

**Imperial College London
Department of Chemical Engineering**

**Chemical Routes for the Valorisation of Biomass into
High Value Added Chemicals using Ionic Liquids as
Solvents**

Amir Al-Ghatta

Thesis submitted as partial fulfilment of the requirements for the degree of Doctoral of Philosophy,
Imperial College London, 2016-2019

Declaration of Originality and Copyright

The work described in this thesis was carried out at Imperial College London between November 2016 and October 2019. The entire body of work is my own unless otherwise stated and has not been submitted previously for a degree at this or another university.

The copyright of this thesis rests with the author and is made available under a Creative Commons Attribution Non-Commercial No Derivatives licence. Researchers are free to copy, distribute or transmit the thesis on the condition that they attribute it, that they do not use it for commercial purposes and that they do not alter, transform or build upon it. For any reuse or redistribution, researchers must make clear to others the licence terms of this work.

All the work of the thesis is going to be subjected to embargo for a period of one year from submission.

The thesis resulted so far in the following publications:

Al Ghatta, A.; Wilton-Ely, J.D. E. T.; Hallett, J.P. Rapid, High-Yield Fructose Dehydration to HMF in the Ionic Liquid [bmim][OTf], *ChemSusChem* 2019, 12, 4452-4460

Al Ghatta, A.; Wilton-Ely, J.D. E. T.; Hallett, J.P. Strategies for the Separation of the Furanic Compounds HMF, DFF, FFCA and FDCA from Ionic Liquids, *ACS Sustainable Chem. Eng.* 2019, 7, 16483-16492

Al Ghatta, A.; Wilton-Ely, J.D. E. T.; Hallett, J.P.. Efficient Formation of 2,5-Diformylfuran in Ionic Liquids at High Substrate Loadings and Low Oxygen Pressure with Separation through Sublimation, *ACS Sustainable Chem. Eng.* 2020, 8, 2462-2471

Abstract

Petrochemical industry has experienced huge development in the last century, dominating different sectors such as plastics, detergents, pharmaceuticals and fertilizers. While technologies for processing of fossil feedstocks are now well established with marginal room for improvements, biorenewable chemicals derived from biomass struggle to be commercialised at large scale due to strong barriers experienced in R&D. Much research is in place to develop catalysts which can achieve high turnover numbers and high yield which can compete with the traditional processes, but the usage of lignocellulosic biomass requires innovative approaches which combine catalyst and solvent design with optimal separation minimizing emissions and waste streams.

In this work, we will investigate ionic liquids as valuable solvents for the synthesis of high value biomonomers such as diformylfuran (DFF) and 2,5-furandicarboxylic acid (FDCA) starting from sugars. So far, the synthesis of these chemicals has seen huge challenges due to the difficulties in isolating the intermediate 5-HMF derived from sugar dehydration, which is the key molecule to produce these monomers. The usage of ionic liquids as solvents can lead to multiple advantages which can allow the production of these molecules at large scale, simplifying process separation and favouring high yield of reaction.

Other bioderived products such as humins and surfactants will be studied as potential applications in the wastewater treatment for removal of heavy metals and detergents industry. A new category of biosurfactants derived from furfural exhibits remarkable proprieties which can have a potential higher cleaning ability compared the current oil derivatives ones.

This thesis copes different aspects for an efficient sugar biorefinery, focused to substitute oil derivative consumer products, such as plastic and detergents, with the aim to achieve the reduction in CO₂ emissions.

Glossary

5-HMF 5-hydroxymethyl furfural

HMF hydroxymethyl furfural

DFF diformylfuran

FDCA 2,5-furandicarboxylic acid

FFCA 5-formyl-2-furancarboxylic acid

HMFCa 5-hydroxy-2-furancarboxylic acid

[bmim] 1-butyl-3-methylimidazolium

[emim] 1-ethyl-3-methylimidazolium

[bmpyr] 1-butyl-3-methylpyrrolidinium

[N(Me)Oct₃] trioctyl methyl ammonium

[OAc] acetate

[OTf] triflate

[NTf₂] bistrimlimide

[PF₆] hexafluoro phosphate

[BF₄] tetrafluoro borate

PEF polyethylene furoate

PET polyethylene terephthalate

BTX benzene toluene xylene

LC lignocellulose

TA terephthalic acid

MEK ethyl methyl ketone

DMSO dimethyl sulfoxide

LC liquid chromatography

MS mass spec

HPLC high performance liquid chromatography

IR infrared spectroscopy

GPC gel permeation chromatography

WWT wastewater treatment

THF tetrahydrofuran

DCM dichloromethane

MIBK	methyl isobutyl ketone
PTSA	p-toluenesulfonic acid
UV	ultraviolet spectroscopy
NMR	nuclear magnetic resonance
TEMPO	2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
MBA	methoxybenzyl alcohol
FA	furfuryl alcohol
TPAP	tetrapropylammonium perruthenate
DABCO	1,4-diazabicyclo[2.2. 2]octane
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
XPS	X-ray photoelectron spectroscopy
SEM	scanning electron microscope
XRD	X-ray crystallography
TGA	thermogravimetric analysis
EDTA	ethylenediaminetetraacetate
STPP	sodium tripolyphosphate
LAS	linear alkyl benzene sulfonate
SDS	sodium dodecyl sulphate
KP	Kraft Point
CMC	critical micelles concentration
CSA	chlorosulfonic acid
SDBS	sodium dodecyl benzene sulphonate

Acknowledgments

It has been my biggest desire to contribute to chemical science in the field of sustainability and green chemistry. After my long education which involved one bachelor and two masters fulfilled in four different countries, I couldn't not spend all my knowledge acquired to the scientific world.

After finishing my masters, I spend a period in an engineering company as process engineer, but I immediately felt that the environment was not suitable for me. Many protocols and low critical thinking due to on working in well-established petrochemical technologies let me feel oppressed and disappointed since I couldn't give enough space to my ideas and I was not contributing in green technologies which could improve the chemical industry. Therefore, when I got my phd offer I didn't think twice on it and I decided to leave my job to cope this new experience.

Since I begin my studies in Chemical Engineering I realised that an understanding of Chemistry it is fundamental to have complete scientific profile and cope in a critical way different topics. While this is not true when working in some traditional engineering companies, I believe that this profile is very important in the academic world and in every field of chemistry involving innovative technologies. In this matter my former education that covered both chemistry and chemical engineering helped me a lot.

I would like to thank:

- My supervisors prof. James Wilton-Ely and prof. Jason Hallett to have given me the opportunity to join their group and contribute to my personal and professional development.
- My colleagues in the Hallett Group. During these 3 years there was a big turnover of people and I was happy to meet different wonderful people from different part of the world. Some of them as Raul, Anthon, Francisco, Andreas will be life friends which I will never forget.
- Aida, for being on my side in every moment during my whole PhD period and being a wonderful sister to share nice and bad moments together.
- The male version of Aida....Coby. One of the persons that have been most comprehensive to me and a big chemistry head. One small suggestion by him could led to huge breakthrough in the experiment.
- Last but not least... to my Mother ,my Angel on earth, for being always encouraging and comprehensive, to have put my happiness before everything else and show optimism in every moment. I am so lucky to have you as a mother, if I was able to achieve all these scores in my life is only thanks to you.

I dedicate this thesis to my parents.

My father which personality and intelligence have fascinating me since I was kid and which he naturally inspired me in coping a scientific career.

*Nothing in life is to be feared,
it is only to be understood.
Now is the time to understand more, so that we may fear less.*

Marie Curie

Contents

Chapter 1 Introduction	22
Chemical Industry: Past and Present	24
How the chemical industry is structured and the role of biomass	27
PEF, a green substitute for PET	33
Green Processes: a critical approach to the 12 principles of green chemistry	36
Solvents in the Chemical Industry.....	42
Ionic Liquids a Replacements for Organic Solvents for Biomass Valorisation.....	45
How “Green” is this thesis.....	48
Prospects	50
References.....	51
Chapter 2 Stability of 5-HMF in Ionic Liquids: Characterization and Valorisation of the Humin Side Products.....	56
Introduction.....	57
Experimental Section.....	60
Materials	60
Synthesis Ionic Liquids.....	60
Stability test of furanic compounds in the ionic liquids.....	61
Synthesis of Humins	61
Metal Extraction	62
Results and Discussions.....	63
Stability of HMF in the ionic liquids	63
Characterization of humins	65
Morphology and molecular weight analysis	71
Application of humins in metal extraction from waste water	73
Conclusions.....	75
References.....	76
Chapter 3 Ionic Liquid as Green Solvents for the Separation of Sugar-derived Furanic Compounds.....	79
Introduction.....	81
Experimental Section.....	87

Materials	87
DFF sublimation.....	87
Precipitation of FFCA and FDCA from ionic liquids by water addition.	87
HMF extraction from a hydrophobic ionic liquid.....	87
Analytical method.....	88
Calculation of the Solubility of Hydrophobic Ionic Liquids in Water.....	88
Esterification of FDCA with ethylene glycol in ionic liquids	89
Results and Discussion	90
Sublimation of DFF from ionic liquids.....	90
Separation of FDCA and FFCA	91
Energy analysis of drying [bmim]Cl and [bmim]Br.....	93
Extraction of HMF from trioctylmethylammonium salts using water.....	97
Study of the interaction between HMF and ionic liquids by FT-IR	99
Study of ionic liquid miscibility with water	100
Solvent selection guidelines for product separation	100
Conclusions.....	102
References.....	103
Chapter 4 Rapid High-Yield Fructose Dehydration to HMF in Mixtures of Water and the Non-Coordinating Ionic Liquid [bmim][OTf]	107
Introduction.....	108
Experimental Section.....	111
Materials	111
Fructose conversion to HMF.....	111
Partition coefficients between ionic liquid and diethyl ether	111
Results and Discussion	113
Stability of HMF in the ionic liquid under acidic conditions	113
Presence of intermediates.....	114
Effect of water content on the yield and rate of the reaction.....	116
Effect of fructose loading.....	118
Effect of temperature	119
Effect of the cation.....	120
Extraction of HMF from Ionic Liquids.....	121

Conclusions.....	124
References.....	125
Chapter 5 Catalytic Oxidation of 5-HMF into DFF in [bmim][OTf] with immobilized TEMPO-pyridine ionic liquid and CuCl.....	130
Introduction.....	131
Experimental Section.....	133
Materials	133
Oxidation Experiments	133
Synthesis of TEMPO-immobilized ionic liquid	134
Synthesis of bipyridine immobilized Ionic Liquid [bbpy][NTf ₂]	135
XPS analysis.....	136
Results and Discussion	137
Screening of catalytic systems.....	137
Solvent and Ligand selection	139
5-HMF and catalyst loading.....	141
Investigation of recycling with immobilised TEMPO	143
Synthesis of DFF from fructose in a two-step reaction.....	144
Study of the overoxidation of 5-HMF	145
Catalyst characterization	146
Conclusions.....	148
References.....	149
Chapter 6 Heterogeneous catalytic oxidation of HMF into FDCA in ionic liquids	153
Introduction.....	154
Experimental Section.....	158
Materials	158
Catalyst preparation	158
Catalyst characterization	159
Oxidation experiments with carbene	159
Oxidation experiments at high pressure.....	159
Results and Discussion	161
Synthesis of FDCA through homogeneous catalysis.....	161
Heterogeneous catalysis: Effect of solvent composition on reaction yield.....	162

Strategy for efficient oxidation of HMF to FDCA in ionic liquids	163
Characterisation of the Mn/Fe oxides support.....	164
Results of oxidation	165
Conclusion	168
References.....	169
Chapter 7 Biorenewable Anionic Surfactants as Valuable Replacements for Current Detergent Formulations	172
Introduction.....	173
Experimental Section.....	179
Materials	179
Esterification reaction to produce the alkyl furoate.....	179
Sulfonation with Chlorosulfonic Acid.....	180
Solubility studies	181
Resistance to hard water	181
Critical Micelle Concentration (CMC).....	182
Results and Discussion	183
Synthesis of the Furoate Ester	183
Synthesis of Sulfonated alkyl furoate	185
Solubility studies	186
Resistance to hard water	186
Critical Micelle Concentration	187
Summary of furoate sulfonated surfactants.....	188
Discussion of the biodegradability	189
Conclusions.....	191
References.....	192
Chapter 8 Conclusions and Prospects.....	194
Prospects	196
Application of ionic liquids in enzymatic and electrochemical reactions.....	196
References.....	198
A. Appendix.....	199
Characterization Ionic Liquids.....	199
Ionic Liquid as Green Solvent for Separation of Furanic Compounds.....	210

Rapid High-Yield Fructose Dehydration to HMF in Mixtures of Water and the Non-Coordinating Ionic Liquid [bmim][OTf]	212
Catalytic Oxidation of 5-HMF into DFF in [bmim][OTf] with immobilized TEMPO-pyridine ionic liquid and CuCl	215
Biorenewable Anionic Surfactants as Valuable Replacement of Current Detergent Formulations	220

List of Figures

Figure 1.1 Global fossil fuel consumption from Our World in Data https://ourworldindata.org/fossil-fuels#coal	24
Figure 1.2 Crude Oil consumption by sector in 2012 (from https://www.globalpetrolprices.com/articles/39/)	25
Figure 1.3 ‘Chemical tree’ for the production of bulk chemicals from fossil fuel feedstocks.....	28
Figure 1.4 Twenty-five biobased chemicals which can substitute most of the oil-derived products and their development status ²⁴	30
Figure 1.5 Chemicals that can be obtained from Furfural and HMF.....	31
Figure 1.6 Chemical route to arrive at FDCA and PEF from lignocellulosic feedstocks	34
Figure 1.7 CO ₂ emission associated with different organic solvents. Reproduced with permission from ref ⁴⁴	43
Figure 1.8 Method for the selection of a solvent for a defined application proposed by Jin et al. Reproduced with permission from ref ⁴⁴	44
Figure 1.9 The most common cations and anions used for ionic liquid synthesis.	45
Figure 2.1 Reaction scheme from sugars to 5-HMF with side reactions.....	58
Figure 2.2 Scheme of humins production in ionic liquid.....	62
Figure 2.3 Effect of temperature (9 h) and time (160 °C) on HMF degradation in different ionic liquids (10 % loading respect the solvent).....	64
Figure 2.4 FT-IR spectra of humins produced in different ionic liquids compared to the HMF spectra	67
Figure 2.5 FT-IR spectra of humins from [bmim][OTf] degradation and monomeric units isolated from the THF soluble fraction.....	68
Figure 2.6 Proposed mechanism of HMF degradation in [OTf] ⁻ ionic liquids. Readapted from study in literature. ²⁵	69
Figure 2.7 IR Spectra of humins formed by acid-catalysed dehydration of fructose and the proposed repeating unit of the humins	70
Figure 2.8 SEM of humins formed in different ionic liquids after 9 h at 160 °C. a) [bmim][OTf]; b) [bmpyr][OTf]; c) [bmim][HSO ₄]; d) dehydration of fructose in [bmim][OTf] with 10 % HCl.	71
Figure 2.9 Particle size distribution for the humins formed in the ionic liquid [bmpyr][OTf].	72
Figure 2.10 Molecular weight distribution of humins produced in different ionic liquids.	73
Figure 3.1 System proposed by Wei and co-workers . 1) oil bath heater, 2) magnetic stirrer, 3) Two neck flask for vapor generator(organic solvent at its boiling point temperature), 4)Nitrogen cylinder, 5) Ring type gas distributor, 6) Three neck flask (ionic liquid and HMF), 7) connector, 8) connection to vacuum oil pump, 9) Product collection , 10) ice bath. Reproduced with the permission of ref ¹² ..	82

Figure 3.2 System of Shi and co-workers for the extraction of HMF from ionic liquid with a mixture of acetone and CO ₂ with continuous concentration. Reproduced with the permission from ref ¹⁴	83
Figure 3.3 Reaction pathway to obtain FDCA from HMF	84
Figure 3.4. Recovery of DFF in 3 h at different temperatures from [bmim][NTf ₂] under vacuum (20 mbar). 10 % loading DFF respect the solvent Reproduced with the permission of ref ¹	91
Figure 3.5. Solubility of FDCA and FFCA in ionic liquid - water mixtures of [bmim]Cl and [bmim]Br (left) and [bmim][OTf] (right) at room temperature; solubility expressed in terms of mg of compound per gram of solvent. Reproduced with the permission of ref ¹	93
Figure 3.6 Equilibrium diagram [bmim]Cl/water estimated by COSMOSAC with the IULAM package	94
Figure 3.7 Multiple effect Aspen flowsheet for ionic liquid dehydration.....	94
Figure 3.8 Yield of the diester as function of temperature and time for acid esterification with PTSA. Catalyst loading 10 % (mole) respect FDCA, FDCA loading 12 mg/g in ionic liquid. Temperature experiments done at 180 °C. Time course experiments at 6 h. Ethylene glycol:FDCA ratio 100:1 (mole).	96
Figure 3.9 Effect of different anions on the partition coefficient for the [N(Me)Oct ₃] ⁺ salts (left) and the effect of the cation for NTf ₂ ⁻ salts (right). Reproduced with the permission of ref ¹	97
Figure 3.10 On the left, water concentration to achieve 90% HMF recovery from [N(Me)Oct ₃]Cl at different phase ratios (R) and different HMF loadings at 20 °C. On the right, water concentration needed to achieve 90% HMF recovery from [N(Me)Oct ₃]Cl and [N(Me)Oct ₃][NTf ₂] ionic liquids at R = 2. Numbers next to the data points represent the number of washes required. Reproduced with the permission of ref ¹	98
Figure 3.11 FT-IR spectra of the hydroxyl and carbonyl group of HMF with anions with different H-bonding ability. Reproduced with the permission of ref ¹	100
Figure 4.1 The cations and anions used in the ionic liquids in this chapter. Reproduced with the permission of Al-Ghatta et al. 2019.	110
Figure 4.2. Degradation of HMF at 90 °C in [bmim][OTf] with a range of water contents and 10% PTSA loading (with respect to HMF) and 10% HMF loading (with respect to the ionic liquid). Reproduced with the permission of Al-Ghatta et al. 2019.....	114
Figure 4.3. Acid selection for fructose dehydration in [bmim][OTf]. Fructose loading = 14% respect the solvent, T = 90 °C, initial water content = 3.5%, acid catalyst loading 10% respect fructose, t = 10 min. Reproduced with the permission of Al-Ghatta et al. 2019.....	115
Figure 4.4. Effect of water content on HMF yield from fructose in [bmim][OTf], fructose loading = 10% respect the solvent, T = 90 °C, t = 10 min, 10 % acid catalyst loading (HCl) respect the substrate. Reproduced with the permission of Al-Ghatta et al. 2019.....	117
Figure 4.5. Effect of water content on the kinetics of HMF production from fructose in [bmim][OTf] at 100 °C, fructose loading = 10 % respect the solvent, catalyst loading = 10% (HCl) respect fructose. Reproduced with the permission of Al-Ghatta et al. 2019.....	118
Figure 4.6. a) The HMF yield from fructose in [bmim][OTf], at different fructose loadings and b) kinetic analysis of the same reaction at two fructose loadings (right). Reaction conditions: T = 90 °C,	

3.5% water content, t = 10 min, 10% HCl loading respect fructose. Reproduced with the permission of Al-Ghatta et al. 2019.	119
Figure 4.7. Effect of temperature on HMF yield from fructose in [bmim][OTf], 10% fructose loading, 10% HCl loading, 3.5% water content. Reproduced with the permission of Al-Ghatta et al. 2019...	119
Figure 4.8. Kinetic analysis of the dehydration of fructose to HMF in [bmim][OTf] at two different temperatures and 14% fructose loading respect the solvent, 10% HCl loading respect fructose, 3.5% water content.	120
Figure 4.9 Partition coefficient of HMF in diethyl ether and ionic liquid mixtures.	122
Figure 4.10 Mass spectrometry of the side products in the DCM layer after washing.	123
Figure 4.11 Proposed side-product from HMF dehydration in ionic liquid.	123
Figure 5.1 Synthesis of the ionic liquid immobilised TEMPO, [TEMPO-bmim][NTf ₂].	134
Figure 5.2 Synthesis of the pyridine immobilised ionic liquid, [bbpy][NTf ₂].	135
Figure 5.3 Oxidation of 5-HMF with catalytic systems reported in literature. Conditions: 10% HMF loading (respect the solvent), 10% catalyst loading (respect HMF), 1 bar O ₂ , 80 °C, 6 h.	138
Figure 5.4 Effect of different promoters on the yields and conversion of 5-HMF. Experiments performed for 6 h with O ₂ balloon at 80 °C, 200 mg [bmim][OTf], 20 mg 5-HMF, TEMPO/CuCl/promoter loading 5 mol% respect HMF. Reproduced with the permission from Al Ghatta et.al. 2020,ACS Sus. Chem. Eng., 2020	140
Figure 5.5 Effect of different promoters on the yields and conversion of 5-HMF after 3 hours. Experiments performed with O ₂ balloon at 80 °C, 200 mg [bmim][OTf], 20 mg 5-HMF, TEMPO/CuCl/promoter loading 5 mol% respect HMF. Reproduced with the permission from Al Ghatta et.al. 2020,ACS Sus. Chem. Eng., 2020	141
Figure 5.6 Influence of 5-HMF loading on conversion and yield in [bmim][OTf]. Higher 5-HMF loading slows down the reaction but retains high selectivity. Experiments performed for 6 h with O ₂ balloon at 80 °C, TEMPO/CuCl/pyridine loading of 5 mol% respect HMF. Reproduced with the permission from Al Ghatta et.al. 2020,ACS Sus. Chem. Eng., 2020	142
Figure 5.7 Yield of DFF and FFCA at different temperatures. Reaction conditions: 4 bar O ₂ partial pressure, 10% 5-HMF loading. 10% catalyst loading (CuCl/[bbpy][NTf ₂]/ TEMPO-[bmim][NTf ₂])	145
Figure 5.8 XPS analysis of the catalyst. On the left, catalyst complex CuCl with different ligands. On the right, fresh and spent catalyst.	146
Figure 5.9 XPS for C1s for fresh and spent catalyst	147
Figure 6.1 Mechanism of formation of carbene and its role with water in the oxidation of the aldehyde	162
Figure 6.2 Oxidation of HMF to FDCA with two different catalysts and different solvent composition (50:50). O ₂ pressure 2 bar, 120 °C, 12.6 mg/g HMF concentration	163
Figure 6.3 SEM image of catalyst support at different Mn:Fe content. Left column 10 µm. Right column 2 µm.	165

Figure 6.4 Oxidation of HMF into FDCA with Ru supported by different mixtures of Mn and Fe (molar ratio). Temperature 120 °C, O ₂ pressure 10 bar, 12.6 mg/g HMF concentration.....	166
Figure 6.5 Chemical path adopted to arrive at FDCA from glucose.	167
Figure 7.1 Typical surfactant formulation for LAS.Reproduced with the permission from ref ⁶	175
Figure 7.2 HMF-derived surfactants reported by Stensrud and Wicklund in 2016 (left hand side), Lee and co-workers (middle) and Hoffman and co-workers (on the right).	176
Figure 7.3 Reaction scheme of the proposed surfactants.....	177
Figure 7.4 Chemical path for the derivation of furoic acid and fatty alcohols.....	178
Figure 7.5 Structure of sulfonating agents.	185
Figure 7.6 Measurement of surface tension at different concentrations of surfactant.	187
Figure A. 1 ¹ H NMR spectrum of [bmim]Cl in deuterated DMSO.....	199
Figure A. 2 ¹³ C{ ¹ H} NMR spectrum of [bmim]Cl in deuterated DMSO.	199
Figure A. 3 Mass spectrum of [bmim]Cl.....	200
Figure A. 4 ¹ H NMR spectrum of [bmpyr]Cl in deuterated DMSO.....	200
Figure A. 5 ¹³ C{ ¹ H} NMR spectrum of [bmpyr]Cl in deuterated DMSO.....	201
Figure A. 6 Mass spectrum of [bmpyr]Cl.....	201
Figure A. 7 ¹ H NMR spectrum of [bmim]OTf in deuterated DMSO.....	202
Figure A. 8 ¹³ C{ ¹ H} NMR spectrum of [bmim]OTf in deuterated DMSO	202
Figure A. 9 ¹ H NMR spectrum of [bmpyr]OTf in deuterated DMSO.....	203
Figure A. 10 ¹³ C NMR spectrum of [bmpyr]OTf in deuterated DMSO.....	203
Figure A. 11 Mass spectrum of [bmpyr]OTf.	204
Figure A. 12 ¹ H NMR spectrum of [bmim]Br in deuterated DMSO.	205
Figure A. 13 ¹³ C{ ¹ H} NMR spectrum of [bmim]Br in deuterated DMSO.....	205
Figure A. 14 Mass spectrum of [bmim]Br.....	206
Figure A. 15 ¹ H NMR spectrum of [bmim][NTf ₂] in deuterated DMSO.	206
Figure A. 16 ¹³ C{ ¹ H} NMR spectrum of [bmim][NTf ₂] in deuterated DMSO	207
Figure A. 17 Mass spectrum of [bmim][NTf ₂].....	207
Figure A. 18 ¹ H NMR spectrum of [bmpyr][NTf ₂] in deuterated DMSO.	208
Figure A. 19 ¹³ C{ ¹ H} NMR spectrum of [bmpyr][NTf ₂] in deuterated DMSO.	208
Figure A. 20 Mass spectrum of [bmpyr][NTf ₂]	209
Figure A. 21 Cold finger apparatus for sublimation of DFF.....	210

Figure A. 22 Sublimed DFF from the IL on the condenser tip (left) and collected DFF (right).....	210
Figure A. 23 Comparison between the commercial DFF and the sublimed material (left) and comparison of the bulk IL after first sublimation and second sublimation (right).....	211
Figure A. 24 Crude 5-HMF product prior DCM washing with impurities in the furan region.....	212
Figure A. 25 ¹ H-NMR spectra for the purified 5-HMF after DCM washing.....	212
Figure A. 26 C-NMR spectra for the purified 5-HMF after DCM washing.....	213
Figure A. 27 ¹ H-NMR of recovered ionic liquid [bmim][OTf].....	213
Figure A. 28 Mass spectra of isolated HMF.....	214
Figure A. 29 ¹ H NMR spectrum of Intermediate A reduced with excess phenylhydrazine in deuterated CDCl ₃	215
Figure A. 30 ¹ H NMR spectrum of [TEMPO-bmim][NTf ₂] reduced with excess phenylhydrazine in deuterated CDCl ₃	215
Figure A. 31 ¹³ C{ ¹ H} NMR spectrum of [TEMPO-bmim][NTf ₂] reduced with excess phenylhydrazine in deuterated CDCl ₃	216
Figure A. 32 Mass spectrum of [TEMPO-bmim][NTf ₂].	216
Figure A. 33 ¹ H NMR spectrum of DFF in deuterated DMSO.....	217
Figure A. 34 ¹³ C{ ¹ H} NMR spectrum of DFF in deuterated DMSO.	217
Figure A. 35 Mass spectrum of DFF.....	218
Figure A. 36 On the left, photograph of the reaction mixture after 6 h showing sublimed DFF (white) while further material precipitates from the reaction mixture. On the right, DFF after vacuum was applied for 6 h at 80°C.....	218
Figure A. 37 ¹ H NMR spectrum of FFCA in deuterated DMSO.	219
Figure A. 38 ¹³ C{ ¹ H} NMR spectrum of FFCA in deuterated DMSO.....	219
Figure A. 39 ¹ H-NMR octyl furoate.....	220
Figure A. 40 C-NMR octyl furoate.....	220
Figure A. 41 ¹ H-NMR Sulphonated Octyl Furoate.....	221
Figure A. 42 C-NMR Sulphonated Octyl Furoate.....	221
Figure A. 43 ¹ H-NMR dodecyl furoate.....	223
Figure A. 44 C-NMR dodecyl furoate.....	223
Figure A. 45 ¹ H-NMR Sulphonated dodecyl furoate.....	225
Figure A. 46 C-NMR Sulponated Dodecyl Furoate.....	225
Figure A. 47 ¹ H-NMR Hexadecyl Furoate.....	226
Figure A. 48 C-NMR hexadecyl Furoate.....	226

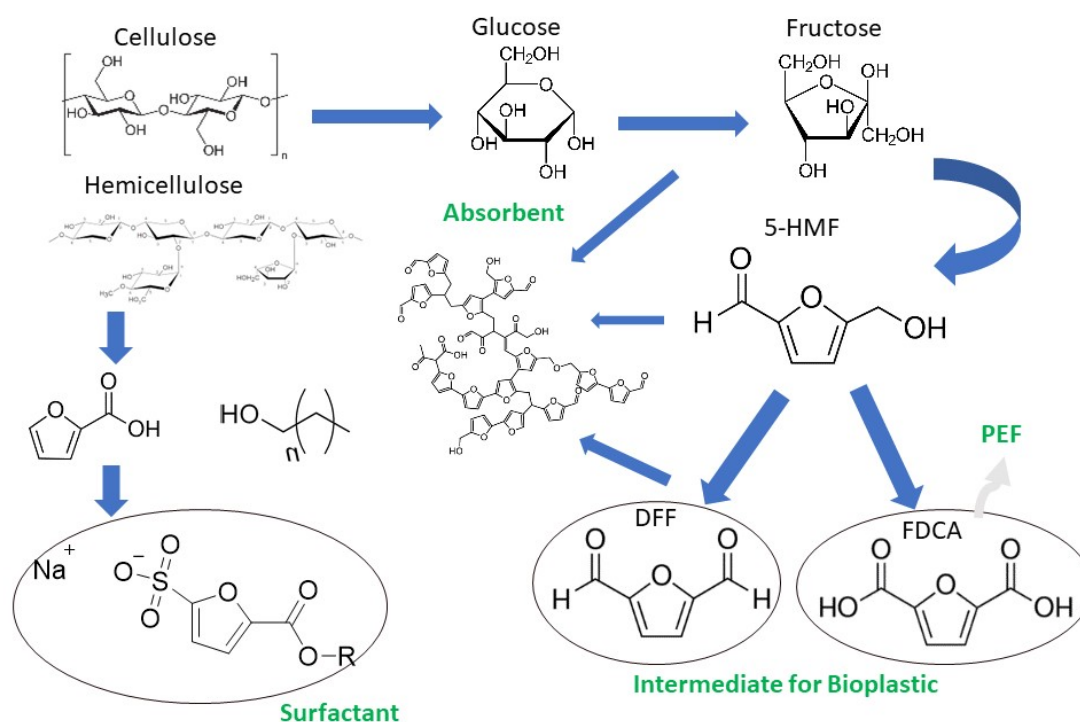
Figure A. 49 H-NMR Sulphonated headecyl furoate	227
Figure A. 50 C-NMR sulphonated hexadecyl furoate	228

List of Tables

Table 2.1 Degradation of different furanic compounds in different [OTf] ⁻ and Cl ⁻ ionic liquids at 120 °C (6 h)	65
Table 2.2 HMF assignments of the IR spectra peaks based on study reported in litterature. ¹¹	66
Table 2.3 Extraction of Pb (100 ppm) from water with humins. Conditions: 20 °C, 0.1 % humins loading respect the solvent, pH 4.	74
Table 3.1 DFF recovered by sublimation at 100 °C under reduced pressure, 10% DFF loading respect the solvent, 12 h.	90
Table 3.2 Energy requirement for the drying of ILs until 1% water content in 4-stage evaporators with a final pressure of 0.01 bar. Calculations were performed using Aspen Plus 8.8V with the IULAM integrated package.	94
Table 3.3 Esterification of FDCA with ethylene glycol using different ionic liquids and catalysts. Temperature 180 °C, FDCA concentration 12.6 mg/g in ionic liquid. Ethylene glycol to FDCA ratio 100:1 (mole). Catalyst loading 10%.	96
Table 3.4 Solubility of hydrophobic ionic liquids in water.	100
Table 3.5 Solvent design guidelines for the separation of DFF, FFCA, FDCA and HMF from ionic liquid media.	101
Table 4.1. Effect of the cation on HMF yield from fructose in different ILs. Reaction conditions: 14% fructose loading, T = 100 °C, t = 10 min, 10% HCl loading, 3.5% water content.	120
Table 5.1 Different catalytic systems for alcohol oxidation reported in literature	137
Table 5.2 Yield (HPLC) of the oxidation of 5-HMF at 40% (mass) loading in the reaction mixture using TEMPO/CuCl/pyridine as the catalyst system. Data shown are the average of 3 repeat experiments.	142
Table 5.3 Recycling experiment in [bmim][NTf ₂] with [TEMPO-bmim][NTf ₂] (5 mol% respect HMF), [bbpy][NTf ₂] (5 mol% respect HMF) at 40% 5-HMF loading respect the solvent and 5 mol% CuCl catalyst loading respect HMF. Conditions: 80 °C, O ₂ balloon, DFF separation through sublimation under vacuum. Results are an average of 3 experiments.	144
Table 5.4 Effect of time on product selectivity. Reaction conditions: 5 mol % loading of CuCl/[bbpy][NTf ₂]/TEMPO-[bmim][NTf ₂] compared HMF, 10% HMF loading respect the solvent , 80 °C, 1 bar.	145
Table 5.5 Binding energies for different CuCl-ligand complexes.....	147
Table 6.1 Result of the oxidation of DFF and FFCA in [bmim][OTf] at room temperature, atmospheric pressure and 10 min. Substrate loading 10% mass respect the solvent. Catalyst loading 1% mol respect the substrate.....	162
Table 6.2 Evaluation of the basic sites derived from TGA analysis	165
Table 7.1 Performance of different furan derivative surfactants evaluated by Daunhaur and co-workers	176

Table 7.2 Score corresponding to the appearance of the liquid. Opalescent is a non-clear solution but through which objects can be seen. Cloudy is a non-clear solution through which objects cannot be seen.....	181
Table 7.3 Mean stability table.....	182
Table 7.4 Physical properties of octanol and octyl furoate.....	184
Table 7.5 Results of solubility tests for different surfactants.....	186
Table 7.6 Results of hard water stability tests.....	186
Table 7.7 Calculated CMC for different surfactants.	188
Table 7.8 Comparison of the properties of tested surfactants and those of Dauenhauer and co-workers.	189

Chapter 1 Introduction



Over the years the chemical industry has evolved to meet different social, environmental and economic needs which resulted in major investment in research and development focused on developing chemical processes at high yield, low energy and reasonable costs. Moreover, the occurrence of major incidents combined with the rising awareness of issues with CO₂ emission in the last 30 years led to a strong involvement of governments and institutions which have implemented regulation on emissions, waste disposal and incentives for green technologies.

To date, most chemicals and fuels are produced from fossil feedstocks with processes which are long established with little room for improvement in terms of process development. Environmental concerns have resulted in stricter legislation to encourage the usage of renewable feedstocks and the development of sustainable green processes. In this matter, huge challenges must be addressed to substitute efficient processes at large scale with new economically competitive ones that are simultaneously more environmentally friendly.

This thesis will discuss different pathways to valorise biomass into valuable furanic chemicals which are outstanding candidates to replace a large variety of fossil derived ones, with applications in

plastics, detergents and adsorbents in wastewater treatment. The main focus will be on the biomonomer 2,5-furandicarboxylic acid (FDCA), which represents the building block for the bioderived plastic polyethylene furanoate (PEF) as a replacement for PET in the food and packaging sector. Challenges will be described and potential solutions provided to current problems which have hindered the application of these biochemicals so far.

Chemical Industry: Past and Present

The chemical industry has seen huge development in the last century, impacting on every type of application from everyday life to industry. Organic and inorganic raw materials are converted into products for consumers or intermediates for other industries. Organic material feedstocks belong to two different categories; fossil fuels and biomass. During the 1800s and 1900s, coal represented the main feedstock for fossil fuels, especially in Europe, and it was used mainly for energy production for transportation and mining. In the beginning of the 20th century, thanks to the development of novel oil extraction technologies, oil (also known as petroleum) started to be used as feedstock, proving to be more efficient than coal in terms of energy production and chemical synthesis, although coal processing continued to experience high activity by countries that couldn't access oil reserves (e.g. Germany). Thanks to oil, the chemical industry experienced tremendous development by opening new areas (e.g. plastics and detergents) and innovation in the pharmaceutical industry, consumer products and agriculture.¹ As can be seen in Figure 1.1 (left), coal consumption dominated until the 1950s when crude oil refineries started to be established worldwide; in the 1960s oil started to become the dominating feedstock over coal and natural gas. While the graph shows the total consumption of each category of feedstock, it does not elucidate how it is consumed. Indeed, of the total fossil fuel production, only a small fraction is not combusted. In the US, of the total amount of fossil fuel production, 93 % is used to satisfy heat and power demand for industry and consumers, while only 7% is intended for non-combustion uses.²

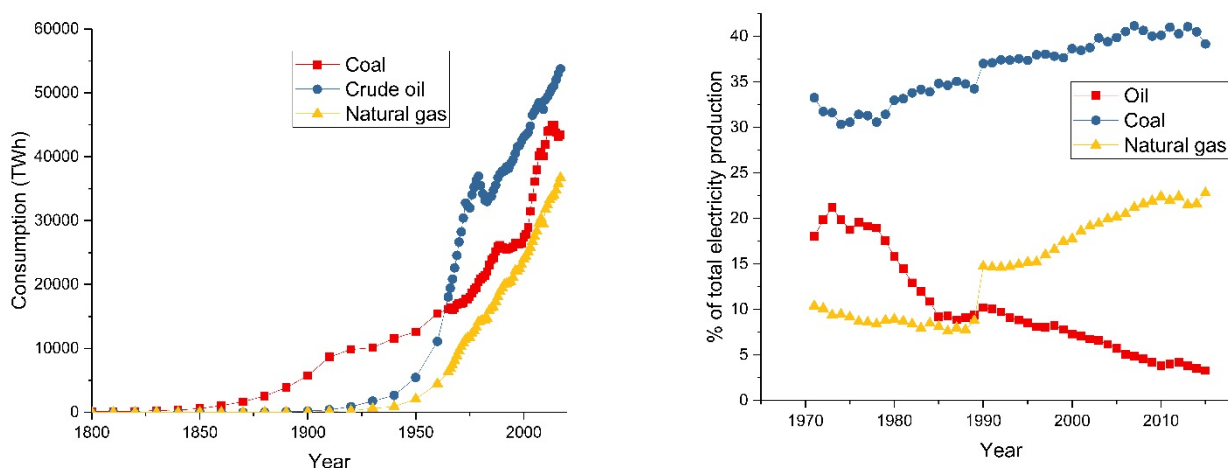


Figure 1.1 Global fossil fuel consumption from Our World in Data <https://ourworldindata.org/fossil-fuels#coal>

Fossil fuels today represent 66% of the total electricity production (the remainder is supplied by nuclear and renewable technologies); of this share coal contributes more than half (45 % in 2014) with the major producer being China with over 50% of the coal demand. For electricity production, coal is followed by natural gas (22%) and finally oil (4%).³ Oil contributes only a small part to the global

electricity production since the greatest part is used in transportation where it is burned as heat source to produce power for the vehicles. As can be seen in Figure 1.2, over 60% of the oil consumption is intended for transportation, of which a negligible part becomes electricity and, considering that transportation is the primary energy consuming sector by volume, oil represents the most important of all the energy feedstocks.

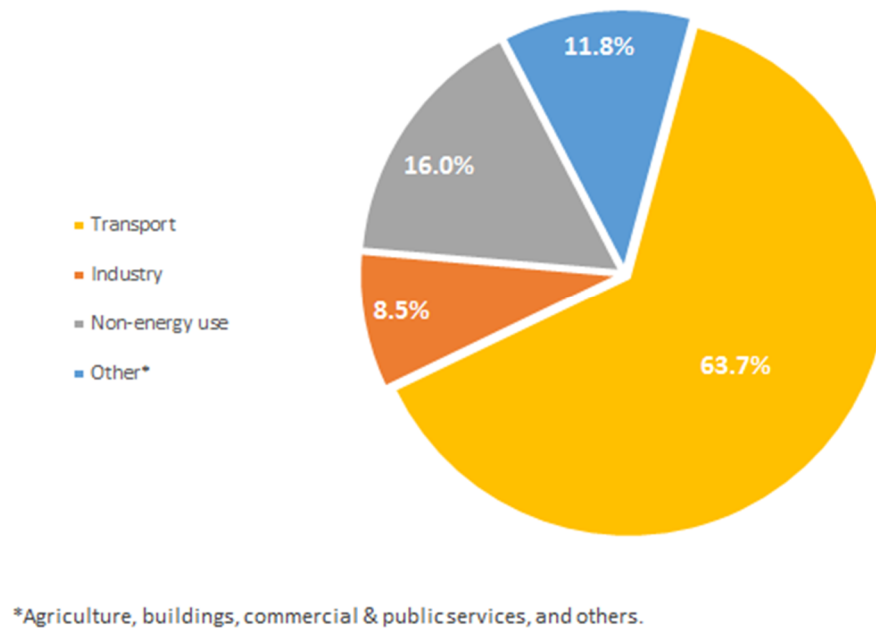


Figure 1.2 Crude Oil consumption by sector in 2012 (from <https://www.globalpetrolprices.com/articles/39/>)

The reserves remaining for the future show a different trend. Coal reserves are projected to last for 107 years, natural gas for 35 years and oil for 37 years⁴ based on current consumption trends. However it should also be taken into account that natural gas reserves are affected by Exploration & Production investment, which has increased over the years and new large reserves are constantly being found (e.g. ENI's Zohr field in Egypt) and new technologies implemented (shale gas technology) increasing drastically the prospects for the usage of natural gas.⁵ Even if fossil fuels have contributed to developing the chemical industry and reducing the price of energy and many consumer products, their limited reserves and the concomitant CO₂ emissions have illustrated the need to seek alternative resources that can partially replace fossil fuels. CO₂ produced from burning fossil fuels accounts for about three quarters of annual greenhouse emissions (GHG). Uncontrolled use of fossil fuel with the consequent emissions of GHG can lead to drastic and dangerous consequences. Different scenarios have been studied, resulting in the Paris Agreement, where a commitment has been reached to limit the temperature increase below 2 °C by the end of this century, with efforts being made to limit it to 1.5 °C.^{6,7} Moreover, further increase in energy demand by 50% in 2050 makes both environmental issues

and limited resources major concerns for sustainable economic growth.⁸ Alternative renewable sources and socio-economic models need to be studied to reduce the dependency on fossil fuels. Governments have devised incentives for the development and implementation of new green technologies. Important goals have been reached in Europe where in 10 years the renewable energy production increased by 67% accounting today for more than 30% of the total energy production, shutting down many traditional fossil-based power plants.⁹ In the transportation field, bioethanol has become one of the major players as a fuel blend to increase the octane number of gasoline by replacing the oil-derived methyltertbutyl ether (MTBE).¹⁰

How the chemical industry is structured and the role of biomass

In recent years, major concerns have been directed at the energy sector and no specific directives have been issued for chemicals even though partial replacement can provide a huge contribution to reducing carbon emissions.¹¹ The potential to expand the biomass share in the energy and chemical sector relies on the facile growth of lignocellulosic plants and availability of waste biomass products in agriculture which do not impact the food chain.¹² The US Department of Energy has seen in biomass a huge potential in replacing transportation fuels using its agricultural and forest resources without impacting the food chain.¹³ However, the sustainability of expanding biomass production to a large volume have to be taken into account since drastic impacts may be felt in water consumption and biodiversity.¹⁴

In the beginning of the 20th century, biomass was one of the main feedstocks for energy and chemical production. Since the mid-20th century the development of technologies for chemical upgrading naphtha has completely overtaken the chemistry of other feedstocks and is still the dominating technology today.

The large-scale synthesis of chemicals can be depicted in the form of a tree-type diagram. Over 80% of chemicals are produced by base chemicals (in total there are around 20) produced from raw materials such as oil, natural gas and coal. Some of these base chemicals are directly produced in the refinery as ethene, propene and butadiene as distillation products of crude oil or by integrated catalytic processes such as steam cracking and dehydrogenation. Others, such as synthesis gas and ammonia, need further chemical processing to be obtained and they are usually produced in facilities outside the refinery (BTX, ammonia and methanol). From these base chemicals, over 300 chemicals can be synthesized as intermediates and these can be used as direct consumer products (acetic acid, formaldehyde, ethanol, etc) or intermediates for other products (terephthalic acid, ethylene oxide, urea etc.). These base and intermediate chemicals cover most of the chemical market and their process feasibility is strictly related to the volume produced; for this reason they are called bulk chemicals. The intermediates are further processed to produce speciality chemicals for specific applications such as solvents, plastics, detergents, pharmaceuticals and insecticides. In optimising the base chemical production, the choice of the feedstock plays a crucial role. Originally coal was the main source to produce aromatic base chemicals called BTX (benzene, toluene and xylene) through pyrolysis, while nowadays 96% are produced from petroleum feedstocks through catalytic reforming of C₅-C₁₀ oil fractions since this approach is more selective and less energy intensive.¹⁵

An approximate idea of the large variety of chemical routes used is depicted in Figure 1.3.

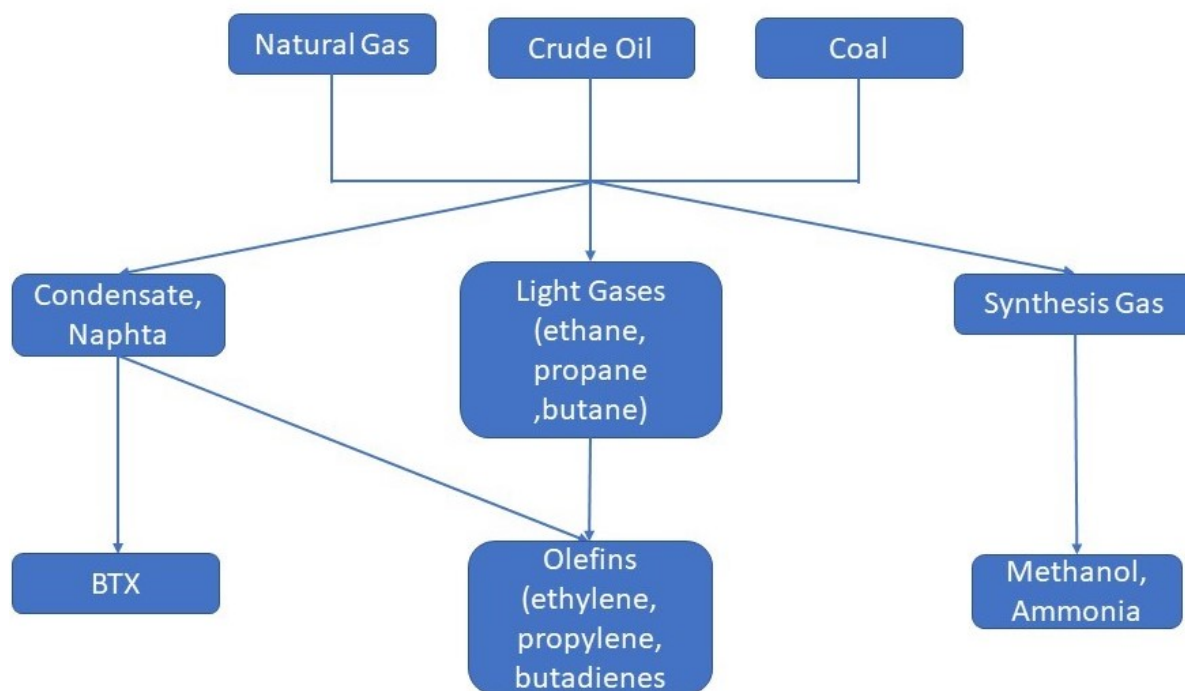


Figure 1.3 ‘Chemical tree’ for the production of bulk chemicals from fossil fuel feedstocks

The branches in Figure 1.3 are further developed through the production of many different chemicals for different applications as plastics, pharmaceuticals, solvents, fertilizers, dyes and many others. Notwithstanding the large differentiation of chemicals, the total amount of chemical output is just a small percentage of the total refinery output (7%), while the rest is used as fuel for transportation. However, these chemicals represent a good source of revenue since they add higher value compared with fuels.¹⁶

In this context, where fossil fuels dominate the chemical industry, the introduction of new technologies based on renewable sources is challenging in terms of process economy and volume production. Biomass is a good candidate to partially replace fossil fuels but the chemical routes to arrive at valuable products still need to be fully developed and fewer chemical routes are currently available for this purpose.¹⁷ However, the incentives to expand the biomass fraction in this field have increased recently thanks especially to the development of new technologies capable of processing lignocellulosic feedstocks which do not impact the food chain. The chemical processes to upgrade biomass into valuable products are referred to as a biorefinery.¹⁸ Here the main constituents of biomass, cellulose, hemicellulose and lignin are fractionated for further processing. Different technologies are commercially available, such as steam explosion, ammonia explosion and dilute acid pre-treatment. Recently ionic liquid pre-treatment technologies have proven promising for the production of cellulose and lignin in high purity.¹⁹

For many years, lignin has attracted interest as a valuable potential source of BTX through hydrocracking which can replace the oil derived option, notwithstanding the high R&D efforts and

different trials performed so far, scale-up of this process has proved to be economically uncompetitive or inefficient due to the low theoretical yield of BTX that can be obtained from lignin.²⁰ For this reason, the burning of lignin is preferred to supply energy to the biorefinery itself and sell the excess as electricity or use it as a feedstock in niche applications.²¹

On the other hand, cellulose represents a valuable feedstock to produce liquid fuels and chemicals besides being itself used as polymers for a large variety of materials.²² Sugars derived from cellulose are key feedstocks for many chemical reactions. The production of sugars from cellulose is an established process and many different chemicals beyond biofuels can potentially replace petrochemicals.¹⁸ They represent the substrate for bioethanol production which today, thanks to government incentives, dominates over the ethanol derived from fossil fuels. The use of biomass derived feedstocks can contribute to replacing the capital and energy intensive processes of the refineries to convert hydrocarbons to oxygenated functionalised compounds (alcohols, aldehydes, carboxylic acids, etc.) since oxygenated compounds (such as sugars) are more suitable feedstocks for these purposes.²³ Important targets were set by the EU in the Renewable Energy Directive (2009/28/EC) that states that ‘the European Council of March 2007 reaffirmed the Community’s commitment to the Community-wide development of energy from renewable sources beyond 2010’. It endorsed a mandatory target of a 20% share of energy from renewable sources in overall EU energy consumption by 2020 and ‘a mandatory 10% minimum target to be achieved by all Member States for the share of biofuels in transport petrol and diesel consumption by 2020, to be introduced in a cost-effective way’. The interest in the biofuel market was thus boosted in the EU but, while specific targets were set for biofuels, none was set for biobased chemicals. For these, more specific goals were set by the US Department of Energy, which specified that 30% of liquid fuels and 25% of organic chemicals must be replaced by sustainable feedstocks, however this target has been difficult to achieve. Indeed, while technologies to valorise biomass feedstocks into biofuels are now established, in the biobased chemicals field substantial investment in R&D has been made but little commercial activity exists at present. The Final Report for the European Commission Directorate-General Energy made by a consortium led by E4tech, Record and Wageningen²⁴ identified 94 green products, ranging from chemicals to biofuels and polymers, that can be derived from sugars obtained from the pretreatment of sustainable biomass feedstocks. These can replace the majority of all oil derived chemicals and represent an energy saving not only in terms of CO₂ emissions from the replacement of fossil fuel feedstocks, but potentially also in process economics since most of the chemical routes studied are biological and chemoenzymatic, which are less energy demanding compared to those based on petrochemical pathways.

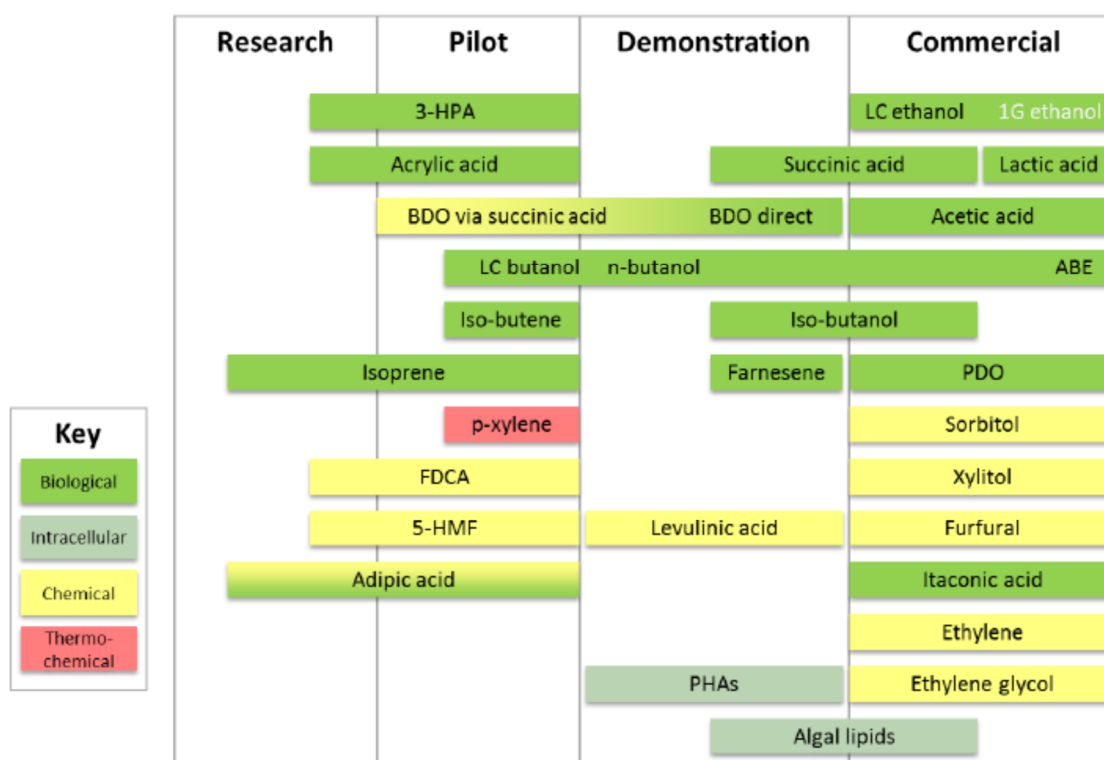


Figure 1.4 Twenty-five biobased chemicals which can substitute most of the oil-derived products and their development status²⁴

Sugars that can be converted into valuable products include glucose, fructose, galactose, xylose, arabinose, ribose, lactose, sucrose and maltose. From the 94 products that can be obtained from these sugars, only 25 chemicals are selected as promising for large-scale prototype that can be tested in the intended environment in a pilot plant. The commercialization status of these chemicals and their synthesis routes are shown in Figure 1.4. These are all chemical intermediates capable of substituting a large variety of petrochemical products, hence referred to as green chemicals.

In terms of commercial impact, lignocellulosic (LC) ethanol has seen major development in the last decade and has been considered as the only sustainable feedstock for ethanol production (replacing starch).²⁵ Large investment and subsidies have been used to increase the commercial market of this fuel because carbon neutrality and transportation costs can be minimised thanks to the ability of these crops to grow on any land.²⁶ This has favoured the development of different technologies for pretreatment of biomass for the production of sugars at high yield that can be fermented into ethanol. So far steam explosion proved to be a valuable technology for the high yield sugar production from biomass and a 40,000 ton/year operating plant was built in Crescentino (Italy).²⁷ The development on a large scale of LC ethanol has permitted the spread of green ethylene and ethylene glycol obtained by the dehydration of ethanol,^{24,28} which provides the basis for the production of a large variety of chemicals exploiting the well-known chemical processing of ethylene and the large scale utilization of ethylene glycol to form polyesters. Other biochemicals produced at large scale are 1,3 propanediol and succinic

acid which, thanks the development of genetically modified microorganisms, they can be produced from sugars replacing the routes which uses fossil derived chemicals.^{29,30}

While ethylene and ethylene glycol can be used to produce green polymers and intermediate chemicals, the substitution of BTX is much more challenging. Furan derivatives from sugar dehydration are a valuable option that can replace most of the oil-derived compounds. One of the main green compounds that in the future is expected to gain more importance is furfural. This is currently already commercialized on a large scale by the dehydration of hemicellulose, which is an extremely low cost feedstock from lignocellulosic plants.³¹ Another high-value molecule derived from cellulose is 5-HMF. Its multifunctional chemical structure has attracted much attention since it has the potential to undergo many reactions that can produce both chemicals and fuels.³² A depiction of the large variety of chemicals^{33,34} that can be obtained from both furfural and HMF is shown in Figure 1.5.

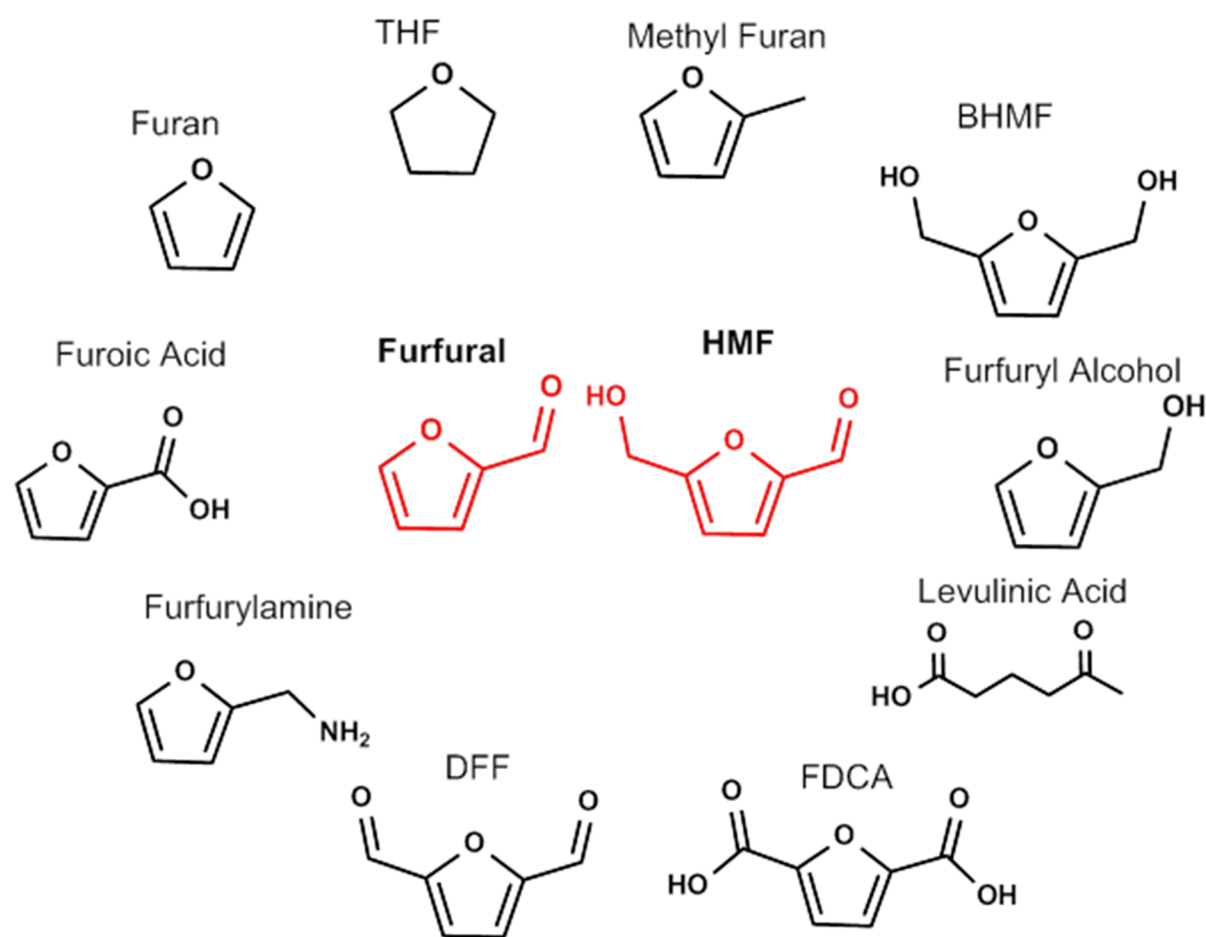


Figure 1.5 Chemicals that can be obtained from Furfural and HMF

While furfural synthesis is relatively easy, the chemical routes to arrive at 5-HMF from sugars still have to be fully established.³⁵ A lot of research has been done toward this purpose, yet no processes have proven to be efficient enough for scale-up. The difficulty in this route lies in the thermal and

chemical instability of 5-HMF, which limits the process conditions. Commercial plants are still at pilot scale: BASF has built a pilot plant of 20 tons/year at a purity of 99.9%.²⁴ This represents a very small scale compared to the actual 5-HMF potential in the market. Indeed, as an intermediate product it has to be commercialized on the order of 40,000-100,000 ton/year to be process efficient and actually to be able to compete in the market.

The most valuable chemical compound that can be produced from furfural and HMF is 2,5-furandicarboxylic acid (FDCA), the base monomer for the synthesis of the bioplastic polyethylene furanoate (PEF), and this will be discussed below.

PEF, a green substitute for PET

Polyethylene terephthalate (PET) is one of the most popular polyester resins with major applications in food and beverage packaging and clothing. It accounts for about 8% of world polymer production and is the 4th most produced polymer. In the last 30 years, the development of technologies for the polymerisation of PET to obtain high molecular weight polymers allowed the expansion of this material in different applications especially in the beverage sector, substituting glass bottles.³⁶ Advantages of PET are its low weight, low cost, low gas permeability, transparency, resistance, malleability, resistance to high temperature, recyclability and easy disposal (it can be burned). As such, it can be classified as a 'first class' polymer with outstanding balance between properties and cost.

The synthesis of PET involves the polycondensation of terephthalic acid (TA) and ethylene glycol (EG). While today there is a gradual replacement of oil-derived EG with greener EG, the substitution of TA has always proved to be challenging and much research has been done in the last 20 years to find an efficient chemical route that can be competitive.³⁷ TA today is produced from oxidation of the BTX derivative *p*-xylene through aerobic oxidation with the Amoco Mid-Century catalyst. This catalytic system consists of a mixture of Mn and Co salts using acetic acid as solvent. The success of such a catalytic system lies in the advantages of using a homogeneous catalyst with a product which is easy to be separated since it is insoluble in the reaction mixture. Moreover the system proves to be recyclable, high yield and uses a cheap catalyst.³⁸ The efficient synthesis of this molecule allows scale-up to large volumes, providing a cheap starting material to produce the polymer, making its substitution very challenging. Recently it has been announced that a TA plant facility at Corpus Christi (US) will be built with a capacity of 1.2 million ton/year with an integrated PET line of 1000,000 ton/year.³⁹

FDCA represents one of the premier candidate to substitute TA for the synthesis of a polymer in the food and beverage sector. The polymerization of FDCA with EG gives PEF, a polyester with superior properties compared to PET in terms of gas permeability. It has been estimated that the substitution of PEF with PET can save up to 50% of carbon emissions related to the life cycle of PET. The market competitiveness of PEF is strictly related to the price of FDCA which is currently estimated to be over \$2/Kg which is considered prohibitive compared with TA (\$1-1.3/Kg).⁴⁰ Moreover, no commercial FDCA plants exist and it is produced only in small batches since no technologies have been developed that can produce this molecule on a large scale. The main reason lies in the chemical downstream process to produce FDCA passing through the molecule 5-HMF according to Figure 1.6. The isolation of 5-HMF at high purity and yield has represented the limiting step for the techno-economic feasibility of FDCA since the cost for HMF isolation and synthesis are high. In order to be competitive, the price of HMF should be similar to that of *p*-xylene (\$0.9-1.1/Kg) and it is currently not close to that value. Avabiochem is the only company currently producing 5-HMF from fructose,

however, it recently announced that only unpurified HMF (88%) will be commercialised, making it unsuitable for conversion to FDCA.

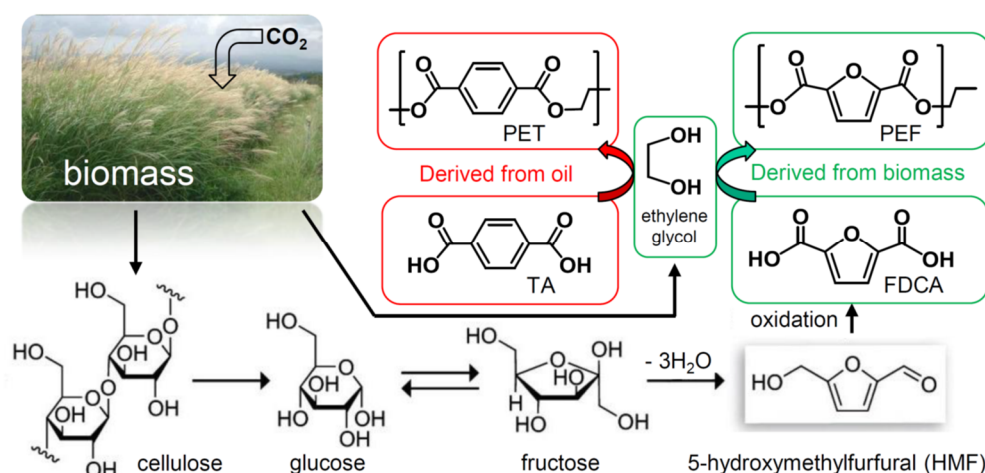


Figure 1.6 Chemical route to arrive at FDCA and PEF from lignocellulosic feedstocks

In recent years, various companies have announced the development of FDCA pilot plants. Avantium and BASF signed a joint venture for the development of the YXY technology at a production of 50,000 ton/year of FDCA by 2016 and 300-500 ktons/year by 2018 at a competitive price < \$1000/Kg from starch feedstock supplied by Cargill (Weastra 2011). However, BASF recently backed out due to technology issues, reducing the chances that the project will be completed.⁴¹

A market report by consulting firm Weastra⁴² has shown the market potential of FDCA in the future and the cost targets that such a chemical has to reach to be feasible and competitive. Today the total production of FDCA is between 3.5-5 tons/year for a total market value of \$10 million. The sample price for the purest FDCA is currently over \$2,300/Kg, which is not feasible compared to that of terephthalic acid. Weastra has estimated that the total FDCA addressable market is \$50.5 billion/year. The target price that Weastra has set for FDCA to be competitive is \$1/Kg to replace all its chemical competitors (terephthalic acid, bisphenol A, adipic acid, phthalic anhydride). The FDCA market is expected to increase to 498,617 tons in 2020 with an economic value of \$498 million. The PET market looks the most accessible for FDCA with an addressable market of \$43 billion from \$55 billion. Other potential market areas identified by Weastra are adipic acid, phthalic anhydride (used in plasticizers) and bisphenol A (used in polycarbonates).

The chemical routes to produce the different chemicals in Figure 1.5 require new catalysts and process conditions to obtain high yields to make the process economically feasible. Challenges lie in the stability of furanic compounds under harsh conditions (substrate loading, high temperature, acidic conditions) since they are affected by side reactions such as cross polymerization forming undesired side products such as humins, which make the conventional petrochemical processes unsuitable for this purpose. In developing a new chemical process, care has to be taken to make sure that the production

of new chemical compounds is done in the most sustainable way with minimal impact on the environment. Focus must be given to the energy demand of the plant and resources required to process the feedstocks. In the next section, the requirements will be outlined for a process to be defined as 'green' since 'green feedstocks' does not necessary imply 'green products' if not synthesized in a sustainable way.

Green Processes: a critical approach to the 12 principles of green chemistry

Beside the use of renewable feedstock, the process economics and sustainability depend on other criteria that cannot be neglected if the goal is to establish a completely green process. Most importantly, safety is the main criteria to be considered when developing a chemical plant with consideration to both human health and the environment. Since a chemical plant needs to process enormous amounts of chemicals every year, its impact on the environment can be significant if the resources are not exploited properly and emissions and waste not controlled. Moreover, accidents in chemical plants can result in catastrophic damage leading to loss of life and environmental pollution according to the chemicals used. Utility consumption, solvents, recyclability, waste generation, and safety are the main factors to be taken into consideration in the design of a new chemical process. The American Chemical Society published “The 12 principles of green Chemistry”⁴³ which represents the basis for evaluating a process:

- 1) **Prevention.** In choosing the chemical route to arrive at the final product, the preferred route is the one that reduces the waste generated per Kg of product (E-factor). Examples of such principles are the pharmaceutical companies whose processes can produce up to 100 Kg of waste per Kg of product, raising concerns in both process economics and environmental impact. More sustainable chemical routes need to be considered to reduce waste disposal;
- 2) **Atom economy.** In part related to the first principle, research should focus on finding chemical routes which incorporate all the reactants in one desired product, accomplishing a more sustainable usage of the resources, preventing waste.
- 3) **Less Hazardous Chemical Synthesis.** The synthesis should focus on preventing hazardous chemicals or conditions which on a large scale can lead to harmful events.
- 4) **Design Safer Chemicals.** Different molecules can have the same chemical function. Research should be oriented to those chemicals that are safer, especially with lower impact on human health and the environment. Toxicology of the compounds used should be strictly evaluated.
- 5) **Safer Solvents and Auxiliaries.** The use of these should be minimized or made innocuous. Most organic solvents are known to be toxic and flammable and yet they account for 50-80% of the total mass in standard batch chemical plants.⁴⁴ The use of solvents can increase the cost of the chemical plants by increasing the pumping and heating expenses due to higher flow rate and penalties due to the safety issues related to plant operation due to their flammability. However, they are needed for many chemical reactions to ensure high selectivity, high mass/heat transfer and in some case they can improve the safety of the chemical reaction by diluting explosive or pyrophoric compounds. Research should be oriented toward replacing

organic solvents with non-flammable and non-toxic solvents such as ionic liquids and deep eutectic solvents. This aspect will be examined later.

- 6) **Design for Energy Efficient processes.** Work at lower temperatures if possible.
- 7) **Use Renewable Feedstocks.** Carbon neutral feedstocks should be a priority even if considerations need to be made regarding their excessive exploitation. In this matter, a good summary is given by Cséfalvay et al.: “Resources including energy should be used at a rate at which they can be replaced naturally and the generation of waste cannot be faster than the rate of their remediation.”⁴⁵
- 8) **Reduce Derivatives.** Protecting groups and temporary modification of the physical chemical properties of the compound (extractive distillation) should be avoided because this compromises the E-factor;
- 9) **Catalytic routes should be prioritized.** Stoichiometric reagents for some chemical reactions (such as oxidation and hydrogenation) can generate huge amounts of toxic waste. Alcohol oxidation with permanganate generates huge quantities of toxic by-products, which are difficult to dispose of, undermining safety and E-factor. For example, catalytic aerobic alcohol oxidation with a catalyst represents a superior alternative since it uses oxygen from the air and produces only water as a by-product;
- 10) **Design for Degradation.** The chemical products should degrade at the end of their function. This concept is strictly related to biodegradability. Accumulation of chemical substances in an environment can cause huge damage to an ecosystem. Furan rings can be degraded much more easily than benzene rings and they retain most of the physical properties;
- 11) **Real-Time analysis for Pollution Prevention.** In chemical plants, monitoring of the emissions and process conditions should be in place. In recent years process instrumentation has been developed considerably by the introduction of Digital Control Systems (DCS) in most chemical plants. Control of the emissions needs to always be in place in units such as incinerators to control unreacted chemical compounds. Strict limits are placed on the use of Volatile Organic Compounds (VOC). For example, dimethyl carbonate is preferred as a solvent compared to ethyl acetate since it is not subjected to VOC legislation;
- 12) **Inherently Safer Chemistry for Accident Prevention.** Chemicals should be handled in a way that minimises chemical accidents (fire, explosion, uncontrolled release).

The application of all of these principles to a chemical process can make the environmental impact negligible and so they represent key features for researchers to improve or create new areas in the chemistry field. However, these principles have been strongly criticized by Winterton and other authors since they do not take into account many factors which, on a large scale, have different impacts.⁴⁶ Further considerations around these ‘12 Principles’ are described below:

- According to the principles, the processes that best reflect all 12 principles are biological ones. Microorganisms and enzymes require water as a solvent (which is considered a green solvent), they work at low temperatures and they are highly selective, minimising the energy requirements. However, their kinetics lie far away from those of a high temperature catalytic process since microorganisms generally grow very slowly. Scaling up an enzymatic technology can result in excessive equipment costs and the need for huge amounts of land. This is a huge drawback considering that one of the key parameters for bulk chemicals is the throughput of product per m^3 of reactor. Indeed, a chemical catalytic process is capable of processing over 10,000-1000,000 m^3 of feedstock per 1 m^3 of reactor. This is mostly due to the high turnover number of metal catalysts that have been developed in the last century, where stability, activity and selectivity are parameters that have been largely optimised in most of the catalytic processes. An enzymatic process is far away from achieving these numbers and they also often suffer deactivation.
- The chemical industry has evolved to place more emphasis on optimising waste and turning it into useful by-products, increasing the profitability of many processes and reducing costs associated with waste disposal. As an example, the production of acetone and phenol proved to be successful with the cumene process where cheap starting materials such as propylene and benzene with oxygen can simultaneously produce both products. On the other hand, processes with better atom efficiency, such as the Wacker process to produce acetone selectively can seem more in line with the 12 principles of green chemistry (principle 2), but this neglects the operational challenges of operating on a large scale such as corrosion from the catalyst, recyclability and profitability.
- One of the major gaps in the 12 principles is the utility usage and how this can influence the environmental impact of the plant. Energy balance is a big issue. This concept has become more and more important over the years and different technologies have been introduced to maximise the heat recovery in chemical processes. An ideal reaction should be carried out at low temperature (principle 6) but this obscures enormous related side effects. The use of high temperature in chemical processes does not necessarily mean high energy expenditure. Irreversible exothermic reactions can be run at high temperature and recover the heat to satisfy the internal energy requirements as well as allowing the excess to be sold as electricity. As many chemical processes can work as power plants by exploiting the heat of reaction produced in the reactor (e.g. sulfur oxidation) to produce steam to power turbines. Moreover, high temperatures also mean fast kinetics, lower reactor volumes and energy savings for separations.
- The CO_2 savings from processing a carbon-neutral feedstock can be seen in different ways. Biomass is an abundant cheap feedstock that can potentially replace fossil fuels. However, the environmental impact that can result from producing such large amounts of biomass can be

catastrophic in terms of the amount of land, fertilizer and water needed, impacting strongly on the food chain and animal ecosystem. Moreover, transportation of such low energy density feedstocks can result in much more CO₂ consumption compared with transporting the equivalent barrel of oil.

According to these considerations, the 12 Principles are a good guide to classify a chemical route according to its environmental impact, but they should always be viewed in a critical way since they lack quantitative analysis on how toxic or how green a process is. This analysis should be supported by a Life Cycle Assessment (LCA) where all the stages of the product life of raw material extraction (oil, mining), processing, manufacturing, distribution, transport and disposal are considered. LCA provides a more quantitative output compared with the 12 Principles and represents a rigorous study of the environmental and human impact of a technology.

Defining the sustainability of a chemical plant is a complex task since many different parameters need to be considered. A high level of sustainability can be achieved by improving existing processes or processing the same feedstock in a different way. Hence research should not only be focused towards chemical routes that satisfy all the 12 principles of Green Chemistry because many factors will be neglected, resulting in a process which will never be applicable. A great example can be seen in the sulfuric acid plants where a combination of catalyst design and process design allowed the reduction of SO₂ emissions to undetectable limits, while maintaining high catalyst stability at moderate conditions. BASF has invested in a process to produce H₂ and hydrothermal carbon from methane by thermal cracking using renewable energy, making a cheap fossil feedstock clean and carbon neutral combined with a solid carbon which can replace coal in the steel industry.⁴⁷

Much research should be focused on improving already existing processes by developing new catalysts, new methods to optimise separations, optimise waste disposal and usage of byproducts, and better study the toxicology of the compounds involved. All this is focused on a general awareness of the danger that chemical plants have towards the environment.

In order to find an intermediate compromise between the 12 principles and their critics, we decided to reformulate the principles which define a sustainable realistic green process to allow a reduction in CO₂ emissions and reduce the impact to humans and the environment:

- a) **Prevention and atom economy.** High atom economy and E-factor should be optimised on the principle of minimising operating costs (including utilities) and reducing environmental impacts. In case multiple products can be produced in one step, the preferred route is the one with best process economy. In cases where the process suffers from side products, these need to be characterized and valorised;

- b) **Chemicals and reaction design.** The impact of chemical compounds can be classified through route of exposure (inhalation, skin contact and ingestion) and toxicity. Route of exposure should be minimized with priority on inhalation since vapours are generally more challenging to remove and can harm a large area and cause more casualties. Toxic compounds should be converted to less harmful ones at near quantitative conversion or high recycling with no purges (high selectivity).
- c) **Operating conditions.** High yield of reaction should be prioritized even if high temperatures are required with the condition that heat integration can be achieved or heat recovered to produce other valuable products (including electricity).
- d) **Feedstocks.** Renewable ones are preferred if they do not exploit excessive resources and impact the food chain. In this matter, lignocellulosic biomass is the preferred one since there is a lot of waste from agriculture which currently is flared.
- e) **Catalysis.** As mentioned previously, the usage of microorganisms for the synthesis of bulk chemicals as 1,3 propanediol, succinic acid and ethanol proved to be successful to replace oil derivative chemicals and they can provide a sustainable economically affordable solution. On the other hand, isolated enzymes are more expensive which associated with their instability and low kinetic make the operating and capital costs of the plant expensive. For bulk or intermediate chemicals, (usually inorganic) chemical catalysts or biological path which uses microbial community are more suitable. The catalytic path particularly allows to maximise the throughput of product per m³ of process unit thanks its higher resistance to temperature, maximising the kinetic therefor reducing the capital costs.
- f) **Design of safer chemicals.** Major focus needs to be given to consumer products where most of the chemicals are dispersed in the environment. Chemicals in this field need to be safe and compatible with the waste water treatment plants. It is desired that most of the organic products are anaerobically digested with high solubility in water to avoid formation of precipitates that will form sludge in the wastewater treatment (WWT).
- g) **Solvents.** In addition to these concepts, a solvent should provide not only modification of the chemical state of the compounds but also favour the yield of the reaction and product purification.

These are going to be the pillars upon which the following thesis will be focused. At the end of this chapter we will recall these principles applied to the aim of the thesis.

One of the main compounds which defines the sustainability of a chemical plant are the solvents. These constitute most of the chemical mass of the plant and represent the main compound

which could be released into the environment; therefore, solvent choices are crucial to reducing the health and safety issues of a plant.

Solvents in the Chemical Industry

Solvents are used in the chemical industry to change the physical state of a compound to favour chemical reactions. The most commonly used solvent in everyday life is water, the second most used are organic solvents. The choice of a solvent depends on many factors, some of which include the boiling temperature, toxicity and affinity for the compounds involved. In terms of process economics, organic solvents are more often used than water for different reasons, such as their lower boiling points, making product separation easier; a wide range of organic compounds are insoluble in water and water is often an undesired impurity that can lead to catalyst deactivation. The role of the solvent is manifold, giving high selectivity, allowing washing for product purification, safety and better handling.

About 20 million tons per year of organic solvents are produced and they find application in all chemical sectors. For the pharmaceutical industry the organic solvent composition can reach up to 85% of the solvent mass due to the need to obtain a high purity product.⁴⁴ The popularity of organic solvents is due mainly to their low price. Acetonitrile is a by-product of acrylonitrile production; the high demand of acrylonitrile and the large size of the chemical plants that make acetonitrile satisfy worldwide demand with only a few plants. Research into different chemical routes for the selective production of acetonitrile makes little economic sense. From 2008 to 2009 the shutdown of the only two chemical plants producing acetonitrile in China and Texas caused a worldwide shortage of acetonitrile, increasing its price drastically.⁴⁸ However, in order to reduce the human exposure to organic solvents which can cause harm due to their toxicity and flammability, much legislation has been put in place to reduce organic solvent emissions (Clean Air Act 1990 and European Union Solvents Emission Directive 1999/13/EC). Their high vapour pressure makes it difficult to control their emission and strict care has to be taken to treat vented gas in chemical plants making sure that it remains below threshold limits. In the EU and US, the Volatile Organic Compound (VOC) legislation defines the maximum amount in ppm that can be released into the atmosphere. One of the few organic compounds which is not subject to this legislation is dimethyl carbonate (DMC). Its exemption from this legislation classifies it as a green chemical compound and it has found widespread application in the paint industry as a replacement for MEK, *tert*-butyl acetate and *p*-chlorobenzotrifluoride even if its exposure through inhalation at high concentrations can lead to the same effects as methanol poisoning.⁴⁹

The use of organic solvents in industry makes chemical processing more demanding also in terms of CO₂ emissions since most of them are flared for energy generation after use rather than recycled since their recovery can be very energy intensive. In Figure 1.7, the emissions associated with the usage of different common organic solvents are shown.

Health and safety are important considerations. Solvent toxicity represents a danger for humans and the environment since potential accidents due to release, fire and explosion can arise.⁵⁰ Indeed, over the years, legislation has been put in place to regulate the handling of chemical compounds. In particular,

the volume of flammable and toxic chemicals cannot exceed a certain amount in a chemical plant including storage and process flowstreams. This and many other laws are in place to avoid major accidents such as the ones at Basel, Flixborough, Bhopal and Seveso. Experience from these scenarios has led to the chemical industry exploring different solutions in order to create effective health and safety measures in a chemical plant.

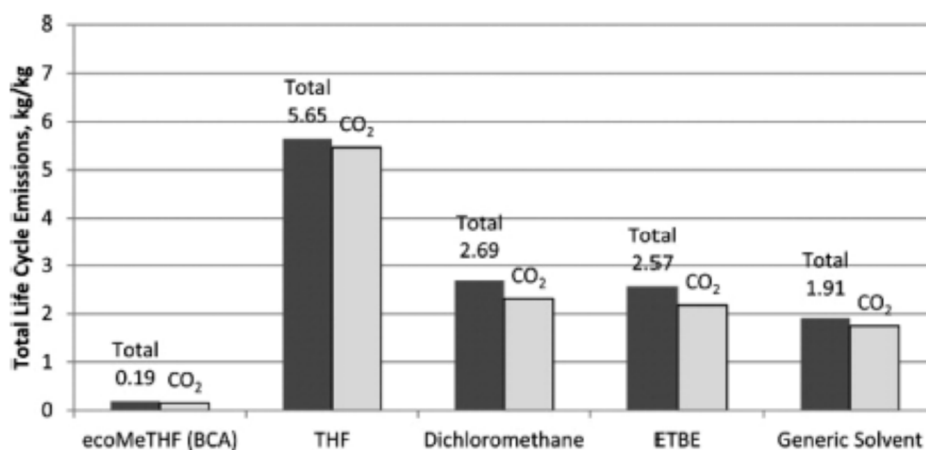


Figure 1.7 CO₂ emission associated with different organic solvents. Reproduced with permission from ref⁴⁴.

The implementation of new solvents in the chemical industry can lead to significant improvements in CO₂ emissions and health and safety, however changing the solvent can lead to a drastic impact on the commercial viability of the process since its choice will affect the material selection of most of the equipment in the chemical plant. Moreover, the choice of one specific solvent can favour one step but penalise other steps. An example of this is the Difasol process, where the application of ionic liquids in a large scale process is hindered by the capital cost of the equipment.⁵¹

A valuable procedure was proposed by Jin et al. (Figure 1.8), which identifies a useful methodology to evaluate the choice of solvent. The procedure uses the Kamlet-Taft parameters to compare the solvent properties. These are three parameters that take into account the hydrogen donating/acceptor and π -bonding ability of the solvent with specific reference molecules. By comparing these parameters, the solvents with the same parameters are the best candidates to substitute another toxic solvent. Further studies have to be performed to identify the physical properties and toxicology of the solvent with the implementation of a Life Cycle Assessment.

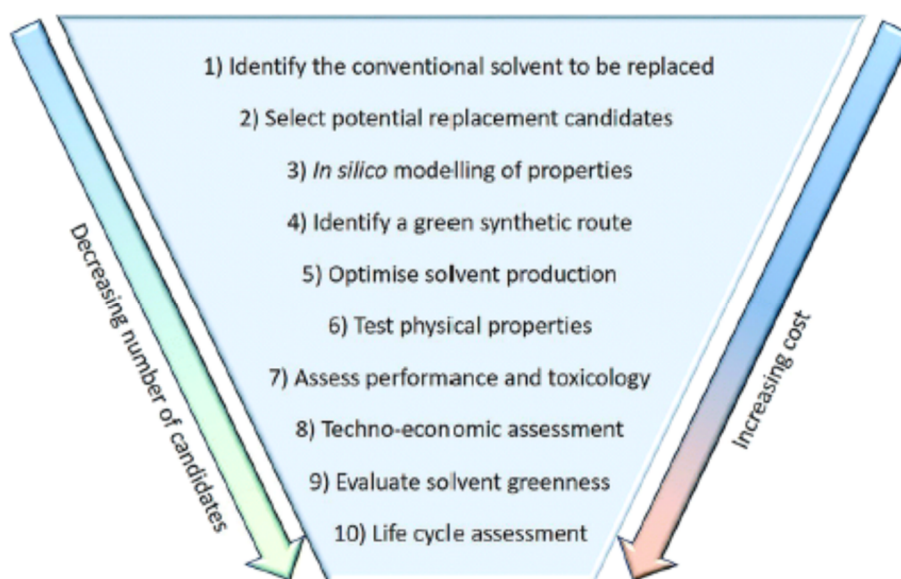


Figure 1.8 Method for the selection of a solvent for a defined application proposed by Jin et al. Reproduced with permission from ref⁴⁴.

Green organic solvents represent a relatively new development and strict guidelines are not yet available. In order to address these issues and rank the solvents based on their health and safety measures, many pharmaceutical companies and organisations have reported their own guidelines for solvent selection.⁵² Ethanol, acetic acid, gamma valerolactone (GVL), 2-MeTHF are considered green solvents since they are derived from biomass but their usage is still affected by their toxicity and flammability. Moreover, the associated costs for some of these solvents are still high.

Neoteric solvents are non-organic solvents that exhibit unique physical and chemical properties that can be exploited for reactions and separations. Examples of neoteric solvents are ionic liquids, deep eutectic solvents and supercritical CO₂. Their properties make them very attractive for implementation in chemical processes since they solve multiple problems associated with the usage of organic solvents, such as flammability and volatility, but careful consideration is needed for the high cost of these solvents, their disposal and toxicity.⁵³

The next section will focus on ionic liquids as valuable green solvents for the valorisation of biomass into FDCA and how their utilization in this field can satisfy all the criteria of a green process.

Ionic Liquids a Replacements for Organic Solvents for Biomass Valorisation

Ionic liquids (IL) are chemical compounds made entirely of ions. Their asymmetric molecular structure, weak interactions and charge delocalization decreases their melting points below 100 °C making them suitable for different applications. However, this definition can be extended to all compounds which melt at the operating condition. ILs are classified as protic and aprotic according to the cation chemical structure. The combination of cation and anion changes remarkably the chemical-physical properties of the ILs (stability, melting point, viscosity, hydrophilicity) making them tunable solvents and thus interesting for many different applications.⁵⁴⁻⁵⁶

As salts, ionic liquids have negligible vapour pressure and are non-flammable, reducing drastically safety issues related to toxicity through inhalation. These properties combined with the high stability of these molecules at high temperatures have led to them being considered green solvents for many years.

Interest in ionic liquids increased drastically when it was demonstrated that many catalyst show higher activity when they are used in ILs as solvents, especially those with non-coordinating anions such as $[\text{BF}_4]^-$ and $[\text{PF}_6]^-$.^{51,56} These features pushed many researchers to study the toxicity of these ILs and this has shown that the $[\text{BF}_4]^-$ and $[\text{PF}_6]^-$ ions undergo hydrolysis at temperatures higher than 50°C, producing HF, a corrosive and lethal gas, undermining their consideration as green solvents.⁵⁷ These ILs were replaced by those with more stable $[\text{OTf}]^-$ and $[\text{NTf}_2]^-$ ions, however their applications are limited by their cost and the strong toxicity of the $[\text{NTf}_2]^-$ anion in the environment.

When considered today, the statement that ‘ionic liquids are green solvents’^{58,59} it is not true and so attention must be focused on a more limited class of ionic liquid that has minimum impact towards the environment. The most common anions and cations studied today are reported in Figure 1.9⁴⁴:

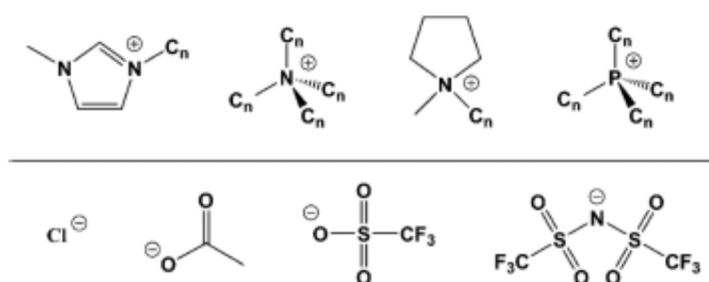


Figure 1.9 The most common cations and anions used for ionic liquid synthesis.

Due to their high cost and recent concerns over toxicity⁶⁰ of some of the aprotic ionic liquids, their application needs to be justified. A study on the biodegradability of imidazolium ionic liquids has shown that these salts are not biodegradable and that their toxicity is related to the length of the alkyl

chain.⁶¹ Different studies have shown that the toxicity of ionic liquids is higher compared with organic solvents respect some microbial community⁶² and the choice of the cation is crucial for that purpose. However, it is worth mentioning that the likelihood of ionic liquids entering the environment is much lower compared to organic solvents due to their negligible vapour pressure, making their recovery straightforward. In a typical petrochemical plant, the use of an organic solvent requires the addition of flares and catalytic burners to ensure that emissions are below the threshold established by legislation. In contrast, ionic liquids do not have any flammability issues and, thanks to their negligible vapour pressure, they do not require the addition of any extra units to dispose of vapours. However, the high cost associated with these solvents and their toxicity to aquatic life requires that quantitative recovery is achieved. In this matter, an efficient separation of the products is needed to guarantee high recovery and minimise the washing steps.

It has been proven that protic ionic liquids can fractionate biomass by dissolving lignin, obtaining a high purity cellulose which can be used for further processing.^{19,63} In contrast, aprotic ionic liquids with halide and acetate anions can dissolve cellulose and establish chemical pathways to valorise it to further chemical compounds.⁶⁴ Hence, they are considered very good candidates for catalyst design and to valorise cellulose to further chemicals. Following work by Dumesic and co-workers, which showed that high yields of 5-HMF can be obtained from fructose in a biphasic system consisting of water and an organic solvent,⁶⁵ Zhao and co-workers⁶⁶ reported in 2007 that high yields from glucose and cellulose can be obtained using ionic liquids with chloride anions as solvents, opening a new path to obtain 5-HMF at a potentially low cost. Moreover, quantitative yields from fructose can be achieved without the addition of an organic solvent. Further studies, however, have proven that isolation of HMF from ionic liquids is unfeasible due to the high affinity of 5-HMF for the solvent. In addition crystallization of 5-HMF in polar solvents is not feasible and the high boiling point and weak stability of 5-HMF at high temperatures are further issues.⁶⁷ Various attempts have been made to isolate 5-HMF from ionic liquids but a consistent solution has yet to be achieved. A high yield chemical path to valorise 5-HMF is thus yet to be exploited.

This thesis will demonstrate that, while 5-HMF separation from ionic liquids is a limiting step, other compounds derived from HMF are much easier to separate, including 2,5-diformylfuran (DFF) and FDCA. Therefore, converting HMF directly to one of these molecules in the ionic liquid is a potential solution to exploit the high yield of HMF from sugars.

It is thus necessary to establish whether the synthesis of these molecules in the ionic liquid represents the most sustainable way to valorise sugars into biobased chemicals compared with other technologies which use cheaper solvents. Current research is moving in various directions in order to develop new catalysts in different solvents to convert sugars and 5-HMF to DFF and FDCA. In Chapter 5 and 6, an outline will be provided of the state of art to synthesize DFF and FDCA from sugars.

In the next section, an outline and motivation for this thesis will be provided. According to the principles of green chemistry, we have attempted to address all the points in order to develop as close to an ideal green process as possible which uses renewable feedstocks and processes them in a sustainable way.

While most of the thesis addresses the chemistry of 5-HMF in ionic liquids, Chapter 7 is devoted to furfural-derived biobased surfactants. This is a promising new field, which needs to be developed due to the stricter legislation to which these compounds are now being subjected. This market is currently dominated by the linear alkylbenzene sulfonates (LAB) which are oil derivatives and have environmental issues due to the formulation needed for different applications. In this thesis, it will be demonstrated how biobased surfactants derived from furfural have the potential to solve all the issues related to this field.

How “Green” is this thesis

The main aim of this work is to study different chemical pathways to valorise biomass-derived feedstocks into value added chemicals which can replace oil derivatives. Furfural and 5-HMF were identified as valuable intermediate compounds to replace BTX in different applications. As described above, FDCA is one of the best candidates to replace terephthalic acid for the synthesis of PEF, passing through 5-HMF derived from cellulose. Moreover, the intermediate DFF can be useful in niche applications for new classes of polymers or speciality chemicals. We believe that the synthesis of these molecules using ionic liquids as solvent through aerobic oxidation represents the most sustainable chemical path to produce these molecules following our green principles:

- a) **Prevention and atom economy.** The chemical path from sugars (Figure 1.6) produces only water as a side product and no toxic waste. Thanks to the high chemical stability of ILs, they can be recycled with high efficiency. Since DFF is an intermediate of FDCA, we demonstrated in Chapter 3 that these molecules are easy to fractionate when using ionic liquids as solvents, opening the possibility to produce multiple valuable products from the same feedstock. All the chemical paths involved are affected by the same side reactions which imply the formation of a large molecular weight product derived from side reaction with sugars or self-condensation of HMF called humins. Chapter 2 will focus on the characterization of humins and their application in metal extraction from waste water treatment (WWT).
- b) **Chemicals and reaction design.** Most ionic liquids are toxic when ingested, which is most likely to happen through spillage and dispersion into the environment. Hence there must be a focus on the recyclability of the solvent. For ionic liquids, this is favoured due to their high stability. Since they are not flammable and not volatile, they are safe for use in a chemical plant.
- c) **Operating conditions.** Ionic liquids give high yields of 5-HMF from sugars and cellulose, making them much more competitive compared with other solvents.
- d) **Feedstock.** Ionic liquids have proved to be extremely efficient in processing lignocellulosic biomass which is a cheap and sustainable feedstock.
- e) **Catalysis.** Homogeneous and heterogeneous catalysis will be studied for aerobic oxidation to valorise HMF into DFF and FDCA in the ionic liquids. Aerobic oxidation uses cheap reactants and produces no toxic side products, unlike other catalysts
- f) **Design of safer chemicals.** FDCA is the monomer to produce PEF, a green and sustainable bioplastic for food and beverage packaging with superior properties compared PET.
- g) **Solvents.** Ionic liquids can boost the yield of the reaction from sugars to 5-HMF. The conversion of 5-HMF in the ionic liquids into more valuable products has received less attention and this will be the main topic of this thesis (Chapter 5 and 6). DFF can be easily separated from the ionic liquids through sublimation under mild conditions, while FDCA can be separated

by precipitation through addition of small amounts of water (Chapter 3). Aerobic oxidation in ionic liquids represents the missing link for a completely sustainable green process.

This thesis will also demonstrate that furfural-derived surfactants are promising substitutes for LAB and be made by esterification of furoic acid with fatty alcohols, leading to potential applications in the detergent industry. While LAB require various formulations to exhibit their detergent properties, it is demonstrated here that their substitution with bioderived alternatives has the potential to display better properties as a detergent without the need for any additional formulation.

Prospects

In this thesis, we wish to define two main concepts which can lead to a significant contribution towards the valorisation of biobased chemicals from biomass. First, that ionic liquids are valuable solvents for the chemical valorisation of furanic compounds and furfural and 5-HMF is the main candidate for the substitution of a large variety of chemicals derived from BTX.

Chapter 2 focuses on the stability of 5-HMF in ionic liquids and the characterization of the humins formed. The motivation for the study is related to finding the best conditions for catalyst design for further valorisation.

Chapter 3 describes the most valuable compounds derived from 5-HMF which can be efficiently separated from ionic liquids, therefore setting the target compounds to be synthesized in these solvents.

In Chapter 4, a different pathway to synthesize 5-HMF from fructose in non-coordinating ionic liquids is described. The advantage of synthesizing this molecule in these solvents is that it facilitates the separation and allows us to further valorise 5-HMF into a more valuable product since catalysis in non-coordinating ionic liquids has already been developed.

Chapter 5 centres on the synthesis of DFF through homogeneous catalysis exploiting the findings in Chapter 4.

Chapter 6 is devoted to catalyst design for the synthesis of FDCA in coordinating ionic liquids which are cheaper compared to non-coordinating ILs.

In Chapter 7, a new category of surfactants derived from furfural are described which have the potential to replace LAB as well as displaying superior performance as detergents.

References

- (1) Speight, J. G. Chapter 12 - Petrochemicals. In *Handbook of Industrial Hydrocarbon Processes*; 2011; pp 429–466. <https://doi.org/10.1016/B978-0-7506-8632-7.10012-X>.
- (2) Matar, S.; Hatch, L. *Chemistry of Petrochemical Processes*; Elsevier, 2001.
- (3) Share of electricity production from renewable sources, World <https://ourworldindata.org/grapher/renewables-share-electricity-production> (accessed Jan 7, 2020).
- (4) Shafiee, S.; Topal, E. When Will Fossil Fuel Reserves Be Diminished? *Energy Policy* **2009**, 37 (1), 181–189. <https://doi.org/10.1016/j.enpol.2008.08.016>.
- (5) Emerson, D. F.; Al Ghatta, A.; Woolston, B. M.; Fay, A.; Kumar, A.; Stephanopoulos, G. Theoretical Analysis of Natural Gas Recovery from Marginal Wells with a Deep Well Reactor. *AIChE J.* **2017**, 63 (9), 3642–3650. <https://doi.org/10.1002/aic.15738>.
- (6) Rogelj, J.; Popp, A.; Calvin, K. V; Luderer, G.; Emmerling, J.; Gernaat, D.; Fujimori, S.; Streffler, J.; Hasegawa, T.; Marangoni, G.; et al. Scenarios towards Limiting Global Mean Temperature Increase below 1.5 °C. *Nat. Clim. Chang.* **2018**, 8 (April). <https://doi.org/10.1038/s41558-018-0091-3>.
- (7) Erickson, P.; Lazarus, M.; Piggot, G. Limiting Fossil Fuel Production as the next Big Step in Climate Policy. *Nat. Clim. Chang.* **2018**, 8 (12), 1037–1043. <https://doi.org/10.1038/s41558-018-0337-0>.
- (8) IEA (2019), “World Energy Outlook 2019”, IEA, Paris <https://www.iea.org/reports/world-energy-outlook-2019>.
- (9) Eurostat-Statistic Explained: Renewable energy statistics https://ec.europa.eu/eurostat/statistics-explained/index.php/Renewable_energy_statistics#Renewable_energy_produced_in_the_EU_increased_by_two_thirds_in_2007-2017.
- (10) ICF; U.S. Department of Agriculture. *A Life-Cycle Analysis of the Greenhouse Gas Emissions of Corn-Based Ethanol*; 2017.
- (11) European Commission. The chemical industry can achieve a 36% reduction in annual greenhouse gas emissions by 2050 <https://ec.europa.eu/jrc/en/news/chemical-industry-can-achieve-36-reduction-annual-greenhouse-gas-emissions-2050-study-shows>.
- (12) Fatma, S.; Hameed, A.; Noman, M.; Ahmed, T.; Sohail, I.; Shahid, M.; Tariq, M.; Tabassum, R. Lignocellulosic Biomass: A Sustainable Bioenergy Source for Future. *Protein Pept. Lett.* **2018**, 25. <https://doi.org/10.2174/0929866525666180122144504>.
- (13) Werpy, T.; Northwest National Laboratory, P.; Petersen, G.; Renewable Energy Laboratory, N. Top Value Added Chemicals from Biomass Volume I—Results of Screening for Potential Candidates from Sugars and Synthesis Gas Energy Efficiency and Renewable Energy. *Northwest Natl. Lab.* **1992**.
- (14) Myllyviita, T.; Holma, A.; Antikainen, R.; Lahinen, K.; Leskinen, P. Assessing Environmental Impacts of Biomass Production Chains - Application of Life Cycle Assessment (LCA) and Multi-Criteria Decision Analysis (MCDA). *J. Clean. Prod.* **2012**, 29–30, 238–245. <https://doi.org/10.1016/j.jclepro.2012.01.019>.
- (15) Moulijn, J. A.; Makee, M.; Van Diepen, A. *Chemical Process Technology*; Wiley-VCH, 2013.

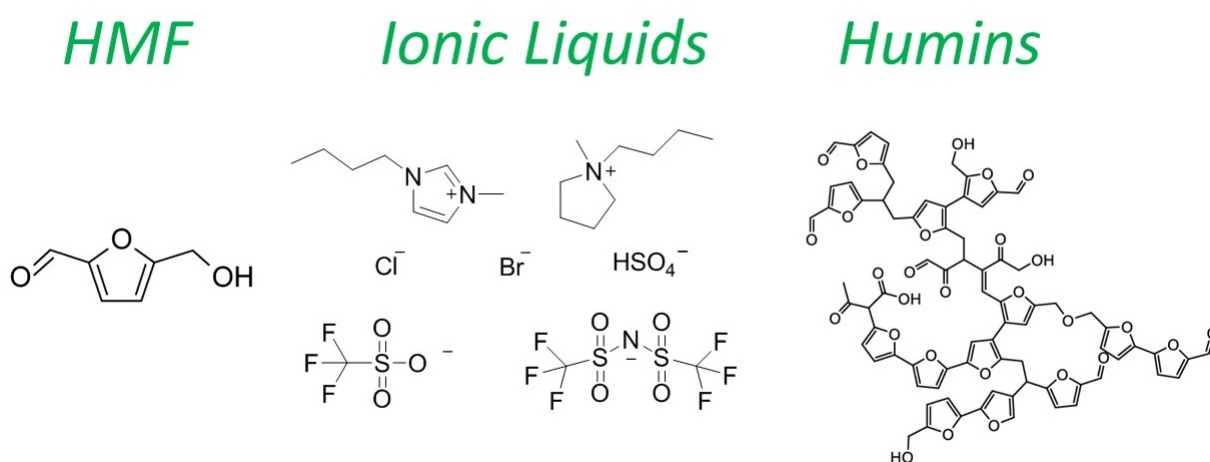
- (16) Clews, R. J. Fundamentals of the Petroleum Industry. In *Project Finance for the International Petroleum Industry*; Elsevier, 2016. <https://doi.org/10.1016/b978-0-12-800158-5.00005-0>.
- (17) Doods, D. R.; Gross, R. A.; Dodds, D. R.; Gross, R. A. Chemicals from Biomass. *Science*. **2007**, *318* (5854), 1250–1251.
- (18) Takkellapati, S.; Li, T.; Gonzalez, M. A. An Overview of Biorefinery-Derived Platform Chemicals from a Cellulose and Hemicellulose Biorefinery. *Clean Technol. Environ. Policy* **2018**, *20* (7), 1615–1630. <https://doi.org/10.1007/s10098-018-1568-5>.
- (19) Brandt, A.; Ray, M. J.; To, T. Q.; Leak, D. J.; Murphy, R. J.; Welton, T. Ionic Liquid Pretreatment of Lignocellulosic Biomass with Ionic Liquid-Water Mixtures. *Green Chem*. **2011**, *13* (9), 2489–2499. <https://doi.org/10.1039/c1gc15374a>.
- (20) Wang, H.; Pu, Y.; Ragauskas, A.; Yang, B. From Lignin to Valuable Products—Strategies, Challenges, and Prospects. *Bioresour. Technol.* **2019**, *271*, 449–461. <https://doi.org/10.1016/J.BIORTECH.2018.09.072>.
- (21) Yuan, T.-Q.; Xu, F.; Sun, R.-C. Role of Lignin in a Biorefinery: Separation Characterization and Valorization. *J. Chem. Technol. Biotechnol.* **2013**, *88* (3), 346–352. <https://doi.org/10.1002/jctb.3996>.
- (22) Li, G.; Liu, W.; Ye, C.; Li, X.; Si, C.-L. Chemocatalytic Conversion of Cellulose into Key Platform Chemicals. *Int. J. Polym. Sci.* **2018**, 1–21. <https://doi.org/10.1155/2018/4723573>.
- (23) Ragauskas, A. J.; Ragauskas, A. J.; Williams, C. K.; Davison, B. H.; Britovsek, G.; Cairney, J.; Eckert, C. A.; Jr, W. J. F.; Hallett, J. P.; Leak, D. J.; et al. The Path Forward for Biofuels and Biomaterials. *Science (80-.)*. **2006**, *311* (5760), 484–489. <https://doi.org/10.1126/science.1114736>.
- (24) E4tech; Re-Cord; Wur. *From the Sugar Platform to Biofuels and Biochemicals*; 2015. [https://doi.org/contract No. ENER/C2/423-2012/SI2.673791](https://doi.org/contract%20No.%20ENER/C2/423-2012/SI2.673791).
- (25) Padella, M.; O’Connell, A.; Prussi, M. What Is Still Limiting the Deployment of Cellulosic Ethanol? Analysis of the Current Status of the Sector. *Appl. Sci.* **2019**, *9* (21). <https://doi.org/10.3390/app9214523>.
- (26) Parsons, S.; McManus, M. C.; Taylor, C. M. Second-Generation Ethanol from Lignocellulose. In *Greenhouse Gas Balances of Bioenergy Systems*; Elsevier Inc., 2018; pp 193–206. <https://doi.org/10.1016/B978-0-08-101036-5.00013-6>.
- (27) Gusakov, A. V. Cellulases and Hemicellulases in the 21st Century Race for Cellulosic Ethanol. *Biofuels* **2013**, *4* (6), 567–569. <https://doi.org/10.4155/bfs.13.55>.
- (28) Stattman, S. L.; Gupta, A.; Partzsch, L.; Oosterveer, P. Toward Sustainable Biofuels in the European Union? Lessons from a Decade of Hybrid Biofuel Governance. *Sustain.* **2018**, *10* (11), 1–17. <https://doi.org/10.3390/su10114111>.
- (29) Lee, C. S.; Aroua, M. K.; Daud, W. M. A. W.; Cognet, P.; Pérès-Lucchese, Y.; Fabre, P. L.; Reynes, O.; Latapie, L. A Review: Conversion of Bioglycerol into 1,3-Propanediol via Biological and Chemical Method. *Renewable and Sustainable Energy Reviews*. Elsevier Ltd February 1, 2015, pp 235–244. <https://doi.org/10.1016/j.rser.2014.10.033>.
- (30) Mazière, A.; Prinsen, P.; García, A.; Luque, R.; Len, C. A Review of Progress in (Bio)Catalytic Routes from/to Renewable Succinic Acid. *Biofuels, Bioprod. Biorefining* **2017**, *11* (5), 908–931. <https://doi.org/10.1002/bbb.1785>.
- (31) Mariscal, R.; Maireles-Torres, P.; Ojeda, M.; Sádaba, I.; López Granados, M. Furfural: A Renewable and Versatile Platform Molecule for the Synthesis of Chemicals and Fuels. *Energy*

- and *Environmental Science*. Royal Society of Chemistry April 1, 2016, pp 1144–1189. <https://doi.org/10.1039/c5ee02666k>.
- (32) Wilson, K.; Lee, A. F. Bio-Based Chemicals from Biorefining: Carbohydrate Conversion and Utilisation. In *Advances in Biorefineries: Biomass and Waste Supply Chain Exploitation*; Elsevier Ltd., 2014; pp 624–658. <https://doi.org/10.1533/9780857097385.2.624>.
 - (33) Mittal, A.; Pilath, H. M.; Johnson, D. K. Direct Conversion of Biomass Carbohydrates to Platform Chemicals: 5-Hydroxymethylfurfural (HMF) and Furfural. *Energy & Fuels* **2020**. <https://doi.org/10.1021/acs.energyfuels.9b04047>.
 - (34) Kabbour, M.; Luque, R. Furfural as a Platform Chemical. In *Biomass, Biofuels, Biochemicals*; Elsevier, 2020; pp 283–297. <https://doi.org/10.1016/b978-0-444-64307-0.00010-x>.
 - (35) Dashtban, M.; Gilbert, A.; Fatehi, P. Recent Advancements in the Production of Hydroxymethylfurfural. *RSC Adv.* **2014**, 4 (4), 2037–2050. <https://doi.org/10.1039/c3ra45396k>.
 - (36) PET Plastic: A Comprehensive Review <https://omnexus.specialchem.com/selection-guide/polyethylene-terephthalate-pet-plastic/key-features-applications-of-pet> (accessed Jan 7, 2020).
 - (37) Cavani, F.; Albonetti, S.; Basile, F.; Gandini, A. *Chemicals and Fuels from Bio-Based Building Blocks* | Wiley Online Books; Wiley-VCH, 2016.
 - (38) Collias, D. I.; Harris, A. M.; Nagpal, V.; Cottrell, I. W.; Schultheis, M. W. Biobased Terephthalic Acid Technologies: A Literature Review. *Ind. Biotechnol.* **2014**, 10 (2), 91–105. <https://doi.org/10.1089/ind.2014.0002>.
 - (39) M&G chemicals Corpus Christi Facility <http://www.mgcorpuschristi.com/en/corpus-christi/the-projects>.
 - (40) Purified Terephthalic Acid (PTA) Prices and Pricing Information | ICIS <https://www.icis.com/explore/resources/news/2007/11/06/9076460/purified-terephthalic-acid-pta-prices-and-pricing-information/> (accessed Jan 7, 2020).
 - (41) <https://www.avantium.com/press-releases/basf-notifies-avantium-of-its-exit-from-synvina/>.
 - (42) Weastra, S. r. o. *Market Study on Succinic Acid, Itaconic Acid and FDCA*; 2011.
 - (43) 12 Principles of Green Chemistry - American Chemical Society <https://www.acs.org/content/acs/en/greenchemistry/principles/12-principles-of-green-chemistry.html> (accessed Jan 7, 2020).
 - (44) Clarke, C. J.; Tu, W. C.; Levers, O.; Bröhl, A.; Hallett, J. P. Green and Sustainable Solvents in Chemical Processes. *Chem. Rev.* **2018**, 118 (2), 747–800. <https://doi.org/10.1021/acs.chemrev.7b00571>.
 - (45) Cséfalvay, E.; Akien, G. R.; Qi, L.; Horváth, I. T. Definition and Application of Ethanol Equivalent: Sustainability Performance Metrics for Biomass Conversion to Carbon-Based Fuels and Chemicals. *Catal. Today* **2015**, 239, 50–55. <https://doi.org/10.1016/j.cattod.2014.02.006>.
 - (46) Winterton, N.; Winterton, N. Green Chemistry : Deliverance or Distraction ? Efficient Chemical Reactions and a Preference for Catalytic. *Clean Technol. Environ. Policy* **2016**, 18 (4), 991–1001. <https://doi.org/10.1007/s10098-016-1118-y>.
 - (47) BASF to develop emission-free H2 production technology | News | gasworld <https://www.gasworld.com/basf-to-develop-emission-free-h2-production-technology-/2016321.article> (accessed Jan 7, 2020).

- (48) Tullo, A. A Solvent Dries Up. *Chem. Eng. News* **2008**, 86 (47), 27. <https://doi.org/10.1021/cen-v086n047.p027>.
- (49) Arico, F.; Tundo, P. Dimethyl Carbonate: A Modern Green Reagent and Solvent. *Russ. Chem. Rev.* **2010**, 79 (6), 479–489. <https://doi.org/10.1070/RC2010v079n06ABEH004113>.
- (50) Firestone, J. A.; Gospe, S. M. Organic Solvents. In *Clinical Neurotoxicology: Syndromes, Substances, Environments*; Elsevier Inc., 2009; pp 401–414. <https://doi.org/10.1016/B978-032305260-3.50041-1>.
- (51) Welton, T. Solvents and Sustainable Chemistry. *Proc.R.Soc.A* **2015**, 471 (2183), 1–26. <https://doi.org/10.1098/rspa.2015.0502>.
- (52) Byrne, F. P.; Jin, S.; Paggiola, G.; Petchey, T. H. M.; Clark, J. H.; Farmer, T. J.; Hunt, A. J.; Robert McElroy, C.; Sherwood, J. Tools and Techniques for Solvent Selection: Green Solvent Selection Guides. *Sustain. Chem. Process.* **2016**, 4 (1), 7–16. <https://doi.org/10.1186/s40508-016-0051-z>.
- (53) Adams, C. J. Neoteric Solvents: An Examination of Their Industrial Attractiveness. In *Ionic Liquids*; 2002; pp 15–29. <https://doi.org/10.1021/bk-2002-0818.ch002>.
- (54) Ghandi, K. A Review of Ionic Liquids, Their Limits and Applications. *Green Sustain. Chem.* **2014**, 4 (1), 44–53. <https://doi.org/10.4236/gsc.2014.41008>.
- (55) Holbrey, J. D.; Seddon, K. R. Ionic Liquids. *Clean Technol. Environ. Policy* **1999**, 1 (4), 223–236. <https://doi.org/10.1007/s100980050036>.
- (56) Rogers, R. D.; Seddon, K. R. Perspective Article: Ionic Liquids Solvents of the Future? *Science (80-.)*. **2003**, 302 (5646), 792–793.
- (57) Freire, M. G.; Neves, C.; Marrucho, I. M. Hydrolysis of Tetrafluoroborate and Hexafluorophosphate Counter Ions in Imidazolium-Based Ionic Liquids. *J. Phys. Chem. B* **2010**, 114 (11), 3744–3749. <https://doi.org/10.1021/jp903292n>.
- (58) Baleizão, C.; Gigante, B.; Garcia, H.; Corma, A. Ionic Liquids as Green Solvents for the Asymmetric Synthesis of Cyanohydrins Catalysed by VO(Salen) Complexes. *Green Chem.* **2002**, 4 (3), 272–274. <https://doi.org/10.1039/b201497c>.
- (59) Earle, M. J.; Seddon, K. R. Ionic Liquids. Green Solvents for the Future. *Pure Appl. Chem.* **2000**, 72 (7).
- (60) Peric, B.; Sierra, J.; Martí, E.; Cruañas, R.; Garau, M. A.; Arning, J.; Bottin-Weber, U.; Stolte, S. (Eco)Toxicity and Biodegradability of Selected Protic and Aprotic Ionic Liquids. *J. Hazard. Mater.* **2013**, 261, 99–105. <https://doi.org/10.1016/j.jhazmat.2013.06.070>.
- (61) Zhao, D.; Liao, Y.; Zhang, Z. D. Toxicity of Ionic Liquids. *Clean - Soil, Air, Water* **2007**, 35 (1), 42–48. <https://doi.org/10.1002/clen.200600015>.
- (62) Sun, X.; Zhu, L.; Wang, J.; Wang, J.; Su, B.; Liu, T.; Zhang, C.; Gao, C.; Shao, Y. Toxic Effects of Ionic Liquid 1-Octyl-3-Methylimidazolium Tetrafluoroborate on Soil Enzyme Activity and Soil Microbial Community Diversity. *Ecotoxicol. Environ. Saf.* **2017**, 135, 201–208. <https://doi.org/10.1016/j.ecoenv.2016.09.026>.
- (63) Brandt-Talbot, A.; Gschwend, F. J. V.; Fennell, P. S.; Lammens, T. M.; Tan, B.; Weale, J.; Hallett, J. P. An Economically Viable Ionic Liquid for the Fractionation of Lignocellulosic Biomass. *Green Chem.* **2017**, 19 (13), 3078–3102. <https://doi.org/10.1039/c7gc00705a>.
- (64) Swatloski, R. P.; Spear, S. K.; Holbrey, J. D.; Rogers, R. D. Dissolution of Cellulose with Ionic Liquids. *J. Am. Chem. Soc.* **2002**, 124 (18), 4974–4975. <https://doi.org/10.1021/ja025790m>.

- (65) Roman-Leshkov, Y.; Chheda, J. N.; Dumesic, J. a. Phase Modifiers Promote Efficient Production of Hydroxymethylfurfural from Fructose. *Science*. **2006**, *312* (4), 1933–1937. <https://doi.org/10.1126/science.1126337>.
- (66) Zhao, H.; Holladay, J. E.; Brown, H.; Zhang, Z. C. Metal Chlorides in Ionic Liquid Solvents Convert Sugars to 5-Hydroxymethylfurfural. *Science*. **2007**, *316* (5831), 1597–1600. <https://doi.org/10.1126/science.1141199>.
- (67) Wang, H.; Liu, S.; Zhao, Y.; Zhang, H.; Wang, J. Molecular Origin for the Difficulty in Separation of 5-Hydroxymethylfurfural from Imidazolium Based Ionic Liquids. *ACS Sustain. Chem. Eng.* **2016**, *4* (12), 6712–6721. <https://doi.org/10.1021/acssuschemeng.6b01652>.

Chapter 2 Stability of 5-HMF in Ionic Liquids: Characterization and Valorisation of the Humin Side Products



The main challenge that exists between the chemical processing of petrochemical and biomass derived feedstocks is the stability and reactivity of the compounds involved. In this matter, petrochemical feedstocks can be processed at high temperature with a catalyst capable of achieving high selectivity. On the contrary, biomass derived chemicals need controlled conditions since sugars and furanic compounds undergo a large variety of side reactions the mechanism of which are currently unknown. The most common side products are humins, high molecular weight water-insoluble compounds derived from thermal and acid degradation of sugars and HMF. Often this side product is considered one of the main reasons for catalyst deactivation due its high functionality which can bind to the active centre of the catalyst. This makes the choice of catalyst, solvent and reaction conditions crucial to achieve an efficient process. The focus of this chapter is to analyse the stability of HMF in different ionic liquids and explore the mechanisms of degradation, morphology and chemical structure of humins. Some ionic liquids enhance the stability of HMF while others catalyse the formation of humins. Focus will be placed on the ionic liquids which enhance the formation of humins and, through FT-IR, mass spectrometry and GPC, the mechanism of the degradation will be explored.

Introduction

In order to carry out an efficient catalytic reaction, it is useful to analyse the stability of the compounds involved under the reaction conditions. The difficulties encountered in the separation of HMF from ionic liquids has led to much research into solutions involving the valorisation of sugars into an intermediate chemical product which can be easier to separate. Different studies have taken different paths, as in the *in situ* conversion of HMF into a more valuable product, such as FDCA. Studies have been carried out on this reaction using Ru-based catalysts in [emim][OAc], obtaining 40% yield of FDCA in 24 h at 140 °C,¹ while Yan and co-workers used a non-noble metal catalyst based on Fe/Zr reaching 60% yield at 160 °C in 24 h.² Recently, Chen and co-workers used polyoxometallates at 140 °C in 6 h to obtain 84 % yield.³ From these reported studies on the catalytic oxidation of HMF, it can be concluded that high temperatures are needed to perform the oxidation and, by considering that all are performed at very low concentrations (0.1 M), the instability of HMF at high temperature is one of the key points which leads to the inefficiency of the reaction.

All processes to valorise HMF need to consider the stability of this compound under the reaction conditions. Galkin and co-workers have highlighted the instability of HMF at room temperature according to its physical state. Since the melting point of this compound is 30-34 °C, it can exist as a solid or liquid metastable state. The liquid state undergoes faster degradation due to the increased self-diffusion of the molecules and residual acidity of the reaction. For this reason, a study proposed 5-methylfurfural as a more versatile chemical for an efficient biorefinery design.^{4,5}

While current theory supports the fact that ionic liquids stabilize HMF towards over-dehydration into formic and levulinic acid, other types of side reactions arise due to the reaction of sugars with the HMF produced and the thermal instability of HMF at high temperatures.⁶⁻⁸ In both cases, the degradation of HMF leads to high molecular weight compounds called humins, generally water insoluble, which consist of a complex organic framework. As humins are considered the main product from glucose dehydration, methods to suppress humin formation are highly desirable. Addition of an organic solvent has proven to be inefficient due to the high affinity of HMF with ionic liquids and the low partition coefficient.⁹ While different reports have highlighted the instability of HMF at high temperatures in ionic liquids, other reports have shown that water has a beneficial effect on HMF stability in ionic liquids.¹⁰ A study done in DMSO by Tsilomelekis and co-workers showed that the solvent can interact with the carbonyl group of HMF, reducing the energy of the LUMO orbital and thereby reducing susceptibility to nucleophilic attack at the carbonyl group, which is considered the main step for its side reaction with sugars.¹¹ In contrast, IR studies performed on the ionic liquid/HMF interactions showed weak interactions of the IL with the aldehyde group, while strong interaction were observed with the hydroxyl group.^{12,13} Even if not proven, it is likely that the energy of the HOMO

orbital of the hydroxyl group is decreased in the presence of ionic liquids, hence reducing the nucleophilic attack of the sugars towards the carbonyl.

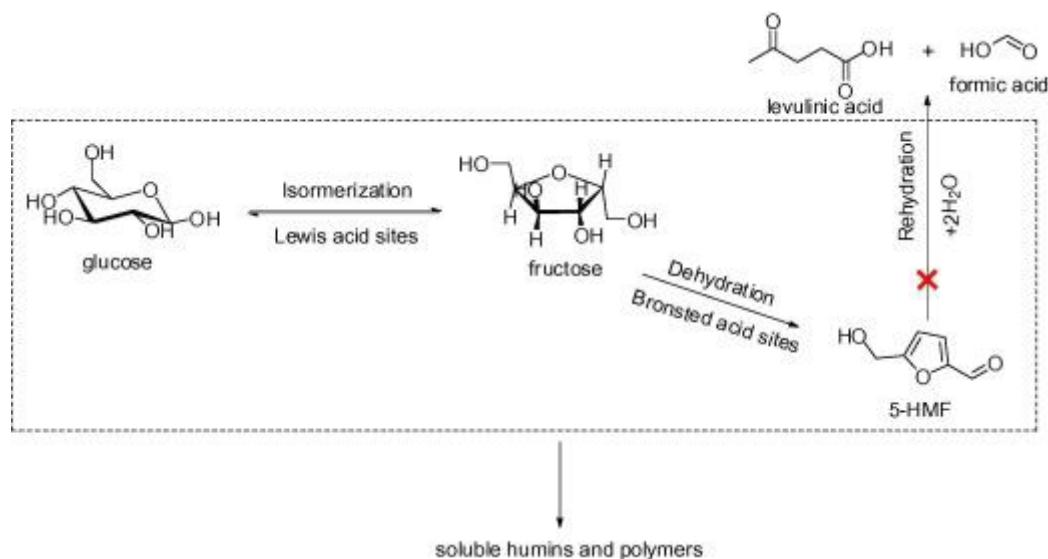


Figure 2.1 Reaction scheme from sugars to 5-HMF with side reactions

Various studies have focused on characterizing the humins derived from different sugars dehydration processes, most of which are carried out in water. However, so far, the exact chemical structure and mechanism are still not completely understood. Hoang and co-workers analysed glucose-derived humins produced under strong acidic conditions and demonstrated their applicability for syngas production. The authors demonstrated that humins grow as spherical particles whose morphology and chemical composition changes upon heating, passing from an amorphous furanic structured material to a benzene graphitized framework.¹⁴

Other studies have been based only on characterization of humins formed under different conditions. Patil and Lund showed that two different morphologies of humins are formed by the addition of an acid or by thermal decomposition due to different relative amounts of functional groups observed.¹⁵ Acid-catalyzed humins resemble those from Hoang and co-workers as spheres which grow with increasing reaction time. In both cases the aldehyde group of humins is not detected by IR, indicating that aldol condensation is the main mechanism involved in the polymerization. A similar study was performed by Cheng and co-workers, which investigated the soluble fractions of humins in different organic solvents with LC-MS, showing that all soluble fractions have the same molecular structure and that solubility in water depends exclusively on molecular weight.¹⁶

Different studies have observed that the thermal degradation of HMF in the ionic liquids is consistent, but this is partially suppressed when a Lewis acid is present at low temperature.^{10,17} The reason for this is unclear. At temperatures higher than 180 °C, cross polymerization between the cation

and the aldehyde group is reported due to the formation of a carbene after deprotonation of the C2 position on the imidazolium ring.¹⁸

While most of the reports studied the humins derived from acid dehydration of sugars, the work described here will focus on the stability of HMF in ionic liquids and the analysis of humins as side products of degradation. It was found that, according to its H-bonding ability and viscosity, the anion of the ionic liquids can trigger humin formation, influencing its morphology and chemical structure. Following the increasing interest in carbonaceous material for water treatment, it is demonstrated that humins derived from HMF are a potential carbonaceous material for the extraction of lead from waste water making it a potential candidate for a large variety of applications.

Experimental Section

Materials

All materials for ionic liquid synthesis and cold finger glassware were purchased from Sigma-Aldrich. Methylimidazole (99%) was distilled under reduced pressure over CaH_2 . Chlorobutane (99.5%) was distilled at atmospheric pressure over P_2O_5 . HMF, DFF, FFCA and FDCA were obtained from Fluorochem.

Synthesis Ionic Liquids

Ionic liquid was synthesised according literature reported procedure¹⁹. [bmim]Cl was synthesized on a large scale (350 g). Manipulation of all chemicals was performed by cannulation under inert conditions. 1-methylimidazole (164.2 g, 2 mol) was transferred to a three neck flask equipped with an air condenser followed by the addition of acetonitrile (100 mL). The mixture was heated at 60 °C under stirring and 1-chlorobutane (203.7 g, 2.2 mol, 1.1 eq) was then added dropwise using a dropping funnel. The reaction mixture was heated for 3 days at 70 °C. Complete consumption of 1-methylimidazole was confirmed by ^1H NMR spectroscopy. [bmim]Cl was precipitated by gradual addition of ethyl acetate at 3 °C. The resultant white crystals were washed under inert conditions with portions of ethyl acetate (2 L in total), dried under vacuum and stored in a glovebox. NMR spectra agreed with those reported in literature.¹⁹

[bmim]Br was synthesized by the same procedure using bromobutane and [bmpyr]Cl was prepared in the same way using *N*-methylpyrrolidine.

For the synthesis of [bmim][OTf], [bmim][NTf₂] and [bmpyr][NTf₂], [bmim]Cl (30 g, 0.17 mol) was dissolved in water (100 mL) and Li[OTf] (30 g, 0.179 mol, 1.1 eq) was dissolved in water (50 mL). The lithium triflate solution was added dropwise to the chloride solution under vigorous stirring and the reaction left overnight. The product was extracted from aqueous solution using a total of 800 mL dichloromethane. The organic extracts were washed repeatedly with water (5 mL) until the silver nitrate test revealed no halide ions (5-6 washes). The organic phase was dried with magnesium sulfate and then evaporated to dryness under reduced pressure. The ionic liquid, [bmim][OTf] was further dried under reduced pressure overnight at 60 °C (final yield: 47 g, 96%) and handled thereafter under an inert atmosphere. [bmim][NTf₂] was synthesized by the same procedure using Li[NTf₂] and [bmpyr]NTf₂ was prepared by the same method using [bmpyr]Cl and Li[NTf₂].

NMR spectra of [bmim]Br, [bmpyr]Cl, [bmim][OTf] and [bmim][NTf₂] were in agreement with literature ones.²⁰⁻²³

Stability test of furanic compounds in the ionic liquids

The mixture of ionic liquids and furanic compound (HMF, methyl furfuryl alcohol, HMFA, furfuryl alcohol) was prepared in large batches. Ionic liquids and HMF were mixed at the desired mass ratio (1:10) followed by addition of a known amount of organic solvent which solubilized both HMF and the ionic liquid. For this purpose, dichloromethane was chosen for [bmim]Cl, [bmim]Br, [bmim][NTf₂] and [bmim][OTf] while methanol was selected for [bmim]HSO₄ (insoluble in dichloromethane). Aliquots of samples were placed in a 3 mL vial followed by complete solvent removal under vacuum (overnight). This was achieved by closing the vials with a rubber septum, purged with a needle and placed in a flask connected to a vacuum pump through a Schlenk line. The flask was left under vacuum overnight to ensure that all the organic solvent (DCM or methanol) is removed. The reaction was started by placing the vials on a preheated heating plate and left for the desired time. The reaction was then quenched with 3 ml of water, filtered and residual HMF measured by chromatography.

In a typical experiment the batch solution was prepared by mixing 1 g of HMF, 10 g of ionic liquid and 10 g of DCM. The mixture was stirred in a vortex mixer until a homogenous solution was formed. Approximately 630 mg of solution were placed in a 3 ml vial. After capping the vial with a rubber septum and purged with a syringe it was placed connected to the Schlenk line through a flask and left it under vacuum overnight. The reaction was started by adding a stirrer bar and placed on the preheated heating block and left it to the desired time under stirring (300 rpm). Degradation was calculated according the following formula:

$$z = \frac{C_i - C_f}{C_i}$$

Where C is the concentration and the subscript i and f stands for initial and final.

Each experiment was repeated multiple times (3-8 times) due to the poor replicability of the system especially for value of degradation less than 30 % which standard deviation could be more than 50 %. On the other hand, when the values of degradation are high (>50 %) the repeat were consistent with low standard deviation (<10 %)

Quantification for HMF, furfuryl alcohol and methyl furfuryl alcohol was performed using a Shimadzu Prominence preparative HPLC (Shimadzu, Kyoto, Japan) with refractive index and ultraviolet (UV) detectors. The instrument was equipped with C18 Agilent reversed phase column using methanol/water (1:9) as the mobile phase with a flow rate of 0.6 ml/min at 40 °C.

For the quantification of HMFA, the same instrument was used but an Aminex HPX-87H column using a 0.005 M H₂SO₄ as the mobile phase at 55 °C.

Synthesis of Humins

HMF and ionic liquids were mixed at a 1:3 ratio (by mass). Typically, 1 g of HMF was mixed with 3 g of ionic liquid in a 30 mL vial and placed on a preheated heating block at the desired time. 10 ml of

water was added to quench the reaction and precipitate the humins which was separated by centrifugation and washed with water (about 1 L) until the liquid phase turned clear. When [bmim]HSO₄ was used, the humins was washed until neutral pH of the washing solution was reached. The humins were then dried in the oven at 60 °C overnight (Figure 2.2). Characterization was performed by SEM, GPC, FT-IR (Agilent Cary) and mass spectroscopy.

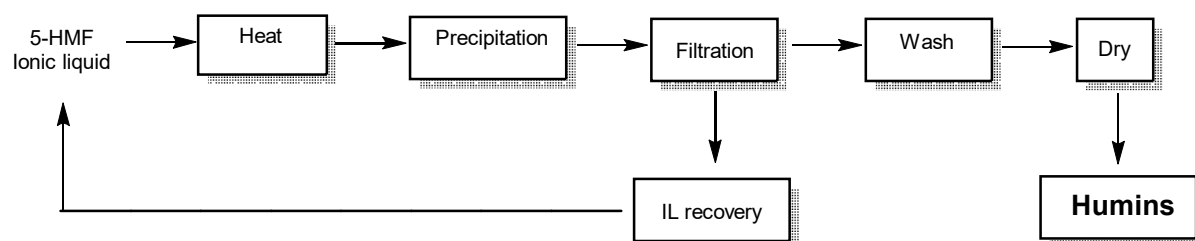


Figure 2.2 Scheme of humins production in ionic liquid

For GPC analysis, samples were prepared by dissolving 20 mg of humins in 1 mL GPC grade DMSO containing LiBr (1 g·L⁻¹) and filtered through a 0.2 µm syringe filter. GPC measurements were performed using an Agilent 1260 Infinity instrument equipped with a Viscotek column set (AGuard, A6000 M and A3000 M) and using GPC grade DMSO used as eluent at a flow rate of 0.4 mL·min⁻¹ at 60 °C. The Agilent 1260 Infinity RID detector was used for detection. Calibration of the instrument was conducted using 10 pullulan standards (Agilent calibration kit, 180 < Mp < 780 000).

Mass spectroscopy was performed with a Waters LCT Premier (ES-ToF)/Acquity i-Class by Dr. Lisa Haigh in the Department of Chemistry (White City).

For particle sizes, the solid was dispersed in water and light scattering was performed using a Malvaren Mastersizer.

Metal Extraction

A mother solution of lead nitrate (100 ppm) was prepared by dilution of an ICP standard solution (1000 ppm) at pH 2. Then the pH was corrected at 4 with a solution of 0.1 M of NaOH. In a typical experiment, 5 mg of humins (or activated carbon) was mixed with 5 ml of lead solution in a 10 ml vial and mixed overnight (12 h) in a vortex mixer. At the end of the reaction the solid was removed with a 0.2 µm filter and diluted by a factor of 100 for ICP analysis to determine the concentration of residual metal. The extraction efficiency is defined as:

$$y = \frac{x_i - x_f}{x_i}$$

Where y is the extraction efficiency, x referred to the initial (i) and final (f) concentration.

The experiments were executed in triplicate.

Results and Discussions

Stability of HMF in the ionic liquids

An initial study focused on analysing the stability of HMF in different ionic liquids at different temperatures by measuring the degree of degradation. This was related to the chemical propriety of the ionic liquids which can be summarized according their hydrogen bond ability and polarizability. These properties can be tuned by varying the cation and anion. Imidazolium ionic liquids were analysed with different anions according to their H-bond ability and hydrophobicity. The H-bond ability varies in the order $\text{Cl}^- > \text{Br}^- > [\text{HSO}_4]^- > [\text{OTf}]^- > [\text{NTf}_2]^-$.¹³

Temperature and time effects on HMF degradation are reported in Figure 2.3. No substantial degradation was observed after 9 h in all the ionic liquids tested at temperature below 100 °C. The ILs with coordinating anions Cl^- and Br^- exhibit similar degradation until 120 °C, after which the chloride shows the greatest degradation while the Br^- anion seems to provide a protective effect to the HMF, limiting the degradation to below 50% at high temperature. Surprisingly, the non-coordinating ionic liquid anions $[\text{OTf}]^-$ and $[\text{NTf}_2]^-$ exhibit different trends. The hydrophobic nature of $[\text{bmim}][\text{NTf}_2]$ seems to guarantee remarkable stability at low temperature, while degradation starts to become evident at 120 °C and remains constant at about 40% until 160 °C. This unusual behaviour, reflected in both temperature and kinetic analysis, could be traced to two different effects. Due the hydrophobicity of the solvent and the water generated by the HMF degradation, a second water phase can be formed during the reaction which partially removes HMF from the ionic liquid and reduces the actual temperature in the mixture due to the boiling effect. This was evident by looking at the top of the reaction vial where reflux was clearly observed. It was concluded that hydrophobicity has a beneficial effect on HMF stability especially at low temperatures (< 100 °C). A different trend was observed for the $[\text{OTf}]^-$ anion, which showed a completely different trend. While the degradation was low until 120 °C, it increased drastically at 140 °C, reaching close to full degradation at 160 °C. Since this solvent is hydrophilic, the water generated during degradation exhibits a protective effect until 120 °C (HMF shows higher stability in $[\text{bmim}][\text{OTf}]/\text{water}$ mixtures⁷); at higher temperatures the water evaporates, speeding up the degradation. In this case, since water and $[\text{bmim}][\text{OTf}]$ are completely miscible, there could be an increase in the boiling point of the water, allowing the temperature in the system to rise, contrary to what was observed for $[\text{bmim}][\text{NTf}_2]$. A greater degree of degradation was observed for $[\text{bmim}][\text{HSO}_4]$, exhibiting full conversion at temperatures higher than 120 °C, indicating HMF degradation is catalysed under acidic conditions.

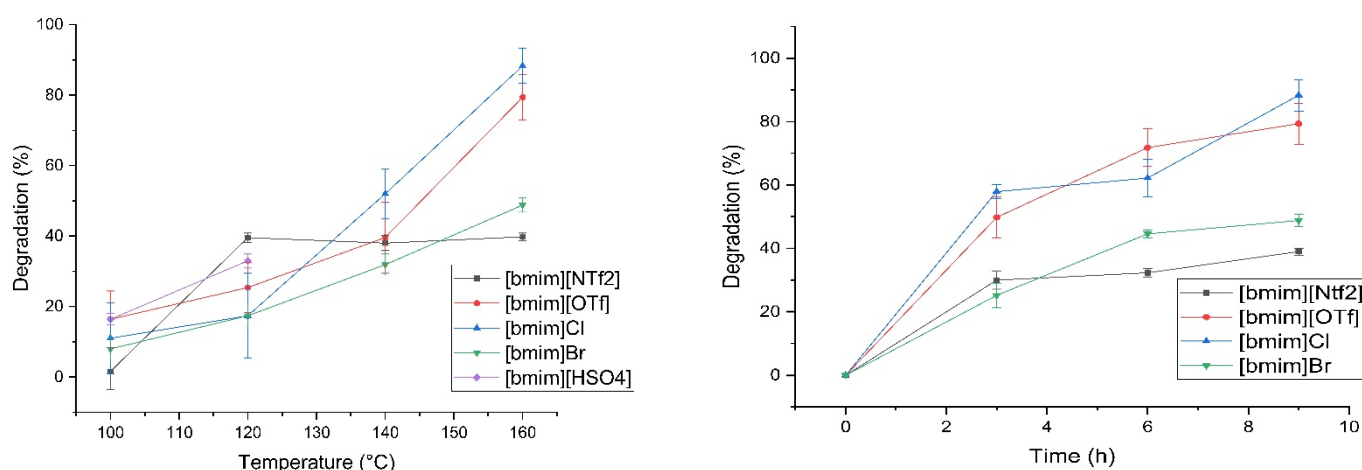


Figure 2.3 Effect of temperature (9 h) and time (160 °C) on HMF degradation in different ionic liquids (10 % loading respect the solvent)

According to the results presented so far, $[\text{OTf}]^-$ and Cl^- ionic liquids exhibit the highest degradation at higher temperatures; in this manner the anions used represent two different extremes in coordination ability, where Cl^- exhibits the highest H-bond accepting strength while $[\text{OTf}]^-$ is neutral, suggesting that an optimum H-bond strength exists to stabilize HMF since the Br, which have an intermediate bonding, exhibits the lowest degradation. In a second study, the effect of the cation was evaluated using $[\text{bmpyr}][\text{OTf}]$ but the degradation observed was the same as $[\text{bmim}][\text{OTf}]$, suggesting that the cation has less influence to the rate of degradation of HMF compared the anion. This is further suggested by FT-IR analysis reported in Wang and co-workers¹² and is confirmed with further analysis in the next chapter,¹³ which shows that cations do not have strong interactions with HMF.

In order to start the investigation of the degradation mechanism, different furanic compounds were tested by varying the substituent on the furan ring, increasing the electron donating effect. For this reason, the aldehyde group of HMF was substituted with different substituents with a range of electron withdrawing abilities. The analysis in Table 2.1 is consistent with the postulate that the hydroxyl group is the main reason for the instability of the compound and a substituent with electron donating ability accelerates the degradation by activating the hydroxyl group towards side reactions. The destabilization is partially protected by Cl^- anions which coordinate with the hydroxyl group. In contrast, electron-withdrawing groups such as COOH strongly stabilize the compounds, leading to negligible degradation. In the next section the mechanism of degradation will be discussed by analysing the humin structures produced in different ionic liquids.

Table 2.1 Degradation of different furanic compounds in different [OTf]⁻ and Cl⁻ ionic liquids at 120 °C (6 h)

	Degradation OTf	Degradation Cl
Me-	100.0	98.8
H-	60.8	30.8
O=C-	37	15.4
HOOC-	2.8	2.3

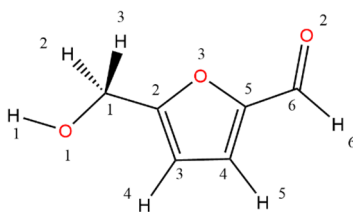
Characterization of humins

The main side products of HMF degradation are classified as humins. Different studies were conducted on humin structures and it has been demonstrated that different morphologies and chemical structures are observed with different media, catalyst and feedstock used. Understanding of the humins' chemical structure is an important feature needed to deduce the mechanism of degradation and the potential to use this byproduct as a value-added material. In this work, humins were synthesized in [bmim]Cl, [bmpyr][OTf], [bmim][OTf] and [bmim][HSO₄] at 160 °C then separated through water addition and washed extensively with water and ethanol. Surprisingly, no humins were formed in [bmim]Cl even when substantial degradation was observed according to Figure 2.3. This suggests that degradation of HMF in this solvent occurs through the formation of water-soluble oligomers whose further polymerization is inhibited by the Cl⁻ anions. On the contrary, large amounts of humins (30% compared to HMF) were collected from the other ionic liquids and analysed by FT-IR (Figure 2.4). The humins recovered from the ionic liquids [bmim][OTf] and [bmpyr][OTf] showed the same IR spectra, confirming that the degradation obeys the same mechanism. In order to gain more information on the structure and gain more insights on which functional groups are reacting, the IR spectra of the humins was compared with the substrate HMF to see which peaks undergo to change. The peaks of HMF was assigned based on the computational study done by Tsilomelekis and co-workers.¹¹

Compared to the HMF spectra, it can be deduced that the furanic structure of HMF remains intact, while the absorption at 3392 cm⁻¹ related to the disappearance of the hydroxy group, indicating that the degradation proceeds through reaction of the hydroxyl group while the aldehyde peak at 1665 cm⁻¹ remains unaffected with a slight shift of the aromatic C=C stretching at 1519 cm⁻¹.²⁴ In contrast, humins recovered from the [HSO₄]⁻ ionic liquid exhibit completely different spectra compared to HMF where the structure in the furanic regions below 1665 cm⁻¹ is completely altered, while the hydroxyl group is transformed into a broad peak typical of a carboxylic acid signal. In this case, a different mechanism of degradation is involved where aldehyde groups and furan rings undergo side reactions. Ring opening of the furan is a potential mechanism that could explain this observation.

Table 2.2 HMF assignments of the IR spectra peaks based on study reported in literature.¹¹

Absorption (cm ⁻¹)	Assignment
3392	O ₁ -H ₁ stretch
3121 - 2925	CH ₂ sym/asym stretches
2835	C ₆ -H ₆ stretch
1665	C ₆ =O ₂ stretch
1519	C ₂ =C ₃ / C ₄ =C ₅ stretches
1396 – 1369	C ₆ -H ₆ rocking, sp ³ C-H wagging
1336	O ₁ -H ₁ twisting
1277 - 1188	Multiple rocking and C ₄ -C ₅ -C ₆ bending
1070	C ₁ -O ₁ stretch
1017	C ₃ -H ₄ /C ₄ -H ₅ scissoring
985	C ₆ -H ₆ rocking out of plane
964	C ₂ -O ₃ -C ₅ symmetric stretch
941	sp ³ C-H and O ₁ -H ₁ rocking
805 – 767	C ₃ -H ₄ /C ₄ -H ₅ twisting and wagging



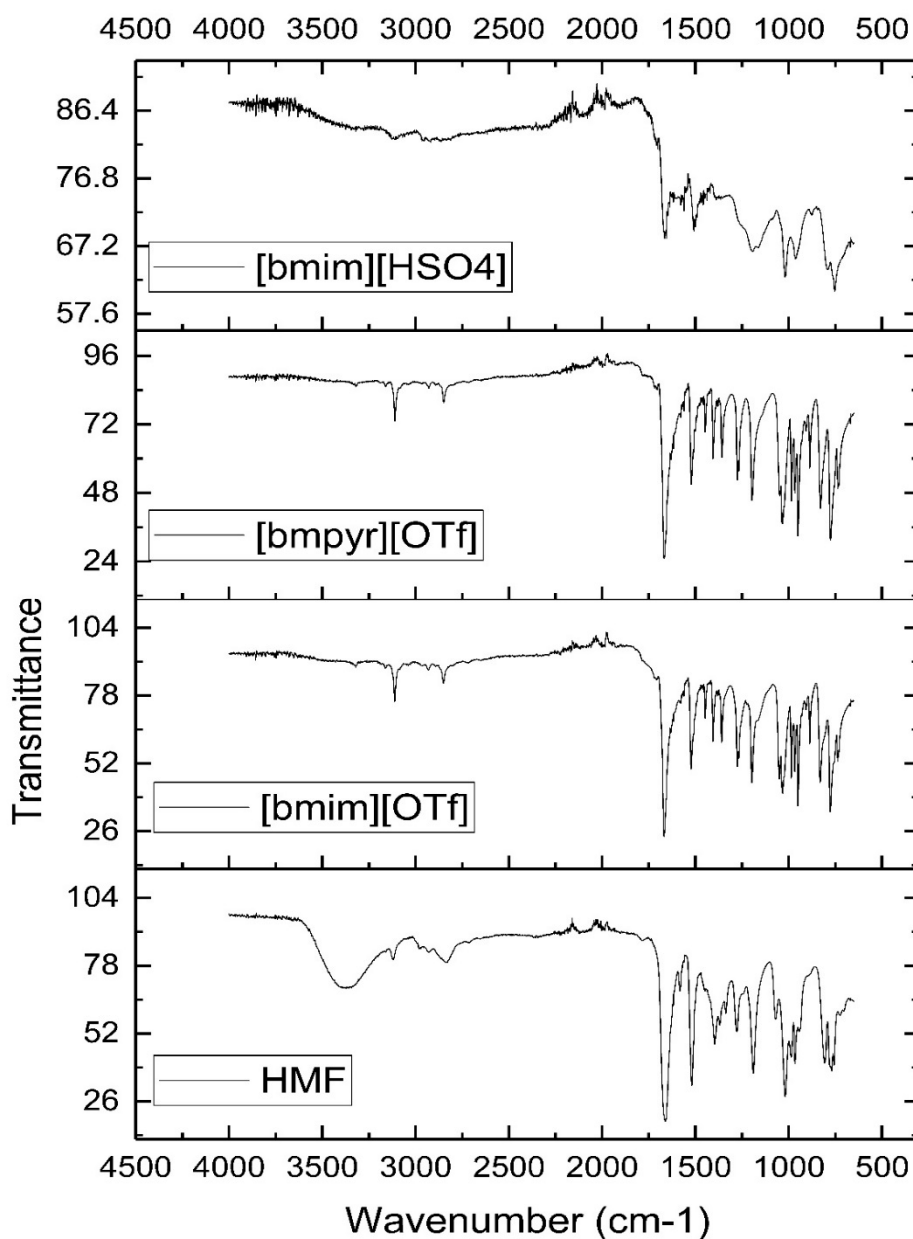


Figure 2.4 FT-IR spectra of humins produced in different ionic liquids compared to the HMF spectra

In order to study the decomposition mechanism in both solvents in more depth, different strategies were adopted. For the humins formed in [bmim][OTf], following the observation that the residue recovered from washing exhibits the same FT-IR spectra as the high molecular weight humins, it was decided to extract this residue with THF to be able to perform mass spectrometry analysis and characterise the repeat unit. The FT-IR spectra of the THF soluble fraction are reported in Figure 2.5 with comparison to those for the high molecular weight humins. The peaks in both spectra exhibit negligible shifts, indicating that the structure of both compounds is similar.

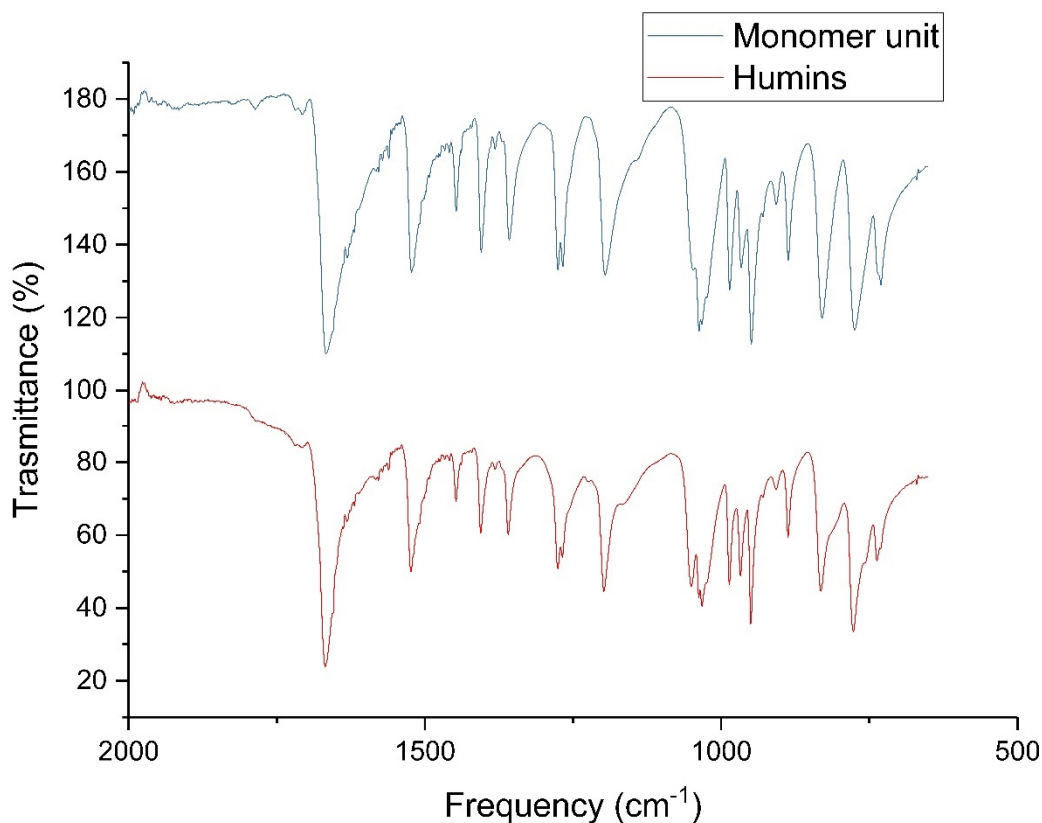
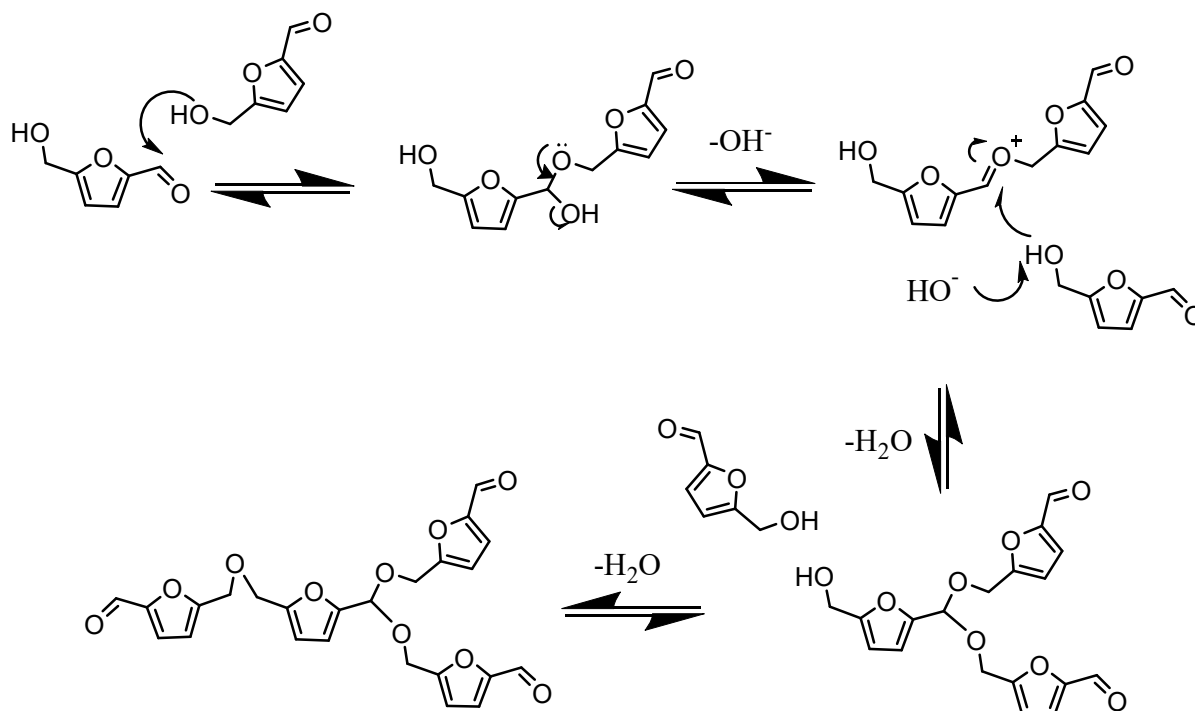


Figure 2.5 FT-IR spectra of humins from [bmim][OTf] degradation and monomeric units isolated from the THF soluble fraction

For the monomeric unit, mass spectrometry analysis indicates a value of m/z 467. Based on this mass, a possible structure was elaborated with a mechanism. From FT-IR data it was concluded that the furanic structure is retained and so the mass is equivalent to 4 furanic rings which are interconnected by units that are not derived from ring opening but result from condensation of the hydroxyl groups (absence of this signal in the FT-IR). It has already been proposed by Summerskii and co-workers²⁵ that furan rings can be interconnected by acetals which involves condensation of two hydroxyl groups with an aldehyde. This is further confirmed by the peaks between 1000-1200 cm^{-1} in Figure 2.4 and Figure 2.5, which are characteristic of acetal signals. While Summerskii proposed an acid catalysed reaction, the high temperatures used in this reaction speed up the kinetics, requiring no catalyst. However longer reaction times were still required since at 3 and 6 hours no humin formation was observed. A structure was thus elaborated with a mechanism and reported in Figure 2.6.



Mass observed: 467.2716
 Mass calculated (positive ion): 467.0973
 Error: 0.038 %

Figure 2.6 Proposed mechanism of HMF degradation in [OTf]⁻ ionic liquids. Readapted from study in literature.²⁵

In the mechanism, one aldehyde group condenses to form an acetal with two hydroxy groups, while the residual hydroxyl group is condensed with another HMF molecule. This mechanism can propagate to form higher molecular weights by condensing other HMF molecules. In this way, the structure has no hydroxyl group and correlates well to the features in the FT-IR spectra obtained.

The mass matches the mass spectra with an error of 0.038%, which is in line with the requirements of most scientific journals (e.g., *ChemSusChem* < 0.4%). From these results, it can be concluded that the structure depicted in Figure 2.6 is a monomeric unit of the humins formed in the non-coordinating ionic liquids with [OTf]⁻ anions.

In contrast, the humins formed by the acidic [bmim][HSO₄] ionic liquid proved to have a more complex structure. The peaks relative to the aldehyde and furan ring in the IR spectra at low frequency had decreased in intensity, probably due to the breakdown of the furanic structure in favour of other types of reactions. Titrici and co-workers have already demonstrated that sugars undergo decomposition to graphene like material at high temperatures in the ionic liquid [bmim][FeCl₄].^{26,27} The consumption of the aldehyde group of HMF under acidic conditions was demonstrated by Patil and co-workers, who proposed an intermediate 2,5-dioxo-6-hydroxy-hexanal (DHH) to explain such behaviour.¹⁵ However, no spectroscopic evidence was reported for DHH to prove its existence and recently Shen and co-workers claimed that HMF can react with levulinic acid and formic acid through aldol condensation.

This contradicts observations from previous studies which suggested that levulinic and formic acid are accumulated in the system and do not participate in humin formation.^{15,28,29} The presence of a strong carboxylic acid signal in the IR spectra of the humins formed in [bmim][HSO₄] indicates that the nature of these side reactions is ring opening. The furan can be converted to a benzene ring which can further be interconnected through an aldol condensation of the open form of the furan ring. The formation of benzene rings is further supported by Raman spectra analysis which exhibits the G and D bands typical of graphitized material. In contrast, humins from ionic liquids with triflate ions proved to be inactive, indicating that benzene rings are not formed in this type of structure. In this case, a lower molecular weight unit could not be isolated, so mass spectrometry analysis was not possible.

The change of the humin structure from furanic to benzene was proposed by Luiks and co-workers,³⁰ in which 1,2,4-benzenetriol was isolated at high yield from HMF treated at high temperature (400 °C) under acidic conditions in water. The authors proposed a mechanism based on ring opening with an intermediate which undergoes cycloaddition. In our study, the benzenetriol can represent the starting molecule for further polymerization reactions, but evidence for this is still lacking. Studies by others have shown that the transition from furan-rich structures to graphitized structures upon heating at high temperature (>700 °C) for gasification purposes, leads to the detection of aromatic compounds by GC-MS. Solid state ¹³C NMR analysis by Hoang and co-workers¹⁴ showed that carboxylic and ketone groups disappeared upon heating at high temperature due to decarboxylation, while the C=C signal increased sharply, indicating an increase in aromatization of the solid.

A different structure was observed with fructose as a starting material and using HCl as catalyst. As can be seen in Figure 2.7, the strong signal associated with the hydroxyl group indicates that most of the fructose functionalities are retained and complete dehydration of the OH groups is not achieved. A 6 h reaction time allowed the isolation of the side product through condensation of HMF and an intermediate from fructose dehydration

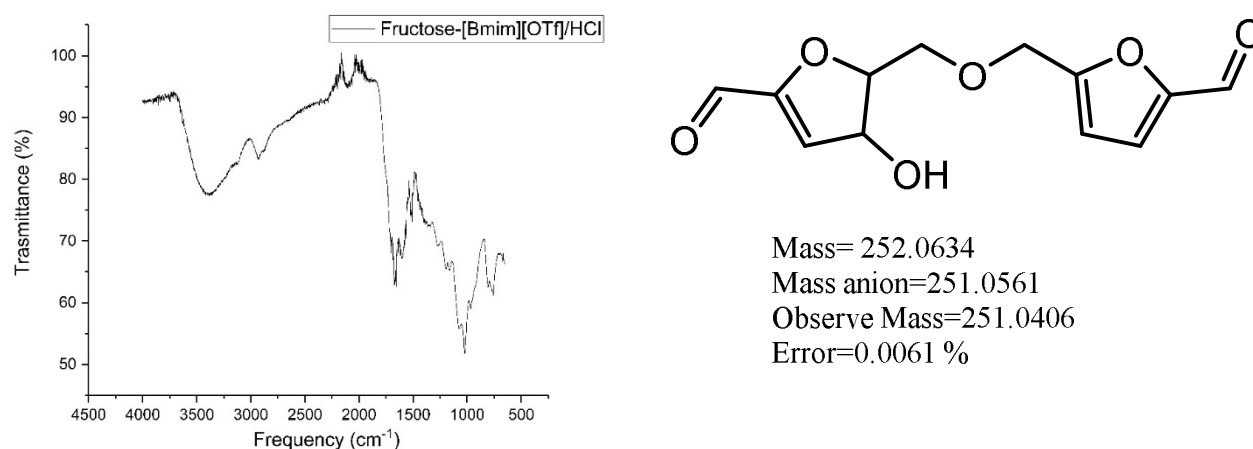


Figure 2.7 IR Spectra of humins formed by acid-catalysed dehydration of fructose and the proposed repeating unit of the humins

. This could be representative of a repeating unit of the humins formed. Further discussion and details of the mechanism will be provided in the next chapter.

Morphology and molecular weight analysis

Besides influencing the molecular structure, the reaction medium influences the morphology and the molecular weight of the humins formed. In Figure 2.8 the SEM images recorded for different humins formed in different ionic liquids are displayed. The cation did not influence the chemical structure of the solid, but SEM analysis proves that it does influence the morphology. The humins formed in [bmim][OTf] exhibited larger particles compared to those formed in [bmpyr][OTf] due to the lower viscosity which favours particle growth due to the higher diffusion of the oligomers formed in the liquid phase, which can further react increasing the molecular weight. In contrast, the higher viscosity of the [bmpyr] salt disfavours the condensation of the particles, creating a flakes of nanostructured material. The acid catalyst [bmpyr][HSO₄] showed similar behaviour, with fructose-derived humins forming nanoparticles.

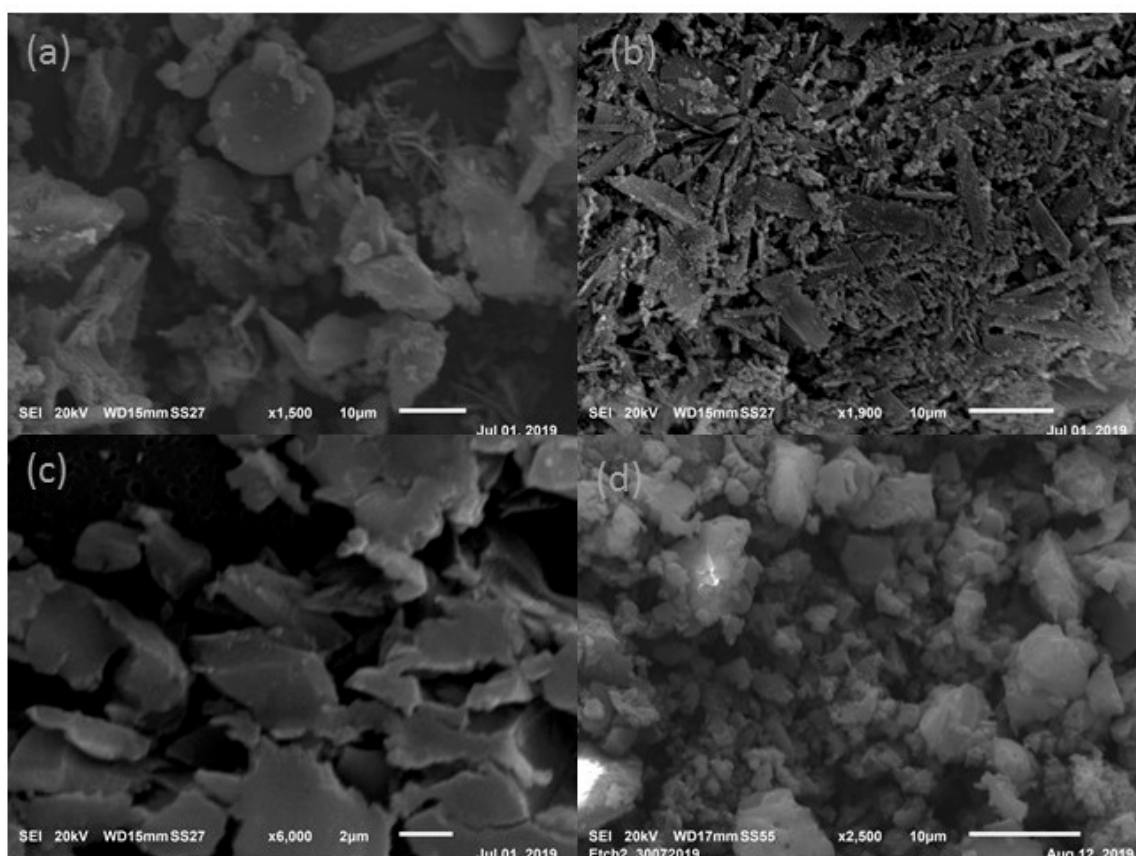


Figure 2.8 SEM of humins formed in different ionic liquids after 9 h at 160 °C. a) [bmim][OTf]; b) [bmpyr][OTf]; c) [bmim][HSO₄]; d) dehydration of fructose in [bmim][OTf] with 10 % HCl.

Insights can be deduced by analysing the molecular weight and particle sizes of the solids. The particle size measurement using the Mastersizer instrument was performed only for the humins formed from [bmpyr][OTf] since the analysis requires a large amount of sample and these humins represent the most interesting structures for the small particle dimensions obtained. The humins obtained from [bmim][HSO₄] could not be analysed as the particles could not be dispersed in the water phase, instead precipitating on the bottom of the instrument. Figure 2.9 reports the particle size distribution of these humins, giving an average size of 37 μm with a broad distribution in the nanoparticle range. This indicates that agglomeration exists as the SEM images show that most of the particles are on the nm scale.

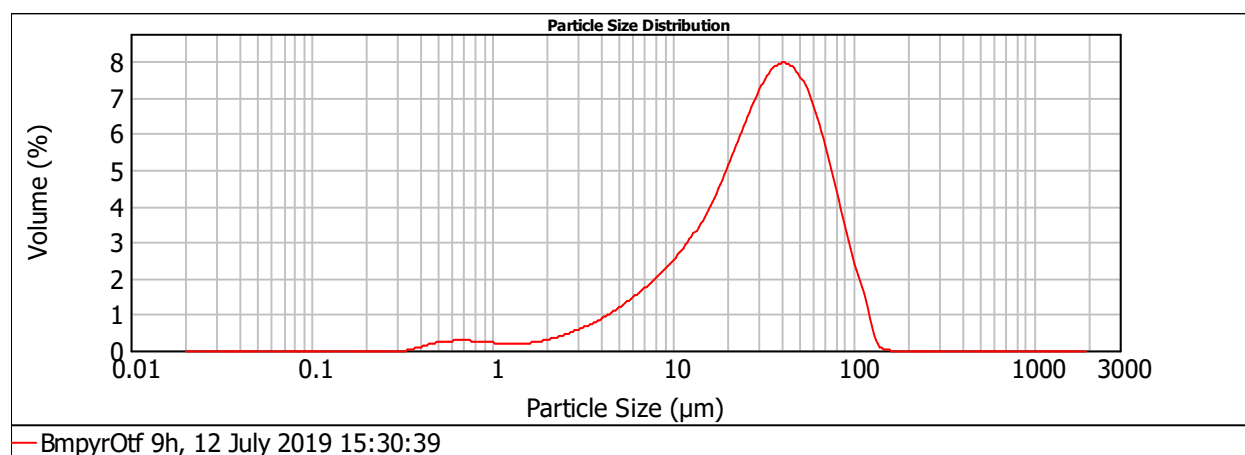


Figure 2.9 Particle size distribution for the humins formed in the ionic liquid [bmpyr][OTf].

Further studies were performed by analysing the molecular weight of the humins by GPC in Figure 2.10. The humins from the [OTf]⁻ ionic liquids exhibited two peaks at low and high molecular weight. While the low molecular weight feature has a sharp peak, its value is not completely reliable since it is below the calibration curve; however these are representative of water insoluble oligomers with low molecular weights. A time course analysis of the reaction reported in

Figure 2.10 (right) shows that these low molecular weight peaks decrease in intensity in favour of the high molecular weight peak. Indeed, by increasing the reaction time the molecular weight of the humins increases two-fold with higher polydispersity being observed as well as a decrease of the peak at lower molecular weight. This indicates that one possible mechanism for humin growth lies in the agglomeration of oligomers rather than direct addition of HMF to the polymer matrix. This is further confirmed by the FT-IR spectra presented in Figure 2.5, indicating that the humins are growing with the same repeating unit depicted in Figure 2.6. In contrast, no peaks in the low molecular weight region were observed for humins produced in [HSO₄]⁻ ionic liquids and in [bmim][OTf] from fructose. In case of [HSO₄]⁻, the high yield of humins suggests that the degradation was achieved much faster hence a direct conclusion cannot be made. In the case of fructose, the low yield of humins obtained indicates

that the polymer is growing from agglomeration of water-soluble compounds, hence a mechanism of growth by fructose addition to the polymer matrix is more plausible.

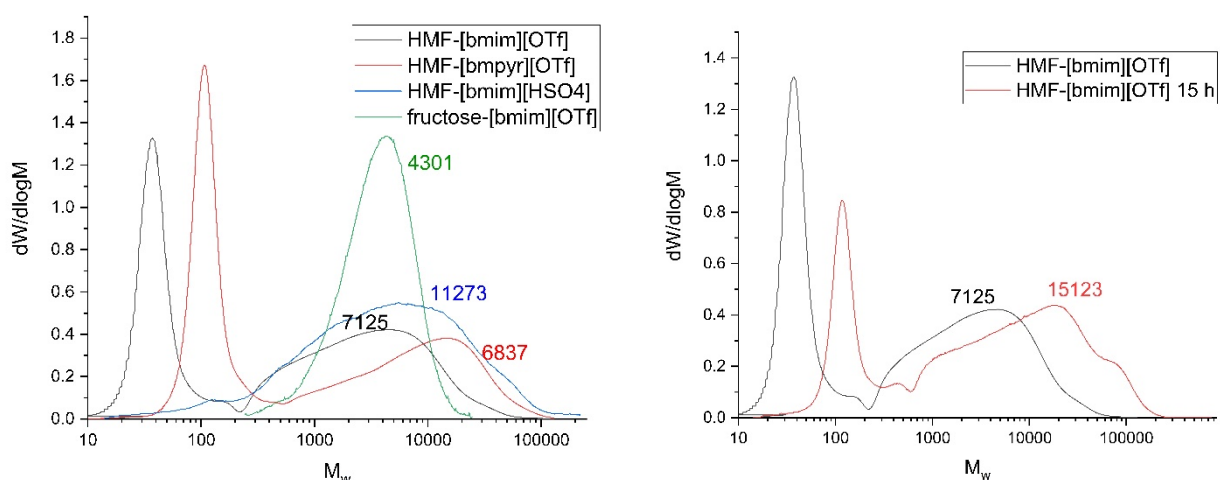


Figure 2.10 Molecular weight distribution of humins produced in different ionic liquids.

Application of humins in metal extraction from waste water

Metal removal from waste water has always represented an important topic for sustainable water use with regulations becoming stricter with time. In this matter, the concentration of heavy metals in the waste water needs to be reduced to ppb levels. Here, the challenge lies on designing an adsorbent with high absorption capacity which can remove the metals efficiently but at the same time being cost efficient. Solid adsorbents are preferred over liquids since they are easier to implement in wastewater treatment (WWT) plants and simplify the phase separation greatly.³¹ Metals are leached into the water phase in the form of ionic salts, hence polar surfaces represent a suitable medium for adsorption of metals. More specifically, functionalized surfaces which can chelate the metals can enhance the adsorption capability. So far, activated carbon has proved to be efficient for this purpose due to its low cost and good adsorption performance. However, the need to achieve high levels of removal have led to much research aimed at developing functionalized materials which can further enhance the adsorption. According to the structure proposed for the humins in the previous paragraph, this material can represent a superior adsorbent for metal removal since furans are more polar compared to benzene rings (representative of carbon materials) and the high oxygen content leads to highly functionalized groups which can potentially chelate the metal. In the following analysis some preliminary results are presented for the removal of lead using humins produced from the thermal degradation of HMF in ionic liquids. In Table 2.3 are the results for humins produced from [OTf]⁻ and [HSO₄]⁻ ionic liquids compared to commercial activated carbon (Sigma-Aldrich). Surprisingly, activated carbon performed better than the humins produced in [OTf]⁻ ionic liquids, which is probably due to the fact that benzene rings interact better than furan rings with metals through π - π stacking. This is further confirmed by the experiment with humins produced from [HSO₄]⁻ ionic liquids, since a graphitized structure was observed by Raman

spectroscopy. This humin exhibits better performance in the extraction at low solid loading, combining both the benefits of having benzene rings in the structure with highly functionalized groups derived from the ring opening of the furans.

It can be concluded that humins produced in [bmim][HSO₄]⁻ represent a potentially valuable adsorbent for metal removal from waste water treatment, exhibiting superior properties compared with the activated carbon tested and double the extraction efficiency.

Table 2.3 Extraction of Pb (100 ppm) from water with humins. Conditions: 20 °C, 0.1 % humins loading respect the solvent, pH 4.

Humins from	Yield of extraction (%)
[bmim][OTf]	14 ± 3.2
[bmim][HSO ₄]	42 ± 5.5
Activated Carbon	19 ± 3.3

Conclusions

HMF exhibits instability in ionic liquids, producing different types of water-insoluble humins. The cation of the ionic liquid was found to influence the morphology of the humins and not the chemical structure. Using [bmim]Cl as solvent, the degradation of HMF is extensive but no humins were formed, indicating that the degradation is limited to small molecular weight oligomers. Bromide anion, which are weaker H-bond acceptors, provides a higher level of stability.

On the contrary, in the non-coordinating ionic liquid [bmim][OTf], HMF form large amounts of humins. A combined analysis of mass spectrometry and FT-IR demonstrated that the repeating unit is formed of furanic rings connected by acetals. In this case a mechanism was proposed.

Using ionic liquids with [HSO₄]⁻ anions, the humins produced have carboxylic acid groups with a graphitized structure, suggesting ring opening followed by cycloaddition. A mechanism for this process was not proposed and further analysis is needed in order to understand which functional groups are involved.

Analysis of the molecular weight with GPC indicates that humins formed from [bmim][OTf] grow with a mechanism of oligomer agglomeration while humins from [HSO₄]⁻ or fructose dehydration involve direct molecular agglomeration of HMF or fructose into the polymer matrix.

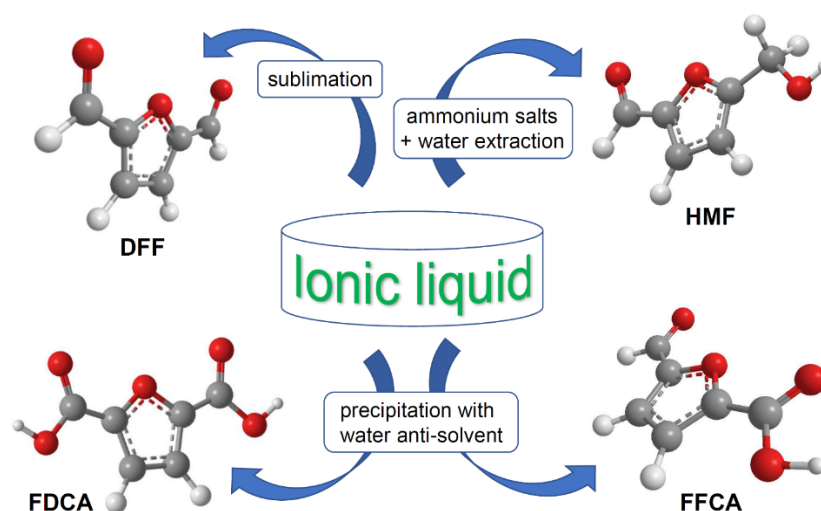
References

- (1) Stahlberg, T.; Eyjolfsson, E.; Gorbanev, Y. Y.; Sdaba, I.; Riisager, A. Aerobic Oxidation of 5-(Hydroxymethyl)Furfural in Ionic Liquids with Solid Ruthenium Hydroxide Catalysts. *Catal. Letters* **2012**, *142* (9), 1089–1097. <https://doi.org/10.1007/s10562-012-0858-5>.
- (2) Yan, D.; Xin, J.; Zhao, Q.; Gao, K.; Lu, X.; Wang, G.; Zhang, S. Fe-Zr-O Catalyzed Base-Free Aerobic Oxidation of 5-HMF to 2,5-FDCA as a Bio-Based Polyester Monomer. *Catal. Sci. Technol.* **2018**, *8* (1), 164–175. <https://doi.org/10.1039/c7cy01704a>.
- (3) Chen, R.; Xin, J.; Yan, D.; Dong, H.; Lu, X.; Zhang, S. Highly Efficient Oxidation of 5-Hydroxymethylfurfural to 2,5-Furandicarboxylic Acid with Heteropoly Acids. *ChemSusChem* **2019**, *12* (12), 2715–2724. <https://doi.org/10.1002/cssc.201900651>.
- (4) Galkin, K. I.; Krivodaeva, E. A.; Romashov, L. V.; Zalesskiy, S. S.; Kachala, V. V.; Burykina, J. V.; Ananikov, V. P. Critical Influence of 5-Hydroxymethylfurfural Aging and Decomposition on the Utility of Biomass Conversion in Organic Synthesis. *Angew. Chemie - Int. Ed.* **2016**, *55* (29), 8338–8342. <https://doi.org/10.1002/anie.201602883>.
- (5) Galkin, K. I.; Ananikov, V. P. Towards Improved Biorefinery Technologies : 5-Methylfurfural as a Versatile C 6 Platform for Biofuels Development. *ChemSusChem* **2019**, *11* 9991, 185–189. <https://doi.org/10.1002/cssc.201802126>.
- (6) Zakrzewska, M. E.; Bogel-lukasik, E.; Bogel-lukasik, R. Ionic Liquid-Mediated Formation of 5-Hydroxymethylfurfural s A Promising Biomass-Derived Building Block. *Chem. Rev.* **2011**, *111* (2), 397–417. <https://doi.org/https://doi.org/10.1021/cr100171a>.
- (7) Al Ghatta, A.; Wilton-Ely, J. D. E. T.; Hallett, J. P. Rapid, High-Yield Fructose Dehydration to HMF in the Ionic Liquid [Bmim][OTf]. *ChemSusChem* **2019**. <https://doi.org/https://doi.org/10.1002/cssc.201901529>.
- (8) Li, Y. N.; Wang, J. Q.; He, L. N.; Yang, Z. Z.; Liu, A. H.; Yu, B.; Luan, C. R. Experimental and Theoretical Studies on Imidazolium Ionic Liquid-Promoted Conversion of Fructose to 5-Hydroxymethylfurfural. *Green Chem.* **2012**, *14* (10), 2752–2758. <https://doi.org/10.1039/c2gc35845j>.
- (9) Hou, Q.; Li, W.; Zhen, M.; Liu, L.; Chen, Y.; Yang, Q.; Huang, F.; Zhang, S.; Ju, M. An Ionic Liquid-Organic Solvent Biphasic System for Efficient Production of 5-Hydroxymethylfurfural from Carbohydrates at High Concentrations. *RSC Adv.* **2017**, *7* (75), 47288–47296. <https://doi.org/10.1039/c7ra10237b>.
- (10) Zhao, H.; Holladay, J. E.; Brown, H.; Zhang, Z. C. Metal Chlorides in Ionic Liquid Solvents Convert Sugars to 5-Hydroxymethylfurfural. *Science (80-.)*. **2007**, *316* (5831), 1597–1600. <https://doi.org/10.1126/science.1141199>.
- (11) Tsilomelekis, G.; Josephson, T. R.; Nikolakis, V.; Caratzoulas, S. Origin of 5-Hydroxymethylfurfural Stability in Water/Dimethyl Sulfoxide Mixtures. *ChemSusChem* **2014**, *7* (1), 117–126. <https://doi.org/10.1002/cssc.201300786>.
- (12) Wang, H.; Liu, S.; Zhao, Y.; Zhang, H.; Wang, J. Molecular Origin for the Difficulty in Separation of 5-Hydroxymethylfurfural from Imidazolium Based Ionic Liquids. *ACS Sustain. Chem. Eng.* **2016**, *4* (12), 6712–6721. <https://doi.org/10.1021/acssuschemeng.6b01652>.
- (13) Al Ghatta, A.; Wilton-Ely, J. D. E. T.; Hallett, J. P. Strategies for the Separation of the Furanic Compounds HMF, DFF, FFCA, and FDCA from Ionic Liquids. *ACS Sustain. Chem. Eng.* **2019**. <https://doi.org/https://doi.org/10.1021/acssuschemeng.9b03613>.
- (14) Hoang, T. M. C.; van Eck, E. R. H.; Bula, W. P.; Gardeniers, J. G. E.; Leffertsa, L.; Seshana,

- K. Humin Based By-Products from Biomass Processing as a Potential Carbonaceous Source for Synthesis Gas Production. *Green Chem.* **2015**, *17* (2), 959–972. <https://doi.org/10.1039/C4GC01324G>.
- (15) Patil, S. K. R.; Lund, C. R. F. Formation and Growth of Humins via Aldol Addition and Condensation during Acid-Catalyzed Conversion of 5-Hydroxymethylfurfural. *Energy and Fuels* **2011**, *25* (10), 4745–4755. <https://doi.org/10.1021/ef2010157>.
 - (16) Cheng, Z.; Vlachos, D. G.; Everhart, J. L.; Tsilomelekis, G.; Nikolakis, V.; Saha, B. Structural Analysis of Humins Formed in the Brønsted Acid Catalyzed Dehydration of Fructose. *Green Chem.* **2018**, *20* (5), 997–1006. <https://doi.org/10.1039/C7GC03054A>.
 - (17) Wei, Z.; Liu, Y.; Thushara, D.; Ren, Q. Entrainer-Intensified Vacuum Reactive Distillation Process for the Separation of 5-Hydroxymethylfurfural from the Dehydration of Carbohydrates Catalyzed by a Metal Salt-Ionic Liquid. *Green Chem.* **2012**, *14* (4), 1220–1226. <https://doi.org/10.1039/c2gc16671b>.
 - (18) Zhang, Z.; Liu, W.; Xie, H.; Zhao, Z. K. An Unexpected Reaction between 5-Hydroxymethylfurfural and Imidazolium-Based Ionic Liquids at High Temperatures. *Molecules* **2011**, *16* (10), 8463–8474. <https://doi.org/10.3390/molecules16108463>.
 - (19) 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), 1–15. <https://doi.org/10.1371/journal.pone.0163835>.
 - (20) 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 Sustain. Chem. Eng.* **2014**, *2* (4), 978–981. <https://doi.org/10.1021/sc400553q>.
 - (21) Wells, T. P.; Hallett, J. P.; Williams, C. K.; Welton, T. Supplementary Information for : Esterification in Ionic Liquids : The Influence of Solvent Basicity. *J. Org. Chem.* **2008**, *73* (14), 5585–5588. <https://doi.org/10.1021/jo8005864>.
 - (22) Correia, I.; Welton, T. An Old Reaction in New Media: Kinetic Study of a Platinum(II) Substitution Reaction in Ionic Liquids. *J. Chem. Soc. Dalton Trans.* **2009**, *35* (21), 4115–4121. <https://doi.org/10.1039/b822152a>.
 - (23) Tsurumaki, A.; Ohno, H. Dissolution Oligo (Tetrafluoroethylene) Preparation. *Chem. Commun.* **2018**, *54* (4), 2–9.
 - (24) van Zandvoort, I.; Wang, Y.; Rasrendra, C. B.; van Eck, E. R. H.; Bruijninx, P. C. A.; Heeres, H. J.; Weckhuysen, B. M. Formation, Molecular Structure, and Morphology of Humins in Biomass Conversion: Influence of Feedstock and Processing Conditions. *ChemSusChem* **2013**, *6* (9), 1745–1758. <https://doi.org/10.1002/cssc.201300332>.
 - (25) Sumerskii, I. V.; Krutov, S. M.; Ya Zarubin, M. Humin-Like Substances Formed under the Conditions of Industrial Hydrolysis of Wood. *Russ. J. Appl. Chem.* **2010**, *83* (2), 321–328. <https://doi.org/10.1134/S1070427210020266>.
 - (26) Xie, Z. L.; White, R. J.; Weber, J.; Taubert, A.; Titirici, M. M. Hierarchical Porous Carbonaceous Materials via Ionothermal Carbonization of Carbohydrates. *J. Mater. Chem.* **2011**, *21* (20), 7434–7442. <https://doi.org/10.1039/c1jm00013f>.
 - (27) Xie, Z. L.; Huang, X.; Titirici, M. M.; Taubert, A. Mesoporous Graphite Nanoflakes via Ionothermal Carbonization of Fructose and Their Use in Dye Removal. *RSC Adv.* **2014**, *4* (70), 37423–37430. <https://doi.org/10.1039/c4ra05146g>.
 - (28) Horvat, J.; Klaić, B.; Metelko, B.; Šunjić, V. Mechanism of Levulinic Acid Formation. *Tetrahedron Lett.* **1985**, *26* (17), 2111–2114. [https://doi.org/10.1016/S0040-4039\(00\)94793-2](https://doi.org/10.1016/S0040-4039(00)94793-2).

- (29) Girisuta, B.; Janssen, L. P. B. M.; Heeres, H. J. A Kinetic Study on the Decomposition of 5-Hydroxymethylfurfural into Levulinic Acid. *Green Chem.* **2006**, 8 (8), 701.
<https://doi.org/10.1039/b518176c>.
- (30) Luijkx, G. C. A.; van Rantwijk, F.; van Bekkum, H. Hydrothermal Formation of 1,2,4-Benzenetriol from 5-Hydroxymethyl-2-Furaldehyde and d-Fructose. *Carbohydr. Res.* **1993**.
[https://doi.org/10.1016/0008-6215\(93\)80027-C](https://doi.org/10.1016/0008-6215(93)80027-C).
- (31) Komjarova, I.; Blust, R. Comparison of Liquid-Liquid Extraction, Solid-Phase Extraction and Co-Precipitation Preconcentration Methods for the Determination of Cadmium, Copper, Nickel, Lead and Zinc in Seawater. *Anal. Chim. Acta* **2006**, 576 (2), 221–228.
<https://doi.org/10.1016/j.aca.2006.06.002>.

Chapter 3 Ionic Liquid as Green Solvents for the Separation of Sugar-derived Furanic Compounds



The synthesis of the platform chemical 5-hydroxymethylfurfural (HMF) from sugars and its conversion to higher value products have been a key area of recent research. This has led to the development of a wide range of catalytic systems for this purpose. In particular, there has been a focus on the synthesis of 2,5-diformylfuran (DFF) and 2,5-furandicarboxylic acid (FDCA) from sugars, passing through HMF as an intermediate. FDCA is attracting attention as it is the key monomer needed to make the bioderived plastic PEF, a sought-after substitute for PET in packaging applications. The synthesis of HMF has proven very efficient in ionic liquids but the process is limited by the high cost in isolating the final product. Efforts to avoid the need to isolate HMF have been driven by the instability of the compound and the difficulties in its separation from the ionic liquid medium. This has led to the catalytic generation of products, such as DFF, FFCA (5-Formyl-2-furancarboxylic acid) and FDCA via HMF. While the focus has rested firmly on the development of catalytic routes to these products, much less attention has been paid to the separation of these compounds from the ionic liquid solvent medium. Ionic liquids are widely used as highly effective solvents for the pre-treatment of biomass and the breakdown of sugars, making use of their stability, negligible volatility and potential for recycling. Despite this, the production of DFF and FDCA in ionic liquid media has been hampered by the lack of information on the separation of these compounds. Perhaps due to this, much research has been done in DMSO (high bp, flammable) to produce FDCA or DFF from fructose and Srinivasan and co-workers addressed the

issue of separation recently¹, quantifying the anti-solvent needed for the precipitation of these compounds from DMSO. Inspired by this study, the following chapter provides a detailed study on the separation of HMF, FDCA, FFCA and DFF from ionic liquids. By exploiting the chemical and physical tunability of the ionic liquids, we were able to achieve very effective separation of these compounds from the medium. In particular, we show that DFF can be separated with high efficiency and high purity from the ionic liquids by sublimation at low temperature. For the first time, we demonstrate that the sublimation properties of DFF are retained even in solution. While so far DFF has played a marginal role compared FDCA (it is far less studied), the highly efficient separation of this compound from ionic liquids can make it a new interesting sugar-derived platform chemical.

The separation of FDCA and FFCA was performed by adding water as anti-solvent and an energy analysis using Aspen² was used to calculate the conditions needed for removal of water to allow recycling of the ionic liquid for further catalytic cycles. It was discovered that the amount of water that needs to be added to ionic liquids in order to separate FDCA is lower than that required when using DMSO. This represents a valuable energy saving and reduced water consumption, which are important factors for potential scale-up of the process.

Furthermore, we analysed the solvent extraction of HMF from hydrophobic ammonium-based ionic liquids. Using ammonium salts has the advantage that water can be used as the extracting phase, favouring the partitioning due to the well-known affinity of HMF for water. In this context, ionic liquids with non-coordinating anions (such as bis(trifluoromethylsulfonyl) imide) proved to be the best solvents for the combined synthesis and extraction of HMF.

The following work was published in the journal *ACS Sustainable Chemistry and Engineering*³.

Introduction

In order to develop an efficient chemical process, different chemical and engineering aspects must be strictly evaluated. While the optimization of the reaction yield with catalyst design and optimization of reaction parameters represents a priority and a milestone for the scale-up of a process, separation represents another fundamental issue which can establish the competitiveness of a technology. Indeed, separation can impact drastically the capital and operating cost of a chemical plant and its optimization it is crucial to obtain a process with low energy input and high yield. The process engineer needs to adopt the most convenient choice in terms of units (distillation, liquid-liquid/gas extraction, membranes, adsorption) and configuration. On the other hand, different reaction pathways can be used to favour the separation. The choice of the solvent will have the main impact on the separation, especially in cases where diluted conditions are used. Toxicity and boiling point will strongly influence the disposal procedure, recycling, selectivity and separation units.

The extensive research carried out in the last 15 years aimed at the efficient synthesis of 5-HMF from sugars has shown that separations represent the main issue for the commercialization at large scale of this molecule.⁴ The high boiling point of this substance, instability at high temperature and room temperature melting point makes the separation and purification of this compound very tedious and inefficient. Due to the instability of 5-HMF at high temperatures and side reactions with the sugars under catalytic conditions, low concentrations of substrates are needed to guarantee high yields, hence the solvent choice plays a key role in the feasibility of the process in terms of process economics and sustainability, since it will inevitably represent the main component of the system. Water, DMSO and ionic liquids have proved so far to be the best candidates for a high yield of product, each with advantages and disadvantages.^{5,6} Water, which is considered by many reports the greenest solvent (price, abundance and disposal), has proven to be inefficient without the addition of an organic solvent, which is needed to partially suppress the side reaction by partial extraction of 5-HMF from the reaction mixture.⁷ This system will not be completely green because of the use of an organic solvent, even if the low cost of catalysts and solvents have attracted the interest for scale-up from AVA Biochem, which is now operating a pilot plant which produces 5-HMF from fructose. The synthesis of 5-HMF using water as a medium allows for easy isolation of the product due to the favourable water/organic partition coefficient.⁸ However, using water as solvent does not allow one to obtain 5-HMF from glucose or cellulose in one-pot, which represents a cheaper and more sustainable solution. For this purpose, DMSO and ionic liquids have proved to be superior solvents and many reports have reported high yields of 5-HMF but with the drawback that the separation of HMF is not feasible. Regarding ionic liquids, extraction with organic solvents (such as ethyl acetate or diethyl ether) is regularly used but the partition coefficient is unfavourable, necessitating excessive washing.⁹ Moreover, the use of organic solvents during product recovery undermines some of the benefits of using ILs such as flammability, volatility

and toxicity, the same issues the use of an ionic liquid was meant to avoid. The idea so far is to convert *in situ* HMF into a product that is easier to separate. Many studies have been performed with DMSO and important results have been obtained with chemical pathways that can go from 5-HMF to DFF or FDCA in two steps.¹⁰ However, the high solvation ability of DMSO makes the separation of any organic compound very tedious.

Srinivasan and co-workers analysed the separation from DMSO of glucose, HMF, DFF and FDCA by antisolvent addition.¹ In their work, glucose was separated by addition of organic solvents, DFF and FDCA by water addition and HMF by addition of water followed by separation using solvent extraction. Many papers report DMSO as efficient for both sugar dehydration and HMF oxidation,^{11–13} however, the applicability of this solvent on a large scale is hindered by its high boiling point (189 °C), its decomposition to toxic sulfur compounds and the need for low substrate loadings in many cases. Moreover, a process based on DMSO would still be dependent on organic solvents and separation through antisolvent addition, which can result in high energy requirements for solvent regeneration. An energy balance analysis would be needed to evaluate the techno-economic impact of such a process.

The separation of HMF from ionic liquids has proven so far to be a challenging problem and the main issue to scale-up of this technology. Different innovative trials have exploited the low vapour pressure of these solvents. Thermal distillation under very high vacuum and high temperature has been proposed, despite the risk posed by the thermal instability of HMF. Wei and co-workers used an entrainer distillation apparatus (Figure 3.1) which at high temperature (180 °C), high vacuum (300 Pa) and rapid gas bubbling (N₂ or saturated organic solvent) was able to achieve over 90% recovery in a short reaction time (10 min).¹⁴ The final purity of 5-HMF achieved was around 90%. However [omim]Cl was used to avoid evaporation under such harsh conditions but it was reported that this ionic liquid exhibits instability at high temperatures.¹⁵

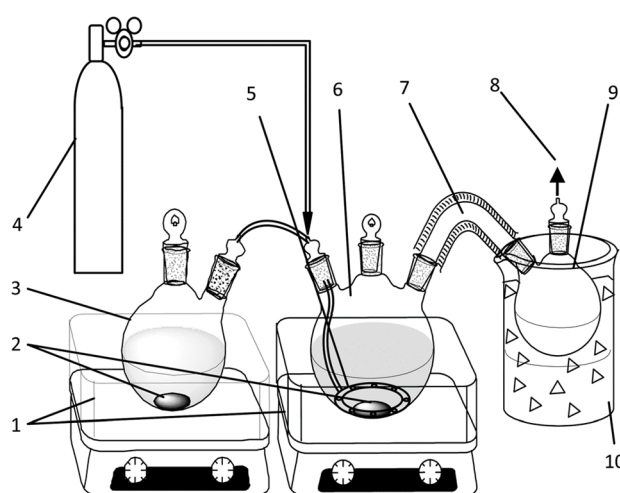


Figure 3.1 System proposed by Wei and co-workers . 1) oil bath heater, 2) magnetic stirrer, 3) Two neck flask for vapor generator(organic solvent at its boiling point temperature), 4)Nitrogen cylinder, 5) Ring type gas distributor, 6) Three neck flask (ionic liquid and HMF), 7) connector, 8) connection to vacuum oil pump, 9) Product collection , 10) ice bath. Reproduced with the permission of ref¹²

Other authors have proposed extraction with supercritical CO₂.¹⁶ In contrast to organic solvents, supercritical CO₂ is considered a green solvent for its non-toxicity and non-flammability; hence extraction with this solvent can establish an organic solvent-free process. Sun and co-workers have studied the partition coefficient of HMF between [bmim]Cl and CO₂ at different pressures and temperatures, showing that lower temperature favours the extraction and a minimum of 20 bar pressure is necessary to achieve 70% extraction, which is considered still too low a partition for a scalable process compared to the high pressure needed.¹⁷ Other studies use CO₂ as a phase separator to increase the extraction with organic solvents. Following the observation that at relatively low CO₂ pressure (7.5 bar) the mixture of [omim]Cl and acetone separate, Shi and co-workers¹⁴ designed a system where HMF is extracted continuously from [omim]Cl with CO₂ and acetone reaching a yield of 84% from fructose. Major drawbacks of the system lie in the selectivity of extraction since catalyst and sugars are partially soluble in the CO₂-acetone mixture.

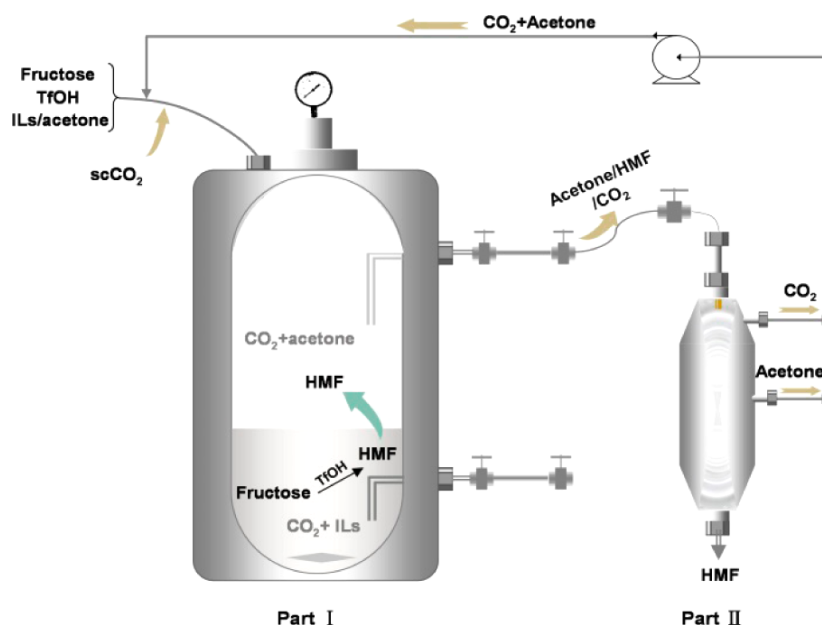


Figure 3.2 System of Shi and co-workers for the extraction of HMF from ionic liquid with a mixture of acetone and CO₂ with continuous concentration. Reproduced with the permission from ref¹⁴

In the systems reported so far, the separation of HMF from ionic liquids requires harsh conditions and a multiphasic continuous system. In this context, the *in situ* conversion of HMF to a chemical compound with a less challenging separation represents a potential solution.

By analysing the chemical path from HMF to FDCA, we can identify several intermediate products that can potentially be synthesized from HMF through aerobic oxidation; 2,5-diformylfuran (DFF), 5-formylfuran-2-carboxylic acid (FFCA) and 2,5-furandicarboxylic acid (FDCA). While DFF and FFCA have potential in the pharmaceutical and consumer product industry,^{18,19} FDCA is the key monomer to produce polyethylene furanoate (PEF), a bioplastic suitable for use as a food and beverage

packaging in place of polyethylene terephthalate (PET).²⁰ The study of the separation will form a basis for a solvent design strategy in which the optimum catalytic performance is combined with suitable conditions for separation.

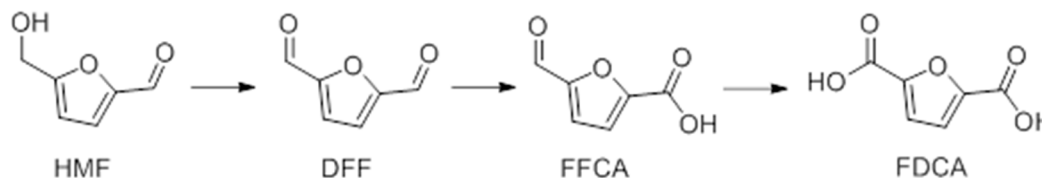


Figure 3.3 Reaction pathway to obtain FDCA from HMF

So far, many systems have been reported for the selective oxidation of HMF to obtain these chemicals based on both noble and non-noble metal catalysts in water or organic solvents. Solvent effects have proved to be a determinant factor for the selectivity of the reaction, influenced by the water content in the system. Organic solvents proved to be more selective towards DFF^{21–26} while water is the most used solvent for the synthesis of the carboxylic acids FFCA and FDCA.^{27–30} Recent research has focused on synthesising these molecules.

In this chapter DFF, FDCA, FFCA and 5-HMF separation will be studied in different ionic liquids thus providing guidelines for a solvent design strategy for scale-up of production of these molecules. The compatibility of the ionic liquids with possible catalytic routes reported in the literature will also be discussed. In the case of homogeneous catalysis, precipitation of the final product from the reaction mixture is preferred in order to avoid expensive thermal separation and favour catalyst recycling. In contrast, under heterogeneous catalytic conditions, the final product should be soluble to avoid catalyst deactivation and the separation has to be performed using heating or by addition of an antisolvent after catalyst removal. While sugar dehydration in ionic liquids is widely studied, only recently has progress has been achieved in the oxidation of HMF and sugars to FDCA in [bmim]Cl but the results described only report HPLC yields at very diluted conditions,^{31–33} hence separation and purification will play a determinant role in defining the feasibility of scale-up using ionic liquid technology for this application.

In order to minimize the use of organic solvents, the extraction of HMF, DFF, FFCA and FDCA from ionic liquids will be investigated in this work in order to establish the most suitable ionic liquid for each compound to allow further processing. If the lack of volatility of the ILs causes difficulties in product separation, this property will be exploited, along with the polarity of the ILs, to achieve an optimum separation of the components from the mixtures. Imidazolium ionic liquids were investigated for the separation of these compounds because of their low viscosity. This is preferred since the catalytic aerobic oxidation route which leads to DFF, FFCA and FDCA requires solvents with low viscosity to avoid mass transfer limitations. In the context of this work, the aim is to demonstrate that the one-pot synthesis of these compounds in the ionic liquids can provide a more favorable environment for the

separation. Different anions were tested to analyse the effect of hydrogen bond acceptor ability on the separation. The study with HMF is carried out by analysing the ammonium ionic liquids to study the hydrophobicity effect on the extraction with water. The final extraction of HMF in water can guarantee a suitable environment for oxidation to FDCA which can be easily separated in water by acidification.

Most literature reports on the synthesis of DFF use organic solvents,^{26,34} raising doubts over the feasibility of potential scale up due to product separation issues and environmental sustainability. Based on our observation in the lab and previous work,³⁵ DFF cannot be sublimed from organic solvents (neither upon heating nor by applying vacuum) but this property is retained in ionic liquids. Hence, the synthesis of DFF in ionic liquids allows separation by sublimation and this represents a solution to large-scale product separation as well as solvent recycling without the need for expensive thermal treatments. Moreover, sublimation usually delivers a high purity product, avoiding the need for further purification.

The separation of FDCA and FFCA is studied by calculating their solubility in different ionic liquid - water mixtures. Only recently was the synthesis of FDCA from HMF in [bmim]Cl described using a Fe/Zr catalyst which makes this system compatible with the formation of HMF from glucose.³³ While this system proved to have great potential for one-pot synthesis of the plastic monomer from sugars, challenges regarding separation still remain. We studied the separation of FDCA from ionic liquids through water addition, by exploiting the low solubility of FDCA in water. However, the addition of water in a system containing ionic liquids requires regeneration of the solvent for further catalytic cycles. Using the thermodynamic ILUAM database package for ionic liquids supplied by Victor Ferro,² a multi-effect evaporation process was simulated in Aspen to estimate the energy requirement for regeneration of the ionic liquid. Compared to the values reported for DMSO,¹ the addition of a smaller quantity of water is required when an ionic liquid is used (*vide infra*), decreasing the water consumption for potential scale up.

For HMF, hydrophobic ionic liquids were studied based on methyltrioctylammonium salts paired with water extraction of HMF. Ammonium salts have been reported as good solvents for the dehydration of glucose to HMF in high yield,³⁶ showing minimal leaching into the water phase.³⁷ The combination of ammonium salts with water could form the basis of a system free of organic solvents for HMF extraction and subsequent oxidation to FDCA, since water has (thus far) proved to be the most efficient medium for the catalytic oxidation of aldehydes and alcohols to carboxylic acids.²⁷ By using hydrophobic ionic liquids, the affinity of HMF towards the water phase can be favoured, providing the basis for an improvement in the partition coefficient for the extraction of HMF. Many catalysts have been studied for this oxidation under base-free conditions, making ready implementation of a two-step reaction possible. Previously, different organic solvents were studied to extract HMF from the ionic liquid phase with the Cl⁻ ionic liquids. An extensive study was reported by Zho and co-workers³⁸ where different organic solvents were tested as extractants from [bmim]Cl, showing the best performance with

glycol dimethyl ether and acetyl acetone with partition coefficient close to 3.33 towards the ionic liquid phase over THF, butyl ether, MIBE, MIBK, cyclohexone, ethyl acetate and n-butanol. Other reports show that by changing the Cl⁻ anion of the ionic liquid for triflate, remarkably the partition coefficient can be increased by one order of magnitude.³⁹ By using a hydrophobic ionic liquid and water, the partition coefficient can be improved even more.

Experimental Section

Materials

Ionic Liquid were synthesized according procedure already reported in Chapter 2 (Experimental Section). All chemicals and cold finger glassware were purchased from Sigma-Aldrich, as were the methyltrioctylammonium salts with anions chloride ($\geq 97\%$), bromide ($\geq 97\%$) and bistriflimide ($\geq 99\%$).

DFF sublimation

The sublimation of DFF was performed using a sublimation apparatus with heating and cooling in small volumes to guarantee optimum recovery of the solid sublimate under vacuum. DFF (40 mg) was placed in a 1 mL vial and mixed with 400 mg of solvent to be tested. The vial was placed inside the cold finger chamber, then heating was applied for 10 min at the operating temperature to test when the solution became clear indicating full solubilisation. Vacuum was applied for the desired time. The DFF was collected on the tip of the condenser, which was cooled to 7 °C.

Trials of sublimation through gas bubbling was also tested by designing a flask adapter to fit the cold finger, but results were not replicable due to the difficulties in controlling the flow rate and in guaranteeing a uniform temperature in the glassware causing non-localized sublimation.

Images of the experimental setup are provided in the Appendix. All experiments were performed two or more times.

Precipitation of FFCA and FDCA from ionic liquids by water addition.

In order to evaluate the separation of FDCA and FFCA from the ionic liquids, the solubility of these compounds in different IL-water mixtures was calculated to estimate the facility to separate these compounds. The saturation point of the mixture was determined by gradual addition of substrate in a certain amount of solvent (~300 mg) followed by stirring overnight (200 rpm). After centrifugation (40,000 rpm) the liquid phase was analysed by HPLC with a UV-detector operating at 254 nm with external standard calibration. Experiments were repeated at least three times.

The energy required for the dehydration was calculated using Aspen Plus 8.8v with the integrated ILUAM package. The process was simulated with a 4-stage multiple effect evaporator.

HMF extraction from a hydrophobic ionic liquid.

The extraction efficiency of HMF from the hydrophobic ionic liquid was evaluated in terms of partition coefficients. In order to replicate the experiments in triplicate and avoid tedious measurements on the order of mg, a stock solution of ionic liquid with HMF at the desired concentration (C_{HMF0}^{IL}) was prepared on a large scale. Since the ionic liquid is solid or exhibits very high viscosity making it difficult to handle and all lie on the bottom of the vial, both compounds were dissolved in dichloromethane.

Aliquot solutions were removed and placed in 1.5 mL centrifuge vials, from which the organic solvent was removed under vacuum for 12 h. A certain amount of water was then added to each vial in order to obtain the desired phase ratio (R) followed by stirring for 12 h to ensure equilibrium had been reached. A small amount of water phase was withdrawn and analysed by HPLC with external standard calibration and the partition coefficient (K) calculated according to the following equation:

$$\frac{1}{K} = 1 - R \frac{C_{HMF}^w}{C_{HMF0}^{IL}}$$

Where K is the partition coefficient, R mass phase ratio, C_{HMF}^w concentration of HMF in the water phase at equilibrium (mg/g), C_{HMF0}^{IL} initial concentration of HMF in the ionic liquid phase (mg/g).

The calculation of the number of washes required to achieve a desired recovery (y) was determined by the following equation:

$$N = \frac{\ln(1 - y)}{\ln(1 - \frac{R}{K + R})}$$

Where N is the number of washes to obtain a desired recovery, y is the desired recovery defined as $R \frac{C_{HMF}^w}{C_{HMF0}^{IL}}$ and R is the mass phase ratio.

Analytical method

Quantification of HMF, FFCA and FDCA was performed using a Shimadzu Prominence preparative HPLC (Shimadzu, Kyoto, Japan) with refractive index (RI) and ultraviolet (UV) detectors. This instrument was equipped with an Aminex HPX-87H column which exhibits outstanding resolution for polar compounds (HMF 27 min, FFCA 20 min and FDCA 14 min) using 0.005 M H₂SO₄ as the mobile phase at 55 °C and a flow rate of 0.6 mL/min. Quantification was done with external standard.

Calculation of the Solubility of Hydrophobic Ionic Liquids in Water

The solubility of the ionic liquids in water was determined by mixing the two phases overnight at room temperature (20 °C). The water phase was analysed by ion chromatography Dionex ICS-5000+ DC using a method reported in the literature.⁴⁰ Anion chromatography (AC) was performed on a Thermofisher ICS5000+ with a Dionex IonPac AS20 (4 × 250 mm) analytical column and an AG20 (4 × 50 mm) guard (45 °C), AERS500e 4 mm analytical suppressor (15 °C), and conductivity detector. The eluents included 18.2 MΩ·cm Milli-Q ultrapure water, HiPerSolv CHROMANORM acetonitrile (≥99.9%), and 200 mM NaOH (from 50% w/w fisher scientific NaOH), typically proportioned at 30% acetonitrile and 10–20% 200 mM NaOH (20–40 mM eluent strength), depending on the sample being analysed. Chromatograms were eluted isocratically at 1 mL/min, and the electrochemical suppressor was regenerated by external 18.2 MΩ·cm Milli-Q ultrapure water. Quantification was done by external standards using LiNTf₂, NaCl and NaBr to quantify the anion.

Esterification of FDCA with ethylene glycol in ionic liquids

In a typical experiment 12.6 mg of FDCA were dissolved in 1 g of ionic liquid with 620 mg of ethylene glycol (100:1 molar respect to FDCA) at 80 °C in a 10 ml vial. 1.7 mg (10 % loading respect FDCA) of para-toluene sulfonic acid (PTA) was loaded in the vial and the mixture heated at the desired temperature and time.

Quantification was done by HPLC with a C18 reverse phase carbon column with the same method reported in Chapter 2 (experimental section).

Results and Discussion

Sublimation of DFF from ionic liquids

The following study was conducted after the observation that following the dissolution of DFF in ionic liquids and, followed by heating overnight, DFF crystals appeared on the top of the vial indicating that the dialdehyde sublimes directly out of the ionic liquid. Since sublimation is slow at 1 atm, vacuum was applied to increase the rate of sublimation and recover the whole product in a short time.

The effect of the hydrogen bonding on the separation of DFF from imidazolium ionic liquids was first studied. Two different anions, chloride and bistriflimide ($[\text{NTf}_2]$), were used since they represent two extremes in hydrogen bond acceptor strength. Under reduced pressure, at 100 °C for 12 hours, 93-95% of the DFF was recovered at 10% loading from both ILs (Table 3.1), showing no influence of the ionic liquid on the sublimation property of DFF.

Table 3.1 DFF recovered by sublimation at 100 °C under reduced pressure, 10% DFF loading respect the solvent, 12 h.

Ionic liquid	DFF recovered from commercial sample	DFF recovered from second sublimation
[bmim]Cl	93.1 $\pm$ 0.1%	96.7 $\pm$ 0.4%
[bmim][NTf ₂]	95.2 $\pm$ 0.3%	97.7 $\pm$ 0.2%

The commercial DFF used was not the highest purity (95 %); therefore, a second sublimation was performed on the same recovered material, achieving a higher recovery. This suggests that the DFF was obtained at higher purity. This is further confirmed by the fact that the brown commercial DFF yields a white powder on sublimation under our conditions (see Figure A224 in Appendix).

In [bmim][NTf₂], heating at 40 °C was required to achieve full dissolution since at room temperature the solubility is low (10.2 $\pm$ 0.6 mg/g). This indicates that precipitation is another useful separation method since [bmim][NTf₂] is a room temperature ionic liquid. However, the high viscosity of the IL and the washing of the product makes the procedure tedious with inevitable loss of ionic liquid and yield. For this reason, precipitation was not considered further in this study. An investigation conducted in [bmim][NTf₂] for 6 hours showed that a minimum temperature of 60 °C is required to fully recover the dissolved DFF by sublimation (Figure 3.4). In contrast, at 40 °C, DFF is fully dissolved with only 7% recoverable by sublimation.

From these results, it appears that the hydrogen bond acceptor ability of the ionic liquid has little effect on the sublimation of DFF, allowing high recovery in both cases. This makes ionic liquids a viable option to valorise HMF through selective alcohol oxidation. In agreement with Wang and co-workers, the major interaction between HMF molecules and the ions in the IL appears to be the hydrogen bonding between the anion and the HMF hydroxyl group, with other interactions being

negligible.³⁹ The absence of any strong interactions between the aldehyde groups of DFF and the ions in the IL favour its separation by conserving the sublimation properties of DFF. The possibility of exploiting this separation technique makes the scale-up of this reaction very attractive. FT-IR analysis was conducted to confirm these statements (described at the end of this chapter).

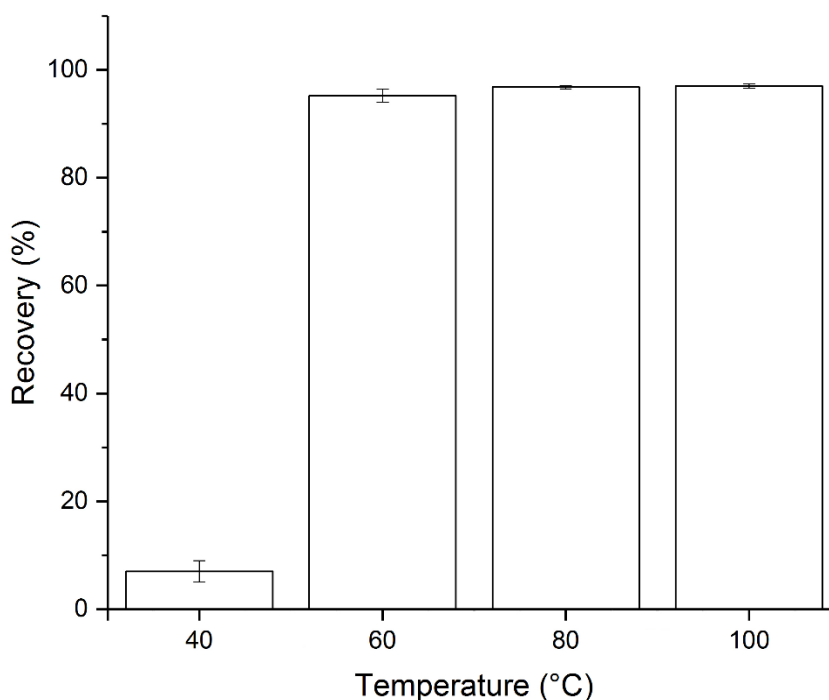


Figure 3.4. Recovery of DFF in 3 h at different temperatures from [bmim][NTf₂] under vacuum (20 mbar). 10 % loading DFF respect the solvent Reproduced with the permission of ref ¹

Separation of FDCA and FFCA

In order to study the separation of FDCA and FFCA from the ionic liquids, the solubility of FDCA and FFCA was calculated in order to provide a threshold parameter at which separation through precipitation can be accomplished. The low solubility of FDCA and FFCA in water is well known,⁴⁰ hence the hydrophilicity of the ILs was exploited to achieve separation through antisolvent precipitation. Solubility was calculated at room temperature since low temperatures are needed to achieve precipitation. However ionic liquids with halide anions are solid at room temperature, hence water contents above 20% were chosen as the minimum amount necessary to achieve a liquid state with sufficiently low viscosity to allow separation at room temperature. The solubility of FDCA in [bmim]Cl at high temperatures is reported to be 49%.⁴³

In the following study, the solubility of FDCA in both [bmim]Cl and [bmim]Br were compared for the separation, however, so far, only [bmim]Cl has been reported as a solvent for the synthesis of FDCA.³³ In Figure 3.5 the solubility at different water contents was calculated showing that FFCA

exhibits higher solubility compared to FDCA in the ILs tested. From the trend observed, the decreased solubility of FDCA at low water content suggests that the hydrogen bonding interactions between the carboxylic acid groups and the anions play a key role. By increasing the amount of water, the strong interaction between the chloride ions and carboxylic groups are broken due to solvation of the chloride ions in favour of the interactions with water which are much weaker.

In light of our studies on DFF sublimation, the high solubility of FFCA was not predicted since aldehydes have a lower affinity for anions, as demonstrated by Wang and co-workers.³⁹ However the presence of water can introduce new interactions with the aldehyde moiety and the formation of geminal diol that can form from the nucleophilic attack of water on the aldehyde, which would dramatically increase the solubility of the aldehyde. Such interactions were already observed in literature hence it is a valid explanation for the higher solubility observed compared to FFCA.⁴¹ At high water contents, the interactions that dominate are between the water and the aldehyde, however the acidity of the carboxylic acid group in FFCA can hinder the formation of the geminal diol, leading to a decrease in its solubility. At low water contents, the molecule can exhibit a combined interaction with both water and chloride anions. This allows water to interact with the aldehyde while hydrogen bonding between the chloride ions and the carboxylic acid increases the pKa of the molecule, favouring the formation of diols. Regarding the role of the anion, FDCA and FFCA proved to be less soluble in the bromide-based ionic liquid, probably due to the lower hydrogen-bonding ability of the bromide toward the carboxylic group.

In order to separately analyse the role of water on the solubility of FDCA and FFCA, a study was carried out with the hydrophilic, non-coordinating ionic liquid [bmim][OTf] over a range of water concentrations. In this way the interaction of the ionic liquid with the OH group is suppressed. The results reported in the data gathered show that both FDCA and FFCA can be separated from [bmim]Cl, [bmim]Br and [bmim][OTf] by addition of water. The results reported by Srinivasan et al in 2017 demonstrate that the solubility of FDCA in DMSO at 20% water content is around 30%.¹ Figure 3.5 (left) shows that this value decreases to 12% for [bmim]Cl and only 3.4% in [bmim]Br with the same water content. In this context, ILs represent a more suitable solution for a possible scale-up to reduce water consumption. The results reported in the data gathered show that both FDCA and FFCA can be separated from [bmim]Cl, [bmim]Br and [bmim][OTf] by addition of water. The results reported by Srinivasan et al in 2017 demonstrate that the solubility of FDCA in DMSO at 20% water content is around 30%.¹ Figure 3.5 (left) shows that this value decreases to 12% for [bmim]Cl and only 3.4% in [bmim]Br with the same water content. In this context, ILs represent a more suitable solution for a possible scale-up to reduce water consumption.

Figure 3.5 (on the right) shows a different trend to that exhibited for [bmim]Cl. In pure [bmim][OTf], FDCA shows very low solubility (< 4 mg/g), while FFCA demonstrates higher solubility, suggesting that the aldehyde group has a superior affinity for this poor hydrogen bond acceptor environment. The maximum solubility observed at 20% water content indicates a synergistic effect

between the ionic liquid and water in the dissolution of these compounds. Since this maximum is observed for both compounds, the interactions may specifically involve the carboxylic acid group. Increasing the water content leads to a plateau where the solubility approaches that in pure water. Higher FFCA solubility at higher water content suggests an interaction of the water with the aldehyde group to form geminal diols already demonstrated in other reports.^{44,45}

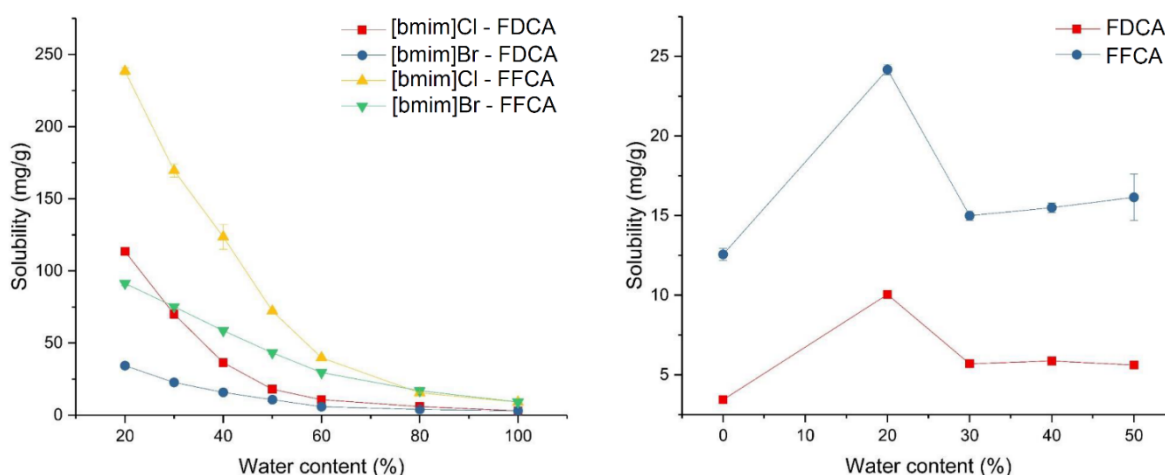


Figure 3.5. Solubility of FDCA and FFCA in ionic liquid - water mixtures of [bmim]Cl and [bmim]Br (left) and [bmim][OTf] (right) at room temperature; solubility expressed in terms of mg of compound per gram of solvent. Reproduced with the permission of ref¹

Energy analysis of drying [bmim]Cl and [bmim]Br

The addition of an antisolvent such as water can drastically impact the operating cost of the plant. In order to evaluate the feasibility of the process, an energy balance of the dehydration step needs to be performed.

The challenge in dehydrating the ionic liquid at low water concentration lies in the high heat of vaporisation of water (2.26 MJ/Kg) and the increasing boiling point at high salt concentration. As can be seen in the phase diagram in Figure 3.6 the boiling point increases exponentially at water content less than 40%.

Multi-effect evaporation represents an efficient process to reduce the energy requirements by exploiting the heat of vaporisation at high pressure to satisfy the energy requirements of the stages operating at lower pressures. Such a configuration is widely used in desalination processes to compensate for the higher energy required by the increased boiling point of salt solutions. In this investigation, we chose four stages at 0.8, 0.5, 0.2 and 0.01 bar to dehydrate the ionic liquid until 1% water remained. 20 mg of product (FDCA or FFCA) per gram of the IL-water mixture was chosen as the threshold level of the residual product in the solvent after precipitation. The corresponding solubility values are shown Figure 3.5 and data on drying the ILs are reported in Table 3.2.

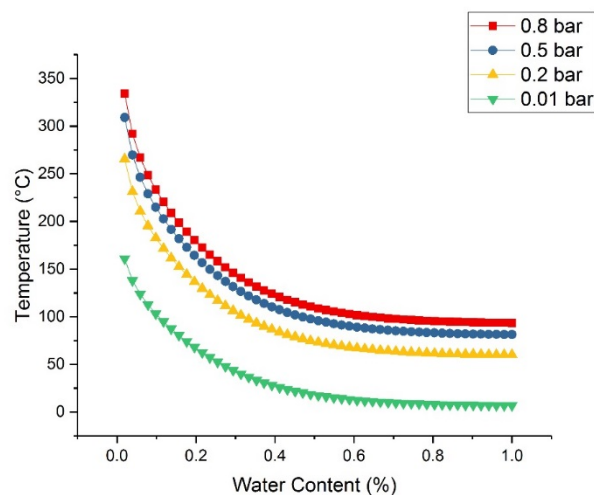


Figure 3.6 Equilibrium diagram [bmim]Cl/water estimated by COSMOSAC with the IULAM package

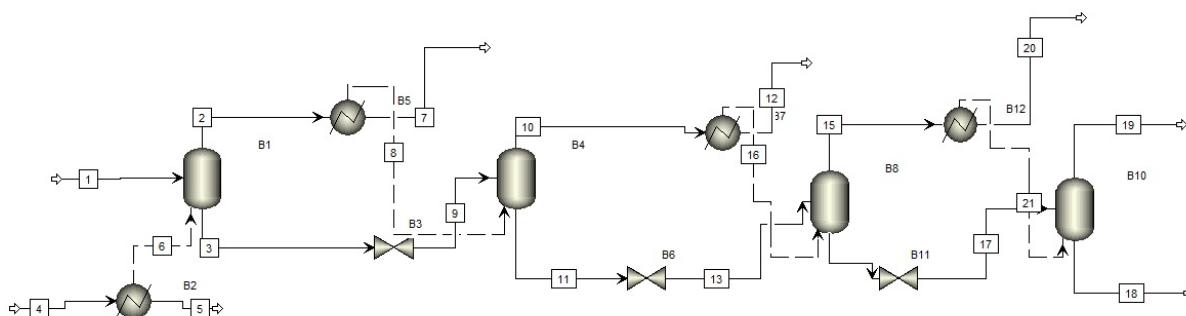


Figure 3.7 Multiple effect Aspen flowsheet for ionic liquid dehydration

Table 3.2 Energy requirement for the drying of ILs until 1% water content in 4-stage evaporators with a final pressure of 0.01 bar. Calculations were performed using Aspen Plus 8.8V with the IULAM integrated package.

Ionic liquid/product	Initial water concentration	Energy Requirement (KJ/Kg)
[bmim]Cl/FDCA	52.0%	409
[bmim]Br/FDCA	37.5%	368
[bmim]Cl/FFCA	83.5%	492
[bmim]Br/FFCA	79.0%	489

According to Table 3.2, removal of the quantity of water required to fully precipitate FFCA from [bmim]Cl or [bmim]Br would lead to high energy requirements, making this approach unsuitable for scale-up purposes. In contrast, the use of [bmim]Cl or [bmim]Br is more favourable for FDCA as less energy is required due to the lower solubility of this product in the IL medium. In both cases the

synthesis of these compounds would be more convenient in [bmim][OTf] for the low solubility in the solvent. However catalytic systems for this purpose are not reported.

A detailed energy analysis for a FDCA plant using ionic liquids would need to be considered in order to optimize the process and minimize operating costs.

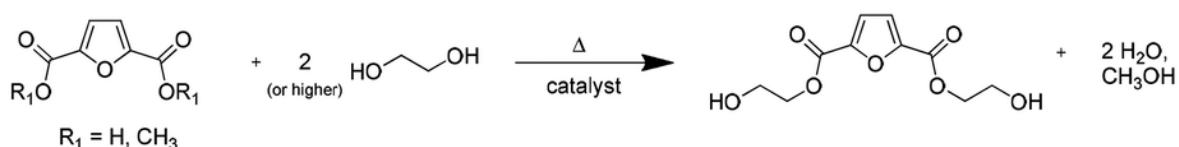
Esterification of FDCA in ionic liquids

Removal of water through the use of multiple effect evaporators represents a typical solution for concentration of salt solutions to reduce the energy consumption of the plant. However, the energy cost can still be high in addition to the fact that capital investments are very high for these types of plants. Membrane separation represents a valid alternative to reduce the investment costs but compatibility in different scenarios must be evaluated for membrane selectivity and stability.

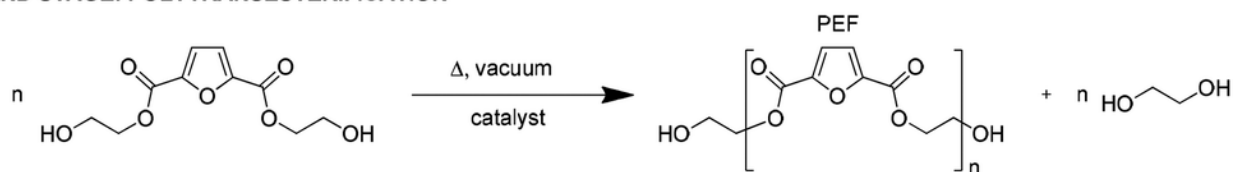
Another possibility is the *in situ* polymerization of FDCA with ethylene glycol which can reduce drastically the water addition due to the hydrophobicity of the resins formed.

The first step of the polymerisation is the formation of the di-substituent oligomer from the carboxylic acid (or ester) with an acid catalyst with release of two molecules of water (or methanol) according the reaction in Scheme 1. In order to form the polymer, higher temperatures and a vacuum need to be applied to remove water and push the reaction towards higher molecular weight products.

1ST STAGE: TRANSESTERIFICATION



2ND STAGE: POLYTRANSESTERIFICATION



Scheme 1 Synthesis of PEF

The effect of the ionic liquid in the first step of reaction will first be discussed. The formation of the di-ester monomer represents a fundamental step for the further polymerization. The reaction conditions were chosen so that FDCA was very diluted in the ionic liquid (12 mg/g) since most of the research so far on the oxidation of HMF in FDCA in ionic liquids are studied at very low concentrations with *p*-toluenesulfonic acid (PTSA) as a Brønsted acid catalyst. The effects of time and temperature are reported in Figure 3.8.

Analysing the reaction at 6 hours shows that temperature exerts a favourable effect on the esterification from being completely inactive at 140 °C to reaching a maximum yield of 22% at 200 °C

(the boiling point of ethylene glycol), while long reaction times decrease the yield probably due to thermal degradation (dark colour of the solution). The optimum yield was found to occur at 3 h.

In order to further analyse the effect of the anion on the esterification, in particular the effect of the H-bond donating ability, tests were performed in the absence of the ionic liquid and with the non-coordinating ionic liquid [bmim][NTf₂] with PTSA as catalyst. The results reported in Table 3.3 indicate that the higher H-bond accepting ability associated with the Cl⁻ anion suppresses the esterification, while the non-coordinating bistriflimide anion has no impact on the reaction. In order to improve the esterification, Lewis acid catalysts (tin and chromium salts) were tested and the results are reported in Table 3.3 with comparison to other reaction conditions.

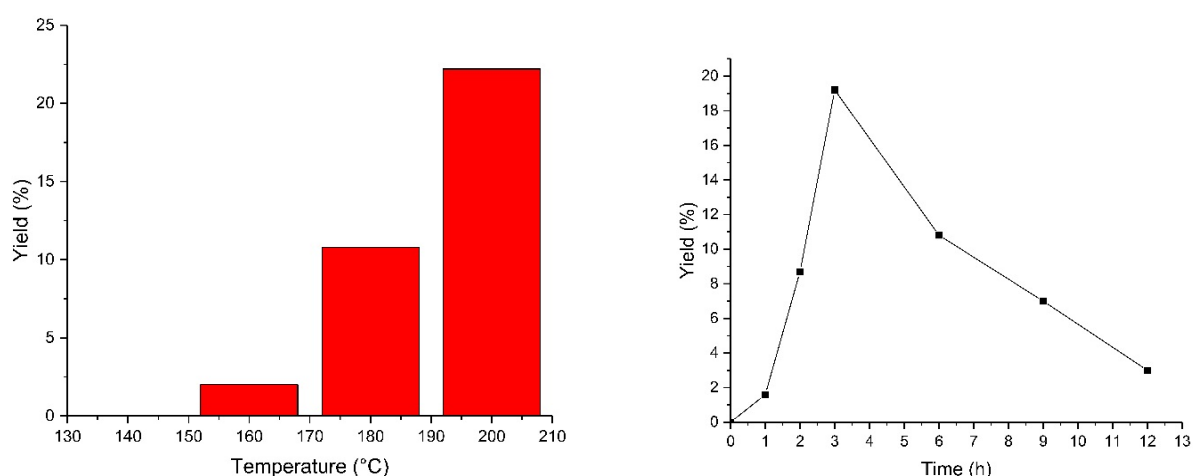


Figure 3.8 Yield of the diester as function of temperature and time for acid esterification with PTSA. Catalyst loading 10 % (mole) respect FDCA, FDCA loading 12 mg/g in ionic liquid. Temperature experiments done at 180 °C. Time course experiments at 6 h. Ethylene glycol:FDCA ratio 100:1 (mole).

Table 3.3 Esterification of FDCA with ethylene glycol using different ionic liquids and catalysts. Temperature 180 °C, FDCA concentration 12.6 mg/g in ionic liquid. Ethylene glycol to FDCA ratio 100:1 (mole). Catalyst loading 10%.

Ionic Liquid	Catalyst	Yield (%)
None	PTSA	67.7
[bmim]Cl	PTSA	19.3
[bmim][NTf ₂]	PTSA	67.5
[bmim]Cl	SnCl ₃	41.9
[bmim]Cl	CrCl ₃	13.5

While chromium exhibits low activity, tin shows the best performance, boosting the yield to 42%. According to the results obtained so far, the esterification of FDCA to the di-substituted monomer proved to be challenging due to low selectivity. This is further compromised by increasing the basicity

of the solvent by adding [bmim]Cl. Further improvements may be achieved by designing an appropriate catalyst.

Recently Qu and co-workers⁴⁶ used ionic liquids as catalyst for the polymerisation of FDCA. In that work 0.5 eq of ethylene glycol were used for the polymerisation at shorter reaction times, achieving a high yield of polymer, demonstrating that a large excess of ethylene glycol is unnecessary for polymerization. The low selectivity can be seen in the instability of the di-ester monomer at high temperature, which, over the longer reaction time, leads to self-degradation.

Extraction of HMF from trioctylmethyammonium salts using water

In this part of the investigation, the extraction of HMF from hydrophobic ionic liquids using water is discussed. While most of the literature discusses the separation from [bmim]Cl with organic solvents, few investigated the extraction using water since it is rare to find studies that report sugar dehydration in hydrophobic ionic liquids. While it has already been proven that the anion plays the key contribution on the yield of dehydration, the cation has a negligible effect on the reaction. Therefore, the polarity of the ionic liquid can be tuned by changing the cation from imidazolium to trioctylammonium, yielding a water-immiscible solvent, so that water extraction can be performed. In order to investigate the nature of affinity both the anion and cation will be varied. As can be seen in Figure 3.9, strong hydrogen bonding anions give an unfavourable partitioning toward the ionic liquid phase, while this is improved remarkably with non-coordinating anions such as [NTf₂]. The cation has a minor impact, obeying the same trend as the polarity of the ionic liquid, as described by the Kamlet-Taft parameter, π . This indicates that secondary interactions between the furan rings exist but the hydrogen bond donating ability of the cation has a minimal effect on the separation.

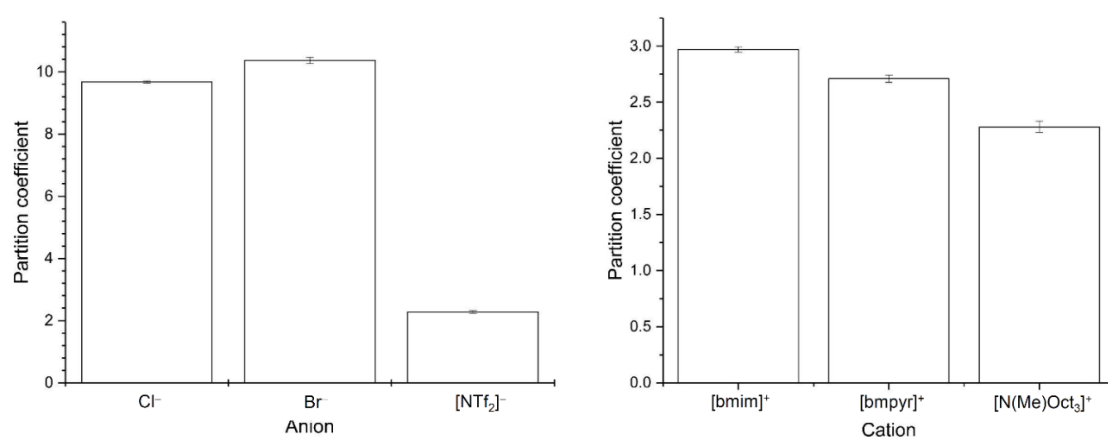


Figure 3.9 Effect of different anions on the partition coefficient for the [N(Me)Oct₃]⁺ salts (left) and the effect of the cation for NTf₂⁻ salts (right). Reproduced with the permission of ref¹

In order to further understand the feasibility of using water to extract HMF from the IL, the number of washes required to obtain 90% recovery and the value for the final HMF concentration in the water phase was calculated. According to most of the literature, in order to further valorise HMF into FDCA through aerobic oxidation, the concentration cannot exceed 0.1 M in the water phase since higher values will cause precipitation of FDCA onto the catalyst surface, requiring the addition of a base.²⁹ However, too low a concentration should also be avoided since it can compromise the efficiency of separation and leads to excessive water consumption for scale-up. The initial loading of HMF and the amount of water used in each stage are therefore crucial factors and these aspects are summarized in Figure 3.10. Using the ionic liquid $[N(Me)Oct_3]Cl$, a minimum of 40% HMF loading is necessary to achieve a concentration close to 0.1 M and an excessive amount of washing is required. As can be seen in Figure 3.10 (right), for an HMF loading of 10% in the IL, 13 washes are required to extract 90% of the HMF, leading to a concentration in the aqueous phase of 0.03 M. In this scenario the chemical path to obtain HMF is an important choice since high loading of sugars are required to achieve the desired HMF concentration, proving to be challenging for the many side reactions which this reaction scheme contains. A reduction in the amount of washing can be accomplished by increasing the water/IL ratio, but this would reduce the HMF concentration in the water phase. Improved yields are indeed often reported under dilute conditions for the production of HMF from cellulose in ILs, for example.⁴⁷ While this is acceptable on a lab scale, more concentrated systems^{48–50} are needed for realistic scale-up. At 10% loading, an HMF concentration of more than 0.1 M can be achieved (compared to 0.03 M using the chloride-based IL) with the bistriflimide anion with only two washes, hence this ionic liquid represents the best solution for an efficient separation.

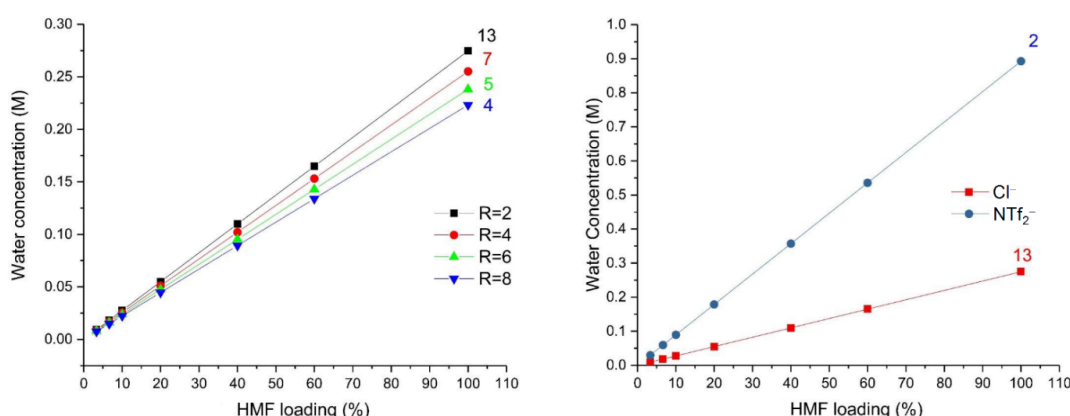


Figure 3.10 On the left, water concentration to achieve 90% HMF recovery from $[N(Me)Oct_3]Cl$ at different phase ratios (R) and different HMF loadings at 20 °C. On the right, water concentration needed to achieve 90% HMF recovery from $[N(Me)Oct_3]Cl$ and $[N(Me)Oct_3][NTf_2]$ ionic liquids at R = 2. Numbers next to the data points represent the number of washes required. Reproduced with the permission of ref¹

Study of the interaction between HMF and ionic liquids by FT-IR

Separation is related to the chemical interaction of the solvent with the product. In order to confirm the interactions mentioned previously, FT-IR analysis was performed for the HMF and ionic liquids to observe the shifts of the -OH and C=O bonds due to their interactions with the anions and cations. This analysis could be done with HMF since the physical state of the ionic liquid [bmim]Cl and [bmim]Br is liquid upon addition of HMF to the mixture. Water could not be added since it reduces the intensity of the peaks related to HMF. This analysis could not be carried out with FFCA, FDCA and DFF since the mixture remains solid, not permitting the dissociation of ions, hence the interactions could not be observed. However, the functional groups in HMF are the same as in the other furanic compounds, therefore the results can be generalised. Whenever hydrogen bonds are broken, the shift related to the -OH moves towards higher wavenumber (blue shift). The opposite of this phenomenon is called a red shift. As observed by Wang and co-workers,⁴¹ the increased addition of ionic liquids is accompanied by a broader and less intense signal for the -OH group. We will neglect in this study the intensity and peak shape since these phenomena are not well understood. It was observed that a minimum amount of 30 mol% ionic liquid provides a good compromise to observe the signal with reasonable intensity. From Figure 3.11, it can be seen that the anion influences both the hydroxyl and carbonyl groups of HMF. For the hydroxyl group the shift follows the order $\text{Cl}^- > \text{Br}^- > [\text{NTf}_2]^-$. The $[\text{NTf}_2]^-$ anion proved to have the lowest H-bond ability (Figure 3.11 left) which leads to a slight blue shift to 3391 cm^{-1} for the $[\text{N}(\text{Me})\text{Oct}_3][\text{NTf}_2]$, while the Cl^- and Br^- salts exhibit red shifts, 3262 cm^{-1} for Cl^- and 3337 cm^{-1} for Br^- , reflecting the higher H-bonding ability of the halide anions in coordinating the -OH unit. This greater interaction of the Cl^- with the -OH group explains the higher solubility of FDCA and FFCA. However, results in Figure 3.11 exhibit a different trend compared to the H-bond ability of the anion since higher partition coefficients are observed for the Br^- anion, suggesting that other interactions are involved. Figure 3.11 (right) reports the spectra for the C=O absorption, showing a slight red shift from the original 1683 cm^{-1} with the strongest belonging to the Br^- (1667 cm^{-1}) and the weakest being $[\text{NTf}_2]^-$ (1678 cm^{-1}) while the Cl^- anion exhibits an intermediate shift (1674 cm^{-1}). The effect of the cation on both functional groups of HMF revealed no relevant contribution of the cation in H-bonding. This confirms that the polarizability of the ionic liquid is a more realistic indication of the more favourable partition coefficient for the ammonium salt and lower interaction with the furan ring. In particular, it was observed that the HMF and the ammonium salt do not exhibit full miscibility as for the [bmim] and [bmpyr] salts, indicating that secondary interactions arise between the cation and the furan ring of HMF.

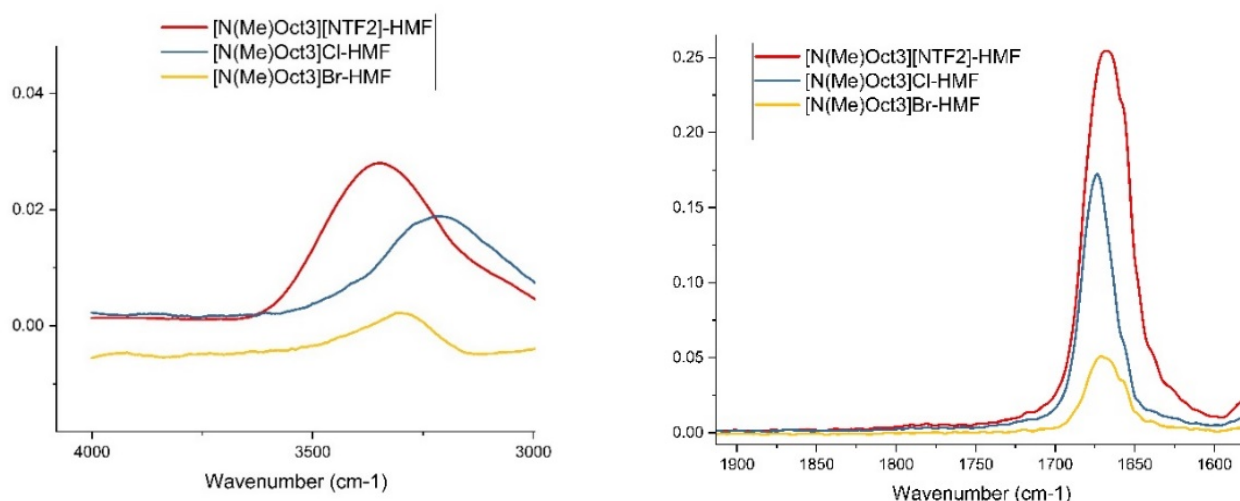


Figure 3.11 FT-IR spectra of the hydroxyl and carbonyl group of HMF with anions with different H-bonding ability. Reproduced with the permission of ref ¹

Study of ionic liquid miscibility with water

The high cost associated with ionic liquids requires a maximised recovery of the solvents for recycling and further use. The solubility of the ionic liquids in the water phase was measured and reported in Table 3.4.

Table 3.4 Solubility of hydrophobic ionic liquids in water.

Ionic Liquid	Solubility (mg IL / g H ₂ O)
[N(Me)Oct ₃]Cl	2.1
[N(Me)Oct ₃]Br	0.9
[N(Me)Oct ₃][NTf ₂]	0.029
[bmim][NTf ₂]	5.5
[bmpyr][NTf ₂]	4.7

Regarding the anions, [NTf₂]⁻ gave the lowest solubility for the three different cations. With the ammonium cation, the solubility is decreased drastically compared to the imidazolium and pyridinium cations. In all cases removal of the [NTf₂]⁻ salt from the water phase is needed for the process to be economically viable because of the high cost associated with preparing this anion and its high toxicity to aquatic life. Other considerations include the high cost associated with imidazolium ionic liquids, while ammonium-based ionic liquids, though exhibiting lower solubility in water, exhibit higher toxicity.⁵¹

Solvent selection guidelines for product separation

In light of this study, different strategies can be adopted for the efficient separation of DFF, FDCA, FFCA and HMF from the ionic liquids. The choice of the separation system will be strongly influenced

by the catalytic route used to synthesize these compounds. If heterogeneous catalysis is used, the product should be soluble in the reaction mixture while the opposite is true for homogeneous catalysis. DFF can be easily separated from the reaction mixture by sublimation at any loading at high purity and yield, so both homogeneous or heterogeneous catalysis can be employed.

The synthesis of FFCA in a hydrophilic coordinating ionic liquid will require the addition of large amounts of water to achieve separation, which for scale-up purposes can result in high energy requirements for ionic liquid regeneration. In this case homogeneous catalysis in a non-coordinating ionic liquid such as [bmim][OTf] is the most suitable solution since FFCA exhibits low solubility. This will lead to precipitation of the product from solution, allowing simple recovery by filtration.

FDCA can be separated by water addition in the presence of a heterogeneous catalyst or by filtration in [bmim][OTf] when operating with homogeneous catalysis.

In the case of HMF, the separation is still challenging even when using hydrophobic ionic liquids since rigorous washing is needed, however remarkable improvements can be achieved when the [NTf₂]⁻ anion is used instead of Cl⁻ or Br⁻. The [N(Me)Oct₃][NTf₂] ionic liquid represents the most suitable solvent to be used since it displayed the minimum amount of washes with minimum loss of ionic liquid into the water phase. In this way high HMF concentration in the water phase can be achieved for further transformation into FDCA. Disadvantages regarding the ammonium salts lie with the high viscosity which make it less than ideal for heterogeneous catalysis, while imidazolium ionic liquids are more suitable.

These findings are summarized in Table 3.5 with the aim to provide solvent design guidelines.

Table 3.5 Solvent design guidelines for the separation of DFF, FFCA, FDCA and HMF from ionic liquid media.

Compound	Homogeneous catalysis	Heterogeneous catalysis
DFF	Sublimation at 60 °C with [bmim]Cl or [bmim][NTf ₂]. Alternatively, filtration from [bmim][NTf ₂] at room temperature	Sublimation from [bmim]Cl or [bmim][NTf ₂]
FFCA	Precipitation and filtration from [bmim][OTf]	Water addition to [bmim]Br or [bmim]Cl but with a high energy cost for drying the IL
FDCA	Precipitation and filtration from [bmim][OTf]	Water addition in [bmim]Cl and separation through filtration
HMF	Synthesis in hydrophobic [N(Me)Oct ₃][NTf ₂], followed by washing with water	Synthesis in [bmim][NTf ₂] with water extraction

Conclusions

This study provides valuable insight for an efficient process design strategy to achieve a good compromise between high yield of reaction and efficient separation. When ionic liquids are used as media for sugar valorisation, four specific products have been identified which can be synthesized from sugars/HMF. By tuning the ionic liquid anion and cation, the interactions with the functional groups can be weakened, favouring separation. Weak interaction of the anions with the aldehyde group make DFF separation by sublimation extremely efficient and non-hydrogen bond dependent making any ionic liquid solvent suitable for this purpose.

FDCA and FFCA can be separated from water-miscible ILs by antisolvent water addition. Lower amounts of water are needed for FDCA making the separation less energy intensive in terms of the subsequent dehydration of the ionic liquids. In contrast, excessive water requirements for FFCA makes the separation unfeasible and non-competitive due to a synergistic interaction between water molecules and the aldehyde groups as well as hydrogen bonding with the carboxylic acid. For FFCA, synthesis by homogeneous catalysis in non-coordinating ionic liquids is recommended.

Concerning the separation of HMF from ionic liquids, despite the many years of research on the synthesis of this molecule, little work has focused on the development of heterogeneous catalysts and insufficient efforts have been directed to improve the separation. The problem can be circumnavigated by swapping from a coordinating ionic liquid to a non-coordinating one. In particular, the hydrophobic, non-coordinating bistriflimide ionic liquids are potential solvents for the generation of HMF due to the possibility of efficient extraction of this product with water. The ammonium-based IL, [N(Me)Oct₃][NTf₂], showed the most favourable partition coefficient (2.28) for HMF, potentially achieving 90% product recovery with only two washes, minimizing water consumption. Once extracted, HMF can be easily be converted to FDCA in water under base free conditions; the latter can be easily separated from water through acidification.

This study has provided an indication as to where future research should be focused in order to achieve a feasible chemical process. While much research is focused on catalyst development, the solvent systems used are often unsuitable for the separation or incompatible with other reaction steps. This work provides efficient guidelines for a solvent design strategy aimed to optimise the whole process from reaction to separation.

References

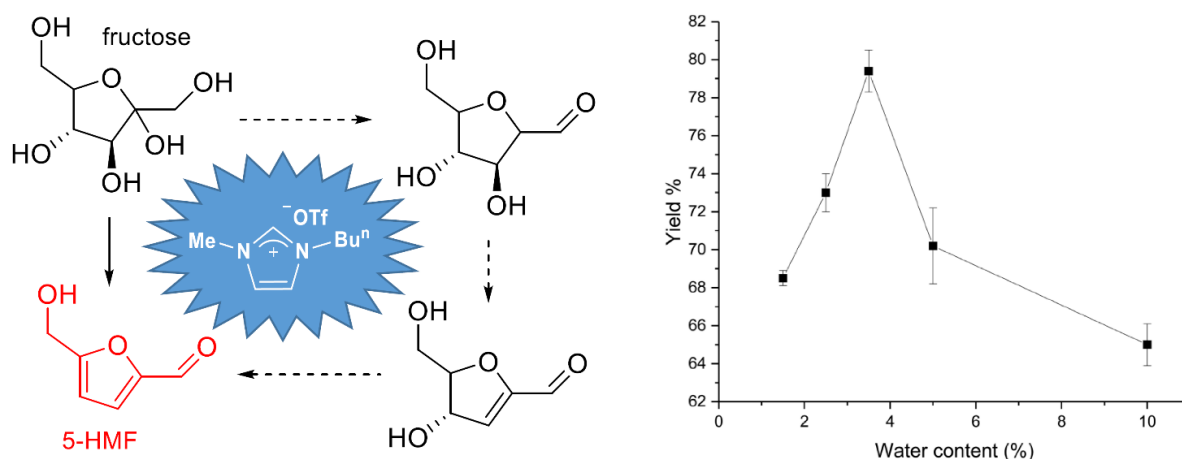
- (1) Gajula, S.; Inthumathi, K.; Arumugam, S. R.; Srinivasan, K. Strategic Designing on Selection of Solvent Systems for Conversion of Biomass Sugars to Furan Derivatives and Their Separation. *ACS Sustain. Chem. Eng.* **2017**, 5 (6), 5373–5381. <https://doi.org/10.1021/acssuschemeng.7b00681>.
- (2) Ferro, V. R.; Moya, C.; Moreno, D.; Santiago, R.; De Riva, J.; Pedrosa, G.; Larriba, M.; Diaz, I.; Palomar, J. Enterprise Ionic Liquids Database (ILUAM) for Use in Aspen ONE Programs Suite with COSMO-Based Property Methods. *Ind. Eng. Chem. Res.* **2018**, 57 (3), 980–989. <https://doi.org/10.1021/acs.iecr.7b04031>.
- (3) Al Ghatta, A.; Wilton-Ely, J. D. E. T.; Hallett, J. P. Strategies for the Separation of the Furanic Compounds HMF, DFF, FFCA, and FDCA from Ionic Liquids. *ACS Sustain. Chem. Eng.* **2019**. <https://doi.org/10.1021/acssuschemeng.9b03613>.
- (4) Yu, I. K. M.; Tsang, D. C. W. Conversion of Biomass to Hydroxymethylfurfural: A Review of Catalytic Systems and Underlying Mechanisms. *Bioresource Technology*. 2017. <https://doi.org/10.1016/j.biortech.2017.04.026>.
- (5) Zou, X.; Zhu, C.; Wang, Q.; Yang, G. Catalytic Dehydration of Hexose Sugars to 5-Hydroxymethylfural. *Biofuels, Bioprod. Biorefining* **2019**, 13 (1), 153–173. <https://doi.org/10.1002/bbb.1932>.
- (6) Saha, B.; Abu-Omar, M. M. Green Chemistry CRITICAL REVIEW Advances in 5-Hydroxymethylfurfural Production from Biomass in Biphasic Solvents. **2014**. <https://doi.org/10.1039/c3gc41324a>.
- (7) Román-Leshkov, Y.; Dumesic, J. A. Solvent Effects on Fructose Dehydration to 5-Hydroxymethylfurfural in Biphasic Systems Saturated with Inorganic Salts. *Top. Catal.* **2009**, 52 (3), 297–303. <https://doi.org/10.1007/s11244-008-9166-0>.
- (8) Gomes, F. N. D. C.; Pereira, L. R.; Ribeiro, N. F. P.; Souza, M. M. V. M. Production of 5-Hydroxymethylfurfural (HMF) via Fructose Dehydration: Effect of Solvent and Salting-Out. *Brazilian J. Chem. Eng.* **2015**, 32 (1), 119–126. <https://doi.org/10.1590/0104-6632.20150321s00002914>.
- (9) Hou, Q.; Li, W.; Zhen, M.; Liu, L.; Chen, Y.; Yang, Q.; Huang, F.; Zhang, S.; Ju, M. An Ionic Liquid-Organic Solvent Biphasic System for Efficient Production of 5-Hydroxymethylfurfural from Carbohydrates at High Concentrations. *RSC Adv.* **2017**, 7 (75), 47288–47296. <https://doi.org/10.1039/c7ra10237b>.
- (10) Liu, H.; Cao, X.; Wang, T.; Wei, J.; Tang, X.; Zeng, X.; Sun, Y.; Lei, T.; Liu, S.; Lin, L. Efficient Synthesis of Bio-Monomer 2,5-Furandicarboxylic Acid from Concentrated 5-Hydroxymethylfurfural or Fructose in DMSO/H₂O Mixed Solvent. *J. Ind. Eng. Chem.* **2019**. <https://doi.org/10.1016/j.jiec.2019.04.038>.
- (11) Chen, G.; Wu, L.; Fan, H.; Li, B. G. Highly Efficient Two-Step Synthesis of 2,5-Furandicarboxylic Acid from Fructose without 5-Hydroxymethylfurfural (Hmf) Separation: In Situ Oxidation of Hmf in Alkaline Aqueous H₂O/DMSO Mixed Solvent under Mild Conditions. *Ind. Eng. Chem. Res.* **2018**, 57 (48), 16172–16181. <https://doi.org/10.1021/acs.iecr.8b03589>.
- (12) Thananattananachon, T.; Rauchfuss, T. B. Efficient Route to Hydroxymethylfurans from Sugars via Transfer Hydrogenation. *ChemSusChem* **2010**, 3 (10), 1139–1141. <https://doi.org/10.1002/cssc.201000209>.

- (13) Shimizu, K. ichi; Uozumi, R.; Satsuma, A. Enhanced Production of Hydroxymethylfurfural from Fructose with Solid Acid Catalysts by Simple Water Removal Methods. *Catal. Commun.* **2009**, *10* (14), 1849–1853. <https://doi.org/10.1016/j.catcom.2009.06.012>.
- (14) Wei, Z.; Liu, Y.; Thushara, D.; Ren, Q. Entrainer-Intensified Vacuum Reactive Distillation Process for the Separation of 5-Hydroxymethylfurfural from the Dehydration of Carbohydrates Catalyzed by a Metal Salt-Ionic Liquid. *Green Chem.* **2012**, *14* (4), 1220–1226. <https://doi.org/10.1039/c2gc16671b>.
- (15) Yuanyuan, C.; Mu, T. Comprehensive Investigation on the Thermal Stability of 66 Ionic Liquids by Thermogravimetric Analysis. *Ind. Eng. Chem. Res.* **2014**, *53*, 8651–8664.
- (16) Shi, C.; Xin, J.; Liu, X.; Lu, X.; Zhang, S. Using Sub/Supercritical CO₂ as “Phase Separation Switch” for the Efficient Production of 5-Hydroxymethylfurfural from Fructose in an Ionic Liquid/Organic Biphasic System. *ACS Sustain. Chem. Eng.* **2016**, *4* (2), 557–563. <https://doi.org/10.1021/acssuschemeng.5b00889>.
- (17) Sun, X.; Liu, Z.; Xue, Z.; Zhang, Y.; Mu, T. Extraction of 5-HMF from the Conversion of Glucose in Ionic Liquid [Bmim]Cl by Compressed Carbon Dioxide. *Green Chem.* **2015**, *17* (5), 2719–2722. <https://doi.org/10.1039/c5gc00092k>.
- (18) Zhang, S.; Li, W.; Zeng, X.; Lin, L. Recent Progress and Prospects in the Selective Catalytic Production of 2,5-Diformylfuran. *J. Bioprocess Eng. Biorefinery* **2014**, *3* (1), 23–34. <https://doi.org/10.1166/jbeb.2014.1072>.
- (19) Ventura, M.; Aresta, M.; Dibenedetto, A. Selective Aerobic Oxidation of 5-(Hydroxymethyl)Furfural to 5-Formyl-2-Furancarboxylic Acid in Water. *ChemSusChem* **2016**, *9* (10), 1096–1100. <https://doi.org/10.1002/cssc.201600060>.
- (20) de Jong, E.; Dam, M. A.; Sipos, L.; Gruter, G.-J. M. Furandicarboxylic Acid (FDCA), A Versatile Building Block for a Very Interesting Class of Polyesters. In *ACS Symposium Series*; American Chemical Society, 2012; Vol. 1105, pp 1–13. <https://doi.org/10.1021/bk-2012-1105.ch001>.
- (21) Pérez-Bustos, H. F.; Lucio-Ortiz, C. J.; de la Rosa, J. R.; de Haro del Río, D. A.; Sandoval-Rangel, L.; Martínez-Vargas, D. X.; Maldonado, C. S.; Rodríguez-González, V.; Garza-Navarro, M. A.; Morales-Leal, F. J. Synthesis and Characterization of Bimetallic Catalysts Pd-Ru and Pt-Ru Supported on γ -Alumina and Zeolite FAU for the Catalytic Transformation of HMF. *Fuel* **2019**, *239*, 191–201. <https://doi.org/10.1016/J.FUEL.2018.10.001>.
- (22) Li, Y.; Li, Y.; Li, P.; Cao, P.; Wang, X.; Guan, H. POM@surf(n)/CeO₂ Electrospun Nanofibers for the Facile Oxidation of 5-HMF to DFF. *Appl. Catal. A Gen.* **2019**, *583*, 117–122. <https://doi.org/10.1016/j.apcata.2019.117122>.
- (23) Zhao, J.; Jayakumar, A.; Hu, Z. T.; Yan, Y.; Yang, Y.; Lee, J. M. MoO₃-Containing Protonated Nitrogen Doped Carbon as a Bifunctional Catalyst for One-Step Synthesis of 2,5-Diformylfuran from Fructose. *ACS Sustain. Chem. Eng.* **2018**, *6* (1), 284–291. <https://doi.org/10.1021/acssuschemeng.7b02408>.
- (24) Wang, Q.; Hou, W.; Meng, T.; Hou, Q.; Zhou, Y.; Wang, J. Direct Synthesis of 2,5-Diformylfuran from Carbohydrates via Carbonizing Polyoxometalate Based Mesoporous Poly(Ionic Liquid). *Catal. Today* **2019**, *319*, 57–65. <https://doi.org/10.1016/j.cattod.2018.07.042>.
- (25) Zhang, W.; Meng, T.; Tang, J.; Zhuang, W.; Zhou, Y.; Wang, J. Direct Synthesis of 2,5-Diformylfuran from Carbohydrates Using High-Silica MOR Zeolite-Supported Isolated Vanadium Species. *ACS Sustain. Chem. Eng.* **2017**, *5* (11), 10029–10037. <https://doi.org/10.1021/acssuschemeng.7b02002>.

- (26) Antonyraj, C. A.; Jeong, J.; Kim, B.; Shin, S.; Kim, S.; Lee, K. Y.; Cho, J. K. Selective Oxidation of HMF to DFF Using Ru/Alumina Catalyst in Moderate Boiling Solvents toward Industrial Production. *J. Ind. Eng. Chem.* **2013**, *19* (3), 1056–1059. <https://doi.org/10.1016/j.jiec.2012.12.002>.
- (27) Sajid, M.; Zhao, X.; Liu, D. Production of 2,5-Furandicarboxylic Acid (FDCA) from 5-Hydroxymethylfurfural (HMF): Recent Progress Focusing on the Chemical-Catalytic Routes. *Green Chem.* **2018**, *20* (24), 5427–5453. <https://doi.org/10.1039/c8gc02680g>.
- (28) Zhou, X.; Song, K.; Li, Z.; Kang, W.; Ren, H.; Su, K.; Zhang, M.; Cheng, B. The Excellent Catalyst Support of Al₂O₃ Fibers with Needle-like Mullite Structure and HMF Oxidation into FDCA over CuO/Al₂O₃ Fibers. *Ceram. Int.* **2019**, *45* (2), 2330–2337. <https://doi.org/10.1016/J.CERAMINT.2018.10.148>.
- (29) Yi, G.; Teong, S. P.; Zhang, Y. Base-Free Conversion of 5-Hydroxymethylfurfural to 2,5-Furandicarboxylic Acid over a Ru/C Catalyst. *Green Chem.* **2016**, *18* (4), 979–983. <https://doi.org/10.1039/C5GC01584G>.
- (30) Zhang, C.; Chang, X.; Zhu, L.; Xing, Q.; You, S.; Qi, W.; Su, R.; He, Z. Highly Efficient and Selective Production of FFCA from CotA-TJ102 Laccase-Catalyzed Oxidation of 5-HMF. *Int. J. Biol. Macromol.* **2019**, *128*, 132–139. <https://doi.org/10.1016/j.ijbiomac.2019.01.104>.
- (31) Chen, R.; Xin, J.; Yan, D.; Dong, H.; Lu, X.; Zhang, S. Highly Efficient Oxidation of 5-Hydroxymethylfurfural to 2,5-Furandicarboxylic Acid with Heteropoly Acids. *ChemSusChem* **2019**, *12* (12), 2715–2724. <https://doi.org/10.1002/cssc.201900651>.
- (32) Yan, D.; Wang, G.; Gao, K.; Lu, X.; Xin, J.; Zhang, S. One-Pot Synthesis of 2,5-Furandicarboxylic Acid from Fructose in Ionic Liquids. *Ind. Eng. Chem. Res.* **2018**, *57* (6), 1851–1858. <https://doi.org/10.1021/acs.iecr.7b04947>.
- (33) Yan, D.; Xin, J.; Zhao, Q.; Gao, K.; Lu, X.; Wang, G.; Zhang, S. Fe-Zr-O Catalyzed Base-Free Aerobic Oxidation of 5-HMF to 2,5-FDCA as a Bio-Based Polyester Monomer. *Catal. Sci. Technol.* **2018**, *8* (1), 164–175. <https://doi.org/10.1039/c7cy01704a>.
- (34) Lv, G.; Wang, H.; Yang, Y.; Li, X.; Deng, T.; Chen, C.; Zhu, Y.; Hou, X. Aerobic Selective Oxidation of 5-Hydroxymethyl-Furfural over Nitrogen-Doped Graphene Materials with 2,2,6,6-Tetramethylpiperidin-Oxyl as Co-Catalyst. *Catal. Sci. Technol.* **2016**, *6* (7), 2377–2386. <https://doi.org/10.1039/c5cy01149c>.
- (35) Halliday, G. A.; Young, R. J.; Grushin, V. V. One-Pot, Two-Step, Practical Catalytic Synthesis of 2,5-Diformylfuran from Fructose. *Org. Lett.* **2003**, *5* (11), 2003–2005. <https://doi.org/10.1021/ol034572a>.
- (36) Hu, L.; Sun, Y.; Lin, L. Efficient Conversion of Glucose into 5-Hydroxymethylfurfural by Chromium(III) Chloride in Inexpensive Ionic Liquid. *Ind. Eng. Chem. Res.* **2012**, *51* (3), 1099–1104. <https://doi.org/10.1021/ie202174f>.
- (37) Xu, J.; Paimin, R.; Shen, W.; Wang, X. An Investigation of Solubility of Aliquat 336 in Different Extracted Solutions. *Fibers Polym.* **2003**, *4* (1), 27–31. <https://doi.org/10.1007/BF02899326>.
- (38) Zhou, J.; Xia, Z.; Huang, T.; Yan, P.; Xu, W.; Xu, Z.; Wang, J.; Zhang, Z. C. An Ionic Liquid-Organics-Water Ternary Biphasic System Enhances the 5-Hydroxymethylfurfural Yield in Catalytic Conversion of Glucose at High Concentrations. *Green Chem.* **2015**, *17*, 4206–4216. <https://doi.org/10.1039/c5gc01039j>.
- (39) Al Ghatta, A.; Wilton-Ely, J. D. E. T.; Hallett, J. P. Rapid, High-Yield Fructose Dehydration to HMF in the Ionic Liquid [Bmim][OTf]. *ChemSusChem* **2019**. <https://doi.org/https://doi.org/10.1002/cssc.201901529>.

- (40) Rutz, C.; Schmolke, L.; Gvilava, V.; Janiak, C. Anion Analysis of Ionic Liquids and Ionic Liquid Purity Assessment by Ion Chromatography. *Zeitschrift für Anorg. und Allg. Chemie* **2017**, *643* (1), 130–135. <https://doi.org/10.1002/zaac.201600437>.
- (41) Wang, H.; Liu, S.; Zhao, Y.; Zhang, H.; Wang, J. Molecular Origin for the Difficulty in Separation of 5-Hydroxymethylfurfural from Imidazolium Based Ionic Liquids. *ACS Sustain. Chem. Eng.* **2016**, *4* (12), 6712–6721. <https://doi.org/10.1021/acssuschemeng.6b01652>.
- (42) Hussain Motagamwala, A.; Won, W.; Sener, C.; Alonso, D. M.; Maravelias, C. T.; Dumesic, J. A. Toward Biomass-Derived Renewable Plastics: Production of 2,5-Furandicarboxylic Acid from Fructose. *Sci. Adv.* **2018**, *4* (1), 1–8. <https://doi.org/10.1126/sciadv.aap9722>.
- (43) Stahlberg, T.; Eyjolfssdottir, E.; Gorbanev, Y. Y.; Sdaba, I.; Riisager, A. Aerobic Oxidation of 5-(Hydroxymethyl)Furfural in Ionic Liquids with Solid Ruthenium Hydroxide Catalysts. *Catal. Letters* **2012**, *142* (9), 1089–1097. <https://doi.org/10.1007/s10562-012-0858-5>.
- (44) Dijkman, W. P.; Groothuis, D. E.; Fraaije, M. W. Enzyme-Catalyzed Oxidation of 5-Hydroxymethylfurfural to Furan-2,5-Dicarboxylic Acid. *Angew. Chemie - Int. Ed.* **2014**, *53* (25), 6515–6518. <https://doi.org/10.1002/anie.201402904>.
- (45) Davis, S. E.; Zope, B. N.; Davis, R. J. On the Mechanism of Selective Oxidation of 5-Hydroxymethylfurfural to 2,5-Furandicarboxylic Acid over Supported Pt and Au Catalysts. *Green Chem.* **2012**, *14* (1), 143–147. <https://doi.org/10.1039/C1GC16074E>.
- (46) Qu, X.; Jiang, M.; Wang, B.; Deng, J.; Wang, R.; Zhang, Q.; Zhou, G.; Tang, J. A Brønsted Acidic Ionic Liquid as an Efficient and Selective Catalyst System for Bioderived High Molecular Weight Poly(Ethylene 2,5-furandicarboxylate). *ChemSusChem* **2019**. <https://doi.org/10.1002/cssc.201902020>.
- (47) Eminov, S.; Filippousi, P.; Brandt, A.; Wilton-Ely, J.; Hallett, J. Direct Catalytic Conversion of Cellulose to 5-Hydroxymethylfurfural Using Ionic Liquids. *Inorganics* **2016**, *4* (32), 1–15. <https://doi.org/10.3390/inorganics4040032>.
- (48) Ilgen, F.; Ott, D.; Kralisch, D.; Reil, C.; Palmberger, A.; König, B. Conversion of Carbohydrates into 5-Hydroxymethylfurfural in Highly Concentrated Low Melting Mixtures. *Green Chem.* **2009**, *11* (12), 1948–1954. <https://doi.org/10.1039/b917548m>.
- (49) Li, Y. N.; Wang, J. Q.; He, L. N.; Yang, Z. Z.; Liu, A. H.; Yu, B.; Luan, C. R. Experimental and Theoretical Studies on Imidazolium Ionic Liquid-Promoted Conversion of Fructose to 5-Hydroxymethylfurfural. *Green Chem.* **2012**, *14* (10), 2752–2758. <https://doi.org/10.1039/c2gc35845j>.
- (50) Li, C.; Zhao, Z. K.; Wang, A.; Zheng, M.; Zhang, T. Production of 5-Hydroxymethylfurfural in Ionic Liquids under High Fructose Concentration Conditions. *Carbohydr. Res.* **2010**, *345* (13), 1846–1850. <https://doi.org/10.1016/j.carres.2010.07.003>.
- (51) Berglind, R.; Dave, G. Influence of a Co-Solvent (Acetone) and Ultrasonication on the Acute Toxicity of a Quaternary Amine (Aliquat 336) and an Organophosphorus Compound (HDEHP) to *Daphnia Magna*. *Bull. Environ. Contam. Toxicol.* **1981**, *27* (1), 316–325. <https://doi.org/10.1007/BF01611026>.

Chapter 4 Rapid High-Yield Fructose Dehydration to HMF in Mixtures of Water and the Non-Coordinating Ionic Liquid [bmim][OTf]



In comparison to most of the literature, the non-coordinating ionic liquid [bmim][OTf] presents a new alternative, valuable solvent for fructose dehydration into the platform chemical HMF. Short reaction times, high substrate loadings and high yields can be achieved in this solvent, making it competitive with reports using [bmim]Cl or [bmim]Br. By increasing the catalytic activity and selectivity, water plays a crucial role where small amounts added to the solvent suppresses the side reaction related to the self-condensation of HMF. Using acid catalysis in [bmim][OTf] with 3.5% water content, yields above 80% can be achieved at 100 °C in only 10 minutes, even at high (14%) fructose loading. The synthesis of HMF in this ionic liquid could pave the way to HMF isolation and further catalytic valorisation since this ionic liquid doesn't contribute to hydrogen bonding which is the main factors behind the difficult separation and inefficient catalysis previously reported.

Introduction

The molecule 5-HMF represents a promising intermediate product from sugars which can replace a large variety of oil derivatives chemical products¹. Its efficient synthesis and isolation at high yield is the important for scale-up and to be competitive in the market.² The main feedstock to produce HMF is cellulose, glucose and fructose, through a tandem of reaction of hydrolysis, isomerisation and dehydration¹ and important results have been achieved using ionic liquids as solvents.^{3–7} The use of biomass derived feedstocks and ionic liquids for processing have provided the basis for a green chemical process where the environmental impact and sustainability of the technology are met, even if recently concerns have been raised over the toxicity of these solvents.⁸ Current research has focused on deep eutectic solvents and water for the dehydration of fructose to HMF but improved yields are still needed.^{9–11} while other research has focused on optimising heterogeneous catalysts for the dehydration reaction both involving metal catalysts^{12–18} and supported ionic liquids.^{19,20}

It is now established that ionic liquids with halide anions are very efficient for the production of HMF from fructose, glucose and cellulose with both Brønsted and Lewis acid catalysts.^{21–23}, due to their ability to dissolve the substrate through hydrogen bonding and favourable catalytic activity²⁴ and so far they have proven to be superior solvents compared to organic solvents in terms of substrate loading, operating conditions and reaction times.^{25,26} It has been reported that homogeneous catalysis proved to be efficient for the reaction of cellulose and glucose using chromium or tin chloride catalysts in combination with Cl[−] or Br[−] ionic liquids.²⁷

While for glucose the choices are restricted to a few catalytic systems, more options are reported for fructose dehydration. The acidic ionic liquid [bmim][HSO₄] in combination with the Lewis acid CrCl₃·6H₂O was found to be a very efficient system to obtain quantitative yield from fructose at high loadings (1:7 with respect to the ionic liquid).²⁸ Metal-free systems are also reported as both [bmim]Br and [Hmim]Cl can dehydrate fructose in high yields and loadings with longer reaction times. With [Hmim]Cl, 92% yield was achieved at 90 °C in 45 min while [bmim]Br required heating to 100 °C and 1 hour to obtain the same yield. While the high activity towards dehydration can be related to the acidity of the cation for [Hmim]Cl, this is still unclear for [bmim]Br since the formation of HBr has complicated the situation^{29,30} in contrast to [bmim]Cl, which needs microwave heating to perform a catalyst-free high yield dehydration (97%).³¹ The addition of a Brønsted acid can reduce the reaction time and temperature of the dehydration, maintaining high selectivity. A comprehensive study was performed by Li and co-workers which tested a large variety of Brønsted acids in different ionic liquids. While most of the acids had a positive effect on the reaction in [bmim]Cl or [bmim]Br, achieving near quantitative yield with HCl in 10 minutes at 80 °C, the dehydration was unsuccessful in non-halogenated and non-coordinating ionic liquids such as [bmim][BF₄] and [bmim][PF₆], with yields less than 10% yield in 30 minutes.³² While the dehydration of fructose is extensively studied in coordinating ionic liquids based

on Br⁻ and Cl⁻, the dehydration of fructose in non-coordinating ionic liquids has not been studied deeply due to the high cost of these ionic liquids and their inability to dissolve cellulose and glucose. A few examples are reported in literature, using the acidic resin Amberlyst-15 in [bmim][PF₆] or a triphasic system but generally satisfactory results were not obtained.^{33,34} Shi and co-workers studied the coordination of the anion with the hydroxyl groups through a molecular dynamic study showing that Cl⁻ tends to form a centralised structure around the fructose molecule through hydrogen bonding,³⁵ while this was not observed in [bmim][OTf]. Such structures may be responsible for the stabilization of HMF towards further side reactions involving the formation of humins or they could actively participate by activating the hydroxyl groups toward dehydration. [Bmim]Cl and [bmim]Br have always been considered as superior solvents for their lower cost and higher selectivity and research has focused on catalyst design to improve yield and selectivity. However, most literature ignores a barrier related to the use of these ionic liquids: separation and valorisation of HMF. Separation of HMF from these ionic liquids has been a challenge for many years^{36,37} and systems proposed for separation via scCO₂ extraction or highly entrained vacuum distillation are more fascinating to observe than commercially viable³⁸⁻⁴⁰ due to their high operating costs. Conversion of HMF *in situ* through oxidation to high value product such as DFF and FDCA has proven to be challenging since coordinating anions alter the selectivity of the noble metals which are commonly used for this reaction.^{41,42} Moreover, a good compromise between reaction time, heating method and catalyst loading still needs to be properly achieved. Some researchers have focused on oxidizing HMF in the reaction media into 2,5-furandicarboxylic acid (FDCA), which is easier to separate by water addition.⁴³⁻⁴⁵

In contrast, alcohol oxidation has proven to be extremely efficient in non-coordinating ionic liquids with [PF₆]⁻, [BF₄]⁻, [NTf₂]⁻ and [OTf]⁻ anions with yields and selectivities higher than those achieved in conventional organic solvents.⁴⁶⁻⁵⁰ The possibility of using these solvents for selective alcohol oxidation to produce DFF is an attractive option since DFF can be isolated in high purity through sublimation according to the study reported in the previous chapter and our publication.⁴⁵ Moreover, the separation of 5-HMF is much more favoured due to the lack of hydrogen bonding between HMF and the ionic liquids, opening up different pathways for the valorisation of this chemical. However, the dehydration reaction from sugars to HMF in these solvents has proven to be inefficient so far, hence the two steps cannot be combined. An efficient chemical pathway that enhances the HMF yield from sugars in these solvents could make the overall process more attractive for both isolation and catalysis. The aim of this study is to focus on improving the yield of HMF in non-halogenated and non-coordinating ionic liquids, such as [bmim][OTf] (Figure 4.1), which is a more suitable media for HMF valorisation. In order to increase the yield at short reaction times, analysis was performed on different reaction parameters. Water content proved to be the most crucial parameter for solvent design as it stabilises HMF towards side reactions. It will be demonstrated that the reason for the low selectivity towards HMF in these solvents is due to the instability of HMF under acidic conditions. Water addition

suppresses the side reaction and stabilizes HMF, leading to a high yield of dehydration of fructose to HMF at short reaction times and high loadings, making these ionic liquids more efficient than the conventional halogenated ones reported to date.

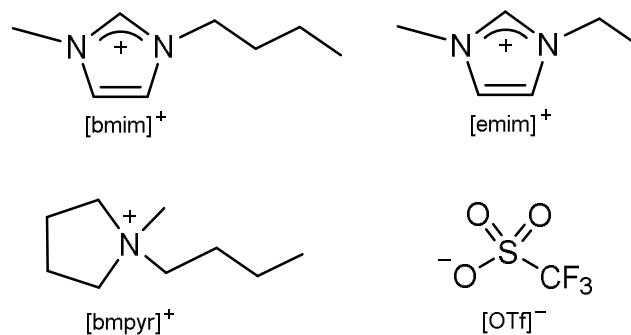


Figure 4.1 The cations and anions used in the ionic liquids in this chapter. Reproduced with the permission of Al-Ghatta et al. 2019.

Experimental Section

Materials

Fructose, 36% hydrochloric acid, calcium hydride, phosphorus pentoxide, lithium triflate and potassium hydroxide and [emim][OTf] were purchased from Sigma Aldrich. 5-Hydroxymethylfurfural (99%, chromatography standard) was obtained from Fluorochem and purified by crystallisation at 3 °C from ethyl acetate and hexane. *N*-methylimidazole, *N*-methylpyrrolidine and chlorobutane for ionic liquid synthesis were purchased from Alfa Aesar. Methylimidazole was purified at reduced pressure (2.1 mbar, 40 °C reflux temperature) in the presence of calcium hydride. Chlorobutane was dried at atmospheric pressure over phosphorus pentoxide. Methylpyrrolidine was distilled at atmospheric pressure over KOH. Acetonitrile, ethyl acetate and hexane were purchased from VWR and further purified by distillation over calcium hydride.

Fructose conversion to HMF

Due to the high cost, long synthesis procedure of the ionic liquids used and large amount of experiments to be carried out, the setup was designed to perform at low volume and minimise the waste of ionic liquid. Difficulties lie in the measurement of low amounts of acid catalyst; hence a large batch was prepared. A larger quantity of the IL was prepared with the desired amount of water and catalyst. Since the experiments are highly sensitive to the water content, the ionic liquid was left under vacuum overnight at 70 °C. All the handling of the ionic liquids was done in a glove box.

Experiments were performed in triplicate in 1.5 mL vials. Each vial was loaded with an appropriate amount of fructose followed by the addition of the solvent to be tested in the desired fructose/solvent ratio. The vials were placed in a preheated heating block for the desired reaction time. At the end of the reaction, the reaction mixture was rapidly quenched with 1 mL of water and then further diluted 6:1 and filtered before HPLC analysis. Kinetic analysis was performed by halting the reaction by addition of water at the desired time and recording the data. Sampling could not be performed for the low volumes used and condensation of water at the top of the vial could not be taken into account, potentially biasing the yield.

Quantification of HMF yield was performed using a Shimadzu Prominence preparative HPLC (Shimadzu, Kyoto, Japan) with refractive index (RI) and ultraviolet (UV) detectors and equipped with an Aminex HPX-87H column using 0.005 M H₂SO₄ as the mobile phase at 55 °C and flow rate of 0.6 mL/min.

Partition coefficients between ionic liquid and diethyl ether

Partition coefficients were calculated using diethyl ether since it is a common solvent used for the extraction of HMF from [bmim]Cl. In a centrifuge tube vial, 300 mg of ionic liquid were mixed with 30 mg of HMF and heated at 60 °C for 30 minutes to obtain a homogeneous solution and then cooled

down to room temperature. Then 1 g of diethyl ether was added to the mixture and vigorously stirred for one hour. An aliquot of the organic phase was withdrawn and analysed by GC with a ThermoFischer GC ULTRA with external standard calibration. Partition coefficients were calculated using the following formula:

$$K = \frac{C_{HMF}^{organic\ phase}}{C_{HMF}^{ionic\ liquid}}$$

The synthesized HMF was extracted from the ionic liquid phase through solvent extraction with diethyl ether. The dehydration experiment was repeated in large scale (1 g of ionic liquid) at 14 % fructose loading (140 mg), 10 % H₂SO₄ loading (respect the substrate), 3.5 % water content, 100 °C and 10 min. At the end of the reaction the ionic liquid phase was diluted with water (20 ml) and neutralised with NaOH at pH 7. The solution was then washed with small amounts of dichloromethane to remove most of the impurities to avoid decreasing the yield to any great extent. 1 mL additions of DCM were used until the organic layer turns clear (average 5 washes). The purified water layer was then extracted with diethyl ether (3 x 100 mL) and concentrated under vacuum, obtaining a yellow liquid which crystallized in the fridge (71 % yield from sugar). The ionic liquid phase was extracted from water with ethyl acetate as a light brown viscous liquid and then characterized by NMR spectroscopy and mass spectrometry. The side products were isolated from the dichloromethane layer by solvent removal and extraction with diethyl ether and analysed by mass spectrometry.

Results and Discussion

Stability of HMF in the ionic liquid under acidic conditions

Literature studies on the mechanism of fructose dehydration appear to agree that a hydrogen bonding environment is necessary for dehydration to be achieved.³⁵ The role of the hydrogen bonding is discussed and different theories and opinions are presented in the literature regarding its role in the catalysis and stabilization of HMF from reaction with fructose to lead to humins. However, the potential for hydrogen bonding is reduced in an ionic liquid with a non-coordinating anion. In order to investigate the role of hydrogen bonding in the reaction, a stability test of HMF was carried out. The stability of HMF in [bmim][OTf] was first investigated under acidic conditions at elevated temperatures with a range of water contents. This was designed to identify conditions where HMF is stable so that it does not undergo self-condensation over long reaction times. Since H-bonding has proven to play a key role for the stabilization,⁵² water was added to the ionic liquid as a hydrogen bond donor. In order to efficiently regulate the water content, *p*-toluenesulfonic acid (PTSA) was tested as acid since HCl and HSO₄ are generally available only as solutions. Moreover *p*-toluenesulfonic acid has already been shown to be a good reagent for fructose dehydration in many different solvent systems when PTSA is used in its immobilised form (Amberlyst-15).^{53–59}

According to the data in Figure 4.2, HMF proved to be extremely unstable under water-free conditions, undergoing 43% degradation at 10% catalyst loading in 10 min at 90 °C. The gradual addition of water hindered the formation of side products, decreasing the decomposition to just 14%. The origin of this behaviour could be linked either to the hydrogen bonding of water with HMF or the decreasing activity of the protons on addition of increasing amounts of water. However, no trace of further hydration to formic and levulinic acids is observed, suggesting that the ionic liquid is still contributing to the stability of HMF even if the anion is not an H-bond donor. In order to find the relationship between water and acid, a stability test was performed at 1.3% water content with HCl and H₂SO₄ as both exhibit a lower pK_a compared to PTSA. The results showed slight changes in the degree of degradation with lower degradation for HCl (18.4 ± 0.8%) and slightly higher value for H₂SO₄ (23.2 % ± 0.2%) compared to PTSA (20.3%). The large difference in acidity of these Brønsted acid catalysts does not correlate with the difference in degradation observed and there appears to be no relationship with the pK_a of the acid. This observation suggests that water is stabilising HMF through H-bonding, protecting it from self-condensation. In the following section this stabilization will be analysed to see if it can lead to improvements in the HMF yield from fructose. It will also aim to discern whether the reason for the low yield observed so far in the literature for the reaction in non-coordinating ionic liquids can be ascribed to the instability of HMF under water free conditions.

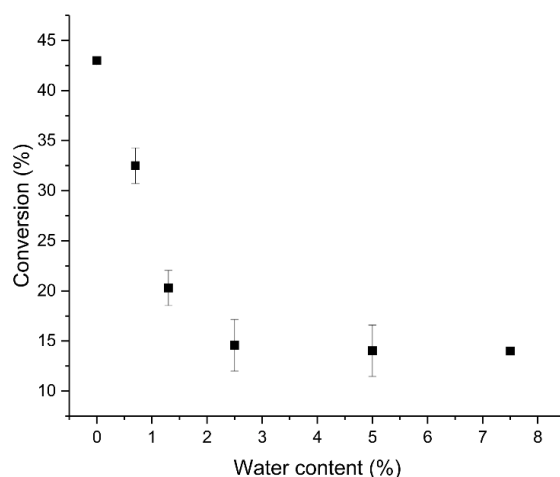
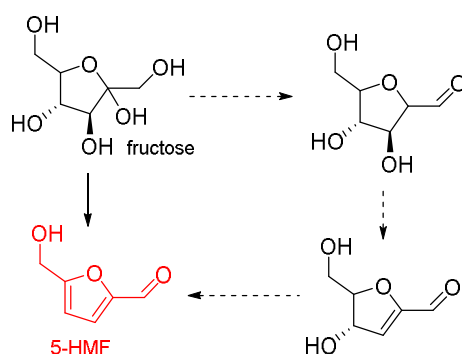


Figure 4.2. Degradation of HMF at 90 °C in [bmim][OTf] with a range of water contents and 10% PTSA loading (with respect to HMF) and 10% HMF loading (with respect to the ionic liquid). Reproduced with the permission of Al-Ghatta et al. 2019.

Presence of intermediates

During the experiments on fructose dehydration, it was observed that the HMF yield did not follow a first order relationship with respect to fructose. In all the experiments at temperatures higher than 90 °C fructose achieved full conversion in less than 1 min while the HMF yield increased over 10 min, suggesting the formation of intermediates during the dehydration process. These were observed in the HPLC chromatogram by two further peaks at 7.7 min and 8.1 min (compared to fructose at 9.3 min). To further confirm that there were two intermediates belonging to the same reaction pathway, kinetic analyses were performed and revealed that the yield was not increasing further after the peaks at 7.7 min and 8.1 min disappeared. Zhang et al.,⁵¹ using ethanol as a solvent at room temperature, demonstrated that two principal intermediates are formed prior to HMF formation, according to the mechanism depicted in Scheme 1. Their analysis with *in situ* NMR spectroscopy and mass spectrometry strongly supporting this reaction path. Due to the difficulty in quantifying the intermediates, the rate limiting steps in the dehydration will not be discussed here. Instead, the reaction was considered completed when the intermediate peaks in the chromatogram were no longer present.



Scheme 1. Fructose dehydration scheme proposed in previous work⁵¹

Selection of the acid catalyst

In light of the stability study described above, three different catalysts were tested operating under conditions where the decomposition of HMF is minimised. Since the dehydration of fructose involves the generation of 3 moles of water per mole of fructose, it was decided to operate with a lower initial water content to avoid a possible excess that could reduce the rate of reaction or lead to further undesired hydrolysis of HMF. Hence a water content of 3.5% and a fructose loading of 14% were selected. Under these conditions, complete dehydration of fructose will lead to a water content of 5% which is below the minimum degradation of HMF according Figure 4.2. The acids, PTSA, H₂SO₄ and HCl were chosen for catalyst screening. The success of PTSA for the dehydration of HMF has already been established in different systems and HCl has been shown to be an effective catalyst in a wide variety of solvents. In the work of Tuerke and co-workers 82% yield at 30% fructose loading was obtained in about 1 minute at 185 °C and 17 bar pressure in a microbatch reactor using HCl in a biphasic system of water/MIBK.⁶⁰ A study published in 2011 reported a 82% HMF yield in isopropanol in 1 hour at 120 °C,⁶¹ while a near quantitative yield was obtained in [bmim]Cl at 80 °C.³² Sulfuric acid proved to be an efficient catalyst in [bmim]Cl and DMSO, reaching over 93% yield.^{32,62}

The results from the screening of different acids are shown in Figure 4.3. Hydrochloric acid proved superior to PTSA or sulfuric acid. The lower pK_a can ensure complete dehydration, reaching 74% yield in 10 minutes at 14% fructose loading. The counterion can also provide further hydrogen bonding to the hydroxyl group and its role seems very important for the high difference in yield compared to the other acids. Water provides stability to HMF but a suitable counterion of the catalyst had to be chosen to provide the necessary catalytic activity. It was thus decided to continue the study with HCl as the catalyst.

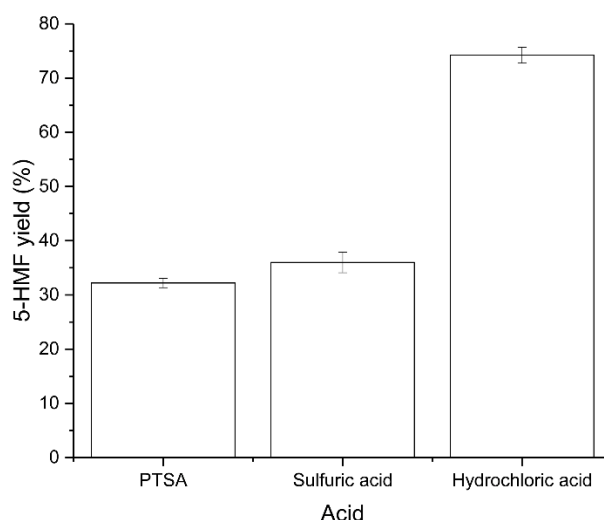


Figure 4.3. Acid selection for fructose dehydration in [bmim][OTf]. Fructose loading = 14% respect the solvent, T = 90 °C, initial water content = 3.5%, acid catalyst loading 10% respect fructose, t = 10 min. Reproduced with the permission of Al-Ghatta et al. 2019.

Effect of water content on the yield and rate of the reaction

In order to further understand the role of water in the reaction medium, a range of water contents in the ionic liquid were investigated. The results in Figure 4.4 clearly suggest that water has a significant effect on the yield of HMF in the reaction. Gradual addition of water improved the yield up to 79% at 3.5% water content, indicating that side reactions are suppressed. On the other hand, in pure water the catalyst was completely inactive. This suggests that at too high water content the catalytic activity of the acidic protons is decreased too much, making it completely inactive for dehydration.

This observation seems at first instance to contradict the previous study on the stability of HMF under acidic conditions. According to those results, different acids with different pKa values did not affect the degradation, while, according to the results below on dehydration, water is clearly decreasing the activity of the protons, affecting the dehydration. The answer to this can be seen in the anion of the acid, since its coordination with the hydroxyl group is needed for the dehydration; high water content will lead to excessive hydration of the Cl⁻ ion, blocking further catalytic activity.

Low water concentration led to a poor yield, which (considering that all the reaction are 100 % conversion) may be due to the overly aggressive activity of the H⁺ ions which may be influenced by the water content, leading to side reactions of HMF, such as self-condensation or reaction with fructose (to produce humins); such phenomena will be further discussed later in this chapter. An optimum was observed at 3.5% water content (79% yield), suggesting a good compromise between stabilisation and acidity for dehydration of HMF. In this medium, water is playing a different role compared to the dehydration in halogenated ionic liquids as [bmim]Cl, [bmim]Br and [Hmim]Cl reported in other work,^{29,30,32} where the only effect is to decrease the rate of reaction, marginally affecting the selectivity. In other catalytic systems, water contamination leads to a drastic decrease in selectivity with overhydration to levulinic acid and formic acid.^{63,64} In our case, the water content has a beneficial effect on the yield while an excessive amount leads to lower efficiency due to the deactivation of the catalyst while in low amounts it acts as a catalyst moderator. This is further suggested by the relative amounts of water and HMF, which in the case of 3.5% water content, is equivalent to 2.5 moles of water per mole of HMF.

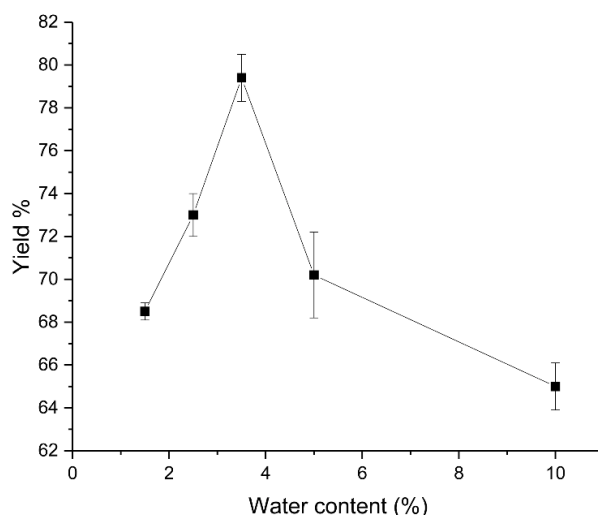


Figure 4.4. Effect of water content on HMF yield from fructose in [bmim][OTf], fructose loading = 10% respect the solvent, $T = 90\text{ }^{\circ}\text{C}$, $t = 10\text{ min}$, 10 % acid catalyst loading (HCl) respect the substrate. Reproduced with the permission of Al-Ghatta et al. 2019.

In order to further understand the role of water content on the stability of HMF and the rate of reaction, kinetic analysis was performed at two different water contents at a higher temperature ($100\text{ }^{\circ}\text{C}$).

The data in Figure 4.5 suggest that the water content contributes to both the stability of HMF and the rate of the reaction. At 2.5% water content, the reaction reached a maximum at 3 minutes with a yield of 76% followed by a gradual decrease of HMF yield of 6% by 10 minutes. This decrease can be ascribed to the trend observed in Figure 4.5, suggesting that the total water content in the system is not enough to stabilise HMF. By increasing the water content to 3.5%, this trend is no longer observed, instead there is a steady increase up to 82% HMF yield. This is further confirmation that water is stabilising HMF from self-condensation side reactions. Compared to the previous results (Figure 4.4), the yield at 3.5% water content was improved, indicating that at $90\text{ }^{\circ}\text{C}$ not all of the sugar was dehydrated due to incomplete conversion of the intermediates. The remaining 20% lost in yield can be ascribed to side reactions between fructose (or the intermediates) with the HMF formed. This will be discussed further below.

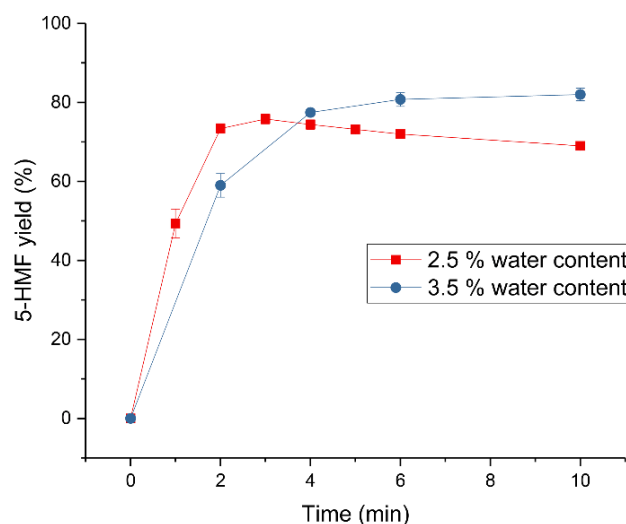


Figure 4.5. Effect of water content on the kinetics of HMF production from fructose in [bmim][OTf] at 100 °C, fructose loading = 10 % respect the solvent, catalyst loading = 10% (HCl) respect fructose. Reproduced with the permission of Al-Ghatta et al. 2019.

Effect of fructose loading

Thus far it has been demonstrated that [bmim][OTf] in combination with HCl as a catalyst is a versatile system for the dehydration of fructose to HMF. However, the high cost associated with this ionic liquid requires careful consideration in terms of the overall process economics. To this end the substrate loading will be studied since this can reduce the cost per unit product. This will also provide an insight into the side reactions involved, which are the cause of the reduced yield. The study on the substrate loading is reported in Figure 4.6. The yield of HMF increased by reducing the substrate loading, indicating that the side reaction of fructose (or the intermediates) with HMF is one reason for the inefficiency. Water addition seems to stabilise HMF towards self-condensation, but not completely from cross-condensation. Further analysis was carried out on the rate of reaction for two substrate loadings, 10 and 14%. Both reactions were carried out over the course of 10 minutes. In both cases no maximum was observed indicating that HMF does not undergo self-condensation under these reaction conditions. At 90 °C, it was observed that even at 14% loading and 3.5% water content, HMF does not undergo any significant decomposition, reaching a plateau (the yield decreases by only 2% from 8 to 10 minutes). At 10% fructose loading, the HMF yield increases to 82% in 10 minutes, showing a trend of increasing yield. While the reaction at 10 % yield has an increasing trend, at higher loading the yield reaches a plateau with incomplete conversion of intermediates. This may due to excessive water formation which reduces the activity of the catalyst. In order to further improve the yield at high loading, the effect of the temperature will be discussed in the next paragraph.

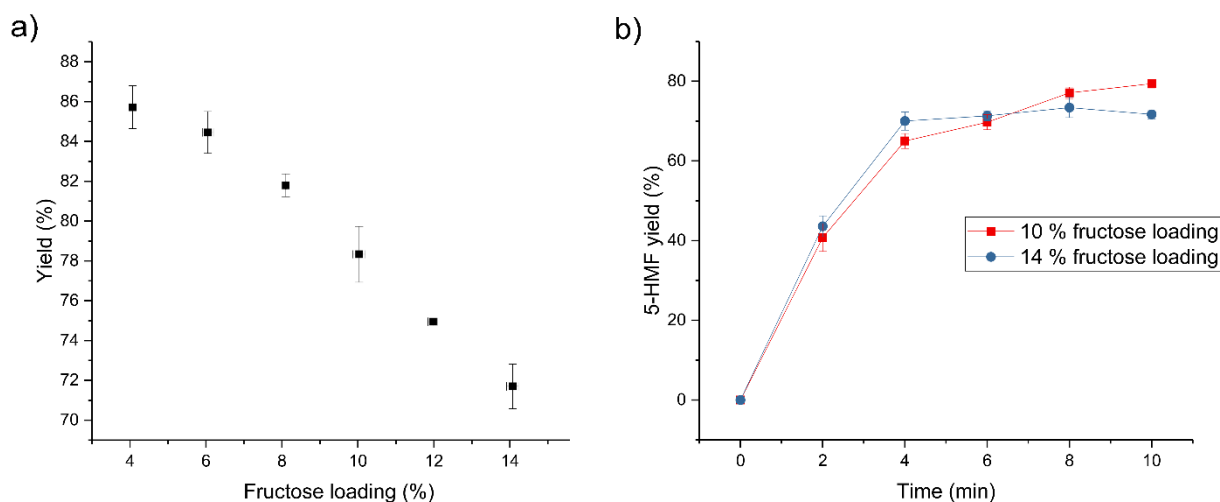


Figure 4.6. a) The HMF yield from fructose in [bmim][OTf], at different fructose loadings and b) kinetic analysis of the same reaction at two fructose loadings (right). Reaction conditions: $T = 90\text{ }^{\circ}\text{C}$, 3.5% water content, $t = 10\text{ min}$, 10% HCl loading respect fructose. Reproduced with the permission of Al-Ghatta et al. 2019.

Effect of temperature

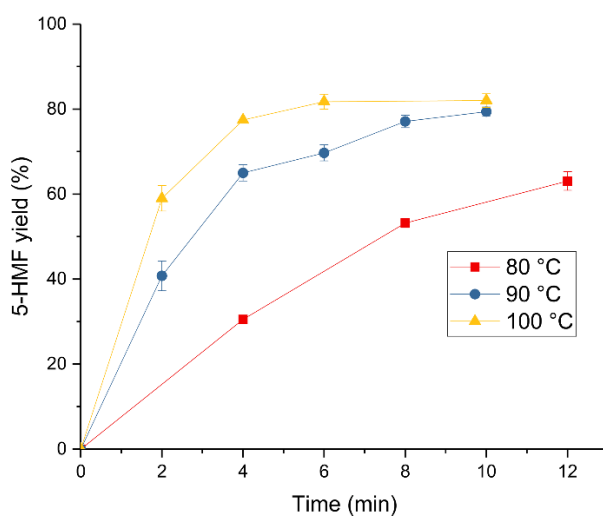


Figure 4.7. Effect of temperature on HMF yield from fructose in [bmim][OTf], 10% fructose loading, 10% HCl loading, 3.5% water content. Reproduced with the permission of Al-Ghatta et al. 2019.

Analysis of the effect of the temperature on the reactions is reported in Figure 4.7 at 10% fructose loading. Higher temperatures have a beneficial effect on the reaction, shortening the reaction time and increasing the yield. This result is expected for all dehydration reaction in which high temperature is needed due to the endothermic nature of the reaction.

Further optimization was performed at higher loadings. Kinetic analysis was carried out for higher HMF loadings at $100\text{ }^{\circ}\text{C}$ as seen in Figure 4.8. In this case the yield was improved from 72% to

81%, making the dehydration at higher concentration a more feasible process from a techno-economic viewpoint.

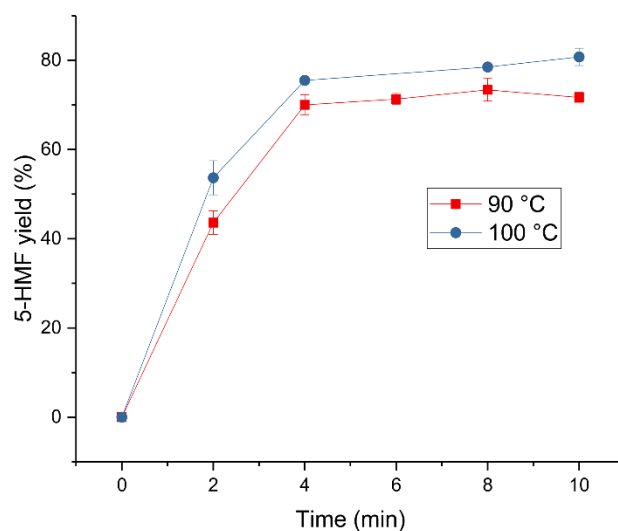


Figure 4.8. Kinetic analysis of the dehydration of fructose to HMF in [bmim][OTf] at two different temperatures and 14% fructose loading respect the solvent, 10% HCl loading respect fructose, 3.5% water content.

Effect of the cation

According to Zhang and co-workers⁵¹, the cation plays a key role in the dehydration of fructose at room temperature since the cation can contribute with weak H-bonding donation to the hydroxyl groups.

Table 4.1. Effect of the cation on HMF yield from fructose in different ILs. Reaction conditions: 14% fructose loading, T = 100 °C, t = 10 min, 10% HCl loading, 3.5% water content.

Ionic Liquid	HMF yield (%)
[bmim][OTf]	80.8 ± 2.0
[emim][OTf]	77.4 ± 0.7
[bmpyr][OTf]	80.1 ± 0.5

The choice of a cation with higher proton donation ability will increase the rate of reaction. In previous work, the imidazolium ionic liquid displayed the best performance as a catalyst using ethanol as solvent. In order to validate this concept in our system, various ionic liquids with different cations and diverse H-bonding donation abilities were tested. The H-bond donating ability can be quantified by the Kamlet-Taft parameter α as reported in the literature.⁶⁵ Pyrrolidinium ionic liquids have a lower H-bond ability compared to imidazolium with an α of 0.4 compared to 0.6 for imidazolium ionic liquids. However, the results reported in Table 4.1 show no significant effect of the cation on HMF yield, suggesting that while the interaction of the cation with hydroxyl groups are significant at low temperature, these play

no role at higher temperatures and no interactions arise with the fructose molecule at higher temperatures.

Extraction of HMF from Ionic Liquids

The synthesized HMF was extracted from the ionic liquid through solvent extraction. Direct extraction with diethyl ether from the ionic liquid phase followed by solvent removal under vacuum resulted in a dark viscous liquid. This indicates the existence of impurities in the crude HMF product confirmed by additional peaks in the furan and aldehyde region in the NMR which were not observed in the ionic liquid liquor. This may be due to residual acidity dragged into the organic phase, which upon concentration leads to degradation of HMF. In order to remove the acidity, the organic phase was washed with a sodium carbonate solution, but this led to poor recovery of HMF because of the high affinity of HMF for the water phase and its instability at high pH. Following these observations, it was decided to neutralise the ionic liquid phase at pH 7 after water addition (20 mL) and adopt the protocol reported in the experimental section. The purification with DCM washing allows the removal of the impurities which visibly contribute to the dark colour. After the washing the water layer became clear and HMF could be extracted with ethyl acetate.

As already mentioned in a previous chapter, since the [OTf]⁻ anion is non-coordinating, the separation of HMF from this type of solvent is favoured. The issue in this step is the higher miscibility of this ionic liquid with organic solvent. For this purpose, diethyl ether was used as its low dielectric constant makes the ionic liquid highly insoluble. In order to analyse the effect of a coordinating environment on the partition coefficient, different extraction experiments were analysed, varying the concentration of Cl⁻ anions in the mixture with diethyl ether. The results reported in Figure 4.9 show a pronounced negative effect of Cl⁻ on the partition coefficient, even at low concentrations. However, at Cl⁻ free conditions the partition coefficient increases by two orders of magnitude, making extraction into the organic phase more favourable even if the absolute value of the partition coefficient suggests extensive washing will still be required in order to achieve a good recovery with this organic solvent. More polar solvents, such as ethyl acetate or MIBK may be able to boost the extraction but they exhibit large miscibility with [bmim][OTf]. An organic solvent screening will be necessary to establish a viable system for scale-up.

By exploiting the higher partition coefficient between [bmim][OTf]/diethyl ether, the isolation of HMF from this solvent was explored working at bigger scales with 1 g of ionic liquid and 14% fructose loading with a yield of 71% (HPLC yield 82%). The loss of yield is due to partial solubilisation of HMF in the DCM layer used for extraction. Mass spectrometry of the isolated HMF shows two peaks at m/z 139 and m/z 83 which correspond to the mass of levulinic acid and formic acid.⁶⁶ However, the fact that these were not seen in either the NMR spectra nor HPLC data suggests that they are present in very small amounts.

By analysing the NMR spectra of the ionic liquid prior to work-up, only peaks related to HMF and ionic liquid were observed and water addition did not lead to any precipitation, meaning that the

side products are likely to be low molecular weight products. This is a further confirmation that water is suppressing the formation of humins since in many other acid catalysed systems reported in the literature, side products are insoluble high molecular weight compounds.^{66,67} By analysing the NMR spectra of the ionic liquid prior to work-up, only peaks related to HMF and the ionic liquid were observed and water addition did not lead to any precipitation, meaning that the side products are likely to be low molecular weight products. This is a further confirmation that water is suppressing the formation of humins since in many other acid catalysed systems reported in the literature, side products are insoluble high molecular weight compounds.^{66,67}

The side products were analysed by mass spectrometry since only HMF was detected by NMR spectroscopy in the DCM layer. Two large peaks arise at m/z 251 and m/z 155, which were not reported in the literature. The mass is slightly higher than that of two molecules of HMF suggesting that it can derive partially from reaction with fructose (Figure 4.10). By calculating the mass, we speculate a product that is a result of the reaction between fructose intermediate and HMF, resulting in two rings linked by an ester group (Figure 4.11). The structure has a mass of m/z 251.0561 with an error of 0.0061% which is within the tolerance accepted by most journals (*ChemSusChem* requires a tolerance within 0.4%).

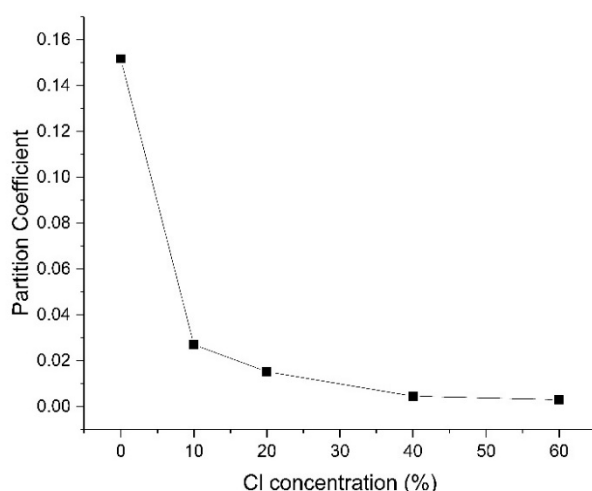


Figure 4.9 Partition coefficient of HMF in diethyl ether and ionic liquid mixtures.

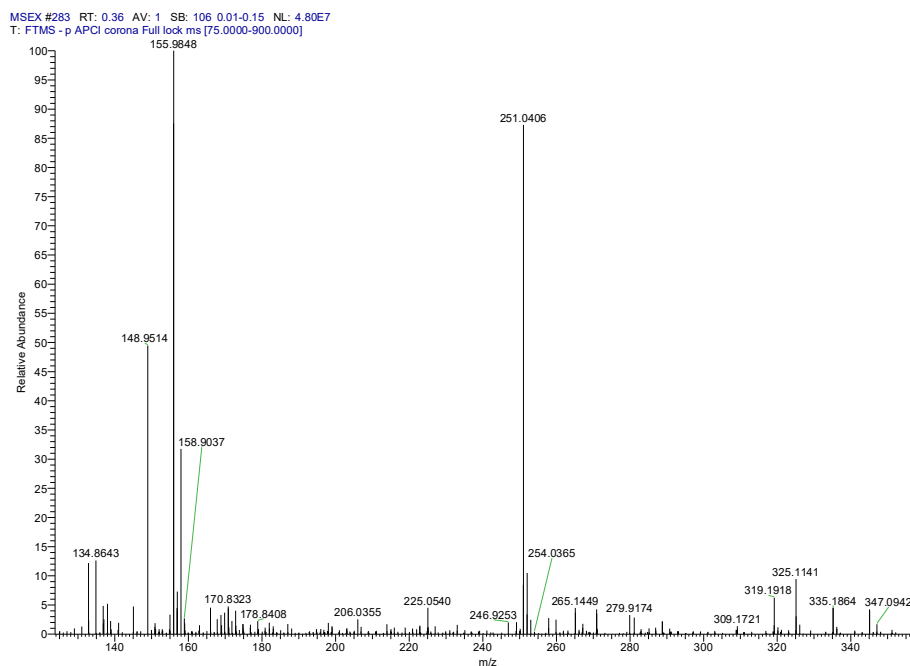
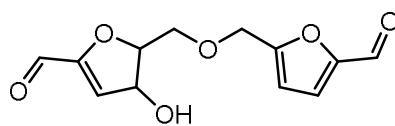


Figure 4.10 Mass spectrometry of the side products in the DCM layer after washing.



Mass= 252.0634

Mass anion=251.0561

Observe Mass=251.0406

Error=0.0061 %

Figure 4.11 Proposed side-product from HMF dehydration in ionic liquid

Conclusions

This study shows that the ionic liquid [bmim][OTf] is a versatile solvent for the dehydration of fructose to HMF permitting a good compromise between high loading (14%), short reaction time (10 min), low temperature (100 °C) and high yield (>80 %). In achieving this important result, it was found that water plays a key role in stabilising HMF and was the key factor in improving the yield of HMF from fructose, making this system very competitive in contrast to all of the negative results reported so far in the literature. The analysis presented here shows that the dehydration of fructose to HMF in non-coordinating ionic liquids is compromised by the instability of HMF in the (pure) ionic liquid under acidic conditions. By regulating the water content, side reactions related to the self-condensation of HMF are suppressed. Cross-condensation of fructose with the formed HMF in the beginning of the reaction is the main source of inefficiency and one oligomer was identified as etherification of one intermediate with HMF. The separation of HMF from this solvent is more favourable compared to halogenated ionic liquids, improving the partition coefficient by two orders of magnitude. However, in terms of process economics the amount of solvent is still enormous for process scale-up and further studies on solvent screening must be done for an efficient separation of HMF. On the other hand, the solvent used is a suitable media for selective alcohol oxidation with the potential to produce DFF which can be separated by sublimation. In the next chapter this aspect will be tackled by developing a catalytic system for the selective production of DFF from HMF in [bmim][OTf], allowing this to be combined with the system developed above.

References

- (1) Van Putten, R.-J. J.; van der Waal, J. C.; de Jong, E.; Rasrendra, C. B.; Heeres, H. J.; de Vries, J. G. Hydroxymethylfurfural, a Versatile Platform Chemical Made from Renewable Resources. *Chem. Rev.* **2013**, *113* (3), 1499–1597. <https://doi.org/10.1021/cr300182k>.
- (2) Ragauskas, A. J.; Ragauskas, A. J.; Williams, C. K.; Davison, B. H.; Britovsek, G.; Cairney, J.; Eckert, C. A.; Jr, W. J. F.; Hallett, J. P.; Leak, D. J.; et al. The Path Forward for Biofuels and Biomaterials. *Science*. **2006**, *311* (5760), 484–489. <https://doi.org/10.1126/science.1114736>.
- (3) Wang, H.; Zhu, C.; Li, D.; Liu, Q.; Tan, J.; Wang, C.; Cai, C.; Ma, L. Recent Advances in Catalytic Conversion of Biomass to 5- Hydroxymethylfurfural and 2 , 5-Dimethylfuran. *Renew. Sustain. Energy Rev.* **2019**, *103*, 227–247. <https://doi.org/10.1016/j.rser.2018.12.010>.
- (4) Ståhlberg, T.; Fu, W.; Woodley, J. M.; Riisager, A. Synthesis of 5-(Hydroxymethyl)Furfural in Ionic Liquids: Paving the Way to Renewable Chemicals. *ChemSusChem* **2011**, *4* (4), 451–458. <https://doi.org/10.1002/cssc.201000374>.
- (5) Wang, T.; Nolte, M. W.; Shanks, B. H. Catalytic Dehydration of C 6 Carbohydrates for the Production of Hydroxymethylfurfural (HMF) as A. *Green Chem.* **2014**, *16* (2), 548–572. <https://doi.org/10.1039/c3gc41365a>.
- (6) Siankevich, S.; Savoglidis, G.; Fei, Z.; Laurenczy, G.; Alexander, D. T. L.; Yan, N.; Dyson, P. J. A Novel Platinum Nanocatalyst for the Oxidation of 5-Hydroxymethylfurfural into 2,5-Furandicarboxylic Acid under Mild Conditions. *J. Catal.* **2014**, *315*, 67–74. <https://doi.org/10.1016/j.jcat.2014.04.011>.
- (7) Siankevich, S.; Fei, Z.; Scopelliti, R.; Jessop, P. G.; Zhang, J.; Yan, N.; Dyson, P. J. Direct Conversion of Mono- and Polysaccharides into 5-Hydroxymethylfurfural Using Ionic-Liquid Mixtures. *ChemSusChem* **2016**, *9* (16), 2089–2096. <https://doi.org/10.1002/cssc.201600313>.
- (8) Clarke, C. J.; Tu, W. C.; Levers, O.; Bröhl, A.; Hallett, J. P. Green and Sustainable Solvents in Chemical Processes. *Chem. Rev.* **2018**, *118* (2), 747–800. <https://doi.org/10.1021/acs.chemrev.7b00571>.
- (9) Istasse, T.; Bockstal, L.; Richel, A. Production of 5-Hydroxymethylfurfural from D-Fructose in Low-Transition-Temperature Mixtures Enhanced by Chloride Anions and Low Amounts of Organic Acids. *Chempluschem* **2018**, *83* (12), 1135–1143. <https://doi.org/10.1002/cplu.201800416>.
- (10) Antonetti, C.; Fulignati, S.; Licursi, D.; Galletti, A. Turning Point toward the Sustainable Production of 5-Hydroxymethyl-2-Furaldehyde in Water: Metal Salts for Its Synthesis from Fructose and Inulin. *ACS Sustain. Chem. Eng.* **2019**, *7* (7), 6830–6838.
- (11) Haung, X.; Kudo, S.; Sperry, J.; Hayashi, J. Clean Synthesis of 5-Hydroxymethylfurfural and Levulinic Acid by Aqueous Phase Conversion of Levoglucosenone over Solid Acid Catalysts. *ACS Sustain. Chem. Eng.* **2018**, *7* (6), 5892–5899.
- (12) Du, M.; Agrawal, A.; Chakraborty, S.; Garibay, S. J.; Limvorapitux, R.; Choi, B.; Madrahimov, S. T.; Nguyen, S. T. Matching the Activity of Homogeneous Sulfonic Acids: The Fructose-to-HMF Conversion Catalyzed by Hierarchically Porous Sulfonic-Acid-Functionalized Porous Organic Polymer (POP) Catalysts. *ACS Sustain. Chem. Eng.* **2019**, *7* (9), 8126–8135.
- (13) Yamada, T.; Kamata, K.; Hayashi, E.; Hara, M.; Uchida, S. Structure-Function Relationships in Fructose Dehydration to 5-Hydroxymethylfurfural under Mild Conditions by Porous Ionic Crystals Constructed with Analogous Building Blocks. *ChemCatChem* **2019**, *11*, 1–6.

<https://doi.org/10.1002/cctc.201900614>.

- (14) Hou, Q.; Zhen, M.; Li, W.; Liu, L.; Liu, J.; Zhang, S.; Nie, Y.; Bai, C.; Bai, X.; Ju, M. Efficient Catalytic Conversion of Glucose into 5-Hydroxymethylfurfural by Aluminum Oxide in Ionic Liquid. *Appl. Catal. B* **2019**, *253*, 1–10. <https://doi.org/DOI:10.1016/j.apcatb.2019.04.003>.
- (15) Wiesfeld, J. J.; Gaquere, R.; Hensen, E. J. M. Mesoporous Doped Tungsten Oxide for Glucose Dehydration to 5-Hydroxymethylfurfural. *ACS Sustain. Chem. Eng.* **2019**, *7* (8), 7552–7562.
- (16) Zhang, T.; Li, W.; Xin, H.; Jin, L.; Liu, Q. Production of HMF from Glucose Using an Al³⁺ - Promoted Acidic Phenol- Formaldehyde Resin Catalyst. *Catal. Commun.* **2019**, *124*, 56–61.
- (17) Rusanen, A.; Lahti, R.; Lappalainen, K.; Karkkainen, J.; Hu, T.; Romar, H.; Lassi, U. Catalytic Conversion of Glucose to 5-Hydroxymethylfurfural over Biomass-Based Activated Carbon Catalyst. *Catal. Today* **2019**.
- (18) Bobbink, F. D.; Huang, Z.; Menoud, F.; Dyson, P. J. Leather-Promoted Transformation of Glucose into 5-Hydroxymethylfurfural and Levoglucosenone. *ChemSusChem* **2019**, *12* (7), 1437–1442. <https://doi.org/10.1002/cssc.201802830>.
- (19) Sidhpuria, K. B.; Daniel-Da-Silva, A. L.; Trindade, T.; Coutinho, J. A. P. Supported Ionic Liquid Silica Nanoparticles (SILnPs) as an Efficient and Recyclable Heterogeneous Catalyst for the Dehydration of Fructose to 5-Hydroxymethylfurfural. *Green Chem.* **2011**, *13* (2), 340–349. <https://doi.org/10.1039/c0gc00690d>.
- (20) Degirmenci, V.; Pidko, E. A.; Magusin, P. C. M. M.; Hensen, E. J. M. Towards a Selective Heterogeneous Catalyst for Glucose Dehydration to 5-Hydroxymethylfurfural in Water: CrCl₂ Catalysis in a Thin Immobilized Ionic Liquid Layer. *ChemCatChem* **2011**, *3* (6), 969–972. <https://doi.org/10.1002/cctc.201000426>.
- (21) Zakrzewska, M. E.; Bogel-lukasik, E.; Bogel-lukasik, R. Ionic Liquid-Mediated Formation of 5-Hydroxymethylfurfural s A Promising Biomass-Derived Building Block. *Chem. Rev.* **2011**, *111* (2), 397–417. <https://doi.org/https://doi.org/10.1021/cr100171a>.
- (22) An, S.; Wang, Z.; Zhang, H.; Mira, H. N.; Song, Y.-F. Self-Organization of Ionic Liquid-Modified Organosilica Hollow Nanospheres and Heteropolyacids: Efficient Preparation of 5-HMF Under Mild Conditions. *ChemCatChem* **2019**, *11*, 1–12.
- (23) Pramod V, R.; Rajendra, M. B.; Wook-Jin, C.; Amol, J. R.; Hern, K. Efficient Dehydration of Glucose, Sucrose, and Fructose to 5-Hydroxymethylfurfural Using Tri-Cationic Ionic Liquids. *Catal. Letters* **2019**, *149* (3), 672–687.
- (24) Swatloski, R. P.; Spear, S. K.; Holbrey, J. D.; Rogers, R. D. Dissolution of Cellulose with Ionic Liquids. *J. Am. Chem. Soc.* **2002**, *124* (18), 4974–4975. <https://doi.org/10.1021/ja025790m>.
- (25) Yong, G.; Zhang, Y.; Ying, J. Y. Efficient Catalytic System for the Selective Production of 5-Hydroxymethylfurfural from Glucose and Fructose. *Angew. Chemie Int. Ed.* **2008**, *47* (48), 9345–9348. <https://doi.org/10.1002/anie.200803207>.
- (26) Zhao, H.; Holladay, J. E.; Brown, H.; Zhang, Z. C. Metal Chlorides in Ionic Liquid Solvents Convert Sugars to 5-Hydroxymethylfurfural. *Science (80-.)*. **2007**, *316* (5831), 1597–1600. <https://doi.org/10.1126/science.1141199>.
- (27) Hou, Q.; Li, W.; Zhen, M.; Liu, L.; Chen, Y.; Yang, Q.; Huang, F.; Zhang, S.; Ju, M. An Ionic Liquid-Organic Solvent Biphasic System for Efficient Production of 5-Hydroxymethylfurfural from Carbohydrates at High Concentrations. *RSC Adv.* **2017**, *7* (75), 47288–47296. <https://doi.org/10.1039/c7ra10237b>.

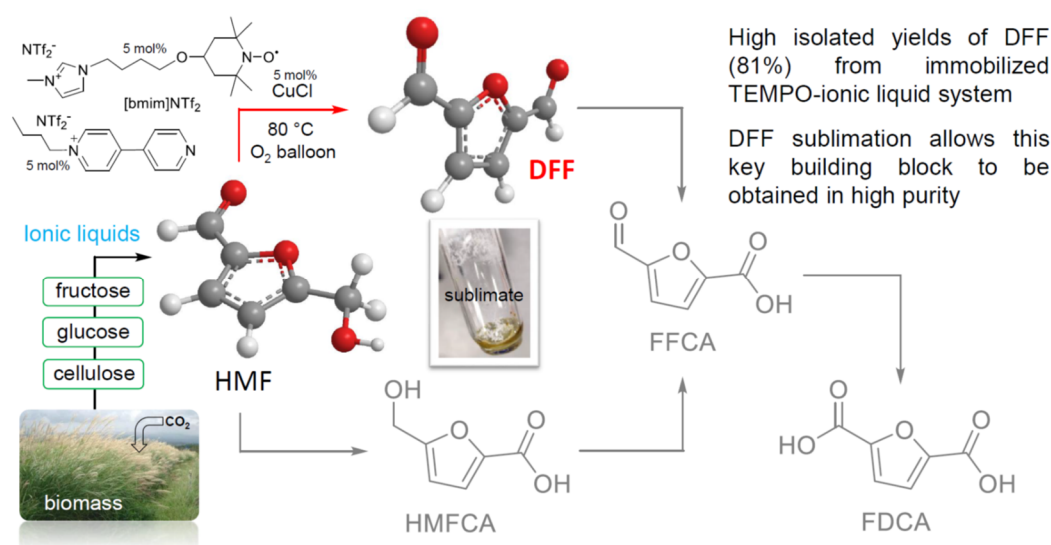
- (28) Eminov, S.; Wilton-Ely, J. D. E. T.; Hallett, J. P. Highly Selective and Near-Quantitative Conversion of Fructose to 5-Hydroxymethylfurfural Using Mildly Acidic Ionic Liquids. *ACS Sustain. Chem. Eng.* **2014**, 2 (4), 978–981. <https://doi.org/10.1021/sc400553q>.
- (29) Li, Y. N.; Wang, J. Q.; He, L. N.; Yang, Z. Z.; Liu, A. H.; Yu, B.; Luan, C. R. Experimental and Theoretical Studies on Imidazolium Ionic Liquid-Promoted Conversion of Fructose to 5-Hydroxymethylfurfural. *Green Chem.* **2012**, 14 (10), 2752–2758. <https://doi.org/10.1039/c2gc35845j>.
- (30) Moreau, C.; Finiels, A.; Vanoye, L. Dehydration of Fructose and Sucrose into 5-Hydroxymethylfurfural in the Presence of 1-H-3-Methyl Imidazolium Chloride Acting Both as Solvent and Catalyst. *J. Mol. Catal. A Chem.* **2006**, 253 (1–2), 165–169. <https://doi.org/10.1016/j.molcata.2006.03.046>.
- (31) Li, C.; Zhao, Z. K.; Cai, H.; Wang, A.; Zhang, T. Microwave-Promoted Conversion of Concentrated Fructose into 5-Hydroxymethylfurfural in Ionic Liquids in the Absence of Catalysts. *Biomass and Bioenergy* **2011**, 35 (5), 2013–2017. <https://doi.org/10.1016/j.biombioe.2011.01.055>.
- (32) Li, C.; Zhao, Z. K.; Wang, A.; Zheng, M.; Zhang, T. Production of 5-Hydroxymethylfurfural in Ionic Liquids under High Fructose Concentration Conditions. *Carbohydr. Res.* **2010**, 345 (13), 1846–1850. <https://doi.org/10.1016/j.carres.2010.07.003>.
- (33) Lansalot-Matras, C.; Moreau, C. Dehydration of Fructose into 5-Hydroxymethylfurfural in the Presence of Ionic Liquids. *Catal. Commun.* **2003**, 4 (10), 517–520. [https://doi.org/10.1016/S1566-7367\(03\)00133-X](https://doi.org/10.1016/S1566-7367(03)00133-X).
- (34) Tian, C.; Zhu, X.; Chai, S. H.; Wu, Z.; Binder, A.; Brown, S.; Li, L.; Luo, H.; Guo, Y.; Dai, S. Three-Phase Catalytic System of H₂O, Ionic Liquid, and VOPO 4-SiO₂ Solid Acid for Conversion of Fructose to 5-Hydroxymethylfurfural. *ChemSusChem* **2014**, 7 (6), 1703–1709. <https://doi.org/10.1002/cssc.201400119>.
- (35) Shi, C.; Zhao, Y.; Xin, J.; Wang, J.; Lu, X.; Zhang, X.; Zhang, S. Effects of Cations and Anions of Ionic Liquids on the Production of 5-Hydroxymethylfurfural from Fructose. *Chem. Commun.* **2012**, 48 (34), 4103–4105. <https://doi.org/10.1039/c2cc30357d>.
- (36) Hu, L.; Sun, Y.; Lin, L. Efficient Conversion of Glucose into 5-Hydroxymethylfurfural by Chromium(III) Chloride in Inexpensive Ionic Liquid. *Ind. Eng. Chem. Res.* **2012**, 51 (3), 1099–1104. <https://doi.org/10.1021/ie202174f>.
- (37) Tian, G.; Tong, X.; Cheng, Y.; Xue, S. Tin-Catalyzed Efficient Conversion of Carbohydrates for the Production of 5-Hydroxymethylfurfural in the Presence of Quaternary Ammonium Salts. *Carbohydr. Res.* **2013**, 370, 33–37. <https://doi.org/10.1016/j.carres.2013.01.012>.
- (38) Wei, Z.; Liu, Y.; Thushara, D.; Ren, Q. Entrainer-Intensified Vacuum Reactive Distillation Process for the Separation of 5-Hydroxymethylfurfural from the Dehydration of Carbohydrates Catalyzed by a Metal Salt-Ionic Liquid. *Green Chem.* **2012**, 14 (4), 1220–1226. <https://doi.org/10.1039/c2gc16671b>.
- (39) Sun, X.; Liu, Z.; Xue, Z.; Zhang, Y.; Mu, T. Extraction of 5-HMF from the Conversion of Glucose in Ionic Liquid [Bmim]Cl by Compressed Carbon Dioxide. *Green Chem.* **2015**, 17 (5), 2719–2722. <https://doi.org/10.1039/c5gc00092k>.
- (40) Shi, C.; Xin, J.; Liu, X.; Lu, X.; Zhang, S. Using Sub/Supercritical CO₂ as “Phase Separation Switch” for the Efficient Production of 5-Hydroxymethylfurfural from Fructose in an Ionic Liquid/Organic Biphasic System. *ACS Sustain. Chem. Eng.* **2016**, 4 (2), 557–563. <https://doi.org/10.1021/acssuschemeng.5b00889>.
- (41) Sajid, M.; Zhao, X.; Liu, D. Production of 2,5-Furandicarboxylic Acid (FDCA) from 5-

- Hydroxymethylfurfural (HMF): Recent Progress Focusing on the Chemical-Catalytic Routes. *Green Chem.* **2018**, *20* (24), 5427–5453. <https://doi.org/10.1039/c8gc02680g>.
- (42) Stahlberg, T.; Eyjolfsson, E.; Gorbanev, Y. Y.; Sdaba, I.; Riisager, A. Aerobic Oxidation of 5-(Hydroxymethyl)Furfural in Ionic Liquids with Solid Ruthenium Hydroxide Catalysts. *Catal. Letters* **2012**, *142* (9), 1089–1097. <https://doi.org/10.1007/s10562-012-0858-5>.
 - (43) Yan, D.; Xin, J.; Zhao, Q.; Gao, K.; Lu, X.; Wang, G.; Zhang, S. Fe-Zr-O Catalyzed Base-Free Aerobic Oxidation of 5-HMF to 2,5-FDCA as a Bio-Based Polyester Monomer. *Catal. Sci. Technol.* **2018**, *8* (1), 164–175. <https://doi.org/10.1039/c7cy01704a>.
 - (44) Yan, D.; Xin, J.; Shi, C.; Lu, X.; Ni, L.; Wang, G.; Zhang, S. Base-Free Conversion of 5-Hydroxymethylfurfural to 2,5-Furandicarboxylic Acid in Ionic Liquids. *Chem. Eng. J.* **2017**. <https://doi.org/10.1016/j.cej.2017.04.021>.
 - (45) Al Ghatta, A.; Wilton-Ely, J. D. E. T.; Hallett, J. P. Strategies for the Separation of the Furanic Compounds HMF, DFF, FFCA, and FDCA from Ionic Liquids. *ACS Sustain. Chem. Eng.* **2019**. <https://doi.org/10.1021/acssuschemeng.9b03613>.
 - (46) Farmer, V.; Welton, T. The Oxidation of Alcohols in Substituted Imidazolium Ionic Liquids Using Ruthenium Catalysts. *Green Chem.* **2002**, *4* (2), 97–102. <https://doi.org/10.1039/b109851a>.
 - (47) Ansari, I. A.; Gree, R. TEMPO-Catalyzed Aerobic Oxidation of Alcohols to Aldehydes and Ketones in Ionic Liquid [Bmim][PF₆]. *Org. Lett.* **2002**, *4* (9), 1507–1509. <https://doi.org/10.1021/ol025721c>.
 - (48) Fall, A.; Sene, M.; Gaye, M.; Gómez, G.; Fall, Y. Ionic Liquid-Supported TEMPO as Catalyst in the Oxidation of Alcohols to Aldehydes and Ketones. *Tetrahedron Lett.* **2010**, *51* (34), 4501–4504. <https://doi.org/10.1016/j.tetlet.2010.06.086>.
 - (49) Wang, Z. G.; Jin, Y.; Cao, X. H.; Lu, M. Bi-Functionalized PEG1000ionic Liquid [Imim-PEG1000-TEMPO][CuCl₂]: An Efficient and Reusable Catalytic System for Solvent-Free Aerobic Oxidation of Alcohols. *New J. Chem.* **2014**, *38* (9), 4149–4154. <https://doi.org/10.1039/c4nj00778f>.
 - (50) Lin, L.; Liuyan, J.; Yunyang, W. Base Promoted Aerobic Oxidation of Alcohols to Corresponding Aldehydes or Ketones Catalyzed by CuCl/TEMPO. *Catal. Commun.* **2008**, *9* (6), 1379–1382. <https://doi.org/10.1016/j.catcom.2007.11.041>.
 - (51) Zhang, J.; Yu, X.; Zou, F.; Zhong, Y.; Du, N.; Huang, X. Room-Temperature Ionic Liquid System Converting Fructose into 5-Hydroxymethylfurfural in High Efficiency. *ACS Sustain. Chem. Eng.* **2015**, *3* (12), 3338–3345. <https://doi.org/10.1021/acssuschemeng.5b01015>.
 - (52) Galkin, K. I.; Ananikov, V. P. Towards Improved Biorefinery Technologies : 5-Methylfurfural as a Versatile C 6 Platform for Biofuels Development. *ChemSusChem* **2019**, *119991*, 185–189. <https://doi.org/10.1002/cssc.201802126>.
 - (53) Jeong, J.; Antonyraj, C. A.; Shin, S.; Kim, S.; Kim, B.; Lee, K. Y.; Cho, J. K. Commercially Attractive Process for Production of 5-Hydroxymethyl-2-Furfural from High Fructose Corn Syrup. *J. Ind. Eng. Chem.* **2013**, *19* (4), 1106–1111. <https://doi.org/10.1016/j.jiec.2012.12.004>.
 - (54) Sampath, G.; Kannan, S. Fructose Dehydration to 5-Hydroxymethylfurfural: Remarkable Solvent Influence on Recyclability of Amberlyst-15 Catalyst and Regeneration Studies. *Catal. Commun.* **2013**, *37*, 41–44. <https://doi.org/10.1016/j.catcom.2013.03.021>.
 - (55) Morales, G.; Melero, J. A.; Paniagua, M.; Iglesias, J.; Hernández, B.; Sanz, M. Sulfonic Acid Heterogeneous Catalysts for Dehydration of C6-Monosaccharides to 5-Hydroxymethylfurfural in Dimethyl Sulfoxide. *Chinese J. Catal.* **2014**, *35* (5), 644–655.

[https://doi.org/10.1016/S1872-2067\(14\)60020-6](https://doi.org/10.1016/S1872-2067(14)60020-6).

- (56) Takagaki, A.; Ohara, M.; Nishimura, S.; Ebitani, K. A One-Pot Reaction for Biorefinery: Combination of Solid Acid and Base Catalysts for Direct Production of 5-Hydroxymethylfurfural from Saccharides. *Chem. Commun.* **2009**, No. 41, 6276–6278. <https://doi.org/10.1039/b914087e>.
- (57) Ohara, M.; Takagaki, A.; Nishimura, S.; Ebitani, K. Syntheses of 5-Hydroxymethylfurfural and Levoglucosan by Selective Dehydration of Glucose Using Solid Acid and Base Catalysts. *Appl. Catal. A Gen.* **2010**, 383 (1–2), 149–155. <https://doi.org/10.1016/j.apcata.2010.05.040>.
- (58) Ilgen, F.; Ott, D.; Kralisch, D.; Reil, C.; Palmberger, A.; König, B. Conversion of Carbohydrates into 5-Hydroxymethylfurfural in Highly Concentrated Low Melting Mixtures. *Green Chem.* **2009**, 11 (12), 1948–1954. <https://doi.org/10.1039/b917548m>.
- (59) Assanosi, A. A.; Farah, M. M.; Wood, J.; Al-Duri, B. A Facile Acidic Choline Chloride-p-TSA DES-Catalysed Dehydration of Fructose to 5-Hydroxymethylfurfural. *RSC Adv.* **2014**, 4 (74), 39359–39364. <https://doi.org/10.1039/c4ra07065h>.
- (60) Tuercke, T.; Panic, S.; Loebbecke, S. Microreactor Process for the Optimized Synthesis of 5-Hydroxymethylfurfural: A Promising Building Block Obtained by Catalytic Dehydration of Fructose. *Chem. Eng. Technol.* **2009**, 32 (11), 1815–1822. <https://doi.org/10.1002/ceat.200900427>.
- (61) Lai, L.; Zhang, Y. The Production of 5-Hydroxymethylfurfural from Fructose in Isopropyl Alcohol: A Green and Efficient System. *ChemSusChem* **2011**, 4 (12), 1745–1748. <https://doi.org/10.1002/cssc.201100489>.
- (62) Sievers, C.; Musin, I.; Marzalletti, T.; Olarte, M. B. V.; Agrawal, P. K.; Jones, C. W. Acid-Catalyzed Conversion of Sugars and Furfurals in an Ionic-Liquid Phase. *ChemSusChem* **2009**, 2 (7), 665–671. <https://doi.org/10.1002/cssc.200900092>.
- (63) Tao, F.; Song, H.; Chou, L. Dehydration of Fructose into 5-Hydroxymethylfurfural in Acidic Ionic Liquids. *RSC Adv.* **2011**, 1 (4), 672–676. <https://doi.org/10.1039/c1ra00088h>.
- (64) Qi, X.; Watanabe, M.; Aida, T. M.; Smith, R. L. Catalytic Dehydration of Fructose into 5-Hydroxymethylfurfural by Ion-Exchange Resin in Mixed-Aqueous System by Microwave Heating. *Green Chem.* **2008**, 10 (7), 799–805. <https://doi.org/10.1039/b801641k>.
- (65) Kirchner, B. *Ionic Liquids*; Springer, 2009.
- (66) Fu, X.; Dai, J.; Guo, X.; Tang, J.; Zhu, L.; Hu, C. Suppression of Oligomer Formation in Glucose Dehydration by CO₂ and Tetrahydrofuran. *Green Chem.* **2017**, 19 (14), 3334–3343. <https://doi.org/10.1039/C7GC01115F>.
- (67) Girisuta, B.; Janssen, L. P. B. M.; Heeres, H. J. A Kinetic Study on the Decomposition of 5-Hydroxymethylfurfural into Levulinic Acid. *Green Chem.* **2006**, 8 (8), 701. <https://doi.org/10.1039/b518176c>.

Chapter 5 Catalytic Oxidation of 5-HMF into DFF in [bmim][OTf] with immobilized TEMPO-pyridine ionic liquid and CuCl



Following our previous study on the separation of furanic compounds from the ionic liquid in Chapter 3, the catalytic upgrading of HMF into a more valuable product is highly desired. However, there is currently a lack of literature describing catalysts capable of efficiently converting HMF to DFF or FDCA in ionic liquids. In the following chapter, a homogeneous catalytic system will be developed for the oxidation of HMF into DFF. According to the solvent design guidelines developed in Chapter 4, this system has the potential to obtain very pure DFF that can be separated through sublimation. For this purpose, the system CuCl/TEMPO was tested in the ionic liquid [bmim][OTf] and high yield was achieved in short reaction times with the addition of a ligand. In order to test the recyclability of the system, TEMPO and the pyridine ligand were immobilized in the ionic liquid to avoid catalyst evaporation during vacuum separation of DFF. The system showed outstanding performances regarding loading, reaction time, temperature and oxygen pressure achieving over 90% yield at 80 °C, 1 bar, in 3 h with 40% HMF loading. By increasing the reaction time, the selectivity can be switched to FFCA with good yield (62%). Starting from fructose as a feedstock, 55% DFF yield was obtained in a two-step reaction. This study proves that ionic liquids are superior solvents for the catalytic conversion and separation of highly valuable, pure, bioderived chemical compounds.

Introduction

2,5-diformylfuran (DFF) represents a bioderived chemical which can be obtained from HMF. Compared with HMF, it has different properties, some of which are advantageous, as DFF is hydrophobic, stable at room temperature and sublimes at a relatively low temperature. While this molecule does not sublime from solution in organic solvents, its sublimation property is retained in ionic liquids, making the recovery easier at high purity.¹ Recently, different heterogeneous catalysts have been reported which are capable of efficiently oxidizing fructose or HMF into DFF. While any organic solvent can be used to carry out the oxidation of HMF, the choice is limited when the conversion has to be carried out from fructose. For this purpose, DMF and DMSO have already been proven to guarantee high yields of fructose dehydration.²⁻⁶ Based on this work, most research is currently focused on developing heterogeneous catalytic systems to combine both reactions and obtain a high yield of DFF from sugars. For example, over 70% yield was obtained in a two-step synthesis using an Amberlyst-15 and Fe/Mn based catalyst or Cs/MnO at temperatures over 110 °C at 10-15 bar O₂ pressure.^{7,8} Other catalytic systems based on polyoxometallates and molybdenum were capable of achieving the same yield.^{9,10} However, notwithstanding the high yield achieved using different catalysts in one or two steps, they possess the same drawbacks since they require high oxygen pressures, high temperatures and low substrate loadings. Moreover, the issue of separation remains since once HMF is converted into DFF, the removal of a high boiling point solvent remains challenging, leading to the same issues related to the separation of HMF.

In this scenario, the development of a catalytic system capable of converting HMF into DFF in an ionic liquid can be extremely useful since DFF sublimes from the ionic liquid, creating a valuable chemical path for the valorisation of sugars into biochemicals. However, even though there are no reported studies on the oxidation of HMF to DFF in ionic liquids, selective aerobic alcohol oxidation is well studied with homogeneous catalysis. Oxidation has been widely studied with catalysts based on Pd,^{11,12} Ru,¹³⁻¹⁷ Co,¹⁸ W,¹⁹ V,^{20,21} Fe/Zr^{22,23} and Cu/TEMPO.²⁴⁻²⁸ In choosing the catalytic system to be used, multiple factors must be considered. First, the ionic liquid used has to be suitable for sugar dehydration, and the catalytic system should be able to oxidise furanic compounds. Indeed, catalyst activity has shown strong dependency on the functionality of the alcohol group. Aromatic alcohols have proven to be the most ideal compounds to oxidise and they are used as model compounds for oxidation and activated alcohols with electron donating groups have generally shown higher activity towards oxidation compared to those with electron withdrawing groups. On the other hand, allylic and heterocycles compounds have proven more challenging for the alcohol oxidation. The reason for this can be deduced from the stability of these compounds compared to the aromatic alcohols. While benzyl alcohol is highly stable at high temperatures, furfuryl alcohol is much less stable, undergoing polymerization. The results of this side reaction can lead to significant effects on the catalyst activity,

possibly leading to deactivation and side products. Therefore, in choosing the catalytic system, it is important first to analyse the substrate scope of the catalyst. Stark and co-workers showed that palladium catalysts, which are commonly used for oxidation, change chemoselectivity to alcohol etherification whenever chloride ions are present in the system, hence palladium catalysts need a solvent which doesn't form H-bonding for an efficient oxidation.¹¹ Another study shows that by adding [emim][NTf₂], the catalytic activity of Pd is boosted, indicating a favourable effect of the ionic liquid on the kinetics of reaction.¹² Few studies use non-noble metal catalysts such as cobalt, tungsten and vanadium. Co-phthalocyanine and vanadyl acetylacetonate show remarkable selectivity for a large variety of substrates, respectively, in [bmim]Br and [bmim][PF₆] at atmospheric pressure,^{18,20,21} while only one substrate was tested with tungsten oxide in [omim]Cl.¹⁹

Ruthenium in different forms was also tested in different ionic liquids. Welton et al. successfully oxidized a large variety of benzyl alcohols using tetrapropylammonium perruthenate (TPAP) in [bmim][NTf₂]¹³ while ruthenium based salts require chloride to exhibit activity towards oxidation.¹⁶

A widely studied catalyst is the combination of CuCl and TEMPO which showed improved kinetics of oxidation in ionic liquids compared to organic solvents which require long reaction times to complete the reaction. In the following chapter, the most suitable catalytic system for the oxidation of HMF to DFF will be explored along with efforts to develop an efficient path from sugars.

Experimental Section

Materials

Materials and procedure for ionic liquid synthesis are the same as the one adopted in Chapter 2 (Experimental Section). 4-hydroxy-TEMPO (97 %), anhydrous benzene (99.8 %), sodium hydride (60 % dispersion in mineral oil), dibromobutane (99%), CuCl (99 %), TEMPO (98%), DABCO, DBU (98%), triethyl amine (>99.5%), VO(acac)₂ (97 %), cobalt phthalocyanine (97%), TPAP (97 %), 4 methoxybenzyl alcohol (98 %) were bought from Sigma Aldrich. 4,4 bypyridine (98%) was bought from Flurorochem.

Oxidation Experiments

Experiments were performed in a 3 mL vial closed with a rubber septum. Different methods to supply oxygen to the system were tested mainly through bubbling with a needle or balloon. Bubbling manifested different practical problems such as high oxygen consumption and reproducibility of the system due to the difficulties in regulating the oxygen flow. This often causes entrainment of the liquid phase, while an oxygen balloon guaranteed consistent results and low oxygen consumption, allowing us to execute more experiments in parallel and in triplicate. The catalyst (CuCl/TEMPO) and HMF were dissolved in the ionic liquid phase prior to the reaction in a 3 ml vial then closed with a rubber septum. Oxygen was introduced in the system through a needle connected to a balloon. The vials were placed in a pre-heated heating block and left under stirring for the desired time.

In a typical experiment, 300 mg of ionic liquid were mixed with the catalyst at 5% loading compared HMF (4.7 mg CuCl, 1.86 mg TEMPO), stirred overnight to assure that all the catalyst is dissolved and then HMF (30 mg) is added to the reaction mixture then capped with a rubber septum and purged with an oxygen balloon. The vial was placed in a preheated heating block and left it for the desired time under stirring. At the end of the reaction the reaction mixture 3 ml of water were added to the reaction mixture and analysed by HPLC.

HPLC quantification was done with H-column with the same method reported in Chapter 3 (Experimental Section).

Synthesis of TEMPO-immobilized ionic liquid

The synthesis of TEMPO-immobilize follow the scheme reported in Figure 5.1 with a modified procedure reported in literature.²⁹

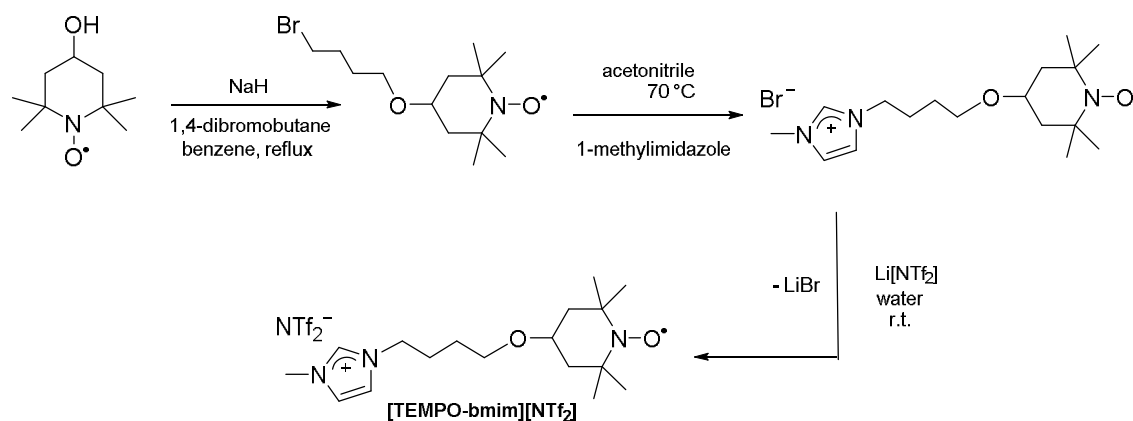


Figure 5.1 Synthesis of the ionic liquid immobilised TEMPO, [TEMPO-bmim][NTf₂].

4-hydroxy-TEMPO (5.0 g, 29 mmol) and dry benzene (100 mL) were added to a 250-mL 3-neck flask equipped with a reflux condenser and nitrogen inlet line. This step is focused on forming the alkoxide of TEMPO to increase its nucleophilicity for the subsequent S_N2 reaction. For this purpose sodium hydride (0.72 g, 30.0 mmol) was chosen since it is stabilized with oil making the handling safe and straightforward. Since chromatography was performed in later steps, the residual oils formed were removed at that stage. Once the addition of NaH was complete, the reaction was brought to reflux for 24 hours. The resulting suspension was cooled in an ice bath and 1,4-dibromobutane (8.6 g, 40.0 mmol) was added and the solution was again brought to reflux for 24 hours. For this purpose, an excess of dibromobutane was needed to guarantee monosubstitution. After the reaction was complete, the reaction solution was cooled and water (50 mL) was added to quench any excess sodium hydride. The contents of the reaction vessel were transferred to a separating funnel and extracted with diethyl ether (100 mL). The organic layer (benzene and diethyl ether) was decanted from the separating funnel and dried over MgSO₄ then concentrated under reduced pressure to afford the crude intermediate product containing unreacted 1,4-dibromobutane. The intermediate was purified by chromatography on silica gel with gradient elution. The column was run first with hexane. In this step the immobilized TEMPO remained on the column (visible due to its characteristic red colour) while all the dibromobutane was washed out. Then diethyl ether/hexane (1:1) was used to separate the side products. One side product was identified and was easily separated as the first fraction by tracking its typical orange colour. The solvent was then removed under vacuum to afford the desired product as a red oil denoted as **intermediate A** (2.0 g, 6.5 mmol, 23%).

The compound that resulted from this (**intermediate A**, 2.0 g, 1 eq) was slowly added to a solution of 1-methylimidazole (0.5 mL, 6.5 mol, 1 eq) in acetonitrile (1 mL). The mixture was stirred for 3 days at 70 °C. After cooling to room temperature, ethyl acetate (2 mL) was added to the mixture causing precipitation of 1-methyl-3-(4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl)butyl)imidazolium bromide as a red solid (1.2 g, 3.0 mmol). The solid was dissolved in water with Li[NTf₂] (0.98 g, 3.4 mmol, 1.1 eq) and stirred overnight at room temperature. The ionic liquid 1-methyl-3-(4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl)butyl)imidazolium bistriflimide precipitated from the solution as a red viscous liquid. This ionic liquid was dissolved in dichloromethane (1 mL) and washed with water to remove all the residual bromide ions that can be detrimental in the catalysis. The washing was tracked with AgNO₃ test. Yield 1.9 g (50%).

The NMR of Intermediate A and final product agrees with literature.²⁹

Synthesis of bipyridine immobilized Ionic Liquid [bbpy][NTf₂]

This molecule was synthesized to avoid evaporation of the ligand during reaction. Below is the detailed procedure for the synthesis with a modified procedure reported in literature.³⁰

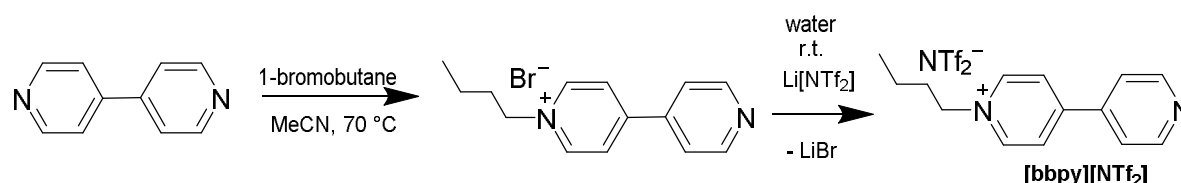


Figure 5.2 Synthesis of the pyridine immobilised ionic liquid, [bbpy][NTf₂].

4,4'-Bipyridine (8.00 g, 51.0 mmol) was dissolved in acetonitrile (90 mL) and 1-bromobutane (8.87 g, 7.00 mL, 61.0 mmol, 1.2 eq.) was added dropwise under an inert atmosphere. The mixture was heated with stirring at 70 °C for 3 days. After cooling, the solution was concentrated and the resulting precipitate was isolated by filtration. The solid product was stirred and heated at reflux in chloroform overnight. The insoluble material was separated and was identified to be the dialkyl product by ¹H NMR spectroscopy. The chloroform solution was evaporated and recrystallized to give a light green solid (10.3 g, 69%). The solid was dissolved in water with LiNTf₂ and stirred overnight. The ionic liquid separated from the water as a viscous liquid. Purification from residual bromide was achieved by dissolution in dichloromethane and washing until AgNO₃ gave a negative test for halide. Yield: 18.1 g (72%).

NMR of the final product agrees with the one reported in literature.³⁰

XPS analysis

Catalyst characterization was performed by XPS analysis, performed using a Thermo NEXSA XPS fitted with a monochromated Al $K\alpha$ X-ray source (1486.7 eV), a spherical sector analyser and 3 multichannel resistive plate, 128 channel delay line detectors. All data was recorded at 19.2W and an X-ray beam size of 200 x 100 μm . Survey scans were recorded at a pass energy of 160 eV, and high-resolution scans recorded at a pass energy of 20 eV. Electronic charge neutralization was achieved using a Dual-beam low-energy electron/ion source (Thermo Scientific FG-03). Ion gun current = 150 μA . Ion gun voltage = 45 V. All sample data was recorded at a pressure below 10^{-8} Torr and a room temperature of 294 K.

XPS spectra was fitted using OriginPro 2017 with Savitzky-Golay method over 10 point of window.

In order to perform the characterization of the catalyst the complex Cu-ligand was prepared in a different batch rather than in-situ. A stoichiometric amount of ligand and CuCl (100 mg) was mixed in dry acetonitrile (10 ml) at room temperature overnight. After solvent removal in vacuum, the catalyst was washed with diethyl ether (3*2 ml) then dried in a vacuum oven overnight at 60 °C.

The recovery of the catalyst after the reaction was done by water addition to the reaction mixture (10:1) when the solvent was hydrophilic ([bmim][OTf]). The copper-ligand complex precipitate from the reaction mixture and recovered by decantation. The catalyst recovery was done only for experiments with recycling and was possible only with the ligand [bbpy][NTf₂] since hydrophobic, avoiding ligand lost in the water phase, keeping intact the interaction with the copper center.

Results and Discussion

Screening of catalytic systems

The strategy adopted to select the best ionic liquid/catalyst combination for our purpose was to test different catalytic systems and measure the selectivity at a defined time under the same conditions.

In order to validate the experimental, the different catalytic systems were replicated with 4-methoxybenzyl alcohol which is the most used substrate to test the catalytic activity. The system that was selected from the literature was based on the substrate scope and the compatibility of the ionic liquid for dehydration. Priority was given to systems that used halogenated ionic liquids, since these are the most efficient solvents for sugar dehydration.³¹ In particular the system of Shaabani and co-workers use [bmim]Br, a solvent which can perform a catalyst-free dehydration of fructose at high loading (33%), low temperature (100 °C) and high yield (>90 %). In their study, different benzyl alcohols were oxidized at high yield in short reaction times and 1 bar O₂ pressure. Moreover the system proved to be recyclable more than 6 times.¹⁸ Other systems which were considered are reported in Table 5.1.

Table 5.1 Different catalytic systems for alcohol oxidation reported in literature

	Author	Ionic Liquid	Catalyst	Temperature	Catalyst Loading
(1)	Jiang & Ragauskas 2006 ²⁰	[bmim][PF ₆]	VO(acac) ₂ /DABCO	80 °C	5%
(2)	Ansari & Green 2002 ²⁴	[bmim][PF ₆]	CuCl/TEMPO	65 °C	10%
(3)	Shaabani et al. 2007 ¹⁸	[bmim]Br	Co-phthalocyanine	70 °C	5%
(4)	Farmer & Welton 2002 ¹³	[bmim][NTf ₂]	TPAP/CuCl	60 °C	5%

Applying these systems to the oxidation of 4-methoxybenzyl alcohol was successful for (1), (2) and (4), achieving more than 80% yield, while (3) was not repeatable since the reaction did not proceed at all. Reasons for this could be related to the catalyst synthesis compared to the commercial one used in this work. Detailed analysis of this system was not carried out and further investigation was limited to (1), (2) and (4). According to these results it was decided that non-coordinating ionic liquids are more suitable for this type of reaction and the results of the oxidation of HMF to DFF are reported in Figure 5.3. The results show that the system reported by Ansari and Green with CuCl/TEMPO exhibits the

highest selectivity over the other systems making it the most suited to further optimization studies focused on increasing the yield. In all cases the yield was much lower compared to that for methoxybenzyl alcohol (MBA). The reason for this can be traced to the electron donating substituent of the MBA in contrast to HMF which has an aldehyde - an electron withdrawing group. Moreover, the furan ring can induce instability since it can interact with the metal leading to side reactions. In order to further understand the reason for this drastic change in the selectivity, a test using furfuryl alcohol (FA) was done to understand the impact of the functional group on the catalysis. System (1) was tested with FA and surprisingly the selectivity was further decreased to 19% (compared to 37% for HMF) forming a solid insoluble side product. This observation indicates that, contrary to the results for benzene-based substrates, more electron-donating substituents on the furan ring compromise the oxidation of the alcohol by decreasing the selectivity. This can be related to the instability of the furan ring towards side reactions, as already demonstrated in Chapter 2, as electron donating groups on the furan ring lead to degradation of the furan alcohol. This observation is reflected by the substrate scope tested in the reports. Ansari and Green tested FA in their reaction while the oxidation of furans are not reported in the Ragauskas and Welton studies. Based on this, the strategy for selecting a potential catalyst was modified to check whether furanic alcohols had been attempted in the literature report.

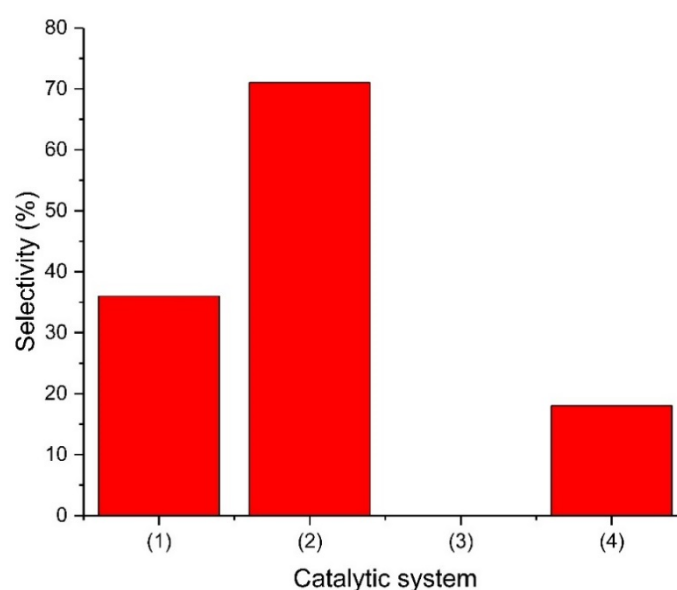


Figure 5.3 Oxidation of 5-HMF with catalytic systems reported in literature. Conditions: 10% HMF loading (respect the solvent), 10% catalyst loading (respect HMF), 1 bar O₂, 80 °C, 6 h.

While Ansari and Green were the first to report CuCl/TEMPO in ionic liquids, the system has been widely studied and used thanks to its wide substrate scope.³² However, this system suffers from recyclability problems and product separation due to the homogeneous nature of the system. Ansari and Green were able to recycle TEMPO up to 5 times by extracting the aldehydes formed with diethyl ether,

however, this method proved to be inefficient due to the high solubility of TEMPO in diethyl ether, resulting in long reaction times due to catalyst leaching.²⁴ Hansen and co-workers successfully achieved high yields for the conversion of 5-HMF to DFF using a CuCl/bipyridine/TEMPO system (without recycling) but long reaction times were required and toxic acetonitrile was used as the solvent.³³ Another report²⁷ demonstrated that a large variety of alcohols can be oxidised in [bmim][PF₆] with high efficiency in less than 3 hours, however, the attractiveness of this system is compromised by the toxicity of this ionic liquid and the alcohols investigated did not include 5-HMF. In this work, a new system is presented based on a TEMPO and pyridine immobilized ionic liquids for use with CuCl in the ionic liquids [bmim][OTf] and [bmim][NTf₂] achieving high isolated yield from 5-HMF at high loading (40%).

Solvent and Ligand selection

In our study the ionic liquid [bmim][PF₆] used by Ansari and Green was replaced by the non-coordinating ionic liquids [bmim][NTf₂] and [bmim][OTf] since these exhibit similar properties to the former but are much more stable and less toxic. Further trials were performed using different anions (Cl⁻, Br⁻, [HSO₄]⁻) but all deactivated the catalyst, leading to the formation of no product. This seems partially in contradiction with the work of Fall and co-workers, in which a PEG-TEMPO ionic liquid with a [CuCl₂]⁻ anion was observed to be the active species used to oxidize the furfuryl alcohol, however in their work a homogeneous oxidant was used. Hence our study focused on optimising the conditions in [bmim][OTf] and [bmim][NTf₂], further analysing the hydrophilic and hydrophobic effects of the solvent. The first trial at 80 °C in [bmim][OTf] resulted in 88% yield of HMF in 12 h achieving full conversion. Overoxidation to FFCA was seen as the main byproduct of the reaction in 9% yield. In order to improve the selectivity and rate, ligands were added to the system. This approach has already proven to be successful in increasing the rate of reaction dramatically.^{20,32} Different amines were tested for a reaction at 6 h to cover a wide range of pK_a from 5 to 13. Some reports discuss the role of a base in the catalytic activity. Various reports state that the role of the base is to partially deprotonate the alcohol to favour the coordination to the metal, while other literature states that is its interaction with the metal which is responsible for the enhanced catalytic activity. Pyridine, DABCO (1,4-diazabicyclo[2.2.2]octane), DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) and triethylamine were chosen for the oxidation. According the results in Figure 5.4, no direct correlation between the pK_a and the final DFF yield was observed, since triethylamine, which has the highest pK_a (13), slows down the reaction compared to having no ligand at all. This can be explained by the low coordination ability of the triethylamine which is not necessarily correlated to the pK_a. This results state that the major effect for the enhanced catalytic activity in ionic liquids is the interaction of metal/ligand combination.

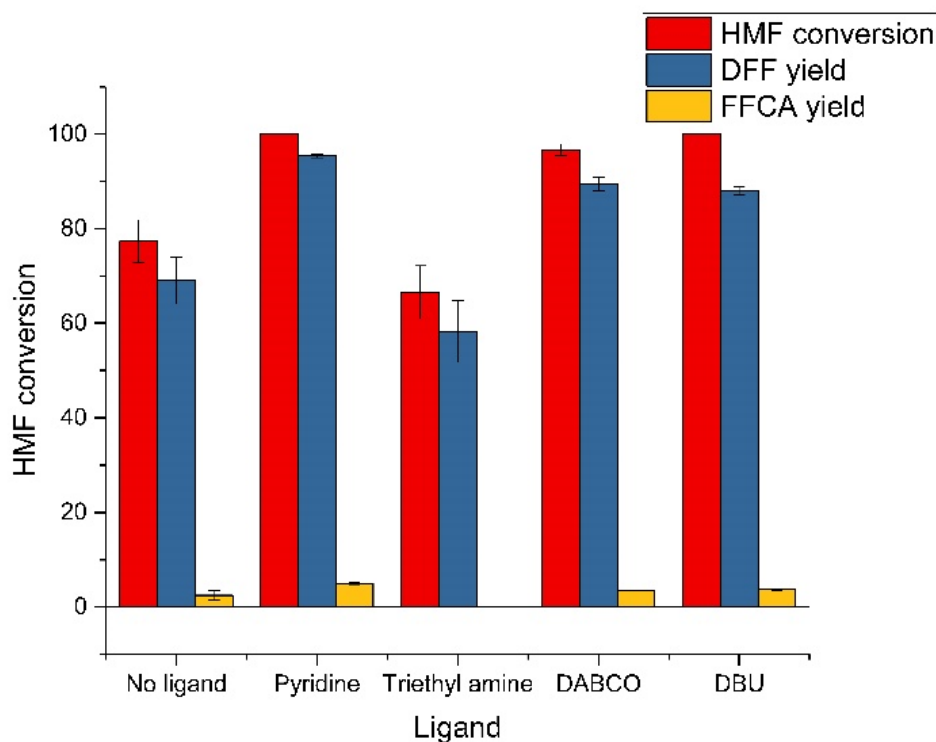


Figure 5.4 Effect of different promoters on the yields and conversion of 5-HMF. Experiments performed for 6 h with O₂ balloon at 80 °C, 200 mg [bmim][OTf], 20 mg 5-HMF, TEMPO/CuCl/promoter loading 5 mol% respect HMF. Reproduced with the permission from Al Ghatta et.al. 2020,ACS Sus. Chem. Eng., 2020

Since satisfactory results with pyridine, DABCO and DBU were achieved in 6 hours at full conversion, running the reaction for 3 hours was investigated and reported in Figure 5.5. In this new study, pyridine proved to be slightly more efficient compared to DBU, while DABCO gave the lowest performance. Comparing the data for 3 and 6 hours, there is a slight increase in selectivity at 100% conversion after 6 hours. In agreement with previous work by Hansen and co-workers, the same reaction performed in acetonitrile does not show a first order reaction due to the formation of an intermediate since conversion and yield do not proceed with the same rate.³³ However, spectroscopic evidence for the presence of the intermediate was not reported. A modest amount of over-oxidation to FFCA is observed in all cases mainly due to the water generated in the system, which forms geminal diols with the electrophilic DFF.

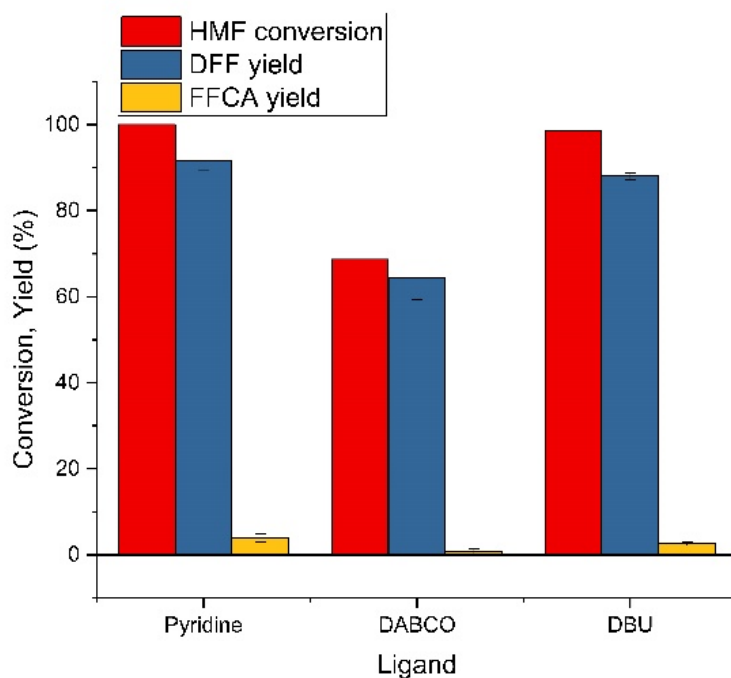


Figure 5.5 Effect of different promoters on the yields and conversion of 5-HMF after 3 hours. Experiments performed with O₂ balloon at 80 °C, 200 mg [bmim][OTf], 20 mg 5-HMF, TEMPO/CuCl/promoter loading 5 mol% respect HMF. Reproduced with the permission from Al Ghatta et.al. 2020,ACS Sus. Chem. Eng., 2020

5-HMF and catalyst loading

Due to the high cost of the ionic liquids used, the initial HMF loading is a fundamental parameter for the techno-economic efficiency of the system. To address this matter, the initial loading was varied from 10 to 50% and the yield recorded. The catalyst loading was also reduced, and these results are reported in Figure 5.6. The selectivity remained close to 100% while a gradual decrease in yield was observed. The same observation was reported by Kumpulainen and Koskinen in 2009 for the oxidation of *trans*-hex-2-ene-1-ol, in which the authors observed no reaction at 1 mol% loading and deactivation when the catalyst reached 100% conversion.³⁴ It has also been proposed by Hoover and co-workers that the deactivation is due to the formation of a copper hydroxide dimer complex at high water content, which is insoluble in the reaction mixture.³⁵ However, in our reactions, insoluble solid was not observed, leading us to suspect a different form of deactivation. This can be attributed to the water generated in the system, hence different conditions were tested to eliminate the water generated in the system, by thermal evaporation (heating up to 100°C), physical removal using a hydrophobic solvent or adding a drying agent.

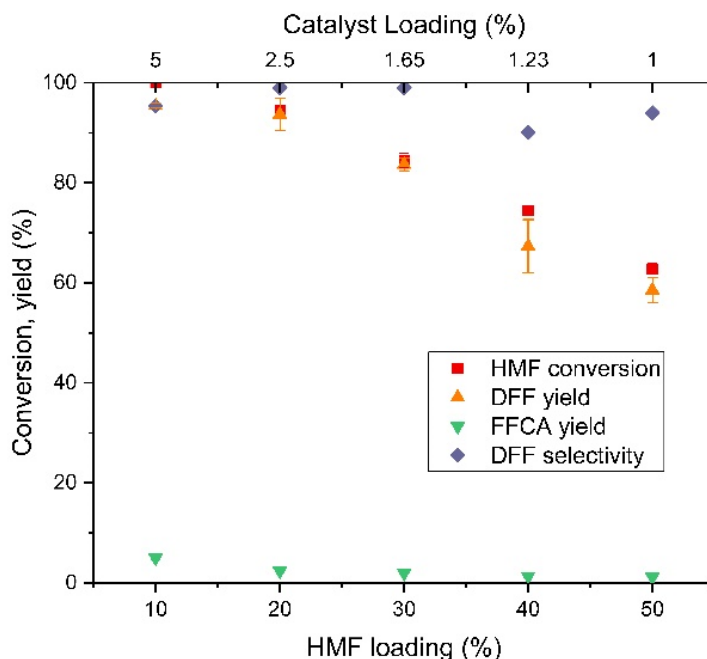


Figure 5.6 Influence of 5-HMF loading on conversion and yield in [bmim][OTf]. Higher 5-HMF loading slows down the reaction but retains high selectivity. Experiments performed for 6 h with O₂ balloon at 80 °C, TEMPO/CuCl/pyridine loading of 5 mol% respect HMF. Reproduced with the permission from Al Ghatta et.al. 2020,ACS Sus. Chem. Eng., 2020

Table 5.2 Yield (HPLC) of the oxidation of 5-HMF at 40% (mass) loading in the reaction mixture using TEMPO/CuCl/pyridine as the catalyst system. Data shown are the average of 3 repeat experiments.

Entry	Ionic Liquid	Temperature °C	Cat. Loading (mol %)	Time (h)	Conversion (%)	DFF yield (%)	FFCA yield (%)
1	[bmim][OTf]	80	1.23	6	74.3±1.6	69.3±5.3	1.0±0.2
2	[bmim][OTf]	100	1.23	6	64.3±0.5	60.7±2.7	1.8±0.2
3	[bmim][OTf] + molecular sieves	80	1.23	6	64.3±0.2	61.3±0.9	0
4	[bmim][NTf ₂]	80	1.23	6	82.0 ±0.8	76.3±2	0
5	[bmim][NTf ₂]	100	1.23	6	72.3 ±2.1	56.6±1.5	0
6	[bmim][NTf ₂]	80	1.23	12	82.5±1.2	75.0±1.8	0
7	[bmim][NTf ₂]	80	5	6	100	90.0±1.0	0

The results reported in Table 5.2 show that higher temperatures decrease the rate of reaction. This is probably due to loss of TEMPO from the solution due to the concomitant sublimation with DFF which we observed sublimes under the same conditions. Addition of molecular sieves proved to be detrimental to the reaction, decreasing kinetics even if selectivity remained high. Swapping to a hydrophobic solvent proved beneficial, improving the yield by 8%. However, increasing the reaction time to 12 h (Entry 6) did not provide any benefit, leading to the same yield and conversion. One possibility is that TEMPO sublimes in 6 h leading to no improvements between 6 h and 12 h. This is further confirmed in literature where it is reported that TEMPO has sublimation proprieties under vacuum.³⁶ Moreover, other studies have reported that the alcohol oxidation reaction with TEMPO can

follow a second order reaction making the yield dependent on the initial concentration of substrate.³⁴ This implies that higher substrate loadings would lead to longer reaction times to reach full conversion, having a further negative impact on the sublimation of TEMPO. To address this, the loading was increased to 5 mol%, restoring the yield beyond 90% at full conversion (Entry 7).

Sublimation of TEMPO represents a limiting factor for the separation of DFF since it constitutes the loss of part of the catalytic system, undermining the recyclability. For this reason, it was decided to exploit the potential of ionic liquids for chemical immobilization of catalysts to cope with the recycling issue. This would keep the catalyst in solution at high temperature and vacuum allowing separation of DFF at high purity and recycling the solvent system for further catalytic cycles. Synthesis of the immobilized TEMPO and ligand was reported in the experimental section.

Investigation of recycling with immobilised TEMPO

The immobilization of TEMPO in the ionic liquid has been mentioned in different reports and most use TEMPO with a functional group to chemically attach it to the ionic liquid. Wang and co-workers used PEG-1000 imidazolium ionic liquid to chemically immobilize TEMPO to the cation, then $[\text{CuCl}_2]^-$ was used as counterion. The system was used as combined solvent and catalyst. In another report, TEMPO triazolium salts were employed to immobilize TEMPO using dibromobutane to form a linker between TEMPO and the imidazolium ring to be used as catalyst with (bis(acetoxy)iodobenzene) to perform oxidation in $[\text{Hmim}][\text{BF}_4]$.²⁵ In the present study it was decided to adopt a modified procedure from the literature to ease handling and separation.²⁹ The reaction scheme is reported in Figure 5.1 and procedure reported in the Experimental Section of this Chapter.

For the same reason the ligand had to be immobilized as well. For this scope, the ligand 4,4'-bipyridine was selected. While other bipyridine complexes can coordinate the metal better as the 2,5-isomer, the 4,4-isomer is better for immobilization since the nitrogen in the 4 position will be less sterically hindered compared the 2,5-disubstituted derivative after immobilization is carried out. The reaction scheme is reported in Figure 5.2. As the TEMPO immobilized ionic liquid, the main challenge of this reaction is to guarantee monosubstitution on the pyridine ring. However, working with an excess of bromobutane allowed the byproducts to be more easily separated compared to bipyridine.

After checking that the immobilised catalyst (TEMPO and pyridine) gave the same HPLC results as the analogous non-immobilised system in Table 5.2 entry 7, the recycling of the solvent was tested. The DFF was separated after each cycle by vacuum sublimation, then the cycle was repeated by adding a further fraction of HMF. With the high loading of HMF (40%) most of the DFF precipitated from the reaction mixture forming a solid block at room temperature. The separation was performed at 80 °C under vacuum for 8 h subliming the DFF in the upper walls as a white block, allowing it to be collected easily. However, the system performed worse during the second cycle over 6 hours. Increasing the

reaction time to 12 h in the second cycle gave slight improvements, but the catalyst was completely inactive by the third cycle.

Addition of pyridine and TEMPO to the third cycle failed to improve the situation suggesting that it is the copper species which undergoes to deactivation. This phenomenon was observed already in the literature when acetonitrile was used as solvent,^{20,21} which suggested that the acid generated in solution by over oxidation is responsible for the deactivation through the formation of copper hydroxide which is insoluble in the reaction mixture. Other reports showed that swapping the chloride counterion in triflate allowed the yield to be improved without ultimately preventing deactivation.³⁴

At the beginning of the project, it was believed that TEMPO sublimation was the main factor for the decreased activity of the catalyst. Subsequent results confirmed that it is the copper component that is actually the cause of the observed catalytic deactivation.

Table 5.3 Recycling experiment in [bmim][NTf₂] with [TEMPO-bmim][NTf₂] (5 mol% respect HMF), [bbpy][NTf₂] (5 mol% respect HMF) at 40% 5-HMF loading respect the solvent and 5 mol% CuCl catalyst loading respect HMF. Conditions: 80 °C, O₂ balloon, DFF separation through sublimation under vacuum. Results are an average of 3 experiments.

Cycle	Time (h)	Conversion (%)	Isolated yield (%)
1	6	100	81.1 ± 7.7
2	6	75.0 ± 1.1	68.0 ± 8.1
2'	12	89.0 ± 2.2	77.0 ± 4.2
3	6	0	0

Synthesis of DFF from fructose in a two-step reaction

Following the study in Chapter 3, the dehydration of fructose to HMF can be achieved efficiently at high loadings and 3.5% water content. By replicating that system, 5-HMF was synthesized at 83% yield and 14% loading with 10% HCl loading at 100 °C and converted *in situ* to DFF by addition of the catalyst at 5 mol% loading, obtaining an overall HPLC yield of 62.1 ± 3.2% (isolated yield 55.2 ± 6.7%). For this reaction, 10 h were needed to achieve full conversion whereas in the previous results 6 h was sufficient. This may due to the protonation of TEMPO at the radical moiety reducing the active species for oxidation.^{36,37}

The attempt to recycle the whole reaction mixture proved unsuccessful since the reaction achieved no conversion. Control experiments with HCl/CuCl and HCl/TEMPO for the dehydration step show that both species act as an inhibitor, deactivating the HCl catalyst. Since CuCl has proven to be a successful catalyst for dehydration,^{38,39} attempts were made to dehydrate fructose in [bmim][OTf] but the catalyst proved to be incompatible with the solvent.

Study of the overoxidation of 5-HMF

The final stage of the study focused on the analysis of the overoxidation of 5-HMF to FFCA to see whether the selectivity can be adjusted by varying the reaction parameters. For this reaction, water is an important parameter since it thermodynamically favours the formation of the carboxylic acid from aldehydes. Hence [bmim][OTf] was used as solvent since it retains water in the system. First the time effect was analysed, increasing the reaction time to 12 h obtaining a consistent product distribution, as reported in Table 5.4.

Table 5.4 Effect of time on product selectivity. Reaction conditions: 5 mol % loading of CuCl/[bbpy][NTf₂]/TEMPO-[bmim][NTf₂] compared HMF, 10% HMF loading respect the solvent, 80 °C, 1 bar.

Time (h)	Yield DFF (%)	Yield FFCA (%)
6	95.4 ± 0.4	4.98 ± 0.3
12	64.2 ± 0.8	26.3 ± 0.5

In order to keep DFF in the solvent phase, oxidation was performed in a high pressure reactor at 4 bar O₂ at various temperatures. At 4 bar, no sublimation of DFF was observed. At high temperature, over 100 °C, traces of FDCA appeared at very low yield (3.1%) but selectivity reached a plateau at 100 °C suggesting catalyst deactivation. A maximum of 63% of FFCA was obtained and collected after sublimation of DFF by diethyl ether washing (5 x 5 mL) as a yellowish powder.

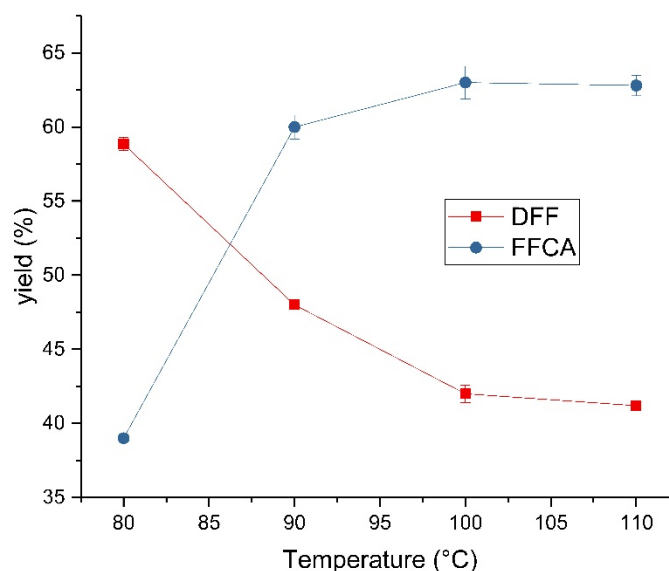


Figure 5.7 Yield of DFF and FFCA at different temperatures. Reaction conditions: 4 bar O₂ partial pressure, 10% 5-HMF loading. 10% catalyst loading (CuCl/[bbpy][NTf₂]/ TEMPO-[bmim][NTf₂])

Catalyst characterization

The copper catalyst with different ligands were characterized by XPS and reported in Figure 5.8. According to its catalytic cycle, copper can exhibit oxidation states +1 and +2, which can be distinguished by XPS by a broad satellite peak centred around 943 and 962 eV, typical of copper(II) due to its d^9 configuration. On the other hand, copper(I) does not show any satellite peak due to its complete full d^{10} shell which does not allow any charge transfer.^{40,41} Two main peaks are characteristic of the copper spectra and relate to the orbitals $2p_{1/2}$ and $2p_{3/2}$. The main peak at $2p_{3/2}$ is broader for Cu(II) and at higher binding energy compared to Cu(I), while the latter is a much sharper peak at lower binding energy.⁴² The presence of the satellites in all our copper complexes indicate that Cu(I) is actually oxidized to Cu(II) prior to the actual reaction taking place, suggesting that, while CuCl is stable, the addition of the ligand makes the catalyst more sensitive to oxygen undergoing oxidation. Hence, TEMPO is needed to reduce the copper and begin the catalytic cycle. According a mechanistic study by Stahl and co-workers, di-oxygen will form a bridge between two Cu(II) complexes which undergoes a breakdown caused by TEMPO to form the active catalytic form of Cu(II) hydroxide complex which will then oxidize the alcohol with the radical TEMPO.⁴¹

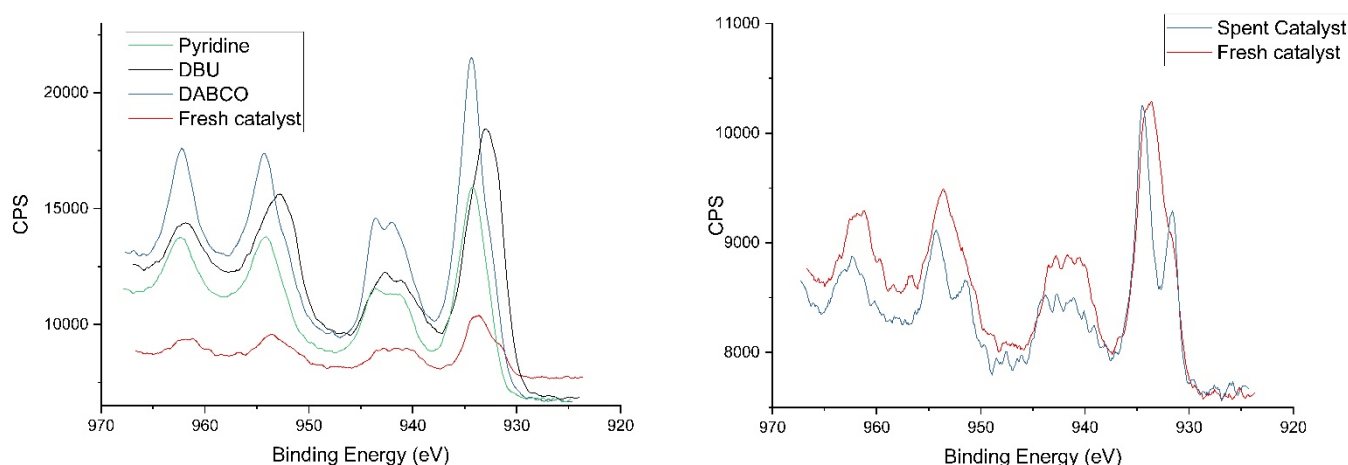


Figure 5.8 XPS analysis of the catalyst. On the left, catalyst complex CuCl with different ligands. On the right, fresh and spent catalyst.

The binding energies are reported in Table 5.5 for the main peak $2p_{3/2}$. Compared to the values reported for CuCl_2 , the shift to lower binding energies indicates that the copper atom is in an environment with lower electron density, indicating that the binding with the Cl counteranion may be broken to form different Cu(II) structures.

Table 5.5 Binding energies for different CuCl-ligand complexes.

Ligand	Cu 2p _{3/2} (eV)
CuCl ⁴³	932.4
CuCl ₂ ⁴³	934.8
[bbpy][NTf ₂]	933.5
DABCO	934.3
DBU	933.1
Pyridine	934.2

The characterization by XPS of the spent catalyst show a different structure of copper with a split of the 2p_{3/2} orbital from a broad peak at 933.54 eV to two sharp peaks at 931.6 and 934.5 eV. The further splitting of the orbital 2p_{1/2} suggests that a combination of copper (I) and (II) co-exists. The peak at 931.6 eV is indicative of copper(I) and is shifted to lower binding energy compared to the original at 932.4 eV for CuCl, while the Cu(II) peaks are shifted to higher binding energy compared to the fresh catalyst.

These data, combined with the formation of sharp peak for Cu(II), suggest that a bimetallic Cu (II)-Cu(I) complex is formed which is inactive toward oxidation. The higher electron density associated with the Cu(I) species can cause the shift of Cu(II) and the same with Cu(I), and vice-versa. The formation of a bimetallic complex associated with the split peaks in the XPS spectra was reported by Yang and co-workers⁴⁴ even if a clear reason for the splitting was not given.

Analysis of the C1s spectra reveals two peaks at 284 eV for C-C bonds, while the peaks at 292 eV can be assigned to the C-N bond of the ligand. Since no further peaks appeared in the C1s spectra (Figure 5.9), this suggested that no insoluble humins (typical side-product with HMF) are formed that can deactivate the catalyst.

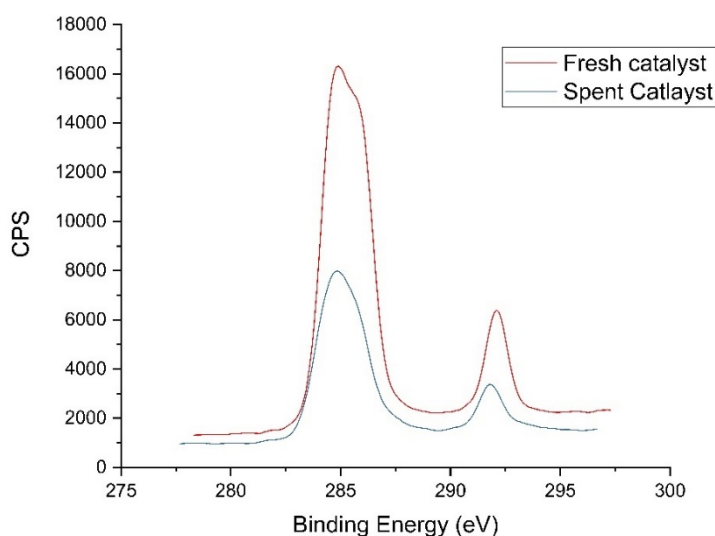


Figure 5.9 XPS for C1s for fresh and spent catalyst

Conclusions

Among the homogeneous catalytic systems reported in the literature in ionic liquids, the copper/TEMPO system represents a valuable catalyst for the oxidation of HMF to DFF. With high loadings, low oxygen pressure and low temperatures, high yields of DFF can be obtained, gaining significant advantages compared to other systems reported previously which use organic solvents, high oxygen pressure and suffer from purification problems. The use of the ionic liquid allows a practical separation of DFF from the reaction mixture starting from fructose and HMF, through sublimation at high purity. Ligands play a crucial role in the catalytic activity and pyridine proved to display the best performance, reducing drastically the reaction time and achieving 100 % conversion in less than 6 hours. Further modification of the catalyst by immobilization of TEMPO and the ligand allowed the recycling to be performed twice but deactivation arises on the third cycle. The reason lies in the deactivation of the copper catalyst, which is probably converted into another, inactive form. Further studies are needed to increase the stability of the catalyst, allowing improved recycling.

This study confirms that DFF is a valuable biochemical sugar-derived product that can be easily synthesized in ionic liquids with significant advantages both in terms of kinetics and separation. In the next chapter, focus will move to the synthesis of FDCA from sugars, an even more valuable product which reveals different catalytic challenges for the ionic liquid medium.

References

- (1) Al Ghatta, A.; Wilton-Ely, J. D. E. T.; Hallett, J. P. Strategies for the Separation of the Furanic Compounds HMF, DFF, FFCA, and FDCA from Ionic Liquids. *ACS Sustain. Chem. Eng.* **2019**. <https://doi.org/10.1021/acssuschemeng.9b03613>.
- (2) Binder, J. B.; Raines, R. T. Simple Chemical Transformation of Lignocellulosic Biomass into Furans for Fuels and Chemicals. *J. Am. Chem. Soc.* **2009**, *131* (5), 1979–1985. <https://doi.org/10.1021/Ja808537j>.
- (3) Sievers, C.; Musin, I.; Marzioletti, T.; Olarte, M. B. V.; Agrawal, P. K.; Jones, C. W. Acid-Catalyzed Conversion of Sugars and Furfurals in an Ionic-Liquid Phase. *ChemSusChem* **2009**, *2* (7), 665–671. <https://doi.org/10.1002/cssc.200900092>.
- (4) Morales, G.; Melero, J. A.; Paniagua, M.; Iglesias, J.; Hernández, B.; Sanz, M. Sulfonic Acid Heterogeneous Catalysts for Dehydration of C6-Monosaccharides to 5-Hydroxymethylfurfural in Dimethyl Sulfoxide. *Chinese J. Catal.* **2014**, *35* (5), 644–655. [https://doi.org/10.1016/S1872-2067\(14\)60020-6](https://doi.org/10.1016/S1872-2067(14)60020-6).
- (5) Jeong, J.; Antonyraj, C. A.; Shin, S.; Kim, S.; Kim, B.; Lee, K. Y.; Cho, J. K. Commercially Attractive Process for Production of 5-Hydroxymethyl-2-Furfural from High Fructose Corn Syrup. *J. Ind. Eng. Chem.* **2013**, *19* (4), 1106–1111. <https://doi.org/10.1016/j.jiec.2012.12.004>.
- (6) Shimizu, K. ichi; Uozumi, R.; Satsuma, A. Enhanced Production of Hydroxymethylfurfural from Fructose with Solid Acid Catalysts by Simple Water Removal Methods. *Catal. Commun.* **2009**, *10* (14), 1849–1853. <https://doi.org/10.1016/j.catcom.2009.06.012>.
- (7) Liu, B.; Zhang, Z.; Lv, K.; Deng, K.; Duan, H. Efficient Aerobic Oxidation of Biomass-Derived 5-Hydroxymethylfurfural to 2,5-Diformylfuran Catalyzed by Magnetic Nanoparticle Supported Manganese Oxide. *Appl. Catal. A Gen.* **2014**, *472*, 64–71. <https://doi.org/10.1016/j.apcata.2013.12.014>.
- (8) Yuan, Z.; Liu, B.; Zhou, P.; Zhang, Z.; Chi, Q. Aerobic Oxidation of Biomass-Derived 5-Hydroxymethylfurfural to 2,5-Diformylfuran with Cesium-Doped Manganese Dioxide. *Catal. Sci. Technol.* **2018**, *8* (17), 4430–4439. <https://doi.org/10.1039/c8cy01246f>.
- (9) Wang, Q.; Hou, W.; Meng, T.; Hou, Q.; Zhou, Y.; Wang, J. Direct Synthesis of 2,5-Diformylfuran from Carbohydrates via Carbonizing Polyoxometalate Based Mesoporous Poly(Ionic Liquid). *Catal. Today* **2019**, *319*, 57–65. <https://doi.org/10.1016/j.cattod.2018.07.042>.
- (10) Zhao, J.; Jayakumar, A.; Lee, J. M. Bifunctional Sulfonated MoO₃-ZrO₂ Binary Oxide Catalysts for the One-Step Synthesis of 2,5-Diformylfuran from Fructose. *ACS Sustain. Chem. Eng.* **2018**, *6* (3), 2976–2982. <https://doi.org/10.1021/acssuschemeng.7b02671>.
- (11) Seddon, K. R.; Stark, A. Selective Catalytic Oxidation of Benzyl Alcohol and Alkylbenzenes in Ionic Liquids. *Green Chem.* **2002**, *4* (2), 119–123. <https://doi.org/10.1039/b111160b>.
- (12) Chen, Y.; Bai, L.; Zhou, C.; Lee, J.-M.; Yang, Y. Palladium-Catalyzed Aerobic Oxidation of 1-Phenylethanol with an Ionic Liquid Additive. *Chem. Commun. (Camb)*. **2011**, *47* (22), 6452–6454. <https://doi.org/10.1039/c1cc11643f>.
- (13) Farmer, V.; Welton, T. The Oxidation of Alcohols in Substituted Imidazolium Ionic Liquids Using Ruthenium Catalysts. *Green Chem.* **2002**, *4* (2), 97–102. <https://doi.org/10.1039/b109851a>.
- (14) Fan, X.; Qu, Y.; Wang, Y.; Zhang, X.; Wang, J. Ru(III)-Catalyzed Oxidation of Homopropargyl Alcohols in Ionic Liquid: An Efficient and Green Route to 1,2-Allenic Ketones. *Tetrahedron Lett.* **2010**, *51* (16), 2123–2126.

<https://doi.org/10.1016/j.tetlet.2010.02.053>.

- (15) De Souza, R. F.; Dupont, J.; Dullius, J. E. D. L. Aerobic, Catalytic Oxidation of Alcohols in Ionic Liquids. *J. Braz. Chem. Soc.* **2006**, *17* (1), 48–52. <https://doi.org/10.1590/S0103-50532006000100007>.
- (16) Wolfson, A.; Wuyts, S.; Vos, D. E. De; Vankelecom, I. F. J.; Jacobs, P. a. Aerobic Oxidation of Alcohols with Ruthenium Catalysts in Ionic Liquids. *Tetrahedron Lett.* **2002**, *43* (45), 8107–8110. [https://doi.org/DOI: 10.1016/S0040-4039\(02\)01921-4](https://doi.org/DOI: 10.1016/S0040-4039(02)01921-4).
- (17) Stahlberg, T.; Eyjolfssdottir, E.; Gorbanev, Y. Y.; Sdaba, I.; Riisager, A. Aerobic Oxidation of 5-(Hydroxymethyl)Furfural in Ionic Liquids with Solid Ruthenium Hydroxide Catalysts. *Catal. Letters* **2012**, *142* (9), 1089–1097. <https://doi.org/10.1007/s10562-012-0858-5>.
- (18) Shaabani, A.; Farhangi, E.; Rahmati, A. Aerobic Oxidation of Alkyl Arenes and Alcohols Using Cobalt (II) Phthalocyanine as a Catalyst in 1-Butyl-3-Methyl-Imidazolium Bromide. **2008**, *338*, 14–19. <https://doi.org/10.1016/j.apcata.2007.12.014>.
- (19) Chen, L.; Zhou, T.; Chen, L.; Ye, Y.; Qi, Z.; Freund, H.; Sundmacher, K. Selective Oxidation of Cyclohexanol to Cyclohexanone in the Ionic Liquid 1-Octyl-3-Methylimidazolium Chloride. *Chem. Commun. (Camb)*. **2011**, *47* (33), 9354–9356. <https://doi.org/10.1039/c1cc12989a>.
- (20) Jiang, N.; Ragauskas, A. J. Vanadium-Catalyzed Selective Aerobic Alcohol Oxidation in Ionic Liquid [Bmim]PF₆. *Tetrahedron Lett.* **2007**, *48* (2), 273–276. <https://doi.org/10.1016/j.tetlet.2006.11.032>.
- (21) Jiang, N.; Ragauskas, A. J. Selective Aerobic Oxidation of Activated Alcohols into Acids or Aldehydes in Ionic Liquids Selective Aerobic Oxidation of Activated Primary Alcohols into Acids or Aldehydes Has Been Developed in Ionic Liquids . Under Optimal Conditions , Various Alcohols . **2007**, No. 1, 7030–7033.
- (22) Yan, D.; Xin, J.; Zhao, Q.; Gao, K.; Lu, X.; Wang, G.; Zhang, S. Fe-Zr-O Catalyzed Base-Free Aerobic Oxidation of 5-HMF to 2,5-FDCA as a Bio-Based Polyester Monomer. *Catal. Sci. Technol.* **2018**, *8* (1), 164–175. <https://doi.org/10.1039/c7cy01704a>.
- (23) Yan, D.; Xin, J.; Shi, C.; Lu, X.; Ni, L.; Wang, G.; Zhang, S. Base-Free Conversion of 5-Hydroxymethylfurfural to 2,5-Furandicarboxylic Acid in Ionic Liquids. *Chem. Eng. J.* **2017**. <https://doi.org/10.1016/j.cej.2017.04.021>.
- (24) Ansari, I. A.; Gree, R. TEMPO-Catalyzed Aerobic Oxidation of Alcohols to Aldehydes and Ketones in Ionic Liquid [Bmim][PF₆]. *Org. Lett.* **2002**, *4* (9), 1507–1509. <https://doi.org/10.1021/ol025721c>.
- (25) Fall, A.; Sene, M.; Gaye, M.; Gómez, G.; Fall, Y. Ionic Liquid-Supported TEMPO as Catalyst in the Oxidation of Alcohols to Aldehydes and Ketones. *Tetrahedron Lett.* **2010**, *51* (34), 4501–4504. <https://doi.org/10.1016/j.tetlet.2010.06.086>.
- (26) Wang, Z. G.; Jin, Y.; Cao, X. H.; Lu, M. Bi-Functionalized PEG1000ionic Liquid [Imim-PEG1000-TEMPO][CuCl₂]: An Efficient and Reusable Catalytic System for Solvent-Free Aerobic Oxidation of Alcohols. *New J. Chem.* **2014**, *38* (9), 4149–4154. <https://doi.org/10.1039/c4nj00778f>.
- (27) Lin, L.; Liuyan, J.; Yunyang, W. Base Promoted Aerobic Oxidation of Alcohols to Corresponding Aldehydes or Ketones Catalyzed by CuCl/TEMPO. *Catal. Commun.* **2008**, *9* (6), 1379–1382. <https://doi.org/10.1016/j.catcom.2007.11.041>.
- (28) Jiang, N.; Ragauskas, A. J. Copper(II)-Catalyzed Aerobic Oxidation of Primary Alcohols to Aldehydes in Ionic Liquid [Bmpy]PF₆. *Org. Lett.* **2005**, *7* (17), 3689–3692.

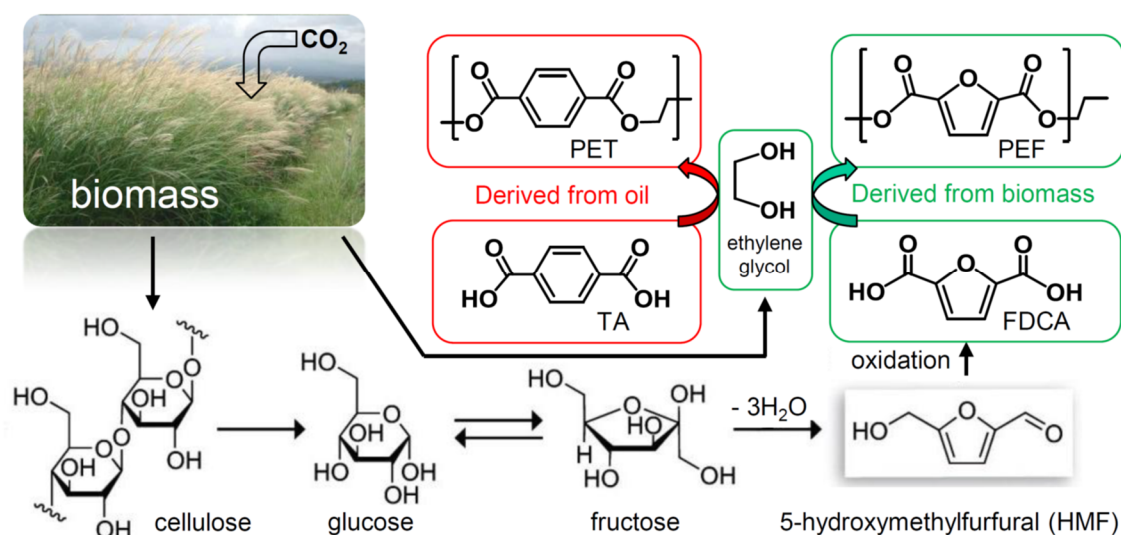
<https://doi.org/10.1021/ol051293+>.

- (29) Qian, W.; Jin, E.; Bao, W.; Zhang, Y. Clean and Selective Oxidation of Alcohols Catalyzed by Ion-Supported TEMPO in Water. **2006**, *62*, 556–562. <https://doi.org/10.1016/j.tet.2005.10.022>.
- (30) Yang, H. U. I.; Tan, Y.; Hao, J.; Yang, H.; Liu, F. Side-Chain Polypseudorotaxanes by Threading Cucurbit [7] Uril onto Synthesis , Characterization , and Properties. **2010**, *48*, 2135–2142. <https://doi.org/10.1002/POLA>.
- (31) Li, Y. N.; Wang, J. Q.; He, L. N.; Yang, Z. Z.; Liu, A. H.; Yu, B.; Luan, C. R. Experimental and Theoretical Studies on Imidazolium Ionic Liquid-Promoted Conversion of Fructose to 5-Hydroxymethylfurfural. *Green Chem.* **2012**, *14* (10), 2752–2758. <https://doi.org/10.1039/c2gc35845j>.
- (32) Hoover, J. M.; Steves, J. E.; Stahl, S. S. Copper(I)/Tempo-Catalyzed Aerobic Oxidation of Primary Alcohols to Aldehydes with Ambient Air. *Nat. Protoc.* **2012**, *7* (6), 1161–1166. <https://doi.org/10.1038/nprot.2012.057>.
- (33) Hansen, T. S.; Sádaba, I.; García-Suárez, E. J.; Riisager, A. Cu Catalyzed Oxidation of 5-Hydroxymethylfurfural to 2,5-Diformylfuran and 2,5-Furandicarboxylic Acid under Benign Reaction Conditions. *Appl. Catal. A Gen.* **2013**, *456*, 44–50. <https://doi.org/10.1016/j.apcata.2013.01.042>.
- (34) Kumpulainen, E. T. T.; Koskinen, A. M. P. Catalytic Activity Dependency on Catalyst Components in Aerobic Copper-TEMPO Oxidation. *Chem. - A Eur. J.* **2009**, *15* (41), 10901–10911. <https://doi.org/10.1002/chem.200901245>.
- (35) Hoover, J. M.; Ryland, B. L.; Stahl, S. S. Copper/TEMPO-Catalyzed Aerobic Alcohol Oxidation: Mechanistic Assessment of Different Catalyst Systems. *ACS Catal.* **2013**, *3* (11), 2599–2605. <https://doi.org/10.1021/cs400689a>.
- (36) Mahoney, L. R.; Mendenhall, G. D.; Ingold, K. U. Calorimetric and Equilibrium Studies on Some Stable Nitroxide and Iminoxy Radicals. Approximate O-H Bond Dissociation Energies in Hydroxylamines and Oximes. *J. Am. Chem. Soc.* **1973**, *95* (26), 8610–8614. <https://doi.org/10.1021/ja00807a018>.
- (37) Amorati, R.; Pedulli, G. F.; Pratt, D. A.; Valgimigli, L. TEMPO Reacts with Oxygen-Centered Radicals under Acidic Conditions. *Chem. Commun.* **2010**, *46* (28), 5139–5141. <https://doi.org/10.1039/c0cc00547a>.
- (38) Sampath, G.; Srinivasan, K. Remarkable Catalytic Synergism of Alumina, Metal Salt and Solvent for Conversion of Biomass Sugars to Furan Compounds. *Appl. Catal. A Gen.* **2017**, *533*, 75–80. <https://doi.org/10.1016/j.apcata.2017.01.004>.
- (39) Zhao, H.; Holladay, J. E.; Brown, H.; Zhang, Z. C. Metal Chlorides in Ionic Liquid Solvents Convert Sugars to 5-Hydroxymethylfurfural. *Science (80-.)*. **2007**, *316* (5831), 1597–1600. <https://doi.org/10.1126/science.1141199>.
- (40) Taher, A.; Kim, D. W.; Lee, I. M. Highly Efficient Metal Organic Framework (MOF)-Based Copper Catalysts for the Base-Free Aerobic Oxidation of Various Alcohols. *RSC Adv.* **2017**, *7* (29), 17806–17812. <https://doi.org/10.1039/c6ra28743c>.
- (41) Hoover, J. M.; Ryland, B. L.; Stahl, S. S. Mechanism of Copper(I)/TEMPO-Catalyzed Aerobic Alcohol Oxidation. *J. Am. Chem. Soc.* **2013**, *135* (6), 2357–2367. <https://doi.org/10.1021/ja3117203>.
- (42) <https://xpssimplified.com/elements/copper.php>.
- (43) Biesinger, M. C. Advanced Analysis of Copper X-Ray Photoelectron Spectra. *Surf. Interface*

Anal. **2017**, *49* (13), 1325–1334. <https://doi.org/10.1002/sia.6239>.

- (44) McMoran, E. P.; Powell, D. R.; Perez, F.; Rowe, G. T.; Yang, L. Synthesis and Characterization of Copper Complexes with CuICuI, Cu_{1.5}Cu_{1.5}m and CuIICuII Core Structures Supported by a Flexible Dipyridylamide Ligand. *Inorg. Chem.* **2016**, *55* (21), 11462–11472. <https://doi.org/10.1021/acs.inorgchem.6b02006>.

Chapter 6 Heterogeneous catalytic oxidation of HMF into FDCA in ionic liquids



In this Chapter we conclude the analysis of HMF valorisation in ionic liquids. FDCA is the most valuable chemical (so far identified) that can be obtained from HMF and much research has been focused on developing an efficient technology which can guarantee a competitive price for this molecule. Here we will focus on catalyst design for the efficient oxidation of HMF into FDCA in ionic liquids. As already demonstrated in Chapter 3, FDCA is a molecule that can be easily separated from these solvents, therefore it can potentially establish a path starting from a cheap feedstock as cellulose and glucose. This study provides principles to establish a starting point for heterogeneous catalyst design for this transformation in ionic liquids.

Introduction

The diacid monomer 2,5-furandicarboxylic acid (FDCA) is considered one of the highest value molecules that can be derived from sugars. As already mentioned in Chapter 1, market demand for this molecule is increasing due to the desire to obtain a completely green bioplastic that can replace PET within the food and packaging sector.¹ However, viable technologies which guarantee an efficient techno-economical path from sugars to FDCA do not currently exist due to the challenges in isolating the HMF intermediate. Most research done so far has focused on designing heterogeneous catalysts to perform a base free oxidation of HMF to FDCA in water and successful catalysts were developed by functionalizing the support, guaranteeing high yield, rapid kinetics and minimal metal leaching.²

Water is the preferred solvent for this purpose since the oxidation of aldehydes is thermodynamically favoured through the formation of geminal diols, which serve as the intermediate for the formation of the carboxylic acid.³ This mechanism is well accepted and can be found in any organic chemistry book.⁴

Other unconventional mechanisms have been reported for the oxidation of aldehydes under anhydrous conditions such as the Amoco Mid-Century catalyst⁵ but this involves a radical mechanism at high temperature which can lead to thermal HMF degradation and probably breakdown of the furan ring through the action of the radicals.

Most literature regarding catalytic oxidations report only homogeneous catalysis for the selective oxidation of alcohols and still fewer to carboxylic acids. Benzaldehydes undergo oxidation to carboxylic acids spontaneously through the formation of radicals (with light) on the carbonyl moiety. This leads to the capture of molecular oxygen, forming a benzoperoxy radical which undergoes disproportionation, forming the carboxylic acid.⁶ Ni(acac)₂ has proven to be an efficient catalyst for the oxidation of different benzyl aldehydes in non-coordinating ionic liquids with [BF₄]⁻ and [PF₆]⁻ anions.⁷ Other examples use stoichiometric oxidants such as H₂O₂ or tertiarybutylperoxide.^{8,9}

In this work, we will focus on the heterogeneous catalytic oxidation of HMF in ionic liquids as a potential path to valorise sugars to high value added biochemicals. The development of a heterogeneous catalyst for oxidation in ionic liquids can be extremely challenging due to the coordination properties of the anion.¹⁰ For this purpose, the use of an ionic liquid which solubilizes FDCA is needed to avoid precipitation onto the catalyst surface, which would cause deactivation of the active sites. Hence coordinating anions as Cl⁻, Br⁻ or acetate have to be used since FDCA is not soluble in non-coordinating ionic liquids.¹¹ It has been demonstrated that even small concentrations of coordinating anions can drastically affect the selectivity of the oxidation when noble metal catalysts are used. Seddon and Stark showed that the activity of a Pd-based catalyst is swapped from oxidation to etherification even at low concentration of Cl⁻ ions.¹²

The use of halide-based ionic liquids to perform this reaction has two main advantages for the cost and feedstock processing. Considering the same cation, Cl^- or Br^- based ionic liquids are cheaper since fewer reaction steps are required for their synthesis, whereas $[\text{OTf}]^-$ and $[\text{NTf}_2]^-$ require a metathesis step (usually from a halide precursor) with expensive fluorinated salts. In addition, Cl^- and Br^- produce ionic liquids that are capable of dissolving cellulose and glucose, raising the possibility of their direct use with a cheaper feedstock that does not impact the food chain. On the other hand, the solubility of oxygen in these ILs is very low compared to those containing $[\text{OTf}]^-$ or $[\text{NTf}_2]^-$ anions, which already show lower oxygen solubility compared to organic solvents or water.¹³ For a possible scale-up, mass transfer limitations can have a strong impact. Therefore, for heterogeneous catalysis, the low viscosity of imidazolium ionic liquids are the most suitable choice.

While the selective alcohol oxidation of furanic compounds in ionic liquids has been successfully achieved in non-coordinating anion environments,^{14,15} the oxidation of 5-HMF in coordinating ionic liquids has only been recently studied and only a few publications exist. Stahlberg and co-workers studied the oxidation of 5-HMF with RuOH on different supports.¹⁶ All catalysts demonstrated poor selectivity toward DFF and FDCA in most of the imidazolium ionic liquids studied. The best selectivity was achieved with $[\text{emim}][\text{OAc}]$ under very harsh conditions (140 °C, 20 bar O_2 pressure) obtaining 40% yield at full conversion after 24 h. This study demonstrated that while Ru proved to be an outstanding catalyst to oxidize HMF to both DFF or FDCA at high yields in organic solvents or water,^{17,18} this was not the case when ionic liquids were used, indicating a strong influence of the ions on the mechanism of reaction. Moreover, it is well known that dialkylimidazolium acetate ionic liquids form carbenes above 60 °C¹⁹ which in this case could be the main species responsible for the oxidation. It has already been demonstrated in many reports that carbenes are very good catalysts for aldehyde oxidation,^{20,21} therefore the role of Ru in that system is marginal. Leaching of the catalyst, separation of FDCA, low yield, harsh conditions, low HMF loadings and poor solvent stability are the main issues in this catalytic system, which represented the first reported example of HMF oxidation in ionic liquids. However, the work of Stahlber and co-workers shows interesting insight regarding the catalytic oxidation in ionic liquids compared to conventional oxidation systems. While 5-HMF is unstable at high temperatures in chloride-based ionic liquids, this degradation seems to be accelerated when the catalyst is added, indicating that a different reaction path is undertaken when the hydroxyl group is engaged in H-bonding with an anion.

Yan and co-workers designed a noble metal-free catalyst for the aerobic oxidation of 5-HMF based on Zr and Fe oxides. The reaction was still affected by modest yields (60%), low substrate loadings and harsh conditions (160 °C, 20 bar O_2).²² The authors demonstrated that the Lewis acidity of the support does not have a remarkable impact on the reaction while the Lewis basicity remarkably impacts the selectivity and reaction rate.²³ A control study done by the authors showed that the rate limiting step is the oxidation of the alcohol moiety of HMF while the aldehydes are oxidized more

rapidly. This suggests that a different mechanism is involved in non-aqueous environment at high temperatures. Probably the low strength of the acid sites due to the absence of the noble metals indicates that the hydroxyl group of 5-HMF is not adsorbed efficiently onto the catalyst surface while the strong basicity allows the adsorption of the aldehyde group (more electrophilic) without the requirement of a geminal diol. Another study performed by the authors revealed that, for this type of catalyst, Ce doping did not bring any additional benefit compared with other types of catalysts,²⁴ indicating that oxygen mobility on the catalyst surface is not a limiting step as shown in other studies carried out in water.²⁵ The authors developed a two-step reaction to produce FDCA directly from sugars. In the first step, fructose was converted to HMF with Amberlyst-15 as the catalyst, then the oxidation was performed in a second step with the Fe/Zr catalyst, achieving 46% yield overall. This represents an innovative chemical system where both reactions are performed with recyclable heterogeneous catalysts. The main drawback lies in the low concentration of HMF (0.1 M) which makes separation unfeasible. Moreover, the prospect of working at high loadings is limited by the harsh conditions used (160 °C) and the long reaction time (24 h) due to the pronounced instability of 5-HMF under these conditions (as demonstrated in Chapter 2).

Significant improvements in catalyst performance in [bmim]Cl have been developed recently by Chen and co-workers, who used heteropoly acids based on Mo and V to achieve 89% yield of FDCA from 5-HMF and 44% yield from glucose at 140 °C and 10 bar O₂ in 6 h. In this work the authors demonstrated a synergic effect between the interaction of the cation and anion of the ionic liquid with the catalytic activity of the molybdenum centre.²⁶ Though the catalytic activity is remarkable, the catalyst suffers from leaching, losing catalytic activity after the third run. Moreover, the system still suffers from difficult product separation due to the low substrate concentration (10 mg/g).

All of the results reported so far in ionic liquids are HPLC yields and product isolation was not attempted due to the low concentrations of FDCA achieved, making the separation unfeasible. Recycling was demonstrated only for the catalyst and not the ionic liquid. Chen and co-workers proposed an *in situ* polymerization with ethylene glycol to form PEF directly. This option would be extremely beneficial since the resin is completely insoluble in water and addition of a small amount would lead to precipitation. However, polycondensation does not seem a feasible option since PEF requires high temperatures (>200 °C) whereas, in the case of ionic liquids, carbenes are often formed under these conditions, favouring depolymerisation.²⁷

Improvements in ionic liquid catalysis for both dehydration and oxidation are needed to achieve product separation and higher yield of reaction. The main problem in achieving high yields of DFF or FDCA from sugars lies in the compatibility of the dehydration and oxidation reactions and the difficulty in oxidizing 5-HMF in halogenated ionic liquids. [bmim]Br and [Hmim]Cl represent the ideal solvents when fructose is used as a feedstock, since no catalyst is needed for the dehydration; therefore catalyst

design would involve only the oxidation step. In this chapter we will investigate new concepts to establish an efficient catalyst design for the oxidation of HMF to FDCA in coordinating ionic liquids.

Experimental Section

Materials

Material and methods for ionic liquid is the same as reported in the Chapter 2 (Experimental Section). Iron (III) nitrate nonahydrate (>98%), manganese (II) nitrate hexahydrate (98 %) , cobalt nitrate hexahydrate (98 %), NaBH_4 (99 %) , 1,4-dimethyl-4H-1,2,4-triazolium iodide (95 %) and DBU (98%) were bought from Sigma Aldrich. $\text{RuCl}_3 \cdot x\text{H}_2\text{O}$ (97 %) was bought from Fluorochem.

Catalyst preparation

The catalyst support was prepared by a co-precipitation method. In a typical preparation, manganese and iron nitrates were dissolved in water in the desired metal ratio at a total salt concentration of 20-40 mg/mL. In a beaker, the metal solution was added dropwise to water at pH 10 with sodium hydroxide solution (1 M) to keep the pH at 10. Sodium hydroxide was chosen as the base because it allows for better control of the pH, accelerating the procedure. However, it generally provides a lower surface area for the final catalyst compared to other bases, such as sodium carbonate. The solution at pH 10 was centrifuged and washed with water until a neutral pH was reached. The particles were dried at 60 °C and then calcined at 400 °C for 8 h to convert the residual metal hydroxides. Ruthenium was deposited onto the catalyst surface via reduction. Catalyst support powder was dispersed in a RuCl_3 solution (1 mg/mL) at the desired mass loading (10%) and stirred overnight under inert atmosphere, then a solution of NaBH_4 (10:1 respect ruthenium) was added dropwise and stirred overnight. The solution was centrifuged and washed with water and ethanol. Since the amount of hydration of RuCl_3 is not known, the calculation were referred to the anhydrous form.

In a typical experiment to prepare a support Mn:Fe 1:1, 100 mg of manganese nitrate (0.348 mmol) and 140.7 mg iron nitrate were mixed with 10 ml of water of water. In a beaker with a 30 ml of NaOH water solution at pH 10 the metal solution was added dropwise with a pipette and the pH corrected to 10 with another solution of sodium hydroxide (1 M). At the end of the addition, the solution was left overnight at room temperature, then centrifuge it to separate the solid and the solid washed with water until neutral pH was reached (about 1 L of water was required). The solid was dried at 60 °C and then calcinated at 400 °C in a furnace.

For ruthenium deposition, in a typical experiment 100 mg of catalyst support was dispersed in 20.5 ml of RuCl_3 solution (1 mg /ml) . 37.5 mg of NaBH_4 were dissolved in 100 ml of water and added dropwise to the ruthium chloride solution. The solution was left overnight under stirring and then centrifuged and washed with water and ethanol (3*100 ml).

The same procedure was adopted for Mn/Co support using cobalt nitrate hexahydrate instead of iron nitrate.

Catalyst characterization

Catalyst morphology was studied by SEM with a JEOL 2100Plus and XRD X'pert Pro. Evaluation of the Lewis basicity was done by temperature programmed desorption experiments with CO₂ according to the following method:

20 mg of sample was placed in a crucible and loaded into the TGA instrument. The sample was exposed to a flow of N₂ (30 mL/min) for 30 min and then to CO₂ at a flowrate of 30 mL/min for 1 h to saturate the basic sites of the sample. After that the sample was exposed to a flow of N₂ (30 mL/min) and warmed at a heating rate of 10 °C/min until 850 °C.

The results were reported as TGA signal relative to the loss of mass with temperature. Conventionally we classify as strong the basic sites which desorb at temperatures higher than 500 °C; medium for 300-500 °C and weak for those which do so lower than 300 °C. Distribution of basic strength was evaluated as the percentage of the area of the related region relative to the total area.

Oxidation experiments with carbene

The oxidation of DFF and FFCA with carbene was done in a 3 ml vials. In a typical experiment 300 mg of [bmim][OTf] were mixed with 30 mg of DFF (0.242 mmol) and 0.54 mg (1 mol % respect the substrate) of carbene precursor (1,4-dimethyl-4H-1,2,4-triazolium iodide) measured in a high precision balance. The reaction was started by adding DBU to the reaction mixture (73.5 mg, 0.48 mmol) and left stirring for 10 minutes with open cap.

Oxidation experiments at high pressure

In order to perform the oxidations, a reactor was designed to run multiple reactions in parallel at high pressure. Oxidation with pure oxygen at high pressure and temperature involves a high risk of explosion due to the presence of debris and residual lubricant oil which can cause ignition and explosion even with small drops.²⁸ Therefore, tubing and fittings were carefully cleaned to remove residual dust from assembly/manufacture of the equipment and strict protocols were adopted to remove the lubricants. A higher risk occurs in continuous flow since the impact of debris can cause a localized, overheated zone which can cause an ignition. Another event that can cause fire is adiabatic compression due to sudden interruption of gas flow. In our case, since the oxidation was performed under static conditions, the risk of ignition was minimized, requiring no cleaning of the fittings. The reactor was designed with a metallic base containing inserts to accommodate reaction vials (3 mL capacity). Each insert was connected through metallic tubing to a gas supply oxygen head connected to the cylinder. Each insert was equipped with a valve to isolate each reaction vial. In order to guarantee good magnetic stirring the vials were designed to be located 2 cm outside the hotplate to be close to the secondary magnetic field of the magnet.

According to the material selection guidelines, stainless steel exhibits excellent compatibility with an oxygen rich environment and so this was chosen as the best compromise between price and resistance.

In a typical experiment, 300 mg of ionic liquid with the desired amount of HMF and 10 mol% catalyst loading were prepared in a 3 mL glass vial. The reaction vials were placed in the reactor inserts and then pressurised. Each cell was isolated by closing the valves. The reactor was heating on a hotplate. In order to avoid the formation of a temperature gradient, the reactor was very well insulated with a minimum two layers of glass wool. The start of the reaction was chosen to be when the desired temperature was reached (30 min after heating was started). At the end of the reaction the products were analysed by HPLC using the same method reported in Chapter 3 (Experimental Section).

Results and Discussion

Synthesis of FDCA through homogeneous catalysis

As mentioned in the introductory paragraph, only a few examples of aerobic homogeneous catalyst have been reported for the oxidation of aldehydes to carboxylic acids. One of the most promising catalytic systems is the one reported by Howarth²⁹ which demonstrates that a relatively inexpensive catalyst such as $\text{Ni}(\text{acac})_2$ at low loading can oxidize different benzaldehydes with different substituents in non-coordinating ionic liquids in the absence of water. In order to check the reproducibility of these experiments, the oxidation of benzaldehyde was performed under the conditions described, leading to a similar yield. In the previous chapter it was demonstrated that DFF can be obtained at high yield from HMF and fructose, DFF was chosen as the substrate for oxidation to FDCA. However, the catalyst proved to be completely inactive towards this substrate. In order to further investigate the oxidation, furfural and FFCA were investigated, proving once more to be inactive in this catalytic system. It can therefore be concluded that the furan ring inhibits the oxidation in this type of system. The absence of water in the solvent suggests that the mechanism of oxidation does not pass through the geminal diol, but instead involves autoxidation with a free radical. Even if not demonstrated, $\text{Ni}(\text{acac})_2$ is likely to form radicals in the absence of light, a mechanism that has been suggested previously.⁶ Therefore, we can speculate that the radical formation at the carbonyl group is thermodynamically unfavoured when furan rings are substituted, and harsher conditions are needed to start the reaction such as those used with the Amoco Mid-Century catalyst.

Another catalytic system is that based on carbene catalysts, which is described in many reports. It has been widely demonstrated that carbenes can catalyse the oxidation of many aldehydes to form carboxylic acids or esters.^{21,30,31} The advantages in using carbenes lies in the fast kinetics (<5 min), room temperature catalysis and atmospheric pressure. It was decided to adopt this technique to oxidize DFF and FFCA to FDCA in $[\text{bmim}][\text{OTf}]$ using a triazolium salt activated with DBU. As can be seen in Table 6.1, water content favours the oxidation of FFCA to FDCA, suggesting that it makes a contribution to the mechanism of reaction as already proposed by other reports³⁰ (reported in Figure 6.1). On the other hand, by reducing the concentration of DBU, the reaction was compromised. Indeed, an equimolar amount of FDCA and DBU was needed to keep the yield high. This can be related to catalyst deactivation due to the acidity of the product since acids inhibit carbene formation. It appears necessary to employ high base concentration to neutralize the FDCA to the FDCA-DBU salts. In contrast to FDCA, its salt is soluble in the reaction mixture, but it could be separated by adding HCl, precipitating the product as a yellowish powder.

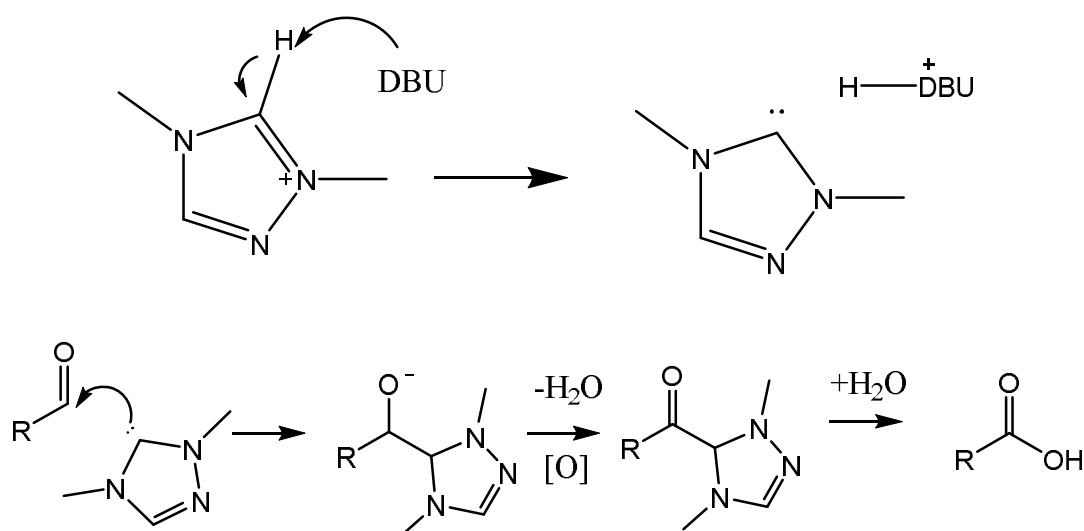


Figure 6.1 Mechanism of formation of carbene and its role with water in the oxidation of the aldehyde

While the oxidation of FFCA proved to be successful, the oxidation of DFF proved to be very inefficient leading to the formation of an insoluble product. It is likely that the electron-withdrawing character of the aldehydes led to a decrease in the energy of the LUMO orbital of the furan ring, favouring attachment to the ring rather than to the carbonyl group.

Table 6.1 Result of the oxidation of DFF and FFCA in [bmim][OTf] at room temperature, atmospheric pressure and 10 min. Substrate loading 10% mass respect the solvent. Catalyst loading 1% mol respect the substrate.

Substrate	Water content (%)	DBU concentration (eq)	Yield FDCA (%)
FFCA	0	2	71
FFCA	1	2	81
FFCA	2	2	93
FFCA	2	1	50
FFCA	2	0.5	10
DFF	2	2	14

The difficulties in optimizing the reaction conditions led us to study a different methodology focusing on heterogeneous catalysis.

Heterogeneous catalysis: Effect of solvent composition on reaction yield

In order to evaluate the effect of the ionic liquids on the oxidation of HMF to FDCA, it was decided to repeat two examples of base-free oxidation from the literature performed in water and change the solvent composition. Two ruthenium catalysts with carbon and metal supports were chosen have already proved to be efficient for this purpose when water is used as solvent.

Yi and co-workers¹⁸ demonstrated that commercial Ru/C can produce HMF at a high yield (88%) but the catalysts suffer from poor recyclability due to catalyst leaching. A different support made of a mixture of manganese and cobalt designed by Mishra and co-workers³² proved to be stable upon recycling and led to a quantitative yield at shorter reaction times.

Figure 6.2 shows the results of the experiments to test the catalytic activity at different solvent compositions with [bmim]Cl and [bmim]Br mixed at 50% with water. Repeating the experiments in water gave lower yields compared with the literature values, probably due to differences in reactor set-up or different catalyst used. The metal support guarantees higher yield compared to the carbon support, achieving about 20% higher yield. By changing the solvent composition, the yield decreases drastically, indicating an inhibition effect of the anions on the reaction. Chloride anions have a higher hydrogen bond ability and exhibit higher inhibition compared with bromide, which has a less marked impact on the catalysis.

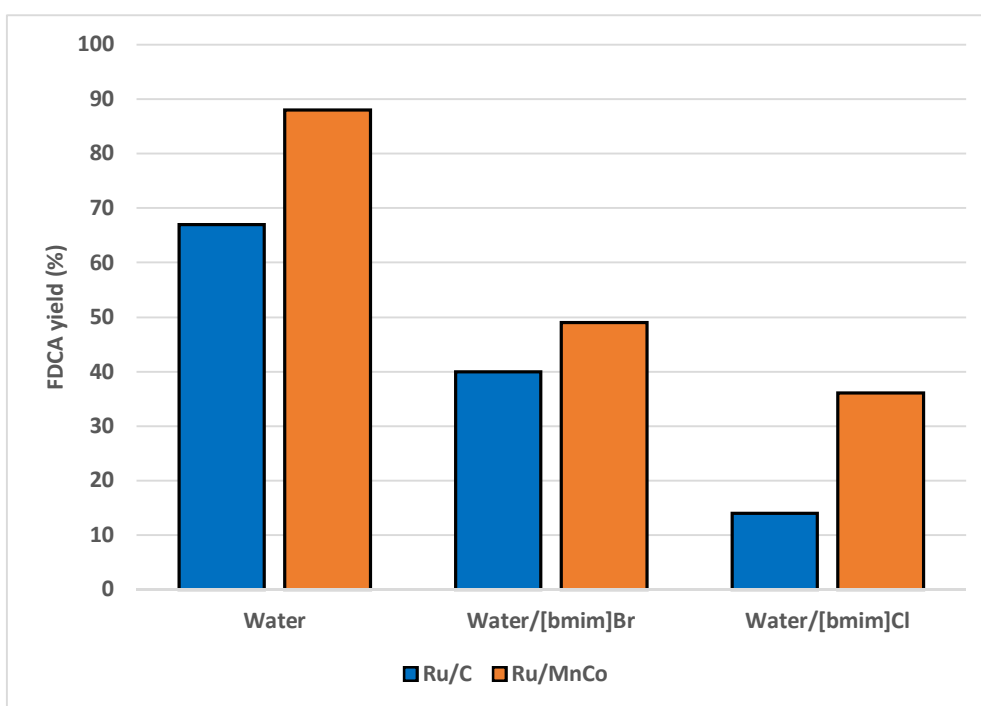


Figure 6.2 Oxidation of HMF to FDCA with two different catalysts and different solvent composition (50:50). O₂ pressure 2 bar, 120 °C, 12.6 mg/g HMF concentration

By considering some observations from the literature, key principles for the design of an efficient catalyst in ionic liquids will be established in the following section.

Strategy for efficient oxidation of HMF to FDCA in ionic liquids

While most of the literature is focused on optimizing catalyst design in water, the application of these catalysts in a non-aqueous environment will likely fail since the catalysts have not been optimized for the intended reaction environment. According to the study done by Yan and co-workers,²³ Lewis basicity performs the key role in the oxidation. Other studies done in DMSO and GVL show that a

minimum amount of water is needed to achieve a successful oxidation. In the work of Yang and co-workers³³ a minimum of 30% water was needed to achieve the oxidation with ruthenium supported by a mixture of Zn and Fe oxides. More specifically the authors observed that an optimum ratio between water and DMSO exists to maximize the yield. Indeed, in pure water their catalyst does not perform well. In another study by Dumesic and co-workers, 50% water was needed to achieve oxidation with a Pt/C catalyst.³⁴ The combination of these studies led us to form two hypotheses:

- Water is necessary for the oxidation even if pure water is not required;
- There is a relationship between the solvent basicity and Lewis basicity of the catalyst support which defines the selectivity and kinetics of reaction.

Following these principles, it was decided to regulate the Lewis basic sites with 20% water in the solvent. Mixtures of metal oxides can show unusual behaviour at different ratios of metals since there can be a synergistic effect between sites that can enhance the basicity of the support. Therefore many metals do not show a linear behaviour in terms of amount and strength of basic sites at different metal ratios. One example is the Fe and Zr oxide mixture where a maximum in basic site strength exists at 60% Zr content.²³ It was decided to investigate a mixture of Fe and Mn oxides since some reports have shown that the strength of the basic sites increases by increasing the manganese content, leading to a linear relationship of the chemical properties of the catalyst support.^{35,36} While manganese guarantees strongly basic sites and high surface area, iron is considered to be a promoter of low surface area and low active sites, therefore it was expected to act as a regulator of the strength of basic sites. Since it has been already proven that Pt and Pd are unsuitable for the aerobic alcohol oxidation,¹² ruthenium is chosen as active centre which will be deposited in the support. This metal proved already to be the most suitable metal for the base free oxidation of HMF into FDCA in water, while Pd and Pt generally require a homogeneous base.^{18,32}

Characterisation of the Mn/Fe oxides support

In Figure 6.3 the morphology of the catalyst at different Mn:Fe molar ratios is reported. It can be deduced that high manganese content leads to a more porous structure while at low manganese content the morphology of the catalysts assumes the form of large particles with low surface area. PXRD showed that all the structure is amorphous since no peaks appeared, indicating that the calcination at 400 °C was not high enough to crystallize the grains.

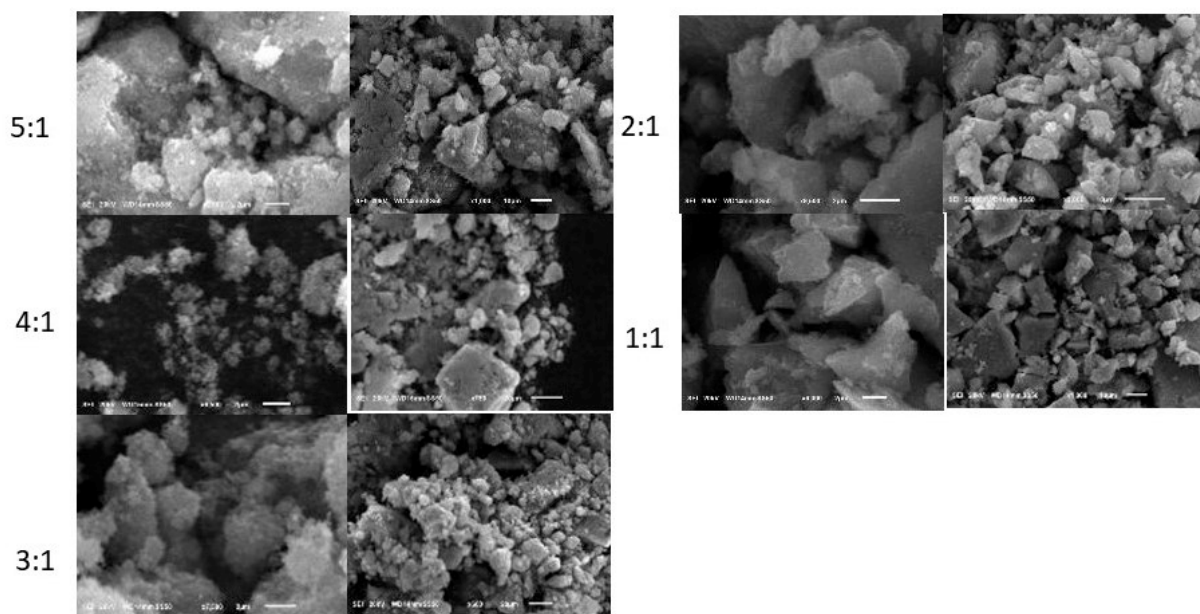


Figure 6.3 SEM image of catalyst support at different Mn:Fe content. Left column 10 μm . Right column 2 μm .

Further insights into the chemical properties of the catalyst can be gained from the CO_2 desorption curves. As predicted, higher manganese content guarantees a higher amount of strong basic sites, and the contrary with higher iron content. The distribution of the basic sites is reported in Table 6.2.

Table 6.2 Evaluation of the basic sites derived from TGA analysis

Mn:Fe	Weak (%)	Medium (%)	Strong (%)
1:1	79	16.5	4.7
2:1	53	30	18.4
3:1	48.9	32	19.4
4:1	20.5	59.2	21.5
5:1	16.8	60.2	24.0

Results of oxidation

The catalysts were tested at 120 $^{\circ}\text{C}$ and 10 bar O_2 pressure with 20% water content over two time courses. As this study is a proof of concept, an HMF loading of 2% was used, since this loading is the typical of that employed in the literature for studies performed in both water and ionic liquids. The results are reported in Figure 6.4. It can be deduced that the support mixture of manganese and iron oxide gives higher yields compared to the systems based on carbon and Mn/Co reported previously. Ratios between 1:1 to 2:1 lead to an optimum yield of 80% in 5 h and 10 h at full conversion. In the

case of too high a manganese content, the yield decreases due to FDCA degradation which could be observed in the HPLC chromatogram by a clear split of the peak related to FDCA. This can be ascribed to the increased amount of strong basic sites which can lead to further reaction of FDCA. At manganese contents of 1:1 or 2:1, the yield reached a maximum of 80% with no FDCA degradation observed in the HPLC, suggesting that FDCA is stable when low amount of strong basic sites are present in the catalyst support Table 6.2. The amounts of strong basic sites regulated by the manganese content also regulates the reaction kinetics, as high amounts speed up the reaction but with the risk of FDCA degradation. The loss of carbon yield can probably be ascribed to side reactions of HMF at the start of the reaction since only FFCA was detected as an intermediate.

While the reaction proved to be easier to control and guarantee high yield with weak basic sites further considerations need to be considered for the ruthenium leaching in the solution which is likely to occur when low amounts of basic sites are present. In this matter, further studies need to be done in studying the leaching in the solution of the metal. This aspect is not considered in this chapter.

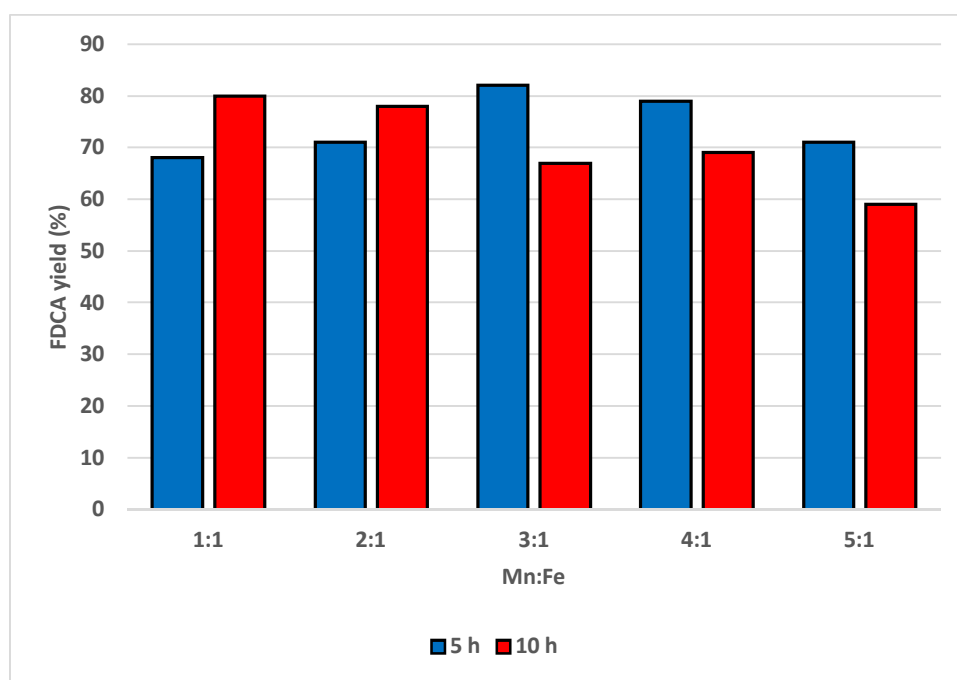


Figure 6.4 Oxidation of HMF into FDCA with Ru supported by different mixtures of Mn and Fe (molar ratio). Temperature 120 °C, O₂ pressure 10 bar, 12.6 mg/g HMF concentration.

Since [bmim]Cl is a very good solvent for glucose dehydration, a two-step reaction was studied to produce FDCA directly from sugars (Figure 6.5). The system used for the dehydration is the one elaborated by Zhao and co-workers which has so far led to the best yield (70%) at high loadings (10%).³⁷ Moreover, it has been demonstrated that water, up to a concentration of 15%, has a beneficial effect on the reaction.³⁸

The first step of the reaction was repeated successfully to give high yields of HMF (68%) from glucose with 10% water content. In the second step, water was added to reach 20% (mass) and the

reaction was performed with the Ru catalyst with a support based on a Mn:Fe ratio 1:1 for 6 h at 120 °C. An overall yield of 41% from glucose was achieved, indicating that the oxidation step is still the limiting step, preventing the theoretical yield being achieved that would be obtained when starting from HMF. This is probably because the HMF concentration achieved after the dehydration is higher than 2%. Further studies need to be performed to establish optimal conditions to increase the yield at higher HMF loading.

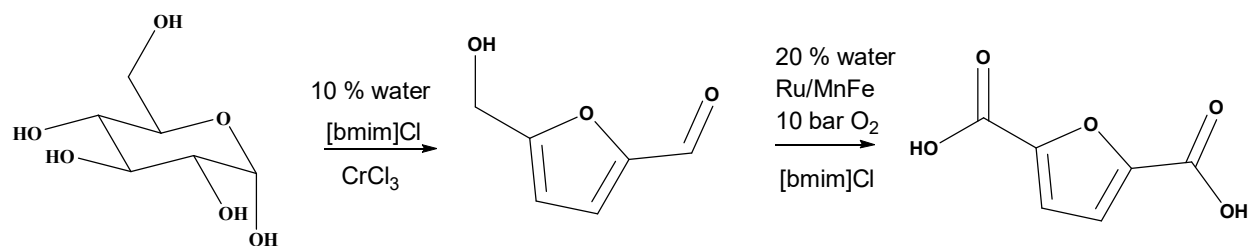


Figure 6.5 Chemical path adopted to arrive at FDCA from glucose.

Conclusion

This study has focused on catalyst design for the efficient synthesis of HMF in the ionic liquid [bmim]Cl. It has demonstrated that a mixture of Mn and Fe oxide can favour the oxidation of HMF to FDCA by regulating the Mn content in the support. Water content has also a determinant effect since a minimum amount is needed to guarantee enough population of geminal diols which will favour the oxidation. By optimizing these parameters, an efficient oxidation has been achieved from HMF to FDCA with yields over 80%. A two-pot reaction starting from glucose allowed us to obtain a yield of 40% which currently is a competitive value compared with other studies.

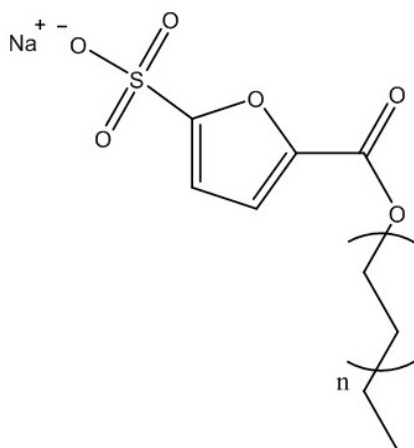
References

- (1) Polyethylene Furanoate Market Size | PEF Industry Report, 2016-2022 <https://www.grandviewresearch.com/industry-analysis/polyethylene-furanoate-pef-market> (accessed Jan 13, 2020).
- (2) Sajid, M.; Zhao, X.; Liu, D. Production of 2,5-Furandicarboxylic Acid (FDCA) from 5-Hydroxymethylfurfural (HMF): Recent Progress Focusing on the Chemical-Catalytic Routes. *Green Chem.* **2018**, *20* (24), 5427–5453. <https://doi.org/10.1039/c8gc02680g>.
- (3) Oxidation of Aldehydes to Carboxylic Acids - Chemgapedia http://www.chemgapedia.de/vsengine/vlu/vsc/en/ch/2/vlu/oxidation_reduktion/oxi_carbs_ald.vlu/Page/vsc/en/ch/2/oc/reaktionen/formale_systematik/oxidation_reduktion/oxidation/ersatz_h_durch_o_n/ox_aldehyde_zu_carbonsaeuren/mechanismus.vscml.html (accessed Jan 13, 2020).
- (4) Clayden, J.; Greeves, N.; Warren, S. *Organic Chemistry*, 2nd ed.; Oxford.
- (5) Tomás, R. A. F.; Bordado, J. C. M.; Gomes, J. F. P. *p*-Xylene Oxidation to Terephthalic Acid: A Literature Review Oriented toward Process Optimization and Development. *Chem. Rev.* **2013**, *113* (10), 7421–7469. <https://doi.org/10.1021/cr300298j>.
- (6) Sankar, M.; Nowicka, E.; Carter, E.; Murphy, D. M.; Knight, D. W.; Bethell, D.; Hutchings, G. J. The Benzaldehyde Oxidation Paradox Explained by the Interception of Peroxy Radical by Benzyl Alcohol. *Nat. Commun.* **2014**, *5* (3322), 1–6. <https://doi.org/10.1038/ncomms4332>.
- (7) Gunasekaran, N. Aerobic Oxidation Catalysis with Air or Molecular Oxygen and Ionic Liquids. *Adv. Synth. Catal.* **2015**, *357* (9), 1990–2010. <https://doi.org/10.1002/adsc.201400989>.
- (8) Mannam, S.; Sekar, G. CuCl Catalyzed Oxidation of Aldehydes to Carboxylic Acids with Aqueous Tert-Butyl Hydroperoxide under Mild Conditions. *Tetrahedron Lett.* **2008**, *49* (6), 1083–1086. <https://doi.org/10.1016/j.tetlet.2007.11.198>.
- (9) Sato, K.; Hyodo, M.; Takagi, J.; Aoki, M.; Noyori, R. Hydrogen Peroxide Oxidation of Aldehydes to Carboxylic Acids: An Organic Solvent-, Halide- and Metal-Free Procedure. *Tetrahedron Lett.* **2000**, *41* (9), 1439–1442. [https://doi.org/10.1016/S0040-4039\(99\)02310-2](https://doi.org/10.1016/S0040-4039(99)02310-2).
- (10) Pârvulescu, V. I.; Hardacre, C. Catalysis in Ionic Liquids. *Chemical Reviews*. June 2007, pp 2615–2665. <https://doi.org/10.1021/cr050948h>.
- (11) Al Ghatta, A.; Wilton-Ely, J. D. E. T.; Hallett, J. P. Strategies for the Separation of the Furanic Compounds HMF, DFF, FFCA, and FDCA from Ionic Liquids. *ACS Sustain. Chem. Eng.* **2019**. <https://doi.org/10.1021/acssuschemeng.9b03613>.
- (12) Seddon, K. R.; Stark, A. Selective Catalytic Oxidation of Benzyl Alcohol and Alkylbenzenes in Ionic Liquids. *Green Chem.* **2002**, *4* (2), 119–123. <https://doi.org/10.1039/b111160b>.
- (13) Lei, Z.; Dai, C.; Chen, B. Gas Solubility in Ionic Liquids. *Chem. Rev.* **2014**, *114* (2), 1289–1326. <https://doi.org/10.1021/cr300497a>.
- (14) Ansari, I. A.; Gree, R. TEMPO-Catalyzed Aerobic Oxidation of Alcohols to Aldehydes and Ketones in Ionic Liquid [Bmim][PF₆]. *Org. Lett.* **2002**, *4* (9), 1507–1509. <https://doi.org/10.1021/ol025721c>.
- (15) Lin, L.; Liuyan, J.; Yunyang, W. Base Promoted Aerobic Oxidation of Alcohols to Corresponding Aldehydes or Ketones Catalyzed by CuCl/TEMPO. *Catal. Commun.* **2008**, *9* (6), 1379–1382. <https://doi.org/10.1016/j.catcom.2007.11.041>.

- (16) Stahlberg, T.; Eyjolfsdottir, E.; Gorbaney, Y. Y.; Sdaba, I.; Riisager, A. Aerobic Oxidation of 5-(Hydroxymethyl)Furfural in Ionic Liquids with Solid Ruthenium Hydroxide Catalysts. *Catal. Letters* **2012**, *142* (9), 1089–1097. <https://doi.org/10.1007/s10562-012-0858-5>.
- (17) Antonyraj, C. A.; Jeong, J.; Kim, B.; Shin, S.; Kim, S.; Lee, K. Y.; Cho, J. K. Selective Oxidation of HMF to DFF Using Ru/Alumina Catalyst in Moderate Boiling Solvents toward Industrial Production. *J. Ind. Eng. Chem.* **2013**, *19* (3), 1056–1059. <https://doi.org/10.1016/j.jiec.2012.12.002>.
- (18) Yi, G.; Teong, S. P.; Zhang, Y. Base-Free Conversion of 5-Hydroxymethylfurfural to 2,5-Furandicarboxylic Acid over a Ru/C Catalyst. *Green Chem.* **2016**, *18* (4), 979–983. <https://doi.org/10.1039/C5GC01584G>.
- (19) Liu, D. (D. J. .; Zhang, Y.; Chen, E. Y.-X. Organocatalytic Upgrading of the Key Biorefining Building Block by a Catalytic Ionic Liquid and N-Heterocyclic Carbenes. *Green Chem.* **2012**, *14* (10), 2738. <https://doi.org/10.1039/c2gc36265a>.
- (20) Bortolini, O.; Chiappe, C.; Fogagnolo, M.; Giovannini, P. P.; Massi, A.; Pomelli, C. S.; Ragno, D. An Insight into the Mechanism of the Aerobic Oxidation of Aldehydes Catalyzed by N-Heterocyclic Carbenes. *Chem. Commun.* **2014**, *50* (16), 2008–2011. <https://doi.org/10.1039/c3cc48929a>.
- (21) Khatana, A. K.; Singh, V.; Gupta, M. K.; Tiwari, B. A Highly Efficient NHC-Catalyzed Aerobic Oxidation of Aldehydes to Carboxylic Acids. *Synth.* **2018**, *50* (21), 4290–4294. <https://doi.org/10.1055/s-0037-1610069>.
- (22) Han, X.; Geng, L.; Guo, Y.; Jia, R.; Liu, X.; Zhang, Y.; Wang, Y. Base-Free Aerobic Oxidation of 5-Hydroxymethylfurfural to 2,5-Furandicarboxylic Acid over a Pt/C-O-Mg Catalyst. *Green Chem.* **2015**, *18*, 1597–1604. <https://doi.org/10.1039/C5GC02114F>.
- (23) Yan, D.; Xin, J.; Zhao, Q.; Gao, K.; Lu, X.; Wang, G.; Zhang, S. Fe-Zr-O Catalyzed Base-Free Aerobic Oxidation of 5-HMF to 2,5-FDCA as a Bio-Based Polyester Monomer. *Catal. Sci. Technol.* **2018**, *8* (1), 164–175. <https://doi.org/10.1039/c7cy01704a>.
- (24) Yan, D.; Xin, J.; Shi, C.; Lu, X.; Ni, L.; Wang, G.; Zhang, S. Base-Free Conversion of 5-Hydroxymethylfurfural to 2,5-Furandicarboxylic Acid in Ionic Liquids. *Chem. Eng. J.* **2017**. <https://doi.org/10.1016/j.cej.2017.04.021>.
- (25) Han, X.; Li, C.; Liu, X.; Xia, Q.; Wang, Y. Selective Oxidation of 5-Hydroxymethylfurfural to 2,5-Furandicarboxylic Acid over MnO:X-CeO₂ Composite Catalysts. *Green Chem.* **2017**, *19* (4), 996–1004. <https://doi.org/10.1039/c6gc03304k>.
- (26) Chen, R.; Xin, J.; Yan, D.; Dong, H.; Lu, X.; Zhang, S. Highly Efficient Oxidation of 5-Hydroxymethylfurfural to 2,5-Furandicarboxylic Acid with Heteropoly Acids. *ChemSusChem* **2019**, *12* (12), 2715–2724. <https://doi.org/10.1002/cssc.201900651>.
- (27) Kubisa, P. Ionic Liquids as Solvents for Polymerization Processes-Progress and Challenges. *Prog. Polym. Sci.* **2009**, *34* (12), 1333–1347. <https://doi.org/10.1016/j.progpolymsci.2009.09.001>.
- (28) Rosales, K. R.; Stoltzfus, J. M. *Guide for Oxygen Compatibility Assessments on Oxygen Components and Systems*; 2007.
- (29) Howarth, J. Oxidation of Aromatic Aldehydes in the Ionic Liquid. *Tetrahedron Lett.* **2000**, *41*, 6627–6629.
- (30) Maki, B. E.; Scheldt, K. A. N-Heterocyclic Carbene-Catalyzed Oxidation of Unactivated Aldehydes to Esters. *Org. Lett.* **2008**, *10* (19), 4331–4334. <https://doi.org/10.1021/ol8018488>.

- (31) Samanta, R. C.; Studer, A. N-Heterocyclic Carbene Catalysed Oxidative Esterification of Aliphatic Aldehydes † ‡. *Cite this Org. Chem. Front* **2014**, *1*, 936. <https://doi.org/10.1039/c4qo00164h>.
- (32) Mishra, D. K.; Lee, H. J.; Kim, J.; Lee, H. S.; Cho, J. K.; Suh, Y. W.; Yi, Y.; Kim, Y. J. MnCo₂O₄ Spinel Supported Ruthenium Catalyst for Air-Oxidation of HMF to FDCA under Aqueous Phase and Base-Free Conditions. *Green Chem.* **2017**, *19* (7), 1619–1623. <https://doi.org/10.1039/c7gc00027h>.
- (33) Chen, L.; Yang, W.; Gui, Z.; Saravanamurugan, S.; Riisager, A.; Cao, W.; Qi, Z. MnOx/P25 with Tuned Surface Structures of Anatase-Rutile Phase for Aerobic Oxidation of 5-Hydroxymethylfurfural into 2,5-Diformylfuran. *Catal. Today* **2019**. <https://doi.org/10.1016/j.cattod.2018.05.049>.
- (34) Hussain Motagamwala, A.; Won, W.; Sener, C.; Alonso, D. M.; Maravelias, C. T.; Dumesic, J. A. Toward Biomass-Derived Renewable Plastics: Production of 2,5-Furandicarboxylic Acid from Fructose. *Sci. Adv.* **2018**, *4* (1), 1–8. <https://doi.org/10.1126/sciadv.aap9722>.
- (35) Neațu, F.; Marin, R. S.; Florea, M.; Petrea, N.; Pavel, O. D.; Pârvolescu, V. I. Selective Oxidation of 5-Hydroxymethyl Furfural over Non-Precious Metal Heterogeneous Catalysts. *Appl. Catal. B Environ.* **2016**, *180*, 751–757. <https://doi.org/10.1016/j.apcatb.2015.07.043>.
- (36) Neatu, F.; Petrea, N.; Petre, R.; Somoghi, V.; Florea, M.; Parvulescu, V. I. Oxidation of 5-Hydroxymethyl Furfural to 2,5-Diformylfuran in Aqueous Media over Heterogeneous Manganese Based Catalysts. *Catal. Today* **2016**, *278*, 66–73. <https://doi.org/10.1016/j.cattod.2016.03.031>.
- (37) Zhao, H.; Holladay, J. E.; Brown, H.; Zhang, Z. C. Metal Chlorides in Ionic Liquid Solvents Convert Sugars to 5-Hydroxymethylfurfural. *Science (80-.)*. **2007**, *316* (5831), 1597–1600. <https://doi.org/10.1126/science.1141199>.
- (38) 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), 1–15. <https://doi.org/10.1371/journal.pone.0163835>.

Chapter 7 Biorenewable Anionic Surfactants as Valuable Replacements for Current Detergent Formulations



- **Biorenewable**
- **Low CMC**
- **Low Kraft Point**
- **High Solubility**
- **High resistance to hard water**
- **Biodegradable**
- **Green** 

The surfactants market represents a key sector in the chemical industry covering many different applications. The commercial volumes involved are large and the products find many applications in everyday life, especially in personal care and the detergents used in household and industry. Due to the large volumes in which they are produced, their sustainability in terms of feedstock, synthesis procedure, biodegradability of the final product and formulations are crucial parameters to assess the environmental impact of the surfactant. As detergent cost is a key factor to be competitive in the market, the design of novel surfactants involves enormous challenges. Linear alkyl sulfonate (LAS) surfactants have proved successful due to their high performance, low cost and biodegradability. However, in order to exhibit their detergent ability, they are used in a formulation with other compounds, raising some limitations due to the cost of these additives and their toxicity. In this study, we present a new class of bioderived surfactants that could replace the petroleum-derived LAS and exhibit improved performance without the need for additives.

Introduction

Surfactants are one of the most used high-volume chemical commodities and find application in many different fields (household, industries, agriculture and personal care).¹ The importance that these compounds play in different sectors makes them one of the synthetic chemicals produced in the highest volume globally. Indeed, the market size of surfactants was estimated at 15 MT/year in 2014 and this is expected to expand further by 4.3% in 2022.²

The chemical structure of the surfactant, consisting of a hydrophilic and a hydrophobic portion, gives them the property to reduce surface tension between two phases and impart a detergent effect, emulsifying, foaming and wetting properties to liquids. These attributes make them ideal for the use in cosmetics, detergents and personal care products.³

Surfactants have different chemical structures which categorize them in four different groups according to their charge localization, anionic, cationic, non-ionic and amphoteric nature. Anionic surfactants predominate in household applications for use in detergents, since they exhibit outstanding performance for the removal of dirt, clay and oil stains. These compounds are composed of a polar ionic head group (sulfate, sulfonate, phosphate or carboxylate) where the anion is the active site which characterizes the surfactant properties. In the early 1940s, fatty acids were widely used as the main component for detergents but later, with the development of the petrochemical industry, these were completely replaced by oil-derived surfactants which show better performance at lower cost. Of these compounds, the linear alkylbenzene sulfonates (LAS) represent the most important surfactants for detergent purposes and represent the highest surfactant market sector by volume produced, finding applications in washing powders, liquid detergents, household products, industrial cleansers and textile production as wetting agents, dispersants and cleansers.^{4,5}

An optimum surfactant design is based on the selection of the chemical structure of the hydrophilic and hydrophobic groups and their relative ratio to meet certain criteria according to the desired application. Finally, the surfactant cost depends on the synthesis procedure and formulation will define the success of the surfactant in the market. The evaluation of the surfactant is accomplished by evaluating different parameters including critical micelle concentration (CMC), Kraft temperature (KP), stability, foaming, solubility, emulsifying properties, toxicity and biodegradability. In order to achieve a good compromise between all these parameters, the final product will be a formulation of different chemical compounds where the surfactant is the active ingredient with a percentage (by mass) between 15 to 30%.⁴ For cleaning applications, the final formulation is referred to as a detergent or soap.

The detergent ability of the surfactant is strictly related to the surface tension measurement of the resulting water/oil interface. Generally, since the composition of the oil phase in everyday practice is variable, most of the characterization of detergency is based on the surface tension between water and air at different surfactant concentrations. Of these factors, the critical micelle concentration (CMC)

and Kraft point (KP) can be measured. CMC is the minimum concentration of surfactant needed to aggregate into micelles, which arbitrarily is chosen as the point at which the surfactant starts to exhibit its detergent ability since micelles can trap the oil drops in the water phase. More specifically, the surfactant needs to aggregate as spherical micelles since these are the ones which guarantee the dispersion of oil in water by stabilizing the oil drops as microemulsions. Other forms of aggregation will reduce the detergent ability, forming a secondary liquid/solid phase (liquid crystal). The Kraft point (KP) is the minimum temperature needed for the surfactant to form micelles. For commercial purpose in the detergents industry, both CMC and KP need to be as low as possible. For this reason it is required that the final formulation has a CMC ideally below 2000 ppm and KP below 30 °C to be used as a detergent.⁶

Other parameters need to be evaluated to fully characterize the performance of the surfactants, including solubility in water and resistance to hard water since calcium salts are generally less soluble compared to sodium salts. These two parameters have a remarkable influence on the formulation of the surfactant since LAS are poorly soluble in water and easily precipitate as calcium salts, reducing the concentration in the water phase, hence decreasing the detergent ability of the surfactant. In order to cope with this problem, additives are used and these are referred to as builders, chelants and hydrotropes. These have the function to increase solubility, retain an effective detergent ability at different conditions and ensure other properties such as anti-encrustation, anti-foam or act as foam ‘boosters’. Hence detergents are produced as formulation of different chemical compounds aimed mainly at reducing precipitation and decreasing the KP and CMC. A typical formulation of the detergent is reported in Figure 7.1. Despite the versatility of LAS in covering a wide range of properties for specific applications, the petroleum-derived nature of these compounds pushes them outside the green chemistry sphere. Moreover, even if they are biodegradable through aerobic digestion, the need for additives raises environmental concerns due to the nature of these chemical compounds.⁷ For example ethylenediaminetetraacetate (EDTA), sodium tripolyphosphate (STPP), sodium nitrilotriacetate, which are typical additives to chelate calcium, exhibit toxicity to human and aquatic life.^{8–10} Other builders that are more environmentally-friendly, such as zeolites or citric acid, are more expensive or have the drawback of forming solid particles or display limited performance, which inevitably increases the cost of the final product.

A solution to improve the detergents industry in terms of sustainability and competitiveness should be focused in using biorenewable feedstocks and seek surfactants that exhibit better intrinsic cleaning ability so that additives are minimised, hence reducing environmental concerns and cost.

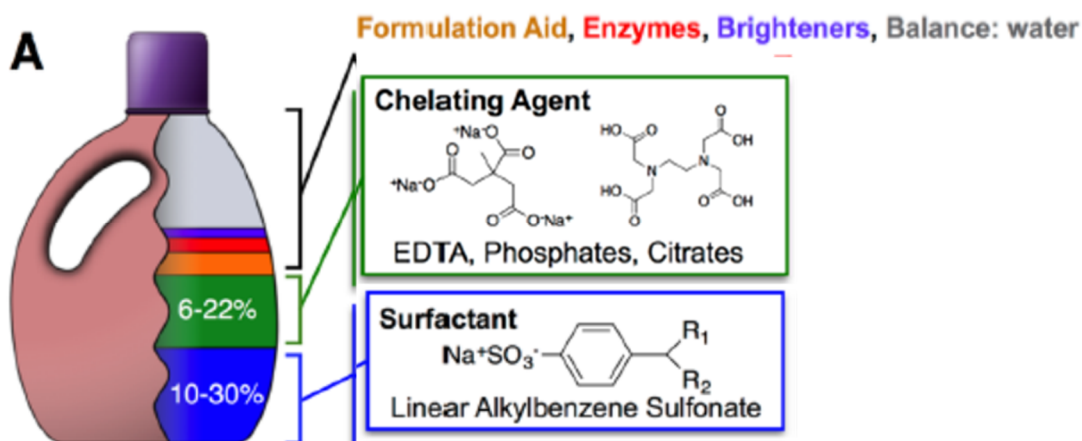


Figure 7.1 Typical surfactant formulation for LAS. Reproduced with the permission from ref⁶

Research efforts have focused on using renewable feedstocks or substituting the hydrophobic chain with renewable materials such as fatty alcohols. Direct sulfonation of fatty alcohols produces fatty alcohol sulfates, a bio-surfactant present in many cleaning and hygiene products. Their bioderived nature (coconut oil or palm kernel), easy synthesis and low toxicity have made them potential substitutes for LAS, however they display limited performance in hard water and higher critical micelle concentration (3-4 times),¹¹ raising drastically the cost and limiting the market for biodegradants to a small percentage (only 3 % of the detergent market).

Investigations have therefore moved towards seeking a biobased and biodegradable surfactant that can display a performance comparable to LAS. Sugar derivatives have attracted much attention for their low toxicity and environmental compatibility. A class of non-ionic surfactants has been reported by Stensrud and Wicklund in a patent in 2016 derived from HMF through esterification of the hydroxyl group and reductive amination of the aldehyde with an amine.¹² Lee and co-workers reported another HMF-derived surfactant formed with a polar head group composed of a sulfate and hydroxyl group but the KP is over 70 °C and its stability is doubtful.¹³

Hoffman and co-workers have proposed a new class of biodegradable surfactants derived from photooxygenation of furfural with air, but applicability of the compound is challenging due to the high KP value.¹⁴ Recently, Daunhauer and co-workers⁶ reported a new class of furan-based surfactants based on the Friedel-Crafts acylation of furan and sulfonation with a sulfur trioxide pyridine complex. In their work, the authors evaluated the effect of substituting the benzene ring of the LAS with a furan ring and analysed different structures with various hydrophobic chains.

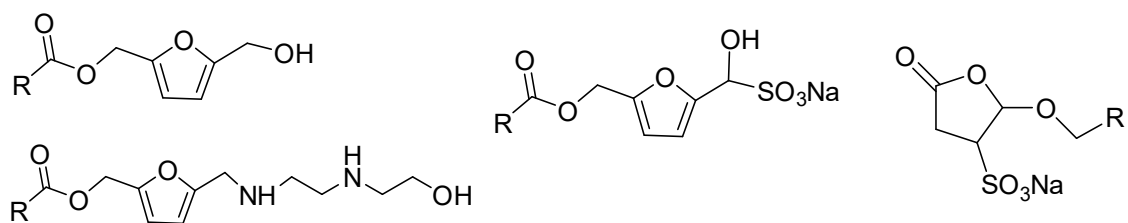


Figure 7.2 HMF-derived surfactants reported by Stensrud and Wicklund in 2016 (left hand side), Lee and co-workers (middle) and Hoffman and co-workers (on the right).

The surfactants analysed by the authors are summarized in Table 7.1. With the same alkyl chain, the new surfactants proved to have superior properties compared to the conventional LAS with higher resistance to hard water and a lower Kraft point. Increasing the polarity of the head group by introducing a ketone had a detrimental effect on both the CMC and turbidity (measure of resistance to water hardness), while branched alkyl chains gave improved CMC performance and turbidity but higher KP. Despite the better overall performance of the branched alkyl chains, the yields reported for their synthesis are low (<20 %) making it a much more costly product compared to the analogous linear ones. Generally, these furan-derived surfactants had better performance compared to LAS since the CMC and KP are already within the boundaries of commercial applicability (CMC < 2000 ppm and KP < 30 °C), moreover the solubility is higher and resistance to hard water is remarkably good. However, the authors did not report the biodegradability of the surfactants despite the fact that furan surfactants can exhibit better degradation properties compared to their benzene-based equivalents.

Table 7.1 Performance of different furan derivative surfactants evaluated by Daunhaur and co-workers

<i>Surfactant</i>	<i>CMC (ppm)</i>	<i>KP (°C)</i>	<i>Turbidity (ppm)</i>
	460	58	< 100
	720	30	>50000
	11520	<0	230
	510	25.7	>50000

This study aims to analyse a new class of furanic surfactants derived from furoic acid and fatty alcohols synthesized by Fischer esterification to achieve the following objectives:

- Development of a low-cost synthesis process using biorenewable sources to provide the basis for industrial application. For this reason, furoic acid represents a sustainable derivative of xylose and is cheap and easy to synthesize. Fatty alcohols are natural compounds that can be derived from fatty acids. In terms of process, Fischer esterification requires mild conditions and proceeds in high yields;
- Development of a surfactant with superior proprieties compared to LAS in terms of CMC, KP, water solubility, biodegradability and turbidity so that no additives are needed.

The new class of surfactants will be referred to as sulfonated alkyl furoates. The routes proposed to obtain the final surfactants are reported in Figure 7.3. Two possible routes are possible depending on which step is performed first. The first reaction pathway consists of the esterification of the carboxylic acid followed by sulfonation at the C4 position. In the second route this is reversed.

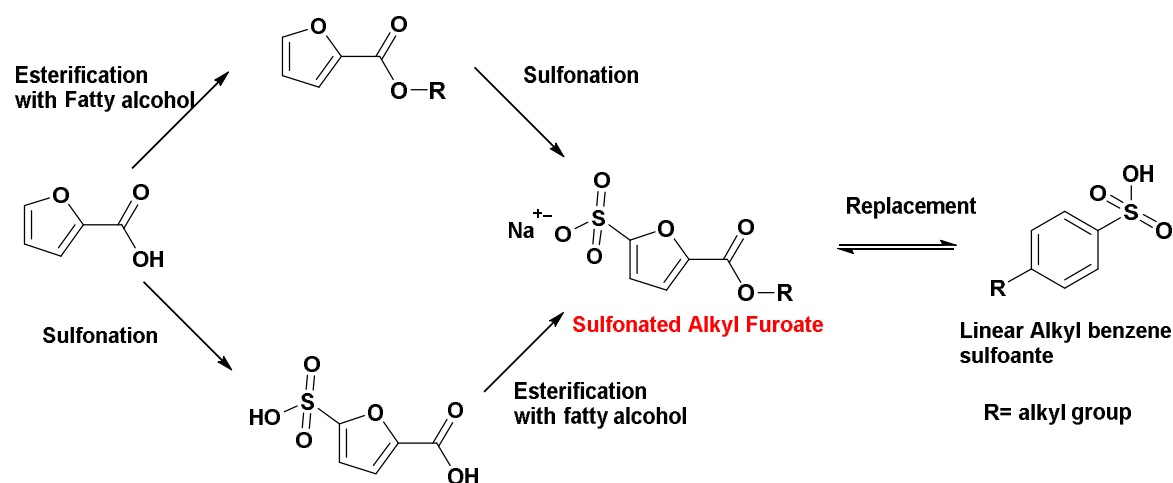


Figure 7.3 Reaction scheme of the proposed surfactants.

Compared to the work of Daunhauer, the proposed surfactants have major potential to be biodegradable thanks the presence of the ester group, which is more easily hydrolysed compared to C-C bonds. Moreover, furoic acid and fatty alcohols are bioderived components and their synthesis has a lower impact on the environment. In contrast, the synthesis route proposed by Daunhauer uses furan, anhydrides and acyl halides, requiring the use of toxic compounds with higher impact on the environment. In our case, both fatty alcohols and furoic acid can be obtained from biomass according the scheme reported in Figure 7.4.

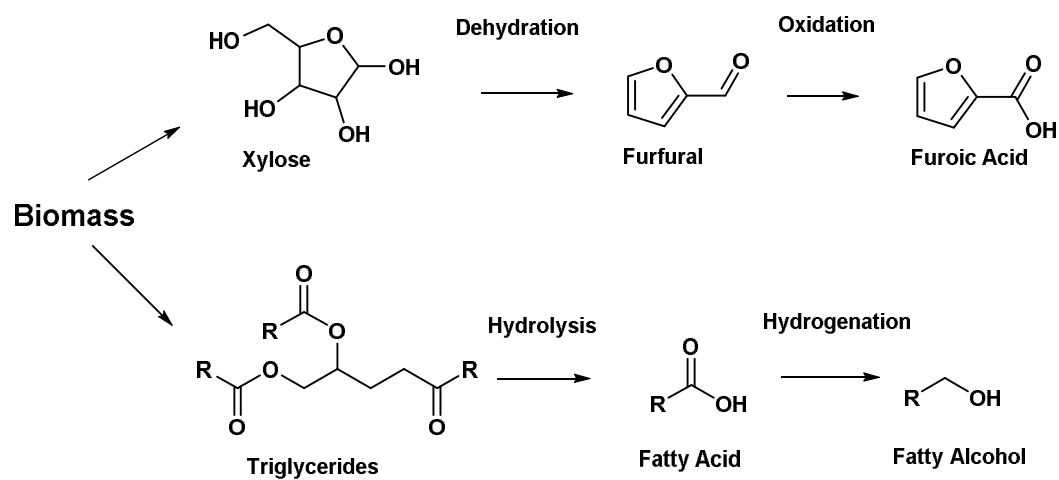


Figure 7.4 Chemical path for the derivation of furoic acid and fatty alcohols.

In this study we will discuss the synthetic pathway used to obtain this surfactant and evaluate its performance compared to those described by Daunhauer and the commercial surfactants LAS and SDS.

Experimental Section

Materials

Furoic Acid (98 %), 1-octanol (>99 %), 1-dodecanol, 1-hexadecanol (99 %), fuming sulfuric acid (20 % SO₃), chlorosulfonic acid (99%), sulfur trioxide pyridine complex (97 %), pharmaceutical grade sodium dodecylbenzenesulfonate (SDBS) and sodium dodecyl sulfate were obtained from Sigma Aldrich. Octyl furoate (>97 %) was obtained by TCI. Dichloromethane (DCM) and chloroform were obtained from VWR.

Chloroform was purified from ethanol by washing with water (3 times 3:1 ratio) and distilled over phosphorous pentoxide in a distillation tower. The solvent was stored in a dark container to avoid decomposition. All other chemicals were used without purification if not otherwise stated.

Esterification reaction to produce the alkyl furoate

The fatty alcohol (1 eq) was mixed with furoic acid (1.2 eq) in a round bottom flask followed by the addition of sulfuric acid (1 mol% with respect to the fatty alcohol). The reaction was heated at 140 °C and left until the alcohol was completely consumed (4-5 h). The reaction mixture was diluted with DCM (2:1 in volume with respect to the reaction mixture) and filtered to remove byproducts and unreacted furoic acid. The organic phase was washed with water (2:1) to remove residual acidity until neutral pH was reached. Since the emulsion could not be broken up by centrifugation, sodium chloride or ethanol had to be added during the washing to separate the phases. Solvent removal under vacuum gave the crude product (75-90 % yield). In the case of the C₁₆ derivative, the product was further purified by crystallization from DCM at -20 °C, while for C₈ and C₁₂ variants, distillation over activated carbon was performed to obtain a purified product as a yellowish liquid. Characterization of the compound was done by NMR.

Octyl Furoate: ¹H NMR (DMSO-d₆): δ 8 (m, -C-CH-O-,), 7.3, 6.7 (m x 2, 2 x 1H, 2 x C-CH-C), 4.23 (t, 2H, O-CH₂-CH₂, J_{HH} = 6.6 Hz), 1.66, 1.4-1.8 (m, CH₂ alkyl chain), 0.86 (m, CH₂-CH₃). ¹³C {¹H} NMR (DMSO-d₆): δ 159.9 (C=O), 147.8 (CH-C-C=O), 144.6 (O-CH-CH), 119, 113 (-C-CH-CH-C), 65 (O-CH₂-CH₂), 31.7, 31.1, 29.1, 28.7, 25.8, 22.7 (6 X C, C-CH₂-C), 14.4 (-CH₂-CH₃) ppm

Dodecyl Furoate: ¹H NMR (DMSO-d₆): δ 7.9 (m, -C-CH-O-,), 7.2, 6.7 (m x 2, 2 x 1H, 2 x C-CH-C), 4.23 (t, 2H, O-CH₂-CH₂, J_{HH} = 6.6 Hz), 1.66, 1.4-1.8 (m, CH₂ alkyl chain), 0.86 (m, CH₂-CH₃). ¹³C {¹H} NMR (DMSO-d₆): δ 159.9 (C=O), 148.2 (CH-C-C=O), 144.5 (O-CH-CH), 119, 112.5 (-C-CH-CH-C), 65.7 (O-CH₂-CH₂), 31.8, 29.5, 29.2, 29.7, 28.8, 25.9, 22.6 (8 X C, C-CH₂-C), 14.1 (-CH₂-CH₃) ppm.

Hexadecyl Furoate.: ¹H NMR (CDCl₃): δ 7.0, 6.9 (m x 2, 2 x 1H, 2 x C-CH-C), 5.8 (m, -C-CH-O-,), 4.1 (t, 2H, O-CH₂-CH₂, J_{HH} = 6.7 Hz), 1.44, 1.37-1.05 (m, CH₂ alkyl chain), 0.85 (m, CH₂-CH₃).

$^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 158.5 (C=O), 145.7 (CH-C=O), 145.5 (O-CH-CH), 117, 111 (-C-CH-CH-C), 64.4 (O-CH₂-CH₂), 32, 29.9-29.3, 28.8, 26, 23 (6 X C, C-CH₂-C), 14.1 (-CH₂-CH₃) ppm.

Sulfonation with Chlorosulfonic Acid

Furoate was added to dry chloroform at a concentration of 30 mg/mL and mixed at room temperature until full dissolution had been achieved. The reaction flask was then connected to a water-filled bubbler through which the HCl produced was vented. Chlorosulfonic acid (CSA) was then added (1.05 eq). The water was first saturated by HCl and then bubbling began, indicating consumption of CSA. The reaction was left until no further bubbling was observed and then analysed by ^1H NMR spectroscopy to confirm that the reaction was complete with full conversion of the ester and reaction of most of the CSA (CSA shift: 10.9 ppm). Chloroform was removed under vacuum to afford a green solution which was diluted with water and neutralized to pH 7. Water was then removed under vacuum to provide the crude product as a black solid. The product needed to be purified to remove residual sodium sulfate salts (formed by neutralization of the excess of chlorosulfonic acid) as well as the impurities responsible for the dark colour. Purification of these latter contaminants failed using activated charcoal and so an organic solvent was chosen that was capable of selectively removing the impurities. A solubility test was carried out for the crude product with hexane, cyclohexane, ethyl acetate, THF, chloroform and DCM. The C₈ and C₁₂ derivatives proved to be soluble in DCM and chloroform, allowing the removal of the sodium sulfate by dissolving the surfactant and filtering. After DCM was removed, diethyl ether and THF were used to further purify the product by washing, exploiting the low dielectric constant of these solvents which renders salts insoluble. Upon washing, the surfactant was obtained as a white powder. In the case of the C₁₆ compound, none of the organic solvents showed good solubility. For that compound, it was decided to wash the product with small amounts of water to remove the sulfate salt by exploiting the low solubility of this surfactant in the water phase. Diethyl ether proved to be unable to purify the product, leaving the C₁₆ in its original darkly coloured state below a clear ether phase. For this surfactant, DCM, chloroform and THF proved to be efficient in removing the impurities, leaving the surfactant as a white powder. Characterization of the compound was done by NMR and MS. For the C₁₆ variant MS was not possible due its low solubility in any solvent tested.

Sulfonated Octyl Furoate: ^1H NMR (D_2O): 6.9, 6.7 (m x 2, 2 x 1H, 2 x C-CH-C), 4.2 (t, 2H, O-CH₂-CH₂, J_{HH} = 6.6 Hz), 1.6, 1.34-1.0 (m, CH₂ alkyl chain), 0.8 (m, CH₂-CH₃).

$^{13}\text{C}\{^1\text{H}\}$ NMR (D_2O): δ 158.5 (C=O), 155.8 (O-CH-CH), 144.5 (CH-C=O), 118.2-112.2 (-C-CH-CH-C), 66.1 (O-CH₂-CH₂), 31.7, 29.2, 29.1, 28.3, 25.7, 22.6 (6 X C, C-CH₂-C), 13.8 (-CH₂-CH₃) ppm.

MS (ES, -ve mode): m/z (abundance) = 303.087 (C₁₃H₁₉O₆S⁻ 100%)

Sulfonated Dodecyl Furoate: ^1H NMR (D_2O): δ 6.9, 6.7 (m x 2, 2 x 1H, 2 x C-CH-C), 4.1 (t, 2H, O-CH₂-CH₂, J_{HH} = 6.6 Hz), 1.52, 1.2-1.1 (m, CH₂ alkyl chain), 0.7 (m, CH₂-CH₃).

$^{13}\text{C}\{^1\text{H}\}$ NMR (D_2O): δ 158.5 (C=O), 155.8(O-CH-CH₂), 144.5 (CH-C-C=O), 118.2-112.2 (-C-CH-CH-C), 66.1 (O-CH₂-CH₂), 31.8, 29.5, 29.2, 29.7, 28.8, 25.9, 22.6 (8 X C, C-CH₂-C), 13.8 (-CH₂-CH₃) ppm.

MS (ES, -ve mode): m/z (abundance) = 359.1534 ($\text{C}_{17}\text{H}_{27}\text{O}_6\text{S}^-$ 100%)

Sulphonated Dodecyl Furoate: ^1H NMR (D_2O): δ 6.9, 6.7 (m x 2, 2 x 1H, 2 x C-CH-C), 4.1 (t, 2H, O-CH₂-CH₂, J_{HH} = 6.4 Hz), 1.54, 1.26-0.95 (m, CH₂ alkyl chain), 0.8 (m, CH₂-CH₃). $^{13}\text{C}\{^1\text{H}\}$ NMR (D_2O): δ 159.5 (C=O), 156.5(O-CH-CH₂), 144.6 (CH-C-C=O), 118.9-112.9 (-C-CH-CH-C), 66.1 (O-CH₂-CH₂), 32.2, 31-29.3, 28.5, 26, 22.8 (10 X C, C-CH₂-C), 13.8 (-CH₂-CH₃) ppm.

Further analysis needs to be done for proof of purity with a chromatography technique. For this purpose a specific surfactant column is needed but this was not available in our lab.

Solubility studies

The solubility studies of different surfactants were performed according to the ISO standard 6839. Different concentrations of surfactant were prepared and heated in a water bath until full dissolution was achieved.

Resistance to hard water

These measurements were performed according to the standard protocol reported in ISO 1063. Calcium chloride was used as the cation source. Three different solutions of Ca^{2+} salts at 6, 9 and 12 molar equivalents (3.0, 4.5, and 6.0 mM, respectively) and a mother solution of surfactant in water at 20 °C at a concentration of 50 mg/mL were prepared. In a 50 mL test tube, a defined aliquot of mother solution was transferred and diluted to 50 mL with the calcium solution to be tested. Five different aliquots of surfactant mother solution were tested: 5.0, 2.5, 1.2, 0.6 and 0.3 mL. Every test was assigned a score according to Table 7.2. The scores of the 15 tests for each surfactant were summed together and the final result was expressed as a mean stability according to Table 7.3.

Table 7.2 Score corresponding to the appearance of the liquid. Opalescent is a non-clear solution but through which objects can be seen. Cloudy is a non-clear solution through which objects cannot be seen.

Appearance of the liquid	Score number
Clear	5
Opalescent	4
Cloudy	3
Slight precipitate	2
Heavy precipitate	1

Table 7.3 Mean stability table.

Total Score	Mean Stability
15-18	1
19-37	2
38-56	3
57-74	4
75	5

Critical Micelle Concentration (CMC)

CMC values were calculated using a Kruss Drop Shape Analyser- DSA25 by the pendant drop method. Different surfactant solutions were prepared at room temperature making sure that no solids were present. These were loaded into a syringe and attached to the apparatus, which allows controlled movement of the plunger. By regulating the plunger progression, a drop was created on the tip of the needle. The software of the instrument calculates the surface tension by acquiring the drop geometry through a camera. The results are presented as a graph surface tension vs surfactant concentration. By increasing the surfactant concentration, the surface tension decreases until reaching a plateau. The intersection between the plateau and the initial slope is identified as the CMC.

Results and Discussion

Synthesis of the Furoate Ester

The main aim of the esterification is to obtain an intermediate furanic ester product compatible with the subsequent sulfonation reaction. Since sulfonation is sensitive to functional groups and residual acidity, it is important to establish a protocol that ensures high purity of the intermediate, minimising the required purification steps. Most importantly the alcohol needs to be completely removed since it can undergo sulfonation, making the separation of the product very difficult.

Most of the esterifications reported in literature were carried out at low temperature (90-100 °C), with solvent and excess of alcohol. The first approach was to follow this procedure using the alcohol as both solvent and reactant in large excess (100:1) to consume all the furoic acid. The reaction mixture was then diluted with DCM and washed with sodium bicarbonate and water until neutral pH was achieved. Different methodologies were then explored to remove efficiently the excess alcohol, while maintaining a high yield of the ester. Column chromatography proved to be unsuccessful since the product undergoes decomposition on silica and alumina.

It was decided to exploit the different physical proprieties of the ester and alcohol. For distillation, the compounds need to have a consistent difference in boiling point, while for crystallization, melting point is the key parameter to take into consideration. However, this latter approach must be considered in terms of the affinity of the compounds for the solvent, which plays a determining role for the separation. Since octyl furoate is the only ester synthesized and characterized in the literature, the melting and boiling points were compared to analyse the possibility of separating the product by distillation or crystallization. Table 7.4 lists the physical properties of the alcohol and ester with different alkyl chains. The data show strong dependency of the boiling and melting point with the nature of the alkyl chain, hence defining the feasibility of the separation technique to be used. Data for both alcohol and ester were reported only for C₈ chains. In this case, distillation represents a potential method due to the large difference in boiling point of the two compounds. By regulating the pressure, the ester can probably be boiled selectively due to the excessive difference in vapour pressure. In contrast, no values have been reported for the melting point of the ester. However, the lower ability for hydrogen bonding of the furan head group compared to the hydroxyl group suggest that the melting point should be much lower. This was confirmed by analysing the C₁₂ ester separated in small amounts by chromatography. The difference in melting point between dodecanol and dodecyl furoate (10 °C) indicates that purification by alcohol precipitation is a valuable option. The purification of the C₁₆ derivative by distillation is more complex due to the high vacuum required and the risk of decomposition at high temperature so, in this case, precipitation is a more viable option.

Table 7.4 Physical properties of octanol and octyl furoate

	Melting Point (°C)	Boiling Point (°C)	Separation
Octanol	-16	129 (0.4 mbar) ¹⁵	Distillation
Octyl-furoate	Not Reported	127 (1.3 mbar)	Distillation
Dodecanol	24	259 (1 atm)	Distillation/Precipitation
Dodecyl-furoate	Not reported	Not reported	Distillation
Hexadecanol	49.3	334 (1 atm)	Precipitation
Hexadecyl-furoate	Not reported	Not reported	Unknown

For this analysis, separation was tested on a small scale (10 g) for C₁₂ and C₁₆. For the former, a distillation apparatus was set up with a condenser at 25 °C. While the separation was achieved efficiently, traces of alcohol were still present in the distillate due to the difficulty in regulating the pressure and the unknown physical properties of the ester. Precipitation was attempted from DCM at -20 °C but no precipitate was formed. In the case of the C₁₆ derivative, the alcohol was efficiently separated by precipitation even though multiple precipitation steps were required to achieve complete purification. This led to a loss of yield since the ester precipitated with the alcohol in small amounts. A consistent and efficient protocol for purification which can maximise the yield was difficult to achieve. Hence a different option was sought.

The difficulties associated with the complete removal of the alcohol and its detrimental effect on the subsequent sulfonation reaction drove us to explore a different chemical route focused on the complete conversion of the alcohol working with an excess of acid. This reaction proved to be limited by the low solubility of the furoic acid in the alcohol at the conventional esterification temperature of 90 °C, which led to low conversion. For this reason, the temperature was increased until full dissolution was achieved (140 °C). At this temperature full conversion of the alcohol was achieved in a short reaction time with a small excess of furoic acid (1.2 eq) thanks to removal of water by evaporation, driving the equilibrium of esterification towards the product according to the Le Chatelier principle. However, the solution became dark black indicating the formation of side products. In the case of the esterification of the C₁₆ derivative, the black product was clearly visible against the characteristic white solid of the C₁₆ ester. In this case the removal of this solid could be achieved by washing with DCM which dissolved the product and allowed subsequent filtration of the by-product along with remaining furoic acid, both of which are insoluble in DCM. The final product was precipitated from DCM at low temperature to obtain a colourless, crystalline solid, which is characteristic of a pure product.

In the case of C₈ and C₁₂ derivatives, most of the solid was removed by dissolution of the product in DCM followed by filtration, however, this was not sufficient to achieve a colourless liquid since the solution remained dark black after filtration. Hence distillation was used to further purify these

compounds. According to these observations, a protocol could be established for the high yield production of furanic esters on a large scale and of high purity and reported in the Experimental Section.

Synthesis of Sulfonated alkyl furoate

Various sulfonation techniques exist to attach a sulfonic group to an aromatic ring. In order to do so a sulfonating agent is required. Three main sulfonating agents are available with different electrophilic reactivity, and these are reported in Figure 7.5. Oleum is an overconcentrated solution of sulfuric acid with free sulfur trioxide (20 %). Chlorosulfonic acid is a strong acid with a chloride bond which can undergo electrophilic substitution; it is considered a strong sulfonating agent although less reactive compared to oleum. Sulfur trioxide complex is an adduct formed from sulfur trioxide and pyridine. This represents a weaker sulfonating agent since pyridine is a weaker leaving group compared to chloride.

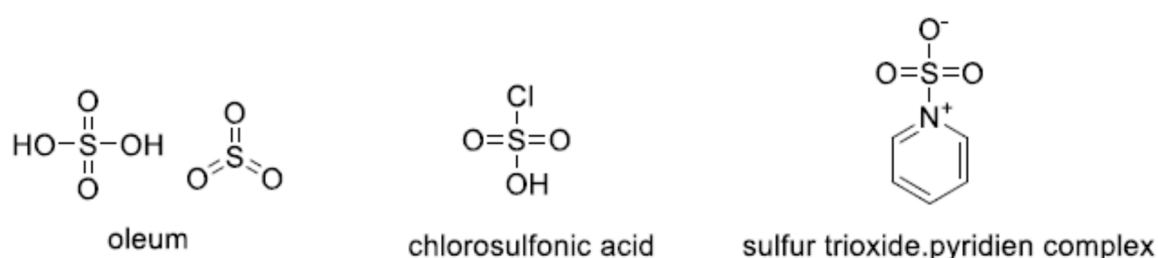


Figure 7.5 Structure of sulfonating agents.

The choice of the most suitable sulfonating agent depends on the nucleophilicity of the substrate to be sulfonated. In our case, since the ester group is electron withdrawing, the nucleophilic behaviour of the furan is decreased. Indeed, sulfonation of octyl furoate with a sulfur trioxide complex failed using the same method used in the literature for the sulfonation of alkyl furans,⁶ leaving the compound untouched.

Oleum was then used as a stronger sulfonating agent. The reaction was carried out at room temperature by simply dissolving the octyl furoate in the oleum and leaving it overnight. Full conversion was achieved. The reaction mixture was then diluted with water, and the product was separated by the addition of stoichiometric amounts of barium carbonate to remove all the sulfate as BaSO₄, which precipitates. The analysis of the crude product by ¹H NMR spectroscopy showed that the reaction was not regioselective and unknown side products were present. Difficulties in purifying the product led us to abandon this route.

Sulfonation with chlorosulfonic acid (CSA) proved to be the most successful approach. Dry chloroform was needed as a solvent to solubilize the CSA and remove ethanol, which is used as a stabilizer. A slight excess was used with respect to the substrate (1.05 eq) at 60 °C. The reaction flask was connected to a bubbler to vent the HCl formed during the sulfonation. The reaction was monitored by ¹H NMR spectroscopy to track the final product. Even if the reaction proved to be slow, it reached completion overnight with no side products observed. The high selectivity of the reaction makes this route

favourable over the others and further optimization of the synthesis was carried out to maximise the yield.

Solubility studies

Results of the solubility tests are reported in Table 7.5.

Table 7.5 Results of solubility tests for different surfactants

Concentration (% weight)	SDS (°C)	SDBS (°C)	C8 (°C)	C12 (°C)	C16 (°C)
22.5	>50	----	<0	<0	>50
20	41-43	>50	<0	<0	>50
17.5	34-35	---	<0	<0	>50
15	27-29	43-45	<0	<0	>50
12.5	27-29	---	<0	<0	>50

The commercial SDBS proved to have the lowest solubility due to the extensive hydrophobicity imparted by the benzene ring while SDS achieved higher solubility of 10-15% at room temperature. Although the solubility is higher compared to LAS, this surfactant will still need hydrotropes to increase the solubility since typical concentrations are between 15-30% of the final formulation. Remarkable improvements were achieved by exchanging a furan head group with an ester linkage, especially for the C₈-C₁₂ alkyl chains, where high solubility was achieved even at very low temperatures, indicating a strong influence of the head group polarity on the solubility. The effect of the alkyl chain becomes evident at C₁₆ where the surfactants proved to have very low solubility (only 0.05% at room temperature). The C₈ and C₁₂ derivatives therefore represent potential solutions to the low solubility of LAS while C₁₆ will need hydrotropes to enable possible application as a detergent.

Resistance to hard water

Further studies were conducted to investigate the resistance to hard water. The results are reported in Table 7.6 based on the criteria reported in Table 7.2 and Table 7.3.

Table 7.6 Results of hard water stability tests

	Total Score	Mean Stability
SDS	21	2
SDBS	50	3
C8	75	5
C12	75	5

SDBS and SDS proved to have very low resistance, exhibiting extensive precipitation in many tests. In contrast, C₈ and C₁₂ derivatives demonstrated outstanding solubility, maintaining a clear solution for all

calcium concentrations. Since most of the additives used commercially are for chelating calcium ions, these results are promising steps toward solving problems related to the toxicity of these compounds and reducing the cost of the final product.

Critical Micelle Concentration

Results for the CMC calculation are reported in Figure 7.6 and summarized in Table 7.7. According to these results, the alkyl chain has a remarkable effect on the CMC, decreasing the concentration about 5 times for every 4 carbon atoms added. For commercial application it is required that the CMC falls below 2000 ppm; usually additives that reduce the CMC (such as NaCl) are required to achieve this target. According to the results presented in Figure 7.6, the furoate alkyl surfactants are capable of achieving low CMCs comparable to the commercial SDBS and SDS. Specifically, C₁₂ and C₁₆ derivatives have CMCs much lower than 2000 ppm. For the C₁₆ compound, the solubility represents a limitation even if it exhibits the lowest CMC. These results seem to contradict the results of Dauenhauer and co-workers which state that higher polarity of the head group leads to lower CMC values. In this regard only the Kraft point (KP) shows remarkable improvements while CMC and water resistance proved to be drastically reduced. The results demonstrated in this study clearly show that this is not valid as a general consideration and CMC is influenced by other factors (e.g. packing factors).¹⁶

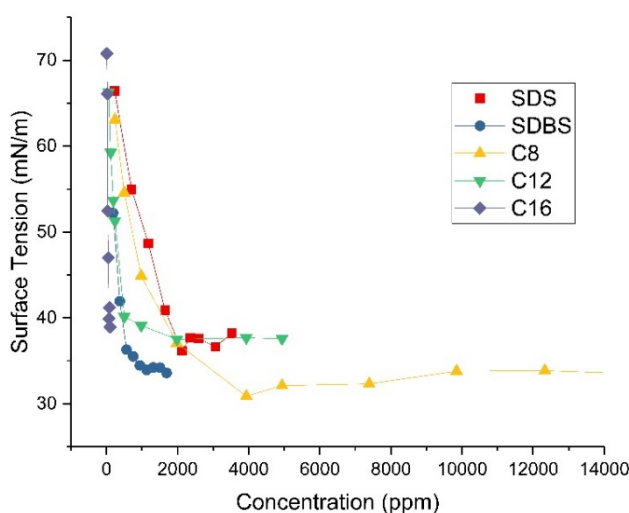


Figure 7.6 Measurement of surface tension at different concentrations of surfactant.

Table 7.7 Calculated CMC for different surfactants.

Surfactant	CMC (ppm)
SDS	2000
SDBS	593
C8	2149
C12	521
C16	60

Summary of furoate sulfonated surfactants

The results obtained so far regarding solubility, resistance to hard water and CMC are consistent with the proposal that furoate alkyl sulfonate surfactants are a potential replacement for LAS and represent a solution to many issues in detergent formulations. The ester linkage proved to be the key to obtaining superior performances compared to C-C and ketone functionalized groups (reported by Park and co-workers⁶). This led to high solubility, low CMC and very high resistance to hard water, thus representing a valuable molecule that can reduce the need for additives and the cost in surfactant formulations.

Of all the surfactant tested, the C₁₂ derivative showed the best performance with high solubility, low CMC and high resistance to hard water. The combination of high solubility and low CMC gave a large population of micelles, which can enhance the detergent ability of the surfactant. It is predicted that this surfactant will exhibit high detergency performance without the need for addition of any additives, while for C₈ and C₁₆ compounds, the addition of salts or hydrotropes to decrease the CMC or increase the solubility will be necessary. Compared to the surfactants reported by Parker and co-workers,⁶ the alkyl furoate sulfonated C₁₂ has the advantage of having a low KP, high solubility (attributed to the ketone functionalization) and low CMC of the furan alkyl linkage. Hence no builder (to decrease the KP), salts (to decrease the CMC) or chelate (to improve the stability in hard water) is needed to improve the detergent properties. This represents the perfect compromise and surfactant C₁₂ proved to have superior properties on all aspects compared with the competitors.

Table 7.8 Comparison of the properties of tested surfactants and those of Dauenhauer and co-workers.

	CMC	Solubility	Hard water stability (ppm)	KP (°C)	Additive
Furoate-C8	2149	High	>250	<0	Salt
Furoate-C12	521	High	>250	<0	None
Furoate-C16	60	Insoluble	Not measured	>50	Hydrotrope, builder
SDBS	593	Low	<100	58 ⁶	Hydrotrope, chelate, builder
SDS	2000	Medium	<100	15 ⁶	Hydrotrope, chelant
Furan sulfonated-ketone C12 ⁶	11520	High	230	<0 ⁶	Salt, chelant
Furan sulfonated C12 ⁶	720	Medium	>250	30 ⁶	Builder

Discussion of the biodegradability

Biodegradability is one of the main properties that the surfactant needs to possess in order to be commercialized since they are primarily disposed of in wastewater treatment (WWT). Water treatment plants are composed of different units focused on degrading all of the compounds that can be degraded through the action of microorganisms. Thus, water can be returned to the environment without causing damage to the ecosystem. The decomposition of the compounds by microorganisms defines the biodegradability of the compound. Usual tests state that a compound can be considered biodegradable if 60% of the compound is degraded within 28 days by a colony of bacteria. Two different categories of microorganisms are used: anaerobic and aerobic. Tests with the first of these are conducted in oxygen free systems and degrade the organic compounds into biogas which can then be used to produce electricity. This represents the first reaction unit in the wastewater treatment plant. Compounds that cannot be degraded anaerobically are then treated by aerobic digestion where, using oxygen, the organic compounds are converted into CO₂ and water. Biodegradability is generally referred to as aerobic digestion in which different protocols are available to assess its decomposition while anaerobic digestion requires a more specific study of the compound to assess its compatibility. From a wastewater treatment point of view, it is highly desirable that most of the organic compounds are anaerobically digested, since biogas is the main added value of the WWT. LAS are not only incompatible with anaerobic digestion but have the potential to exhibit an inhibitory effect on the anaerobic bacteria community.¹⁷ On the other hand, SDS are highly biodegradable in both anaerobic and aerobic digestion making them an environmentally friendly surfactant.¹⁸

Although it has been largely demonstrated that LAS and SDS are readily biodegradable by aerobic bacteria,¹⁹ different considerations have to be taken into account according to the surfactant resistance to hard water. Additives are designed not to precipitate the surfactant during its application nor when it is diluted in a richly diverse environment. In this case the surfactant can precipitate before entering the digestors with a higher chance of being dispersed in the environment. This was reported by different studies of raw sewage, where they reported very high concentrations (up to 35%) of LAS in primary settling tanks where insoluble materials are filtered before entering the digestors.^{18,20} Moreover, since LAS are not biodegradable, they have a positive net CO₂ emission after aerobic digestion.

In this study, biodegradability tests were not performed on our surfactants but the structure suggests that they should be able to biodegrade. We can simplify the mechanism by cleavage of the ester group and degradation of the furoic acid and fatty alcohol. Since both feedstocks (furoic acid and fatty alcohol) are biodegradable and aerobic cleavage of ester groups has already been demonstrated,²¹ it is very likely that the furoate alkyl sulfonated surfactant is also going to be biodegradable.

In the same way, it is possible to anticipate the digestion by anaerobic microorganisms. Ester cleavage by anaerobic digestion and fatty alcohol digestion it has already been well demonstrated.^{22,23} Data on furoic acid are not reported for anaerobic digestion, but furfural has been demonstrated as a highly compatible feedstock for anaerobic digestion, indicating that the furan ring can be digested in an efficient way, in contrast to the benzene ring characteristic of LAS.^{24,25} The anaerobic degradation of the furoate alkyl sulfate are therefore likely to be possible.

However, in this analysis, major considerations have to be performed on the type of microbial community used and standard protocols have to be adopted to assess the compatibility of the two different steps.

Conclusions

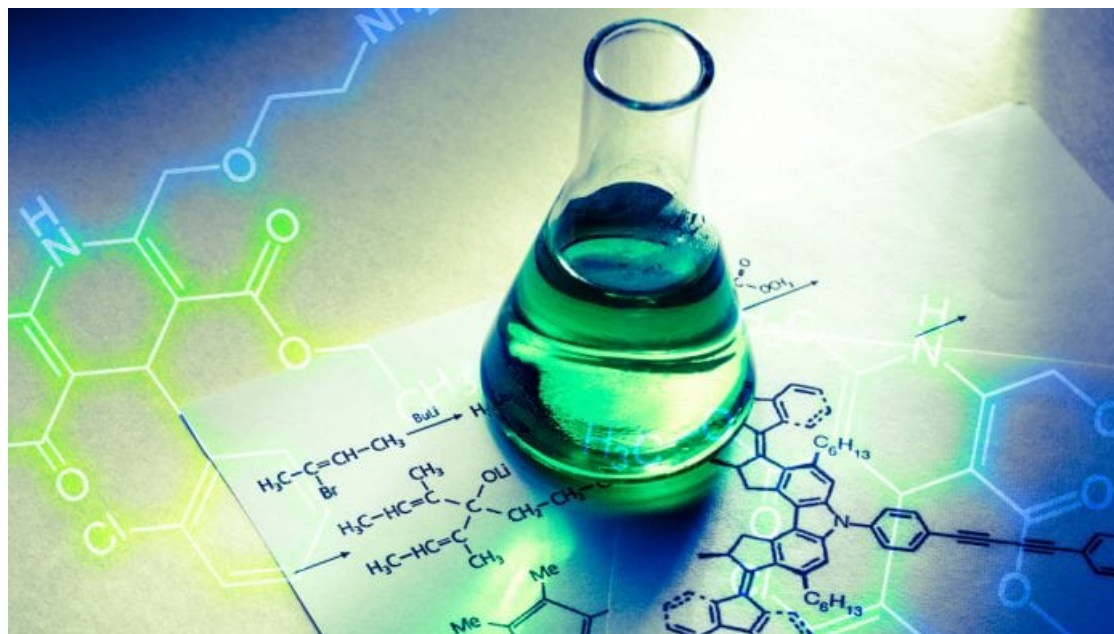
The sulfonated alkylfuroate compounds represent potential substitutes for LAS for application as detergents. The chemical structure consists of a sulfonated furan head with an ester linkage to an alkyl chain, which yields superior performance compared to that of the commercial surfactants (LAS and SDS) and other biobased surfactants synthesized in the literature. The CMC decreases by increasing the alkyl chain, with the C₁₆ derivative exhibiting the lowest CMC although its solubility is too low. The C₁₂ compound represents the best compromise between solubility and CMC, showing very high solubility even at 0 °C in hard water. The superior properties of this surfactant have the potential to reduce drastically the need for additives, which represents an environmental concern. Further studies need to be done to assess the biodegradability of these surfactants.

References

- (1) Benvegna, T.; Plusquellec, D.; Lemiègre, L. Surfactants from Renewable Sources: Synthesis and Applications. In *Monomers, Polymers and Composites from Renewable Resources*; Elsevier, 2008; pp 153–178. <https://doi.org/10.1016/B978-0-08-045316-3.00007-7>.
- (2) Surfactants Market Size Growth & Share | Global Industry Report, 2022 <https://www.grandviewresearch.com/industry-analysis/surfactants-market> (accessed Nov 4, 2019).
- (3) Porter, M. R. Handbook of Surfactants
- (4) Waldhoff, H.; Spilker, R. Handbook of Detergents; 2005.
- (5) Handbook for Cleaning/Decontamination of Surfaces | ScienceDirect <https://www.sciencedirect.com/book/9780444516640/handbook-for-cleaning-decontamination-of-surfaces#book-info> (accessed Nov 4, 2019).
- (6) Park, D. S.; Joseph, K. E.; Koehle, M.; Krumm, C.; Ren, L.; Damen, J. N.; Shete, M. H.; Lee, H. S.; Zuo, X.; Lee, B.; et al. Tunable Oleo-Furan Surfactants by Acylation of Renewable Furans. *ACS Cent. Sci.* **2016**, 2 (11), 820–824. <https://doi.org/10.1021/acscentsci.6b00208>.
- (7) Morse, G. K.; Perry, R.; Lester, J. N. The Life-Cycle Environmental Impact of Key Detergent Builder Systems in the EU. *Sci. Total Environ.* **1995**. [https://doi.org/10.1016/0048-9697\(95\)04530-E](https://doi.org/10.1016/0048-9697(95)04530-E).
- (8) Final Report on the Safety Assessment of EDTA, Calcium Disodium EDTA, Diammonium EDTA, Dipotassium EDTA, Disodium EDTA, TEA-EDTA, Tetrasodium EDTA, Tripotassium EDTA, Trisodium EDTA, HEDTA, and Trisodium HEDTA. *Int. J. Toxicol.* **2002**, 21 (2_suppl), 95–142. <https://doi.org/10.1080/10915810290096522>.
- (9) Liu, Y.; Chen, J. *Encyclopedia of Ecology*, 2nd ed.; Elsevier, 2014.
- (10) Scharpf, L. G.; Hill, I. D.; Wright, P. L.; Plank, J. B.; Keplinger, M. L.; Calandra, J. C. Effect of Sodium Nitrilotriacetate on Toxicity, Teratogenicity, and Tissue Distribution of Cadmium. *Nature* **1972**, 239 (5369), 231–234. <https://doi.org/10.1038/239231b0>.
- (11) Rahman, A.; Brown, C. W. Effect of PH on the Critical Micelle Concentration of Sodium Dodecyl Sulphate. *J. Appl. Polym. Sci.* **1983**, 28 (4), 1331–1334. <https://doi.org/10.1002/app.1983.070280407>.
- (12) Stensrud, K.; Wicklund, L. Synthesis of Non-Ionic Surfactants From 5-Hydroxymethyl-2-Furfural, Furan-2,5-Dimethanol and Bis-2,5-Dihydroxymethyl-Tetrahydrofurans. US20170226075, 2016.
- (13) Kraus, G. A.; Lee, J. J. A Direct Synthesis of Renewable Sulfonate-Based Surfactants. *J. Surfactants Deterg.* **2013**, 16 (3), 317–320.
- (14) Gassama, A.; Ernenwein, C.; Youssef, A.; Agach, M.; Riguet, E.; Marinković, S.; Estrine, B.; Hoffmann, N. Sulfonated Surfactants Obtained from Furfural. **2013**, 15 (6), 1558–1566 <https://doi.org/10.1039/c3gc00062a>.
- (15) Fisher, G. B.; Fuller, J. C.; Harrison, J.; Goralski, C. T.; Singaram, B. Aminoborohydrides. 3. A Facile Reduction of Tertiary Amides to the Corresponding Amines and Alcohols in High Purity Using Lithium Aminoborohydrides. Sterically Controlled Selective CN or CO Bond Cleavage. *Tetrahedron Lett.* **1993**, 34 (7), 1091–1094. [https://doi.org/10.1016/S0040-4039\(00\)77498-3](https://doi.org/10.1016/S0040-4039(00)77498-3).
- (16) Oremusová, J.; Vitková, Z.; Vitko, A.; Tárník, M.; Miklovičová, E.; Ivánková, O.; Murgaš, J.; Krchňák, D. Effect of Molecular Composition of Head Group and Temperature on Micellar

- Properties of Ionic Surfactants with C12 Alkyl Chain. *Molecules* **2019**, *24* (3), 651-656 <https://doi.org/10.3390/molecules24030651>.
- (17) Gavala, H. N.; Ahring, B. K. *Inhibition of the Anaerobic Digestion Process by Linear Alkylbenzene Sulfonates*; 2002; Vol. 13.
 - (18) Scott, M. J.; Jones, M. N. The Biodegradation of Surfactants in the Environment. *Biochim. Biophys. Acta - Biomembr.* **2000**. [https://doi.org/10.1016/S0304-4157\(00\)00013-7](https://doi.org/10.1016/S0304-4157(00)00013-7).
 - (19) M. Leon, V.; Gomez-Parra, A.; Gonzalez-Mazo, E. Biodegradation of Linear Alkylbenzene Sulfonates and Their Degradation Intermediates in Seawater. **2004**, *38*(8), 2359-2367 <https://doi.org/10.1021/es034813>.
 - (20) Berna, J. L.; Moreno, A.; Ferrer, J. The Behaviour of LAS in the Environment. *J. Chem. Technol. Biotechnol.* **2007**, *50* (3), 387–398. <https://doi.org/10.1002/jctb.280500310>.
 - (21) Baker, I. J. A.; Matthews, B.; Soares, H.; Krodziewska, I.; Furlong, D. N.; Grieser, F.; Drummond, C. J. Sugar Fatty Acid Ester Surfactants: Structure and Ultimate Aerobic Biodegradability. *J. Surfactants Deterg.* **2000**, *3* (1), 1–11. <https://doi.org/10.1007/s11743-000-0107-2>.
 - (22) VanEtten, R. L.; Clowes, G. A.; Sebastian, J. F.; Bender, M. L. The Mechanism of the Cycloamylose-Accelerated Cleavage of Phenyl Esters. *J. Am. Chem. Soc.* **1967**, *89* (13), 3253–3262. <https://doi.org/10.1021/ja00989a028>.
 - (23) Florencio, L.; Field, J. A.; Lettinga, G. High-Rate Anaerobic Treatment of Alcoholic Wastewaters. *Brazilian J. Chem. Eng.* **1997**, *14* (4), 409–416. <https://doi.org/10.1590/S0104-66321997000400016>.
 - (24) Akobi, C.; Hafez, H.; Nakhla, G. The Impact of Furfural Concentrations and Substrate-to-Biomass Ratios on Biological Hydrogen Production from Synthetic Lignocellulosic Hydrolysate Using Mesophilic Anaerobic Digester Sludge. *Bioresour. Technol.* **2016**, *221*, 598–606. <https://doi.org/10.1016/j.biortech.2016.09.067>.
 - (25) Wang, Z.; Liu, Z.; Noor, R. S.; Cheng, Q.; Chu, X.; Qu, B.; Zhen, F.; Sun, Y. Furfural Wastewater Pretreatment of Corn Stalk for Whole Slurry Anaerobic Co-Digestion to Improve Methane Production. *Sci. Total Environ.* **2019**, *674*, 49–57. <https://doi.org/10.1016/j.scitotenv.2019.04.153>.

Chapter 8 Conclusions and Prospects



The research reported in this thesis has focused on a different approach to synthesizing chemical compounds so that both catalysis and separation can be favoured. Chapter 1 describes the reasons why we consider our approach the most suitable and 'green' for a future application of biochemicals on a large scale. By exploiting the high stability, recyclability and great ability to process biomass/sugars of the ionic liquids, chemical processes can benefit from great advantages in terms of environmental impact. In Chapter 2, ionic liquids were used as solvent to produce carbonaceous material starting from HMF. By using spectroscopy and analytical techniques we discovered that ionic liquids can result in different humin structures, each with different functional groups and morphology. In particular, humins derived from acidic ionic liquids proved to be superior for the extraction of lead from waste water treatment.

In Chapter 3, we demonstrated that ionic liquids are good solvents for the separation of valuable furanic compounds derived from HMF. DFF and FDCA can be separated, respectively, by sublimation and precipitation by water addition, demonstrating that ionic liquids are superior solvents compared to traditional organic solvents for HMF valorisation. While this aspect is very attractive, so far no catalysts have been developed for the synthesis of these DFF and FDCA in ionic liquids, therefore we devoted two chapters to the synthesis of these molecules in ionic liquids by developing catalysts for the oxidation reaction. The CuCl/TEMPO catalytic system proved to be very efficient for the oxidation of furanic compounds in non-coordinating ionic liquids. However, it proved to be incompatible with the

dehydration reaction in coordinated and halogenated ionic liquids, where the dehydration of sugars to HMF is very efficient at high yield and mild reaction conditions. Therefore, in order to apply the CuCl/TEMPO system, it was decided to devise a system where the dehydration of fructose can be carried efficiently in a non-coordinating ionic liquid so that the HMF formed can be oxidised to DFF in a two-step reaction. It was discovered that the key to achieve high yields of HMF from fructose in non-coordinating ionic liquid was the water content (Chapter 4). Indeed, small variations of the water content led to remarkable changes in yield. An optimum water content was found which optimized the yield of HMF at high fructose concentration under mild reaction conditions.

The findings in Chapter 4 were used in Chapter 5 to achieve the oxidation with TEMPO/CuCl leading to a near quantitative yield of DFF from HMF at low temperature. The two-step reaction starting from fructose proved to be efficient giving an isolated yield of 55%. We believe that this reaction is innovative since it combines a good yield with facile separation of the product, however, issues arise due to the poor recyclability of the system upon catalyst deactivation. Further studies are needed to improve the recyclability of the system and stabilize the copper catalyst. While DFF is a valuable molecule, its direct application is still not well explored. It can be converted to FDCA and then polymerized to PEF, but that would add one chemical step which will inevitably increase the cost of the process. However, as with many bifunctional molecules, there is interest in using these compounds for application in polymers and speciality chemicals. Since most research have focused on the synthesis of FDCA rather DFF, due to its higher value, more studies need to be carried out on DFF.

In Chapter 6, we concentrated on developing a catalyst for the oxidation of HMF into FDCA in coordinating ionic liquids. The challenge was the fact that noble metal catalysts as Pt and Pd suffer from deactivation in halogenated environments, necessitating a different approach to solve the problem. We chose to operate in [bmim]Cl since this solvent has proven to be very efficient in the production of HMF from cellulose and glucose. A combination of Mn and Fe oxides proved to be very efficient in this reaction achieving 80% yield from HMF and 40% glucose in a two-step reaction.

Finally, Chapter 7 focuses on surfactants derived from pentose derivatives of furans. The surfactant derived from furoic acid and fatty alcohol proved to have superior proprieties compared to the commercial LAS and SDS with major resistance to hard water, lower Kraft Point, lower CMC and higher solubility. The low cost of the feedstock makes these surfactants a potential substitute for current detergent formulations with superior proprieties and lower environmental impact.

We believe that this thesis represents a new approach to solve various issues related to sugar processing in the chemical industry. Ionic liquids favour the separation of valuable furanic compounds which could be used as substitutes for applications typically reliant on the aromatic oil fraction, BTX. However, improvements are needed in terms of recyclability of the catalysts and full recovery of the solvents is needed to minimise the waste. In the section below, some prospects for further use of ionic liquids in biomass processing are described.

Prospects

Biomass-derived feedstocks need sustainable processing to be competitive in the market. Emission of CO₂ due to energy and chemicals usage needs to be limited. We demonstrate that ionic liquids are solvent capable of simplifying the process in terms of reaction conditions and product separation. Moreover, the humin side products can be further valorised to a valuable adsorbent. Further valorisation can be achieved by finding different applications in batteries and as catalyst supports. Indeed, carbonaceous materials attract much interest due to their environmentally-friendly nature, compared to classical metal supports, since they are easier to dispose and not harmful to the environment. However, noble metals have been shown to leach from classical carbon supports derived from fossil feedstocks during the catalytic process, causing environmental problems for metal dispersion in the environment. According our experiments, humins have a potential to have high affinity to metal thanks its high functionalization, in this matter further studies need to be addressed to analyse the possibility to use this material as a catalyst supports that reduce the leaching of metals.

For a catalytic process, high levels of ionic liquid recovery are needed in a process to guarantee high recyclability. In our case, homogeneous catalysis suffers from deactivation, therefore further efforts are needed to find ligands which stabilise the copper salts. Regarding heterogeneous catalysts, the support that we developed for the oxidation of HMF directly to FDCA was tested under dilute conditions, meaning that FDCA still cannot be separated by precipitation. The catalyst needs to be tested at higher concentration with no significant loss of yield.

In the surfactant field, the bioderived furoate surfactants proved to be very promising for application in the detergent industry. However, in this field, cost is a key parameter to be considered for the success of the surfactant. Furoic acid represents a more expensive product compared to furfural. Therefore, a direct synthesis of the furoate from furfural is highly desirable to lower the cost. Oxidative esterification of the aldehyde moiety to the ester could be a solution, allowing furfural to be used directly as a feedstock for the synthesis of the surfactant. Moreover, biodegradability test need to be performed.

Since selectivity is the main issue for the oxidation to FDCA in ionic liquids. The use of enzymes and electrochemistry could offer a potential solution since these approaches are more selective. Herein we describe the potential for ionic liquids in this type of system and the advantages they could deliver.

Application of ionic liquids in enzymatic and electrochemical reactions

Enzymatic routes for the catalytic oxidation of HMF to DFF and FDCA proved to be very efficient using enzymes (oxoreductases) of the category EC 1.1.3 and EC 1.2.3, respectively. These two categories of enzymes are able to oxidase primary alcohols and aldehydes using oxygen as the electron acceptor. In order for these enzymes to exhibit their catalytic activity, a co-factor (co-enzyme) needs to

be added. McKenna and co-workers^{1,2} have combined the galactose oxidase (GOase M3-5) with peroxidase from horseradish (HRP) to oxidise HMF to DFF in high yield. Subsequently they used an aldehyde oxidase PaoABC to oxidise DFF to FDCA, again in high yield. However, this reaction proved to have multiple drawbacks since the kinetics are slow, low substrate loadings are needed and catalase is required to remove peroxides from the by-products.

Another enzyme reported by Dijkman and co workers^{3,4} belonging to the category EC 1.1.347 (alcohol dehydrogenase) named HMFO has been tested for the oxidation of HMF to FDCA in one pot. The enzyme uses FAD as co-factor which is already present in the enzyme as a prosthetic group. This has the function of acting as active site for the electron transfer of the α -carbon of HMF to molecular oxygen. Despite the high performance of this enzyme at high loadings, it still deactivates due to leaching of FAD.

According to these studies, enzymatic catalysis for HMF oxidation suffers from instability and deactivation. A new approach has been developed for the stabilization of enzymes in ionic liquids which allows an increase in temperature, allowing the increase in the kinetics of reaction and limits the deactivation of the enzyme.^{5,6} The application of this methodology for the enzymes used in HMF oxidation could be beneficial for combining the high selectivity of the enzymes with the faster kinetics that can be achieved through stabilization.

Electrochemical oxidation is another field to be explored for this reaction. Trials have been performed using water as solvent,⁷⁻⁹ achieving high yields. Ionic liquids have the potential to enhance the reaction kinetics and selectivity thanks to the higher conductivity of the solvent, achieving higher current with lower voltage in the electrochemical cell.

This thesis sets out the case for the use of ionic liquids in sugar processing, showing that they have great potential for rendering the synthesis of economically feasible bioderived products to compete with oil-derivative ones. Industry can be reluctant to adopt such techniques, since most chemical processing is inspired by traditional petrochemical approaches, which rely heavily on organic solvents and non-carbon neutral processes. A different approach needs to be adopted to achieve a more sustainable approach to the processing and valorisation of feedstocks that can reduce waste and CO₂ emissions.

“The human mind adjusts itself to a certain point of view, and those who have regarded nature from one angle, during a portion of their life, can adopt new ideas only with difficulty.”

Antoine Lavoiser

References

- (1) McKenna, S. M.; Leimkühler, S.; Herter, S.; Turner, N. J.; Carnell, A. J. Enzyme Cascade Reactions: Synthesis of Furandicarboxylic Acid (FDCA) and Carboxylic Acids Using Oxidases in Tandem. *Green Chem.* **2015**, *17* (6), 3271–3275. <https://doi.org/10.1039/C5GC00707K>.
- (2) McKenna, S. M.; Mines, P.; Law, P.; Kovacs-Schreiner, K.; Birmingham, W. R.; Turner, N. J.; Leimkühler, S.; Carnell, A. J. The Continuous Oxidation of HMF to FDCA and the Immobilisation and Stabilisation of Periplasmic Aldehyde Oxidase (PaoABC). *Green Chem.* **2017**, *19* (19), 4660–4665. <https://doi.org/10.1039/c7gc01696d>.
- (3) Dijkman, W. P.; Binda, C.; Fraaije, M. W.; Mattevi, A. Structure-Based Enzyme Tailoring of 5-Hydroxymethylfurfural Oxidase. *ACS Catal.* **2015**, *5* (3), 1833–1839. <https://doi.org/10.1021/acscatal.5b00031>.
- (4) Dijkman, W. P.; Groothuis, D. E.; Fraaije, M. W. Enzyme-Catalyzed Oxidation of 5-Hydroxymethylfurfural to Furan-2,5-Dicarboxylic Acid. *Angew. Chemie - Int. Ed.* **2014**, *53* (25), 6515–6518. <https://doi.org/10.1002/anie.201402904>.
- (5) Brogan, A. P. S.; Hallett, J. P. Solubilizing and Stabilizing Proteins in Anhydrous Ionic Liquids through Formation of Protein–Polymer Surfactant Nanoconstructs. *J. Am. Chem. Soc.* **2016**, *138* (13), 4494–4501. <https://doi.org/10.1021/jacs.5b13425>.
- (6) Brogan, A. P. S.; Bui-Le, L.; Hallett, J. P. Non-Aqueous Homogenous Biocatalytic Conversion of Polysaccharides in Ionic Liquids Using Chemically Modified Glucosidase. *Nat. Chem.* **2018**, *10* (8), 859–865. <https://doi.org/10.1038/s41557-018-0088-6>.
- (7) Kubota, S. R.; Choi, K. S. Electrochemical Oxidation of 5-Hydroxymethylfurfural to 2,5-Furandicarboxylic Acid (Fdca) in Acidic Media Enabling Spontaneous Fdca Separation. *ChemSusChem* **2018**, *11* (13), 2138–2145. <https://doi.org/10.1002/cssc.201800532>.
- (8) Zhang, N.; Zou, Y.; Tao, L.; Chen, W.; Zhou, L.; Liu, Z.; Zhou, B.; Huang, G.; Lin, H.; Wang, S. Electrochemical Oxidation of 5-Hydroxymethylfurfural on Nickel Nitride/Carbon Nanosheets: Reaction Pathway Determined by In Situ Sum Frequency Generation Vibrational Spectroscopy. *Angew. Chemie Int. Ed.* **2019**, *58* (44), 15895–15903. <https://doi.org/10.1002/anie.201908722>.
- (9) Weidner, J.; Barwe, S.; Sliozberg, K.; Piontek, S.; Masa, J.; Apfel, U.-P.; Schuhmann, W. Cobalt–Metalloid Alloys for Electrochemical Oxidation of 5-Hydroxymethylfurfural as an Alternative Anode Reaction in Lieu of Oxygen Evolution during Water Splitting. *Beilstein J. Org. Chem.* **2018**, *14*, 1436–1445. <https://doi.org/10.3762/bjoc.14.121>.

A. Appendix

Characterization Ionic Liquids

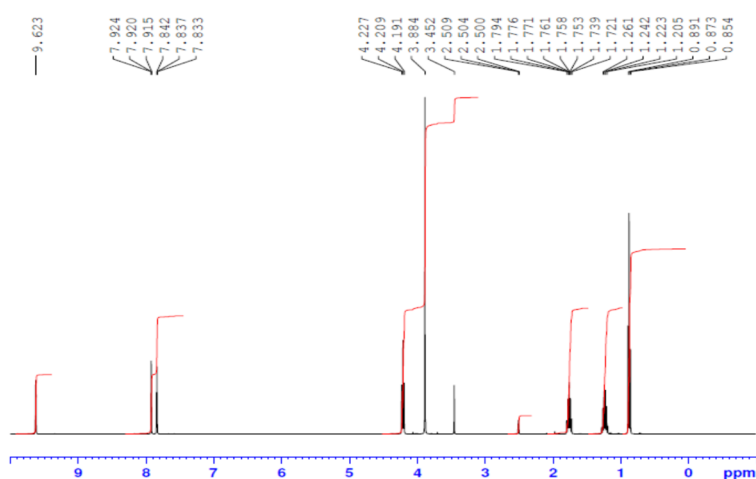


Figure A. 1 ^1H NMR spectrum of [bmim]Cl in deuterated DMSO.

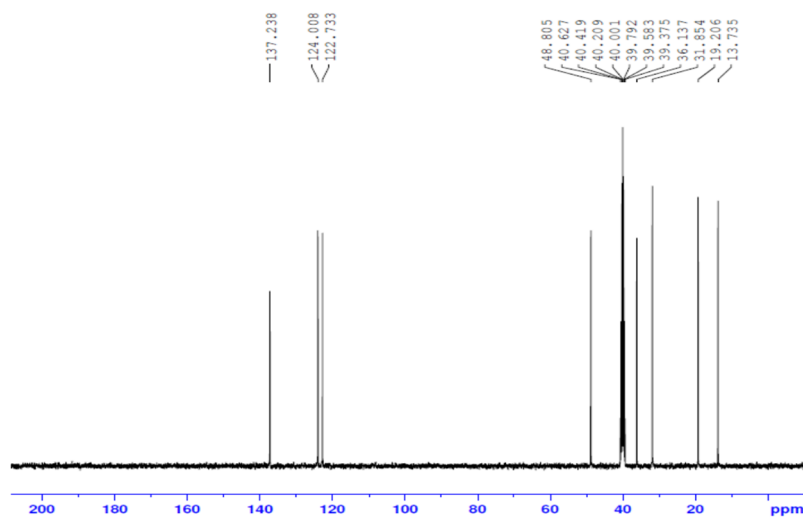


Figure A. 2 $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [bmim]Cl in deuterated DMSO.

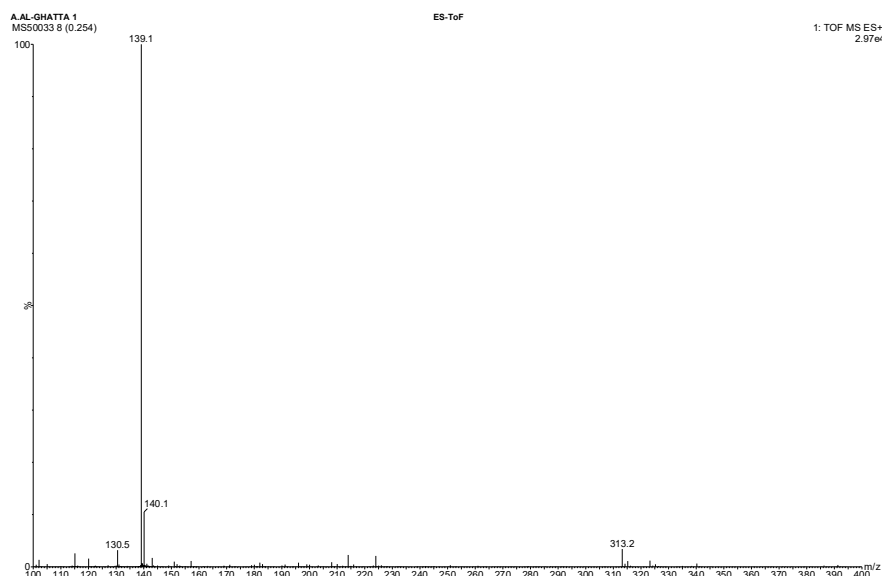


Figure A. 3 Mass spectrum of [bmim]Cl.

[bmim]Cl.: ^1H NMR (DMSO- d_6): δ 9.62 (s, 1H, N_2CH), 7.92, 7.84 (m x 2, 2 x 1H, 2 x N-CH), 4.20 (t, 2H, N- CH_2 -CH $_2$, $J_{\text{HH}} = 7.2$ Hz), 3.88 (s, 3H, N-CH $_3$), 1.77, 1.24 (m x 2, 2 x 2H, N-CH $_2$ -CH $_2$ -CH $_2$ -CH $_3$), 0.87 (t, 3H, -CH $_2$ -CH $_3$, $J_{\text{HH}} = 7.3$ Hz) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (DMSO- d_6): δ 137.2 (N_2 -CH), 124.1, 122.7 (2 x N-CH), 48.8 (N-CH $_2$ -CH $_2$ -CH $_2$ -CH $_3$), 36.14 (NCH $_3$), 31.8 (NCH $_2$ -CH $_2$ -CH $_2$ -CH $_3$), 19.2 (NCH $_2$ -CH $_2$ -CH $_2$ -CH $_3$), 13.7 (N-(CH $_2$) $_2$ -CH $_2$ -CH $_3$) ppm. MS (ES, +ve mode): m/z (abundance) = 357 (31) $[(\text{bmim})_2\text{Br}]^+$, 139 (100) $[\text{bmim}]^+$.

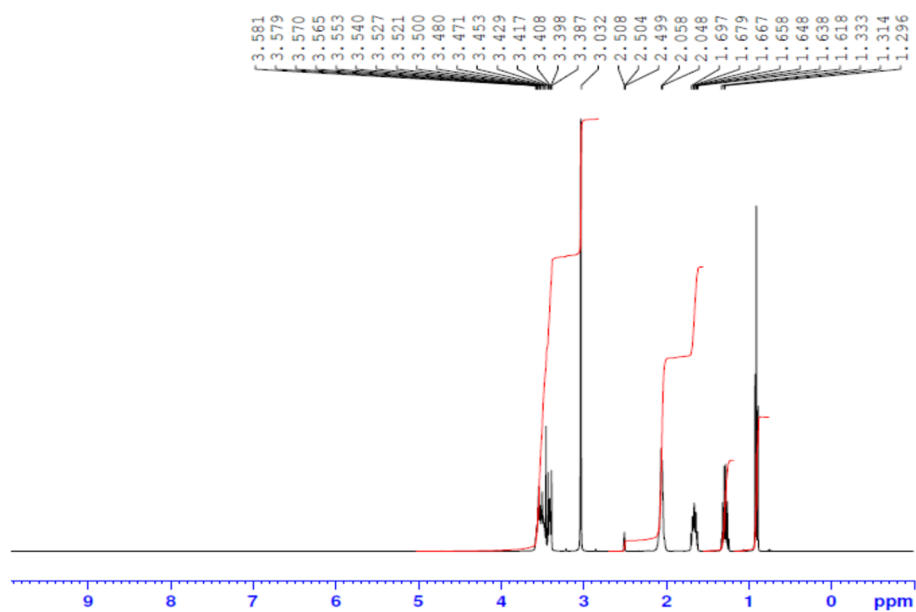


Figure A. 4 ^1H NMR spectrum of [bmim]Cl in deuterated DMSO.

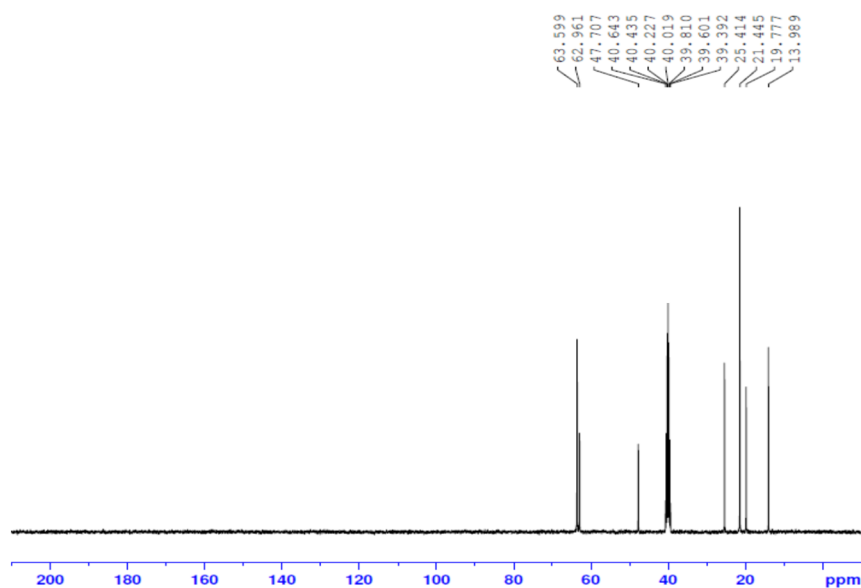


Figure A. 5 $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [bmpyr]Cl in deuterated DMSO.

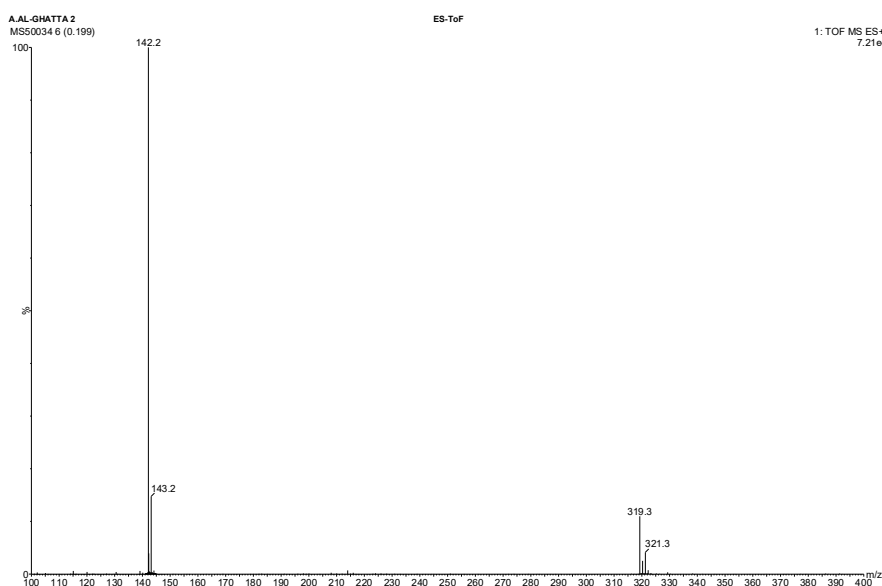


Figure A. 6 Mass spectrum of [bmpyr]Cl.

[bmpyr]Cl: ^1H NMR (DMSO- d_6): 3.58-3.39 (m, 6H, 2,5-pyrrole- CH_2 and N- CH_2 - CH_2 - CH_2 - CH_3), 3.03 (s, 3H, N- CH_3), 2.02-2.05 (m, 2 x 2H, 3,4-pyrrole- CH_2), 1.65 (m, 2H, N CH_2 CH_2 CH_2 CH_3 , $J_{\text{HH}} = 7.2$ Hz), 1.2 (m, 2H, N CH_2 CH_2 CH_2 CH_3 , $J_{\text{HH}} = 7.3$ Hz), 0.86 (t, 3H, N- CH_2 - CH_2 - CH_2 - CH_3 , $J_{\text{HH}} = 7.3$ Hz) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (DMSO- d_6): 63.7 (s, N- CH_2 - CH_2 -), 63.0 (s, 2,5-pyrrole- CH_2), 47.6 (s, N CH_3), 25.4 (s, 3,4-pyrrole- CH_2), 21.4 (s, N- CH_2 - CH_2 - CH_2 - CH_3), 19.8 (s, N-(CH_2) $_2$ - CH_2 - CH_3), 14.0 (s, N-(CH_2) $_3$ - CH_3). m/z (abundance) = 142(100) [bmpyr] $^+$.

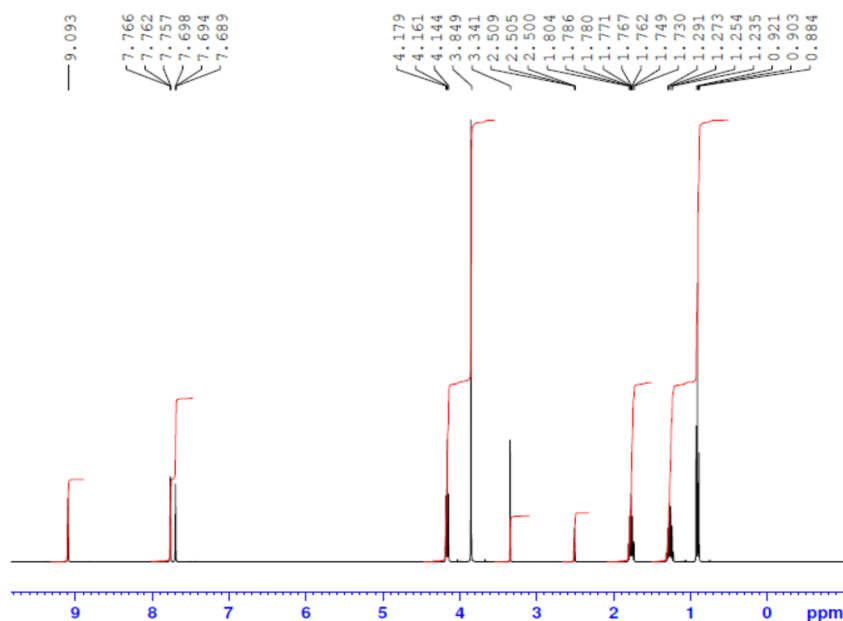


Figure A. 7 ^1H NMR spectrum of [bmim]OTf in deuterated DMSO.

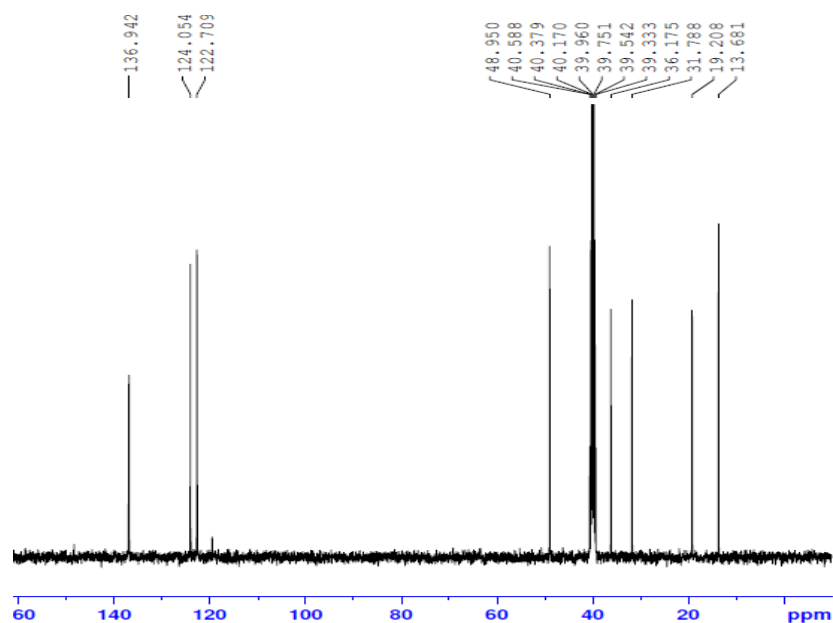


Figure A. 8 $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [bmim]OTf in deuterated DMSO

[bmim]OTf : ^1H NMR (DMSO-d_6): δ 9.08 (s, 1H, N_2CH), 7.76-7.69- (m x 2, 2 x 1H, 2 x N-CH), 4.17 (t, 2H, N- $\underline{\text{CH}_2}$ - CH_2 , $J_{\text{HH}} = 7.2$ Hz), 3.85 (s, 3H, N- CH_3), 1.77- 1.26 (m x 2, 2 x 2H, N- CH_2 - $\underline{\text{CH}_2}$ - $\underline{\text{CH}_2}$ - CH_3), 0.9 (t, 3H, - CH_2 - $\underline{\text{CH}_3}$, $J_{\text{HH}} = 7.4$ Hz) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (DMSO-d_6): δ 137.7 (N_2 -CH), 123.6-122.4 (2 x N-CH), 119.2 (CF_3), 49.1 (N- $\underline{\text{CH}_2}$ - CH_2 - CH_2 - CH_3), 35.8 (N CH_3), 32.0 (N CH_2 - $\underline{\text{CH}_2}$ - CH_2 - CH_3), 19.0 (N CH_2 - CH_2 - $\underline{\text{CH}_2}$ - CH_3), 13.8 (N-(CH_2) $_2$ - CH_2 - $\underline{\text{CH}_3}$) ppm. MS (ES, +ve mode): m/z (abundance) = 139 (100) $[\text{bmim}]^+$.

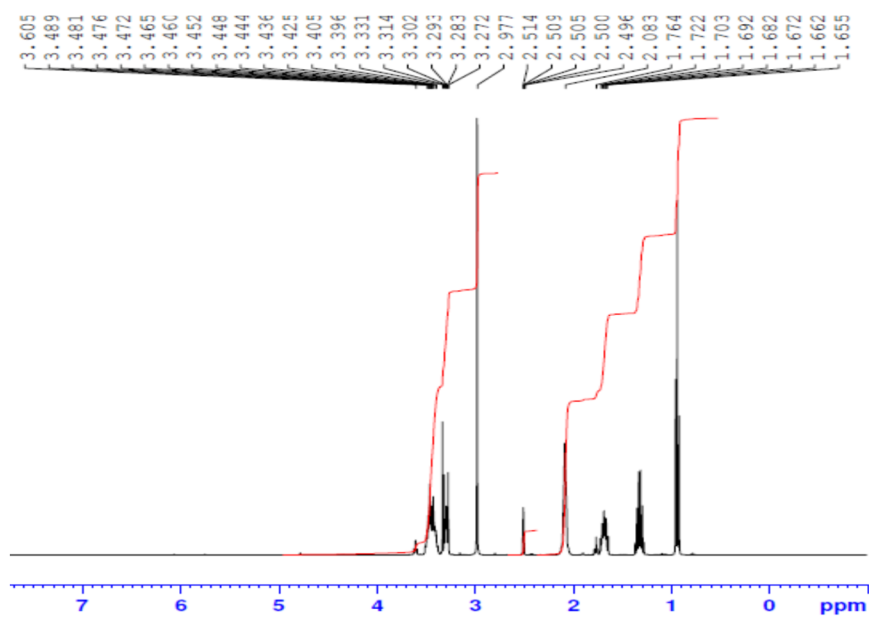


Figure A. 9 ^1H NMR spectrum of [bmpyr]OTf in deuterated DMSO.

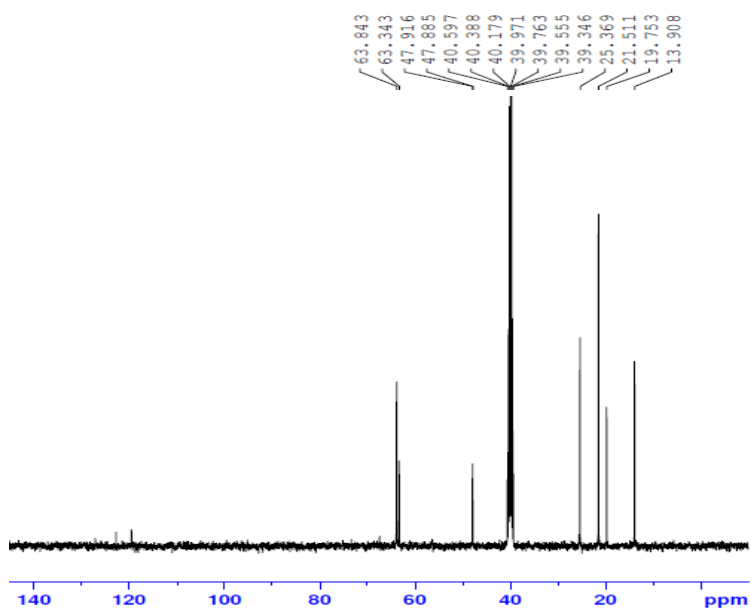


Figure A. 10 ^{13}C NMR spectrum of [bmpyr]OTf in deuterated DMSO.



Figure A. 11 Mass spectrum of [bmpyr]OTf.

[bmpyr]OTf: ^1H NMR (DMSO- d_6): 3.51-3.26 (m, 6H, 2,5-pyrrole- CH_2 and N- CH_2 - CH_2 - CH_2 - CH_3), 2.98 (s, 3H, N- CH_3), 2.02-2.08 (m, 2 x 2H, 3,4-pyrrole- CH_2), 1.68 (m, 2H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$, $J_{\text{HH}} = 7.2$ Hz), 1.32 (m, 2H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$, $J_{\text{HH}} = 7.3$ Hz), 0.94 (t, 3H, N- CH_2 - CH_2 - CH_2 - CH_3 , $J_{\text{HH}} = 7.3$ Hz) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (DMSO- d_6): 119.4 (s, CF_3), 63.9 (s, N- CH_2 - CH_2 -), 63.3 (s, 2,5-pyrrole- CH_2), 47.8 (s, N CH_3), 25.2 (s, 3,4-pyrrole- CH_2), 21.5 (s, N- CH_2 - CH_2 - CH_2 - CH_3), 19.7 (s, N-(CH_2) $_2$ - CH_2 - CH_3), 14.1 (s, N-(CH_2) $_3$ - CH_3).

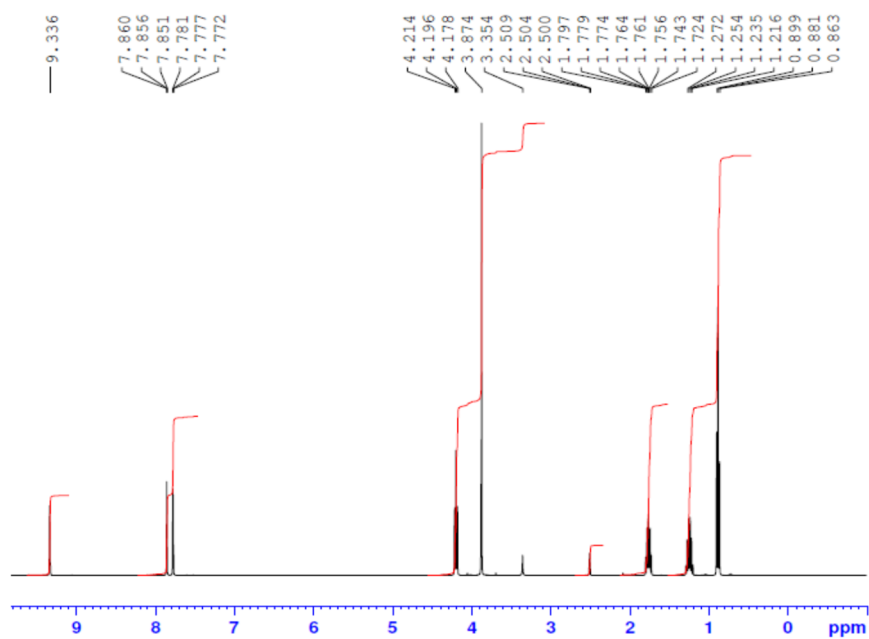


Figure A. 12 ^1H NMR spectrum of [bmim]Br in deuterated DMSO.

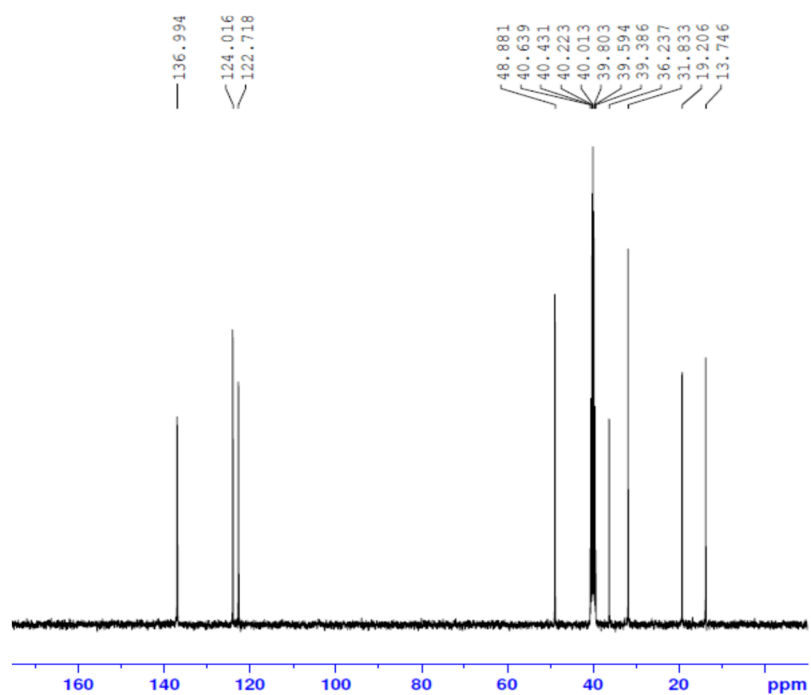


Figure A. 13 $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [bmim]Br in deuterated DMSO.



Figure A. 14 Mass spectrum of [bmim]Br.

[bmim]Br: ^1H NMR ($\text{DMSO}-d_6$): δ 9.33 (s, 1H, N_2CH), 7.86, 7.78 (m x 2, 2 x 1H, 2 x N-CH), 4.20 (t, 2H, N- CH_2 - CH_2 , $J_{\text{HH}} = 7.2$ Hz), 3.87 (s, 3H, N- CH_3), 1.76, 1.25 (m x 2, 2 x 2H, N- CH_2 - CH_2 - CH_2 - CH_3), 0.88 (t, 3H, - CH_2 - CH_3 , $J_{\text{HH}} = 7.3$ Hz) ppm. ^{13}C $\{^1\text{H}\}$ NMR ($\text{DMSO}-d_6$): δ 137.2 (N_2 -CH), 124.1, 122.7 (2 x N-CH), 48.8 (N- CH_2 - CH_2 - CH_2 - CH_3), 36.14 (N CH_3), 31.8 (N CH_2 - CH_2 - CH_2 - CH_3), 19.2 (N CH_2 - CH_2 - CH_2 - CH_3), 13.7 (N-(CH_2) $_2$ - CH_2 - CH_3) ppm. MS (ES, +ve mode): m/z (abundance) = 357 (31) $[(\text{bmim})_2\text{Br}]^+$, 139 (100) $[\text{bmim}]^+$.

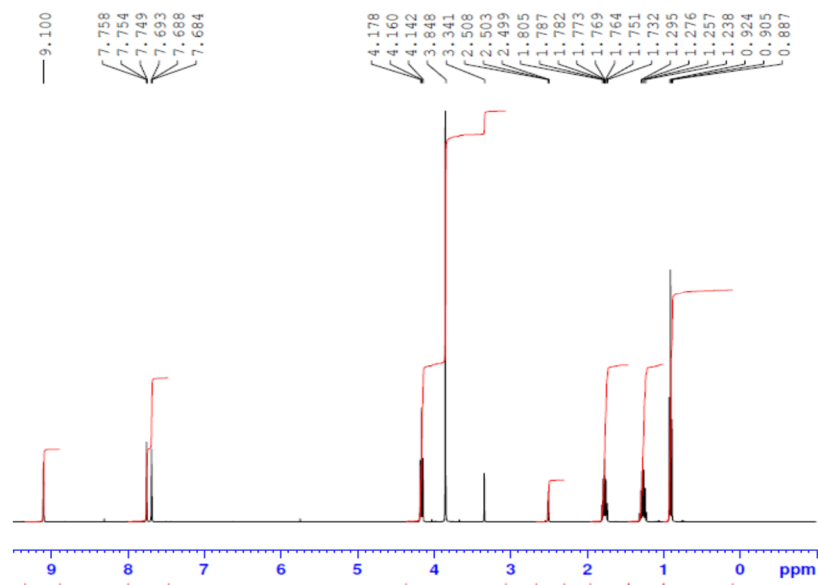


Figure A. 15 ^1H NMR spectrum of [bmim][NTf₂] in deuterated DMSO.

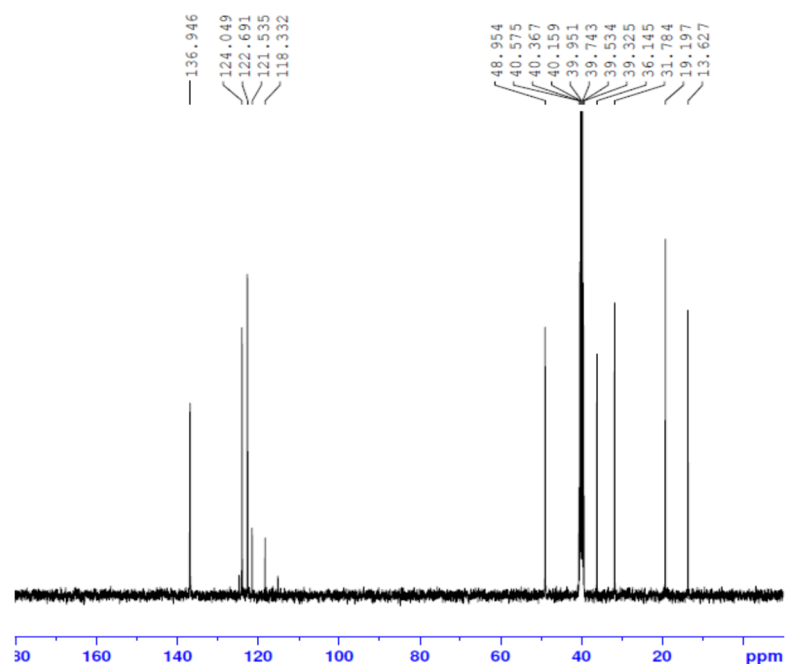


Figure A. 16 $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [bmim][NTf₂] in deuterated DMSO



Figure A. 17 Mass spectrum of [bmim][NTf₂].

[bmim][NTf₂]: ^1H NMR (DMSO-*d*₆): δ 9.33 (s, 1H, N₂CH), 7.86, 7.78 (m x 2, 2 x 1H, 2 x N-CH), 4.20 (t, 2H, N-CH₂-CH₂, $J_{\text{HH}} = 7.3$ Hz), 3.87 (s, 3H, N-CH₃), 1.76, 1.25 (m x 2, 2 x 2H, N-CH₂-CH₂-CH₃), 0.88 (t, 3H, -CH₂-CH₃, $J_{\text{HH}} = 7.4$ Hz) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (DMSO-*d*₆): δ 136.7 (N₂-CH), 124.06, 122.6 (2 x N-CH), 121.7 (CF₃) 48.9 (N-CH₂-CH₂-CH₂-CH₃), 36.1 (NCH₃), 31.7 (NCH₂-CH₂-CH₂-CH₃), 19.1 (NCH₂-CH₂-CH₂-CH₃), 13.5 (N-(CH₂)₂-CH₂-CH₃) ppm. MS (ES, +ve mode): m/z (abundance) = 558 (100) [(bmim)₂NTf₂]⁺, 139 (25) [bmim]⁺.

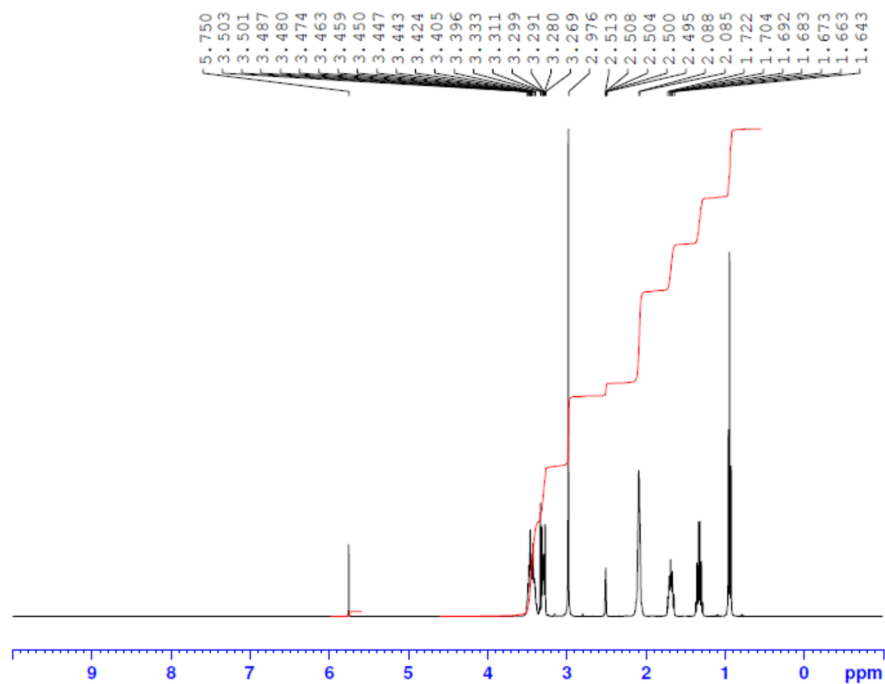


Figure A. 18 ^1H NMR spectrum of [bmpyr][NTf₂] in deuterated DMSO.

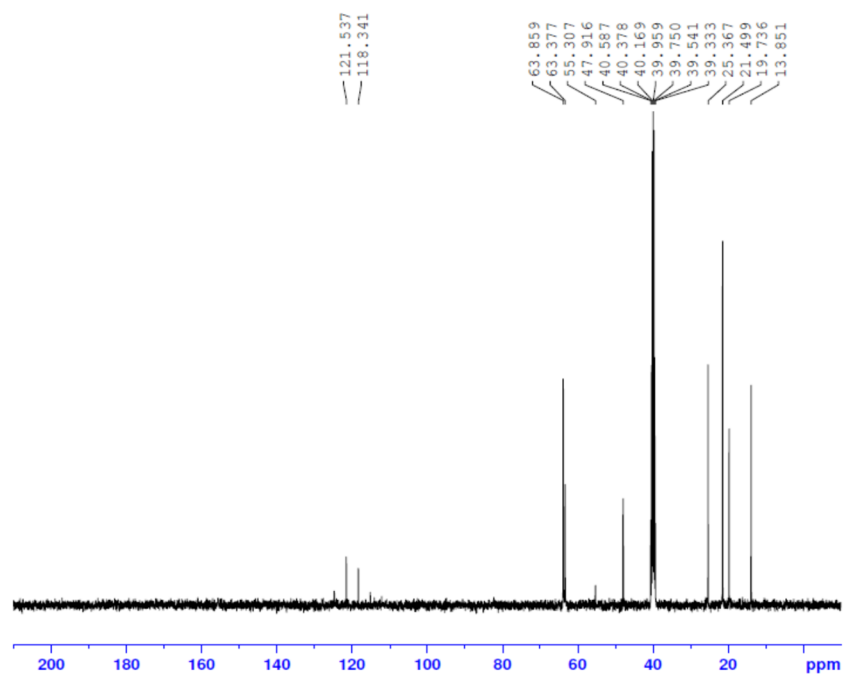


Figure A. 19 $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [bmpyr][NTf₂] in deuterated DMSO.

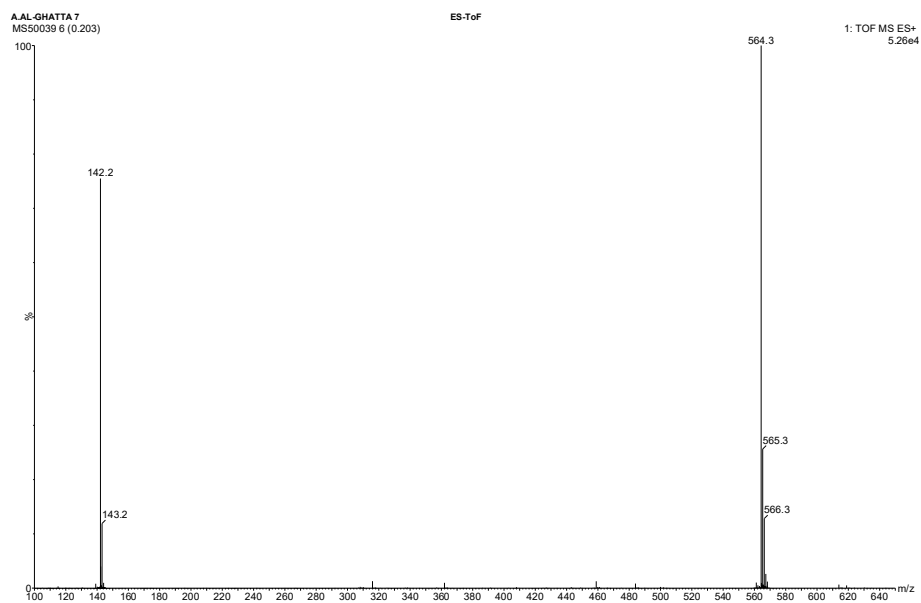


Figure A. 20 Mass spectrum of [bmpyr][NTf₂]

Ionic Liquid as Green Solvent for Separation of Furanic Compounds

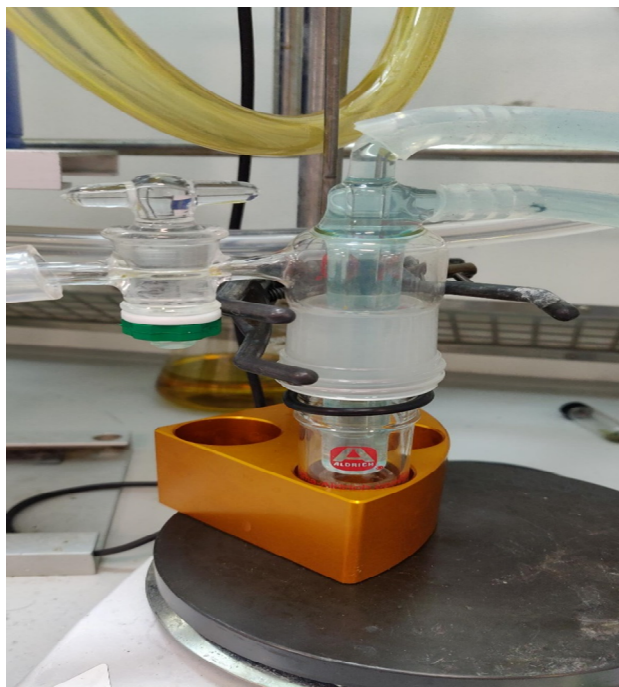


Figure A. 21 Cold finger apparatus for sublimation of DFF.



Figure A. 22 Sublimed DFF from the IL on the condenser tip (left) and collected DFF (right).



Figure A. 23 Comparison between the commercial DFF and the sublimed material (left) and comparison of the bulk IL after first sublimation and second sublimation (right).

Rapid High-Yield Fructose Dehydration to HMF in Mixtures of Water and the Non-Coordinating Ionic Liquid [bmim][OTf]

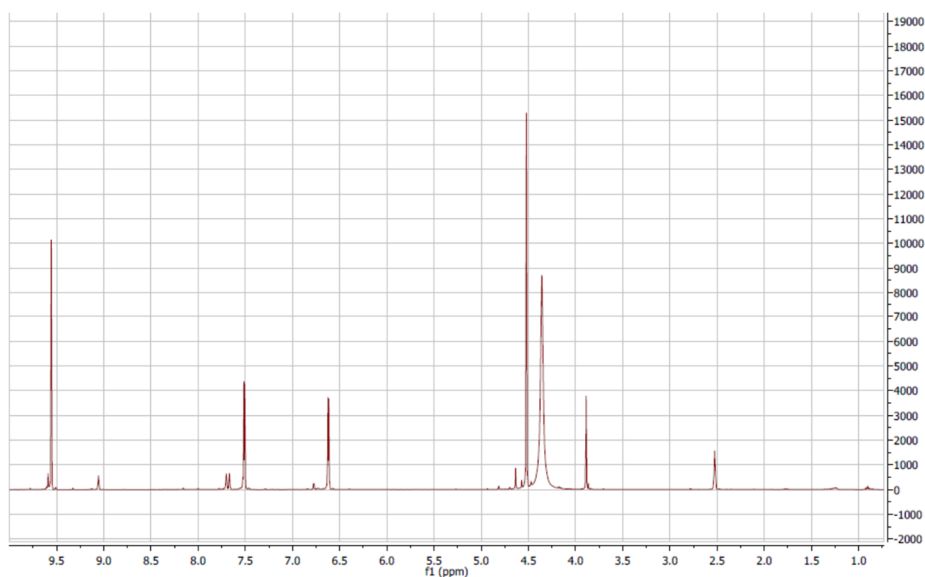


Figure A. 24 Crude 5-HMF product prior DCM washing with impurities in the furan region

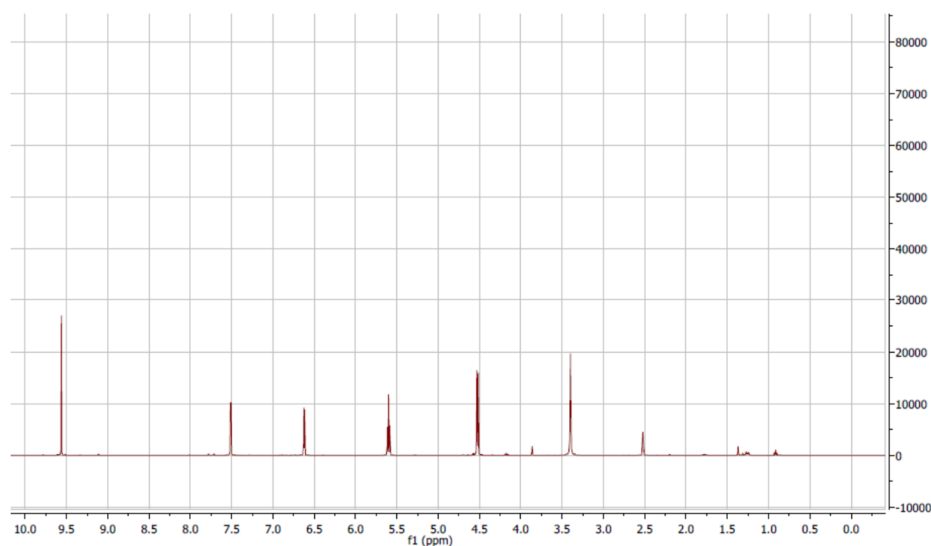


Figure A. 25 ¹H-NMR spectra for the purified 5-HMF after DCM washing

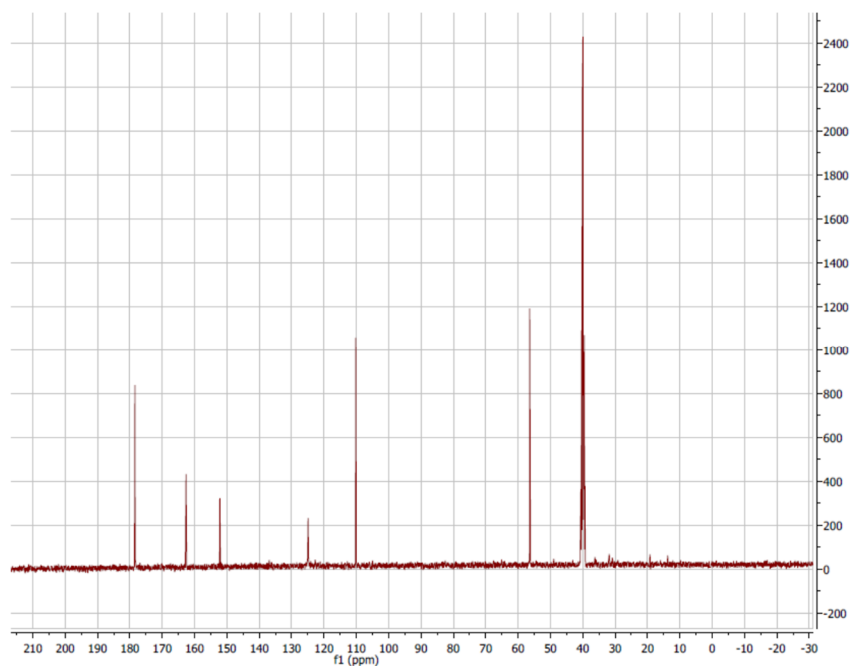


Figure A. 26 C-NMR spectra for the purified 5-HMF after DCM washing

5-HMF: ^1H NMR (DMSO-d_6): 9.56 (s, 1H, O=CH), 7.51 (d, 1H, H-furan), 6.62 (s, 1H, H-furan), 5.60 (t, 1H, $\text{CH}_2\text{-OH}$), 4.52 (d, $\text{CH}_2\text{-OH}$) . $^{13}\text{C}\{^1\text{H}\}$ NMR (DMSO-d_6): δ 178 (s, O=CH), 161, 151 (s, O-C-C furan), 123, 110 (s, C-furan), 57 (C-C-OH)

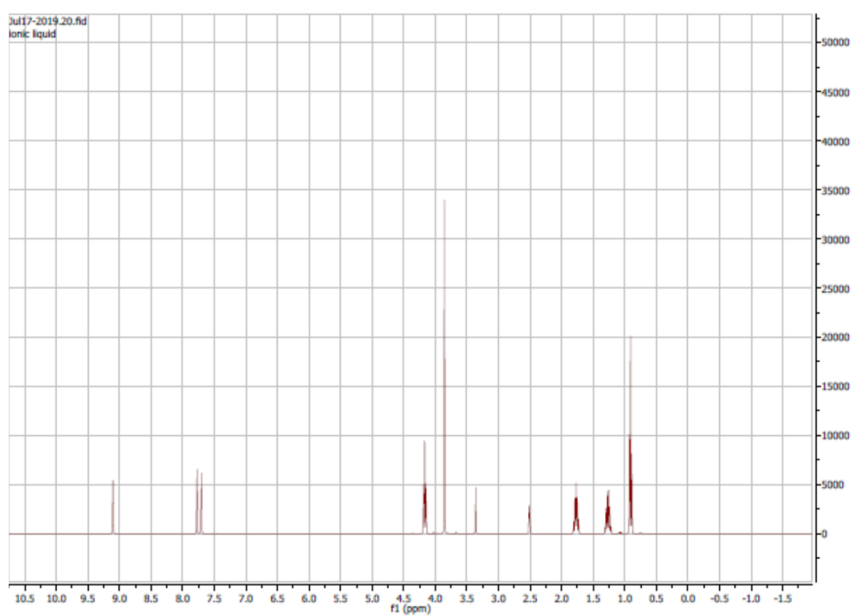


Figure A. 27 H-NMR of recovered ionic liquid [bmim][OTf]

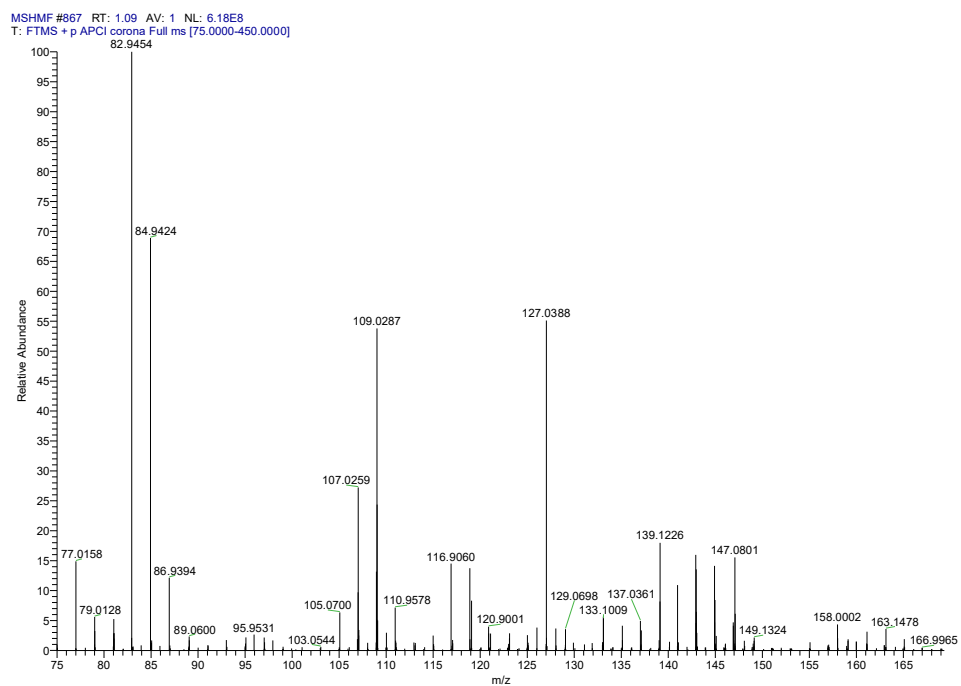


Figure A. 28 Mass spectra of isolated HMF

149 HMFNa⁺

139 Levelunic acid Na⁺

127 HMF H⁺

109 (HMF H⁺)-H₂O

83 Formic acid Na⁺

Catalytic Oxidation of 5-HMF into DFF in [bmim][OTf] with immobilized TEMPO-pyridine ionic liquid and CuCl

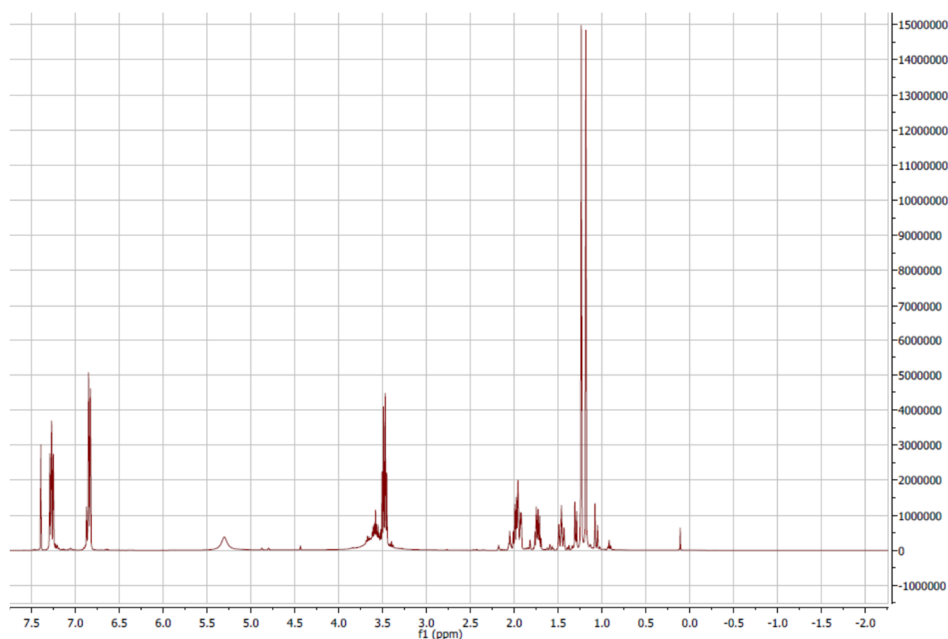


Figure A. 29 ${}^1\text{H}$ NMR spectrum of Intermediate A reduced with excess phenylhydrazine in deuterated CDCl_3 .

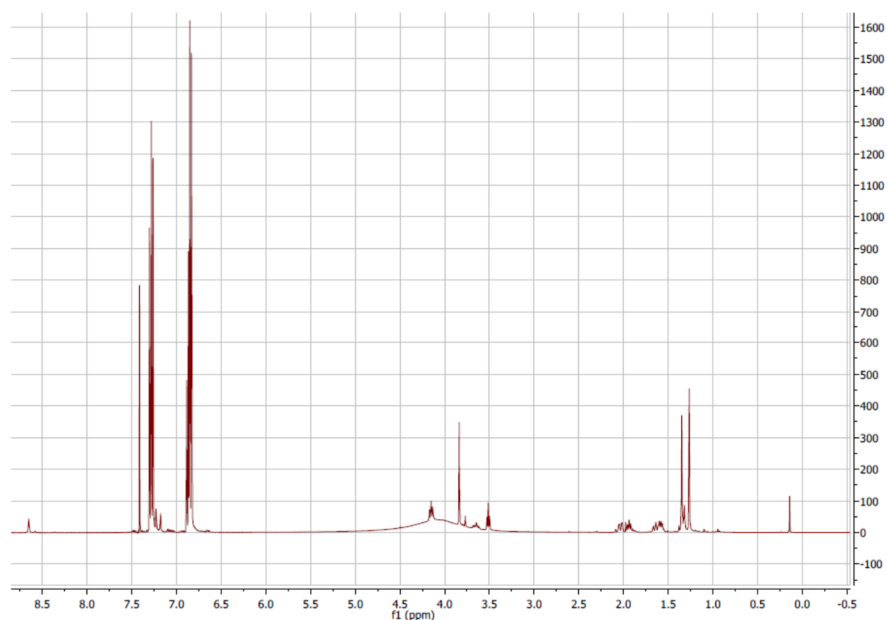


Figure A. 30 ${}^1\text{H}$ NMR spectrum of $[\text{TEMPO-bmim}][\text{NTf}_2]$ reduced with excess phenylhydrazine in deuterated CDCl_3 .

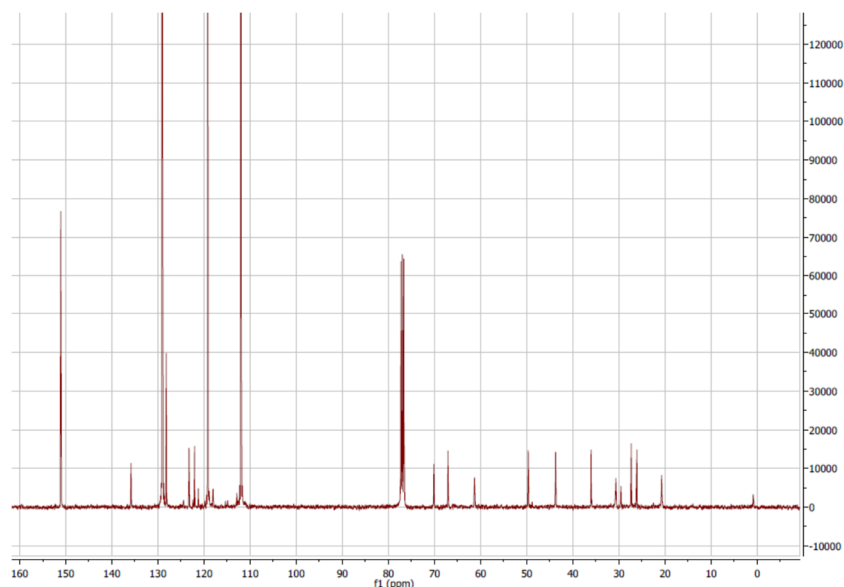


Figure A. $^{31}\text{C}\{^1\text{H}\}$ NMR spectrum of [TEMPO-bmim][NTf₂] reduced with excess phenylhydrazine in deuterated CDCl₃.

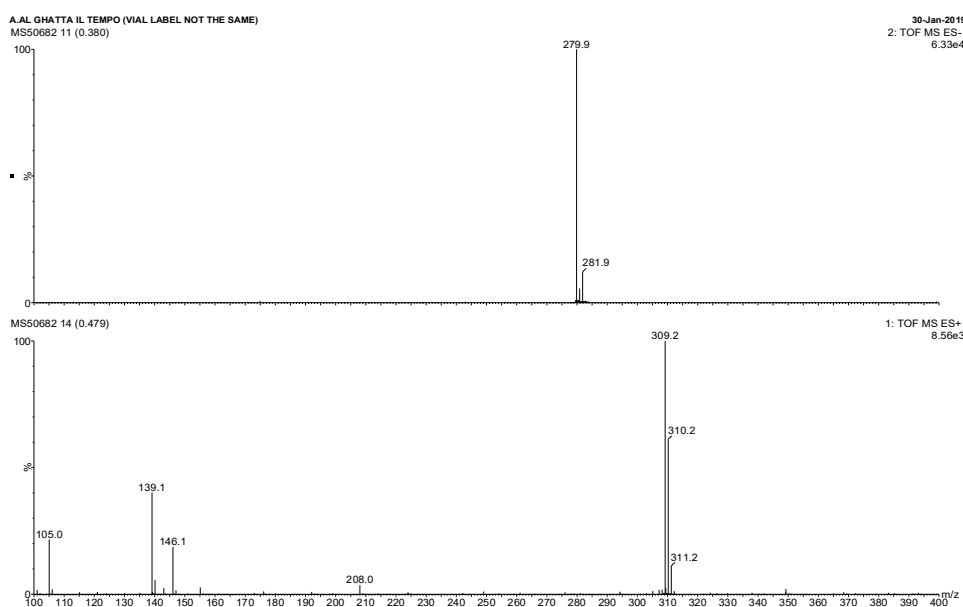


Figure A. 32 Mass spectrum of [TEMPO-bmim][NTf₂].

Intermediate A (reduced form, phenylhydrazine resonances omitted): ^1H NMR (400 MHz, CDCl₃): δ 1.18 (s, 6H, piperidine-Me), 1.24 (s, 6H, piperidine-Me), 1.46 (t, 2H, piperidine-CH, $J_{\text{HH}} = 11.8$ Hz), 1.69 - 1.77 (m, 2H, O-CH₂-CH₂-CH₂-CH₂-Br), 1.91 - 2.08 (m, 4H, O-CH₂-CH₂-CH₂-CH₂-Br, piperidine-CH), 3.44 - 3.63 (m, 5H, O-CH₂, BrCH₂, piperidine-CH) ppm.

[TEMPO-bmim][NTf₂] (reduced form, phenylhydrazine resonances omitted): ^1H NMR (400 MHz, CDCl₃): δ 1.26 (s, 6H, piperidine-Me), 1.35 (s, 6H, piperidine-Me), 1.53 - 2.12 (m, piperidine-CH; O-CH₂-CH₂-CH₂-CH₂-imidazolium; O-CH₂-CH₂-CH₂-CH₂-Br; piperidine-CH), 3.51 (t, 2H, imidazolium-

CH₂, $J_{\text{HH}} = 11.9$ Hz), 3.59 - 3.72 (m, 3H, O-CH₂, piperidine-CH), 3.84 (s, 3H, CH₃-imidazolium), 7.18 (m, 1H, CH-imidazolium), 7.22 (m, 1H, CH-imidazolium), 7.41 (s, 1H, C-CH-C) ppm. ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 137.1 (N₂CH), 123.0 – 121.0 (2 x NCH), 69.1 (N-CH₂-CH₂-CH₂-CH₂), 67.1 (-CH₂-CH₂-O), 61.0 (piperidine O-C-C), 49.6 (piperidine, C-C-N), 43.8 (piperidine, C-C-C), 36.1 (NCH₃), 26.1 - 27.2 (N-CH₂-CH₂-CH₂-CH₂), 20.9 (piperidine, 2 x C-CH₃) ppm. MS (ES, +ve mode): 309 (100) [TEMPO-bmim]⁺. MS (ES, -ve mode): 279 (100) [NTf₂]⁻.

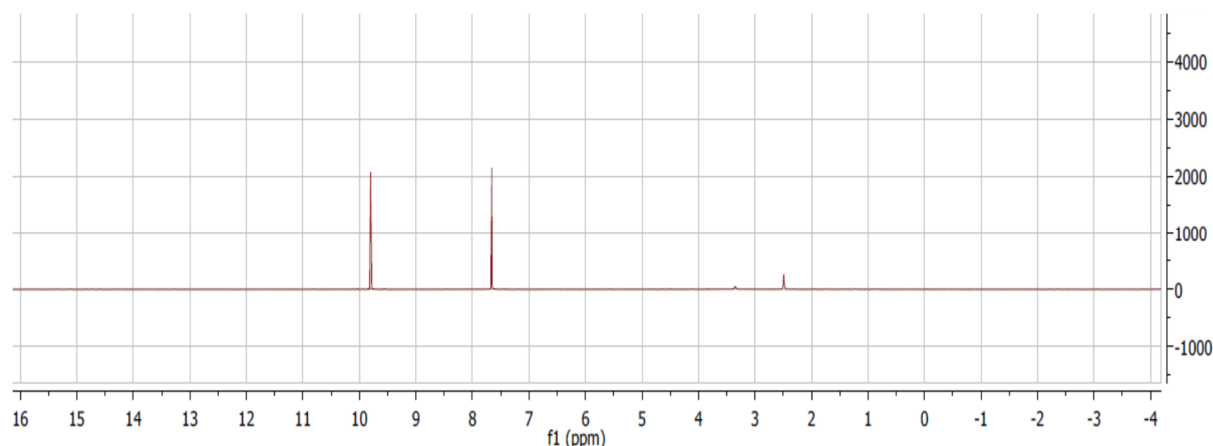


Figure A. 33 ¹H NMR spectrum of DFF in deuterated DMSO.

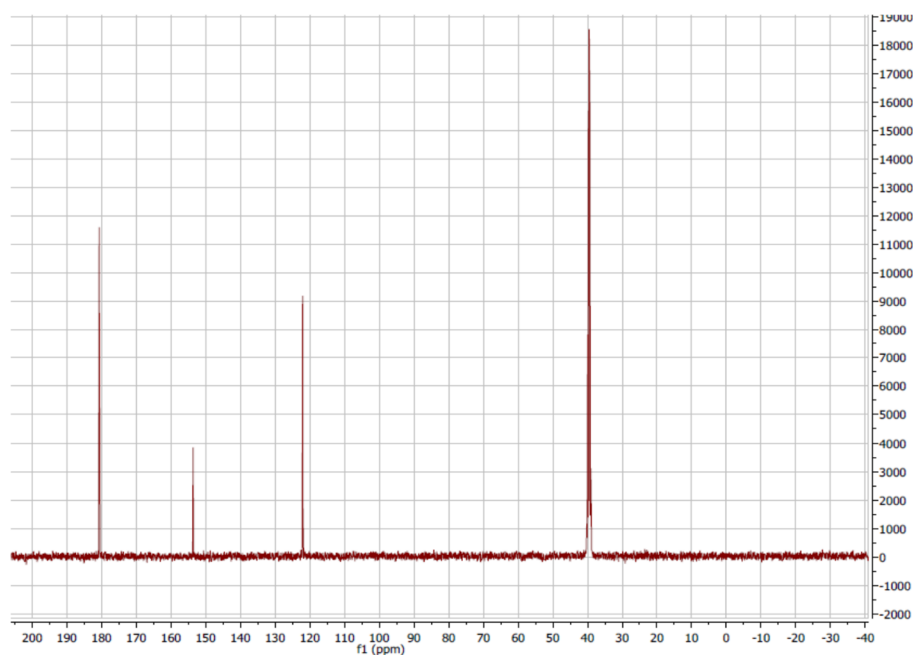


Figure A. 34 ¹³C{¹H} NMR spectrum of DFF in deuterated DMSO.

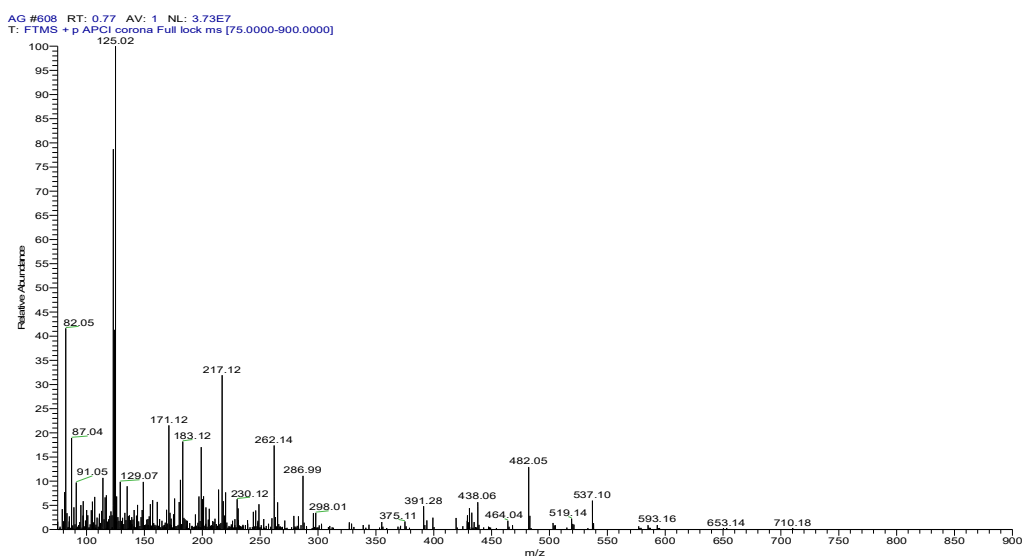


Figure A. 35 Mass spectrum of DFF.

DFF: ^1H NMR (400 MHz, DMSO) δ 9.78 (s, 2H, CH=O), 7.64 (s, 2H, furan CH) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO) δ 121.9 (furan C=C), 154.0 (O=C), 180.7 (O=C) ppm. MS (ES, +ve mode): m/z 125 (100) $[\text{M}+\text{H}]^+$.

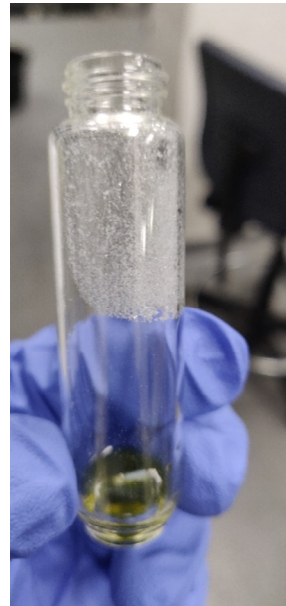
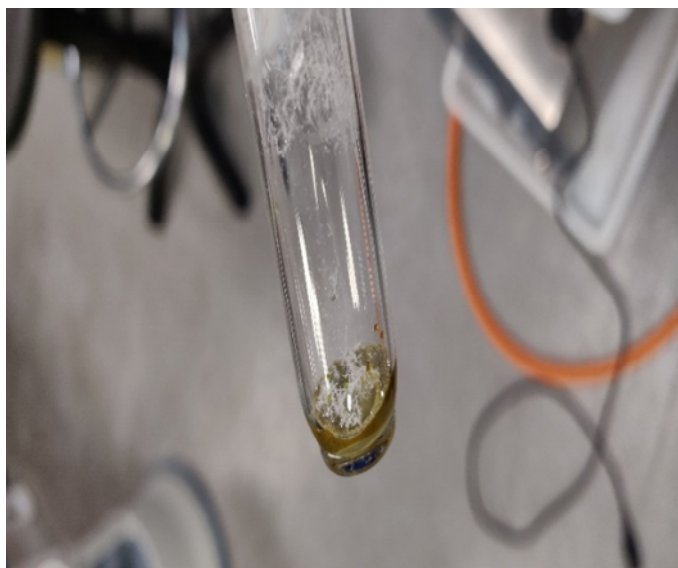


Figure A. 36 On the left, photograph of the reaction mixture after 6 h showing sublimed DFF (white) while further material precipitates from the reaction mixture. On the right, DFF after vacuum was applied for 6 h at 80°C.

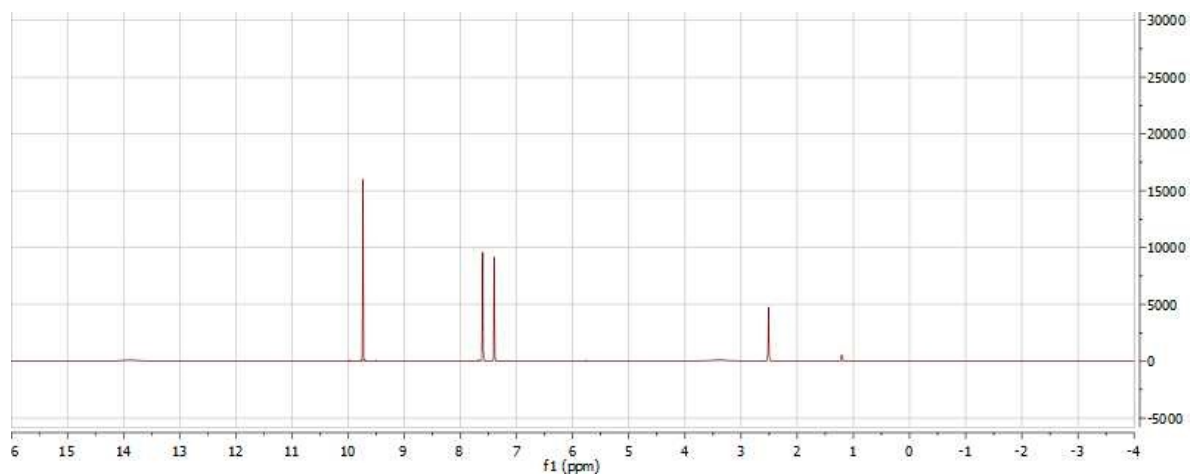


Figure A. 37 ^1H NMR spectrum of FFCA in deuterated DMSO.

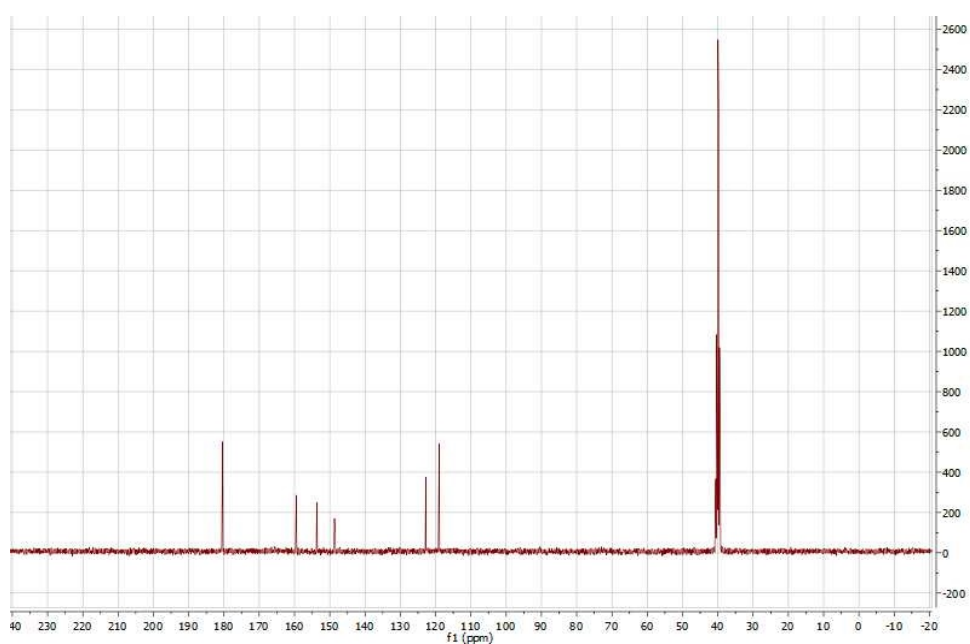


Figure A. 38 $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of FFCA in deuterated DMSO.

FFCA: ^1H NMR (400 MHz, DMSO) δ 9.73 (s, 1H, $\text{CH}=\text{O}$), 7.60 - 7.40 (d, 2 x 1H, 2 x C- $\text{CH}=\text{CH}-\text{C}$, $J_{\text{HH}}=7.4$ Hz) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO) δ 193.3 (O= $\text{CH}-\text{C}$), 159.5 - 153. (2 x C- $\text{CH}=\text{CH}-\text{C}$), 149.0 ($-\text{COOH}$), 122.7-118.9 (2 x C- $\text{C}=\text{O}$) ppm. MS (ES, +ve mode): m/z 141 (100) $[\text{M}+\text{H}]^+$.

Biorenewable Anionic Surfactants as Valuable Replacement of Current Detergent Formulations

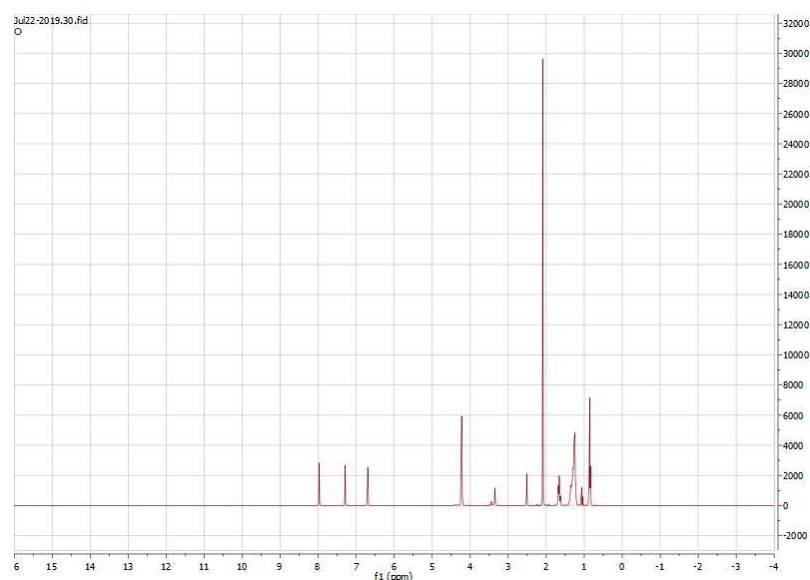


Figure A. 39 ^1H -NMR octyl furoate

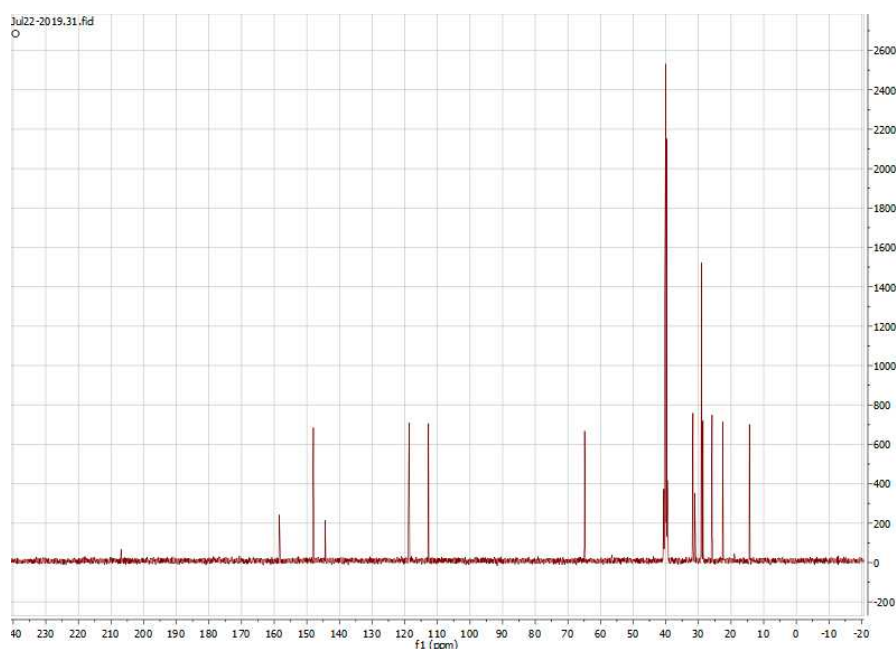


Figure A. 40 ^{13}C -NMR octyl furoate

Octyl Furoate: ^1H NMR ($\text{DMSO}-d_6$): δ 8 (m, $-\text{C}-\underline{\text{CH}}-\text{O}-$), 7.3, 6.7 (m x 2, 2 x 1H, 2 x $\text{C}-\underline{\text{CH}}-\text{C}$), 4.23 (t, 2H, $\text{O}-\underline{\text{CH}}_2-\text{CH}_2$, $J_{\text{HH}} = 6.6$ Hz), 1.66, 1.4-1.8 (m, CH_2 alkyl chain), 0.86 (m, CH_2-CH_3). $^{13}\text{C}\{^1\text{H}\}$

NMR (DMSO- d_6): δ 159.9 (C=O), 147.8 (CH-C-C=O), 144.6 (O-CH-CH), 119, 113 (-C-CH-CH-C), 65 (O-CH₂-CH₂), 31.7,31.1,29.1,28.7,25.8,22.7 (6 X C, C-CH₂-C), 14.4 (-CH₂-CH₃) ppm.

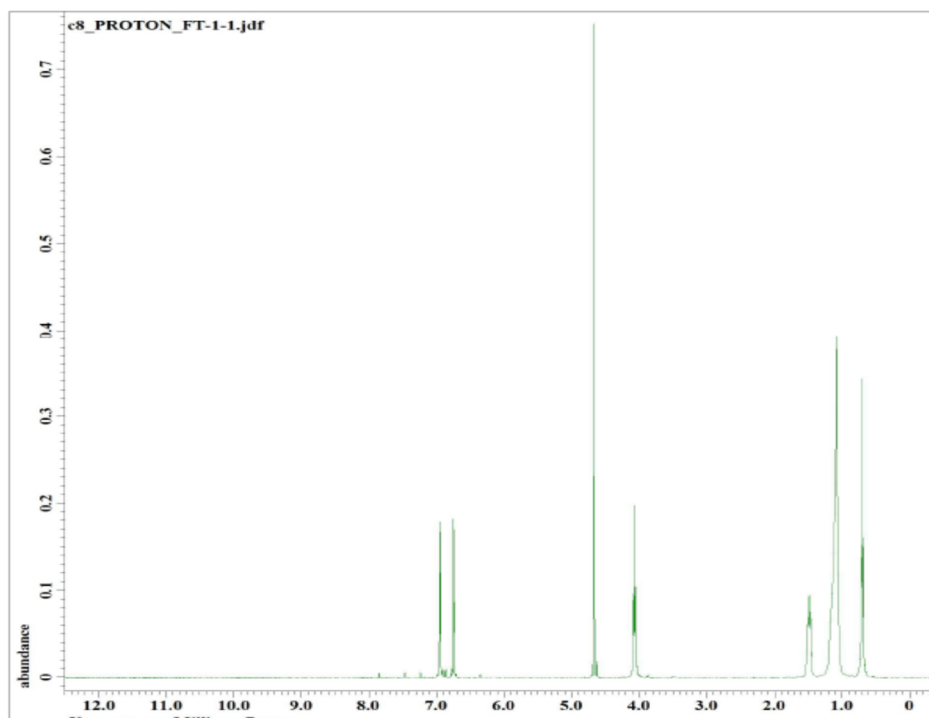


Figure A. 41 ¹H-NMR Sulphonated Octyl Furoate

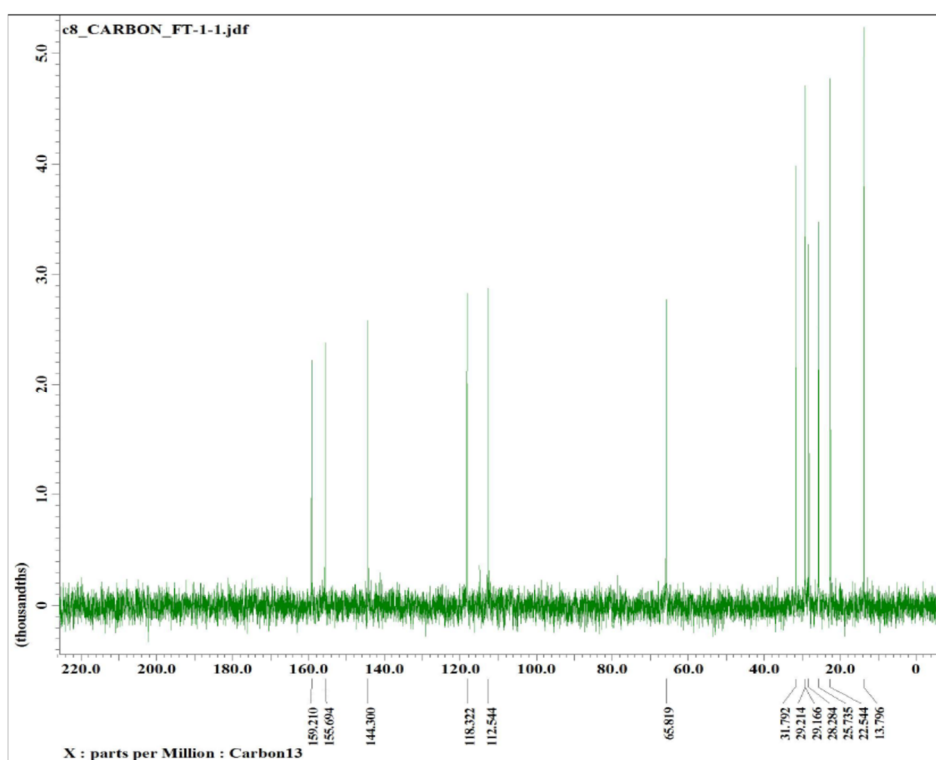


Figure A. 42 ¹³C-NMR Sulphonated Octyl Furoate

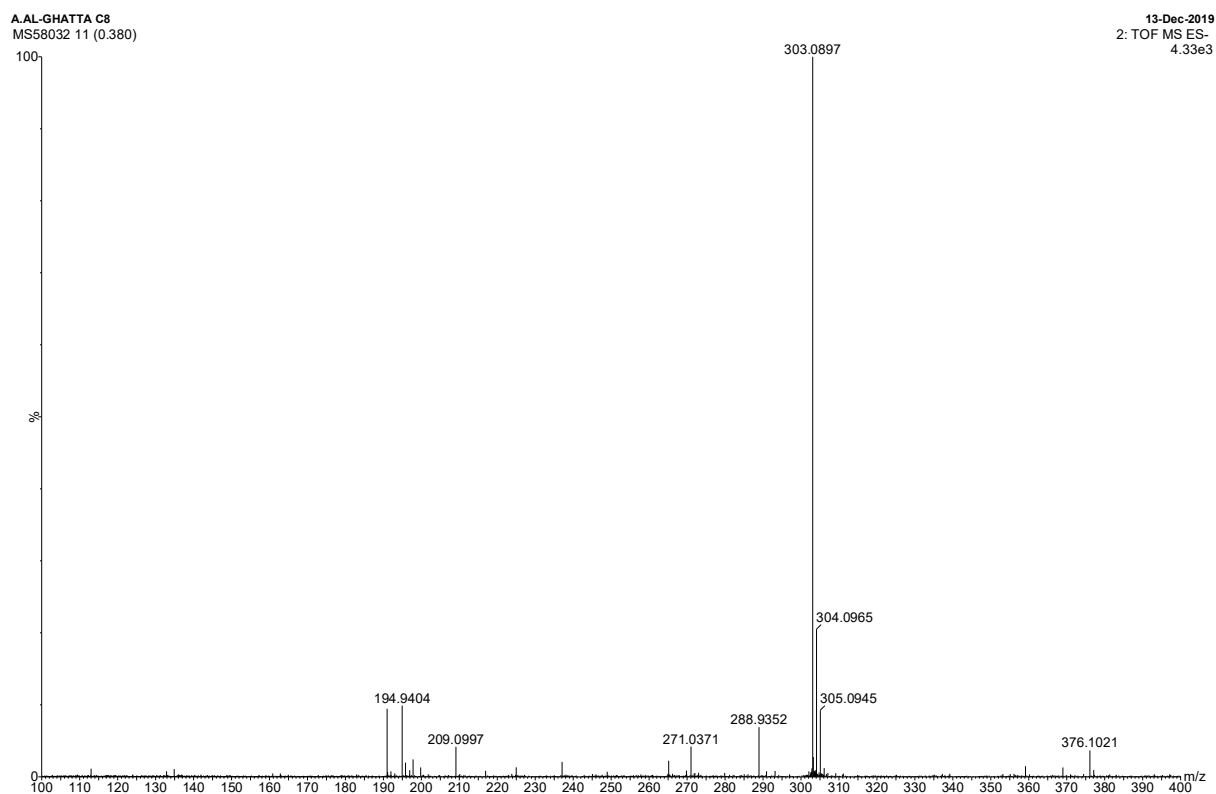


Figure A. 43 Mass spectrum Sulfonated Octyl Furoate

Sulphonated octyl furoate.: ^1H NMR (D_2O): 6.9, 6.7 (m x 2, 2 x 1H, 2 x C-CH-C), 4.2 (t, 2H, O-CH₂-CH₂, J_{HH} = 6.6 Hz), 1.6, 1.34-1.0 (m, CH₂ alkyl chain), 0.8 (m, CH₂-CH₃). ^{13}C { ^1H } NMR (D_2O): δ 158.5 (C=O), 155.8 (O-CH-CH), 144.5 (CH-C-C=O), 118.2-112.2 (-C-CH-CH-C), 66.1 (O-CH₂-CH₂), 31.7, 29.2, 29.1, 28.3, 25.7, 22.6 (6 X C, C-CH₂-C), 13.8 (-CH₂-CH₃) ppm.

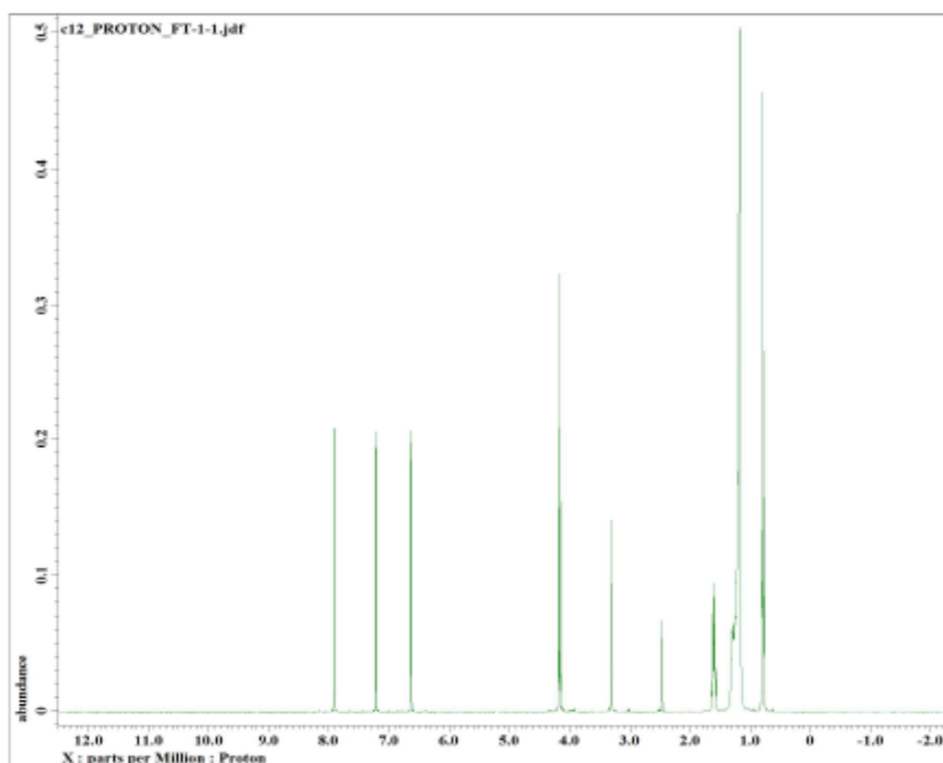


Figure A. 44 ¹H-NMR dodecyl furoate

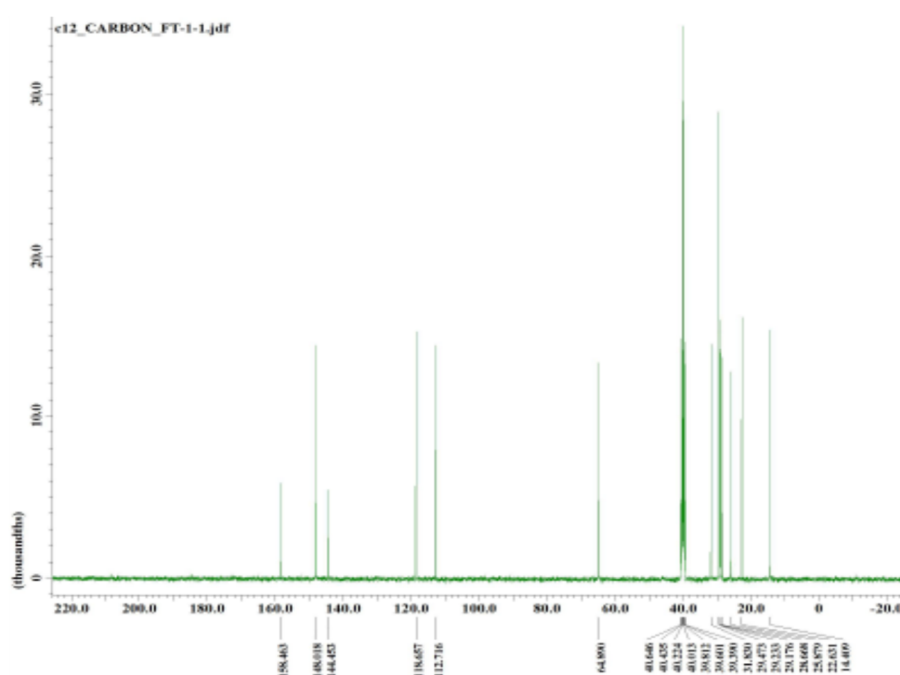


Figure A. 45 ¹³C-NMR dodecyl furoate

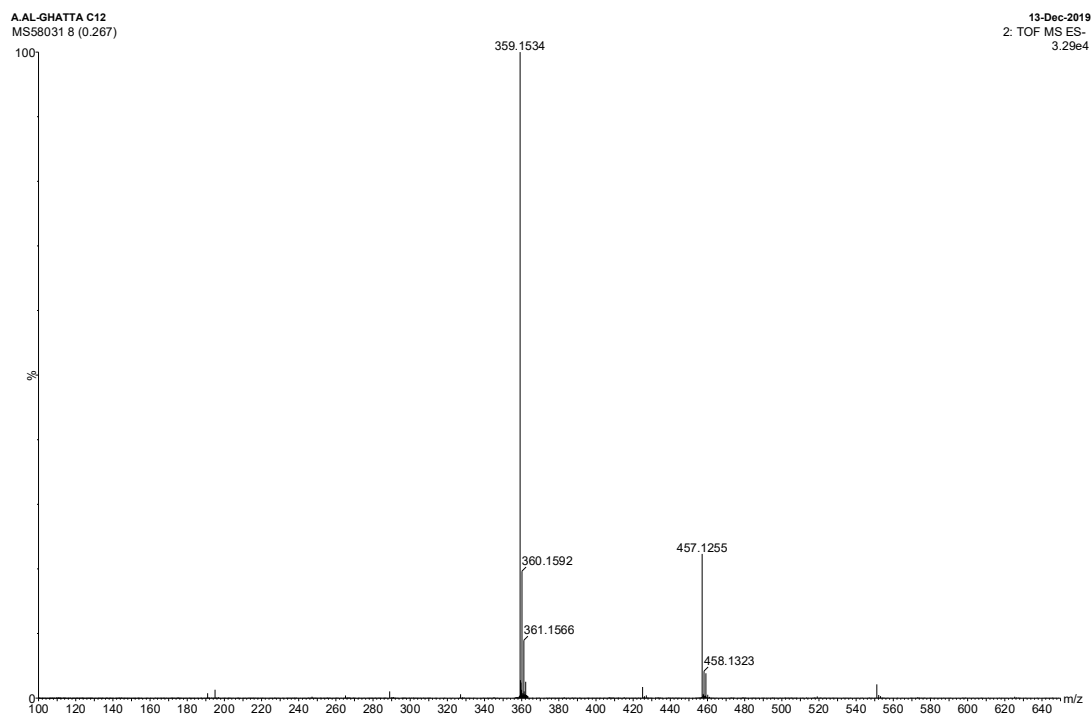


Figure A. 46 Mass spectrum Sulfonated Dodecyl Furoate

Dodecyl Furoate.: ^1H NMR (DMSO-d_6): δ 7.9 (m, $-\text{C}-\underline{\text{CH}}-\text{O}-$), 7.2, 6.7 (m x 2, 2 x 1H, 2 x $\text{C}-\underline{\text{CH}}-\text{C}$), 4.23 (t, 2H, $\text{O}-\underline{\text{CH}_2}-\text{CH}_2$, $J_{\text{HH}}=6.6$ Hz), 1.66, 1.4-1.8 (m, CH_2 alkyl chain), 0.86 (m, CH_2-CH_3). $^{13}\text{C}\{^1\text{H}\}$ NMR (DMSO-d_6): δ 159.9 ($\text{C}=\text{O}$), 148.2 ($\text{CH}-\underline{\text{C}}-\text{C}=\text{O}$), 144.5 ($\text{O}-\underline{\text{CH}}-\text{CH}$), 119, 112.5 ($-\text{C}-\underline{\text{CH}}-\underline{\text{CH}}-\text{C}$), 65.7 ($\text{O}-\underline{\text{CH}_2}-\text{CH}_2$), 31.8, 29.5, 29.2, 29.7, 28.8, 25.9, 22.6 (8 X C, $\text{C}-\underline{\text{CH}_2}-\text{C}$), 14.1 ($-\text{CH}_2-\underline{\text{CH}_3}$) ppm.

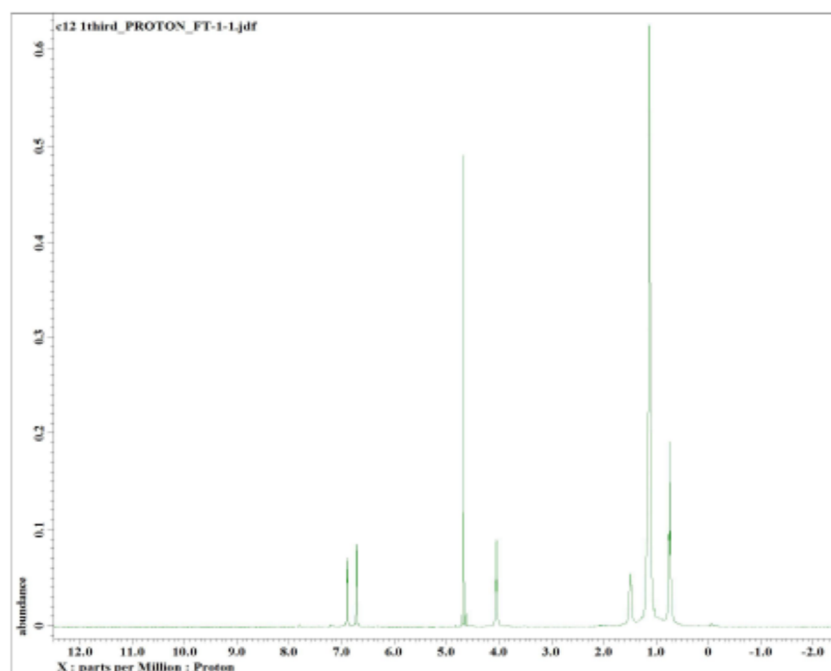


Figure A. 47 ^1H -NMR Sulphonated dodecyl furoate

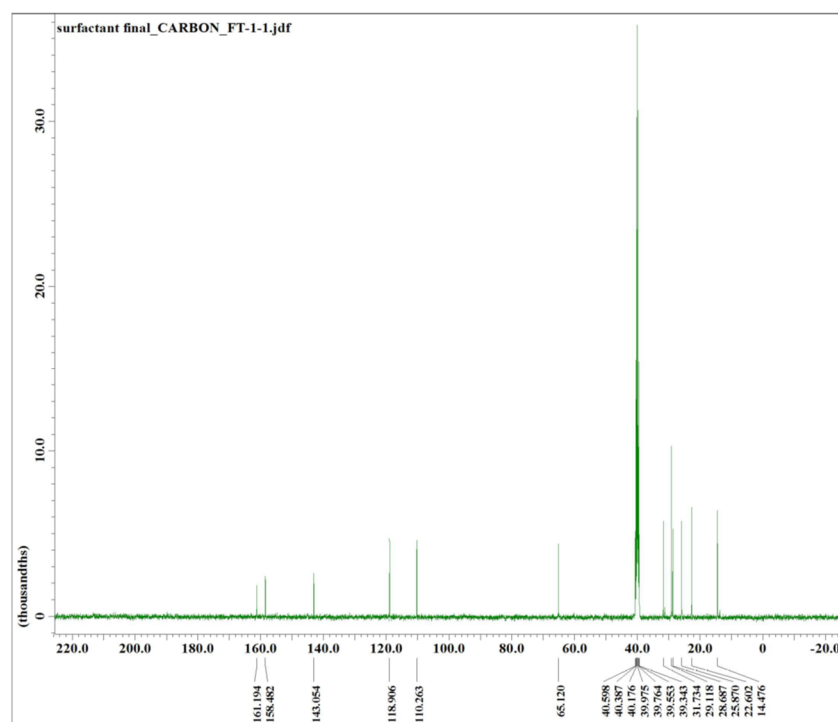


Figure A. 48 ^{13}C -NMR Sulphonated Dodecyl Furoate

Sulphonated Dodecyl Furoate: ^1H NMR (D_2O): δ 6.9, 6.7 (m x 2, 2 x 1H, 2 x C-CH-C), 4.1 (t, 2H, O-CH₂-CH₂, J_{HH} = 6.6 Hz), 1.52, 1.2-1.1 (m, CH₂ alkyl chain), 0.7 (m, CH₂-CH₃).

$^{13}\text{C}\{^1\text{H}\}$ NMR (D_2O): δ 158.5 (C=O), 155.8 (O-CH-CH), 144.5 (CH-C-C=O), 118.2-112.2 (-C-CH-CH-C), 66.1 (O-CH₂-CH₂), 31.8, 29.5, 29.2, 29.7, 28.8, 25.9, 22.6 (8 X C, C-CH₂-C), 13.8 (-CH₂-CH₃) ppm.

MS (ES, -ve mode): m/z (abundance) = 359.1534 ($\text{C}_{17}\text{H}_{27}\text{O}_6\text{S}^-$ 100%)

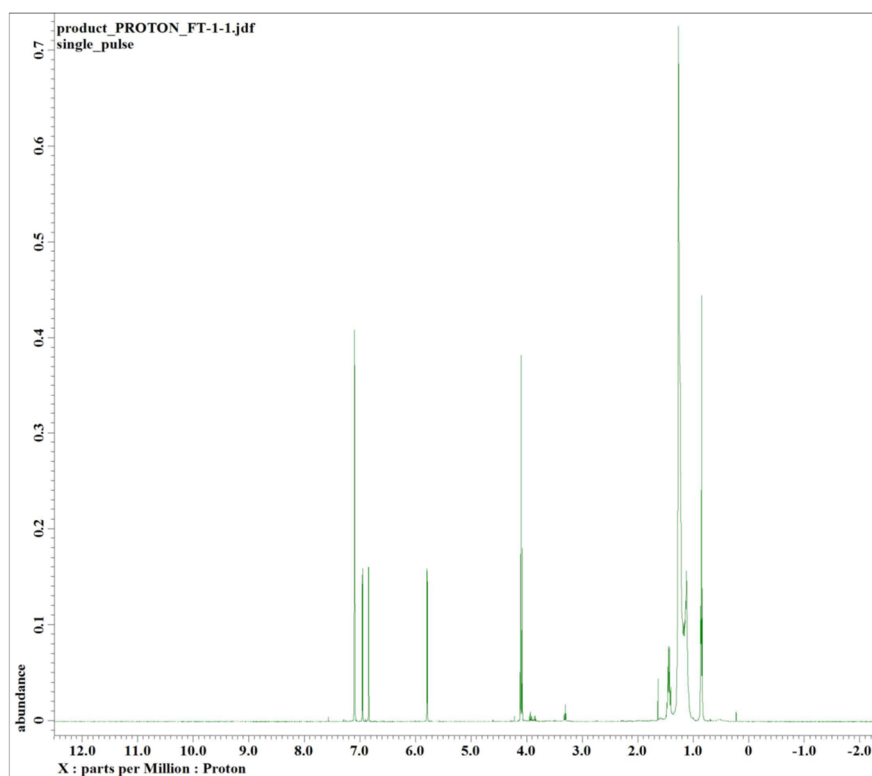


Figure A. 49 ^1H -NMR Hexadecyl Furoate

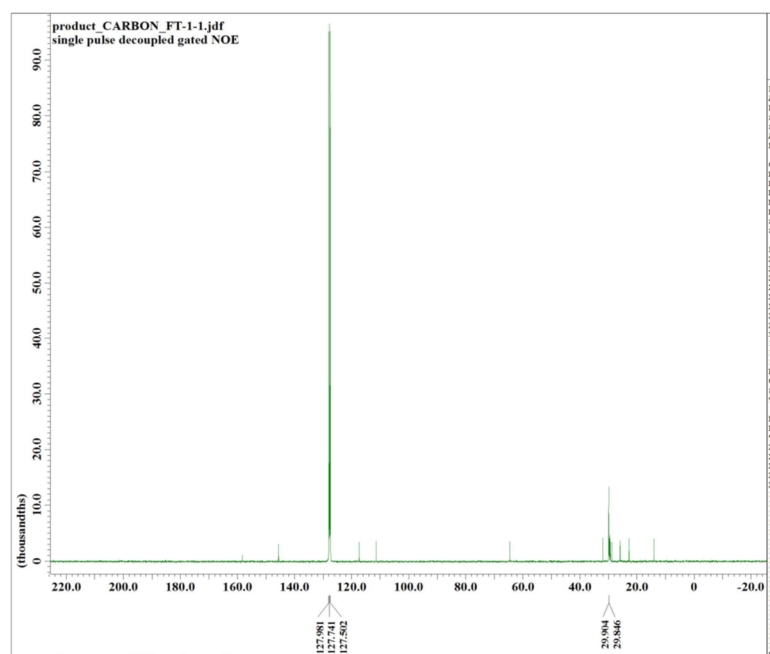


Figure A. 50 ^{13}C -NMR hexadecyl Furoate

Hexadecyl Furoate.: ^1H NMR (benzene- d_6): δ 7.0, 6.9 (m x 2, 2 x 1H, 2 x C-CH-C), 5.8 (m, -C-CH-O-), 4.1 (t, 2H, O-CH $_2$ -CH $_2$, J_{HH} = 6.7 Hz), 1.44, 1.37-1.05 (m, CH $_2$ alkyl chain), 0.85 (m, CH $_2$ -CH $_3$).
 $^{13}\text{C}\{^1\text{H}\}$ NMR (benzene- d_6): δ 158.5 (C=O), 145.7 (CH-C=O), 145.5 (O-CH-CH), 117, 111 (-C-CH-CH-C), 64.4 (O-CH $_2$ -CH $_2$), 32, 29.9-29.3, 28.8, 26, 23 (6 X C, C-CH $_2$ -C), 14.1 (-CH $_2$ -CH $_3$) ppm.

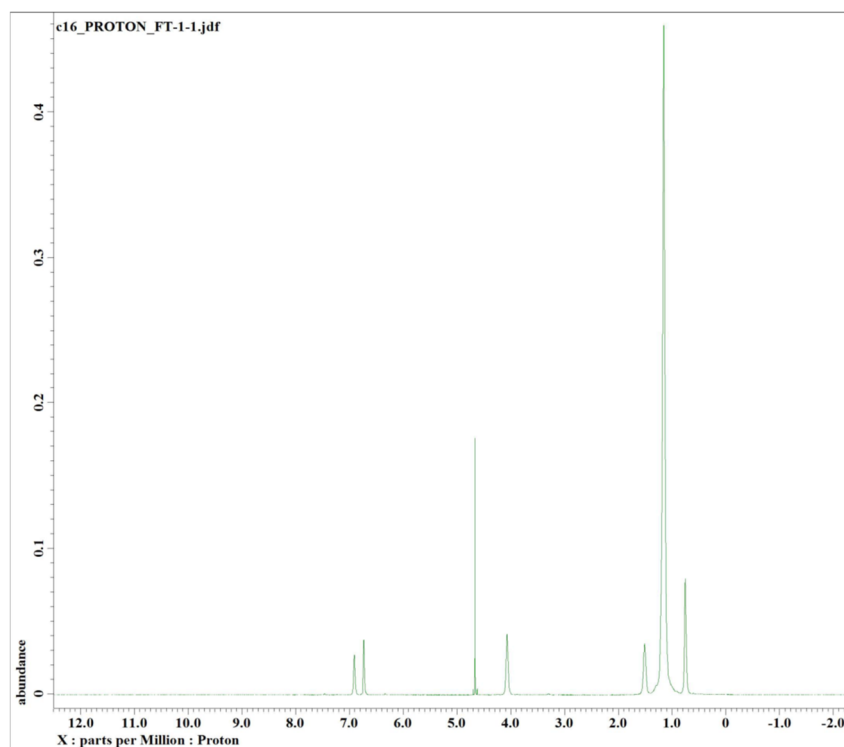


Figure A. 51 ^1H -NMR Sulphonated hexadecyl furoate

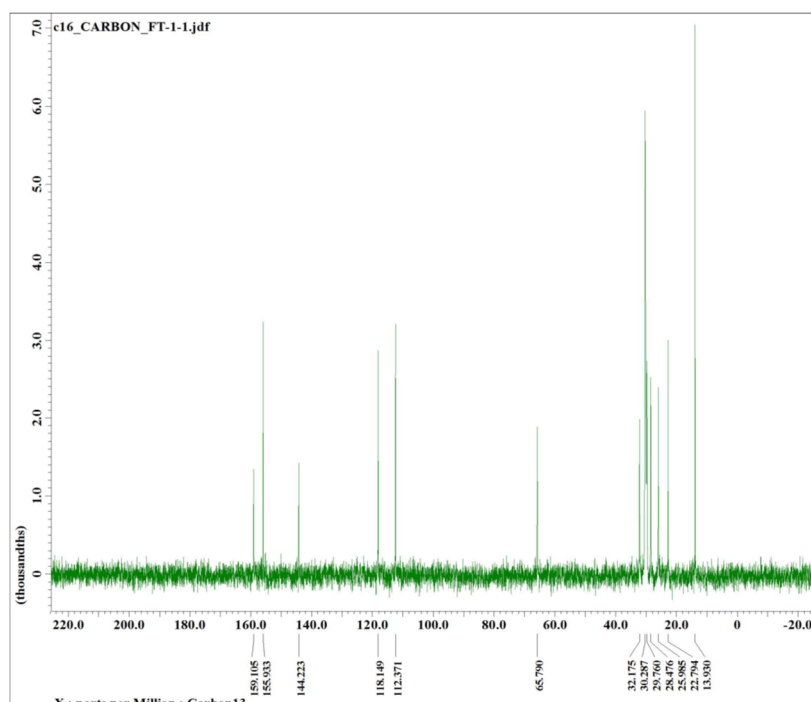


Figure A. 52 C-NMR sulphonated hexadecyl furoate

Sulphonated Hexadecyl Furoate.: ^1H NMR (D_2O): δ 6.9, 6.7 (m x 2, 2 x 1H, 2 x C-CH-C), 4.1 (t, 2H, O-CH₂-CH₂, J_{HH} = 6.4 Hz), 1.54, 1.26-0.95 (m, CH₂ alkyl chain), 0.8 (m, CH₂-CH₃). $^{13}\text{C}\{^1\text{H}\}$ NMR (D_2O): δ 159.5 (C=O), 156.5 (O-CH-CH), 144.6 (CH-C-C=O), 118.9-112.9 (-C-CH-CH-C), 66.1 (O-CH₂-CH₂), 32.2, 31-29.3, 28.5, 26, 22.8 (10 X C, C-CH₂-C), 13.8 (-CH₂-CH₃) ppm.