glucose	0	15	15	-	-	-	-
8	CrCl ₂	100 °C	Glucose	0	15	15	-	-	-	-
9	no catalyst	100 °C	Glucose	0	0	0	-	-	-	-
10	CrCl ₃ ·6H ₂ O	100 °C	Glucose	-	-	-	15	33	15	10
11	CrCl ₂	100 °C	Glucose	-	-	-	15	27	33	10
12	no catalyst	100 °C	Glucose	-	-	-	0	<15	<15	0
13	CrCl ₃ ·6H ₂ O	100 °C	Galactose	0	<3	15	-	-	-	-
14	CrCl ₂	100 °C	Galactose	0	<3	15	-	-	-	-
15	no catalyst	100 °C	Galactose	0	0	0	-	-	-	-

All experiments were replicated based on 3 runs

0.1 g glucose in 0.7 g $[C_4C_{1im}][HSO_4]$; 7 mol% catalyst where present. Non-isolated yields shown.

In order to probe whether this result is specific to the glucose-to-fructose isomerisation, the CrCl₃/[C₄C_{1im}][HSO₄] catalytic system was applied to galactose, which is a C4 epimer of glucose. Table 3.1 demonstrates that the conversion of galactose to HMF showed essentially the same yields as the transformation of glucose to HMF (Table 3.1, entries 13-15). This suggested that the glucose/fructose isomerisation was limiting the HMF yield, as the galactose system must also undergo a similar transition.

Once the variation of catalysts and temperature had been investigated, the duration of the glucose conversion reaction was increased (Table 3.1, entries 10-12) in order to determine if slow kinetics were solely responsible for the low yield, or if HMF/sugar degradation (levulinic acid and humin formation) would occur over extended reaction times. A yield of glucose to HMF of 33% was obtained using $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ at 100 °C after 48 h (Table 3.1, entry 10), an increase from 27% after 24 h. The duration of the reaction was also extended to 72 h, at which point the HMF production dropped to 10% as the expected formation of humins became unavoidable after this extended period at elevated temperatures.

❖ Ionic liquid selection

These investigations confirmed that the $\text{CrCl}_3/[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ catalytic system, which had been successful for the production of HMF from fructose (Chapter 2), was unsuitable for converting glucose to HMF. The focus thus moved to the $\text{CrCl}_3/[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ system,¹⁰ which is widely used for this conversion, and also to mixtures of ionic liquids (Table 3.2).

Table 3.2. *HMF yields in different ionic liquids and mixtures.*

	Ionic Liquid	5min	10min	15min	20min	30min	1h	3h
16	$[\text{C}_4\text{C}_1\text{im}]\text{Cl}$	51	61	65	65	65	65	65
17	$[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$	-	-	-	-	<3	6	21
18	$[\text{C}_4\text{C}_1\text{im}]\text{Cl} + [\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$ (1:1)	-	-	-	-	19	19	19
19	$[\text{C}_4\text{C}_1\text{im}]\text{Cl} + [\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$ (1:3)	-	-	-	-	23	23	23
20	$[\text{C}_4\text{C}_1\text{im}]\text{Cl} + [\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$ (3:1)	-	-	-	-	21	21	21
21	$[\text{C}_4\text{C}_1\text{im}]\text{Br}$	29	35	35	35	35	-	35

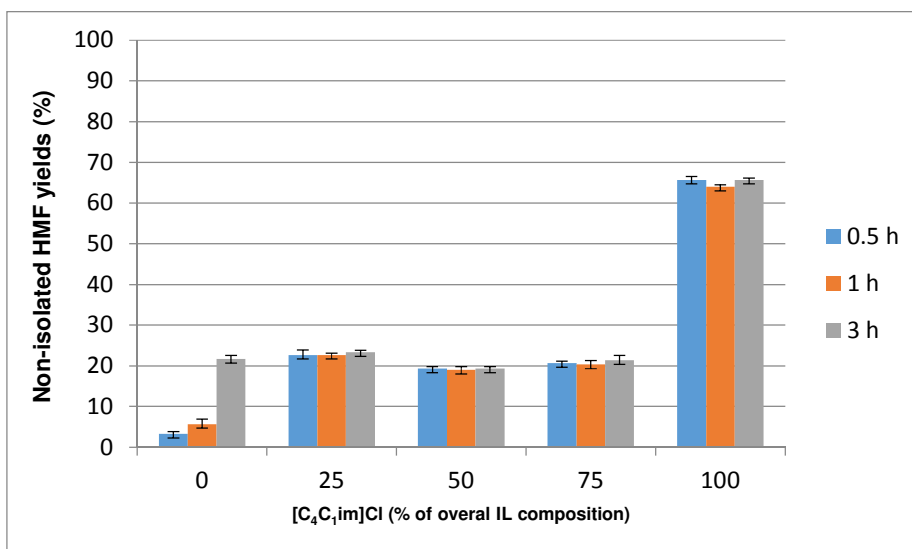
All experiments were replicated based on 3 runs

0.1 g glucose in 0.7 g ionic liquid; 7 mol% $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ catalyst, 120 °C. Non-isolated yields shown.

In our laboratory, the use of $\text{CrCl}_3/[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ led to 65% HMF yield at 120 °C, which is very similar to published results for this system (Table 3.2, entry 16).¹⁰ An equimolar mixture of $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ and $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ was also tested in the chromium-based catalytic system, however this mixture did not perform well and a yield of only 19 % was obtained after 3 h (Table 3.2, entry 18). It appears that the $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ ionic liquid, which promotes fructose to HMF conversions, inhibits the glucose to HMF reaction. From this result it can be inferred that the initial step of the transformation – the isomerisation of glucose to fructose – is the most important catalytic step in the overall conversion of glucose to HMF. Furthermore, it is clear that the Lewis basic IL (with Cl^- anions) is more suitable than the Brønsted acidic solvent (HSO_4^- anions). This is likely to be due to the formation of $[\text{CrCl}_4]^-$ ions in solution, which would be a powerful Lewis base species capable of promoting the glucose isomerisation. In contrast, the non-coordinating $[\text{HSO}_4]^-$ ion cannot form such a complex, and therefore it is less able to catalyse the glucose isomerisation reaction, leading to lower HMF production. It has also been suggested that HMF is formed through an acyclic mechanism involving an enediol,¹⁵⁹⁻¹⁶² produced from the isomerisation of glucose to fructose. Glucose is also susceptible to competing reactions that lead to formation of by-products. In one pathway, dehydration forms non-furan cyclic ethers; in another, C-C bond scission occurs through reverse aldol condensation.⁴⁶ Effective methods for selective *in situ* isomerisation to fructose are thus required to obtain high HMF yields from glucose. NMR spectroscopy studies showed that the glucose starting material, when dissolved in $[\text{C}_2\text{C}_1\text{im}]\text{Cl}$, is predominantly an α -anomer.¹³² It is suggested that solvation of sugars occurs through hydrogen bonding of the chloride ions in the solvent with the carbohydrate hydroxy groups. However, this interaction is not sufficient to cause mutarotation

(α - to β -anomer conversion) as little interconversion of the α - and β -anomers was found to occur in $[\text{C}_2\text{C}_1\text{im}]\text{Cl}$, even after several hours at 80 °C. However, in the presence of a catalytic amount of metal chloride salts, mutarotation was observed to be rapid, leading to an equilibrium mixture of anomers.¹³² This supports the hypothesis proposed here that, the use of a chloride-based ILs, together with chromium (III) chloride improves the isomerisation of glucose to fructose in contrast to a hydrogensulfate-based IL, which is able only to promote the dehydration of fructose.

Other ionic liquid mixtures with different proportions were investigated in order to understand the effect of each ionic liquid component on the conversion of glucose to HMF (Table 3.2, entries 19, 20). Since $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ enhances the isomerisation of glucose to fructose through the Lewis basicity of the Cl^- anions, and $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ accelerates the conversion of fructose to HMF, as previously shown, it was considered possible that an optimum mixture exists with which to accomplish the conversion of glucose to fructose, and then fructose to HMF. However, very similar yields (19-23%) were obtained using various ionic liquids mixtures (containing 25%-75% HSO_4^-), with pure $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ leading to the highest yield (Figure 3.2) by a substantial margin. These results suggested that the presence of significant amounts of $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ actually lowers the yield of HMF from glucose, and strongly suggests that the HSO_4^- anion actually inhibits the glucose-fructose interconversion.



All experiments were replicated based on 3 runs
 0.1 g glucose in 0.7 g ionic liquid, 7 mol% CrCl₃·6H₂O catalyst, 120°C. Non-isolated yields.

Figure 3.2. Yield of HMF from glucose in pure [C₄C₁im]Cl and mixed with [C₄C₁im]HSO₄.

Four different experiments were conducted at 85 °C with sampling after 1 h; a control experiment in water, water plus catalyst, IL alone and IL plus catalyst. In water and water plus catalyst systems there was no conversion at 85 °C and so it was concluded that water is not an effective solvent system for this transformation under the conditions tested (Table 3.3).

Table 3.3. Conversion of glucose to HMF in the presence or absence of 7 mol% CrCl₃·6H₂O.

Entry	Solvent	Glucose (g)	Temp. (°C)	Time (h)	Cat.	Yield (%)
1	Water	0.1	85	1	No	0
2	Water	0.1	85	1	Yes	0
3	[C ₄ C ₁ im]Cl	0.1	85	1	No	14
4	[C ₄ C ₁ im]Cl	0.1	85	1	Yes	35

0.7 g of IL used; Non-isolated yields shown; all experiments were repeated 3 times.

The formation of humins was observed in glucose, IL and catalyst system again according to the mass balance the missing carbon was due to the formation of humins.

It is assumed that the conversion of glucose to HMF proceeds via isomerisation of glucose to fructose and then conversion of fructose to HMF. It was thought that, if the isomerisation of glucose to fructose were to be catalysed by an enzyme, it could lead to higher conversions as, glucose will rapidly isomerise to fructose in the presence of the enzyme, allowing the fructose formed to be readily converted to HMF. However, the enzyme (Sweetzyme, and immobilised glucose isomerase) used for this purpose failed to function at all since the optimal operating temperature for Sweetzyme is between 60-70 °C, which is much lower than the temperature required for the subsequent conversion of fructose to HMF in this system (Table 3.4).

Table 3.4. *The use of Sweetzyme enzyme with $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ in different ILs.*

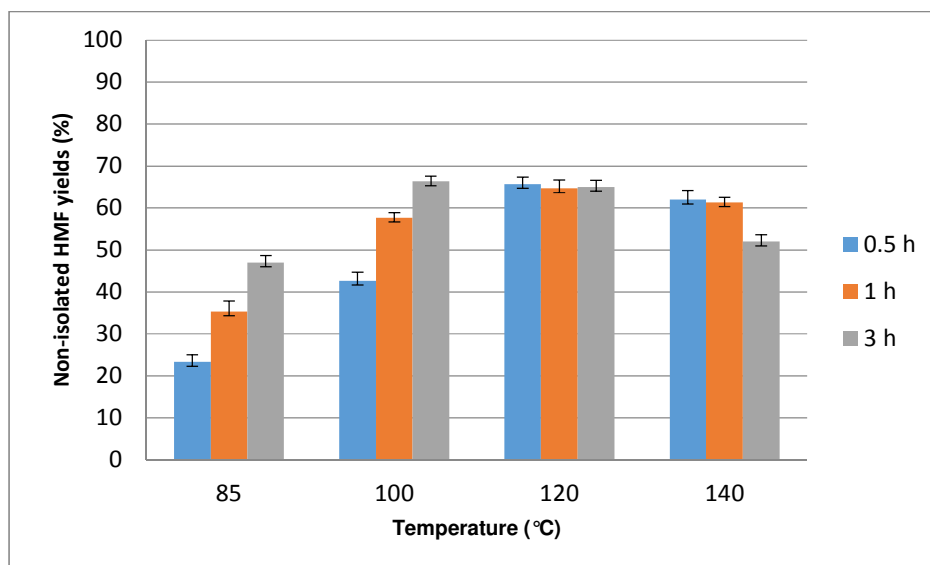
Entry	Solvent	Temp. (°C)	0.5 h	1 h	3 h
1	$[\text{C}_4\text{C}_1\text{im}]\text{Cl}$	120	65	65	65
2	$[\text{C}_4\text{C}_1\text{im}]\text{HSO}_4$	120	3	6	21
3	$[\text{C}_4\text{C}_1\text{im}]\text{HSO}_4 + [\text{C}_4\text{C}_1\text{im}]\text{Cl}$ (1:1)	120	19	19	19

0.7 g of IL used; Non-isolated yields shown; all experiments were repeated 3 times.

Considering the substantial drawbacks surrounding the use of $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$, the effect of different reaction conditions on the performance of $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ as the solvent was examined. This was done in order to attempt to identify the key factors required for high HMF production from glucose. As described above, this study had shown 65% HMF yields from glucose conversion was possible after only 0.5 h, indicating a fast reaction. However, the yield obtained levels off after 0.5 h (the 65% yield is unchanged after 1 h and 3 h) due to the formation of humins as a by-product. The reaction duration was then decreased to a matter of minutes in order to ascertain when the reaction had reached completion. In this part of the study, an additional halide-based IL, $[\text{C}_4\text{C}_1\text{im}]\text{Br}$, was used as a comparison. Higher yields were obtained using $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ than for the bromide IL. It was discovered that the reaction reached

completion after only 15 minutes (65% yield, Table 3.2, entry 16) in $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$, a substantially shorter duration than the standard 3 hours reported previously in the literature (though faster times have been reported with microwave irradiation). The reaction duration was prolonged to 0.5 h and 1 h in $[\text{C}_4\text{C}_1\text{im}]\text{Br}$ but the yield (35%) remained constant (Table 3.2, entry 21).

The effect of temperature on the $\text{CrCl}_3/[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ system was also explored. The yield to HMF decreased to 49% and reaction was slowed considerably by lowering the temperature from 120 °C (the standard conditions employed here) to 85 °C (only 21% yield after 30 min, Figure 3.3). The yield was restored to 65% yield after 3 h at 100 °C, but the reaction was still slow (43% yield after 0.5 h, Figure 3.3). Furthermore, raising the temperature to 140 °C achieved 65% yield to HMF after 0.5 h, but at this temperature the yield dropped to 50% after 3 h due to the formation of humins (Figure 3.3). It is well known that, at high temperatures, the combination of HMF and sugars leads to the unavoidable formation of humins.¹⁵⁸ The catalyst loading was increased in order to confirm that there was sufficient catalyst to perform the conversion and that catalyst poisoning in the reaction medium was not a significant factor. This was confirmed as a fourfold increase in the catalytic loading (to 28 mol%) had a minimal effect on HMF production (61% after 0.5 h at 120 °C).



All experiments were replicated based on 3 runs
0.1 g glucose in 0.7 g [C₄C₁im]Cl, 7 mol% CrCl₃·6H₂O catalyst. Non-isolated yields.

Figure 3.3. Yield of HMF (%) from glucose as a function of reaction temperature.

To calculate the activation energy of glucose conversion to HMF with the use of [C₄C₁im]Cl ionic liquid, two different temperatures 85 °C and 100 °C have been studied (Table 3.5).

Table 3.5. Initial rates of glucose conversion at different temperatures.

Entry	Solvent	Temp. (°C)	Time (h)	k (s ⁻¹)	Rate (mol l ⁻¹ s ⁻¹)
1	[C ₄ C ₁ im]Cl	85	0.5	4E-05	3.34205E-05
2	[C ₄ C ₁ im]Cl	85	1	4E-05	2.81917E-05
3	[C ₄ C ₁ im]Cl	85	3	4E-05	2.30937E-05
4	[C ₄ C ₁ im]Cl	100	0.5	9E-05	5.62745E-05
5	[C ₄ C ₁ im]Cl	100	1	9E-05	4.15686E-05
6	[C ₄ C ₁ im]Cl	100	3	9E-05	3.30392E-05

0.1 g glucose in 0.7 g [C₄C₁im]Cl, 7 mol% CrCl₃·6H₂O catalyst. Non-isolated yields. 3 runs.

$$E_a = \ln \frac{k_2}{k_1} \times \frac{R}{\left(\frac{1}{T_1} - \frac{1}{T_2}\right)} = \ln \frac{9 \times 10^{-5}}{4 \times 10^{-5}} \times \frac{8.314}{\left(\frac{1}{358} - \frac{1}{373}\right)} = 60020 \text{ J/mol}$$

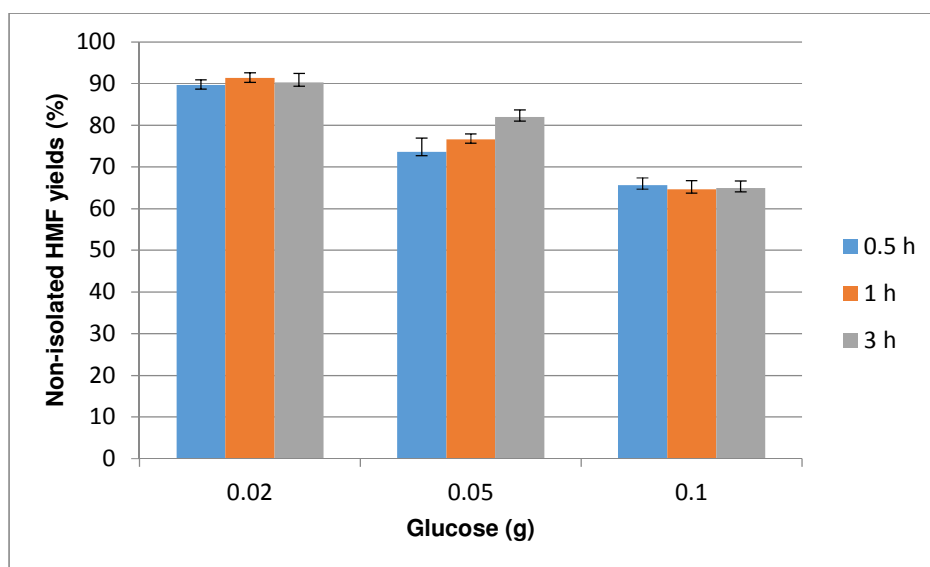
k₂ = rate constant at 100 °C (373 K)

k₁ = rate constant at 88 °C (358 K)

E_a = 60020 J/mol = 14.35 kcal/mol

Compared to the conversion of fructose to HMF in $[\text{C}_4\text{C}_{1\text{im}}]\text{HSO}_4$ with a chromium catalyst, which has the activation energy of 10.45 kcal/mol, the glucose conversion to HMF has an activation energy of 14.35 kcal/mol which is slightly higher. Consequently, the fructose conversion exhibits a lower activation energy thus leading to higher reaction rates.

In order to address the issue of humin formation, the sugar concentration was reduced, based on the hypothesis that the HMF formed would have less sugar with which to react and so reduce the generation of humins. The rapid nature of the reaction also limits the formation of humins as the amount of glucose present in the reaction medium is quickly reduced, preventing it from reacting with the HMF being generated. This is demonstrated in Figure 3.4, which illustrates that lowering the glucose loading from 0.1 g to 0.05 g and ultimately 0.02 g, led to yields to HMF of 80% and 90%, respectively. These results support our hypothesis that the rapid nature of the glucose to HMF conversion does not leave sufficient sugar available to react with HMF to produce humins, thus improving the yield of HMF dramatically.



0.7 g $[\text{C}_4\text{C}_{1\text{im}}]\text{Cl}$, 7 mol% $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ catalyst, 120 °C. Non-isolated yields. 3 runs.

Figure 3.4. Yield (%) of HMF from glucose as a function of substrate loading.

The apparent negative order dependence of this conversion is due to the side reactions which lead to the formation of humins. Lowering the concentration of glucose in this system leads to higher yields, which is an apparent negative order of dependence but this is due to the greater control over the side reactions. In order to address the issue of humin formation, the sugar concentration was reduced, based on the hypothesis that the HMF formed would have less sugar with which to react and so reduce the generation of humins. The rapid nature of the reaction also limits the formation of humins as the amount of glucose present in the reaction medium is quickly reduced, preventing it from reacting with the HMF being generated.

3.4 Conclusion

The conversion of glucose to the established platform chemical, 5-hydroxymethylfurfural (HMF) is an important transformation within the biorefinery concept. Generating HMF from glucose rather than fructose removes an extra step from the overall goal of using biomass to produce this polyfunctional starting material. In Chapter 2, it was shown that $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ was highly effective at producing HMF from fructose, however, the results reported in this Chapter illustrate the additional challenge of generating HMF directly from glucose, for which a Lewis base is advantageous for the isomerisation step to form fructose but Brønsted acidic conditions are needed to dehydrate the fructose to obtain HMF. From this study it appears that the isomerisation is the most important catalytic step in the overall conversion of glucose to HMF. It is clear that $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ (or mixtures thereof) does not provide the desired balance of properties and so is unsuitable for glucose as a feedstock. Instead, an IL with coordinating Cl^- anions, such as $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$, is required to form powerful Lewis basic species with the metal catalyst in solution, e.g. $[\text{CrCl}_4]^-$. These are then capable of promoting the glucose

isomerisation. Other approaches to overcome this rate limiting isomerisation, such as the use of the enzyme Sweetzyme (glucose isomerase), proved incompatible with the high temperatures required for the reaction. The high temperatures at which the reaction is typically performed (120 °C) led to reaction of the HMF formed with unreacted sugars to generate insoluble humins, limiting the yield of HMF to around 65% using the $\text{CrCl}_3/[\text{C}_4\text{C}_{1\text{im}}]\text{Cl}$ system. However, this study has found that reducing the concentration of glucose leads to HMF yields of 90% in only 30 minutes (7 mol% catalyst at 120 °C), without the need for further additives. Future work in the group will aim to adapt this approach to a flow process which operates at low concentrations of glucose.

CHAPTER 4

CELLULOSE TO HMF

4.1 Overview

Many different feedstocks are used to produce the array of useful chemical and biochemical products, on which the world population relies. The key concept in this approach is the production of useful and valuable chemicals from inexpensive biomass resources.^{163,164} Biomass encompasses all organic compounds which are available on a renewable basis, such as animal and plant waste, lignocellulosic biomass, aquatic plants, agricultural food, GM plants and various other waste materials. Biomass can be divided into five main categories which are shown in Figure 4.1.¹⁵⁸

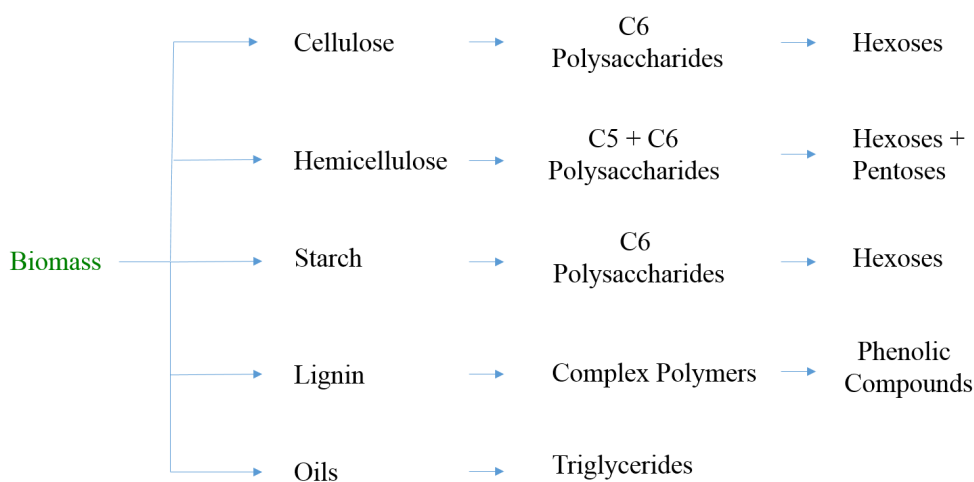


Figure 4.1. *Important biomass components.*¹⁶⁵

By mass, lignocellulosic biomass is composed of cellulose (~50%), hemicellulose (~35%) and lignin (~5-30%) with other extracted components (~10%) depending on biomass type.¹⁶⁶ The

main studies on biomass utilisation have concentrated on cellulose, hemicellulose and lignin transformation with less attention being given to other components, which could also prove a good resource for fine chemicals.¹⁶⁷ For example, extracted compounds from wood include sterols, terpenes, phenolic substances and lignans, which are all important components for chemical synthesis.¹⁶⁸ Essential oils are mainly present in secondary plant metabolites and are very important components in flavourings, fragrances as well as in the health and pharmaceutical industry.¹⁶³

More than 20% of the total mass of Earth's biosphere contains lignin but the complex composition of lignin requires harsh processes in order to obtain phenol derivatives. Due to the lack of effective methods to valorise lignin, it is often simply used as an energy source to be burnt. In 2007, a US Department of Energy survey demonstrated that lignin could be a good precursor of important chemicals, especially aromatics, which could be used to replace their production from oil.¹⁶⁹

Cellulose and hemicellulose make up the largest part of biomass and they account for 50%-80% of the total mass.¹⁶⁸ Many recent papers have reviewed the use of ionic liquids for the dissolution of lignocellulosic biomass, however, these articles focus mainly on the advantages of ionic liquids in the pretreatment of cellulose compared with traditional methods. It has been shown that ionic liquids can decrystallise the cellulose portion of biomass and disrupt the hemicellulose and lignin portion.⁴⁵ Brandt *et al.* studied the possibility of removing lignin from the other biomass constituents using ionic liquids and selectively extracting the lignin fraction.⁴⁵

The hydrolysis of cellulose and hemicellulose produces different sugar units, from which a wide range of important chemicals could be produced. Several papers have been published on the chemical transformation of low-molecular weight carbohydrates to chemicals with useful industrial application profiles.¹⁷⁰ Chedda and coworkers studied the catalytic transformation of biomass-derived oxygenated feedstocks into useful fuels and chemicals. These processes included hydrolysis, dehydration, isomerisation, aldol condensation, reforming, hydrogenation, and oxidation.¹⁷¹ A summary of the alternative methods used to catalytically transform lignocellulose biomass are shown in Figure 4.2.¹⁷²

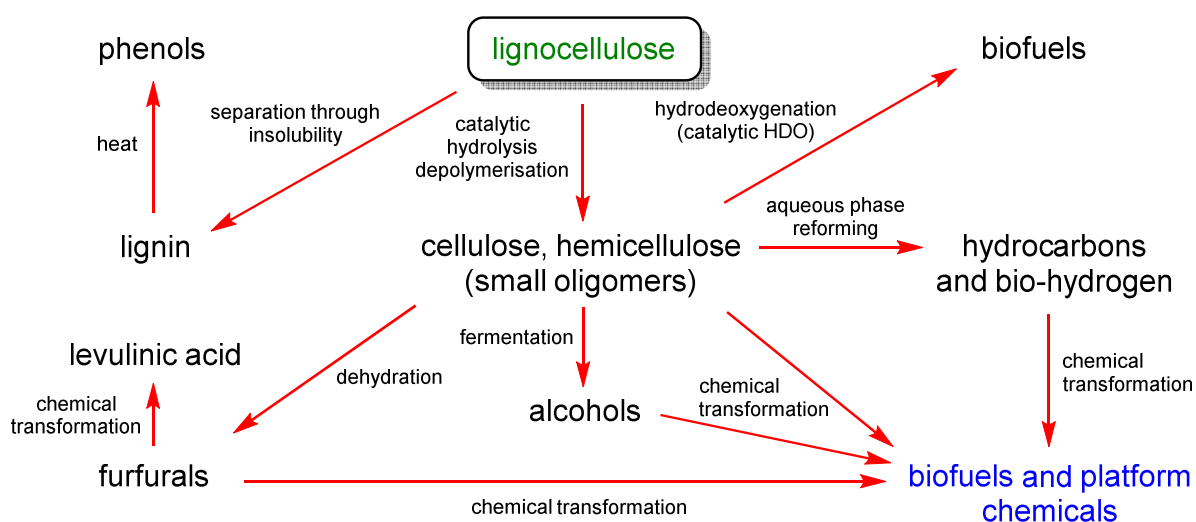
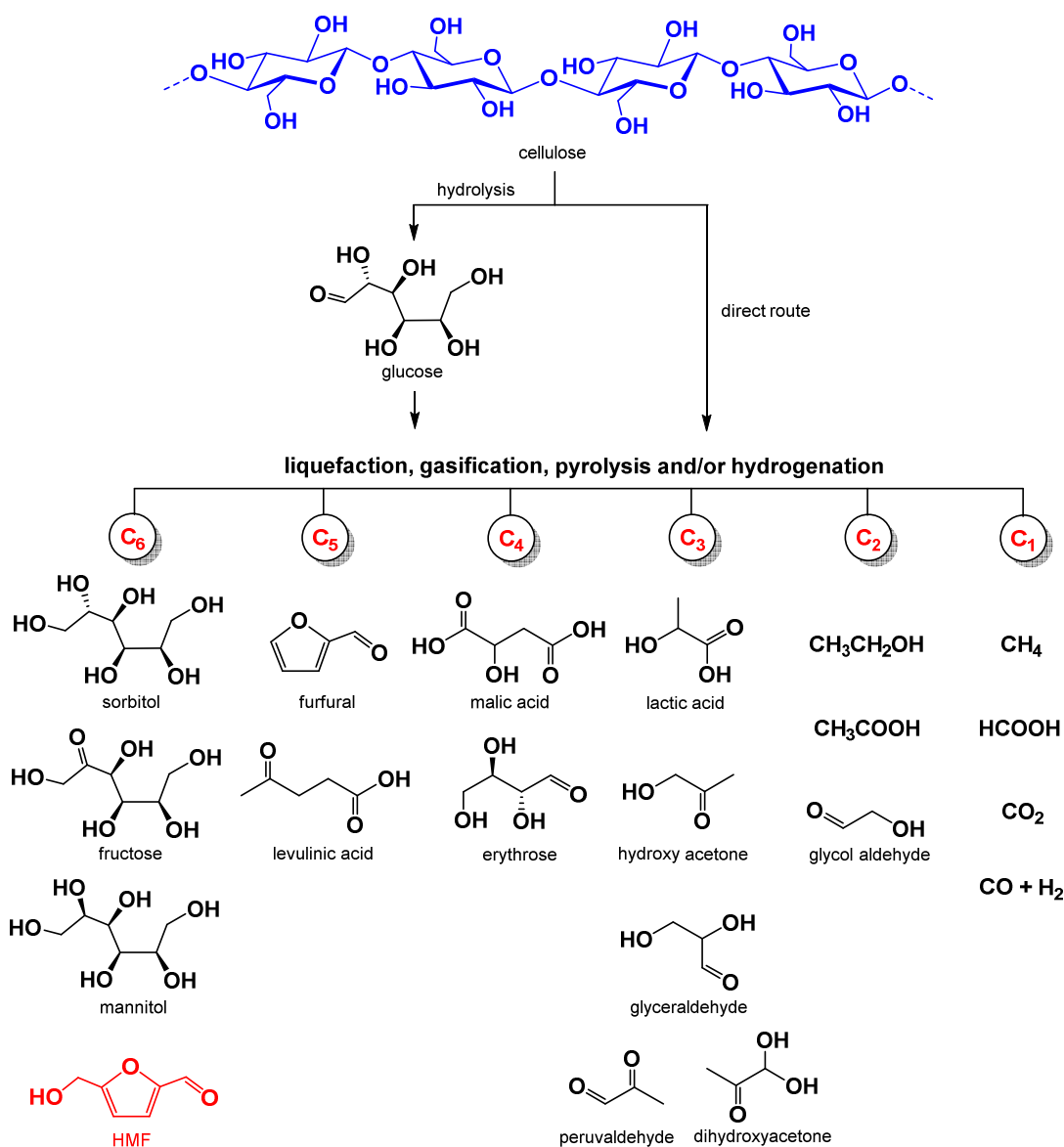


Figure 4.2. Lignocellulosic pathways: A scheme for a chemo-catalytic biorefinery.¹⁷²

Catalytic hydrolysis of lignocellulose produces cellulose and hemicellulose which can then be converted to small sugar molecules and oligomers. Insoluble lignin is separated from the mixture and transformed into phenols by heating. Catalytic hydrodeoxygenation converts small sugar molecules and oligomers into biofuels, while fermentation produces alcohols which can

then be converted to biofuels and other useful chemicals. Dehydration produces furfurals which lead to biofuels and levulinic acid. Aqueous phase reforming produces hydrocarbons and biohydrogen which also can be used as precursors for biofuels and useful chemicals. The catalytic conversion of cellulose to useful chemicals and fuels using different chemical pathways is shown in Scheme 4.1.¹⁶⁷



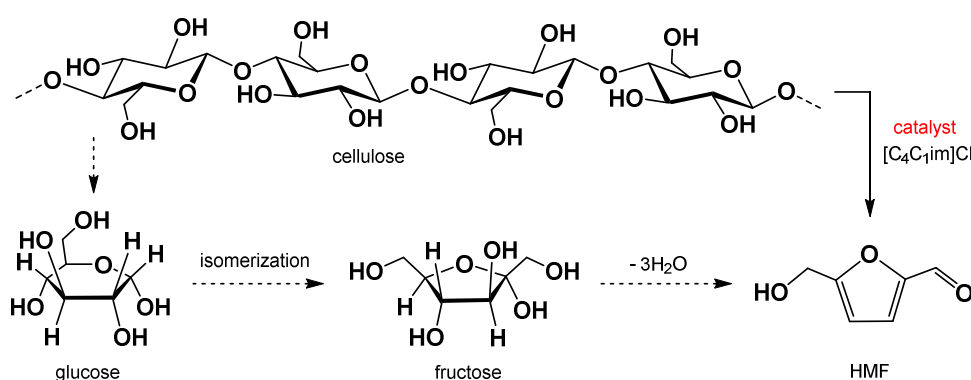
Scheme 4.1. Useful chemicals and fuels obtained from cellulose conversion.¹⁷³

Various review articles have provided an overview of key areas, such as the synthesis and use of sugar derivatives from hemicellulose and cellulose¹⁷⁴ and the methods used for valorisation of biomass waste by conversion to useful platform chemicals.¹⁷⁵ Among the important building blocks derived from lignocellulosic biomass resource, 5-hydroxymethylfurfural (HMF) has been reported as one of the most promising building blocks for industrial chemistry.^{176,177} It is a versatile intermediate between biomass-based carbohydrate chemistry and the petroleum-based industrial chemistry. These find use in a wide variety of chemical manufacturing applications and industrial products.^{178,179}

The most desirable and challenging route to produce HMF involves widely available renewable sources such as cellulose.¹⁸⁰ However, a high-yield, low-cost, energy-efficient and direct conversion of cellulose into HMF is still a challenge and the subject of substantial research. Many different routes and methods have been proposed but the routes published to date are low yielding, high in cost or energy inefficient methods.

The proposed synthetic route from cellulose to HMF is a multistep approach consisting of the production of glucose from cellulose, followed by glucose isomerisation to fructose, and finally HMF formation from the dehydration of fructose.¹⁸¹ Interestingly (in the context of this work), the conversion of cellulose to HMF has also been shown to occur in the absence of a catalyst using ionic liquids, albeit in low yields.⁴⁴

The key step in the conversion of cellulose to HMF (Scheme 4.2) is the hydrolysis of cellulose to sugar molecules, which is hampered by the poor solubility of polymeric cellulose in most solvents. Acid-catalysed hydrolysis of cellulose is one method which has been studied widely, in which the hydroxonium cation and hydroxide anions interact with the cellulose network, leading to breakdown of the polymer.



Scheme 4.2. Pathway to HMF from cellulose.

The most common acids used in cellulose hydrolysis are mineral acids (H₂SO₄, HCl) and organic acids, such as *p*-toluenesulfonic acid as well as different carboxylic acids. Thus far, sulfuric acid has been used most frequently in this reaction, which is unsurprising due to its low cost.¹⁸² The reaction requires relatively high temperatures and is performed under atmospheric pressure. Higher temperatures and longer reaction times are required when dilute acid is used.¹⁸³ The treatment of cellulose with concentrated acid accelerates the hydrolysis markedly, such that the polymer molecules depolymerise to monomers.¹⁸⁴ However, the use of concentrated acid substantially increases the amount of further uncontrolled degradation of glucose or xylose, for example to HMF.¹⁸⁵ However, considering the issues surrounding waste disposal, hazard to the

environment, handling safety, and equipment corrosion, dilute acid is preferable for the hydrolysis of cellulose.¹⁸²

The effect of pressure on the hydrolysis of cellulose has been scarcely investigated, however, at atmospheric pressure the hydrolysis of cellulose is reasonable with dehydrated and hydrolytic products being isolated.¹⁸⁶ The same study shows that the optimum conditions for the depolymerisation of cellulose are elevated temperature, long reaction time and concentrated acid.

In addition to reaction conditions such as temperature, pressure, and reaction time, the type of acid is also an important factor in hydrolysis of cellulose. For example, in the presence of HCl, hydrolysis of cellulose leads to levulinic acid with a yield of 12%.¹⁸⁷ This indicates that hydrochloric acid promotes the further catalytic reaction of the depolymerised products. The effect of dilute phosphoric acid on cellulose depolymerisation is to produce hydrolytic saccharides, HMF and furfural.¹⁸⁸ These results have indicated that dilute phosphoric acid could play an important role in the degradation of cellulose to useful products. Different acid types show different conversion routes depending on their strength. However, despite the high catalytic activity of H_3PO_4 , HCl and H_2SO_4 in cellulose hydrolysis, their large-scale use in this process is uneconomical, causes severe corrosion, involves costly separation and neutralisation as well as the safety and disposal issues associated with concentrated acids.

Heterogeneous solid acid catalysts have several advantages over the homogenous acid catalysts described above. First of all, solid catalysts can easily be removed from the liquid mixture, which allows the possible reuse of the catalyst while minimising corrosion. These advantages have stimulated research on solid acid catalysts as replacements for liquid acid catalysts in the depolymerisation of cellulose.¹⁸⁹⁻¹⁹¹

Recently, various solid catalysts such as H-form zeolites, heteropolyacids, metal oxides, and sulfonated silica have been explored by different research groups (Table 4.1). Solid Brønsted acid catalysts have also been shown to be efficient catalysts for cellulose hydrolysis.

Catalyst	Feedstock	Reaction conditions	Typical products	Yield (%)	Researchers/Year
AC-SO ₃ H + COOH + OH	Cellulose	373 K, 3 h	Glucose	4.0 ^a	Suganuma <i>et al.</i> /2008
AC-SO ₃ H + COOH + OH	Cellulose	373 K, 3 h	β-1,4-glucan	64.0	Yamaguchi <i>et al.</i> /2009
AC-SO ₃ H	Cellulose	423 K, 24 h	Glucose	~8.1 ^b	
AC-SO ₃ H	Cellulose	423 K, 24 h	β-1,4-glucan	0.93	Onda <i>et al.</i> /2008
AC-SO ₃ H (Sulfonation <i>T</i> = 523 K)	Cellulose	423 K, 24 h	Glucose	40.5	
BC-SO ₃ H	Cellulose	423 K, 24 h	Glucose	61.0	Pang <i>et al.</i> /2010
HNbMoO ₆	Cellulose	MW (350 W), 373 K, 1 h	Glucose	19.8	Wu <i>et al.</i> /2010
H ₃ PW ₁₂ O ₄₀	Cellulose	403 K, 12 h	Glucose	21.0	Takagaki <i>et al.</i> /2008
H ₃ PW ₁₂ O ₄₀	Cellulose	453 K, 2 h	Glucose	50.5	Tian <i>et al.</i> /2010
H ₃ PW ₁₂ O ₄₀	Cellulose	—	Levulinic acid	0.14	
H ₃ PW ₁₂ O ₄₀	Cellulose	—	HMF	1.6	Deng <i>et al.</i> /2010
H ₃ PW ₁₂ O ₄₀	Cellulose	≤473 K, 0.5 h	Methyl Glucosides	50.0–60.0	
CrCl ₃ /LiCl + [C ₄ MIM]Cl	+ CH ₃ OH	3 MPa	5-HMF	62.3	Wang <i>et al.</i> /2011
CrCl ₃ /LiCl + [C ₄ MIM]Cl	Cellulose	433 K, 10 min	5-HMF	62.3	Wang <i>et al.</i> /2011
Nafion/silica	Cellulose	463 K, 24 h	Glucose	9.0	Hegner <i>et al.</i> /2010
Sulfonated silica/carbon nanocomposites	Cellulose	—	Levulinic acid	2.0	Van de Vyver <i>et al.</i> /2010
Sulfonated silica/carbon nanocomposites	Cellulose	423 K, 24 h	Glucose	50.0	

AC: Active carbon. BC: Biomass char. [C₄MIM]Cl: 1-butyl-3-methylimidazolium chloride. MW: Microwave-assisted. ^a catalyst: 0.300 g; cellulose: 0.025 g; distilled water: 0.7 g. ^b catalyst: 0.300 g; cellulose: 0.25 g; distilled water: 2.25 g.

Table 4.1. Typical hydrolysis of cellulose with different solid catalysts.¹⁷³

The use of solid catalysts does not simply cause breakdown of the biopolymer into sugars but also leads to other degradation products such as furfural, HMF, and levulinic acid. Overall, while offering advantages for removal of the catalyst from the medium, the catalytic activity and selectivity of such solid acids are very low and so longer reaction times are required for these systems compared with liquid acid catalysts.

Besides the acid catalysed depolymerisation of cellulose there exist many other different methods to achieve this transformation, such as solvolysis, catalytic hydrothermal liquefaction etc. However, none of these methods has provided an effective and selective ‘one pot’ transformation of cellulose to useful chemicals such as HMF and furfurals and, as a result, are either uneconomical or environmentally unfriendly (or both). For this reason, is the challenge remains to find a potentially economically viable method for cellulose conversion to useful products without significant environmental impact.

The research reported here combines ionic liquids as low impact solvents (easily handled, negligible vapour pressure, recyclable) with low-toxicity metal catalysts for the ‘one pot’ conversion of cellulose to value-added chemicals. For this purpose, two ionic liquids have been systematically studied under different conditions in order to arrive at an effective system for cellulose dissolution. In Chapter 2, the key step identified for glucose to HMF conversion was the isomerisation of glucose to fructose, which directly affects the yield, due to competing humin formation.

When using cellulose as the feedstock for HMF formation, it appears that the key step is the dissolution and depolymerisation of cellulose to glucose monomers rather than the glucose to fructose isomerisation and subsequent fructose dehydration. Ionic liquids appear to overcome these problems as they can play the role of both solvent and catalyst.

4.2 Catalyst and IL selection

The important aspect before the selection of catalyst and ILs is the isolation of cellulose from biomass. The microbial fermentation sugars in biomass and the thermochemical conversion of the lignocellulose via pyrolysis or gasification are the proposed methods for the transformation of lignocellulosic biomass into useful chemicals. For each method, deconstruction of the lignocellulosic matrix is necessary before the carbohydrates can be released. There are many pre-treatment methods available in the literature, such as concentrated and dilute acids, organosolv processes as well as lime and ammonia fibre expansion pretreatment. Depending on the tissue structure and the cell wall composition of different plants, methods can vary due to the resistance to deconstruction. Steam explosion (SE) is one of the methods used in the pretreatment of biomass and contains both physical and chemical methods to break down the lignocellulosic material.²⁰⁹ High pressure steam at high temperature is applied for a short time to the biomass. It is then depressurised and the structure is destroyed by this explosive decompression. The drawback of this method is the production of toxic derivatives which inhibit the hydrolysis and fermentation steps. Liquid Hot Water (LHW) treatment is another method which requires high temperatures and pressures. This is a chemical free process which leads to complete removal of hemicellulose, 5-20 % removal of cellulose and 30-60 % removal of lignin. Ammonia fibre explosion is a similar method to SE in which biomass is exposed to

liquid ammonia at high pressure and temperature. Most of these methods are very harsh and require energy-intensive and expensive use of high temperatures and pressures. Recently, Welton and co-workers obtained the best saccharification yields reported so far by using $[\text{C}_4\text{C}_1\text{im}][\text{MeSO}_4]$.¹⁹² Pretreatment of miscanthus with this ionic liquid resulted in the release of 92% glucan content from the biomass.

In previous Chapters yields of 96% HMF were achieved from fructose (Chapter 2) and 90% from glucose (Chapter 3) by employing hydrogensulfate-based and chloride-based ILs, respectively. The next goal was to find suitable conditions and ionic liquid media for the conversion of cellulose, which is another step closer to raw biomass than glucose (and two steps closer than fructose). As cellulose is readily isolated from biomass using ionic liquids, there exists potential to design a system based on ionic liquids which could deliver HMF directly from biomass using only one medium. However, the conversion of cellulose to HMF is more challenging than either fructose or glucose as it requires suitable conditions to dissolve and hydrolyse this biopolymer to monosaccharides before they can be converted to HMF. The conditions and ionic liquids used successfully in Chapters 2 and 3 were used as a starting point and this allowed a comparison to be achieved between HMF yields using cellulose as a substrate and the yields from the monosaccharides, glucose and fructose. The Sigmacell cellulose was used in all experiments which was ordered from Sigma Aldrich. It is type 50 white powder and has a particle size of 50 μm . The Sigmacell cellulose is synthetic and only contains the crystalline region.

Two ionic liquids, $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ and $[\text{C}_4\text{C}_1\text{im}][\text{Cl}]$, were examined with the use of Cr and Zn catalysts which have been reported previously as good catalysts for dehydration of sugars to

HMF and aliquots were collected after 1.5 and 3 h.¹⁹³ Samples were not collected earlier than 1 h due to the time required for dissolution of the cellulose under these conditions. After 1.5 and 3 h, formation of HMF was very low using chromium catalysts (or mixtures with other metals) in [C₄C₁im][HSO₄] ionic liquid (Table 4.2). Only 5% yield was observed (by ¹H NMR spectroscopy) using CrCl₃ and CrCl₃-CuCl₂ catalysts after 3 h at 120 °C (Table 4.2, entries 1 and 2). In the presence of the ionic liquid without any catalyst, no HMF formation was detected after 3 h (Table 4.2, entry 3). In contrast to the hydrogensulfate-based ionic liquid, the yields were found to be much higher using [C₄C₁im][Cl] as the solvent medium. HMF yields of 54% and 11% were observed using CrCl₃ and CrCl₃-CuCl₂ catalysts, respectively (Table 4.2, entry 4 and 5). Only 3% yield was observed in the presence of [C₄C₁im][Cl] without any catalyst (Table 4.2, entry 6). Based on the success [C₄C₁im][Cl] with CrCl₃, this medium was used to investigate another pair of catalysts, however maximum yields of 3% and 30% were obtained using ZnCl₂ and CrCl₃-ZnCl₂ catalysts (Table 4.2, entry 8 and 9).

Table 4.2. Yield (%) of HMF from cellulose using some IL and catalyst combinations.

Entry	Ionic Liquid	Catalyst	1.5 h	3 h
1	[C ₄ C ₁ im][HSO ₄]	CrCl ₃ ·6H ₂ O	<5	<5
2	[C ₄ C ₁ im][HSO ₄]	CrCl ₃ ·6H ₂ O + CuCl ₂ (1:1)	<5	<5
3	[C ₄ C ₁ im][HSO ₄]	No catalyst	0	0
4	[C ₄ C ₁ im]Cl	CrCl ₃ ·6H ₂ O	36	54
5	[C ₄ C ₁ im]Cl	CrCl ₃ ·6H ₂ O + CuCl ₂ (1:1)	11	11
6	[C ₄ C ₁ im]Cl	No catalyst	<3	<3
7	[C ₄ C ₁ im]Cl + [C ₄ C ₁ im][HSO ₄] (1:1)	CrCl ₃ ·6H ₂ O	<3	<5
8	[C ₄ C ₁ im]Cl	ZnCl ₂	0	3
9	[C ₄ C ₁ im]Cl	CrCl ₃ ·6H ₂ O + ZnCl ₂ (1:1)	8	30

0.1 g cellulose in 0.7 g ionic liquid; 7 mol% catalyst, 120 °C. Non-isolated yields shown.

All yields were calculated based of NMR spectrum of reaction mixtures which was already described before. The conversion of three different sugars at exactly same conditions are displayed in Table 4.3.

Table 4.3. *Conversion of fructose, glucose and cellulose under the same conditions.*

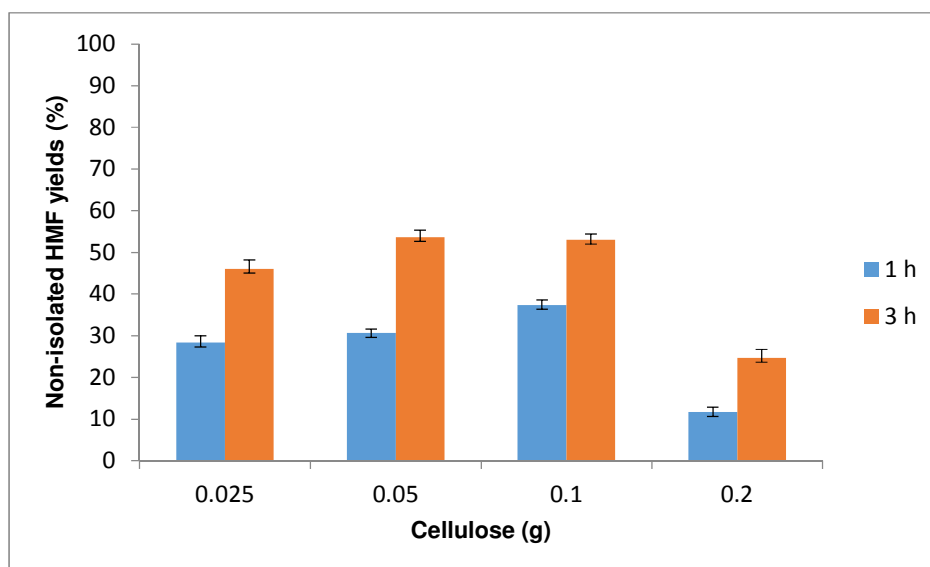
Substrate	Ionic Liquid	T (°C)	Yield (%)	Reference
Cellulose	[C ₄ C ₁ im]Cl	120	54	this work
Glucose	[C ₄ C ₁ im]Cl	120	65	this work
Fructose	[C ₄ C ₁ im]Cl	120	71	43

Our previous findings with glucose and fructose indicated that the ionic liquid, [C₄C₁im]Cl, enhances the isomerisation of glucose to fructose through the Lewis basicity of the chloride anions (Chapter 3), while [C₄C₁im][HSO₄] accelerates the conversion of fructose to HMF (Chapter 2). It was also assumed that the acidity of [C₄C₁im][HSO₄] would promote the hydrolysis of cellulose to monomers. In order to probe this, a mixture of ionic liquids was tested for the conversion of cellulose to HMF, however, a very poor 5% yield of HMF was determined by ¹H NMR spectroscopy (Table 4.2, entry 7). This result suggested that the presence of [C₄C₁im][HSO₄] actually lowers the conversion to HMF, and indicated that the [HSO₄][−] anion actually inhibits the glucose-fructose interconversion as was already verified in the previous investigations of glucose as a precursor to HMF (Chapter 3). These shown in Table 4.2 indicate that, while the choice of chromium catalyst is effective for a reasonable level of cellulose conversion to HMF, the [C₄C₁im][HSO₄] ionic liquid and the systems employing ZnCl₂, CrCl₃-ZnCl₂, CrCl₃-CuCl₂ catalysts perform worse at 120 °C.

4.3 Effect of reaction conditions

4.3.1 Sugar Concentration

Sugar concentration has been shown to be an important factor in this conversion pathway, as shown in Chapter 3, where a reduction in glucose concentration was found to improve the HMF yield. This was suggested to be due to the prevention of humin formation through limiting the amount of sugar present with which the HMF can react to form humins. The rapid nature of the reaction between glucose and the catalyst also helps limit the formation of humins as the amount of sugar present in the reaction medium is quickly reduced, preventing it from reacting with the HMF being generated. Bearing this in mind, the amount of cellulose was reduced and results are illustrated in (Figure 4.3).



All experiments were replicated based on 3 runs
0.7 g ionic liquid; 7 mol% catalyst, 120 °C. Non-isolated yields.

Figure 4.3. *Effect on HMF yield (not isolated) of cellulose concentration.*

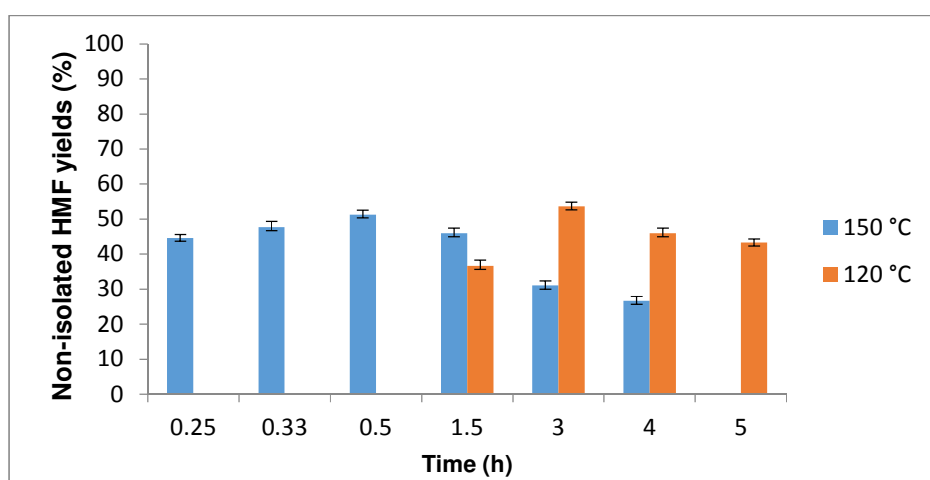
A maximum yield of 54% was obtained after 3 hours using a cellulose loading of 0.1 g. Lowering this loading from 0.1g to 0.05 g and then to 0.02 g led to lower yields of HMF of 53%

and 45%, respectively. Increasing the cellulose concentration from 0.1 g to 0.2 g also led to lower yields of HMF (25% after 3 hours). This can be explained in terms of the poor solubility of cellulose in the ionic liquid and revealed that 0.1 g cellulose in 0.7 g of ionic liquid was approximately the optimal concentration for maximum yield under these conditions. To explore further this solubility issue, the amount of ionic liquid was tripled (0.7 g to 2.1 g) and the yield using 0.1 g of cellulose was found to be 39% after 3 hours. The results suggest that decreasing the cellulose loading does have an effect on the HMF yield and that an optimum concentration can be achieved that provides a balance between successful dissolution of cellulose and sufficient material to make the process effective which could also mean that the heterogeneous reactions is less selective.

In Chapter 3, it was hypothesised that the isomerisation of glucose to fructose was the limiting step, rather than the conversion of fructose to HMF, and therefore decreasing the glucose concentration will lead to the rapid conversion to HMF. The HPLC study assisted the estimation of the rate of glucose to fructose isomerisation in our system. The rate constant for this reaction is calculated to be $2 \times 10^{-6} \text{ s}^{-1}$ and the rate of isomerisation is $1.5 \times 10^{-5} \text{ mol s}^{-1}$. Under the same conditions, and compared with dehydration of fructose to HMF, which has rate of $4.2 \times 10^{-5} \text{ mol s}^{-1}$, the rate of isomerisation is three times lower than the rate of dehydration. This supports our hypothesis that the isomerisation is the rate determining step in the conversion of glucose to HMF under these conditions. This leaves less sugar to react with HMF at 120 °C and thus prevents the formation of humins. However, when using cellulose as the feedstock, it appears that the limiting step is the dissolution and hydrolysis of cellulose to glucose monomers rather than the isomerisation of glucose to fructose.

4.3.2 Reaction time

Figure 4.4 shows the effect of time on the yield of HMF at 120 °C and 150 °C. Prolonging the reaction time improved the HMF yield but, after reaching the maximum yield, the yield declined by 9% at 120 °C between 3 h and 4 h after the start of the reaction. This effect was also observed at 150 °C, where a 6% reduction in yield was observed from 0.5 h to 1.5 h. Measurements were not taken before 1 h at 120 °C since the cellulose only dissolved completely after 1 h at this temperature. At elevated temperatures (e.g., 150 °C), the reaction is very rapid at and the maximum yield was obtained after only 0.5 h (51% HMF yield). However, in all these reactions, prolonged reaction time led to a decrease in yield and this is postulated to be due to the formation of insoluble humins, through reaction of the HMF produced with the monosaccharides from cellulose breakdown. Higher temperatures exacerbate this effect but do lead to rapid reaction times. It should be noted that the HMF yield of 51% after 30 minutes and 44% only after 15 minutes at 150 °C are some of the best so far reported for such a short period of time but still less if compared with glucose and fructose. This could be due to the barriers to dissolution and depolymerisation of cellulose under these conditions.



0.1 g cellulose, 0.7 g ionic liquid; 7 mol% catalyst. Non-isolated yields, based on 3 runs

Figure 4.4. Effect on (non-isolated) HMF yield of two different temperatures.

4.3.3 Effect of water and catalyst loading

The addition of water significantly effects the yield of HMF from cellulose (Table 4.4). Different amounts of water were added to the reaction mixture at 150 °C. An increase in the water content was found to cause a significant decrease in the HMF yield (Table 4.4, entry 1 and 2). This could be due to the effect of water on the solubility of cellulose in [C₄C₁im][Cl] as the hydrogen bonds between [C₄C₁im][Cl] and the hydroxyl group of cellulose are thought to be necessary for the breakage of the β -1,4-glycosidic bonds.¹⁹⁴ However, the presence of substantial amounts of water can lead to the hydrogen bonding interactions with [C₄C₁im]Cl being substituted with those of the water molecules, also reducing the solubility of cellulose in [C₄C₁im]Cl.¹⁹⁴ However, the existence of small amounts of water (Table 4.4, entry 2) seems to increase the yield slightly which could be due the effect of this water content on the hydrolysis of cellulose.

Table 4.4. Effect of water on the (non-isolated) yield of HMF from cellulose.

Entry	Ionic Liquid	Catalyst (mol%)	0.5 h	1 h	3 h
1	[C ₄ C ₁ im]Cl + H ₂ O (1:1)	7	-	22	28
2	[C ₄ C ₁ im]Cl + H ₂ O (3:1)	7	-	51	44
4	[C ₄ C ₁ im]Cl	7	51	45	30
3	[C ₄ C ₁ im]Cl	21	44	37	22

All experiments were replicated based on 3 runs

0.1 g glucose in 0.7 g ionic liquid; CrCl₃·6H₂O catalyst, 150 °C. Non-isolated yields shown.

The catalyst loading was also investigated in order to confirm that there was sufficient catalyst to perform the conversion of cellulose to HMF and that catalyst poisoning was not a significant factor in the reaction medium. The catalyst loading was increased threefold (to 21%) and, surprisingly, the yield was found to decrease slightly (Table 4.4, entry 4). This may be due to

some side reactions taking place, which are promoted by high catalyst loadings. One possibility is the formation of humins, which would be consistent with the darkening of the reaction medium observed (Figure 4.5).

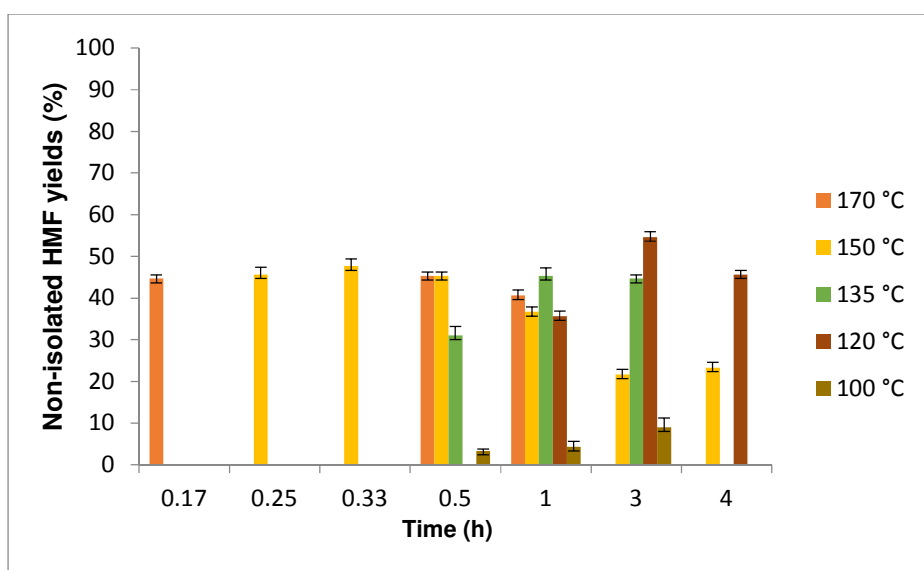


Figure 4.5. *Darkening of reaction medium due to humin formation.*

4.3.4 Effect of reaction temperature

The reaction temperature is clearly an important factor in the conversion of cellulose to HMF, which directly affects the yield and reaction rate. Increasing the temperature of the reaction causes an increase in both the yield and reaction rate. However, after reaching a maximum yield of HMF, this product is consumed by the reaction with any remaining unreacted sugars to form humins (Figure 4.6). Further experiments were conducted to explore this behaviour in more detail. The reaction is very rapid at 150 °C, reaching 44% HMF yield after only 15 minutes, while the same yield is achieved in only 10 minutes at 170 °C. Raising the temperature from 100 °C to 150 °C led to a 41% higher HMF yield, after 30 minutes, while even a more modest rise, from 100 °C to 120 °C, yielded 46% more HMF yield after 3 hours (Figure 4.6).

Although the reaction rate increased with temperature, the HMF yield drops was seen to drop after 30 minutes, which can be attributed to the formation of humins under these high temperature conditions. The best HMF yield at 120 °C of 54% was obtained after 3 hours, indicating the long reaction times required at this lower temperature. This can also be attributed in part to the low level of solubility and degradation of cellulose in the ionic liquid at this temperature. The onset of humin formation was also observed after 3 hours at 120 °C, which is very obvious from the formation of dark solid in reaction mixture.



All experiments were replicated based on 3 runs
0.1 g glucose in 0.7 g ionic liquid; $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ catalyst. Non-isolated yields.

Figure 4.6. *Effect of temperature on yield of HMF from cellulose.*

At temperatures above 120 °C, the reaction rate was accelerated and moderate yields were obtained even after only 10 minutes. Another contributory factor could also be the reduced

viscosity of the reaction medium at this temperature, which accelerates the mass transfer for cellulose dissolution and degradation. Moreover, the HMF yield of 44% obtained from the conversion of cellulose after only 10 minutes is one of the highest yields reported in the literature. However, when the reaction temperature is very high, the formation of humins is unavoidable and the yield drops significantly after only a short period of time. In order to overcome this problem, low cellulose concentrations were tested to limit the formation of humins at high temperatures which will also improve the rate of dissolution (having already explored this aspect at 120 °C – see Figure 4.3). It was hypothesised that, as the reaction rate is rapid at high temperatures, lowering the cellulose concentration could limit the formation of humins as the HMF formed would have less sugar with which to react. Different cellulose concentrations were investigated at elevated temperatures in order to explore this possibility (Table 4.5).

Table 4.5. *Non-isolated yields (%) of HMF from cellulose at elevated temperatures.*

Entry	Ionic Liquid	Cellulose (g)	Temp. (°C)	10 min	0.5 h	1 h	3 h
1	[C ₄ C ₁ im]Cl	0.025	150	40	52	58	58
2	[C ₄ C ₁ im]Cl	0.015	150	25	45	57	51
3	[C ₄ C ₁ im]Cl	0.1	170	44	44	41	-
4	[C ₄ C ₁ im]Cl	0.015	170	31	50	50	-

All experiments were replicated based on 3 runs

0.7 g ionic liquid; 7 mol% CrCl₃·6H₂O catalyst. Non-isolated yields shown.

It was discovered that lowering the cellulose concentration did indeed improve the yield at elevated temperatures, which supports the hypothesis outlined above. When the cellulose loading was decreased to 0.025 grams, the best HMF yield for the entire investigation using

cellulose as a feedstock was obtained. A (non-isolated) yield of 58% was obtained after only 1 h. The reaction was very rapid and 40% yield was obtained only after 10 minutes. Decreasing the cellulose concentration still further to 0.015 grams did not have any positive effect on the yield, possibly because this rendered the solution too dilute. This could be seen from Table 4.5 (entry 1 and 2), in which lowering the concentration actually decreased the reaction rate and the yield dropped by 15% after 10 minutes. Raising the temperature to 170 °C increased the reaction rate to provide a 6% greater HMF yield after 10 minutes (Table 4.5 entry 2 and 4). However, the overall yield dropped by 7% after 3 hours (Table 4.5, entry 2 and 4) due to the onset of humin formation.

4.4 Conclusion

The conversion of cellulose to HMF was probed using a range of different variables, including the nature of the ionic liquid medium, the catalyst selection and modification of the reaction conditions. The conversion of cellulose to HMF is clearly much more challenging than the generation of HMF from sugar monomers due to the polymeric nature of cellulose and its resulting low solubility. Lowering the cellulose concentration led to an increase in the yield of HMF but only to a certain level, beyond which the yield decreased. This suggests that there is a balance to be struck between successful dissolution of cellulose and sufficiency of material to make the process effective when an optimum concentration is achieved. Prolonged reaction time led to a decrease in HMF yield due to the formation of humins over longer reaction periods. The reaction temperature is one of the important factors in the conversion of cellulose to HMF, as it directly affects the yield and reaction rate. At 150 °C, 47% yield of HMF was obtained after only 30 minutes, however, the best HMF yield at 120 °C (54%) was obtained after 3 hours,

indicating the longer reaction times required at this lower temperature. Both prolonged reaction times at lower temperature and shorter reaction times at higher temperatures led to the formation of humins. A compromise was found to achieve a 58% HMF yield after one hour at 150 °C using a relatively low cellulose concentration. This result needs to be viewed in the context of leading HMF yields (as opposed to cellulose conversion) in the literature, which fall in the range 50-60% over longer reaction times (e.g., 5 hours¹⁹⁵) or (non-scalable) microwave heating.¹⁹⁶

CHAPTER 5

EXPERIMENTAL SECTION

5.1 Equipment, reagents, solvents

NMR spectra were recorded on a Bruker DRX-400 (400 MHz) spectrometer at 25 °C with tetramethylsilane as an internal standard. Mass spectra were obtained using an Autospec Q instrument at the Mass Spectrometry Service at Imperial College. Solvents were distilled and dried under N₂ atmosphere before use. Moisture-sensitive compounds were kept under dry nitrogen in a glove box. Chemicals were ordered from Sigma Aldrich and purities are on the table below.

Chemicals	Supplier Purity
1-chlorobutane	99.5 %
1-methylimidazole	>99.0 %
Ethanol	>99.8 %
Cellulose	High purity
Glucose	>99.5 %
Fructose	>99.0 %
Acetonitrile	99.8 %
Ethyl Acetate	99.8 %
Dichloromethane	>99.8 %
Methanol	99.8 %
1-butyimidazol	98.0 %
Toluene	99.8 %
Dimethyl sulfate	>99.0 %
ZnCl ₂	>98.0 %
NiCl ₂	98.0 %
RuCl ₃	45.0-55.0 %
CS ₂	>99.0 %
CrCl ₃ ·6H ₂ O	96.0 %
KOH	90.0 %
CuCl ₂	99.0 %
CrCl ₂	95.0 %
WCl ₄	95.0 %
MoCl ₃	99.9 %
Y(OTf) ₃	N/A
LaCl ₃	99.9 %
La(OTf) ₃	N/A
K ₂ PtCl ₄	98.0 %
Sc(OTf) ₃	N/A
RhCl ₃	98.0 %

5.2 Preparation of the ionic liquids

1-Butyl-3-methylimidazolium chloride, [C₄C₁im]Cl

A flask containing freshly distilled 1-methylimidazole (162 mL, 0.88 mol, 1.0 eq.) and ethyl acetate (150 mL) was cooled in a dry ice bath. Freshly distilled 1-chlorobutane (100 mL, 0.96 mol, 1.1 eq.) was added dropwise by dropping funnel under the N₂ atmosphere. The reaction mixture was allowed to reach room temperature and heated slowly under reflux for 1 hour until the solution became turbid. Then, the solution was heated under N₂ atmosphere to 70 °C for 48 hours. The solvent was removed by cannula filtration in order to avoid atmosphere contaminations. The resultant viscous liquid was dissolved in acetonitrile (25 mL) and ethyl acetate (75 mL) mixture. The solution was allowed to cool at –25 °C freezer. White crystals were formed after 14 hours. The ethyl acetate and acetonitrile mixture was removed by cannula filtration. The product was washed with ethyl acetate (4 x 25 mL). After the removal of solvents, the crystals obtained were dried *in vacuo* overnight, which provided [C₄C₁im]Cl (115 g, 93 %) as colourless crystalline solid.

¹H NMR (400 MHz, DMSO-*d*₆): δ 9.45 (s, 1H, N₂CH), 7.86, 7.79 (m x 2, 2 x 1H, NCH), 4.20 (t, 2H, NCH₂, *J*_{HH} = 7.2 Hz), 3.88 (s, 3H, NCH₃), 1.77, 1.24 (m x 2, 2 x 2H, CCH₂), 0.90 (t, 3H, CH₃, *J*_{HH} = 7.3 Hz) ppm.

¹³C{¹H} NMR (100 MHz, DMSO-*d*₆): δ 137.2 (N₂CH), 124.1, 122.7 (2 x NCH), 48.8 (NCH₂CH₂CH₂CH₃), 36.2 (NCH₃), 31.8 (NCH₂CH₂CH₂CH₃), 19.3 (NCH₂CH₂CH₂CH₃), 13.6 (N(CH₂)₂CH₂CH₃) ppm.

MS (FAB, +ve mode): *m/z* (abundance) = 139 (100) [C₄C₁im]⁺.

Potassium diethyldithiocarbamate

To a solution of diethylamine (25 mL, 239 mmol) in methanol (50 mL) was added potassium hydroxide (13.4 g, 239 mmol) and the solution was left to stir for 5 minutes. Carbon disulfide (14.5 mL, 239 mmol) was then added dropwise by dropping funnel and the solution was stirred for 2 hours. This produced a pale yellow solution. The volatile solvent was evaporated by the use of rotary evaporator. The solid obtained was recrystallised several times from methanol to provide a colourless crystalline product (Yield: 32 g, 85%).

¹H NMR (400 MHz, DMSO-*d*₆): δ 3.92 (t, 4H, NCH₂, *J*_{HH} = 7.3 Hz), 1.58 (m, 4H, NCH₂CH₂), 1.21 (m, 4H, CH₂CH₃), 0.88 (t, 6H, CH₃, *J*_{HH} = 7.4 Hz) ppm.

¹³C{¹H} NMR (100 MHz, DMSO-*d*₆): δ 213.0 (NCS₂), 52.5 (CH₂), 29.6 (CH₂), 20.5 (CH₂), 14.4 (CH₃) ppm.

MS (FAB, -ve mode): *m/z* (abundance) = 138 (100) [S₂CNEt₂][−].

***1-butyl-3-methylimidazolium diethyldithiocarbamate* [C₄C₁im][S₂CNEt₂]**

To a flask containing potassium di-*n*-ethyldithiocarbamate (30, 0.17 mol, 1.0 eq.) was added a solution of [C₄C₁im]Cl (29.7 g, 0.17 mol, 1.0 eq.) in acetonitrile (150 mL) while stirring under N₂ atmosphere. The reaction mixture was stirred for 72 hours under N₂ atmosphere and white precipitate allowed to settle. After the precipitation of potassium chloride, the ionic liquid [C₄C₁im][S₂CNEt₂] was collected by cannula filtration. The purification of the solution included washing several times with water to remove any chloride. Moreover, the remaining potassium chloride was precipitated out of the acetonitrile. The 1-butyl-3-methylimidazolium di-

ethyldithiocarbamate product (38.8 g, 82%) was successfully obtained as a dark-yellow free-flowing liquid.

¹H NMR (400 MHz, DMSO) δ 9.62 (s, 1H, N₂CH), 7.83, 7.75 (m x 2, 2 x 1H, 2 x NCH), 4.22 (t, 2H, NCH₂, J_{HH} = 7.2 Hz), 3.99 (q, 4H, DTC NCH₂), 3.90 (s, 3H, NCH₃), 1.78, 1.25 (m x 2, 2 x 2H, CCH₂), 1.09 (t, 6H, DTC NCCH₃), 0.89 (t, 3H, CCH₃, J_{HH} = 7.3 Hz) ppm.

¹³C NMR (100 MHz, DMSO) δ 212.0 (CS₂), 137.6 (N₂CH), 123.9, 122.6 (2 x NCH), 49.1 (NCH₂), 46.5 (DTC NCH₂), 36.1 (NCH₃), 31.9 (NCCH₂), 19.3 (NCCCCH₂), 13.9 (DTC NCCH₃), 13.0 (NCCCCCH₃) ppm.

MS (FAB, +ve mode): m/z (abundance) = 139 (100) [bmim]⁺ (-ve mode): m/z (abundance) = 148 (100) [S₂CN(CH₂CH₃)₂]⁻.

IR (neat) cm⁻¹: 3133 (ν_{CH} aromatic), 2962, 2936 and 2876 (ν_{CH} aliphatic), 1569 ($\nu_{\text{C=N}}$ aromatic), 1457 (ν_{CN}), 1248 (ν_{CS}), 1169 ($\nu_{\text{C=C}}$ aromatic), 963 (ν_{CS}), 748 (ν_{CH} cation). No amine N-H stretch was observed in the region between 3500-3300 cm⁻¹, providing evidence for the loss of N-H on formation of the dithiocarbamate.

***1-butyl-3-methylimidazolium hydrogensulfate* [C₄C₁im][HSO₄]**

1-Butylimidazole (100 mL, 0.76 mol) was diluted in toluene (60 mL) and cooled in an ice bath. Dimethylsulfate (72 mL, 0.76 mol) was added dropwise to the reaction mixture (flow rate 0.5 drops/sec) while stirring. The reaction mixture was stirred for a further hour at room temperature before the upper toluene layer was removed. The lower ionic liquid layer was washed with toluene (3 x 50 mL) before it was dried overnight at 65 °C under vacuum with

stirring. The yield was 172.5 g (92%). This material was used directly for the synthesis of [C₄C₁im][HSO₄].

[C₄C₁im][MeSO₄] (40.0 g, 0.16 mol) was diluted with deionised water (5 mL). The reaction vessel was kept open to the air and placed in a heating block at 215 °C. The internal temperature of the reaction mixture was continuously monitored and kept between 170 to 180 °C for four hours by dropwise addition of deionised water. The reaction mixture was cooled to 65 °C and kept under vacuum while stirring overnight to remove all residual water. The yield was 37.8 g (98%).

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.19 (s, 1H, N₂CH), 7.79, 7.72 (m x 2, 2 x 1H, NCH), 4.17 (t, 2H, NCH₂, *J*_{HH} = 7.2 Hz), 3.86 (s, 3H, NCH₃), 1.74, 1.23 (m x 2, 2 x 2H, CCH₂), 0.88 (t, 3H, CCH₃, *J*_{HH} = 7.3 Hz) ppm.

¹³C{¹H} NMR (100 MHz, DMSO-*d*₆) δ 137.1 (N₂CH), 124.1, 122.7 (2 x NCH), 48.9 (NCH₂), 36.1 (NCH₃), 31.8 (NCH₂CH₂), 19.2 (CH₂CH₃), 13.7 (CH₃) ppm.

Elemental Analysis: Calc.: C 40.7, H 6.8, N 11.9%; Found: C 40.6, H 6.9, N 11.8%

MS (FAB, +ve mode): *m/z* (abundance) = 139 (100) [C₄C₁im]⁺.

(FAB, -ve mode): *m/z* (abundance) = 97 (100) [HSO₄]⁻.

5.3 Catalytic formation of HMF

Fructose conversion to HMF

Fructose (0.1 g, 0.55 mmol) was added to round bottom flasks containing [C₄C₁im][HSO₄] (0.7 g, 2.96 mmol) mixtures were stirred at standard conditions. Different catalysts CrCl₂,

CrCl₃·6H₂O, CrCl₃, WCl₄, MoCl₃, LaCl₃, Sc(OTf)₃, La(OTf)₃, Y(OTf)₃, RuCl₃, K₂PtCl₄, NiCl₂, RhCl₃, and ZnCl₂ (0.039 mmol, 7 mol%) were added to each flask. The reaction mixtures were stirred at 80 °C under reflux condenser for 24 hours. The samples were collected after various reaction times. The same procedure was repeated at 100 °C and 120 °C for 3 hours and higher HMF yields were achieved. HMF yields are calculated from the integration of HMF peaks against the ionic liquid [C₄C₁im][HSO₄] itself. The ionic liquid was considered to be an internal standard, as it has a negligible vapour pressure. The HMF peak at low field value of 9.55 ppm (see data below) was chosen for calculation of the yields as it does not interfere with any of the solvent regions in ¹H NMR spectrum.

¹H NMR spectrum of 5-hydroxymethylfurfural (HMF)

(400 MHz, DMSO-d₆): δ 9.55 (s, 1H, CHO), 7.50 (d, 1H, 2 x CHOCCH, *J*_{HH} = 3.40 Hz), 6.61 (d, 1H, 2 x CCHCH, *J*_{HH} = 3.5 Hz), 5.57 (t, 1H, OH, *J*_{HH} = 6.0 Hz), 4.51 (d, 2H, CH₂O, *J*_{HH} = 5.9 Hz) ppm.

Glucose conversion to HMF

In each run, glucose (0.1 g, 0.55 mmol) was added to a round bottomed flask containing either [C₄C₁im]Cl (0.7 mg, 4.00 mmol) or [C₄C₁im][HSO₄] (0.7 mg, 2.96 mmol). The catalyst (0.039 mmol, 7 mol%) under study (CrCl₂, CrCl₃·6H₂O, K₂PtCl₄, NiCl₂, ZnCl₂) was added to the flask. The flask was equipped with a reflux condenser and the reaction mixture was stirred at the desired temperature (80, 100, 120 or 140 °C) for 24 hours and in certain cases for 72 hours. Samples were collected after various reaction times (see Tables Chapter 3) and analysed by ¹H NMR spectroscopy. HMF yields were calculated from the integration of HMF resonances

against those of the ionic liquid $[\text{C}_4\text{C}_{1\text{im}}]\text{Cl}$ itself. The ionic liquid was considered to be an internal standard, as it has negligible vapour pressure. The HMF peak at the lowest field chemical shift value of 9.55 ppm was chosen for calculation of the yields as it does not interfere with any of the solvent resonances in ^1H NMR spectrum.

Cellulose conversion to HMF

Cellulose (0.1 g, 0.61 mmol) was added to a round bottomed flask containing $[\text{C}_4\text{C}_{1\text{im}}][\text{Cl}]$ (0.70 g, 2.96 mmol). The catalyst (0.039 mmol, 7 mol%) under study ($\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$, CuCl_2 , ZnCl_2) was added to the flask. The flask was equipped with a reflux condenser and the reaction mixture was stirred at the desired temperature (100, 120, 135, 150 and 170 °C) for 3 hours. Cellulose was completely dissolved in the ionic liquid after 3 hours so it was not isolated from the mixture. Samples were collected after various reaction times (0.5, 1, 3, 24 hours) and analysed by NMR spectroscopy. Cellulose was dissolved in ionic liquid at these temperatures after 3 hours so it was not isolated from mixture. HMF yields were calculated from the integration of HMF peaks against the ionic liquid $[\text{C}_4\text{C}_{1\text{im}}][\text{Cl}]$ itself. The ionic liquid was considered to be an internal standard, as it has negligible vapour pressure. The HMF peak at the lowest field chemical shift value of 9.55 ppm was chosen for calculation of the yields as it does not interfere with any of the solvent resonances in ^1H NMR spectrum.

Thermal stability data for the three ionic liquids employed in the experiments are presented in Table 5.1. Thermogravimetric analysis (TGA) of these ILs suggests that all three ionic liquids are stable under the conditions used in all experiments. The harshest conditions used were for

the conversion of cellulose in [C₄C₁im]Cl at 170 °C, which is a lower temperature than the decomposition temperature of [C₄C₁im]Cl (Table 1).

Table 5.1 Stability of ionic liquids as determined by TGA.

Ionic Liquid	T_{onset} (°C)	T_{peak} (°C)	Reference
[C ₄ C ₁ im]Cl	257	284	197
[C ₄ C ₁ im]HSO ₄	345	377	197
[C ₄ C ₁ im][S ₂ CNR ₂]	192	N/A	198

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