Acid-catalysed conversion of cellulosic biomass into value added small molecules

Thesis submitted in fulfilment of the requirements
for the degree Doctor of Philosophy
at
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Faculty of Science
School of Mathematical and Physical Sciences
by
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Certificate of original authorship

I, Iurii Bodachivskyi declare that this thesis, is submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the Faculty of Science at the University of Technology Sydney.

This thesis is wholly my own work unless otherwise referenced or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

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Statement and list of papers

This *thesis by compilation* originates from the published and accepted works.

1. Bodachivskyi, I.; Kuzhiumparambil, U.; Williams, D.B.G. Acid-catalyzed conversion of carbohydrates into value-added small molecules in aqueous media and ionic liquids. *ChemSusChem* **2018**, *11*, 642–660.
2. Bodachivskyi, I.; Kuzhiumparambil, U.; Williams, D.B.G. A systematic study of metal triflates in catalytic transformations of glucose in water and methanol: identifying the interplay of Brønsted and Lewis acidity. *ChemSusChem* **2019**, *12*, 3263–3270.
3. Bodachivskyi, I.; Kuzhiumparambil, U.; Williams, D.B.G. Metal triflates are tunable acidic catalysts for high yielding conversion of cellulosic biomass into ethyl levulinate. *Fuel Process. Technol.* **2019**, *195*, 106159.
4. Bodachivskyi, I.; Kuzhiumparambil, U.; Williams, D.B.G. Acid-catalysed conversion of carbohydrates into furan-type molecules in zinc chloride hydrate. *ChemPlusChem* **2019**, *84*, 352–357.
5. Bodachivskyi, I.; Kuzhiumparambil, U.; Williams, D.B.G. The role of the molecular formula of $ZnCl_2 \cdot nH_2O$ on its catalyst activity: a systematic study of zinc chloride hydrates in the catalytic valorisation of cellulosic biomass. *Catal. Sci. Technol.* **2019**, *9*, 4693–4701.
6. Bodachivskyi, I.; Kuzhiumparambil, U.; Williams, D.B.G. Towards furfural from the reaction of cellulosic biomass in zinc chloride hydrate solvents. *Ind. Crops Prod.* **2020**, *146*, 112179.
7. Bodachivskyi, I.; Kuzhiumparambil, U.; Williams, D.B.G. High yielding acid-catalysed hydrolysis of cellulosic polysaccharides and native biomass into low molecular weight sugars in mixed ionic liquid systems. *ChemistryOpen* **2019**, *8*, 1316−1324.
8. Bodachivskyi, I.; Kuzhiumparambil, U.; Williams, D.B.G. Catalytic valorization of native biomass in a deep eutectic solvent: a systematic approach towards high yielding reactions of polysaccharides. *ACS Sustainable Chem. Eng.* **2020**, *8*, 678–685.
9. Bodachivskyi, I.; Page, C.J.; Kuzhiumparambil, U.; Hinkley, S.F.R; Sims, I.M.; Williams, D.B.G. Dissolution of cellulose: are ionic liquids innocent or non-innocent solvents?. *ACS Sustainable Chem. Eng.* **2020**, *8*, 10142–10150.
10. Bodachivskyi, I.; Kuzhiumparambil, U.; Williams, D.B.G. Chapter 2, Biomass processing via acid catalysis. In *Biomass valorization: sustainable methods for the production of chemicals*; Ravelli, D.; Samori, C., Eds.; Wiley. *Accepted*.

Statement of contribution of authors

Iurii Bodachivskyi (graduate research student) developed methodology, conducted research, including experimental work, data collection and data analysis (except for size exclusion chromatography-analysis), and drafted all manuscripts. Prof. D. Bradley G. Williams (principal supervisor) and Dr Unnikrishnan Kuzhiumparambil (co-supervisor) supervised Iurii Bodachivskyi's research activities, provided conceptual advice, and revised all manuscripts. Charlotte J. Page, Dr Simon F. R. Hinkley and Dr Ian M. Sims (co-investigators) performed size exclusion chromatography-analysis and revised the manuscript No. 9, 'Dissolution of cellulose: are ionic liquids innocent or non-innocent solvents?'

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Abstract

Acid-catalysed conversion of carbohydrates into organic building block molecules is a promising way to create renewable replacements for fossil fuel-based products. Despite this promise, it is presently not known how to usefully and economically convert native non-food-competitive cellulosic materials into sustainable carbon zero fuels and chemicals in high yields and with low losses. With the aim to remove the blockage towards the biorefinery, this project systematically studies the acid-catalysed transformation of cellulosic (poly)carbohydrates and provides innovative methods to efficiently convert raw, unrefined biomass into value added derivative products.

To explore catalytic reactions of cellulosic polysaccharides, this work starts with model transformations of monomer glucose under the action of Lewis acidic metal trifluoromethanesulfonates (metal triflates), Brønsted acids or combined Lewis/Brønsted acid catalysts in water and methanol. The work underscores the notion that metal triflates are highly tunable catalysts, which under optimised conditions can selectively convert glucose into disaccharides and oligosaccharides, fructose, methyl glycosides, or methyl levulinate. The tunable acidic catalyst systems are further employed in the high-yielding transformation of microcrystalline cellulose into ethyl levulinate in ethanol. The pretreatment of raw and unrefined cellulosic biomass with a biobased deep eutectic solvent affords similarly efficient transformation thereof into ethyl levulinate.

In parallel, the project interrogates the valorisation of cellulosic biomass in ionic liquids. Firstly, it researches zinc chloride hydrates with a molecular formula $ZnCl_2 \cdot nH_2O$ (n = 2.5–4.5) as solvent-catalyst media for the production of low molecular weight saccharides and furan type molecules. It defines the preferred reaction conditions to select furyl hydroxymethyl ketone and furfural, or low molecular weight saccharides and 5-(hydroxymethyl)furfural, from the processing of cellulosic materials. In addition, the work employs a co-solvent system, comprising 1-butyl-3-methylimidazolium chloride and the deep eutectic solvent choline chloride/oxalic acid for the selective depolymerisation of cellulosic biomass into derivative monomer sugars and water-soluble oligoglucans. It separately probes the reactivity of native polysaccharides in the neat deep eutectic solvent and identifies preferred conditions for the direct transformation of structurally branched polysaccharides into monosaccharides and furans, simultaneously providing fine cellulosic powder. The unreacted cellulose may be further beneficiated into additional useful chemicals, optimising towards total use of the biomass.

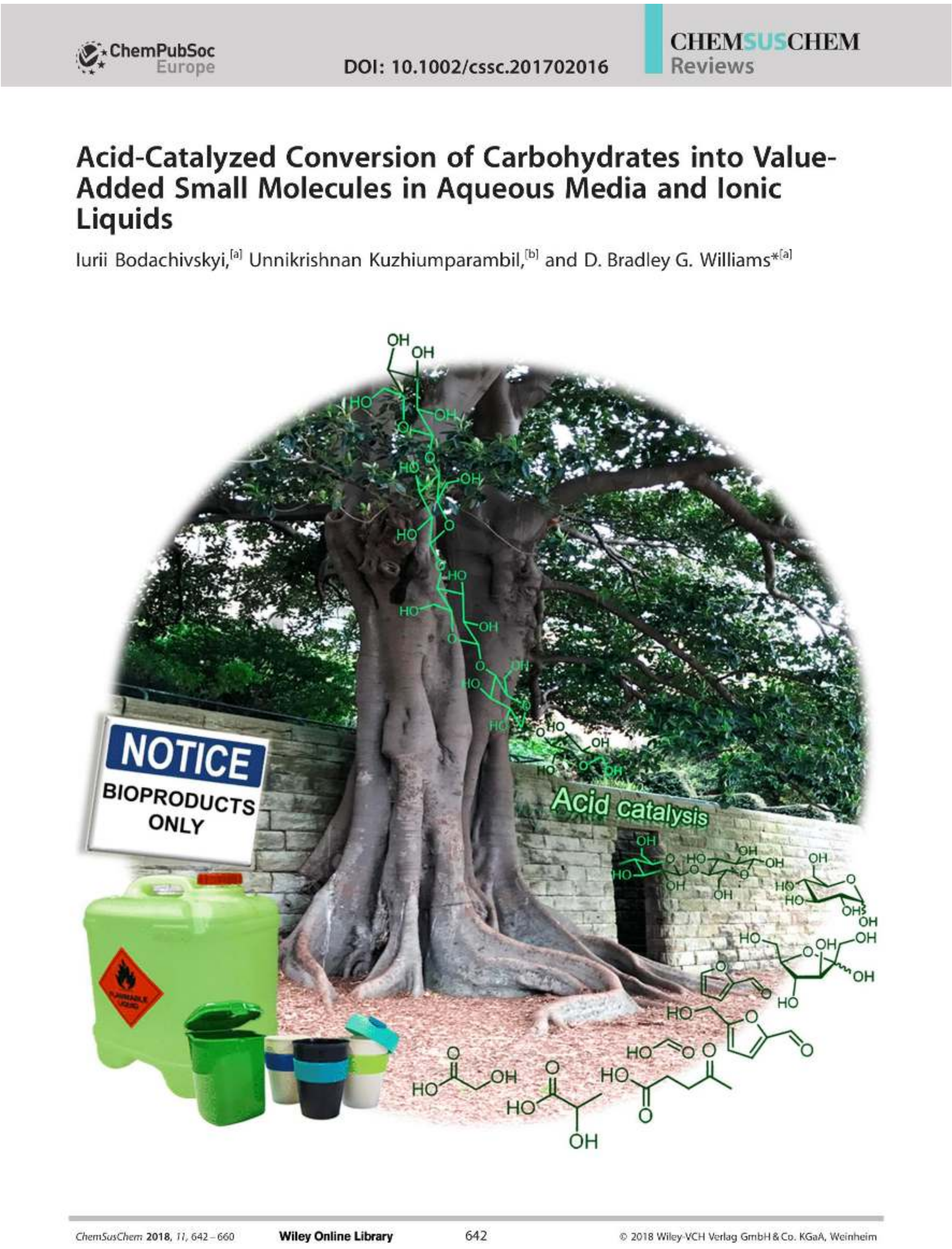
Finally, the work targets a deeper understanding of the dissolution, recovery, and characterisation of cellulose in various classes of ionic solvents. It combines the obtained knowledge of the processing of cellulose in the abovementioned ionic systems, providing practical recommendations for their use in cellulose refinery.

In memory of DSc Grigoriy Pop, Dr Leonid Zheleznyi and Prof. Valery Kukhar, who directed me towards chemical research, and whom I lost along the way.

Chapter 1:

Literature review and scope of the thesis

1.1. Acid-catalysed conversion of carbohydrates into value-added small molecules in aqueous media and ionic liquids (literature review)



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Acid-Catalyzed Conversion of Carbohydrates into Value-Added Small Molecules in Aqueous Media and Ionic Liquids

Iurii Bodachivskyi,[a] Unnikrishnan Kuzhiumparambil,[b] and D. Bradley G. Williams*[a]

ChemSusChem 2018, 11, 642 – 660   Wiley Online Library   642

Biomass is the only realistic major alternative source (to crude oil) of hydrocarbon substrates for the commercial synthesis of bulk and fine chemicals. Within biomass, terrestrial sources are the most accessible, and therein lignocellulosic materials are most abundant. Although lignin shows promise for the delivery of certain types of organic molecules, cellulose is a biopolymer with significant potential for conversion into high-volume and high-value chemicals. This review covers the acid-catalyzed conversion of lower value (poly)carbohydrates into valorized organic building-block chemicals (platform molecules). It focuses on those conversions performed in aqueous media or ionic liquids to provide the reader with a perspective on what can be considered a best case scenario, that is, that the overall process is as sustainable as possible.

1. Introduction

Acids are widely used to promote manifold organic chemical transformations. The versatility of acids makes them outstanding catalysts, as reflected by their widespread adoption in manufacturing and in research and development settings.[1] They can catalyze bond-forming reactions, such as addition, rearrangement, nucleophilic substitution, and electrophilic substitution, or bond-cleavage reactions, such as fragmentation or elimination processes. Acid catalysts can be liquid or solid (in some rare cases, gaseous) and be present as homo- or heterogeneous systems. Some of them catalyze reactions through proton transfer, others through accepting electron density of another atom. It has become usual to name the first group Brønsted acid catalysts, of which typical representatives are hydrochloric, sulfuric, phosphoric, or *p*-toluenesulfonic acids (PTSA). Members of the second group are Lewis acid catalysts, among which $AlCl_3$, BF_3, $SnCl_4$, or $TiCl_4$ are common.[2] Although this convention is typically applied, it is difficult to achieve pure Lewis acidity because Brønsted acidity usually arises as a consequence of Lewis acid–Lewis base complexation.[3,4] This phenomenon led to the discovery and exploitation of combined acid catalysis, in which there is a high degree of research interest.

Combined acid catalysis often is defined as a conjunction of two different acids promoting a synergistic increase in the particular type of acidity (Brønsted or Lewis). The combined acids can be mixtures of two Brønsted acids (Brønsted acid assisted Brønsted acid catalysts), Lewis acids (Lewis acid assisted Lewis acid catalysts), or Brønsted and Lewis acids (Brønsted acid assisted Lewis acid catalysts, or Lewis acid assisted Brønsted acid catalysts).[5] Combined acid catalysis improves the outcomes of numerous processes, as effectively employed in asymmetric synthesis by the groups of Yamamoto[5,6] and Williams[7–9] in applied organic reactions, including the conversion of cellulosic materials.[9]

Growing trend towards green chemistry and sustainable technology has driven the research community to develop efficient new catalytic systems. These state-of-the-art catalysts are intended to meet the following requirements relating to sustainability:[10] 1) be easily separable and not produce waste products; 2) be reusable many times without loss of activity; 3) promote reactions with catalytic amounts, rather than stoichiometric quantities, of the catalyst; 4) provide high selectivity under mild reaction conditions; and 5) be nontoxic and/or nonhazardous.

Apart from its applications in other areas, acid catalysis has made a significant impact on biomass conversion. Since the first synthesis of furfural from saccharides performed by Döbereiner[11] in 1832 and the synthesis of levulinic acid accomplished by Malaguti[12] in 1836, catalysis has been applied to the valorization of biomaterials into fuels, monomers for plastics and plasticizers for them, coatings, surfactants, lubricants and lubricant additives, and so forth, the bulk of which are currently produced from fossil sources.[13–22] Although natural substances, such as saccharides, lipids, and proteins, may all be convertible into useful chemicals, only lignocellulosic materials possess the scale and general ease of accessibility (i.e., physical accessibility as well as scale of renewable production) to be realistic contenders to replace substantial portions of petrochemical products. Cellulose is the most naturally abundant, nonfood, terrestrial polymer. It consists of hundreds to thousands of $\beta(1\rightarrow4)$ linearly linked glucose units, and is normally entangled into plant cell walls with hemicellulose, another polysaccharide, along with the aromatic polymer lignin. Cellulose has a rigid crystalline structure, in comparison with other natural polyglucosides, such as starch or glycogen, as a corollary of the beta-anomeric linkage. This leads to strong inter- and intrachain hydrogen bonding between hydroxyl groups, along with hydrophobic interactions. Therefore, it is virtually insoluble in water and in common organic solvents, which is a cause of substantial difficulties during chemical processing.[23] In this field of endeavor, the philosopher's stone is the direct conversion, preferably selective, of non-pretreated cellulose into value-added small molecules.

Conversion of cellulose into platform molecules is a complex cascade of reactions, in which the direction and rate are determined by the nature of the catalysts present and the process conditions. The first step is solvolysis (typically hydrolysis) of cellulose into glucose or its oligomers, and is catalyzed by Brønsted acids (see Scheme 1).[24] Under the influence of Lewis acids, glucose can either be isomerized into fructose or undergo a retro-aldol reaction to produce other low-molecular-

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weight substances.[25,26] Fructose is the major product under moderate reaction conditions, whereas C_2–C_4 sugars appear at higher temperatures. In the presence of an appropriate catalyst under suitable reaction conditions, these compounds can be converted into carboxylic acids or their derivatives.[26] Fructose can also follow a retro-aldol pathway in the presence of Lewis acids, causing bond cleavage. However, fructofuranose dehydrates in the presence of Brønsted acids, forming 5-(hydroxymethyl)furfural (HMF), which can rehydrate into levulinic acid at elevated temperature and in the presence of water.[27] These transformations are shown pictorially in Scheme 1, and it is immediately evident that the conversion of carbohydrates into smaller molecules proceeds as a complex set of reactions. The complexity arises principally because each stage of the conversion of cellulose is catalyzed by acids, sometimes Lewis acids and sometimes Brønsted acids. The differing roles of the acid catalysts make the selection of appropriate acids for transformations directly from cellulose challenging.

Iurii Bodachivskyi is a PhD candidate in Professor Williams's group at the University of Technology Sydney and is working on the development of methods for the conversion of algal biomass into industrially useful small molecules. His doctorate focusses on the field of homogeneous acid catalysis and alternative solvents as a means to valorize cellulosic materials within green and sustainable processes. His interests also embrace the chemistry of lipids, sulfur organic chemistry, surface processes, and molecular modeling of organic chemical transformations.

Unnikrishnan Kuzhiumparambil obtained his BSc in chemistry, followed by Masters and PhD degrees in biomolecular sciences (2011). He carried out postdoctoral research at the Centre for Forensic Science, University of Technology Sydney, in the area of doping control analysis and metabolism studies of designer steroids (2011–2014). Currently, he is a research associate at the Climate Change Cluster (C3), University of Technology Sydney, and mainly focuses on analytical method development, metabolomics, and the development of high-value products from algal biomass.

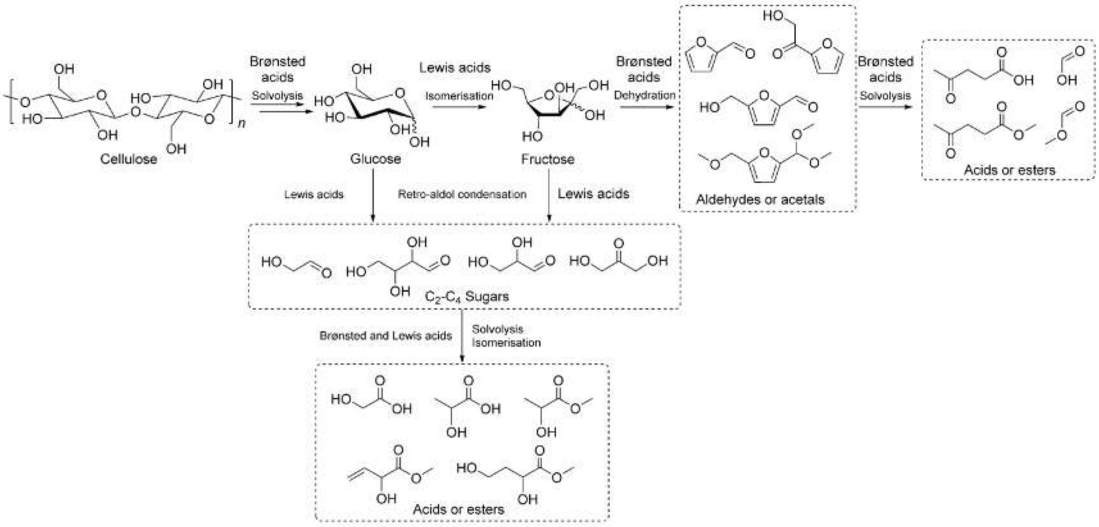
Bradley Williams has a passion for method development. His work has focused on the use of transition-metal catalysts and acidic catalysts, both Lewis and Lewis acid assisted Brønsted acids, in high-efficiency organic transformations. His interests span industrially oriented value-added processes, such as hydroformylation and hydroalkoxycarbonylation to advanced multi-step reactions involving carbohydrate substrates. In his spare time, he poses as an analytical chemist.

At the same time, the selectivity of the set of reactions is influenced by the nature of solvent(s) present: sometimes products interact with solvent molecules in the presence of an acid catalyst to form different compounds. For instance, aldehydes and acids are the main products in water media and water-containing systems,[26–28] whereas acetals and esters predominate in alcohol solutions.[27,29]

Several reviews dedicated to the catalytic conversion of mono-, oligo-, and polysaccharides into platform molecules, along with details of their applications, have been published.[14–18,22,28,30–35] Herein, we focus specifically on acid-catalyzed conversions in water and in ionic liquids (ILs). Both of these types of solvents have shown significant potential for the processing of cellulose into value-added small molecules for different reasons. In the first, it relates, in many instances, to the solubility of the catalyst or hydrophilic product in the aqueous medium. In the second, the alternative solvent is, in many examples, functional and serves to separate the catalyst from the products, thereby preventing side reactions, leading to enhanced yields. It will become evident during the course of this review that these solvents hold tremendous potential to lead to commercially viable processes. Hallmarks of a viable process include high yields and selectivities towards platform molecules, preferably making use of native cellulose, thereby avoiding the need for costly pretreatment, and the process should be conducted under mild reaction conditions. Ideally, it should be capable of being engineered into a continuous process rather than a batch process.

2. Conversion of Carbohydrates in Water and Organic Solvents

The use of water as a solvent for organic synthesis has become popular, owing to its natural abundance, extra-low toxicity, and safety during operation.[36] Catalytic conversion of saccharides in water is no exception. Water is nonetheless a challenging solvent on an industrial scale because of treatment requirements to improve the quality of wastewater before discharge and the huge energy implications if distillation is being considered. A serious problem with the processing of saccharides in water is the selection of appropriate catalyst systems that are stable and active in aqueous media. In addition, in aqueous solutions, some reaction products can be transformed into insoluble polymers, known as humins; a process that noticeably decreases yields of valuable molecules and compromises catalyst activity. These confounding issues render the selective conversion of carbohydrates into specific target compounds in high yields in water a challenging task. This section covers advances in acid-catalyzed transformation of sugars in aqueous systems and systematically portrays sustainable processes that lead to various platform molecules. The section is



Scheme 1. Acid-catalyzed cascade of cellulose conversion into small molecules.

structured to follow the cascade of events in Scheme 1. In this way, it tracks the chemistry as cellulose is converted into various products, and enables the reader to refer back to Scheme 1 and its logic.

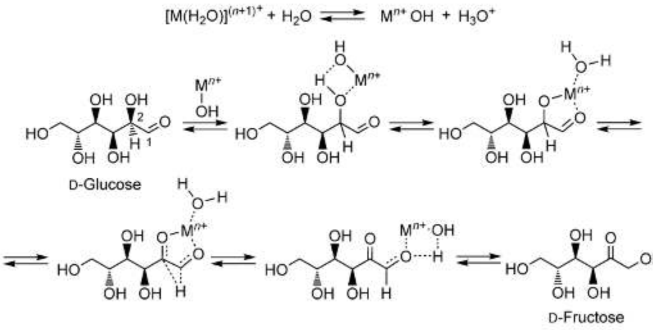
2.1. Oligoglucans and glucose

The first stage of the catalytic cascade of cellulose processing in water media is the hydrolysis of the natural polymer into oligomer glucans and ultimately into monomer sugar glucose, which are of great industrial interest, primarily for fermentative production of ethanol or lactic acid.[37,38] Importantly, cellulose-derived low-molecular-weight sugars are not competitive with food, which avoids potential ethical and social issues associated with the use of food sources as substrates for chemical products. Hydrolysis of glycosidic linkages can be productively catalyzed by concentrated solutions of mineral acids or cellulase mimetic catalysts, examples include sulfonated chloride containing resins or sulfonated carbonized polyvinyl chloride.[39,40] This system requires forcing reaction conditions, produces a large amount of acidic wastewater, and is corrosive towards equipment. It also requires a high loading of solid catalysts that have proved difficult to recover. An aqueous solution of NaCl under hydrothermal conditions (220 °C) overcomes some of these issues.[41] Although this system possesses modest acidity (pH $\approx$ 5.6), it substantially lowers the molar weight of polysaccharides of microcrystalline cellulose (MCC) and lignocellulose (corncob residue, mulberry wood, and corn stover) assisted by nearly complete dissolution of carbohydrates in the solvent. Potentially, such systems can be applied to large-scale depolymerization processes of cellulose and become industrially viable.

An outstanding example of an acid catalyst for the direct conversion of cellulose into glucose in aqueous media was synthesized by the solvent-free mechanochemical oxidation of activated carbon with $KHSO_4$ or $(NH_4)_2S_2O_8$.[42] The oxidative functionalization of activated carbon is proposed to increase the number of acidic sites (e.g., carboxylic, ketonic, or phenolic groups), while mechanical processing enlarges the surface area of the catalyst. Glucose yields of up to 85 % are attainable during acid-catalyzed hydrolysis of ball-milled cellulose, which is remarkable compared with yields achievable for cellulase enzymes ($\approx$65 %). If the energy demands of ball milling, as a means of biomass pretreatment, can be overcome, or if the need for it can be obviated, then this process could become commercializable. Until then, it remains uncompetitive compared with the direct fermentation of cellulose into alcohols or acids.[43–45]

2.2. Fructose

The next step of the cascade given in Scheme 1 is an aldose–ketose isomerization of glucose to fructose named the Lobry de Bruyn–van Ekenstein transformation. Mechanistic studies suggest that the rate-limiting step of this reaction is a hydride shift from the C2 to the C1 position catalyzed by Lewis acids.[46–49] The most probable pathway is thought to involve the formation of a hydroxy–metal species that enables deprotonation of the C2-OH group (Scheme 2). Simultaneously, the Lewis acidic metal cation, M^{n+}, facilitates the C2 $\rightarrow$ C1 hydride shift, which results in the formation of the ketose. This idea has been corroborated in the $AlCl_3$-catalyzed isomerization of glucose.[50] In this instance, the formation of an aluminum aquo complex, $[Al(OH)_{2(aq)}]^+$, as a major catalytic species was



Scheme 2. Proposed mechanism for Lewis acid catalyzed glucose–fructose isomerization.[46–50] M = metal, n = integer.

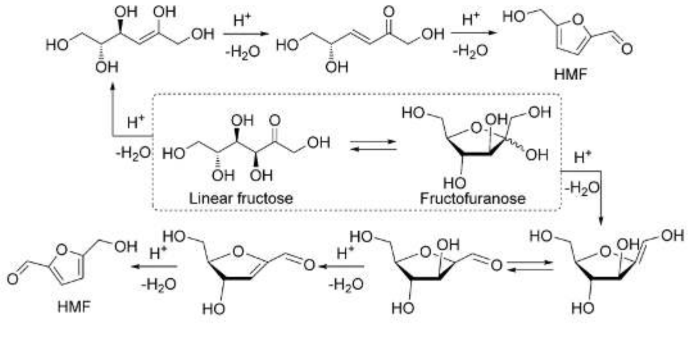
identified. Conversely, under base catalysis, the process is thought to proceed through hydrogen-ion transfer instead.[51]

Unfortunately, there are few catalysts able to promote aldose–ketose isomerization with a high degree of efficacy in water media. A promising hydrophobic tin-containing zeolite with beta-framework topology provides the highest fructose yield (of all catalyst systems) of 31 % directly from glucose.[52] An elegant indirect approach involves a one-pot isomerization–etherification of glucose into methyl fructoside in methanol followed by hydrolysis of the glycoside into fructose in a solution of methanol–water.[53,54] Various aluminosilicates have been tested in this process and the best output of fructose was obtained with the large pore-containing H-USY zeolite. This solid acid can be easily recovered and affords fructose in yields of 55 %. It is remarkable that the current industrially applied method, which is based on isomerase enzymes, provides fructose in yields of only 42 %.[52,55]

2.3. HMF and its derivatives

There is currently particular interest in the conversion of fructose into HMF, which is one of the most important platform molecules within the portfolio of products that can be produced from cellulose.[28,33,34] This compound is a raw material in the production of biobased monomers for the polymer industry, as well as a prominent candidate for the production of biofuel.[22,56,57] The synthesis of HMF requires the consecutive Brønsted acid catalyzed dehydration of fructofuranose, and is proposed to proceed as illustrated in Scheme 3.[58–60] However, alternative reaction pathways through an acyclic mechanism have been proposed.[61,62] Because HMF is rather reactive and readily converts into humins under certain conditions, the procedure is usually conducted in the presence of organic solvents, which separate HMF from the catalyst. In many instances, water-miscible solvents, such as dimethyl sulfoxide (DMSO) or dimethylformamide have been used, but the complexity of their recovery from aqueous systems has led to the use of nonpolar and volatile solvents, such as ethers, ketones, alcohols, aromatics, or their mixtures.[63,64] The immiscibility of such systems is often maintained by the addition of inorganic electrolytes (NaCl, KCl, KBr, etc.), which additionally support the dehydration of fructose.[64–66]

Despite a number of examples demonstrating the successful conversion of fructose into HMF,[28,33,34,67–69] most of them do not meet practical requirements, due to the high cost of the refined input carbohydrate substrates (mostly, fructose and sucrose). If naturally abundant glucose or polyglucosides can be converted selectively into HMF in high yields, the process



Scheme 3. Brønsted acid catalyzed fructose dehydration into HMF.[58–62]

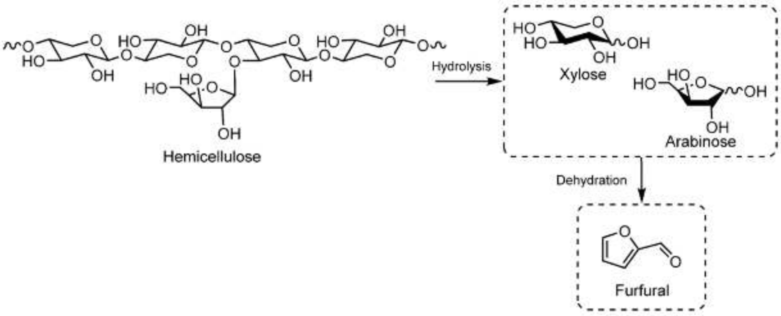
could become industrially viable and so the high-yielding conversion of glucose into fructose is desirable. Glucose conversion into HMF requires catalysts suitable for consecutive aldose–ketose isomerization and fructose dehydration, and therefore, must possess both Brønsted and Lewis acid sites or activity. One solution is to employ Lewis acidic metal chlorides or their combinations with hydrochloric acid.[25,70] As shown above, metal-cation hydrates can cause the release of a Brønsted base aquo complex and H_3O^+, which can catalyze glucose isomerization into fructose (Scheme 2) and dehydration of fructose into HMF. Although Brønsted acids are conventionally denoted as a cation H^+ or H_3O^+ (including instances herein), the structure of the hydrogen ion in water varies with the concentration of the acid, and is shown to be $H_{13}O_6^+$ in less concentrated acidic aqueous media.[71,72] The rate of the second reaction is usually quite low and the addition of a Brønsted acid is necessary to improve the conversion and selectivity to the product.[25,73] The combination of acids increases the rate of fructose dehydration over that obtained with HCl alone, but decelerates the isomerization steps. One way to overcome this negative effect is to raise the reaction temperature, which accelerates all reactions in the system.[25] In addition, Román-Leshkov and Dumesic reported that small temperature increments (for instance, from 150 to 160 °C) improved the rate of dehydration of fructose,[71] thereby reducing the degradation of HMF. The same observations have been noted for combinations of various metal halides and mineral acids (HCl, H_2SO_4, HNO_3, H_3PO_4).[65]

A peculiarity of the activity of metal chlorides in the transformation of glucose into HMF is that the conversion in biphasic systems increases with a reduction of the ionic radius of the cations in the order $Al^{3+} > Ga^{3+} > In^{3+}$ and for the lanthanide series in the order $Yb^{3+} > Dy^{3+} > La^{3+}$.[74] This phenomenon is a result of the greater ability of small cations to coordinate hydroxyl groups in a manner that facilitates the requisite transformations, and is related to the notion of charge density (i.e., the ratio of charge to ionic radius, z/r).[8,75] This trend has been recently confirmed and extended in a study,[76] which showed that the tetravalent Lewis acid $SnCl_4$, in combination with H_3PO_4, afforded the highest activity towards the conversion of cellobiose. However, this method fails in the attempted synthesis of HMF from cellulosic or starch-based food waste, presumably associated with the poor hydrolysis of glycosidic bonds under the reaction conditions employed. An approach that might solve this problem is to change the reaction media from a mixture of water/solvent extractant to that of water/ethanol.[77] Under these conditions, HMF and HMF–ethanol acetals are produced in higher overall yield than that in other solvent systems. It is possible that this is a consequence of the higher rate of alcoholysis of polysaccharides, compared with hydrolysis thereof.[78] Table 1 provides a summary of the outcomes of a number of combinations of substrate, catalyst, and reaction medium, as discussed above.

HMF may be produced through $AlCl_3$-catalyzed transformation of biomass in a biphasic system, H_2O–NaCl/THF, under microwave heating.[79,80] These conditions enable a range of lignocellulosic materials (corn stover, pine wood, grass, poplar) to be transformed into HMF in high yields (Table 1), and this solvent system can also be used to produce furfural in high yield (77 %).[81] Additionally, furfural was obtained as a second major product in impressive yields of up to 65 % (based on the weight of pentose in the substrate), which is in the order required for a commercializable processes.[82] The appearance of furfural is ascribed to the presence of hemicellulose in the lignocellulosic biomass, which consists primarily of D-pentose sugars (xylose, arabinose, rhamnose, etc.) and transforms according to Scheme 4. Despite these promising results, the high cost of microwave reactors, as well as increased energy consumption as a consequence of their operation, restrict their use on an industrial scale at present.

Ferric phosphate has also been applied to the conversion of cellulose in a biphasic system of H_2O–NaCl/THF.[83] Although almost insoluble in the reaction medium at ambient temperature, $FePO_4$ becomes soluble, and therefore, a homogeneous catalyst at the reaction temperature (160 °C; Table 1). The variable catalyst solubility during the process facilitates the recovery thereof by filtration and recrystallization of the iron salt and enables it to be reused without marked loss of activity.

Another relevant class of water-soluble Lewis acids is metal trifluoromethanesulfonates (metal triflates). Li et al. observed that metal triflates provided substantial yields of HMF during the conversion of glucose, without the addition of protic



Scheme 4. Hemicellulose transformation into furfural.

Table 1. Conditions and results for the acid-catalyzed conversion of carbohydrates into HMF.

Substrate	Reaction media	Catalyst[a]	*t* [min]	Reaction *T* [°C]	HMF yield or selectivity [mol %]	Ref.
glucose	water, NaCl/*sec*-butylphenol	$AlCl_3/HCl$	40	160	68[b]	[74]
		$GaCl_3/HCl$	120		50[b]	
		$InCl_3/HCl$	150		52[b]	
		$YbCl_3/HCl$	120		46[b]	
		$DyCl_3/HCl$	160		41[b]	
		$LaCl_3/HCl$	240		44[b]	
cellobiose	water/DMSO	$SnCl_4/H_3PO_4$	20	140	12	[76]
cooked rice					8	
bread crust					10	
cellobiose	water/ethanol	$AlCl_3$	15	160	56[c]	[77]
maltose					46[c]	
starch					47[c]	
corn stover	water, NaCl/THF	$AlCl_3$	30	180	19[d]	[79]
pine wood					35[d]	
grass					24[d]	
poplar					27[d]	
MCC	water, NaCl/THF	$FePO_4$	60	160	50	[83]
α-cellulose					32	
glucose	water, NaCl/*sec*-butylphenol	$Al(OTf)_3$	25	160	49	[84]
		$Sc(OTf)_3$			38	
		$La(OTf)_3$			37	
		$Yb(OTf)_3$			25	
		$Hf(OTf)_4/HCl$			60	
glucose	water/diglyme	$Zr(HPO_4)_2\cdot n\,H_2O$[e]	180	180	63	[91]
ball-milled cellulose	water/THF/*N*-methyl-2-pyrrolidone	$TiO_2/PO_2(OH)_2$	80	180	75	[92]
glucose	water/THF/CO_2	CO_2	240	190	52	[93]
glucose	water	$Nb_2O_5\cdot n\,H_2O$[e]	–	180	36	[97]
sucrose					36	
cellulose	water	$Cr[(C_{12}H_{25}OSO_3)H_2PW_{12}O_{40}]_3$	120	150	53	[98]
corn stover					31	
corn husk					36	

[a] OTf = trifluoromethanesulfonate. [b] HMF selectivity. [c] Total yield of HMF and HMF–ethanol acetals. [d] Yield based on the weight of hexose in biomass. [e] *n* = integer.

acids.[84] This discovery relies on the ability of triflates to induce both Lewis and Brønsted acidity, as previously shown by Williams and Lawton.[3] The conversion of glucose into HMF with metal triflates follows the same pattern as that of metal chlorides, in accordance with the ionic radius of the metal cations in the series $Al^{3+} > Sc^{3+} > La^{3+} > Yb^{3+}$. On the other hand, the use of higher valence-state metal triflates, such as $Hf(OTf)_4$, and the addition of hydrochloric acid significantly improves the yields of HMF (Table 1). These results show promise for the application of metal triflates to the conversion of cellulose, with the additional benefit that it is, in principle, possible to recycle the metal triflate catalyst.[84] Despite the promise of this chemistry, there is an absence of information on the metal triflate catalyzed synthesis of HMF from polymers of glucose (e.g., cellulose).

Heterogeneous acid catalysts dominate over their homogeneous counterparts in large-scale reactions and in industry.[85] This is also reflected in a large number of reports dedicated to the catalytic conversion of carbohydrates into HMF by using typical acidic resins, functionalized silica, zeolites, heteropolyacids, and other solids.[86–88] Notwithstanding the ability to recover heterogeneous catalysts by filtration, homogeneous catalysts can often be efficiently recovered by the simple removal of the organic phase, which contains products,[84,89] leaving the acid catalyst in the aqueous phase. On the other hand, solid acids are frequently disposed of due to their irreversible deactivation by the formation of byproduct polymer humins on their surface.[90] Strategies to overcome this adverse effect might involve the selection of catalysts with a surface that is resistant to adsorption of macromolecular byproducts or with pores large enough to remove them from the matrix of the solid. A promising group of catalysts is composed of mesoporous solid acids. For example, mesoporous zirconium phosphate ($Zr(HPO_4)_2\cdot n\,H_2O$) provides reasonable yields of HMF from glucose, and can be reused in five consecutive cycles without loss of activity.[91] Phosphated TiO_2 also shows promise in appropriate biphasic systems: it enables the conversion of appropriately pretreated MCC into HMF in surprisingly high yields (Table 1).[92] A major downside, however, is the high energy consumption during the 10 h of ball-milling of MCC and the 4 h recovery of the solid acid catalyst at 600 °C. Ball-milling is a technique rather frequently used as a pretreatment method for cellulose. The fact that such drastic pretreatment is required before acceptable yields of products are attainable reflects the very high hurdle and ongoing challenge in the direct conversion of cellulose into valorized small molecules.

In an unusual setup, glucose can be converted into HMF in a mixture of water/THF under the pressure of carbon dioxide.[93] Notably, under the applied conditions, this medium forms a triphasic system, H_2O–CO_2(liquid)/THF–CO_2(liquid)/CO_2(gas), which results in high yield and selectivity of HMF (Table 1). It is apparent that CO_2 possesses Lewis acidity, whereas in situ generated H_2CO_3 offers Brønsted acidity; therefore, the reaction medium contains the acid catalyst requisite to the transformation of glucose into the major product. Usefully, the process requires only a mild pressure of CO_2 (1 MPa) and enables relatively easy recovery of products and solvents.[93] Application of the process to polysaccharides will prove interesting from a scientific and practical perspective.

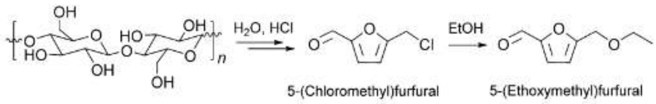
There remains a drive towards the efficient synthesis of HMF directly from cellulose in a single water phase to avoid the use of organic solvents in high-temperature processes. Zhang et al. recently explored a homogeneous catalyst mixture of $AlCl_3$ and maleic acid in the conversion of glucose into HMF in pure water.[94] Kinetic studies reveal that this combination of acids provides high reaction rates, low activation energy for glucose–fructose isomerization, and simultaneously shows superior selectivity towards HMF by avoiding the formation of humins. Previously, de Souza et al. tested 17 different solid acids and bases, including zeolites, heteropolyacids, metal salts, and oxides, as catalysts for glucose conversion into HMF.[90] Among them, only amorphous hydrated niobium oxide, $Nb_2O_5 \cdot n H_2O$, also known as niobic acid, provided HMF in yields above 5%, and up to 28% under optimized conditions. A water-tolerant modified form of niobic acid has been used in the conversion of fructose.[95,96] The feasibility of this kind of catalyst has been improved by the synthesis of a mesoporous niobium oxide with a large number of Lewis and Brønsted acid sites and greater surface area.[97] The yield of HMF was 36% from glucose and sucrose and the reactions were characterized by high rates of conversion of the carbohydrates into product (Table 1).

As far as can be determined, the catalyst providing the highest yield of HMF directly from cellulose in aqueous mixtures is a combined Brønsted–Lewis–surfactant heteropolyacid: $Cr[(C_{12}H_{25}OSO_3)H_2PW_{12}O_{40}]_3$.[98] The micellar nature of the heteropolyacid overcomes difficulties associated with solid–solid interactions between cellulose and the catalyst, leading to milder reaction conditions and improved yields of HMF (Table 1). Additionally, the hydrophobic nature of the catalyst surface prevents the adsorption of polar products and subsequent degradation of HMF into levulinic acid or humins, and enables the catalyst to be reused at least six times. This catalyst was also used for the transformation of lignocellulosic residues (corn stover and corn husk of *Xanthoceras sorbifolia*). Notably, the catalyst works well, even for untreated biomass, to give HMF yields of 31 and 36% for corn stover and corn husk, respectively. Furfural was produced as an additional major product in yields of up to 30%, which were very close to that of requirements for an industrially viable process.[82] Although the catalyst is, in principle, heterogeneous, it is possible that leaching inherent to heteropolyacids leads to the process proceeding through a homogeneous pathway.[21,98]

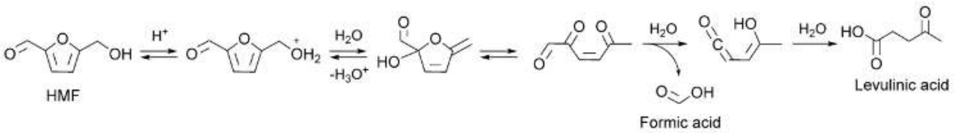
There is some progress towards the synthesis of derivatives of HMF, such as the direct conversion of cellulose into 5-(chloromethyl)furfural.[99–101] This molecule is readily accessible from lignocellulose in high yields of up to 80% (based on the hexose content in biomass) and can be transformed into a large range of derivatives,[100,101] such as a high-quality biofuel in the form of 5-(ethoxymethyl)furfural (95% yield of product isolated).[102] The overall process for the conversion of cellulose into 5-(ethoxymethyl)furfural is pictorially represented in Scheme 5. A downside of the synthesis of 5-(chloromethyl)furfural is the use of concentrated hydrochloric acid and an organochlorine solvent, both of which detract from the elegance of the process and which require a solution to reduce the environmental footprint thereof. Attempts to produce 5-(ethoxymethyl)furfural in high yield directly from carbohydrates are restricted to the use of fructose, glucose, and food-grade di- or oligosaccharides (e.g., sucrose and starch); this leaves room for improvement in future developments.[103–106]

2.4. Levulinic acid, formic acid, and alkyl levulinates

Another versatile organic building block is levulinic acid; a product of the hydrolytic Brønsted acid catalyzed ring-opening reaction of HMF (Scheme 6). In contrast to the synthesis of HMF, which is sensitive to high concentrations of protic acids at elevated temperatures, the production of levulinic acid is promoted by such conditions. At the same time, levulinic acid



Scheme 5. Conversion of cellulose into 5-(ethoxymethyl)furfural via 5-(chloromethyl)furfural.



Scheme 6. Brønsted acid catalyzed HMF rehydration into levulinic acid.[108]

is a relatively stable product and does not require isolation by a nonpolar extractant, thereby simplifying the operating conditions. It is evident in Scheme 6 that rehydration of HMF into levulinic acid also leads to the formation of formic acid, which has a wide use in applied chemistry and agricultural, fuel, and pharmaceutical industries.[107,108] There is also evidence that formic acid, a useful small molecule, can be obtained directly from glucose and fructose.[66]

Levulinic acid is commercially produced by the technology developed by Biofine Renewables, LLC.[109] The process comprises a two-step hydrolytic transformation of biomass catalyzed by sulfuric acid. The first step is a rapid high-pressure hydrolysis of polysaccharides into sugar monomers and their dehydration into HMF; this is performed in a plug flow reactor under a pressure of 25 bar (1 bar$=10^5$ Pa). The second step is the rehydration of HMF into levulinic acid and formic acid in a back-mix reactor under a pressure of 14 bar. Importantly, the ratios of the main products can be easily adjusted through variation in the catalyst concentration and temperature of the second stage.[110] In this process, the yield of levulinic acid also depends on the origin of the feedstock and is produced at 59–83% of the theoretical value, depending on this variable.[108] Some examples of hydrolytic lignocellulose conversion by means of Biofine technology are given in Table 2.

Although the Biofine process is efficient and flexible, the sulfuric acid catalyst also promotes side reactions that produce waste products during the hydrolysis of biomass and separation of products. In addition, the corrosive nature of the reaction mixture, together with the forcing reaction conditions, leave room for improvement. Some of the efforts to solve these problems are discussed below.

For homo- versus heterogeneous catalysis, current information suggests that the former are more suitable for the synthesis of levulinic acid. For example, Weingarten et al. described the production of levulinic acid in a yield of only 27% in the conversion of cellulose catalyzed by the acidic resin Amberlyst 70.[111] Despite these low yields and irreversible catalyst loss, a noticeable benefit of this approach is the significant reduction of byproduct formation. Other resins, such as Nafion SAC 13 and Dowex 50 modified with Fe^{3+} ions, have also been applied in the conversion of cellulose into levulinic acid, but none of them can be recovered with the same catalytic activity.[112,113] In addition, these processes require long reaction times, measured in days in the case of Nafion (Table 2).

There are several successes in the homogeneous acid-catalyzed transformation of polysaccharides into levulinic acid. The efficacy of metal chlorides in these reactions has been reported.[114] Among the metal chlorides, $CrCl_3$ shows the highest activity and affords levulinic acid in an appealing yield of 67% (Table 2). However, the authors also found that $CrCl_3$ was consumed during the process and that chromium hydroxides precipitated during the course of the reaction; this is an issue that remains to be solved. In other work, $AlCl_3$ was found to be useful in the conversion of the hemicellulosic portion of *Pubescens*.[115] The combination of $AlCl_3$ and SiO_2 in water/THF affords reasonable selectivity of levulinic acid of 48% (Table 2). Importantly, this process has become a precedent for the production of another platform molecule, γ-valerolactone.[116] γ-Valerolactone is obtained by the addition of the catalyst Pt/C to the reaction media, which promotes both in situ generation of H_2 from formic acid and reductive cyclization of levulinic acid into its corresponding lactone. Usefully, it is possible to recover the catalyst system.

Pseudo-homogeneous catalytic systems have been developed by Sels et al.[117,118] These are macromolecular water-soluble catalysts based on sulfonated hyperbranched poly(arylene oxindoles). Derivatives with chlorine or fluorine atoms as substituents provide the best catalytic activity (Table 2). It was demonstrated that the catalyst did not change in its chemical composition after the reaction, and thus, could probably be reused. However, catalyst recovery involves ultrafiltration that may cause processing difficulties in industrial-scale processes.

A method with substantial potential is based on the application of gaseous acid SO_2.[119] SO_2 plays a dual role to act as

Table 2. Conditions and results for the acid-catalyzed conversion of cellulosic materials into levulinic acid.

Substrate	Catalyst	*t*	Reaction *T* [°C]	Yield[a,b] [%]	Ref.
paper sludge	H_2SO_4	14 s	215	71[a]	[109]
		0.42 h	200		
paper pulp	H_2SO_4	15 s	205	61[a]	[110]
		0.42 h	185	(82 for formic acid)	
MCC	noncatalytic Amberlyst 70	0.5 h	220	27[a]	[111]
		8 h	160		
cellulose	Nafion SAC 13	120 h	190–200	72[b]	[112]
MCC	Fe resin	5 h	200	33[a]	[113]
MCC	$CrCl_3$	3 h	200	67[b]	[114]
hemicellulose (*Phyllostachys heterocycla cv. Pubescens*)	$AlCl_3/SiO_2$	4 h	160	48[c]	[115]
ball-milled MCC	5Cl-SHPAO[d]	5 h	165	48[b]	[118]
	5F-SHPAO[d]			47[b]	
cellulose	SO_2	0.75 h	210	45[b]	[119]

[a] Levulinic acid yield in % from theoretically possible 71.6% *w/w*. [b] Levulinic acid yield in mol% based on the anhydroglucose unit. [c] Levulinic acid selectivity. [d] 5Cl-SHPAO or 5F-SHPAO are sulfonated hyperbranched poly(arylene oxindole)s with chloride or fluoride substituents in the fifth position of isatin.

both a Lewis acid and Brønsted acid catalyst. The Brønsted activity is provided through the dissolution of SO_2 and formation of H_2SO_3 in aqueous media. The dual acidity of the catalyst led to good yields of levulinic acid from untreated cellulose (Table 2). Usefully, the catalyst could be recovered by steam stripping. The major drawback of this process is the high reaction temperature and pressure, which do not significantly differ from those of the Biofine technology, and therefore, offer little improvement. Nevertheless, sulfurous acid does not induce severe metal corrosion, in comparison with sulfuric acid, which may reduce capital costs.

A particular trend in the conversion of carbohydrates is towards the synthesis of alkyl levulinates for use as solvents or fuel additives.[120] For example, methyl levulinate can be selectively produced in the presence of methanol during the conversion of cellulose catalyzed by combinations of various metal triflates and sulfonic acids.[121] Although the efficacy of single-entity triflate catalysts is high, the presence of PTSA improves the ester yield by boosting the rate of cellulose solvolysis into sugars (Figure 1). As seen in Figure 1, $In(OTf)_3$ affords the highest activity, compared with the other metal triflates, and gives the most active catalyst pair with NSA. Turning now to industrial-scale synthesis, we note that the Eni S.p.A. company has published a patent based on the conversion of lignocellulose with NSA as a catalyst in ethanol, 2-propanol, or 1-butanol.[122] It is noteworthy that the technology can deliver ethyl, propyl, and butyl levulinate in excellent yields of 95, 89, and 85 %, respectively, from coniferous wood. An advantage of processes performed in alcohols is the facile recovery of the catalytic system after distillation of the products.[121]

The opportunity to deliver formic acid from carbohydrates is also of particular interest; formic acid is usually produced as a byproduct of the synthesis of levulinic acid. The most striking instance of the direct conversion of carbohydrates into formic acid is the OxFA process commercialized by OxFA GmbH. This process employs the oxidative conversion of sugars with molecular oxygen by using as a homogeneous catalyst the Keggin-type polyoxometalate $H_5PV_2Mo_{10}O_{40}\cdot 35\,H_2O$ as a means of oxygen insertion into C–C σ-bonds, ultimately leading to formic acid and CO_2 through electron–oxygen transfer mechanisms.[123,124] The catalyst provides some activity towards the hydrolysis of glycosidic bonds and enables mono- and oligosaccharides, such as xylans, to be converted into formic acid in good yields (33 %) under comparably mild conditions (80 °C, 26 h, 30 bar O_2).[124] However, cellulose is rather unreactive under such conditions and there is a need to promote the hydrolysis of the polymer by using an additional source of Brønsted acid. In one approach,[125] PTSA was employed in the process, which led to the improved conversion of various cellulosic materials (beech, poplar, pine, waste paper, cyanobacteria, etc.) into formic acid in improved yields (up to 40 %) and selectivity (40–56 %) towards the target molecule.

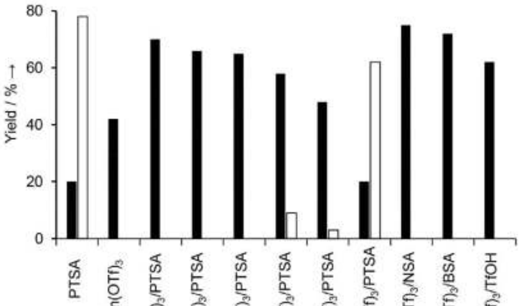


Figure 1. Acid-catalyzed synthesis of methyl levulinate from cellulose. Reaction conditions: cellulose (2.5 mmol; as a glucose unit), Lewis acid (0.02 mmol), Brønsted acid (0.1 mmol), methanol (20 mL), N_2 (0.5 MPa), 180 °C, 30 min.[121] ■: yield of methyl levulinate; □: yield of sugars. NSA = -naphthalenesulfonic acid, BSA = benzenesulfonic acid, TfOH = trifluoromethanesulfonic acid.

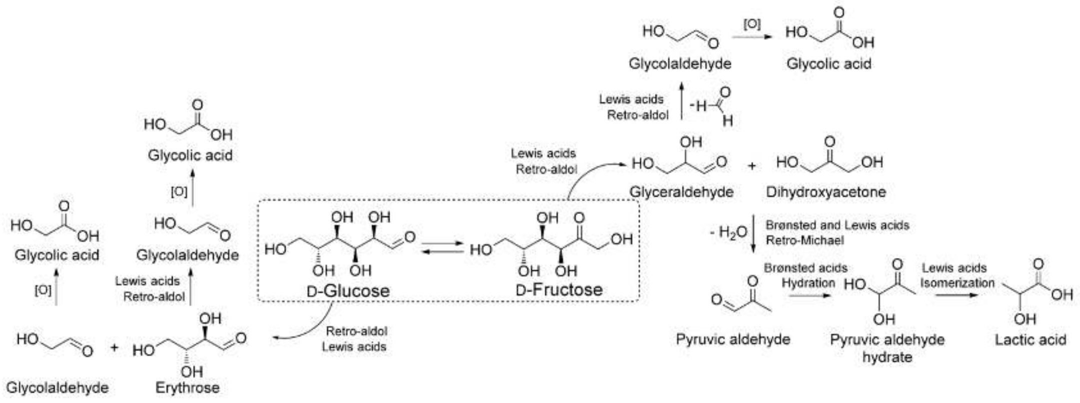
2.5. α-Hydroxy acids

In contrast to the studies described above, the application of a retro-aldol pathway as a method of valorization of cellulose is more complex and less deeply investigated. However, there are some examples of acid catalysts that enable selective processes (Table 3). The major products of the retro-aldol pathway are α-hydroxy acids, primarily lactic and glycolic acids. These acids are also key platform chemicals used widely for the production of commercial bioplastics and for the synthesis of pyruvic and acrylic acids and other monomers.[126]

The retro-aldol reaction gives C_2 and C_4 sugars from glucose, and trioses (dihydroxyacetone and glyceraldehyde) from fructose, as depicted in Scheme 7. This step can normally be performed at elevated temperature with Lewis acid catalysts.[33] Trioses are intermediates in the formation of lactic acid through the sequential stages of a retro-Michael dehydration into pyruvic aldehyde and its hydration and isomerization into 2-hydroxy carboxylic acids. Retro-Michael dehydration is catalyzed by both Lewis and Brønsted acids, whereas the hydration of aldehydes is typically induced by Brønsted acids and isomerization reactions are most frequently promoted by Lewis acids (Scheme 7).[26,127] The synthesis of glycolic acid is also achievable from C_2–C_4 sugars; however, this reaction requires an additional retro-aldol condensation step and hydration and isomerization reactions.[128]

Metal chlorides and other salts have been used to good effect to promote the synthesis of lactic acid from glucose.[129] It was established that $AlCl_3$ provided the highest activity toward lactic acid, which was produced in a yield of 20 % at comparably low reaction temperatures. However, $Pb(NO_3)_2$ is more active in this reaction with ball-milled cellulose to produce a surprisingly high yield (68 %) of lactic acid,[130] and the catalyst could be recovered through the capture of Pb^{2+} on a cation-exchange resin. Nonetheless, the toxicity of lead catalysts poses problems within the concepts of green chemistry and is avoided on an industrial scale.

The application of lanthanide triflates to the hydrothermal conversion of untreated cellulose into α-hydroxy acids represents something of a breakthrough.[131] A yield of 90 % based



Scheme 7. Acid-catalyzed transformation of hexoses into α-hydroxy acids.[26,127,128]

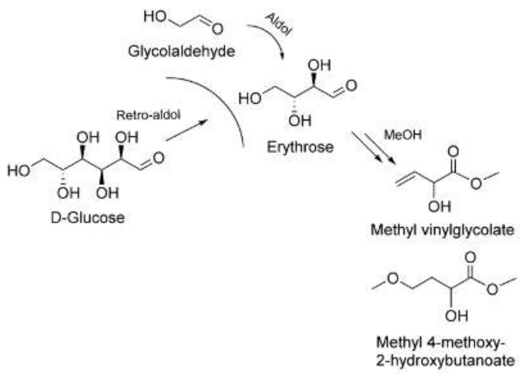
Table 3. Conditions and results for the acid-catalyzed conversion of carbohydrates into α-hydroxy acids.

Substrate	Catalyst	*t* [h]	Reaction *T* [°C]	Lactic or glycolic acid[a] yield [mol %]	Ref.
glucose	$AlCl_3$	6	140	20	[129]
ball-milled MCC	$Pb(NO_3)_2$	4	190	68	[130]
MCC	$Er(OTf)_3$	0.5	240	90[b]	[131]
	$Lu(OTf)_3$			62	
	$Yb(OTf)_3$			62	
	$Er(OTf)_3$			62	
	$Ho(OTf)_3$			61	
	$Dy(OTf)_3$			60	
	$Sm(OTf)_3$			58	
	$Nd(OTf)_3$			55	
	$Pr(OTf)_3$			53	
	$Ce(OTf)_3$			48	
	$La(OTf)_3$			46	
α-cellulose	$H_3PMo_{12}O_{40}$	1	180	49[a]	[128]
bagasse				32[a]	
hay				28[a]	

[a] Yield of glycolic acid. [b] Yield of lactic acid under the optimized catalyst loading.

on the anhydroglucose unit was achieved under optimized conditions with $Er(OTf)_3$ as a catalyst (Table 3). Importantly, this catalyst provided the same result after four cycles of recovery and recycling. Its recovery required only simple distillation of water and reaction products, but on a large scale this may be too energy intensive to be economically feasible. The study also found that the catalyst activity depended on the metal ionic radii in an opposite manner to that of the above examples for the synthesis of HMF. The yield of lactic acid goes up with an increase in cation ionic radius and is approximately equal for $Er^{3+} \approx Yb^{3+} \approx Lu^{3+}$.

Recent investigations into the metal triflate catalyzed conversion of cellulose by the retro-aldol process are based on reactions in methanolic media.[29] This medium leads to the production of α-hydroxy methyl esters, including methyl lactate, methyl vinylglycolate, and methyl 4-methoxy-2-hydroxybutanoate. The last two esters are believed to form from tetrose sugars (Scheme 8), and are also considered to be platform molecules with significant potential for industrial application.[132,133] Importantly, careful selection of the metal triflate catalyst enables the preferred reaction pathway to be followed. For example, $Sn(OTf)_2$ primarily catalyzes the retro-aldol reaction and further conversion of sugars into α-hydroxy esters (Figure 2). Conversely, $Al(OTf)_3$, AgOTf, and $Cu(OTf)_2$ are the best choices for selectivity towards methyl levulinate because they accelerate dehydration–rehydration reactions.[29] It is possible that the outcomes of the reactions depend on the interplay between Brønsted and Lewis acidic components of metal triflates. The prevailing type of catalyst acidity is usually determined by the strength of metal–ligand versus metal–solvent interactions.[3] The first phenomenon relies on Lewis acidity and leads to retro-aldol pathways. In contrast, binding of the sol-



Scheme 8. Conversion of C_2–C_4 sugars into α-hydroxy methyl esters.

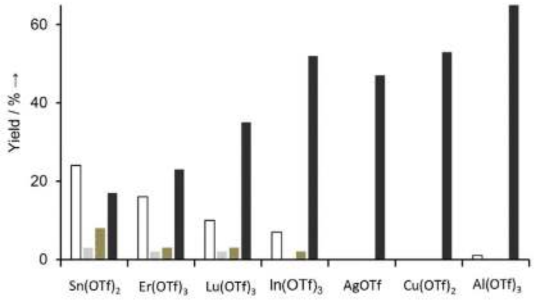


Figure 2. Metal triflate catalyzed conversion of cellulose into value-added esters. Reaction conditions: ball-milled cellulose (1 g), catalyst (0.24 mmol), methanol (50 mL), 200 °C, 2 h.[29] □: yield of methyl lactate, ▪: yield of methyl 4-methoxy-2-hydroxybutanoate, ■: yield of methyl vinylglycolate, ■: yield of methyl levulinate.

vent to the metal induces the release of a Brønsted acid, which leads to rehydration products.

As far as can be established, there is only one instance of a successful acid-catalyzed synthesis of glycolic acid from cellulose.[128] This method is based on a phosphomolybdic heteropolyacid, $H_3PMo_{12}O_{40}$, as a catalyst under an oxygen atmosphere. Optimization of the reaction conditions led to the production of glycolic acid in a yield of 49% for α-cellulose as a substrate (Table 3). Usefully, untreated bagasse and hay produce remarkably high yields of glycolic acid, along with additional products, such as formic, acetic, propionic, and glyceric acids. Importantly, the catalyst can be recovered and reused without loss of activity in nine consecutive runs.

There is a little progress towards the production of other value-added molecules from carbohydrates: products such as C_2–C_4 saccharides, 2,4-dihydroxybutanoic acid, 2,5-dihydroxybut-3-enoic acid, 2,4,5-trihydroxypentanoic acid, 2,4,5,6-tetrahydroxyhexanoic acid, and 5-(1,2-dihydroxyethyl)-3-hydroxydihydrofuran-2(3*H*)-one, which have been found in reaction media as intermediates or side-reaction products.[134] Unfortunately, there are no known chemocatalysts that support the selective production of these molecules, which leaves significant scope for research in this field.

3. Transformation of Saccharides in Ionic Liquids

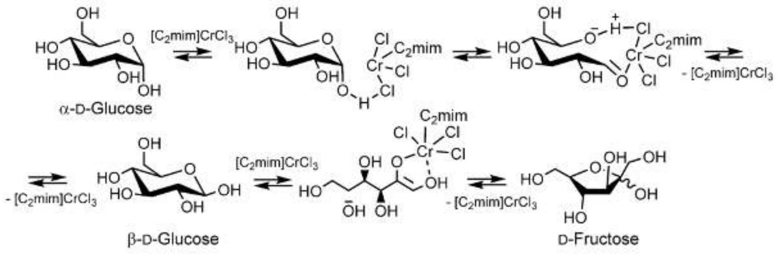
ILs are referred to as a class of alternative solvents that consist solely of ions and have melting points below 100 °C. Over the past few decades, there has been significant focus on the chemistry of ILs[135] and chemical processes in IL media,[135–138] with respect to their specific properties and the wide range of applications, including the synthesis of platform molecules.[138] Chemical transformations of carbohydrates in alternative solvents possess manifold benefits, compared with reactions in aqueous systems. The loss of products, and catalyst deactivation, is markedly diminished in IL media; this is likely to be due to the inhibition of side reactions involving solvent molecules. Some ionic systems are able to dissolve cellulose, and therefore, allow processes to be performed under comparably mild conditions with a high degree of efficacy. The prime disadvantage of common ILs is their high cost, which implies that only outstanding technologies are likely to be competitive in terms of the sustainable biorefinery. To demonstrate the promise and opportunity of ILs, this section focuses on the conversion of carbohydrates in various ionic solvents that are quaternary ammonium salts, deep eutectic solvents (DESs), and inorganic molten salt hydrates.

3.1. Quaternary ammonium ILs

The cascade of cellulose conversion in ILs is somewhat similar to the steps occurring in aqueous media because water is usually added to support hydrolytic reactions. As with other reaction media, the hydrolysis of cellulose into its monomer glucose is considered to be the first stage. In this respect, there are several studies that reveal highly efficient catalytic production of glucose in 1-butyl-3-methylimidazolium chloride ([C_4mim]Cl). For example, a sulfonated carbon-based catalyst prepared by incomplete hydrothermal carbonization and sulfonation of glucose has been applied to the degradation of MCC.[139] A total yield of reducing sugars of 73% was achievable under optimized conditions ($T = 110\,^{\circ}C$, reaction time = 4 h). This yield is significantly higher than those realized with other solid acids, such as HY zeolite, Amberlyst 15, or Nafion NR50, which provide yields of reducing sugars of 48, 28, and 35%, respectively.[139] The latest investigations show that glucose yields can be improved by using dilute sulfuric acid as a catalyst.[140] The highest yield of reducing sugars in this instance is 92% at 180 °C for 60 min reaction time.

The majority of papers reporting the conversion of carbohydrates in alternative solvents focus on the production of HMF. A theoretical comparative study of reaction mechanisms in water and the IL 1,3-dimethylimidazolium chloride ([C_1mim]Cl) found that major differences in outcomes were due to solvent effects in water and IL media.[141] First, it should be noted that deprotonation of the C2 hydroxyl group may be performed by the Cl^- ion of [C_1mim]Cl, similar to the C2–C1 hydride shift proposed during glucose–fructose isomerization catalyzed by Lewis acids in water (Scheme 2). On the other hand, according to the calculated energy values, isomerization occurs through an open-chain mechanism in ILs and a cyclic mechanism in aqueous systems. The authors also propose a variety of side reactions in water that are likely to be absent in ILs, and thereby account for the higher selectivity in alternative solvents.

Metal chlorides are widely used for the catalytic transformation of carbohydrates in ILs. One of the pioneering studies by Zhao et al. showed the high activity of some metal chlorides for glucose conversion in 1-ethyl-3-methylimidazolium chloride ([C_2mim]Cl).[142] From a mechanistic perspective, the solvent–metal chloride interaction induces the formation of MCl^{n-} ions (M = metal, n = integer), which are proposed to catalyze the reaction. Primarily, these catalytic species boost the rate of proton transfer during mutarotation between α- and β-glucose anomers, but only $CrCl^{n-}$ is able to catalyze subsequent isomerization into fructose (Scheme 9). In addition, it was noted



Scheme 9. Isomerization of glucopyranose α-anomer into fructose.[142] [C$_2$mim] = 1-ethyl-3-methylimidazolium.

that metal chlorides tended to stabilize HMF, and this effect was highest for $CrCl_2$, $CuCl_2$, and VCl_4.[142] Conditions and results of the most successful instances are given in Table 4.

Inspired by the abovementioned results, many research groups have applied metal chlorides in the direct conversion of polysaccharides into HMF under various reaction conditions. For example, $CrCl_3$ was applied as a catalyst in the transformation of MCC in [C$_4$mim]Cl under microwave irradiation.[143] HMF yields achieved under these conditions within several minutes are comparable to or higher than those obtained from glucose or cellulose under conventional heating (Table 4). This positive outcome has been ascribed to the rate of heat transfer compared with that of traditional heating and a decrease of activation energy, as a result of orientation effects of polar species in the electromagnetic field of the microwave reactor.[144,145] In addition, it has been reported that $CrCl_3$ can catalyze the conversion of crude lignocellulose under microwave irradiation in [C$_4$mim]Cl.[146] The yields of HMF from corn stalk, rice straw, or pine wood were 45, 47, or 52%, respectively, along with furfural in yields of 23, 25, or 31%, respectively. As mentioned above, the use of microwave reactors in industry is restricted due to cost implications, and so this proposed method is not industrially viable at present.

A notable advance in cellulose valorization into HMF employs [C$_4$mim]Cl as the solvent and $CrCl_3$ as the catalyst.[147] To facilitate the transformation of the polysaccharide into HMF, the cellulosic material was pretreated with a dilute aqueous solution of sodium hydroxide (3 wt%) before the acid-catalyzed reaction. This approach became useful for the conversion of a range of lignocellulosic substrates (wood chips, rice straw) to afford high yields of the target furaldehyde (Table 4). Another benefit of the process is the mild reaction conditions; these are likely to be a consequence of the decrease of the intermolecular linkages between the fibrils of polymer after pretreat-

Table 4. Conditions and results for the acid-catalyzed conversion of carbohydrates into HMF in various ILs.[a]

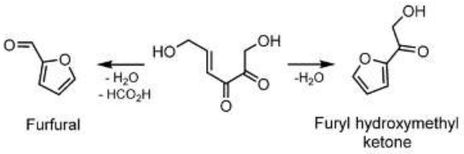
Substrate	Reaction media	Catalyst	t [min]	Reaction T [°C]	HMF yield [mol%]	Ref.
glucose	[C$_2$mim]Cl	$CrCl_2$	180	100	70	[142]
		$CrCl_3$			45	
		$PtCl_4$			15	
		$AlCl_3$			10	
MCC	[C$_4$mim]Cl	$CrCl_3$	2	400 W[b]	61	[143]
wood chips	[C$_4$mim]Cl	$CrCl_3$	120	120	79	[147]
rice straw					76	
MCC	[C$_2$mim]Cl	$CuCl_2$/$CrCl_2$	480	120	57	[148]
MCC	[C$_2$mim]Cl	$CuCl_2$/$CrCl_3$	10	140	39	[150]
MCC	[C$_4$mim]Cl	SCC	15	160	41	[151]
MCC	[C$_2$mim]OAc/[C$_4$SO$_3$Hmim]CH$_3$SO$_3$	$CuCl_2$	210	160	70	[153]
MCC	[C$_3$SO$_3$Hmim]HSO$_4$/DMSO/	$InCl_3$	300	160	45	[154]
ball-milled MCC	[C$_2$OHmim]Cl/[C$_4$SO$_3$Hmim]CF$_3$SO$_3$	$CrCl_2$	240	140	62	[155]
cotton linters	[C$_4$mim]Cl/DMA/LiCl	$CrCl_2$/HCl	120	140	54	[157]
corn stover		$CrCl_3$/HCl			48	
MCC	[C$_4$mim]Cl/DMSO	$AlCl_3$	540	150	55	[159]
MCC	TBAC	$CrCl_3$/HCl	90	140	44	[160]
inulin	ChCl/$C_2H_2O_4\cdot 2\,H_2O$/AcOEt	–	120	80	64	[163]
pretreated MCC[c]	$ZnCl_2\cdot 4.44\,H_2O$	HCl	–	120	30	[174]
MCC	$ZnCl_2\cdot 3\,H_2O$/MIBK	HCl	40	150	81	[175]

[a] [C$_2$mim]OAc = 1-ethyl-3-methylimidazolium acetate, [C$_2$OHmim]Cl = 1-(2-hydroxyethyl)-3-methylimidazolium chloride, [C$_3$SO$_3$Hmim]HSO$_4$ = 1-methyl-3-(3-sulfopropyl)imidazolium hydrogen sulfate, [C$_4$SO$_3$Hmim]CH$_3$SO$_3$ = 1-(4-sulfobutyl)-3-methylimidazolium methanesulfonate, [C$_4$SO$_3$Hmim]CF$_3$SO$_3$ = 1-(4-sulfobutyl)-3-methylimidazolium trifluoromethanesulfonate, ChCl = choline chloride, DMA = dimethylacetamide, MIBK = methyl isobutyl ketone, SCC = sulfonated carbonized cellulose, TBAC = tetrabutylammonium chloride. [b] Heating under microwave irradiation at 400 W. [c] Cellulose was heated in $ZnCl_2\cdot 4.44\,H_2O$ at 70 °C for 12 h.

ment. However, no data were provided with regard to the recovery of the ionic system.

An interesting approach has been developed by Su et al., who employed paired metal chloride Lewis acid assisted Lewis acid catalysts in the conversion of carbohydrates in [C$_2$mim]Cl.[148,149] First, the combination of $CrCl_2/CuCl_2$ at a high loading of the copper salt (85–95 mol% based on the total amount of catalyst added) boosts the rate of the hydrolysis of glycosidic bonds, and therefore, of the yield of glucose. However, optimum selectivity for HMF requires an excess of chromium salt (83 mol% of the catalyst). Regulation of the reaction parameters and elaboration of the recovery procedure through a multistep extraction with MIBK enable the process to reach a steady yield of HMF of 57%. The same group also studied combinations of $PdCl_2/CuCl_2$ in cellulose transformations.[149] Despite the low yield of HMF (17%), these paired metal chlorides efficiently disrupt the long-range interactions between the solvent ions, and thereby, improve cellulose solubility and its hydrolysis.

An important finding in paired Lewis acid catalyzed reactions was the discovery that various combinations of metal chlorides catalyzed the conversion of cellulose in [C$_2$mim]Cl not only to HMF, but also to other furan derivatives, such as furfural and furyl hydroxymethyl ketone, which are all important high-value commodity products.[150] The general hypothesis is that intermediate 1,2-diketones transform into furfural or furyl hydroxymethyl ketone (Scheme 10). It is interesting to point out that the combination $CrCl_3/CuCl_2$ provides the highest yield of HMF in reaction times as brief as 10 min. In turn, $FeCl_3/CuCl_2$ improves the selectivity to and yield of furfural and furyl hydroxymethyl ketone (16 and 11%, respectively) under the same process conditions. In both cases, longer reaction times result in losses of products as a consequence of side processes.



Scheme 10. Formation of furfural and furyl hydroxymethyl ketone from a 1,2-diketone intermediate.[150]

Heterogeneous acid catalysis has also been applied to the transformation of carbohydrates into HMF in alternative solvents. The conversion of glucose in [C$_4$mim]Cl in reactions catalyzed by various solid acids (clays, zeolites, resins, heteropolyacids, sulfated oxides, and carbonized carbohydrates) has been investigated.[151] As seen in Figure 3, the highest conversion of glucose and yield of HMF are delivered by sulfonated carbonized saccharides, primarily derived from cellulose. This material has been identified as a recoverable, efficient catalyst that is also suitable for cellulose conversion (Table 4). Notwithstanding problems associated with the high loading of the sulfonated carbocatalysts (optimally found to be 40 wt% based on starting materials), they show promise with regard to low cost and high selectivity. However, it is important to note the major role performed by [C$_4$mim]Cl in the catalytic reactions, as explained above (i.e., to promote proton transfer reactions). Neither water nor common organic solvents are able to afford high yields of HMF within the process (Figure 4). It is likely that the benefits of the IL system are derived from several phenomena, namely, simultaneous enhancement of the solubility of carbohydrates in the IL, improved stability of the products in the IL, and improved glucose–fructose isomerization.

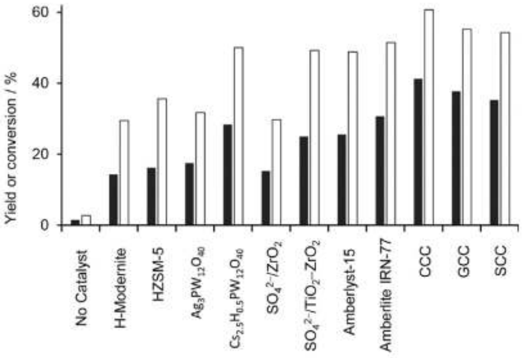


Figure 3. Transformation of glucose into HMF catalyzed by various solid acids. Reaction conditions: glucose (100 mg), catalyst (40 mg), [C$_4$mim]Cl (1 g), 140 °C, 30 min.[151] ■: yield of HMF, □: conversion of glucose. CCC, GSS, and SCC are cellulose-, glucose-, and starch-derived carbonaceous catalysts, respectively.

The potential of acidic ILs to perform the dual roles of reaction medium and cocatalyst has been explored.[152] For example, various acidic ILs combined with [C$_2$mim]OAc have been investigated for the transformation of cellulose into HMF.[153] Mixtures of [C$_4$SO$_3$Hmim]CH$_3$SO$_3$ and $CuCl_2$ provide the highest yield of HMF. Subsequent work with [C$_3$SO$_3$Hmim]HSO$_4$ combined with $InCl_3$ suffered lower yields of the major products and a requirement for longer operation times (Table 4).[154] The combination of $CrCl_2$ and [C$_4$SO$_3$Hmim]CF$_3$SO$_3$, used in the bi-

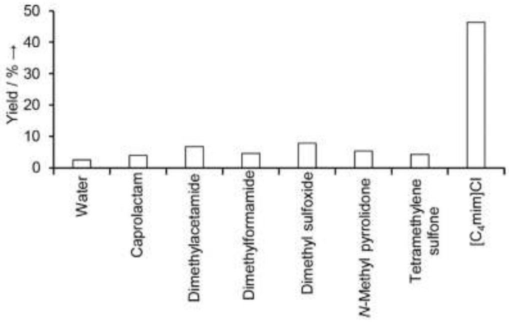


Figure 4. Glucose conversion into HMF in various solvents. Reaction conditions: glucose (100 mg), SCC (40 mg), solvent (1 g), 160 °C, 15 min.[151]

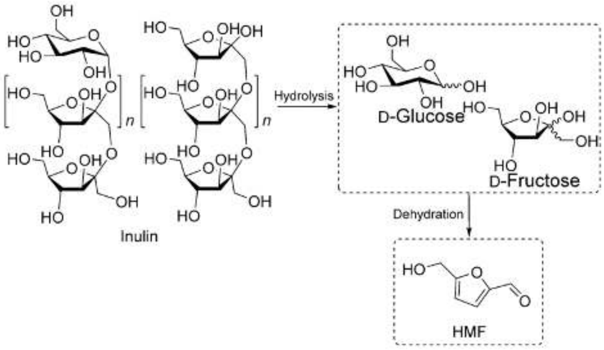
phasic system [C$_2$OHmim]Cl and 1,2-dimethoxyethane, gives significant yields of HMF (Table 4).[155] It is possible to shift the process towards the formation of levulinic acid by using the IL [C$_3$SO$_3$Hmim]HSO$_4$ and an excess of water.[156] This shift is likely to be induced by the rehydration of HMF at higher loadings of water and by hydrolysis of the IL into sulfuric acid, which promotes this reaction. One major disadvantage of this approach is the application of microwave heating before a reasonable yield can be realized.

Imidazolium-based ILs improve the efficacy of the process in terms of higher HMF output and some flexibility of the product portfolio, in comparison with conventional solvents. On the other hand, ILs are costly, which represents something of a stumbling block for the industrial application of the chemistry. One potential resolution has been the addition of the well-known cellulose solvent mixture of *N*,*N*-DMA/LiCl to [C$_2$mim]Cl, to decrease the amount of IL consumed during the cellulose conversion processes.[157,158] This ionic system, in the presence of a catalytic mixture of CrCl$_2$ or CrCl$_3$ and hydrochloric acid, is suitable for the direct conversion of cellulose, and lignocellulosic biomass, to provide HMF in yields of up to 54 and 48 %, respectively (Table 4). In addition, furfural was recovered in a yield of 34 % from corn stover. However, the toxicity of DMA, the high catalyst loading (up to 35 mol % based on the anhydroglucose unit), and problems of solvent reuse complicate the implementation of this method. This issue can be partially resolved by the combination of DMSO and [C$_4$mim]Cl.[159] AlCl$_3$ afforded a reasonable yield of HMF in this mixture under optimized reaction conditions and the system could be reused in five reaction cycles with only slight loss of activity (Table 4). TBAC, which is considered to be a relatively inexpensive alternative to imidazolium-based ILs,[160] also shows some promise. A yield of 44 % HMF was obtained in TBAC during the conversion of cellulose, as catalyzed by a combination of CrCl$_3$ and HCl. The possibility of solvent and catalyst recovery has been surveyed and stable synthetic results have been determined for five reaction cycles.

3.2. DESs

Although common ILs suffer a number of drawbacks as mentioned, DESs show significant promise. DESs are a class of ionic systems formed from a eutectic mixture of Brønsted or Lewis acids and bases and have general formula Cat$^+$X$^-$$z$Y, in which Cat$^+$ is commonly ammonium, phosphonium, or sulfonium cation; X is a halide ion; and z is the number of acid molecules Y.[161] A major advantage of DESs is the ease of their preparation, which usually involves a single-step combination of ammonium salts with a metal salt or hydrogen-bond donor under solvent-free conditions. Additionally, DESs may be prepared from environmentally benign and inexpensive materials, and many of these solvents are considered to be relatively nontoxic and biodegradable substances.[162]

DESs that consist of ChCl and organic acids possess the intrinsic Brønsted acidity needed for certain catalyzed reactions. For instance, the solvent produced by blending ChCl and oxalic or citric acid has been applied for the ready synthesis of HMF from inulin.[163] Inulin is a nondigestible fructose oligomer with occasional chain-terminating glucosyl moieties, which transforms into HMF according to Scheme 11. The high yield of the value-added molecule can be attained at the surprisingly low temperature of 80 °C (Table 4). This result is perhaps the lowest known temperature for the efficient conversion of oligosaccharides into HMF. DESs based on ChCl and citric acid have been used for the conversion of hemicellulose into furfural, in the presence of the Lewis acid catalyst AlCl$_3$.[164] The proposed mechanism suggests that the combined acids are able to promote both xylose–xylulose isomerization and xylulose dehydration into furfural. As a result, the furfural yield can reach 73 %. It is noteworthy that in both cases the acidic DES could be recovered and reused in the process.



Scheme 11. Conversion of inulin into HMF. n = integer.

Another type of DES derived from natural molecules is a eutectic mixture of ChCl and certain carbohydrates. Ilgen et al. reported the acid-catalyzed conversion of various saccharides into HMF in their highly concentrated low-melting mixtures (the ratio of carbohydrate to ChCl was between 1:1 and 1.5).[165] All of the mono-, di-, and oligosaccharides explored gave stable melts in combination with ChCl at temperatures below 100 °C, but their conversion into product strongly depended on the nature of the starting materials and catalyst (Figure 5). A possible explanation for this observation is the likelihood that each saccharide is converted by a different mechanism. As far as can be determined, there is no information relating to the chemical conversion of cellulose in DESs, despite several papers dedicated to cellulose pretreatment in ChCl-based melts.[166–169]

3.3. Inorganic molten salt hydrates

Recent research applying alternative solvents for cellulose conversion has been particularly focused on the use of inorganic molten salt hydrates. These are inorganic salts that contain water tightly bound to the inner coordination sphere of the

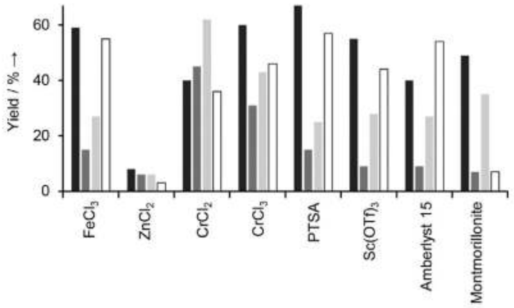


Figure 5. Acid-catalyzed transformations of various sugars into HMF in their highly concentrated melting mixtures. Reaction conditions: catalyst (10 mol%; Amberlyst 15 and Montmorillonite 10.0–12.5 wt% based on sugar), 100 °C, 30 min.[165] ■: fructose/ChCl (1:1.5), ■: glucose/ChCl (1:1.5), ■: sucrose/ChCl (1:1), □: inulin/ChCl (1:1).

cation in quantities approaching the highest coordination number of the central ion.[170] Bearing in mind that such inorganic salts possess intrinsic Lewis acidity, along with extremely low vapor pressures, they demonstrate characteristics consistent with green precepts and are therefore budding candidates for cellulose processing.

A number of molten salt hydrates have been demonstrated to be suitable for the dissolution, swelling, and decomposition of cellulose.[171,172] However, only $ZnCl_2 \cdot n H_2O$ ($n = 3$–4) has presently found an application in the chemical conversion of this polysaccharide into platform molecules.[173–175] $ZnCl_2 \cdot n H_2O$ is considered to be an IL, possessing the formula $[Zn(OH_2)_6][ZnCl_4]$ in the case of $n = 3$.[176,177] The high dissolving power of such ILs might be attributed to the coordination and strong interaction between the hydroxyl groups of the solvent and polymer.[177] These solvent–substrate interactions may lead to the specific pathways in the transformation of cellulose described below.

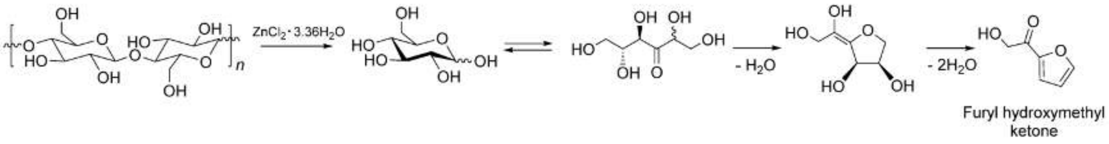
Furyl hydroxymethyl ketone may be prepared from cellulose in $ZnCl_2 \cdot 3.36 H_2O$ under microwave irradiation, and without the addition of a solvent extractant.[173] In contrast to the method detailed above for the formation of this ketone (Scheme 10), the authors postulated another mechanism that proceeded through the intermediate sugar with a carbonyl group on the third carbon atom (Scheme 12). The highest yield of furyl hydroxymethyl ketone was only 12%; this is probably attributable to the decomposition of the product/s in the acidic reaction media.

A study dedicated to the conversion of cellulose in $ZnCl_2 \cdot n H_2O$, in which the number n was carefully controlled, showed that selectivity could be shifted to the formation of HMF through the addition of Brønsted acid catalysts and the use of conventional heating.[174,175] For example, in $ZnCl_2 \cdot 4.44 H_2O/HCl$, HMF is obtained in a yield of 30% from treated cellulose (Table 4).[174] This result can be markedly improved upon through the addition of MIBK to the reaction system as a solvent extractant, and sodium chloride to enhance the removal of HMF from the polar phase.[175] Usefully, a high yield of HMF of about 80% was reproducibly obtained in 4 catalytic runs. This is arguably the benchmark result in HMF synthesis directly from cellulose. The major weakness of the processes is the high loading of HCl catalyst (up to 3 equiv based on anhydroglucose), which provides a barrier to its acceptance in larger scale processes. It therefore remains an unsolved problem to successfully convert cellulose in such systems into one or two major products in high yields under relatively mild reaction conditions.

4. Summary and Outlook

There is current and growing interest in the chemocatalytic conversion of carbohydrates into industrially important products. The dramatic growth in numbers of publications and patents during the past two decades clearly exemplifies the movement towards the acid-catalyzed synthesis of bioderived building-block chemicals with promise to be replacements for common nonrenewable crude oil based products. Notwithstanding the many successful laboratory approaches, a number of problems persist for practical applications. For instance, in most examples, the production of HMF remains based on refined digestible sugars, such as fructose or sucrose, which on a large scale becomes food competitive, potentially becoming a source of moral, ethical, and social problems. Nevertheless, laboratory-scale investigations add substantial knowledge and understanding relating to these transformations, upon which next-generation technologies will no doubt be based. Meanwhile, the technology itself demands a substantial improvement to mitigate significant losses of product during the purification of the target molecule.[33]

Substantial opportunities exist within waste and low-value streams of agriculture, horticulture, and forestry. Examples include lipid-extracted algal residues that are generated during biodiesel production; side branches from plantation trees remaining unused in timber and paper manufacture; the nonedible portion of food crops, peels, and skins from vegetables and fruits that derive from the food-processing industry; and wastes from fermentation processes, such as in the manufacture of bioalcohol, or the use of algal residues (i.e., residual



Scheme 12. Cellulose conversion into furyl hydroxymethyl ketone in $ZnCl_2 \cdot 3.36 H_2O$.[173]

biomass from these processes). Although there have been excellent discoveries towards the conversion of cellulosic materials (preferably native, untreated cellulose or lignocellulosic feedstocks, including their fractionation in benign processes[116,178]) into platform chemicals, and, although these efforts have led to deeper insights and provided glimpses of potential solutions, the problem remains unsolved. Many current practices rely on pretreatment processes that add unwanted levels of complexity or energy consumption. If cellulose can be converted into valuable materials in a process that improves significantly upon the commercial Biofine or OxFA processes, then substantial scientific and, potentially, industrial progress will have been made. The optimum system will be able to operate directly on cellulose or lignocellulose, without requirements for its pretreatment, under mild conditions; will produce high yields of desirable target molecules in selective transformations; and will employ robust catalysts. Preferably, the catalysts will be inexpensive, recoverable, and reusable, and will contain the functionality required to perform the complexity of tasks necessary to convert cellulose into platform chemicals, namely, hydrolysis, isomerization, dehydration, retro-aldol reactions, and rehydration steps. This is a lofty goal for workers in this area, one to which real progress is being made by building on the foundations of a deep understanding that is being achieved by fundamental studies. Despite the progress that has been made, there is much to be done before this problem will be solved.

Arguably, the most promising line of investigation at present includes the use of ILs, which frequently perform as functional solvents that are instrumental in simplifying the role of added catalysts. Ionic solvents have undoubtedly become recognized as highly suitable media for the synthesis of valuable small-molecule products from cellulose and, in some instances, lignocellulosic biomass. The wide variety of conventional imidazolium-based ILs and the availability of cheap alternatives, such as DESs and inorganic molten salt hydrates, provide substantial scope for deeper investigations.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: acid catalysis · biomass · carbohydrates · green chemistry · solvent effects

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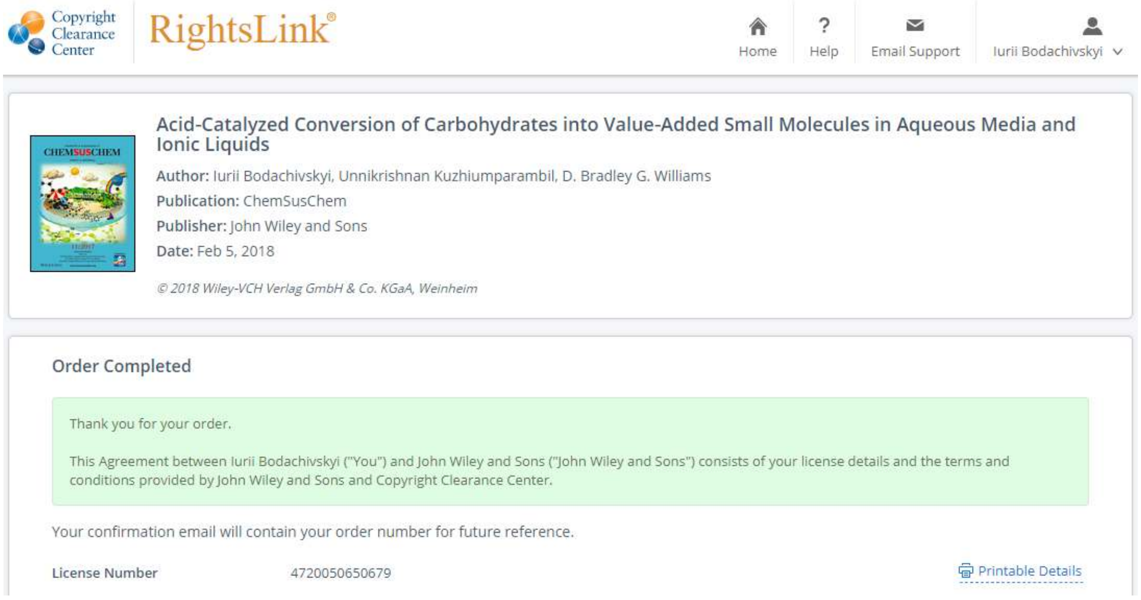

Acid-Catalyzed Conversion of Carbohydrates into Value-Added Small Molecules in Aqueous Media and Ionic Liquids

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1.2. Formulation of project tasks

The above-represented literature survey highlights the knowledge gaps and practical problems that plague the progress towards sustainable valorisation of cellulosic biomass. It also defines the scope for future investigations, among which the use of catalytic metal triflates, along with alternative ionic liquid systems, are arguably the most promising lines for beneficiation within the biorefinery.[1] As discussed, metal triflates are robust and recoverable acidic catalysts that have been successfully deployed in several transformations of carbohydrates.[1] Ionic solvents have been demonstrated to dissolve cellulosic substances and, in separate examples, to catalyse their reactions, consequently enabling the valorisation of polysaccharides under milder reaction conditions and in better yields of some targeted products.[1] The present work will systematically research acid-catalysed conversions of cellulosic carbohydrates and native cellulosic biomass into value added low molecular weight derivatives under the action of metal triflates and/or ionic liquid systems. To do this, experimental work is oriented towards the following tasks:

- **Detail the activity of metal triflates in transformations of (poly)carbohydrates into value added molecules.**

A range of Lewis acidic metal triflates, Brønsted acids, and combined Lewis/Brønsted acid systems are to be explored in model reactions of refined saccharide substrates, such as glucose and microcrystalline cellulose (MCC), under differing processing conditions. These conditions will include the catalyst, solvent, temperature regime and sometimes additives to modify the catalyst.

- **Investigate ionic solvents for the dissolution and acid-catalysed processing of cellulosic materials.**

Various classes of ionic liquids (ILs), including zinc chloride hydrates, imidazolium salts and deep eutectic solvents (DESs), will be researched for the dissolution and acid-catalysed transformation of cellulose. This study will also include the processing of low molecular weight derivatives to detail the course of hydrolytic conversion of polysaccharides in ionic systems.

- **Optimise reaction conditions for the conversion of polysaccharide substrates into target compounds and apply them to the valorisation of native cellulosic biomass.**

Defined optimum catalytic systems based on metal triflates, or ILs, will be employed to the conversion of native cellulose and cellulosic biomass from terrestrial or aquatic sources. The processing parameters will be adjusted for each targeted substrate to maximise yields and selectivity of desirable product(s).

1.3. Thesis overview

This thesis by compilation comprises three chapters with processed research data (**Chapter 2, 3** and **4**), one summative chapter generally discussing the results and concluding the work (**Chapter 5**).

Chapters 2 and **3** are combinations of published research articles directly relating to the thesis.[2–8] They are separated into two sub-projects, namely acid-catalysed conversion of (poly)carbohydrates in aqueous and alcohol media (**Chapter 2**),[2,3] and catalytic valorisation of cellulosic biomass in various classes of ILs (**Chapter 3**), respectively. These chapters are formed by sections which consist of publications with self-contained aims and objectives, description and justification of research methods and rationalisation of data. They are arranged in a logical order, to develop a foundation for research for each subsequent section.

The work in **Chapter 2** starts from model transformations of glucose (the monomer of cellulose) in water and methanol under the action of acidic metal triflates as catalysts, including their derivative Brønsted acid-assisted or Brønsted base-modified systems (**Section 2.1**).[2] **Section 2.1** details the course of the catalytic conversion of glucose into value added molecules, and defines the specific type of acid activity (Brønsted or Lewis) to promote desirable reaction pathways. It determines preferred catalyst, solvent, and temperature regime, to select for disaccharides, fructose, methyl glycosides, or methyl levulinate. The improved fundamental knowledge is further translated into the acid-catalysed conversion of MCC into ethyl levulinate in ethanol (**Section 2.2**).[3] Herein,[3] superb outcomes of the targeted ester are attained with tunable catalytic combinations of metal triflates and Brønsted acids. This study[3] additionally develops the pretreatment process using a renewable deep eutectic mixture of choline chloride and oxalic acid dihydrate (ChCl/oxalic acid), which enables high-yielding and highly selective transformation of raw and unrefined cellulosic materials thereof into ethyl levulinate.

Chapter 3 interrogates catalytic valorisation of cellulosic substrates in various ILs, including zinc chloride hydrate solvents, 1-butyl-3-methylimidazolium chloride ([C_4mim]Cl), and ChCl/acid (oxalic, citric, or *p*-toluenesulfonic acid) deep eutectic systems.[4–8] This chapter is formed by five sections (research articles), as detailed below.

Sections 3.1–3.3 explores the transformation of polysaccharides and native cellulosic biomass in catalytic zinc chloride hydrates solvents.[4–6] The prelude of this study details the unusual conversion of carbohydrates into furyl hydroxymethyl ketone and furfural, defining biphasic solvent system $ZnCl_2{\cdot}3.0H_2O$/anisole as an optimum media for this process (**Section 3.1**).[4] It also highlights some changes of the reaction outcomes in response on the hydration number *n* of $ZnCl_2{\cdot}nH_2O$, and obstacles pertaining to the high reactivity of furanoid products in the acidic ionic solvent.[4] **Section 3.2** continues this research, systematically exploring the role of the molecular formula of $ZnCl_2{\cdot}nH_2O$ (n = 2.5–4.5) on its catalyst activity in chemical transformations of cellulose and other native polysaccharides.[5] This study[5] subsequently applies new insights into highly selective valorisation of lignocellulosic and algal biomass into low molecular weight reducing saccharides, 5-(hydroxymethyl)furfural and furfural. Additionally, **Section 3.3** identifies optimal processing conditions to simultaneously and very efficiently valorise native hexosans and pentosans into furfural as principal product.[6]

Section 3.4 shifts the focus towards the hydrolytic conversion of cellulose in quaternary ammonium salts.[7] It develops a highly selective method for depolymerisation of cellulose into water-soluble (oligo)carbohydrates in the mixed ionic media comprising [C_4mim]Cl and ChCl/acid (oxalic, citric or *p*-toluenesulfonic acid) as co-solvent-catalyst. In this study,[7] a combined ionic system [C_4mim]Cl / ChCl/oxalic acid is established to be optimal and is adopted to the direct depolymerisation of crude cellulose and native cellulosic biomass into significantly value added low molecular weight reducing carbohydrates.

Section 3.5 investigates catalytic processing of cellulosic polysaccharides in the neat deep eutectic system ChCl/oxalic acid.[8] This work[8] characterises the activity of the acidic DES as a solvent-catalyst for reactions of purified (poly)carbohydrates and of the macromolecular portion of unrefined lignocellulose in a systematic study. It details reactivity of native glucans, xylans and fructans and uncovers preferred conditions to efficiently convert native cellulosic biomass into high value monosaccharides, furan derivatives, and into refined cellulose. **Section 3.5** culminates with a subsequent acid-catalysed processing of the recovered cellulosic material using earlier established methods, given in **Sections 2.2, 3.2** and **3.4**, delivering additional value added chemicals in high yields from the undervalued biomass.

Chapter 4 poses an individual study (a published research article), combining the information relating to the dissolution, regeneration, and characterisation of cellulose in ILs.[9] It defines the integrity of cellulose from various sources in different classes of ionic solvents and uses insights given in **Chapters 2** and **3** to rationalise observations. It classifies ILs as *innocent* or *non-innocent* processing media based on the extent of cellulose stability under applied conditions, to provide practical recommendations for the use of these systems in cellulose refining technologies.

Chapter 5 synthesises principal findings of the project in a form of the account, additionally delivering general conclusions and springboard for future research. This is an unpublished material but some of the concepts and conclusions are taken from the currently accepted, co-authored with supervisors book chapter.[10]

Appendices present supporting information for each research article included in **Chapter 2, 3** and **4**.[2–9]

Chapter 2:

Acid-catalysed conversion of (poly)carbohydrates in aqueous and alcohol media

2.1. A systematic study of metal triflates in catalytic transformations of glucose in water and methanol: identifying the interplay of Brønsted and Lewis acidity

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A Systematic Study of Metal Triflates in Catalytic Transformations of Glucose in Water and Methanol: Identifying the Interplay of Brønsted and Lewis Acidity

Iurii Bodachivskyi,[a] Unnikrishnan Kuzhiumparambil,[b] and D. Bradley G. Williams*[a]

The specific type of acidity associated with the given metal trifloromethanesulfonates (Brønsted or Lewis acidity) dramatically influences the course of reactions, and it is possible to select for disaccharides, fructose, methyl glucosides, or methyl levulinate. Glucose is transformed into a range of value-added molecules in water and methanol under the action of acidic metal triflates as catalysts, including their analogous Brønsted acid-assisted or Brønsted base-modified systems. A systematic study is presented of a range of metal triflates in methanol and water, pinning down the preferred conditions to select for each product.

Introduction

The production of bulk chemicals from naturally derived materials is a foundation of sustainable chemical industrial development. Among the various resources that are available, cellulose-derived glucose in principle possesses the scale of manufacture and overall availability to sustain a large chemical industry.[1] In the presence of an acid catalyst, glucose may be converted into a large portfolio of valuable organic building-block chemicals (platform molecules), all of which are realistic contenders to substitute petrochemical products.[1–3] Despite this promise, the acid-catalyzed valorization of glucose is challenging: complexities arise because of the low selectivity of processes that are typically performed in water and that require both Lewis *and* Brønsted acid catalysts, as pictorially presented in Scheme S1 (Supporting Information).[1] It is considered that Lewis acids promote the isomerization of glucose into fructose at moderate temperatures,[3,4] and at elevated temperatures facilitate retro-aldol reactions into low-molecular-weight sugars from which α-hydroxy acids are produced.[5] In turn, Brønsted acids usually catalyze the dehydration of fructose into 5-(hydroxymethyl)furfural (HMF) and rehydration thereof into levulinic acid under more forcing reaction conditions.[6] Whereas Brønsted acidity is achievable by the addition of protic acids to the media, it is more difficult to ensure Lewis acidity owing to the deactivation of many Lewis acids in aqueous solvents.[7] The differing role of the acid catalysts at each stage of the conversion of glucose, along with the difficulties in sustaining Lewis acidity in water, requires the judicious selection of robust catalysts that are capable of providing the requisite activity to enable the substrate to be transformed into the desired product with high yield and selectivity.

The general understanding of the role of solid acid catalysts in these processes has improved over the past few years, owing to several elegant studies.[8–10] Metal triflates are water-tolerant homogeneous Lewis acid catalysts, which has fostered their use in a number of chemical processes in aqueous and protic media, including the synthesis of platform molecules.[7,11–14] Replacing the aqueous solvent with alcohols permits the conversion of carbohydrates into desirable platform molecules in enhanced yields and sometimes under milder reaction conditions.[6,15–17] In the present work, we detail a systematic study of a range of metal triflates and the responses of the reactions in question to the prevailing conditions. In particular, we probe the type of acidity (Brønsted or Lewis) associated with metal triflates and their performance in transformations of glucose into defined valuable molecules, in aqueous media and methanol. This helps to build an improved and more unified view of how to structure the chemical processing of glucose into platform chemicals. Specifically, we probe the conversion of glucose into disaccharides, into fructose and methyl glucosides (MG), and into methyl levulinate (MLev). Along the way, we consider HMF and 5-(methoxymethyl)furfural (MMF), which are intermediates toward MLev.

Results and Discussion

Metal triflates are efficient in the synthesis of some platform molecules in both aqueous and alcohol media at elevated temperatures (180–240 °C).[14–16] Highly selective transformations at lower temperatures are desirable and are an object of the present study. To achieve this, we explored the activity of a number of metal triflates [$Hf(OTf)_4$, $Sn(OTf)_2$, $In(OTf)_3$, $Al(OTf)_3$,

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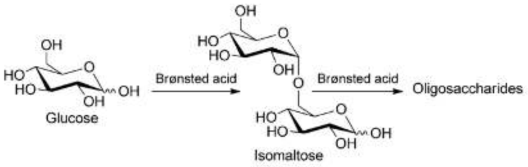
AgOTf, LiOTf, $La(OTf)_3$, or $Y(OTf)_3$], Brønsted acids [*p*-toluenesulfonic acid (TsOH) and H_3PO_4], and Lewis acid-assisted Brønsted acids [$La(OTf)_3/H_3PO_4$, $La(OTf)_3$/TsOH] for the conversion of glucose at lower temperatures and in water or methanol under reflux at atmospheric pressure. In water, fructose, an isomerization product of glucose, is the desired and expected major product,[3,4] but the maximum yield of fructose was only 9 mol% (based on glucose, Table S1, Supporting Information). Metal triflates such as $Sn(OTf)_2$ and $Hf(OTf)_4$ promoted the formation of dark-brown high-molecular-weight byproducts called humins (insoluble condensation products of HMF with saccharides[18]; HMF is a dehydration product of fructose), accounting for the substantial mass losses noted. In contrast, AgOTf or LiOTf showed no catalytic activity, possibly owing to weak complexation with the substrate. Interestingly, the dominant reaction noted with Brønsted acids or Lewis acid-assisted Brønsted acids was the catalyzed condensation of glucose into isomaltose and oligosaccharides, as represented pictorially in Scheme 1. This condensation process has been known since Emil Fischer's day, but most current research shows a distinct focus on enzymatic methods, with little information relating to the targeted chemical synthesis of disaccharides.[19–22] A selective chemical method would therefore provide an exciting alternative to enzymatic methods. As expected, the self-condensation of glucose was more efficient in concentrated aqueous solutions (30 wt% glucose in water) and with extended reaction times (12 h). The highest conversion of glucose (43 wt%, of which 42 wt% is accounted for immediately below, implying 98% selectivity to the named products) into saccharide condensation products was achieved by employing a combination of $La(OTf)_3/H_3PO_4$, and isomaltose was isolated as a main product (yield 17 wt% based on glucose, Table S1, Supporting Information) together with other water-soluble di-, tri-, and oligosaccharides (yields: 5, 6, and 14 wt%, respectively, Table S2, Supporting Information). For comparison, analogous enzymatic processes provide isomaltose in 14 wt% and oligosaccharides in 4 wt% yield.[19] In our work, if water was allowed to distill slowly from the reaction mixture to promote condensation reactions, trisaccharides and oligomeric products predominated, along with water-insoluble material the color of caramel. In this reaction, it is the Brønsted acidity associated with the catalysts, including the metal triflates,[12,13,23,24] that leads to the self-condensation of glucose.



Scheme 1. Self-condensation of glucose into oligosaccharides.

A density functional study at the B3LYP/6-31+g(d) level of theory considering the experimental reaction parameters (temperature, pressure, solvation) found the transition state toward isomaltose to be substantially more stable than those toward other disaccharides (Schemes S2 and S3, Supporting Information, show the series of glucose dimers considered, and a reaction mechanism with intermediates, respectively). This finding implies a kinetic preference for isomaltose (Figure S1, Supporting Information). This observation, coupled with a stable product (thermodynamically the second most favored product of the entire series, Table S3, Supporting Information), would account for the predominance of isomaltose over other glucose disaccharides under Brønsted acid-catalyzed conditions, as observed experimentally.

Aldose–ketose isomerization, required for the glucose–fructose conversion, is more efficient in alcohols than in water, affording alkyl glycosides [glucoside (non-isomerization product) and fructoside (isomerization product)] as major products.[3,8,17] Because the yields of fructose were low in our first set of reactions, consistent with dominant Brønsted acid activity, and to improve the outcome toward fructose, we adopted a two-step, one-pot process, conducting the isomerization in methanol (under reflux at atmospheric pressure, 1 h), and then the hydrolysis of methyl glycosides into fructose and glucose in water (under reflux at atmospheric pressure, 1 h); Table 1 gives the results after the second step.

This approach has been employed favorably in the presence of zeolites.[8,17,25,26] Glucose, fructose, and MG (as a 1:1 mixture of α- and β-anomers of methyl glucopyranoside, as established by quantitative NMR spectroscopic analysis of the product mixture after step 2; Figure S2, Supporting Information) were ob-

Table 1. Acid-catalyzed transformation of glucose in methanol and water[a]

Catalyst	Conv [%]	Fructose yield [%]	MG yield [%]	pH[b] (0.01 M, H_2O)	pH[b] (0.01 M, MeOH)
$La(OTf)_3/H_3PO_4$	12	0	9	2.04	0.72
$Hf(OTf)_4$	41	3	9	2.05	0.50
TsOH	8	0	7	2.08	0.59
H_3PO_4	0	0	0	2.21	2.74
$La(OTf)_3$/TsOH	7	0	5	2.39	1.07
$Sn(OTf)_2$	29	4	9	2.61	0.53
$In(OTf)_3$	29	15	9	3.12	1.09
$Al(OTf)_3$	42	24	5	3.60	1.75
$Al(OTf)_3$/TBP[c]	64	47	1	3.66	2.66
AgOTf	0	0	0	5.16; 4.85[d]	6.10; 4.04[d]
LiOTf	4	3	0	5.33	6.90
$La(OTf)_3$	12	5	0	6.31; 6.05[d]	4.63; 3.77[d]
$Y(OTf)_3$	6	2	2	6.64; 6.02[d]	3.98; 3.20[d]
H-USY[e]	72	55	–	–	–

[a] Yields are specified in mol% based on glucose; "0" or "99" for the product were identified on the basis of trace analysis by HPLC. Reaction conditions: glucose (50 mg), methanol (2 mL), catalyst (20 mol% based on glucose), reflux at atmospheric pressure, 1 h, then solvent exchange with water (2 mL), reflux at atmospheric pressure, 1 h. [b] pH readings were performed in triplicate in water or aqueous methanol (98% alcohol) at 20 °C. [c] Reaction conditions: glucose (50 mg), methanol (2 mL), $Al(OTf)_3$ (20 mol% based on glucose), TBP (60 mol% based on glucose), reflux at atmospheric pressure, 36 h, then solvent exchange with water (2 mL), reflux at atmospheric pressure, 1 h. [d] pH values measured at 40 °C. [e] Reaction conditions:[17] glucose (125 mg), methanol (4 g), H-USY zeolite (75 mg), 120 °C, 2 h, then addition of water (2 g), 120 °C, 1 h.

tained after two-step processing in methanol and water; $Al(OTf)_3$ was found to possess optimal Lewis acidity to drive the isomerization reaction (24 mol% yield of fructose). Given that 1) conversion of glucose into fructose is favored by Lewis acids, and 2) conversion of glucose or fructose into methyl glycosides is favored by Brønsted acidity (similar to the self-condensation of glucose, mentioned above), it might be possible to improve selectivity to fructose by minimizing the Brønsted acid activity associated with the metal triflate catalysts. 2,6-Di-*tert*-butyl-4-methylpyridine (TBP) is known to discriminate between Brønsted and Lewis acidity because it interacts exclusively with hydrogen cations owing to the extreme steric hindrance exerted by the *tert*-butyl-groups, which prevents interactions at the N atom with any larger cations,[27] including Al.[24] Pleasingly, the addition of TBP as Brønsted base [3:1 based on $Al(OTf)_3$] reduced the amount of Brønsted acid-catalyzed production of MG and simultaneously improved the selectivity to and yield of fructose, albeit through a process that required longer reaction times (Table 1 and Table S4, Supporting Information). This outcome demonstrates that catalyst systems displaying both Lewis and Brønsted acidity can be modulated toward Lewis acidity to develop improved chemical selectivity (see below and Table 1 for a discussion on the acidity of the metal triflates). Note that the yield of the isomerization product fructose (47%), produced under mild processing conditions, compares very favorably with the industrially applied enzymatic method (42%).[1] In rare instances, higher yields of fructose are achievable under more forcing reaction conditions (Table 1).[17]

Investigation of the product after step 1 by NMR spectroscopy led to important observations. In particular, the first step delivers high yields of a combination of methyl fructosides and methyl glucofuranosides during the conversion in methanol, with the Lewis acid $Al(OTf)_3$ present, and only small amounts of glucopyranosides (Figure 1). This is entirely consistent with recent work with zeolite catalysts, in which methyl furanosides were also identified as kinetic products.[8] In our work, in all instances, diagnostic signals map perfectly onto those determined previously for similar mixtures.[8] As anticipated, the addition of TBP to $Al(OTf)_3$ suppresses the Brønsted acidity associated with the Lewis acid catalyst and favors the formation of methyl fructosides in preference to methyl glucosides (Figure 2). If only a Brønsted acid (TsOH), Lewis acid-assisted Brønsted acid [$La(OTf)_3/H_3PO_4$], or hard Lewis acid [$Hf(OTf)_4$] is present, very high yields of methyl glucosides are obtained (up to 94% as a mixture of glucopyranosides and glucofuranosides, Figure 3, and Figures S3 and S4, Supporting Information), with no evidence of the formation of fructosides. The softer Lewis acid $La(OTf)_3$ provides only little conversion into methyl glucofuranosides under the applied conditions (Figure S5, Supporting Information). These observations also provide evidence that hard and soft Lewis acids [$Hf(OTf)_4$ and $La(OTf)_3$, respectively] mostly catalyze the isomerization of glucose into fructose in water during the second step; with these acids, the gains of fructose after the two-step conversion in methanol and water are similar to those obtained after the one-step transformation in water (Tables 1 and S1, Supporting Information). Methyl glucofuranosides and fructosides are readily con-

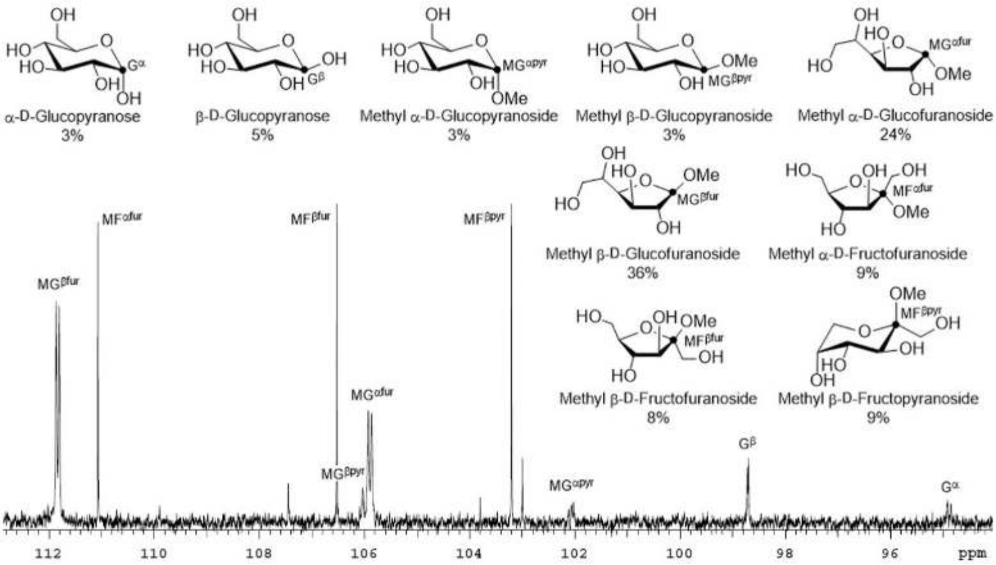


Figure 1. ^{13}C NMR spectrum and the ratio of carbohydrates obtained after $Al(OTf)_3$ processing in methanol (step 1). Reaction conditions: glucose (50 mg), methanol (2.00 mL), $Al(OTf)_3$ (20 mol% based on glucose), reflux at atmospheric pressure, 1 h. Parameters of NMR analysis: sample (50 mg), D_2O (0.60 mL), 25 °C. G^{α} = α-D-glucopyranose, G^{β} = β-D-glucopyranose, $MG^{\alpha pyr}$ = methyl α-D-glucopyranoside, $MG^{\beta pyr}$ = methyl β-D-glucopyranoside, $MG^{\alpha fur}$ = methyl α-D-glucofuranoside, $MG^{\beta fur}$ = methyl β-D-glucofuranoside, $MF^{\alpha fur}$ = methyl α-D-fructofuranoside, $MF^{\beta fur}$ = methyl β-D-fructofuranoside, and $MF^{\beta pyr}$ = methyl β-D-fructopyranoside. The anomeric C atoms (C-1) of the various compounds are labelled on the spectrum.

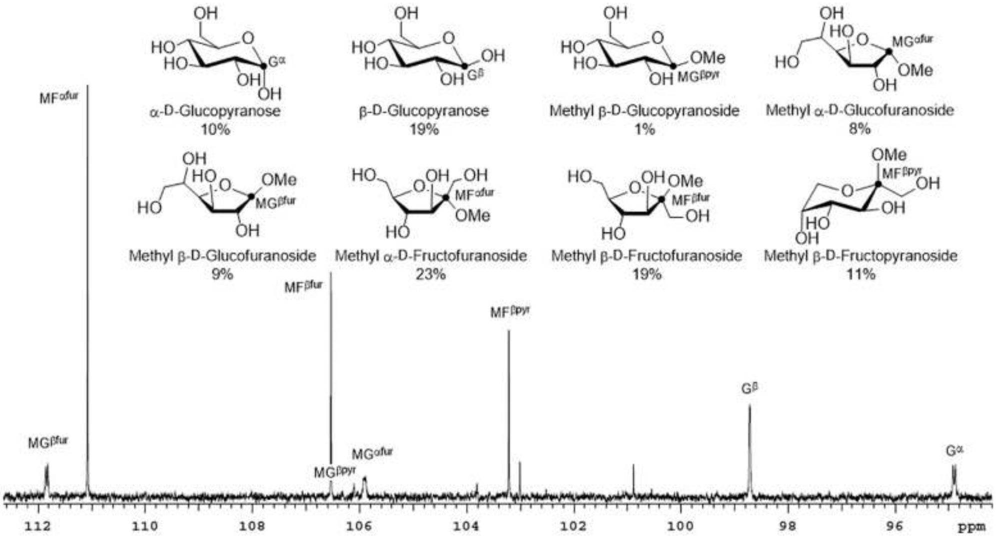


Figure 2. ^{13}C NMR spectrum and the ratio of carbohydrates obtained after Al(OTf)$_3$/TBP processing in methanol (step 1). Reaction conditions: glucose (50 mg), methanol (2.00 mL), Al(OTf)$_3$ (20 mol% based on glucose), TBP (60 mol% based on glucose), reflux at atmospheric pressure, 36 h. Parameters of NMR analysis: sample (50 mg), D$_2$O (0.60 mL), 25 °C. G$^{\alpha}$ = α-D-glucopyranose, G$^{\beta}$ = β-D-glucopyranose, MG$^{\beta pyr}$ = methyl β-D-glucopyranoside, MG$^{\alpha fur}$ = methyl α-D-glucofuranoside, MG$^{\beta fur}$ = methyl β-D-glucofuranoside, MF$^{\alpha fur}$ = methyl α-D-fructofuranoside, MF$^{\beta fur}$ = methyl β-D-fructofuranoside, and MF$^{\beta pyr}$ = methyl β-D-fructopyranoside. The anomeric C atoms (C-1) of the various compounds are labelled on the spectrum.

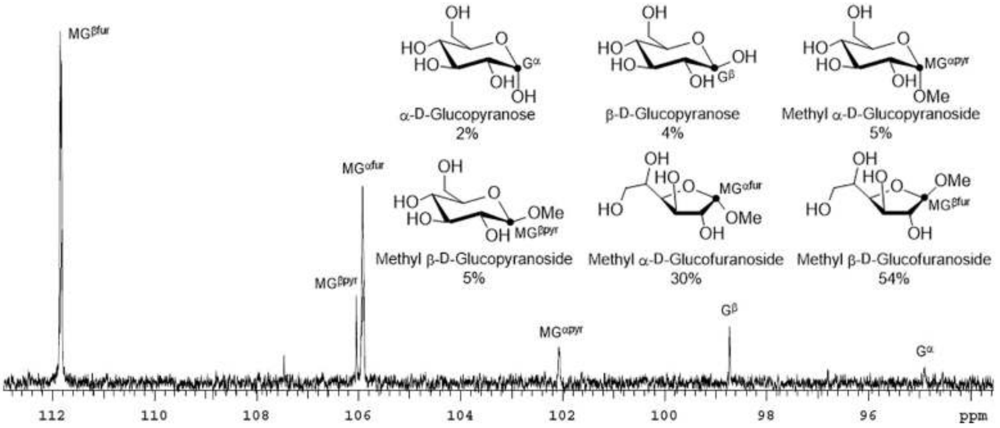


Figure 3. ^{13}C NMR spectrum and the ratio of carbohydrates obtained after TsOH processing in methanol (step 1). Reaction conditions: glucose (50 mg), methanol (2.00 mL), TsOH (20 mol% based on glucose), reflux at atmospheric pressure, 1 h. Parameters of NMR analysis: sample (50 mg), D$_2$O (0.60 mL), 25 °C. G$^{\alpha}$ = α-D-glucopyranose, G$^{\beta}$ = β-D-glucopyranose, MG$^{\alpha pyr}$ = methyl α-D-glucopyranoside, MG$^{\beta pyr}$ = methyl β-D-glucopyranoside, MG$^{\alpha fur}$ = methyl α-D-glucofuranoside, and MG$^{\beta fur}$ = methyl β-D-glucofuranoside. The anomeric C atoms (C-1) of the various compounds are labelled on the spectrum.

verted into glucose and fructose during the processing in water (i.e., the second step, Figure S2, Supporting Information). In turn, glucopyranosides were somewhat stable to hydrolysis under the conditions we employed: in all cases with Lewis acids present, the amount of MG after step 2 was identical to the amount of MG found after step 1 (formed in a 1:1 ratio, as determined by quantitative NMR spectroscopy after each step).

The pH determinations of solutions of various metal triflates in water and methanol, respectively, revealed the strength of the Brønsted acids formed in solution (Table 1). Metal triflates are typically considered to be Lewis acids, but clearly possess Brønsted acidity, sometimes comparable to strong protic Brønsted acids (TsOH and H$_3$PO$_4$). This phenomenon is caused by Lewis acid-assisted Brønsted acidity through complexation of the metal center with the protic solvent and release of hydrogen cations (typically present as $H_{13}O_6^+$ in dilute aqueous solutions),[28] as was disclosed earlier for $Al(OTf)_3$.[23,24] This effect is observed in both media (water and methanol) and is prominent for $Hf(OTf)_4$ and $Sn(OTf)_2$. Certain mixed acids (Lewis + Brønsted), specifically the $La(OTf)_3/H_3PO_4$ pair, deliver the highest Brønsted acidity (Table 1), consistent with our previous studies.[13] TBP reduces the Brønsted acidity of metal triflates, but this effect was noted mostly in methanol and hardly in water, probably owing to the poor solubility of TBP in water.

Considering the combined experimental data, the following points emerge:

1) the strongest Brønsted acids (in which the acidity comes from a protic acid or an assisted Brønsted acid), as determined by pH measurements, provide the highest yields of disaccharides in aqueous media and of MG in methanol;
2) Lewis acids catalyze the isomerization of glucose into fructose, but those that induce the highest Brønsted acidity also promote the formation of methyl glucopyranosides and methyl glucofuranosides (in methanol) and humins;
3) TBP is capable of selectively neutralizing the Lewis acid-assisted-Brønsted acidity while maintaining Lewis acidity in methanol, and therefore improves the selectivity of the conversion of glucose into fructose.

With a view to converting glucose into other platform molecules, which requires elevated temperatures, we conducted the two-step processing in methanol for longer reaction times and at higher temperatures from 65 to 120 °C in the presence of $Al(OTf)_3$ as catalyst (Figure 4), followed by hydrolysis in water. We used a sealed glass pressure-tube for temperatures above 65 °C. As is evident from Figure 4a, extended reaction times do not influence the yield of fructose (for solvent under reflux at ambient pressure) but do improve the conversion of glucose into MG, HMF, MMF, and MLev. Higher temperatures reduce the yield of fructose, owing to its conversion into furaldehydes and their ultimate rehydration into MLev (Figure 4b–d). Arguably, methyl glucosides are also converted into MLev at elevated temperatures after hydrolysis into glucose. Furaldehydes appear as their dimethyl acetals after the processing in methanol, and these readily hydrolyze into HMF and MMF after methanol/water solvent exchange (Figure S6, Supporting Information).

MLev is the major product at elevated temperatures, formed in an excellent 59% yield in a highly selective reaction (120 °C, 8 h, Figure 4d; the yield remains unchanged at 12 and 18 h). Model transformations of fructose and HMF with TsOH as catalyst (Table S5, Supporting Information) highlight the notion that the dehydration/rehydration processes are catalyzed by Brønsted acids. Scheme 2 provides a summary of the conversion of glucose in methanol and water, as discussed above, distinguishing between Lewis acid-promoted reactions and Brønsted acid-catalyzed transformations.

Various other metal triflates and Brønsted acids transform glucose into the derivative products MG and/or MLev in the two-step transformation of glucose in methanol and water, to a greater or lesser extent. Table 2 perfectly exemplifies the interplay between Brønsted and Lewis acidity in these conversions of glucose to product. Typical Brønsted acid catalysts or Lewis acid-assisted Brønsted acids promoted the transformation of glucose into MG, especially highlighted by TsOH (MG

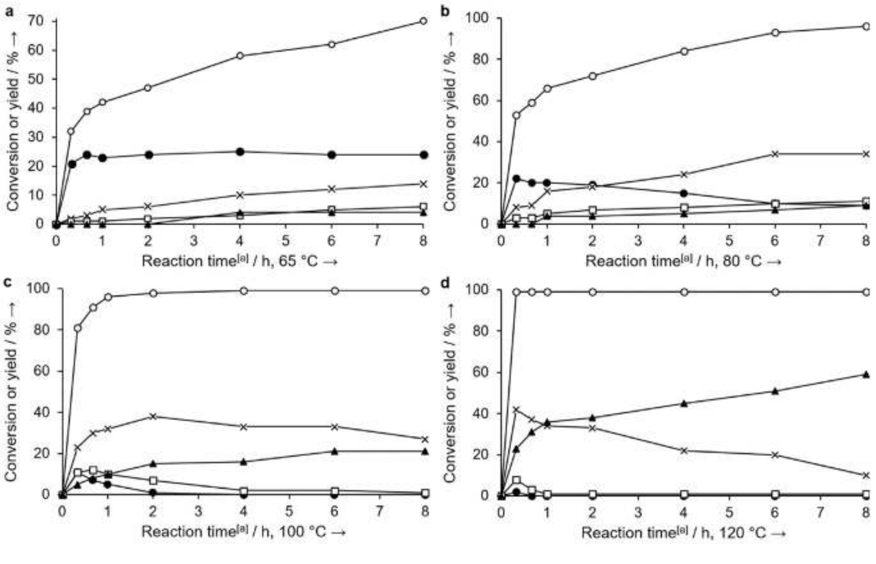
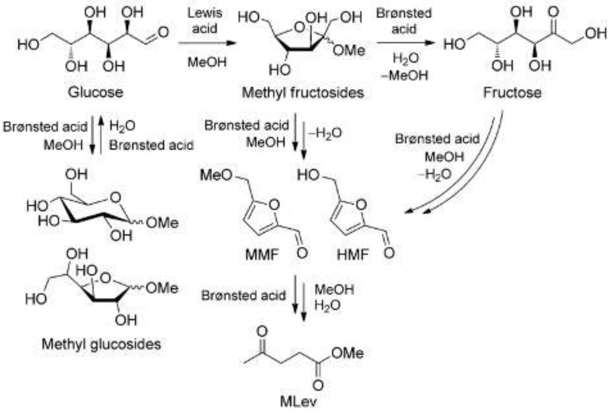


Figure 4. $Al(OTf)_3$-catalyzed conversion of glucose through a two-step process in methanol and water: a) Processing in methanol under solvent reflux at atmospheric pressure. b–d) Temperature of the processing in methanol: 80, 100, 120 °C, respectively. [a] Time of the processing in methanol. Reaction conditions: glucose (50 mg), methanol (2 mL), $Al(OTf)_3$ (20 mol% based on glucose), then solvent exchange with water (2 mL), solvent under reflux at atmospheric pressure (1 h). ○ conversion of glucose, ● yield of fructose, × yield of MG, □ total yield of HMF and MMF, ▲ yield of MLev (identified immediately after the processing in methanol).



Scheme 2. Acid-catalyzed transformation of glucose into platform molecules in methanol and water, highlighting either Lewis acid or Brønsted acid catalysis at each step.

Table 2. Acid-catalyzed transformation of glucose in methanol and water[a]

Catalyst	Conv [%]	Fructose yield [%]	MG yield [%]	HMF and MMF yield [%]	MLev yield[b] [%]
$Al(OTf)_3$	99	0	10	0	59
$La(OTf)_3/H_3PO_4$	84	0	71	0	7
$Hf(OTf)_4$	90	0	14	0	39
TsOH	93	0	93	0	0
H_3PO_4	13	0	13	0	0
$La(OTf)_3$/TsOH	89	0	89	0	0
$Sn(OTf)_2$	90; 97[c]	0; 0[c]	46; 18[c]	1; 0[c]	43; 67[c]
$In(OTf)_3$	99	0	8	1	52
AgOTf	95	0	90	0	0
LiOTf	13	8	0	0	0
$La(OTf)_3$	99	0	89	1	9
$Y(OTf)_3$	99	0	72	0	9

[a] Yields are specified in mol% based on glucose; "0" or "99" for the product were identified on the basis of trace analysis by HPLC. Reaction conditions: glucose (50 mg), methanol (2 mL), catalyst (20 mol% based on glucose), 120 °C, 8 h, then solvent exchange with water (2 mL), reflux at atmospheric pressure, 1 h. [b] Yield of MLev was identified immediately after the processing in methanol. [c] Reaction at 140 °C, 4 h.

yield 93%, α-anomer as major product). In these reactions, the thermodynamic preference for methyl glucopyranosides was evident, with minimum formation of the kinetic product methyl glucofuranosides (determined by quantitative NMR analysis of the product mixture after step 1, Figures S7 and S8, Supporting Information).[8] The anomalous apparent diminished Brønsted acid activity of $La(OTf)_3/H_3PO_4$, evidenced by only 77% yield of MG compared with superior yields afforded by weaker Brønsted acids, probably relates to precipitation of the catalyst at elevated temperatures, with a concomitant reduction of the reaction rate, as is typical for heterogeneous systems.[29] Surprisingly, Lewis acidic catalysts AgOTf, $La(OTf)_3$, and $Y(OTf)_3$, with low Brønsted acidity at low temperatures (Table 1), showed high selectivity towards MG at elevated temperatures, which relies upon Brønsted acid activity. pH measurements of solutions of these catalysts at 20 and 40 °C show the increased Brønsted acidity in methanol and water (Table 1) associated with elevated temperatures. This would be even higher at the elevated temperatures under which the reactions are performed, suggesting that the complexation of the catalyst and solvent leads to sufficient Brønsted acidity under more forcing reaction conditions, but with insufficient Lewis or Brønsted acidity to promote subsequent reactions, giving high selectivity. Catalysts considered to be hard Lewis acids [e.g., $Hf(OTf)_4$, $Sn(OTf)_2$, and $In(OTf)_3$, which also produce high Brønsted acidity] delivered excellent outcomes toward MLev (Tables 1 and 2). MLev is formed by Lewis acid-catalyzed isomerization of glucose into fructose followed by (Lewis acid-assisted) Brønsted acid-catalyzed dehydration/rehydration processes. $Sn(OTf)_2$ offers superb selectivity toward desirable products without significant formation of the byproduct humins that were observed in aqueous media at lower temperatures, affording MLev in 67% yield.

Conclusions

This systematic study of a range of metal triflates and some associated (induced) Brønsted acid systems shows that the selectivity is determined by the dominating Brønsted or Lewis acidity. The nature of the dominant acidity can be manipulated by varying the reaction conditions. First, this includes the addition of a protic acid to form Brønsted acidic combined acid complexes, such as $La(OTf)_3/H_3PO_4$, which promote high conversion of glucose into disaccharides in aqueous solvent. Second, it includes the addition of the Brønsted base 2,6-di-*tert*-butyl-4-methylpyridine (TBP) to inhibit Brønsted acidity, and thereby, enhance the yield of fructose in two-step processing in methanol and water. The activities of metal triflates can be altered dramatically by raising the reaction temperature: whereas some less active metal triflates show poor catalyst activity at lower temperatures, their activity is enhanced at elevated temperatures and is accompanied by very high selectivity to the product, MG or MLev, with very little byproduct formation. Notably, Lewis acids offering the lowest Brønsted acidity under mild conditions, namely AgOTf, $La(OTf)_3$, and $Y(OTf)_3$, promoted Brønsted acid-catalyzed conversion of glucose into MG at higher temperatures, and thus, become a source of hydrogen cations under such conditions, but in highly selective processes. Alternatively, harder Lewis acids (i.e., acids that interact preferentially with protic solvents) with enhanced Brønsted acidity in water and methanol [e.g., $Hf(OTf)_4$, $Sn(OTf)_2$, $In(OTf)_3$, and $Al(OTf)_3$] can efficiently catalyze the transformation of glucose into MLev through an initial Lewis acid-catalyzed isomerization step. These transformations of glucose employing metal triflates afford a deeper insight into the overall role of the acid catalyst in the production of target platform molecules under specified reaction conditions. These insights provide a springboard for future studies toward the selective acid-catalyzed conversion of glucose, as well as other naturally abundant carbohydrates, into a range of functional molecules. Among the options of catalysts for the processing of native biomass such as lignocellulose, metal triflates hold significant promise for sustainable industrial development.

Experimental Section

Reagents and metal triflate catalysts [Hf(OTf)$_4$, Sn(OTf)$_2$, In(OTf)$_3$, Al(OTf)$_3$, AgOTf, LiOTf, La(OTf)$_3$, or Y(OTf)$_3$] and phosphoric acid (H_3PO_4, 85 wt% aqueous solution) were used as supplied from commercial sources. *p*-Toluenesulfonic acid monohydrate was dried under reduced pressure (60 °C, 1 mbar, 12 h) to generate anhydrous TsOH. HPLC-grade solvents were employed for experiments. Methanol was dried over activated 3 Å molecular sieves, according to the established optimum method.[30] The analytical data for synthesized products described in this manuscript have been reported previously.[31–40] Details of analytical procedures and theoretical methods are specified in the Supporting Information.

Acid-catalyzed conversion of glucose in water

Glucose (50 mg), water (2.00 mL), and acid catalyst (20 mol% based on glucose) were introduced into a round-bottomed flask equipped with a condenser and magnetic follower. The mixture was heated and stirred under reflux at atmospheric pressure for 2 h. The reaction was quenched by the addition of an aqueous solution of sodium hydrogen carbonate (2.0 mL, 0.05 M) to neutralize the catalyst. The neutralized aqueous systems were centrifuged (20 000×g for 10 min) and decanted, and recovered solutions were analyzed by using an HPLC system, as detailed in the Supporting Information, to provide the results given in the main text.

For the targeted synthesis of disaccharides, glucose (500 mg), water (1.65 mL), and catalyst (20 mol% based on glucose) were charged into a round-bottomed flask equipped with a condenser and magnetic follower, and the reaction mixture was heated and agitated under reflux at atmospheric pressure for 12 h. The reaction mixture was diluted with aqueous sodium hydrogen carbonate (40.0 mL, 0.05 M). An aliquot of the neutralized aqueous system was centrifuged (20 000×g for 10 min) and decanted, and the recovered solutions were analyzed by using the HPLC system to provide the results detailed in the main text. A detailed method for preparative separation of carbohydrates is presented in the Supporting Information. NMR, IR, and MS spectra for the isolated disaccharides were assigned by comparison with literature data and spectra produced from an authentic commercial sample of isomaltose.[31–34]

Isomaltose (reference sample):[31–34] ^{13}C NMR [125 MHz, D_2O, 25 °C, [D$_4$]trimethylsilylpropionic acid (TMSP)]: $\delta = 97.9$, 96.0, 92.1, 75.9, 74.2, 74.0, 73.0, 71.7, 71.4, 71.3, 70.0, 69.5, 69.4, 69.3, 65.7, 65.6, 60.4 ppm; IR (neat): $\tilde{\nu}_{max} = 3267$, 2922, 1643, 1421, 1348, 1263, 1149, 1102, 1007, 913, 842, 764, 501 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{12}H_{21}O_{11}$ $[M-H]^-$: 341.1089; found: 341.1096.

Isolated disaccharides:[31–34] ^{13}C NMR (125 MHz, D_2O, 25 °C, [D$_4$]TMSP): $\delta = 97.9$, 96.0, 92.1, 75.9, 74.2, 74.0, 73.0, 72.4, 71.7, 71.4, 71.3, 70.0, 69.6, 69.5, 69.4, 69.3, 65.7, 65.6, 60.4 ppm; IR (neat): $\tilde{\nu}_{max} = 3261$, 2921, 1642, 1567, 1421, 1353, 1149, 1099, 1011, 918, 842, 766, 495 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{12}H_{21}O_{11}$ $[M-H]^-$: 341.1089; found: 341.1088.

Two-step acid-catalyzed conversion in methanol and water

Glucose (50 mg), methanol (2.00 mL), and acid catalyst (20 mol% based on glucose), and in some instances base (2,6-di-*tert*-butyl-4-methylpyridine, 60 mol% based on glucose), were introduced into a round-bottomed flask equipped with a condenser and magnetic follower. The mixture was heated and stirred under reflux at atmospheric pressure for a fixed period of time (step 1). Then, methanol was evaporated under reduced pressure (30 °C, 90 mbar), and water (2.00 mL) was added to the reactor (solvent exchange). The resulting mixture was heated and stirred under reflux at atmospheric pressure for 1 h (step 2). The reaction was quenched by the addition of an aqueous solution of sodium hydrogen carbonate (2.00 mL, 0.05 M), and the mixture was centrifuged (20 000×g for 10 min) and decanted. The recovered solutions were analyzed by using an HPLC system, as detailed in the Supporting Information, to provide the results given in the main text.

Reactions at elevated temperatures of 80–120 °C in step 1 were conducted in a sealed glass pressure-tube. Glucose (50 mg), methanol (2.00 mL), and acid catalyst (20 mol% based on glucose) were introduced into a glass pressure tube equipped with a magnetic follower, and the reactor was sealed. The mixture was heated and stirred at the predetermined temperature for a fixed period of time (step 1). After cooling, the mixture was transferred to a round-bottomed flask, and methanol was evaporated under reduced pressure (30 °C, 90 mbar). Then, water (2.00 mL) was added to the reactor (solvent exchange), and the resulting mixture was heated and stirred under reflux at atmospheric pressure for 1 h (step 2). The reaction was quenched by the addition of an aqueous solution of sodium hydrogen carbonate (2.00 mL, 0.05 M), and the mixture was centrifuged (20 000×g for 10 min) and decanted. The recovered solutions were analyzed by using an HPLC system to provide the results detailed in the main text. Additional details of synthesis methods and preparative isolation of products are presented in the Supporting Information.

Methyl α-D-glucopyranoside:[35–37] ^{1}H NMR (500 MHz, D_2O, 25 °C, [D$_4$]TMSP): $\delta = 4.82$ (d, $J = 3.5$ Hz, 1 H), 3.88 (dd, $J = 12.5$, 2.0 Hz, 1 H), 3.76 (dd, $J = 12.5$, 5.5 Hz, 1 H), 3.69–3.63 (m, 2 H), 3.56 (dd, $J = 9.5$, 3.8 Hz, 1 H), 3.43 (s, 3 H), 3.41–3.38 ppm (m, 1 H); ^{13}C NMR (125 MHz, D_2O, 25 °C, [D$_4$]TMSP): $\delta = 102.2$, 102.1, 76.0, 74.4, 74.1, 72.4, 63.4, 57.9 ppm; IR (neat): $\tilde{\nu}_{max} = 3542$, 3232, 2912, 1460, 1430, 1372, 1340, 1302, 1226, 1185, 1103, 1025, 991, 898, 842, 745, 666 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_7H_{13}O_6$ $[M-H]^-$: 193.0718; found: 193.0715.

HMF:[38] TLC: $R_f = 0.213$ (1.5:1 hexane/EtOAc; UV, KMnO$_4$); ^{1}H NMR (500 MHz, CDCl$_3$, 25 °C): $\delta = 9.56$ (d, $J = 1.0$ Hz, 1 H), 7.21 (d, $J = 3.5$ Hz, 1 H), 6.50 (d, $J = 3.5$ Hz, 1 H), 4.70 (s, 2 H), 2.97 ppm (br s, 1 H, OH); ^{13}C NMR (125 MHz, CDCl$_3$, 25 °C): $\delta = 177.7$, 160.7, 152.3, 123.0, 110.0, 57.5 ppm; IR (neat): $\tilde{\nu}_{max} = 3339$, 3120, 2841, 1657, 1582, 1519, 1396, 1368, 1336, 1278, 1188, 1070, 1017, 986, 965, 806, 768, 511 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_6H_6O_3H$ $[M+H]^+$: 127.0390; found: 127.0379.

MMF:[39] TLC: $R_f = 0.563$ (1.5:1 hexane/EtOAc; UV, KMnO$_4$); ^{1}H NMR (500 MHz, CDCl$_3$, 25 °C): $\delta = 9.61$ (s, 1 H), 7.21 (d, $J = 3.5$ Hz, 1 H), 6.52 (d, $J = 3.5$ Hz, 1 H), 4.48 (s, 2 H), 3.42 ppm (s, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$, 25 °C): $\delta = 177.7$, 158.2, 152.6, 121.8, 111.1, 66.5, 58.7 ppm; IR (neat): $\tilde{\nu}_{max} = 3119$, 2930, 2824, 1673, 1584, 1520, 1450, 1401, 1370, 1275, 1192, 1092, 1022, 1001, 970, 944, 907, 810, 784, 756, 732, 509 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_7H_8O_3H$ $[M+H]^+$: 141.0546; found: 141.0536.

MLev:[40] TLC: $R_f = 0.438$ (1.5:1 hexane/EtOAc; $KMnO_4$); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 3.67$ (s, 3 H), 2.75 (t, $J = 7.0$ Hz, 2 H), 2.57 (t, $J = 7.0$ Hz, 2 H), 2.19 ppm (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 206.6$, 173.2, 51.8, 37.9, 29.8, 27.7 ppm; IR (neat): $\tilde{\nu}_{max} =$ 3000, 2954, 1736, 1718, 1438, 1362, 1315, 1213, 1162, 1068, 1029, 1000, 970, 894, 812, 766, 574, 480 cm^{-1}; HRMS (ESI): m/z calcd for $C_6H_9O_3$ $[M-H]^-$: 129.0557; found: 129.0549.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: acidity · carbohydrates · catalysis · glucose · green chemistry

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Iurii Bodachivskyi (graduate research student) developed the methodology, conducted research, including experimental work, data collection and data analysis, and drafted the manuscript. Prof. D. Bradley G. Williams (principal supervisor) and Dr Unnikrishnan Kuzhiumparambil (co-supervisor) supervised Iurii Bodachivskyi's research activities, provided conceptual advice and revised the manuscript.

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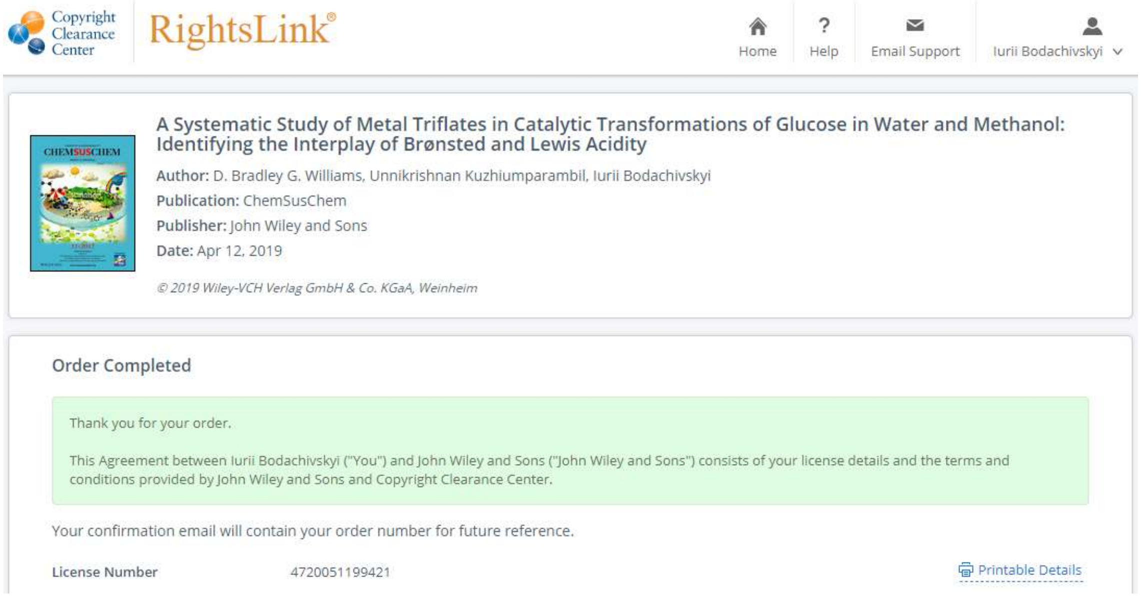

A Systematic Study of Metal Triflates in Catalytic Transformations of Glucose in Water and Methanol: Identifying the Interplay of Brønsted and Lewis Acidity

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2.2. Metal triflates are tunable acidic catalysts for high yielding conversion of cellulosic biomass into ethyl levulinate

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Research article

Metal triflates are tunable acidic catalysts for high yielding conversion of cellulosic biomass into ethyl levulinate

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ABSTRACT

Metal triflates and their mixtures with Brønsted acids are excellent catalysts for the selective and high yielding transformation of microcrystalline cellulose into ethyl levulinate, in ethanol, producing synergistic catalyst effects in some instances. The pretreatment of raw and unrefined cellulosic materials with a deep eutectic solvent enables similarly excellent catalysed conversion thereof into ethyl levulinate in superb yield (up to 75%) and selectivity (up to 88%). When using fermentation-derived ethanol, the product possesses 100% renewable content.

1. Introduction

Cellulose is the most naturally abundant polysaccharide with the scale and potential to reduce reliance on fossil-derived resources [1,2]. In the presence of acid catalysts, cellulose may be transformed into a large portfolio of organic building block molecules (platform chemicals) creating a potentially inexhaustible source of carbon neutral bulk chemicals [1–4]. The direct conversion of cellulosic materials into desirable products is challenging, involving a complex set of reactions that relies differentially upon Brønsted acid catalysis and Lewis acid catalysis [2,5]. Besides these stringent requirements of the catalyst, complexities arise because of the low selectivity of many processes and the forcing conditions required to promote catalytic reactions [2]. To circumvent the difficulties associated with cellulosic substances, many current practices employ edible low molecular weight saccharides as substrates (e.g., sucrose, glucose, or fructose), or pretreated cellulose, such as microcrystalline cellulose (MCC is obtained by treatment of wood pulp with mineral acids) or ball-milled cellulose [2,6–8]. The use of food sources in chemical processes, along with energy demanding pretreatment of native cellulose, reduce the overall sustainability of biorefinery and may become a source of ethical and social concerns. There is thus an imperative to develop new and efficient catalytic systems to perform the complexity of tasks requisite to transform native cellulose into desirable platform chemicals under mild processing conditions.

Metal trifluoromethanesulfonates (metal triflates) are a class of green homogeneous acidic catalysts, which have been efficiently employed in a number of chemical processes, including valorisation of polysaccharides [5,9–13]. These catalysts are able to selectively promote Lewis acid catalysed reactions, or Brønsted acid catalysed processes through Lewis acid-assisted Brønsted acidity [5,14,15]. Several elegant studies have led to deeper insights into the role of metal triflates in the catalytic valorisation of carbohydrates in methanol [5,8,11]. The processes detailed in these papers demonstrate the transformation of glucose, MCC, or ball-milled cellulose, into methyl levulinate or into α-hydroxy methyl esters. For example, $Sn(OTf)_2$ catalyses the formation of a small range of α-hydroxy methyl esters in good yield, directly from cellulose [8]. Such cellulose-derived low molecular weight esters hold significant promise for industrial applications, including the production of fuels, plastics and other speciality chemicals [8,16,17]. The valorisation of cellulosic biomass into alkyl levulinates other than methyl levulinate, has remained somewhat overlooked. Very few catalysts, such as sulfuric acid or aluminium sulfate, have been reported for the direct transformation of cellulose into ethyl levulinate and other alkyl levulinates, with moderate performance. Other methods rely mostly on the catalytic reaction of low molecular weight saccharides and levulinic acid [17,18]. In the present work, we develop a method to perform the direct and selective conversion of cellulosic biomass into ethyl levulinate (ELev). In particular, we investigate the activity of metal triflates, Brønsted acids, and Lewis acid-assisted Brønsted acids in catalytic reactions of MCC in ethanol. We develop a sustainable method to pretreat unrefined cellulose using a deep eutectic solvent (DES) and ultimately apply the optimised methods to the valorisation of low-value cellulosic materials.

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Table 1
Acid-catalysed transformation of microcrystalline cellulose into ELev.[a]

Entry	Acid catalyst	Conv (%)	ELev yield (%)	ELev selectivity (%)	pH[b] 0.01 M
1	$Al(OTf)_3$	74	32	43	1.82
2	$Al(OTf)_3/TsOH$	68	59	87	1.81
3	$Al(OTf)_3/H_3PO_4$	60	20	33	1.64
4	$In(OTf)_3$	79	20	25	1.59
5	$In(OTf)_3/TsOH$	63	45	71	1.63
6	$In(OTf)_3/H_3PO_4$	61	37	61	1.52
7	$Sn(OTf)_2$	50	23	46	1.51
8	$Sn(OTf)_2/TsOH$	60	52	87	1.59
9	$Sn(OTf)_2/H_3PO_4$	43	25	58	1.65
10	$Hf(OTf)_4$	73	24	33	1.33
11	$Hf(OTf)_4/TsOH$	82	57	70	1.49
12	$Hf(OTf)_4/H_3PO_4$	78	47	60	1.51
13	$Y(OTf)_3$	15	0	0	3.97
14	$Y(OTf)_3/TsOH$	46	27	59	1.89
15	$Y(OTf)_3/H_3PO_4$	78	68	87	1.54
16[c]	$Y(OTf)_3/H_3PO_4$	85	75	88	1.54
17	AgOTf	2	0	0	4.63
18	AgOTf/TsOH	22	0	0	1.95
19	$AgOTf/H_3PO_4$	1	0	0	2.08
20	$La(OTf)_3$	10	0	0	4.23
21	$La(OTf)_3/TsOH$	42	14	33	1.88
22	$La(OTf)_3/H_3PO_4$	68	53	78	1.54
23	$Yb(OTf)_3$	23	0	0	3.62
24	$Yb(OTf)_3/TsOH$	50	24	48	1.91
25	$Yb(OTf)_3/H_3PO_4$	83	53	64	1.59
26	TsOH	35	0	0	1.69
27	H_3PO_4	12	0	0	3.50
28	none	0	0	0	5.60

[a] Reaction outcomes are specified in mol% based on anhydroglucose unit present in cellulose.

OTf = trifluoromethanesulfonate. TsOH = *p*-toluenesulfonic acid. Reaction conditions: MCC (50 mg), ethanol (4.00 mL), catalyst (0.05 mmol; 0.05 mmol each acid for combined catalysts), 160 °C, 4 h.

[b] pH readings were performed in triplicate in aqueous ethanol (95 vol% of alcohol) at room temperature.

[c] Reaction temperature = 180 °C, time = 2 h.

2. Materials and methods

2.1. Materials

Microcrystalline cellulose, metal triflate catalysts ($Al(OTf)_3$, $Y(OTf)_3$, AgOTf, $In(OTf)_3$, $Sn(OTf)_2$, $La(OTf)_3$, $Yb(OTf)_3$, or $Hf(OTf)_4$, with purity 97.0–99.9%) and choline chloride (> 98%) were used as supplied from Sigma-Aldrich (Australia). *p*-Toluenesulfonic acid monohydrate (> 98%, Sigma-Aldrich, Australia) was dried under reduced pressure (60 °C, 1 mbar, 12 h) to generate anhydrous TsOH [5]. Analytical grade ethanol (water content of < 0.2%), phosphoric acid (H_3PO_4, 85 wt% aqueous solution) and oxalic acid dihydrate (> 99%) were used as received from Chem-Supply (Australia). Wood pulp (*Pinus*), cellulose extracted from eucalyptus and *Pinus* (unbleached and bleached, BKT, Kinleith, New Zealand) were a generous gift from Dr. Simon Hinkley, The Ferrier Research Institute, Victoria University of Wellington (New Zealand). Softwood chips were sourced from local growers (Australia). The content of cellulose in the substrates was established by a standard analytical procedure NREL/TP-510-42618 [19]. The DES based on choline chloride and oxalic acid dihydrate (1:1 molar ratio) was prepared according to reference [20].

2.2. Acid-catalysed conversion of cellulose

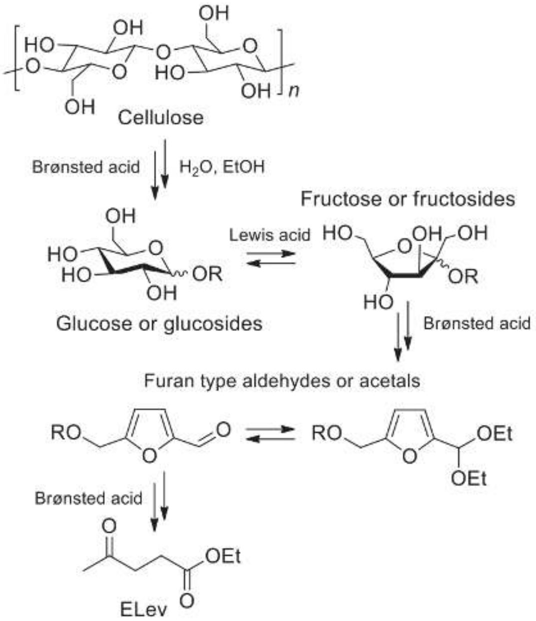
Cellulose (50 mg), ethanol (4.00 mL), metal triflate ($Al(OTf)_3$, $Y(OTf)_3$, AgOTf, $In(OTf)_3$, $Sn(OTf)_2$, $La(OTf)_3$, $Yb(OTf)_3$, or $Hf(OTf)_4$, 0.05 mmol) and/or Brønsted acid (H_3PO_4, or TsOH, 0.05 mmol) were introduced to a 10 mL teflon lined stainless steel autoclave equipped with a magnetic follower and the reactor was sealed. The mixture was heated and stirred at the predetermined temperature for a fixed period of time. After completion of the process, the reactor was cooled in an ice bath. The reaction mixture was centrifuged (3000 ×g for 20 min) to recover the ethanol phase and unreacted substrate. The recovered solution was analysed by chromatography, as detailed in the Supporting information, to provide the yield of ELev specified in the main text. The recovered solids were washed with aqueous ethanol (95 vol%, 3 × 10.0 mL), vacuum oven-dried (60 °C, 1 mbar, 6 h) and weighed to calculate the conversion of substrate specified in the main text. Isolated ELev gave satisfactory analytical data (Figs. S1 and S2, Supporting information) [21]. Additional details of analytical procedures and general methods are specified in the Supporting information.

2.3. Pretreatment of cellulose

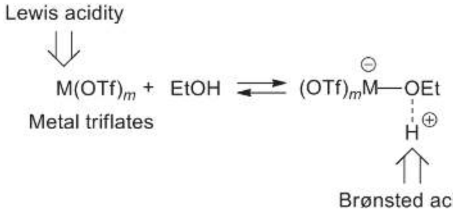
Cellulosic biomass (eucalyptus cellulose, *Pinus* cellulose, wood pulp, or softwood chips, 500 mg) and choline chloride/oxalic acid dihydrate solvent (1:1 molar ratio, 10.000 g) were introduced to a round-bottom flask equipped with a thermometer and magnetic follower and the mixture was heated and agitated at 80 °C for 2 h, resulting in a turbid suspension. The mixture was diluted with water (30.0 mL) to precipitate cellulose, which was recovered, washed with aqueous ethanol (3 × 30.0 mL, 95 vol%), vacuum oven-dried (60 °C, 1 mbar, 6 h) and weighed to determine the yield (Table S1, Supporting information). The recovery of the DES comprised extraction with ethyl acetate (2 × 30 mL) to remove traces of non-polar by-products (5-(hydroxymethyl)furfural, furyl hydroxymethyl ketone, and furfural, as established by HPLC trace analysis), followed by evaporation of water under reduced pressure (45 °C, 10 mbar).

3. Results and discussion

The activity of a range of metal triflates ($Al(OTf)_3$, $In(OTf)_3$, $Sn(OTf)_2$, $Hf(OTf)_4$, $Y(OTf)_3$, AgOTf, $La(OTf)_3$, or $Yb(OTf)_3$) was explored for the catalytic conversion of MCC in ethanol media at 160 °C for 4 h



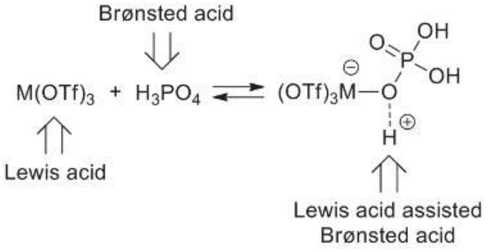
Scheme 1. Acid-catalysed transformation of cellulose into ELev. n = integer, R = H or Et.



Scheme 2. Origin of Brønsted acidity by the interaction of Lewis acidic metal triflates and ethanol. m = 1–4, M = metal.

(reaction parameters were selected based on exploratory work probing the conversion of cellulose in ethanol under various processing conditions (not shown); the specified reaction temperature and time are optimal for the present catalytic study). Table 1 demonstrates that *hard* Lewis acids (based on Pearson's HSAB principles) [22,23], such as Al$(OTf)_3$, In$(OTf)_3$, Sn$(OTf)_2$, or Hf$(OTf)_4$, catalysed the direct transformation of cellulose into ELev (yield up to 32 mol%, based on anhydroglucose units present in cellulose, Table 1, entries 1, 4, 7, 10), in moderate selectivity towards the product (ELev selectivity up to 46 mol %, Table 1, entries 1, 4, 7, 10); no conversion of cellulose was observed without addition of the acidic catalyst (Table 1, entry 28). The conversion of cellulose into alkyl levulinates proceeds via the cascade of Brønsted acid and Lewis acid catalysed reactions shown in Scheme 1. This involves solvolysis into low molecular weight carbohydrates, aldose-ketose isomerisation, dehydration into furaldehydes (converting into acetals in the presence of ethanol), and rehydration thereof into levulinic acid derivatives [2,5]. This suggests that *hard* Lewis acids (Al$(OTf)_3$, In$(OTf)_3$, Sn$(OTf)_2$, and Hf$(OTf)_4$) possess the Brønsted acidity required to catalyse the various processes towards ELev, as represented in Scheme 1. In previous instances, the required Brønsted acidity was achieved by the addition of sulfonic acids [11] or the hydrolysis of Al salts [18]. pH measurements of aqueous ethanolic solutions of various metal triflates confirmed that *hard* Lewis acids possess strong Brønsted acidity. This acidity is attributed to Lewis acid-assisted Brønsted acidity, derived from the complexation of the metal centre with a protic solvent (Scheme 2) [5,15]. The origin of the acidity with metal triflates is thus distinctive: Metal salts such as sulfates, chlorides, or nitrates hydrolyse into the corresponding Brønsted acids in aqueous methanol [18]. Conversely, and in distinct contrast, metal triflates provide Lewis acid-assisted Brønsted acidity, without hydrolysis [5,10,13,15,24]. Chromatographic-analysis of the reaction mixture (details of are presented in the Supporting information) showed only trace amounts of glucose, 5-(hydroxymethyl)furfural, diethyl acetals of the furan derivatives, and 5-(ethoxymethyl)furfural, respectively. These are putative intermediates towards ELev (Scheme 1), supporting the proposed pathway. However, there was also a mass of dark-brown high molecular weight by-product humins (condensation products of intermediate saccharides with aldehydes [5,25]), which immediately accounts for the mass losses and reduced selectivity to ELev (Table 1). In contrast to *hard* Lewis acids, *soft* Lewis acidic metal triflates, such as Y$(OTf)_3$, AgOTf, La$(OTf)_3$, or Yb$(OTf)_3$, failed altogether to catalyse the conversion of the MCC into ELev or into by-product humins. Instead, they provided only moderate mass losses of cellulose (conversion of MCC up to 23 mol%, Table 1, entries 13, 17, 20, 23), possibly due to the ethanolysis thereof into ethanol-soluble oligosaccharides. The poor performance of soft Lewis acids is likely due to their weak interaction with hard *O*-containing substrate and the ensuing overall lower Brønsted acidity, as is evident from pH measurements (Table 1). Brønsted acid catalysts (TsOH and H_3PO_4, Table 1, entries 26, 27) provided similar outcomes, i.e. low conversion of MCC. In previous work, TsOH enabled conversion of MCC in methanol at the higher temperature of 180 °C, predominantly into 'sugars' (yield 78%) but also into some methyl levulinate (yield 20%) [11].

We have previously reported significant improvements to catalysed processes when employing specific targeted mixed Lewis-Brønsted acid systems with demonstrated synergistic effects [5,13,24]. Mixed acid systems have been specifically employed in the catalytic transformation of (poly)carbohydrates into platform chemicals in aqueous or methanol media [5,11], and we considered that this approach may benefit the present research. In particular, our previous work has highlighted that the combination of low activity metal triflates such as La, Gd, and Yb in combination with phosphoric acid, not sulfonic acids, produces synergistic effects [24]. That study also showed that a 1:1 ratio of metal triflate/H_3PO_4 was optimum. We therefore investigated the conversion of MCC in ethanol applying mixtures of Lewis acidic metal triflates and TsOH or H_3PO_4. As is evident from Table 1, combined acids provided higher yield and selectivity to ELev, with the exception of AgOTf (Table 1, entries 17–19), which gave no transformation of cellulose into ELev under the prevailing reaction conditions. Specifically, *hard* Lewis acids in combinations with TsOH improved the yield of ELev (yield up to 59 mol% with Al$(OTf)_3$/TsOH, Table 1, entry 2), most likely due to the selective solvolysis of cellulose into intermediate low molecular weight saccharides catalysed by the Brønsted acidic counterpart (Scheme 1) [2,11]. This is consistent with previous studies [11]. In the previous work [11], similar effects were achievable with mixed In$(OTf)_3$ and various sulfonic acids in the transformation of cellulose into methyl levulinate. The authors [11] note that TsOH (Brønsted acid) mostly improved the rate of the solvolysis into soluble sugars, while In$(OTf)_3$ (Lewis acid) effectively promoted the subsequent conversion of monosaccharides into methyl levulinate, likely via Lewis acid-catalysed aldose-ketose isomerisation (Scheme 1). Therefore, the two acids (Brønsted sulfonic acid and *hard* Lewis) separately and independently improved different catalytic reactions of cellulose towards methyl levulinate by additive effects [11]. H_3PO_4 had an inhibitory effect on *hard* Lewis acids. In contrast, we have shown that *soft* Lewis acid-Brønsted acid combinations produce *synergistic* effects [5,13,24] leading to



Scheme 3. Origination of Lewis acid assisted Brønsted acid complex by the interaction of metal triflates and phosphoric acid. M = Y, La or Yb.

dramatic increases of the catalytic activity through a Lewis acid-assisted Brønsted acidity mechanism [14,15], especially highlighted by combinations of group 3 metal triflates with H_3PO_4 (Table 1, entries 15, 16, 22, 25). Noticeably, individual *soft* Lewis acids, or Brønsted acids, did not promote the conversion of cellulose into ELev (Table 1, entries 13, 20, 23, 26, 27), affording only low conversions of cellulose. In combination, however, rather active catalysts are formed via an assisted acidity mechanism (Scheme 3), which is capable of promoting all stages of catalytic process (Scheme 1) [14,15].

The manifestation of the Lewis acid-assisted Brønsted acidity is immediately apparent from pH readings of aqueous ethanolic solutions of mixed Lewis acids and H_3PO_4 or TsOH. It is notable that triflates of Al, In, Sn, and Hf produced more or less consistent pH reading in the presence or absence of added Brønsted acids. Evidently, the *hard* Lewis acids already produce high Brønsted acidity from the metal-solvent interactions, which is scarcely strengthened by the presence of the Brønsted acids. Also notable is that mixtures of soft Lewis acids with TsOH gave mixtures with higher pH (i.e. less acidic) than neat TsOH. The standout is the mixtures of soft Lewis acids with phosphoric acid (Table 1, entries 15, 19, 22, 25), where highly acidic media are generated, which are significantly more acidic than either reacting partner. Soft metal triflates have been demonstrated by NMR spectroscopy to strongly coordinate to phosphoric acid [24], thereby enhancing its acidity. The experimental results shown in Table 1, entries 15, 19, 22, 25, perfectly reflect the improved catalysts; in particular, $Y(OTf)_3/H_3PO_4$ offered superb selectivity towards desirable products without significant formation of by-product humins (ELev yield 68 mol%, selectivity 87 mol%, Table 1, entry 15). Even higher yields and selectivity to ELev can be reached with combined acid catalyst $Y(OTf)_3/H_3PO_4$ at slightly elevated temperatures (75 mol% yield and 88 mol% selectivity, 180 °C, 2 h, Table 1, entry 16).

We sought to better understand the origins of the catalyst activity and conducted a spectroscopic study of metal triflates in ethanol media. Interrogation of the IR spectra confirmed that individual Lewis acids coordinate to solvent molecules, possibly as represented in Scheme 2. This is shown by changes to the O–H stretching mode of ethanol (Fig. 1) [26]. Deconvolution of the hydroxyl region confirmed the occurrence of two peaks (Fig. 1), which we assign to free solvent and secondly to ethanol present in the coordination sphere of the metal centre (Scheme 2). The complexation of ethanol with metal triflates is also evidenced by the appearance of a C–O stretching vibration near 1175 cm^{-1} (Figs. 2c and S3, Supporting information) [26]. The free solvent has corresponding vibrations at 1087 and 1044 cm^{-1} (Fig. S3, Supporting information). This solvent-solute interaction accounts for the formation of Lewis acid-assisted Brønsted acid complexes (in the form of $[M(OTf)_n]$—OEt···H, where M = metal), explaining the amplified Brønsted acidity of metal triflates (Table 1 and Scheme 2) [5,10,15]. IR studies of mixed Lewis-Brønsted acids revealed that characteristic vibrations for TsOH were only slightly perturbed in the presence of metal triflates, suggesting weak or no interactions between the two entities (Figs. 2a, d and S4, Supporting information). In sharp contrast, the P–OH stretching mode at 995 cm^{-1} and $O{=}PO_3$ deformation mode at 490 cm^{-1} associated with free H_3PO_4 reduced dramatically in combination with *soft* Lewis acids (Figs. 2b, e and S4, Supporting information) [27,28]. It remains evident with $Al(OTf)_3$ and to a lesser extent with $In(OTf)_3$, indicative of poorer binding. This observation points to the favourable complexation between Lewis acids and phosphoric acid, which, in the cases of soft Lewis acids, leads to high Lewis acid-assisted Brønsted acidity (Scheme 3). These data perfectly correlate with the synthesis outcomes and help to rationalise the experimental observations in the catalytic reactions of cellulose (Table 1). Importantly, the results show definite *synergistic* effects in the present work, which are clearly distinct from the previously noted *additive* effects [11], or catalysts generated by hydrolysis of metal salts [18].

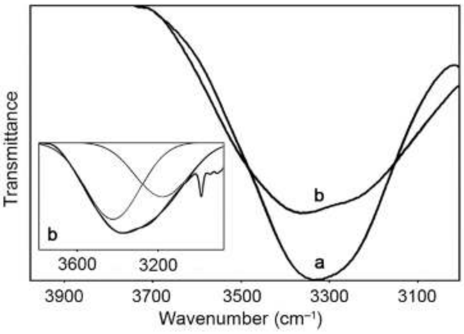


Fig. 1. IR spectra of a) ethanol and b) ethanol 0.1 M solution of $Y(OTf)_3$ in ethanol. The inset shows the deconvoluted spectra of b.

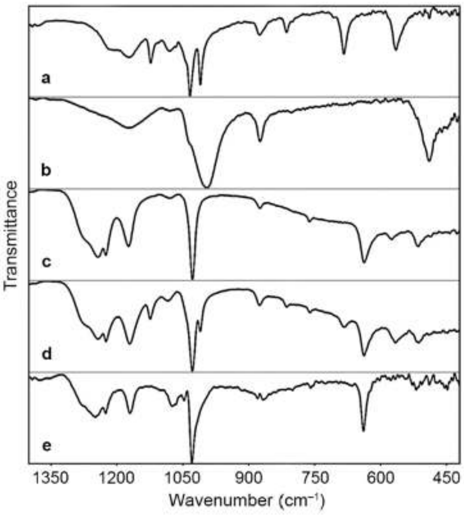


Fig. 2. IR spectra of 0.1 M ethanol solutions of a) TsOH, b) H_3PO_4, c) $Y(OTf)_3$, d) $Y(OTf)_3$/TsOH and e) $Y(OTf)_3/H_3PO_4$. Ethanol peaks were subtracted from spectra. Characteristic vibrations of triflates (1244, 1226, 1030, 763, 640, 577 and 517 cm^{-1}) correspond with data reported in the literature [29].

With the view to converting other cellulosic sources into ELev, we conducted the direct processing of cellulose obtained from eucalyptus and *Pinus* (bleached and unbleached cellulose), wood pulp and softwood chips, in ethanol, employing our catalytic system $Y(OTf)_3/H_3PO_4$ at 180 °C for 2 h (Table 2). As mentioned, MCC is a material obtained by

Table 2
Acid-catalysed transformation of cellulosic biomass into ELev.[a]

Entry	Substrate	Conv (%)	ELev yield (%)	ELev selectivity (%)
1	MCC	85	75	88
2	Eucalyptus cellulose	78	59	76
3[b]		81	72	89
4	*Pinus* cellulose	81	68	84
5[b]		83	73	88
6	*Pinus* cellulose (unbleached)	80	65	81
7[b]		85	75	88
8	Wood pulp (*Pinus*)	64	53	–
9[b]		80	62	–
10[b,c]		81	62	–
11	Softwood chips	77	52	–
12[d] [36]	Wood pulp (*Pinus*)	–	26	–
13[d] [36]	Wood chips (*Pinus*)	–	17	–
14[e] [37]	Cellulosic fibre	–	45	–
15[f] [11]	MCC	–	75 (MLev)	–
16[g] [18]	MCC	100	71 (MLev)	71 (MLev)

[a] Reaction outcomes are specified in mol% based on anhydroglucose unit present in cellulose. Conversion and yield are specified in wt% based on the total carbohydrate content in substrate for wood pulp and softwood chips because both cellulose and hemicellulose (another polysaccharide present in lignocellulose) are convertible into ELev. MLev = methyl levulinate. Reaction conditions: substrate (50 mg), ethanol (4.00 mL), $Y(OTf)_3$ (0.05 mmol), H_3PO_4 (0.05 mmol), 180 °C, 2 h.

[b] Pretreated substrate is employed. Pretreatment conditions: substrate (0.500 g), choline chloride/oxalic acid dihydrate (1:1 molar ratio, 10.000 g), 80 °C, 2 h.

[c] Reaction conditions: substrate (300 mg), ethanol (24.00 mL), $Y(OTf)_3$ (0.3 mmol), H_3PO_4 (0.3 mmol), 180 °C, 2 h.

[d] Reaction conditions: substrate (60 g), aqueous sulfuric acid (0.4 N, 300 g), 190 °C, 2 h, then solvent exchange with ethanol (150 g), 145 °C, 2 h [36].

[e] Reaction conditions: substrate (20 g), ethanol solution of sulfuric acid, 200 °C [37].

[f] Reaction conditions: substrate (2.5 mmol as glucose unit), methanol (20 mL), $In(OTf)_3$ (0.02 mmol), 2-naphthalenesulfonic acid (0.1 mmol), 180 °C, 5 h [11].

[g] Reaction conditions: substrate (3 mmol), methanol (14 mL), H_2O (0.6 mL), $Al_2(SO_4)_3$ (1.2 mmol), 800 W, 180 °C, 40 min [18].

the treatment of native cellulose and is relatively widely used as a medium value commercial product [7]. However, the use of low value or waste cellulosic streams is more desirable and is investigated in the present study. Reactions of native cellulose were less efficient than MCC (Table 2, entry 1, 2, 4, 6, 8, 11). Apparently, the rigid molecular structure of bulk cellulose affected the mass transfer processes restricting the accessibility of the catalyst and the solvent-reagent to the substrate [1,2,6a]; this is mostly because of the larger particle size of the bulk cellulose and higher molecular weight of the native polysaccharides, which factors altogether reduced the rate of catalytic reactions [2,8]. In addition, the transformation of native cellulose was accompanied by the formation of humins, reducing selectivity of the valuable product. This may become a serious obstacle for large volume processes. While this potential hurdle is commonly overcome at a bench scale by ball-milling of cellulosic substrates [2,8], or other drastic methods [30], the problem of energy efficient pretreatment remains essentially unsolved.

DESs are a class of green, and sometimes fully renewable, ionic liquids, in which there is significant interest for the valorisation of cellulosic biomass [31]. In particular, the deep eutectic mixture of choline chloride and oxalic acid has been efficiently applied to the fractionation of lignocellulosic biomass, production of cellulose nanocrystals and nanofibres by treatment of cellulose in this DES and subsequent microfluidic homogenisation or ball-milling, respectively [32–34]. In the present study, we established that native cellulose is amenable to deconstruction in a DES based on choline chloride and oxalic acid dihydrate (1:1 molar ratio) into fine particulate cellulosic material (details of the structure of the recovered materials are provided in the Supporting information, Table S1 and Fig. S5). This was accomplished by treatment of native cellulose in the DES at 80 °C for 2 h. Dilution of the DES with water, followed by washing and drying, afforded a fine cellulosic powder in 67–98 wt% yield (based on substrate loading) with particle size and structure consistent with MCC (Table S1, Fig. S5, Supporting information). This approach was effectively applied to reactions of cellulose from eucalyptus and *Pinus* (bleached and unbleached), and to wood pulp, providing fine cellulosic powders in each instance (average particle size 54–86 μm, Table S1, Supporting information). The yield of cellulose was diminished only for wood pulp (67 wt%, Table S1, Supporting information), likely associated with losses of other macromolecules such as hemicellulose and lignin, which are known to be soluble in DESs [31]. It is noteworthy that the DES may be recovered by extraction of nonpolar furanoids with ethyl acetate (trace amounts of furanoids were identified, which causes the formation of humins during recycling) and evaporation of water (the antisolvent used to precipitate cellulose powder from the DES) from the ionic solvent. The recovered media can be reused without any changes to the recovered cellulose (Table S1, Supporting information). One persistent drawback in this set of reactions is that softwood resisted the pretreatment under the conditions applied (80 °C, 2 h), likely due to the more intractable molecular structure of raw biomass [2,35]. Longer processing of wood chips and higher temperatures caused the formation of humins, and thus we found this method inappropriate for raw lignocellulose. Nevertheless, the subsequent conversion of DES-pretreated cellulosic materials (eucalyptus and *Pinus* cellulose, wood pulp) in ethanol and applying the combined acid catalyst $Y(OTf)_3/H_3PO_4$ enabled notable increases in the yield and selectivity of ELev (Table 2, entries 3, 5, 7, 9). Similarly excellent yields of ELev were obtained for the conversion of pretreated wood pulp performed at larger scale (Table 2, entry 10). The results compare very favourably with benchmarks in the literature (Table 2, entries 12–16) [11,17,18,36,37]. Moreover, our method does not require solvent exchange during the processing, prolonged reaction times, use of corrosive mineral acids or energy demanding microwave irradiation, as was previously employed in other studies (Table 2). These outcomes improve on the state-of-the-art methods, and offer a new technique to produce valuable ELev in high yield and selectivity, from low value cellulosic substrates, employing green solvents and catalysts.

4. Conclusions

This work demonstrates the acid-catalysed high yielding and selective transformation of cellulosic materials in ethanol into value added ELev. The use of metal triflates and their analogous Brønsted acid-assisted systems as catalysts, delivered superb yields (up to 75 mol%) and selectivity (up to 89 mol%) of the target platform molecule. To deliver such outcomes, the use of hard Lewis acids or the combined acid catalyst $Y(OTf)_3/H_3PO_4$ are preferred. Such systems deliver the necessary Lewis acidity and Brønsted acidity to expedite the cascade of reactions required for this transformation. The pretreatment of cellulosic biomass using the renewable deep eutectic system choline chloride/oxalic acid, with subsequent acid-catalysed processing in ethanol, enabled the high-yielding and highly selective direct conversion of the cellulosic raw materials that are available via large volume cellulose refining technologies. These new methods offer a springboard for biorefinery activities, involving green solvents and catalysts in the valorisation of biomass, even though not all of the problems have been solved. Native lignocellulose, such as wood biomass, is less efficiently converted under our conditions. The technology itself still requires efficient methods to recover the product and the catalyst before the method could be scaled up.

Acknowledgment

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.fuproc.2019.106159.

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Declaration, author contributions and copyright information

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Iurii Bodachivskyi (graduate research student) developed the methodology, conducted research, including experimental work, data collection and data analysis, and drafted the manuscript. Prof. D. Bradley G. Williams (principal supervisor) and Dr Unnikrishnan Kuzhiumparambil (co-supervisor) supervised Iurii Bodachivskyi's research activities, provided conceptual advice and revised the manuscript.

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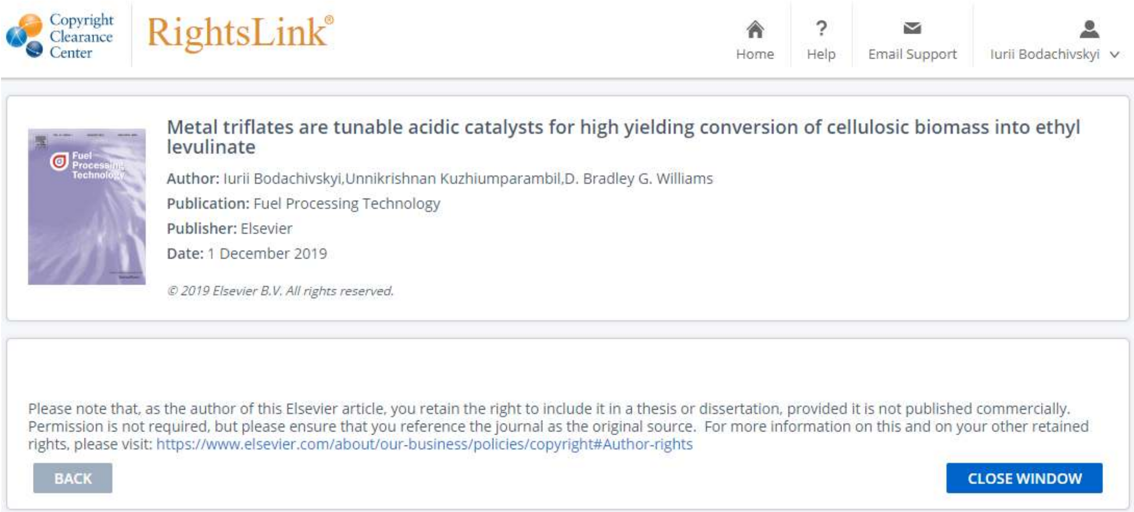

Metal triflates are tunable acidic catalysts for high yielding conversion of cellulosic biomass into ethyl levulinate

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Chapter 3:

Catalytic valorisation of cellulosic biomass in ionic liquids

3.1. Acid-catalysed conversion of carbohydrates into furan-type molecules in zinc chloride hydrate

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Acid-Catalysed Conversion of Carbohydrates into Furan-Type Molecules in Zinc Chloride Hydrate

Iurii Bodachivskyi+,[a] Unnikrishnan Kuzhiumparambil+,[b] and D. Bradley G. Williams+*[a]

Acid-catalysed conversion of biomass, specifically cellulose, holds promise to create value-added, renewable replacements for many petrochemical products. We investigated an unusual acid-catalysed transformation of cellulose and cellobiose in the biphasic solvent system zinc chloride hydrate (ionic liquid)/anisole. Here, furyl hydroxymethyl ketone and furfural are obtained as major products, which are valuable but less commonly formed in high yields in transformations of cellulosic substrates. We explored this chemistry in small-scale model reactions and applied the optimised methods to the conversion of cellulose in bench-scale processes. The optimum reaction system and preferred reaction conditions are defined to select for highly desirable furanoid products in the highest known yields (up to 46%) directly from cellulose or cellobiose. The method avoids the use of added catalysts: the ionic solvent zinc chloride hydrate possesses the intrinsic acidity required for the hydrolysis and chemical transformation steps. The process involves inexpensive media for the catalytic conversion of cellulose into high-value products under mild processing conditions.

Introduction

In the past few decades there has been a significant and growing interest in acid-catalysed transformations of carbohydrates into value-added organic building block chemicals (platform molecules). These molecules are diverse and represent a platform with the potential to replace a large portion of crude oil-based products such as fuels, plastics, coatings, detergents, and other useful commodities.[1–5] The application of ionic liquids (ILs), as alternative reaction media to common aqueous and organic solvents, in the valorisation of polysaccharides has enabled substantial progress towards mild reaction conditions and improved yields and selectivities.[5,6] That many ILs fully dissolve cellulosic material under mild conditions is a primary enabler towards high yields and selectivity, although secondary reasons exist for the success of ILs in this context.[6] Pertinent examples of successful applications of ILs include the transformation of cellulose into low-molecular-weight reducing sugars in 99% yield within 1 h at 100 °C (solvents 1-methyl-3-butylimidazolium chloride and triethyl-(3-sulfopropyl)-ammonium hydrogen sulfate),[7] into 5-(hydroxymethyl)furfural (HMF) in 79% yield within 2 h at 120 °C (solvent 1-butyl-3-methylimidazolium chloride),[8] or into levulinic acid in 40% yield in 2 h at 120 °C (solvent 1-(4-sulfobutyl)-3-methylimidazolium hydrogen sulfate),[9] all of which are arguably benchmark instances of the chemical processing of cellulose into target platform molecules. Drawbacks of the use of ILs include the complexity of recovery of ionic solvents and products from the reaction media, along with their high cost, and these pose potential hurdles to their widespread acceptance in industrial scale processes.[6] There is thus an imperative to develop and employ inexpensive ILs that are able to facilitate the efficient processing of polysaccharides and which are easy, or relatively so, to recover; this remains a goal for workers in this field.

While common ILs suffer some drawbacks as mentioned, inorganic molten salt hydrates show promise to avoid some of these issues. Such ionic systems possess inherent acidity, as well as low viscosity compared to common quaternary ammonium salts, and have been demonstrated to be suitable media for the dissolution of cellulose.[10–12] With commodity level pricing of some inorganic salts and the ease of preparation of their hydrates, these ILs are budding candidates for the chemical conversion of cellulose. Zinc chloride hydrate with the formula $ZnCl_2 \cdot nH_2O$ ($n = 3$–4; this system is considered to be an IL. Although the conventional presentation of the molecular formula of zinc chloride hydrate is $ZnCl_2 \cdot nH_2O$, its formula is more accurately represented as $[Zn(OH_2)_6][ZnCl_4]$ in the case of $n = 3$, based on solid state and liquid state determinations.[13,14]) is useful in the conversion of polysaccharides into furan-type molecules, typically into HMF.[15–18] The processes detailed in these papers require lengthy pretreatment of the substrates, the use of microwave irradiation, or high loading of acid catalyst, all of which inhibit the ability to scale up such processes.[6] It remains an unsolved problem to convert polysaccharides in such IL solvent systems into one or two major products under mild reaction conditions using techniques that are potentially scalable.

The present work discloses the functionality and potential of zinc chloride hydrate solvent in the catalytic conversion of carbohydrates into unusual furan-type molecules (i.e. products

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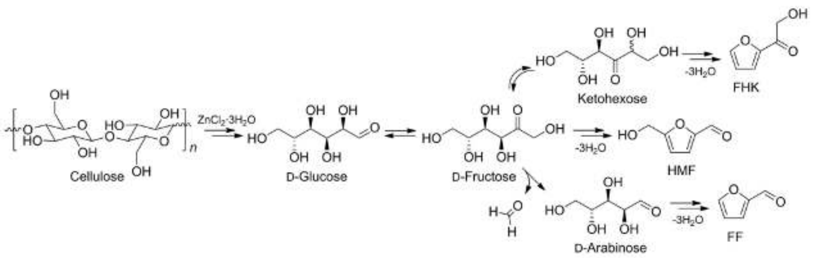

Scheme 1. Catalytic conversion of cellulose into furan-type molecules in ZnCl$_2$·3H$_2$O.

that are valuable but less seldom obtained during the conversion of cellulose) under mild reaction conditions.

Results and Discussion

To explore the course of the hydrolytic conversion of polysaccharides towards platform molecules in ZnCl$_2$·3H$_2$O, the processing of microcrystalline cellulose (MCC) was performed. Firstly, MCC was dissolved in this IL (loading of cellulose 1 wt% based on IL, 80 °C, 1 h) and then the solution was heated under constant agitation at 120 °C for 1 h during which the mixture became dark-brown coloured. Dilution of the reaction medium after completion of the process, with aqueous sodium hydrogen carbonate, led to precipitation of the unreacted cellulose and conversion of zinc chloride into insoluble zinc salts. The aqueous phase yielded three main products, being HMF, its isomer furyl hydroxymethyl ketone (FHK), and furfural (FF), each in yields below 3.0 mol% based on the number of anhydroglucose units present in the cellulose substrate. It is worth noting that low-molecular-weight sugars, and the product of rehydration of furanoids, namely, levulinic acid, were identified in trace amounts only. However, there was a mass of dark-brown colour solids in the water phase: these are typically considered to be high-molecular-weight by-product humins.[6] The portfolio of products suggests that cellulose hydrolyses into monomer glucose under these reaction conditions, and that the glucose transforms rapidly into HMF and FHK in the acidic reaction media. We propose that this process proceeds, under our conditions, via hydrolysis of cellulose into glucose, followed by isomerisation of glucose into ketohexoses and their subsequent dehydration into furanoid products. To test this proposal, we performed liquid chromatography-mass spectrometry (LC-MS) analysis of the recovered reaction media. The results confirmed the presence of glucose and its two isomers fructose and an unidentified ketohexose sugar, as proposed in Scheme 1 and presented in Figure S1 (see the Supporting Information). FF is most likely formed in a sequence that involves conversion of the intermediate hexose sugar fructose into one or more pentose products (e.g., arabinose) followed by dehydration into furan derivatives, as has been disclosed in the literature.[19] This dehydration process would be catalysed by the ZnCl$_2$, which is acidic in nature, and is driven by aromatic stabilisation. The furan-type molecules are unstable in ZnCl$_2$·3H$_2$O and are converted into high-molecular-weight by-products, arguably by condensation with low-molecular-weight sugars as was recently highlighted.[20]

To improve the outcome towards platform molecules, we investigated the influence of loading of cellulose in the medium, and reaction temperature and time. In no case did the reaction afford products in yields higher than 5 mol%, persistently accompanied by humins. The only useful strategy was the continuous extraction of furan derivatives by *m*-xylene during the process, which separates reactive furan derivatives from the acidic medium/catalyst. This was accomplished by the addition of this solvent-extractant from the start of the reaction. Additionally, we identified that dilution of ZnCl$_2$·3H$_2$O with a small amount of water (1 equivalent volume based on the weight of IL) after completion of the process serves to better extract products into the organic solvent phase, likely due to disruption of the ionic solvent and a salting out effect. Analysis of the products in the polar and *m*-xylene phases showed improved yields of FHK and FF of 16 and 13 mol%, respectively, but HMF was present only in trace amounts (Table 1). It is worth noting that FF was found predominantly in the xylene phase, while FHK was present in both the organic solvent and the polar aqueous phase. The incomplete separation of the polar product FHK from the acidic IL by xylene would prolong its exposure to the acidic conditions, leading to its partial decomposition.

Table 1. Yields of furan derivative from the processing of cellulose in the biphasic system ZnCl$_2$·3H$_2$O/organic solvent and partition coefficients of products.

Solvent	FHK yield, [mol%][a]	log P[b]	FF yield, [mol%][a]	log P[c]
m-Xylene	16	−0.93	13	0.64
tert-Butylbenzene	16	−0.45	11	0.48
Anisole	20	0.03	8	0.98
4-Methylanisole	14	−0.37	1	0.97
1,2-Dimethoxybenzene	12	−0.57	11	−0.63
2-*sec*-Butylphenol	6	0.79	2	1.79

[a] mol% based on anhydroglucose unit. [b,c] Logarithm of partition coefficient of product between the organic solvent and the water-diluted ionic liquid (1:1 wt/v IL/water) for FHK and FF, respectively. Reaction conditions: MCC (5 mg), ZnCl$_2$·3H$_2$O (500 mg), solvent-extractant (2.00 mL), 120 °C, 1 h.

It had become clear that one method to improve the yield of desirable products, FHK in particular, was to extract them into a phase separate from the reaction medium, such as into an organic solvent. But a more efficient means of removal of products from the IL phase was required, and so we investigated various organic solvents for this purpose. It is worth noting that common polar high boiling solvents, such as dimethylformamide, dimethylsulfoxide, γ-valerolactone, and methyl isobutyl ketone, which are useful for the conversion of carbohydrates in water-based biphasic systems,[4,6] are miscible with $ZnCl_2 \cdot 3H_2O$, and cause precipitation of cellulose. In turn, aromatic solvents like *tert*-butylbenzene, anisole, 4-methylanisole, 1,2-dimethoxybenzene, or 2-*sec*-butylphenol form a second phase, and therefore maintain the polar phase of the reaction system, in which cellulose remains dissolved. All of these aromatic solvents were applied to the conversion of MCC in a biphasic system; among them, anisole afforded high overall yields of and selectivity to FHK and FF (20 and 8 mol%, respectively, Table 1). This result may be rationalised by the higher partition coefficients of products in anisole, which serves to efficiently remove them from the catalytic system and therefore limits side reactions. A measure of miscibility between the ionic solvent and the organic solvent is deleterious to the course of the reaction. For instance, the occurrence of humins was observed when 1,2-dimethoxybenzene, or 2-*sec*-butylphenol, was used as the organic phase; the partial miscibility led to degradation of the furan-type products with concomitant diminished yields. Conversely, the less polar aromatic solvent anisole demonstrates lower miscibility with the IL, which protects the extracted products from side reactions.

Aiming to improve the conversion of cellulose into FHK and FF in the biphasic system $ZnCl_2 \cdot 3H_2O$/anisole, we conducted some parameter testing. Firstly, the influence of the loading of cellulose to IL (1, 1.25, 1.5, 1.75 and 2 wt% based on the IL) with a low amount of extractant (2 v/w based on IL) was examined. While the yields of FHK and FF remained essentially unchanged in these reactions (Figure S2), ranging from 18–20 mol% and 7–8 mol%, respectively, there was an increase in the amount of humins formed when employing higher concentrations of cellulose. This is most likely due to longer residence times of furanoids in the IL phase, consistent with the literature,[21] which would promote acid-catalysed by-product formation. This occurs because of non-exhaustive extraction of the FHK and FF into the organic phase, leaving open the possibility of reaction between the furanoids and sugars present.

In response, and to enhance the efficiency of the extraction, the conversion of MCC at a loading of 1 and 2 wt% in $ZnCl_2 \cdot 3H_2O$ was performed making use of larger volumes of anisole. The yields of FHK and FF are slightly improved to 23 mol% and 10 mol%, respectively, at 6 v/wt (based on IL) of anisole and 1 wt% cellulose in the IL (Figure S3). The overall yields of FHK are lower at 2 wt% loading of MCC, and the formation of humins was observed in all instances. Overall there was no significant difference in yield between the two loadings of cellulose nor in the formation of humins.

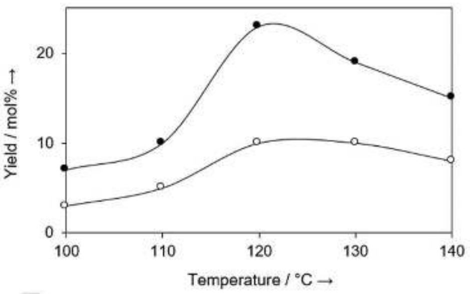

Figure 1. Production of furanoids from reaction of cellulose in the biphasic system $ZnCl_2 \cdot 3H_2O$/anisole at various reaction temperatures. Reaction conditions: MCC (5 mg), $ZnCl_2 \cdot 3H_2O$ (500 mg), anisole (3.00 mL), 1 h. ●: yield of FHK; ○: yield of FF.

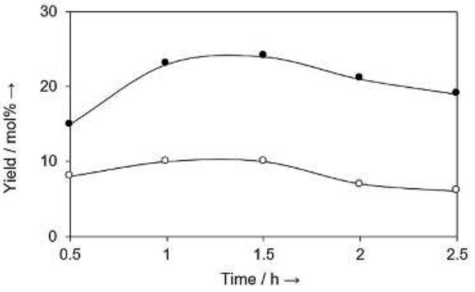

Figure 2. Production of furanoids from reaction of cellulose in the biphasic system $ZnCl_2 \cdot 3H_2O$/anisole at various reaction times. Reaction conditions: MCC (5 mg), $ZnCl_2 \cdot 3H_2O$ (500 mg), anisole (3.00 mL), 120 °C. ●: yield of FHK; ○: yield of FF.

Reaction temperature and the time for which the reactions were conducted substantially influence the outcomes (Figure 1, 2). For instance, the highest yields of FHK and FF were produced at 120 °C (Figure 1) and yields of FHK reached a peak at 1.5 h (24 mol%, Figure 2). Longer reaction times led to diminished yields through by-product formation. At 100 °C (low temperature) we identified small amounts of HMF (2 mol%), and only at that temperature. Presumably, elevated temperatures favour reaction pathways leading to FHK and FF, in preference to those producing HMF (Scheme 1).

To test this proposal, low molecular-weight sugars, such as cellobiose, glucose, and fructose, respectively, which putatively appear during the course of the transformation of cellulose,[6] were subjected to reaction in the IL. As is evident from Figure 3, HMF is one of the products of the conversion of sugars at temperatures below 100 °C, reaching yields up to 16 mol% (based on sugar substrate) from cellobiose or glucose. At higher temperatures FHK and FF become the dominant furanoid products, with yields of HMF falling away dramatically above 100 °C.

The processes with cellobiose, glucose and fructose at elevated temperature was accompanied by complete conversion of substrates (99% conversion of all substrates at the

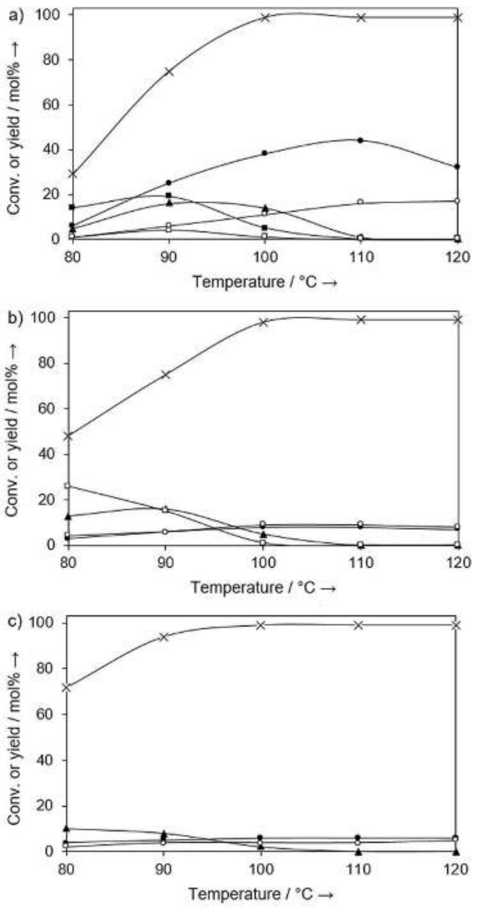

Figure 3. Conversion of carbohydrates (a: cellobiose; b: glucose; c: fructose) and the yields of the major products obtained in the biphasic system $ZnCl_2 \cdot 3H_2O$/anisole at various reaction temperature. Reaction conditions: sugar (5 mg), $ZnCl_2 \cdot 3H_2O$ (500 mg), anisole (3.00 mL), 1 h. ×: conversion; ■: yield of glucose; □: yield of fructose; ●: yield of FHK; ○: yield of FF; ▲: yield of HMF.

temperature above 100 °C, Figures 3a–c). Losses in yields of desirable products is most likely associated with the formation of humins, which were noted in some instances. Apart from furan derivatives and humins, we identified glucose and fructose during the transformation of cellobiose at lower temperatures (yields up to 19 and 4 mol%, respectively, Figure 3a); the occurrence of fructose (yield up to 26 mol%) is also apparent during the conversion of glucose (Figure 3b). The portfolio of compounds identified maps perfectly onto the acid-catalysed cascade of cellulose conversion proposed in Scheme 1, involving hydrolysis, aldose-ketose isomerisation and dehydration steps, respectively. It is likely that the dehydration of fructose into HMF is only favourable at temperatures below 100 °C. At higher temperatures the rates of fructose isomerisation into ketohexose or the pentose intermediate are increased, leading to FHK and FF becoming major products. From the outcomes it appears that the rates of the fructose isomerisation and further dehydration into FHK are higher, relative to the processes forming FF, accounting for the fact that FHK often appears in somewhat higher yields than FF. There is an interesting contrast in this set of reactions compared to those involving cellulose. With cellulose, a reaction temperature of 120 °C affords highest yields of furan derivatives; with low molecular weight substrates the optimum temperature is 110 °C. This finding presumably reflects the need for elevated temperatures to hydrolyse the glycosidic bonds in cellulose at an appreciable rate compared to subsequent reactions that lead to furan derivatives. Reactions converting glucose into furans appear to proceed at higher rate than the hydrolysis reaction of cellulose into glucose, and the optimum temperature that we identified is likely a trade-off between optimised hydrolysis, optimised formation of furans and minimised conversion into humins.

It is possible, in theory, to advantage the hydrolysis of polysaccharides by the addition of water or an acid catalyst, and thus improve the yields of target products. However, reaction of cellulose in zinc chloride with higher ratios of water ($ZnCl_2 \cdot 3.25H_2O$ and $ZnCl_2 \cdot 3.5H_2O$), or $ZnCl_2 \cdot 3H_2O$ with added acid catalysts (*p*-toluenesulfonic acid, oxalic acid, aluminium(III)-, lanthanum(III)-, gadolinium(III)-, ytterbium(III)- or hafnium(IV) trifluoromethanesulfonates, or lanthanum(III)- or gadolinium(III) chlorides) afforded similar or diminished yield of furanoids (Table S1). Arguably, the excess of water, or added catalyst, increases the overall acidity of the reaction media leading to decomposition of the ketone before its extraction, or to rehydration reactions potentially affording levulinic acid.[2,6] However, levulinic acid was not detected during the analysis of the reaction media and so this process appears not to prevail. Overall, the conversion in neat $ZnCl_2 \cdot 3H_2O$ remains the best process to date.

All of the reactions performed to this stage had been conducted at 5 mg scale. A subsequent set of reactions was performed at 10× this scale under identical reaction conditions (Table 2). The scaling operations revealed that the yields of the desired products were reduced to 15% for FHK and remained relatively stable at 9% for FF (Entry 1). Arguably, this relates to reduced mass transfer of products into the anisole phase leading to decomposition of unstable molecules in the polar acidic reaction media. To improve the outcome, the volume of anisole was increased to 8 vol/wt of IL and the reaction temperature was slightly reduced (by 5 °C). This improved the yield of FHK to 20% while the yield of FF remained constant at 9% (Entry 2). It is noteworthy that total selectivity of furan-type molecules was 48% (Entry 2), based on conversion of substrate (recovered unreacted substrate), indicating that the transformation of MCC in $ZnCl_2 \cdot 3H_2O$ is a reasonably selective process. Even higher yields of FHK and FF can be achieved from cellobiose in bench-scale processes. The total yield of furan products is excellent (46% yield of furan products, being a combination of 32% FHK and 14% FF, Entry 3). To the best of our knowledge, these outcomes set the benchmark in terms of yields of FHK and FF during the conversion of poly- or

Table 2. Results of scaling and comparative literature data of the conversion of carbohydrates in $ZnCl_2 \cdot nH_2O$.[a]

Entry	Substrate	Time [h]	Temp [°C]	FHK yield [mol %]	FF yield [mol %]	*S* [%]	*X* [%]
1[b]	MCC	1.5	120	15	9	33	73
2[c]	MCC	1.5	115	20	9	48	61
3[c]	Cellobiose	1.5	115	32	14	46	99
4[d,15]	Cotton fibre	5 min	135	12	–	–	–
5[e,17]	Cotton cellulose	1.67	190	1	1	–	–
6[f,22]	Cellulose	2.5	270	–	6	–	–

[a] *S*—total selectivity of furan-type molecules. *X*—conversion of substrate. [b] Reaction conditions: MCC (50 mg), $ZnCl_2 \cdot 3H_2O$ (5,000 mg), anisole (30.0 mL). [c] Reaction conditions: MCC or cellobiose (50 mg), $ZnCl_2 \cdot 3H_2O$ (5,000 mg), anisole (40.0 mL). [d] Reaction conditions: cotton fibre (1,000 mg), $ZnCl_2 \cdot 3.36H_2O$ (140 mL), heating under microwave irradiation 600 W.[15] [e] Reaction conditions: cotton cellulose (650 mg), $ZnCl_2 \cdot 3.56H_2O$ (100 mL), *n*-butanol (600 mL).[17] [f] Reaction conditions: cellulose (1,000 mg), compressed steam and nitrogen (2.5 MPa), calcined $Ca(H_2PO_4)_2$ (0.1 mmol).[22]

oligoglucans under mild reaction conditions. For comparison purposes, the targeted synthesis of FHK from polysaccharides was hitherto possible only for processes conducted under microwave heating in comparably lower yield than those achieved in this work (12% yield of FHK, Entry 4).[15] Otherwise, FHK and FF are attainable only in small amounts as by-products of the degradation of cellulose (Entries 5, 6);[17,22,23] usually, the major product secured from cellulose is HMF. It is worth noting that zinc chloride hydrate solvent is amenable to recovery and can potentially be reused, as has been shown in the reproducible conversion of cellulose into HMF in 4 catalytic runs in aqueous zinc chloride solvent.[18]

Conclusion

This work details the one-pot transformation of cellulose, into the furan-type platform products FHK and FF in high yield, in biphasic media containing $ZnCl_2 \cdot 3H_2O$ and anisole. These two products are valuable but are less commonly formed in high yield in the transformation of cellulosic substrates. The optimum method avoids the use of added catalysts because the ionic solvent possesses the intrinsic acidity required to facilitate all requisite transformations, namely hydrolysis, isomerization, and dehydration. In turn, anisole promotes the extraction of products from acidic media and preserves them from decomposition. These outcomes improve on the state of the art and provide a framework, involving inexpensive, recoverable media for the efficient direct conversion of cellulose into platform chemicals under mild conditions. The work highlights the ongoing challenge of removal of the reactive (under the reaction conditions) furanoid products from the catalyst, which is likely the current major obstacle to larger scale reactions and improved yields and selectivities.

Experimental Section

Preparation of ionic liquids and processing of carbohydrates were performed in oven-dried glassware at atmosphere pressure. Reagents were used as supplied from commercial sources. All details about analytical methods and equipment are specified in the Supporting Information (SI).

Preparation of Zinc Chloride Hydrate Solvent and Dissolution of Carbohydrates

Anhydrous zinc chloride and deionised water in a molar ratio 1 to 3.0, 3.25 or 3.5, to form $ZnCl_2 \cdot 3H_2O$, $ZnCl_2 \cdot 3.25H_2O$ or $ZnCl_2 \cdot 3.5H_2O$ (Table S2), respectively, were introduced to a round-bottom flask equipped with a thermometer and magnetic follower. The mixture was heated and agitated at 80 °C for 30 minutes, resulting in a transparent colourless ionic liquid. Then the microcrystalline cellulose (100–200 mg, to form a 1–2 wt% solution based on the solvent) was introduced to the flask with the prepared zinc chloride hydrate solvent (10.00 g) and the mixture was heated and agitated at 80 °C for 1 h, resulting in a yellowish transparent solution. The same method was employed for the dissolution of low-molecular-weight carbohydrates (cellobiose, glucose, or fructose) but the processing temperature was 60 °C.

Microscale Model Reactions

A solution of microcrystalline cellulose or low-molecular-weight sugars (cellobiose, glucose or fructose, 5–10 mg) in $ZnCl_2 \cdot nH_2O$ ($n = 3.0–3.5$, 500 mg, 1–2 wt% solution of carbohydrate based on the ionic liquid) and organic solvent (2.00–6.00 mL of *m*-xylene, *tert*-butylbenzene, anisole, 4-methylanisole, 1,2-dimethoxybenzene or 2-*sec*-butylphenol, respectively) were introduced to a two-neck round-bottom flask equipped with a condenser, thermometer and magnetic follower. The mixture was heated and stirred at a predetermined reaction temperature and for a fixed period of time. In some instances, Brønsted acids (*p*-toluenesulfonic acid or oxalic acid, 1–20 mol% based on the number of anhydroglucose units present in cellulose) or Lewis acids (aluminium(III)-, lanthanum(III)-, gadolinium(III)-, ytterbium(III)- or hafnium(IV) trifluoromethanesulfonates, or lanthanum(III)- or gadolinium(III) chlorides, 1–20 mol% based on the number of anhydroglucose units present in cellulose) were added to the reaction media when investigating the role of the catalyst on the outcome of the conversion of cellulose. Recovery of the product included dilution of the ionic liquid with 1 equivalent volume of water based on the weight of ionic liquid in the reactor, followed by agitation of the biphasic system at room temperature for 30 minutes, after which the organic solvent phase was removed from the reactor. Work-up of the aqueous phase was performed by the addition of aqueous sodium hydrogen carbonate (0.50 mL, 1 M), followed by centrifugation and decantation (20,000×g for 10 minutes) to remove precipitated zinc salts. The aqueous and organic solvent phases were analysed using high performance liquid chromatography (HPLC), as detailed in SI, to provide the results described in the main text. All microscale reactions were repeated at least three times.

Bench Scale Processes

A solution of microcrystalline cellulose or cellobiose (50 mg) in $ZnCl_2 \cdot 3H_2O$ (5.00 g, 1 wt% solution of carbohydrate based on the ionic liquid) and anisole (30.0 or 40.0 mL) were introduced to a two-neck round-bottom flask equipped with a condenser, thermometer and magnetic follower. The mixture was heated and stirred at a predetermined reaction temperature (115 or 120 °C) for 1.5 h.

Recovery of the products included dilution of ionic liquid with 1 equivalent volume of water based on the weight of ionic liquid in reactor followed by agitation of the biphasic system at room temperature for 30 minutes. The two phases were separated and a small amount of each (0.5 mL) was processed, as detailed above, before chromatographic analysis using an HPLC system to provide the outcome shown in the main text. The remaining aqueous phase was diluted with aqueous hydrochloric acid (25.0 mL, 0.2 M) to precipitate the unreacted cellulose, which was recovered, washed with deionised water (3×25.0 mL), vacuum oven-dried (60°C, 1 mbar, 12 h) and weighed to provide the conversion of cellulose detailed in the manuscript.

Isolation of Furan-type Molecules and Recovery of Solvents

Isolation of furan-type molecules from anisole phase comprised adsorption of products on the solid adsorbents. A solution of products in anisole (40.0 mL, combined anisole phases after microscale conversion of carbohydrates) was diluted with 1 equivalent volume of hexane and was passed through a glass funnel containing silica gel (10.00 g) and activated carbon (1.00 g) under ambient pressure. The polar products were trapped on the solid adsorbents, while the anisole and hexane were removed as a filtrate. Then furan-type molecules were desorbed with ethyl acetate (3×20.0 mL) and collected as a mixture. The recovery of products from the diluted with 1 equivalent volume of water ionic liquid (10.0 mL, combined aqueous phases after microscale conversion of carbohydrates) comprised extraction with ethyl acetate (3×20.0 mL) under vigorous agitation at room temperature for 10 min. The achieved solutions of products in ethyl acetate after recovery from anisole and aqueous phases were combined and dried over $MgSO_4$ and the solvent was removed under reduced pressure. The mixture of furan-type molecules was subjected to flash column chromatography (hexane–ethyl acetate, 1.5:1) to isolate FHK, FF and HMF. The HPLC analysis of the recovered anisole and diluted with water ionic liquid showed only trace amounts of furanoids remained in both solvents implying almost complete recovery.

Furyl hydroxymethyl ketone:[15] TLC: R_f=0.308 (1.5:1 hexane/EtOAc; UV, $KMnO_4$); ^{1}H NMR (500 MHz, $CDCl_3$, 25°C): δ = 7.63 (dd, J=1.5, 0.5 Hz, 1H), 7.30 (dd, J=3.5, 0.5 Hz, 1H), 6.60 (dd, J=3.5, 1.5 Hz, 1H), 4.74 (s, 2H), 3.27 (br s, 1H, OH); ^{13}C NMR: (125 MHz, $CDCl_3$, 25°C): δ=187.6, 150.1, 147.0, 117.9, 112.6, 65.1; IR (neat): ν_{max}=3331, 3133, 3115, 1678, 1563, 1468, 1421, 1321, 1270, 1168, 1113, 1029, 976, 912, 880, 774, 636, 590, 504 cm^{-1}; HRMS (ESI): m/z calcd for $C_6H_6O_3H$ $[M+H]^+$: 127.0390, found: 127.0378.

Furfural:[24] TLC: R_f=0.532 (1.5:1 hexane/EtOAc; UV, $KMnO_4$); ^{1}H NMR (500 MHz, $CDCl_3$, 25°C): δ = 9.63 (s, 1H), 7.68 (t, J=1.0 Hz, 1H), 7.23 (dd, J=3.5, 1.0 Hz, 1H), 6.58 (dd, J=3.5, 1.0 Hz, 1H). ^{13}C NMR: (125 MHz, $CDCl_3$, 25°C): δ=177.8, 152.9, 148.0, 121.0, 112.5. IR (neat): ν_{max}=3132, 2807, 1673, 1568, 1473, 1394, 1367, 1278, 1157, 1081, 1021, 930, 883, 759, 595 cm^{-1}. HRMS (ESI): m/z calcd for $C_5H_4O_2H$ $[M+H]^+$: 97.0284, found: 97.0278.

Hydroxymethylfurfural:[25] TLC: R_f=0.213 (1.5:1 hexane/EtOAc; UV, $KMnO_4$); ^{1}H NMR (500 MHz, $CDCl_3$, 25°C): δ=9.56 (s, 1H), 7.21 (d, J=3.5 Hz, 1H), 6.51 (d, J=3.5 Hz, 1H), 4.70 (s, 2H), 2.97 (br s, 1H, OH). ^{13}C NMR: (125 MHz, $CDCl_3$, 25°C): δ =177.7, 160.7, 152.3, 123.0, 110.0, 57.6. IR (neat): ν_{max}=3339, 3120, 2841, 1657, 1582, 1519, 1396, 1368, 1336, 1278, 1188, 1070, 1017, 986, 965, 806, 768, 511 cm^{-1}. HRMS (ESI): m/z calcd for $C_6H_6O_3H$ $[M+H]^+$: 127.0390, found: 127.0379.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: biomass · carbohydrates · catalysis · ionic liquids · sustainable chemistry

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Iurii Bodachivskyi (graduate research student) developed the methodology, conducted research, including experimental work, data collection and data analysis, and drafted the manuscript. Prof. D. Bradley G. Williams (principal supervisor) and Dr Unnikrishnan Kuzhiumparambil (co-supervisor) supervised Iurii Bodachivskyi's research activities, provided conceptual advice and revised the manuscript.

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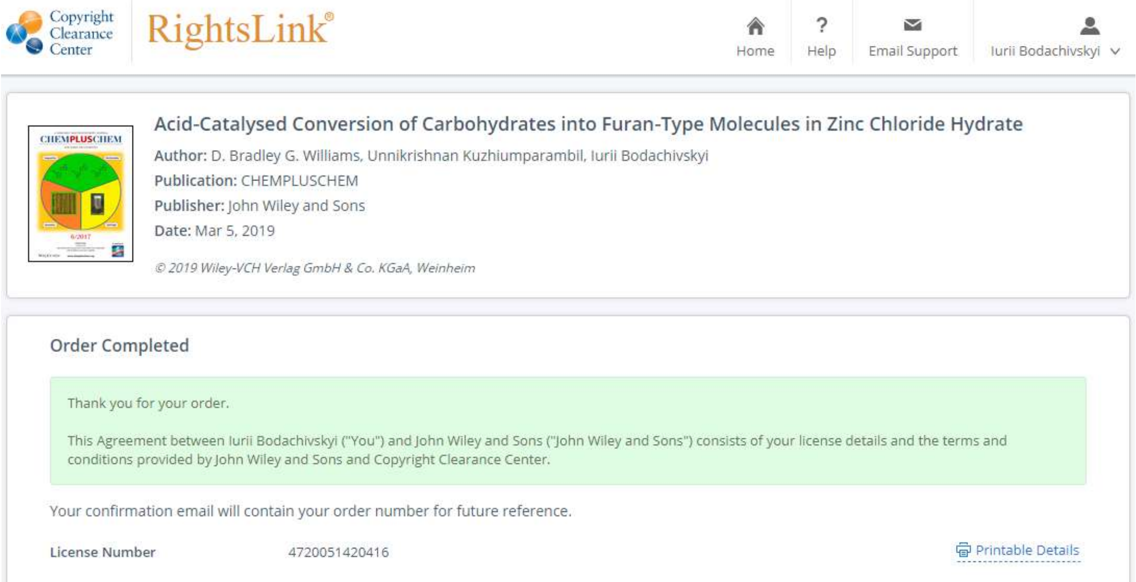

Acid-Catalysed Conversion of Carbohydrates into Furan-Type Molecules in Zinc Chloride Hydrate

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3.2. The role of the molecular formula of $ZnCl_2 \cdot nH_2O$ on its catalyst activity: a systematic study of zinc chloride hydrates in the catalytic valorisation of cellulosic biomass

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The role of the molecular formula of $ZnCl_2 \cdot nH_2O$ on its catalyst activity: a systematic study of zinc chloride hydrates in the catalytic valorisation of cellulosic biomass†

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We demonstrate the efficient and direct transformation of a range of low value substrates, such as lignocellulose and algal biomass, into significantly higher value chemicals, including low molecular weight reducing saccharides, 5-(hydroxymethyl)furfural, furyl hydroxymethyl ketone and furfural. This is based on a systematic study of $ZnCl_2 \cdot nH_2O$ (n = 2.5–4.5), in particular the role of the molecular formula (the amount of H_2O) on its activity in the catalytic transformation of cellulosic materials into value added small molecules. The study includes various model transformations based on refined saccharides and applies the new insights to the highly selective transformation of raw biomass.

Introduction

The acid-catalysed conversion of cellulosic biomass is a promising way to produce organic building block chemicals (platform molecules), as renewable replacements to many petrochemical products.[1–4] There is a current focus on the application of ionic liquids (ILs) in the catalytic valorisation of (poly)carbohydrates into platform chemicals.[1,5] In distinct contrast to common aqueous or organic solvents, ILs are able to dissolve cellulosic material enabling its conversion into desirable products under mild processing conditions.[1–7] While imidazolium salts are most commonly employed, inorganic molten salt hydrates remain less investigated ionic media for the processing of carbohydrates.[1,5] Many of these salts fully dissolve polysaccharides and in due course catalyse their transformation into platform molecules.[4,8] Zinc chloride hydrate, with the conventional formula $ZnCl_2 \cdot nH_2O$ (this system is a true IL with the molecular formula $[Zn(OH_2)_6][ZnCl_4]$ in the case of n = 3),[9,10] is excellent for the synthesis of some useful molecules directly from cellulose (*e.g.*, cotton fibres, microcrystalline cellulose, or cellobiose).[11–13] Some remarkable examples include the transformation of polysaccharides into glucose (solvent $ZnCl_2 \cdot 3.73H_2O$),[11] HMF (biphasic solvent system $ZnCl_2 \cdot 3H_2O$/methyl isobutyl ketone),[12] or into a mixture of furyl hydroxymethyl ketone and furfural (FHK and FF, biphasic solvent system $ZnCl_2 \cdot 3H_2O$/anisole),[13] all of which present a significant advantage relative to the existing processes based on aqueous solvents or commonly used imidazolium salts. Within these exemplary findings, including our recent work in which some changes in response to the molecular formula of $ZnCl_2 \cdot nH_2O$ were noted,[13] the exact role of the molecular formula of the $ZnCl_2 \cdot nH_2O$ system is unclear, on the outcomes and the catalyst activity. For example, a study on the low temperature (70 °C) pretreatment of corncob[14] for n = 3, 4, 5, 6, 7 in $ZnCl_2 \cdot nH_2O$ revealed an ability of the lower hydrates (n = 3, 4) to dissolve and convert small amounts of the biomass but with no rationalisation of the differences in underpinning features of these systems. An improved fundamental understanding would therefore be an enabler for the selective transformation of varied cellulosic substrates in this IL. The successful conversion of cellulosic substrates such as hemicellulose, algal materials (an upcoming non-terrestrial source of energy), and lignocellulose (the most readily available terrestrial biomaterial), is a key step towards sustainable industrial development,[1,4,15] and the present study addresses this topical issue.

In the present work, we systematically probe the activity associated with given $ZnCl_2 \cdot nH_2O$ systems‡ in model

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‡ The authors of the work cited in ref. 9 used highly purified sublimed $ZnCl_2$ when determining the structure of zinc chloride trihydrate to be $[Zn(OH_2)_6][ZnCl_4]$. The same authors employed dried anhydrous $ZnCl_2$ without sublimation to assess the solubility of cellulose at 25 °C in zinc chloride hydrate (ref. 10). No specific rationale is provided in either case. Accordingly, we followed the method described in ref. 10 to prepare the zinc chloride hydrate ionic liquids, employing dried anhydrous $ZnCl_2$ without prior sublimation as a practical approach to our work. Nevertheless, we used double-sublimed $ZnCl_2$ in selected instances for comparative purposes, as indicated in the main text and Table 1.

reactions of purified saccharides, building our understanding, which we ultimately apply to the high yielding selective conversion of lignocellulose and algal biomass. We detail the acid-catalysed transformation of polysaccharides into low molecular weight carbohydrates and furan type molecules in $ZnCl_2{\cdot}nH_2O$ (n = 2.5–4.5).

Experimental

Materials

Microcrystalline cellulose (MCC), corn starch, low molecular weight sugars, metal chlorides (anhydrous), hydrochloric acid (HCl, 32 wt% aqueous solution), phosphoric acid (H_3PO_4, 85 wt% aqueous solution), sulfuric acid (H_2SO_4, 98 wt% aqueous solution) and *p*-toluenesulfonic acid monohydrate (TsOH) were used as supplied from commercial sources. Lignocellulose (softwood chips and corncob) was sourced from local growers (Australia). The macroalga *Ulva lactuca* was provided as a generous gift by Dr. Wayne O'Connor, Department of Primary Industries Fisheries, Port Stephens Fisheries Institute (Australia). The microalga *Porphyridium cruentum* was grown and supplied by Climate Change Cluster (C3), University of Technology Sydney (Australia). Hemicellulose was extracted from corncob by treatment with aqueous NaOH using an optimised method.[16] Polysaccharides from *Ulva lactuca* were obtained following the method described by Mihranyan *et al.*[17] Dried algal powder (10.00 g) was defatted with repeated extraction with toluene/ethanol (5 × 30 mL, 7 : 3 v/v) for 24 h with stirring, treated with 4% aqueous NaOH for 2 h at 80 °C, followed by bleaching with 50.0 mL acetate buffer (pH 4.8) containing $NaClO_2$ (0.9 g) at 70 °C for 2 h. The residue was washed repeatedly with water (5 × 30 mL), filtered and dried at room temperature. The dried product was heated to boiling in 1.5% aqueous hydrochloric acid (50 mL) and the resultant slurry was kept overnight at ambient temperature (30 °C), followed by washing with water (5 × 30 mL). The precipitate was filtered and lyophilised to obtain the polysaccharide fraction. Vacuum oven-dried (60 °C, 1 mbar, 12 h) cellulosic materials were used for acid-catalysed reactions. The carbohydrate content of the cellulosic substrates was established by standard analytical procedures: NREL/TP-510-42618 (ref. 18) for lignocellulose, NREL/TP-5100-60957 (ref. 19) for algal biomass. The total amount of carbohydrates in the given biomass is specified in ESI† Table S1. Zinc chloride hydrate solvents ($ZnCl_2{\cdot}nH_2O$) were prepared by mixing the anhydrous salt‡ with the appropriate amount of deionised water, resulting in transparent colourless IL.[10]

Chromatography-analysis

Carbohydrates was analysed employing liquid chromatography-mass spectrometry on a Shimadzu LCMS-8060 instrument with electrospray ionisation source in negative ion mode. The separation was performed on a Supelco apHera NH2-Polymer analytical column (150 mm × 4.6 mm, 5 μm) using a mixture of acetonitrile and water (65 : 35 v/v) as the mobile phase at a flow rate 0.6 mL min^{-1} and a run time of 18 min. Five transitions *m*/*z* 149.10 → 89.05 (fragmentor voltage 12 V, collision energy 7 eV; detection of xylose), *m*/*z* 178.85 → 89.15 (fragmentor voltage 19 V, collision energy 8 eV; detection of glucose and fructose), *m*/*z* 341.30 → 161.20 (fragmentor voltage 16 V, collision energy 8 eV; detection of cellobiose and cellobiulose), *m*/*z* 503.35 → 161.20 (fragmentor voltage 24 V, collision energy 13 eV; detection of cellotriose) and *m*/*z* 665.25 → 503.10 (fragmentor voltage 26 V, collision energy 12 eV; detection of cellotetraose) were monitored. Liquid chromatography analysis of furan type molecules was conducted using an Agilent 1290 LC instrument equipped with an Agilent Zorbax Eclipse XDB-C18 analytical column (150 mm × 4.6 mm, 3 μm) and Agilent 1260 DAD VL+ detector (detection wavelength 278 nm). The mobile phase was a mixture of methanol and water (15 : 85 v/v) at a flow rate of 1.1 mL min^{-1} with a run time of 20 min. Quantitative analysis was performed with the use of a standard curve plotted with analytical standards.

pH measurements

pH measurements were performed at room temperature (22–23 °C) using a Mettler Toledo pH meter adapted with a standard glass electrode with prior calibration with two buffer solutions (pH = 4.00, pH = 7.00). Measurements were performed in triplicate and the average values are presented.

Acidity readings by the ^{13}C NMR probe method[20]

The binding ability of the various zinc chloride hydrate solvents to mesityl oxide was performed using a ^{13}C NMR method described in the literature.[20] $ZnCl_2{\cdot}nH_2O$ (5.000 g) and mesityl oxide (250 mg to form a 5 wt% solution based on the solvent) were introduced to the round-bottom flask equipped with a magnetic follower and the mixture was agitated at room temperature for 1 h, resulting in a yellowish transparent solution. The solution (0.5 g) was transferred in a 5 mm NMR tube equipped with a coaxial insert containing deuterodimethyl sulfoxide-d_6 (external lock, ^{13}C: δ = 39.7 ppm) and the sample was immediately analysed by NMR spectroscopy (Agilent 500 MHz NMR) at 25 °C.

Dissolution and recovery of cellulose in/from zinc chloride hydrate

MCC (50 mg) and $ZnCl_2{\cdot}nH_2O$ (5.000 g) were introduced to a round-bottom flask equipped with a thermometer and magnetic follower and the mixture was heated and agitated at 80 °C for 2.5 h, resulting in a transparent solution, or a turbid suspension in the case of $ZnCl_2{\cdot}4.5H_2O$. The mixture was diluted with aqueous hydrochloric acid (40.0 mL, 0.01 M aqueous HCl was used to avoid co-precipitation of water-insoluble zinc salts, which commonly form upon dilution with neat water)[8] to regenerate cellulose, which was recovered, washed with deionised water (3 × 25.0 mL), vacuum oven-dried (60 °C, 1 mbar, 12 h) and weighed to determine the conversion of polysaccharide (ESI† Table S2). A small amount of the diluted IL (0.25 mL) was neutralised with aqueous sodium bicarbonate (0.75 mL, 1 M), centrifuged (20 000 × *g* for 10 minutes) to remove water insoluble zinc salts, and decanted. The recovered solution was analysed employing the chromatographic methods given above.

Catalytic conversion of carbohydrates in zinc chloride hydrate

Polysaccharides (MCC, starch, hemicellulose, algal saccharides, 50 mg) and $ZnCl_2 \cdot nH_2O$ (5.000 g) were introduced to a round-bottom flask equipped with a condenser, thermometer, and magnetic follower and the mixture was heated and agitated at 80 °C for 2.5 h, resulting in a transparent solution, or turbid suspension when $ZnCl_2 \cdot 4.5H_2O$ was used as a solvent. The mixture was heated and stirred at the predetermined temperature for a fixed period of time to promote the catalytic conversion (Table 1). In one instance (Table 1), water (0.71 mL) was added to $ZnCl_2 \cdot 3.0H_2O$ after dissolution of MCC when assessing the role of cellulose solubility in $ZnCl_2 \cdot 4.5H_2O$; this approach permitted the processing of cellulose in $ZnCl_2 \cdot 4.5H_2O$ under homogeneous conditions.§ In some instances (Tables 3 and 4 only), Brønsted acids (HCl, H_3PO_4, H_2SO_4, or TsOH, 0.03 mmol) or Lewis acids ($AlCl_3$, $InCl_3$, $LaCl_3$, $GdCl_3$, $YbCl_3$ or $HfCl_4$, 0.03 mmol) were added to the reaction media when investigating the role of added catalyst in the transformations of cellulose in zinc chloride hydrate solvent. After completion, the reaction mixture was cooled and diluted with deionised water (5.00 mL). A small amount of aqueous phase (0.25 mL) was retained for HPLC analysis. Work-up of the aqueous phase before chromatography-analysis included addition of aqueous sodium hydrogen carbonate (0.75 mL, 1 M), followed by centrifugation (20 000 × *g* for 10 minutes) and decantation. The recovered solutions were diluted with a known volume of deionised water, for analysis. The remaining reaction mixture was diluted with aqueous hydrochloric acid (40.0 mL, 0.01 M) to precipitate the unreacted substrate. The recovered solids were washed with deionised water (3 × 25.0 mL), vacuum oven-dried (60 °C, 1 mbar, 12 h) and weighed to calculate the conversion of substrate specified in the main text. The isolation of furanoid products from the diluted with water zinc chloride hydrate solvent was performed according to ref. 13. The furanoids all gave satisfactory analytical data.[13,21–23]

With low molecular weight sugars, the substrate (cellobiose, glucose, or fructose, 50 mg) and $ZnCl_2 \cdot nH_2O$ (5.000 g) were introduced to a round bottom flask equipped with a condenser, thermometer, and magnetic follower and the mixture was heated and stirred at the predetermined temperature for a fixed period of time. The products were recovered and analysed as detailed above. The conversion of substrates was established by chromatography-analysis.

For the conversion studies, the biomass (75, 75, 122, or 217 mg) corresponding to 50 mg of polysaccharides of corncob, wood chips, *Ulva lactuca*, or *P. cruentum*, respectively, and $ZnCl_2 \cdot 4.25H_2O$ (5.000 g) were introduced to a round bottom flask equipped with a condenser, thermometer, and magnetic follower and the mixture was heated and agitated at 80 °C for 5 h, resulting in a transparent solution, or a turbid suspension in case of wood chips or algal biomass. Hydrochloric acid (0.03 mmol of HCl) was added and the reaction mixture was heated and stirred at 120 °C for a fixed period of time. In some instances, hydrochloric acid (0.03 mmol of HCl) was added from the start of the processing, maintaining the ratio of Zn/H_2O within ±1%. The products were recovered and analysed as specified above to provide the results detailed in the main text.

Results and discussion

To understand the role of the molecular formula of $ZnCl_2 \cdot nH_2O$ on the conversion of cellulose, $ZnCl_2 \cdot nH_2O$ with hydration number $n = 2.5–4.5$ was employed under various processing conditions. Firstly, we probed the dissolution of MCC in $ZnCl_2 \cdot 2.5–4.5H_2O$ (1 wt% of MCC, based on solvent, 80 °C, 2.5 h); dissolution is usually considered to be the first step of the conversion of cellulose in aqueous zinc chloride systems.[12,13] All of $ZnCl_2 \cdot 2.5–4.25H_2O$ permitted complete dissolution of MCC, while $ZnCl_2 \cdot 4.5H_2O$ formed a suspension thereof in the IL. Presumably, the most hydrated IL is unable to efficiently disrupt the extensive hydrogen bonding that characterises the macromolecular structure of cellulose, similar to water or to common organic solvents.[1,4,7] Note that this suspension became a homogeneous solution under our reaction conditions of 120 °C (see text below and Table 1). Regeneration of the dissolved cellulose from ILs by precipitation with 0.01 M aqueous hydrochloric acid, washing, and drying, revealed the extent to which the polysaccharide transforms in ionic media (ESI† Table S2). There is no significant change of the mass with the cellulose regenerated from $ZnCl_2 \cdot 3.5–4.5H_2O$ (*i.e.* the weight of the loaded and recovered cellulose from the ILs was similar), implying that the substrate is stable to hydrolysis in such media under the applied conditions. In contrast, $ZnCl_2 \cdot 2.5–3.25H_2O$ initiates the conversion of cellulose during the dissolution, as evidenced by some mass losses (ESI† Table S2). Possibly, the systems with lower hydration number possesses higher acidity, and therefore promote conversion of cellulose into water-soluble molecules. Analysis of the neutralised aqueous phases recovered from the zinc salts (as detailed above) identified only trace amounts of water-soluble saccharides (we detect mono-, di-, tri-, and tetrasaccharides) and furan derivatives (HMF, FHK, and FF). This suggests that cellulose likely converts into higher oligosaccharides (*e.g.*, with five or six glucose units) under our conditions, a matter we are currently investigating. The dissolution and regeneration of MCC in/from $ZnCl_2 \cdot 2.5–4.5H_2O$ demonstrate that these media have differing influences on the cellulose, and it can be reasonably anticipated that this will affect the acid-catalysed transformation of polysaccharides at elevated temperatures.

To test this proposal, we dissolved MCC in $ZnCl_2 \cdot 2.5–4.5H_2O$ (80 °C, 2.5 h) and then attempted the hydrolysis-

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§ Cellulose fully dissolves in $ZnCl_2 \cdot 3.0H_2O$ and remains soluble after dilution with water to a net of $n = 9$.[10]

Table 1 Catalytic conversion of cellulose in $ZnCl_2{\cdot}nH_2O$[a]

Solvent-catalyst	Conv (wt%)	Yield glucose (wt%)	Yield fructose (wt%)	Yield cellobiose (wt%)	Yield cellobiulose (wt%)	Yield cellotriose (wt%)	Yield cellotetraose (wt%)	Yield HMF (mol%)	Yield FHK (mol%)	Yield FF (mol%)
$ZnCl_2{\cdot}2.5H_2O$	86	0	0	0	0	0	0	7	10	8
$ZnCl_2{\cdot}2.75H_2O$	95	1	1	0	0	0	0	14	9	7
$ZnCl_2{\cdot}3.0H_2O$	98 (97)[b]	1 (1)[b]	1 (0)[b]	0 (0)[b]	0 (0)[b]	0 (0)[b]	0 (0)[b]	15 (12)[b]	7 (4)[b]	6 (9)[b]
$ZnCl_2{\cdot}3.25H_2O$	99	5	3	1	1	0	0	19	7	5
$ZnCl_2{\cdot}3.5H_2O$	99	7	4	1	1	0	0	20	7	5
$ZnCl_2{\cdot}3.75H_2O$	99	7	4	1	1	0	0	20	6	4
$ZnCl_2{\cdot}4.0H_2O$	99	18	8	3	2	2	1	20	6	3
$ZnCl_2{\cdot}4.25H_2O$	99	19	9	4	2	3	1	21	5	3
$ZnCl_2{\cdot}4.5H_2O$	94 (99)[c]	21 (10)[c]	10 (1)[c]	7 (6)[c]	4 (1)[c]	5 (4)[c]	1 (6)[c]	16 (14)[c]	5 (5)[c]	2 (3)[c]

[a] Conversion is specified in wt% based on cellulose input. Yields are specified in wt% based on cellulose input for carbohydrates and in mol% based on anhydroglucose units present in the substrate for furan derivatives (HMF, FHK, and FF). Reaction conditions: MCC (50 mg), solvent-catalyst (5.000 g), 80 °C, 2.5 h, then 120 °C, 1 h. [b] The processing was performed in the IL prepared from the double sublimed $ZnCl_2$.† [c] Reaction conditions: MCC (50 mg), $ZnCl_2{\cdot}3.0H_2O$ (5.000 g), 80 °C, 2.5 h, addition of water (0.71 mL) to form $ZnCl_2{\cdot}4.5H_2O$, then 120 °C, 1 h.

conversion of cellulose at 120 °C for 1 h. Table 1 shows that less hydrated solvents, in particular $ZnCl_2{\cdot}2.5\text{–}3.0H_2O$, yielded predominantly furan derivatives, namely HMF, FHK, and FF (total yield up to 30 mol% based on anhydroglucose units present in cellulose), and only trace amounts of low molecular weight saccharides. The chemistry using MCC in $ZnCl2{\cdot}3.0H_2O$ was repeated but employing highly purified doubly sublimed zinc chloride. A similar portfolio of products appeared, in which the total yield of furans was slightly lower (Table 1) but the results were otherwise unsurprising.‡ Furan derivatives are considered to form by a cascade of acid-catalysed reactions, involving the hydrolysis of cellulose into glucose, aldose–ketose isomerisation, and dehydration, respectively, as pictorially represented in Scheme 1.[4,5,13,22,25] HMF is an anticipated dehydration product, while FHK and FF are less commonly obtained as major transformation products of carbohydrates.[4,13,22] In our former study, the occurrence of FHK was attributed to the formation of the intermediate ketohexose (isomerisation product derived from fructose); FF was proposed to form from fructose via an intermediate pentose (*e.g.*, arabinose).[13] In the present work, we identified that cellobiose, glucose, and fructose, which putatively appear during the conversion of cellulose (Scheme 1), fully convert into furanoids and humins[24] in $ZnCl_2{\cdot}2.5H_2O$ under the reaction conditions (120 °C, 1 h, total yield of furanoids up to 16 mol%, based on sugar substrate). This result evidences that low molecular weight saccharides are unstable in less hydrated solvents ($ZnCl_2{\cdot}2.5\text{–}3.0H_2O$), which mediate both the transformation of cellulose into furan derivatives and into by-product humins. In contrast, zinc chloride presented as higher hydrates, namely, $ZnCl_2{\cdot}3.25\text{–}4.5H_2O$, demonstrates improved conversion and selectivity towards HMF (the anticipated dehydration product) and low molecular weight carbohydrates (as hydrolysis products, namely, glucose, cellobiose, cellotriose, and cellotetraose, and isomerisation products, namely, fructose and cellobiulose). Usefully, only small amounts of humins were noted. The yields of HMF (yield up to 21 mol%) and low molecular weight saccharides (total yield up to 48 wt% based on cellulose input) improve with increasing hydration number; however, HMF yield decreased with the most highly hydrated solvent ($ZnCl_2{\cdot}4.5H_2O$, Table 1). It is reasonable to posit that the dissolution of cellulose is the rate limiting step before the acid-catalysed transformations, and thus the overall conversion towards HMF is lower in $ZnCl_2{\cdot}4.5H_2O$ (recall that cellulose is less soluble in this IL, as discussed above, but dissolves at the reaction temperature). To assess whether solubility played a significant role, cellulose was dissolved in $ZnCl_2{\cdot}3.0H_2O$ (80 °C, 2.5 h), after which the reaction medium was diluted with water to form $ZnCl_2{\cdot}4.5H_2O$ and processed at 120 °C for 1 h under homogeneous conditions (Table 1).§ While there was some variability in the accumulation of low molecular weight saccharides under these conditions, yields and ratios of the furanoid products were essentially identical to the principal reaction directly employing $ZnCl_2{\cdot}4.5H_2O$. We also identified trace amounts of other oligosaccharides, likely to be the isomerisation products derived from cellotriose and cellotetraose (ESI† Fig. S1). Model reactions with cellobiose as a substrate confirmed the conversion thereof into cellobiulose and glucose in 23% and 4% yield, respectively, in $ZnCl_2{\cdot}4.25H_2O$, when mild reaction conditions are employed (80 °C, 2h). This confirms that isomerisation can take place in zinc chloride hydrates at earlier stages of the catalytic cascade involving reducing oligosaccharides (Scheme 1). The isomerisation of aldo-oligosaccharides into keto-oligosaccharides has been identified in subcritical aqueous ethanol.[26,27]

Evidently, the level of hydration plays a determinative role in the catalyst activity, most likely related to the acidity of the system. pH measurements¶ of $ZnCl_2{\cdot}nH_2O$ (Table 2) reveal the dramatic extent to which the molecular formula influences the acidity of the zinc chloride hydrate solvent system,

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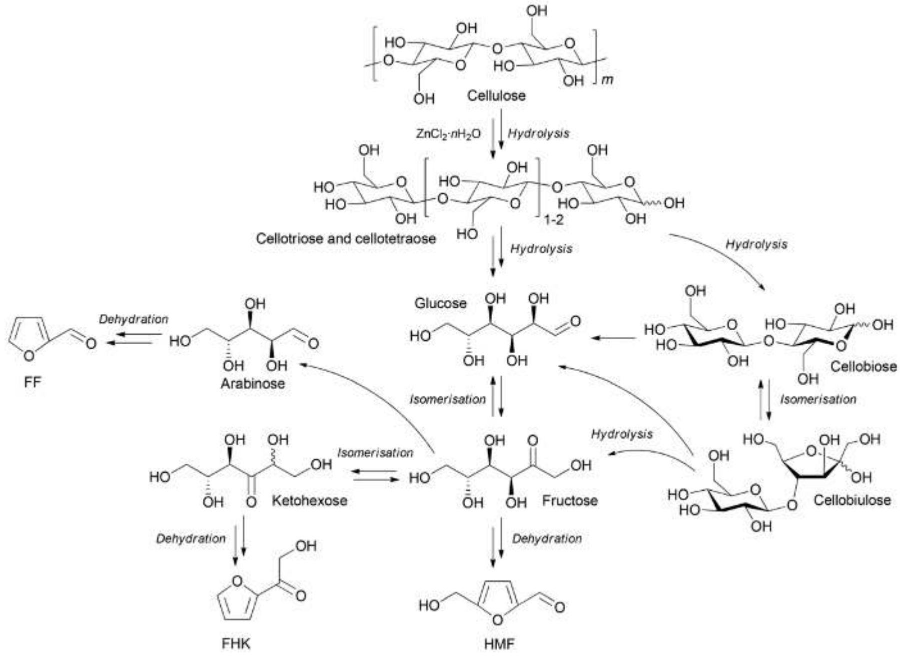
¶ pH measurements in concentrated systems are workable in both concentrated alkaline[49] and acidic media,[50] but subject to error, requiring corrections if accurate data are sought. Our pH measurements provide qualitative uncorrected data, supplemented by quantitative data using the mesityl oxide probe as determined by NMR spectrometry.



Scheme 1 Proposed acid-catalysed cascade of cellulose conversion into small molecules. n = 2.5–4.5. m = integer.

and the very high acidity associated with lower hydration states. Table 2 shows a systematic decrease of acid strength from less hydrated (n = 2.5) media to more highly hydrated (n = 4.5) solvents. $ZnCl_2$ is commonly considered to be a Lewis acid, but clearly the hydrated form becomes a source of Brønsted acidity comparable to concentrated protic acids (*e.g.*, the reported pH of 37 wt% aqueous HCl is −1.1).[28] This phenomenon is caused by Lewis acid assisted Brønsted acidity through binding of the metal centre to water and release of hydrogen cation.[25,29,30] We also probed the binding ability of zinc chloride hydrates with mesityl oxide using ^{13}C NMR spectroscopy to provide a deeper insight into the acidity of inorganic solvents.[20] Acids are known to form complexes with α,β-unsaturated carbonyl compounds, whose binding strength correlates to a difference between the chemical shifts of the α and β carbons ($\Delta\delta$), thereby providing a measure of acidity: the greater the $\Delta\delta$ value, the stronger the binding between the acid and the mesityl oxide and correspondingly the stronger the acid.[20,31,32] The $\Delta\delta$ values for $ZnCl_2\cdot2.5–4.5H_2O$ are equivalent to those of strong Brønsted acids (Table 2),[20,32] and there is a perfect correlation between pH and the $\Delta\delta$ values. The values obtained for $ZnCl_2\cdot3.0H_2O$ prepared from the anhydrous salt and separately from the double sublimed salt showed only marginal differences in $\Delta\delta$ values, implying that any residual impurities from the manufacturing process (*e.g.* HCl) play little or no role in this chemistry.‡ These data help to rationalise the experimental observations in the catalysed reactions of the saccharides.

The changes in acidity are most likely affected by the structure of ILs. It has been established that $ZnCl_2\cdot nH_2O$ comprises a hydrated zinc cation and a tetrachlorozincate anion, as pictorially presented in Scheme 2.[9,10,33] When n = 2–3, the hydrated water is present only in the inner coordination shell of zinc cation. With these entities, hydrogen cation H^+ is directly sourced from the metal aquo complex, accounting for the impressive acid strength (Table 2). With higher hydrates (n = 3.25–4.5), there is water present in excess of the inner coordination sphere, and available to hydrate the H^+ into the less

Table 2 The probe of acidity of neat $ZnCl_2\cdot nH_2O$

Solvent/acid	pH[a]	$\Delta\delta$[b]
$ZnCl_2\cdot2.5H_2O$	−0.5	44.7
$ZnCl_2\cdot2.75H_2O$	−0.4	43.7
$ZnCl_2\cdot3.0H_2O$	−0.2	42.7 (43.0)[c]
$ZnCl_2\cdot3.25H_2O$	0.0	41.9
$ZnCl_2\cdot3.5H_2O$	0.3	41.1
$ZnCl_2\cdot3.75H_2O$	0.5	40.4
$ZnCl_2\cdot4.0H_2O$	0.7	39.7
$ZnCl_2\cdot4.25H_2O$	0.9	39.1
$ZnCl_2\cdot4.5H_2O$	1.1	38.6
HCl (37 wt%)	−1.1 (ref. 27)	—
H_2SO_4 (10 wt%)	—	37.6 (ref. 32)

[a] pH readings were performed in triplicate at room temperature. [b] Difference between the chemical shifts of α and β carbons of mesityl oxide (5 wt% based on IL) in $ZnCl_2\cdot nH_2O$ (0.5 g) with external lock DMSO-d_6 at 25 °C. [c] $\Delta\delta$ of $ZnCl_2\cdot3.0H_2O$ prepared from the double-sublimed anhydrous $ZnCl_2$.‡

a) $[Zn(H_2O)_6]^{2+}\,[ZnCl_4]^{2-} \equiv [Zn(H_2O)_5OH]^{+}\cdots H^{+}\,[ZnCl_4]^{2-}$

b) $[Zn(H_2O)_6]^{2+}\,[ZnCl_4]^{2-}\cdot 3(H_2O) \rightleftharpoons [Zn(H_2O)_5OH]^{+}\,[ZnCl_4]^{2-}\cdot 3(H_2O)\cdots H^{+}$

Scheme 2 Proposed formation of hydrogen cation from zinc chloride hydrate. a) Hydrogen ion generation in the presence of a 'proton' acceptor. b) Sample provision of hydrated hydrogen ion for n = 4.5.

active H_3O^+ cation or even more highly hydrated species.[34,35] This hydration effect is known to suppress the Brønsted acid activity,[35] and is consistent with our experimental results. The higher acidity with lower levels of water present would be consistent with the notion of a less well hydrated hydrogen cation. Nevertheless, discrete species of hydrated H^+ such as $H_{13}O_6^+$ may not exist within these concentrated ionic solvents, unlike in dilute aqueous solutions.[34,35] H^+ is presumably delocalised between the water molecules in the outer coordination sphere, remaining a part of the ionic system.

In the present context, the $ZnCl_2{\cdot}nH_2O$ fulfils two roles. In the first, it acts as ionic liquid solvent for the cellulose. As is evident from the results presented above, some embodiments of $ZnCl_2{\cdot}nH_2O$ are less good than others, as solvents for cellulose (*e.g.* $ZnCl_2{\cdot}4.5H_2O$). The second role is the provision of an acid catalyst to cause the hydrolysis of cellulose into low molecular weight saccharides and their further reaction into furanoid products. While the exact nature of the catalyst remains to be established, we have unambiguously established that the $ZnCl_2{\cdot}nH_2O$ provides acidity in differing degrees.

Now with reference to the synthesis results and the acidity measurements (Tables 1 and 2), there are distinct experimental outcomes associated with the different reaction media. The high acidity of the less hydrated media (*e.g.*, $ZnCl_2{\cdot}2.5H_2O$) leads the conversion of cellulose towards furan-type molecules but also promotes the production of large amounts of humins. In contrast, more highly hydrated ILs (*e.g.*, $ZnCl_2{\cdot}4.0–4.5H_2O$) possess good activity for the hydrolysis-conversion into low molecular weight saccharides (glucose, fructose, cellobiose, cellobiulose, cellotriose, and cellotetraose) and HMF, avoiding the formation of humins.

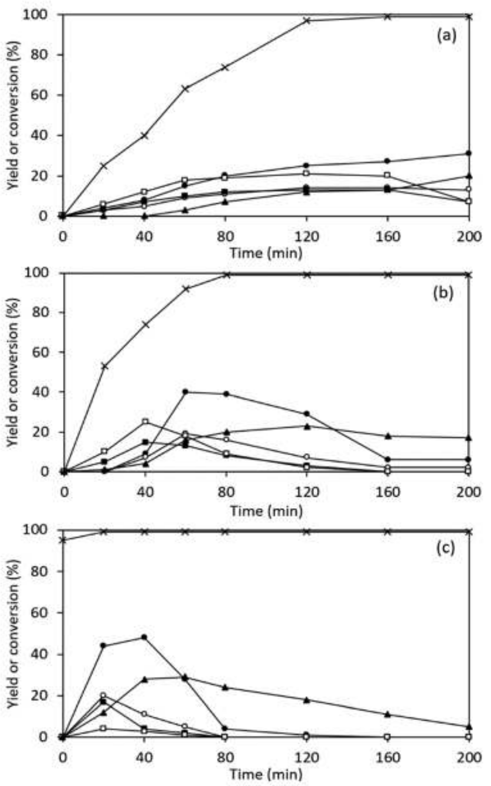


Fig. 1 Catalytic conversion of carbohydrates in $ZnCl_2{\cdot}4.25H_2O$ at various reaction conditions. a), b) and c) T = 100, 110, 120 °C, respectively. Reaction conditions: MCC (50 mg), $ZnCl_2{\cdot}4.25H_2O$ (5.000 g). × = conversion. ● = yield of monosaccharides. ○ = yield of disaccharides. ■ = yield of cellotriose. □ = yield of cellotetraose. ▲ = yield of furanoids.

Of the systems investigated, $ZnCl_2{\cdot}4.25H_2O$ is capable of dissolving cellulose and providing high yields of low molecular weight carbohydrates and HMF (Table 1 and S2†). Accordingly, we conducted the hydrolytic processing of MCC in $ZnCl_2{\cdot}4.25H_2O$ under various reaction parameters. Firstly, the influence of the reaction temperature and time was surveyed. At 100 °C (Fig. 1a), reaction of MCC favours formation of cellotriose and cellotetraose (yields up to 13 wt% and 20 wt%, respectively) up to 160 min, but at 200 min disaccharides (cellobiose and cellobiulose, 9 wt% and 8 wt% yields, respectively), monosaccharides (glucose and fructose, 22 wt% and 9 wt% yield, respectively) and furanoids (HMF, FHK and FF, yields 15, 5 and 1 mol%, respectively) predominate. This suite of products perfectly exemplifies the acid-catalysed cascade of reaction portrayed in Scheme 1, namely hydrolysis of cellulose into low molecular weight glucans, aldose–ketose isomerisation, and dehydration into furan derivatives. It is evident (Fig. 1) that higher reaction temperatures accelerate the catalytic transformations leading to the rapid formation of monosaccharides (glucose and fructose yields up to 33 wt% and 15 wt%, respectively, 120 °C, 40 min) and ultimately dehydration products (HMF, FHK and FF, yields up 21, 5 and 3 mol%, respectively, 120 °C, 60 min) in shorter reaction times (Fig. 1b and c). However, extended reaction at elevated temperatures resulted in the formation of humins, diminishing the yields and selectivity of the target products. From these results, it can be concluded that shorter reaction times are preferred at elevated temperatures to ensure high yields of glucose and HMF (these molecules are commonly desirable products of the cellulose valorisation),[2,4,5] and minimal formation of humins.

Under certain conditions the addition of acids, usually hydrochloric acid, to zinc chloride hydrate improves the yields of saccharides or HMF,[11,12,36] although sulfated titania has been used to good effect in the depolymerisation of cellulose.[37] The added HCl would produce a system akin to Lucas's reagent.[38] To investigate whether this would equally apply to our circumstances, we employed a range of Brønsted acids (hydrochloric, phosphoric, sulfuric or *p*-toluenesulfonic acid) and Lewis acidic metal chlorides ($AlCl_3$, $InCl_3$, $LaCl_3$, $GdCl_3$, $YbCl_3$ or $HfCl_4$) in the hydrolytic processing of MCC in $ZnCl_2·4.25H_2O$ at 120 °C for 1 h. The addition of Brønsted acids substantially improves yields of carbohydrates and provides more complete hydrolysis of cellulose into the monomer glucose (Table 3).

This is consistent with the general view that Brønsted acids promote the hydrolysis of polysaccharides.[4] With Brønsted acids, HMF remains the major furanoid product but the yield of this molecule reduces dramatically for reactions involving H_3PO_4 or, H_2SO_4. A drawback of H_3PO_4 and H_2SO_4 is the formation of insoluble salts in the reaction media, representing a potential hurdle if the recovery of the molten salt is considered. When Lewis acids were added, the reactions afforded lower yields of low molecular weight small saccharides and furan type molecules. The metal chlorides presumably coordinated to the excess of water in the outer coordination shell of zinc chloride hydrate, reducing the effective amount of free water present. This would tend to induce a strongly acidic environment, as shown in Table 1 for the less hydrated zinc chloride hydrate solvents, which is conducive to the formation of humins. Hard Lewis acids ($AlCl_3$, $InCl_3$, and $HfCl_4$), which are more likely to bind strongly to the 'hard' Lewis base O atom of H_2O, or to hydrolyse to [M]–OH + HCl, afforded very low yields of valuable molecules.[39,40] This effect is less prominent with soft Lewis acids ($LaCl_3$, $GdCl_3$, $YbCl_4$), even though the yields of desirable products were lower. Both sets of observations are consistent with the notion of Lewis acid-assisted Brønsted acidity,[29,30,41–43] which these Lewis acids would introduce (in the form of $[MX_3–OH]\cdots H$) in addition to existing effects contributed by the zinc chloride hydrate system. Such Lewis acid-assisted Brønsted acids have been demonstrated to possess very high acidity in some instances.[25,42] Overall, the conversion of cellulose in the presence of HCl is more efficient, compared to the processes with other added catalysts or in the neat inorganic solvent. Therefore, the conversion in $ZnCl_2·4.25H_2O$ with added HCl remains the best process to this stage (Table 3).

We turned our attention to the conversion of other substrates, including starch, hemicellulose, and polysaccharides extracted from the macroalga *Ulva lactuca* in $ZnCl_2·4.25H_2O$ + HCl (Table 4). These polysaccharides are fully soluble in the molten salt hydrate (no added HCl) at lower temperature (80 °C). Once dissolved, the HCl is added and the temperature

Table 4 Catalytic conversion of polysaccharides in zinc chloride hydrate solvent[a]

Entry	Substrate	Conv (wt%)	Yield glucose (wt%)	Yield HMF (mol%)	Yield FF (wt%)
1	MCC	99	50	23	1
2	Starch	99	46	21	2
3	*Ulva lactuca* saccharides	99	55	18	8
4	Hemicellulose	99	—	—	28
5[b]		99	—	—	52
6	Corncob	81	26	23	15
7[c]		85	61	30	22
8	Softwood chips	70	22	18	10
9[c]		74	26	22	11
10	*Ulva lactuca*	85	38	22	10
11[c]		90	52	25	15
12	*P. cruentum*	88	13	33	11
13[c]		94	49	35	29

[a] Conversion is specified in wt% based on substrate input. Yields are specified in wt% for carbohydrates, based on glucan content in the substrate, and in mol% for HMF, based on anhydroglucose units present. Yields are specified in wt% for FF, based on the total carbohydrate content in substrate because both glucans and xylans are convertible into FF. Reaction conditions: polysaccharide (50 mg), solvent-catalyst (5.000 g), 80 °C, 5 h, then addition of HCl (0.03 mmol) 120 °C, 1 h, maintaining the ratio of Zn/H_2O within ±1%. [b] Reaction conditions: hemicellulose (50 mg), solvent-catalyst (5.000 g), 80 °C, 2.5 h, then addition of anisole (40.0 mL), 120 °C, 1 h.[13] [c] Reaction conditions: polysaccharide (50 mg), solvent-catalyst (5.000 g), HCl (0.03 mmol), 80 °C, 5 h, then 120 °C, 1 h.

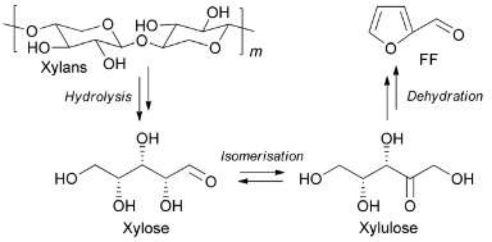
Table 3 Catalytic conversion of cellulose in $ZnCl_2·4.25H_2O$ in the presence of additional Brønsted or Lewis acids[a]

Co-catalyst	Conv (wt%)	Yield glucose (wt%)	Yield fructose (wt%)	Yield cellobiose (wt%)	Yield cellobiulose (wt%)	Yield cellotriose (wt%)	Yield cellotetraose (wt%)	Yield HMF (mol%)	Yield FHK (mol%)	Yield FF (mol%)
None	99	19	9	4	2	3	1	21	5	3
HCl	99	50	2	1	0	1	1	23	0	2
H_3PO_4	99	57	0	0	0	0	0	14	0	2
H_2SO_4	99	58	0	0	0	0	0	7	0	2
TsOH	99	30	2	1	0	1	0	22	1	3
$AlCl_3$	97	3	2	0	0	0	0	12	0	2
$InCl_3$	94	4	0	0	0	0	0	15	3	4
$LaCl_3$	95	7	0	2	1	4	1	15	4	3
$GdCl_3$	94	6	0	0	0	3	0	14	4	3
$YbCl_3$	93	8	0	2	1	5	1	13	5	3
$HfCl_4$	99	1	0	0	0	0	0	2	0	0

[a] Yields are specified in wt% based on input of cellulose for carbohydrates and in mol% based on anhydroglucose units present in the substrate for furan derivatives (HMF, FHK, and FF). Reaction conditions: MCC (50 mg), $ZnCl_2·4.25H_2O$ (5.000 g), 80 °C, 2.5 h, then addition of acid co-catalyst (0.03 mmol), 120 °C, 1 h, maintaining the ratio of Zn/H_2O within ±1%.

raised to 120 °C. The $ZnCl_2 \cdot 4.25H_2O$ + HCl system is capable of converting the various polysaccharides into monomer sugars and furan derivatives. Other products, such as oligosaccharides, fructose, or FHK, were identified in trace amounts only. While the conversion of starch and algal saccharides, consisting of glucans (ESI† Table S1), delivered somewhat similar portfolios of products to that obtained from MCC (Table 4, entries 1–3), the transformation of hemicellulose (Table 4, entry 4) provided mostly the dehydration product FF (28 wt%) and a little xylose (5 wt%). This suggests that xylans, a major component of hemicellulose,[15] are more amenable to conversion into furfural, relative to glucans. The transformation of xylans occurs through hydrolysis into xylose, xylose–xylulose isomerisation and then dehydration into FF, as demonstrated in Scheme 3.[44] Pleasingly, FF can be obtained in impressive yields when performing the catalytic reaction in the biphasic solvent system $ZnCl_2 \cdot 2.5H_2O$/anisole[13] (Table 4, entry 5, FF 52 wt% yield; as shown above in Table 1, this solvent system afforded good selectivity to furfural during the transformation of cellulose). The given outcomes evidence that the functionality of zinc chloride hydrate solvent can be tuned to promote the conversion of target substrate into a defined product.

Finally, we probed the transformation of lignocellulose and algal biomass in zinc chloride solvent. To do this, we conducted the dissolution of biomass in $ZnCl_2 \cdot 4.25H_2O$ under mild conditions (80 °C, 5 h), followed by the catalytic conversion of the substrates at elevated temperature (120 °C, 1 h) with added hydrochloric acid (Table 4). The dissolution of the biomass required extended times compared with the purified saccharides. Even after lengthy processing under mild conditions, softwood and algal biomass remained insoluble. Apparently, the rigid molecular structure of the native biomass resists complete dissolution in zinc chloride hydrate solvent, in contrast to refined saccharides.[45] This solubility issue likely affected the processing at elevated temperature affording low yields of glucose from the given substrates (Table 4, entries 5, 7, 9, 11). A method to overcome this hurdle is to add hydrochloric acid from the start, at low temperature. This approach substantially improved the conversion of corncob and algal substrates into glucose (yields up to 61 wt%, based on the glucan content in the biomass), HMF (up to 35 mol% yield, based on glucan content in the biomass) and FF (up to 29 wt% yield, based on total carbohydrate in the biomass). The processing of wood chips was less efficient, compared to other cellulosic materials, likely due to the more recalcitrant molecular structure and concomitant difficulties during depolymerisation (Table 4, entries 7, 8). Wood biomass remains one of the most challenging substrates for chemical processing.[4,45] Nonetheless, it is worth mentioning that processing of lignocellulose in zinc chloride hydrate enabled the recovery of lignin (so-called acid insoluble lignin) as an unreacted portion of substrate (ESI† Fig. S2 and Table S3). This macromolecule is known to be somewhat stable in zinc chloride solvent,[46,47] and is another raw material holding promise to deliver a range of useful bio-based chemicals.[2,48] This set of reactions presents an efficient transformation of native cellulosic materials directly into glucose, HMF and FF, together with the simultaneous extraction of lignin.



Scheme 3 Proposed acid-catalysed transformation of xylans into furfural in zinc chloride hydrate. *m* = integer.

Conclusions

The present work provides an improved understanding of $ZnCl_2 \cdot nH_2O$ (n = 2.5–4.5) as reaction media for the catalytic transformation of cellulosic substrates into value added products. The molecular formula for the IL solvent is critical to determining the acidity of the mixture, which has a defining role on the outcomes of the transformations. It shows that the amount of water present in inorganic molten salt and the processing conditions significantly influence the course of catalytic reactions enabling selectivity towards furyl hydroxymethyl ketone and furfural, or 5-(hydroxymethyl)furfural and low molecular weight reducing saccharides. The optimised methods enable the direct processing of lignocellulose and algal biomass into significantly value added chemicals under mild processing conditions and in high yields. This work improves our fundamental knowledge of the $ZnCl_2 \cdot nH_2O$ system but there remain some fundamental questions to be answered before firm conclusions about the causality within the system can be fully ascribed. There also remain technical problems to be solved. One in particular is the efficient recovery of ionic liquids and products, which represents a challenge to be solved before practical application of the methods. If this challenge can be overcome, then substantial industrial progress will potentially have been made.

Conflicts of interest

There are no conflicts to declare.

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Iurii Bodachivskyi (graduate research student) developed the methodology, conducted research, including experimental work, data collection and data analysis, and drafted the manuscript. Prof. D. Bradley G. Williams (principal supervisor) and Dr Unnikrishnan Kuzhiumparambil (co-supervisor) supervised Iurii Bodachivskyi's research activities, provided conceptual advice and revised the manuscript.

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The role of the molecular formula of $ZnCl_2 \cdot nH_2O$ on its catalyst activity: a systematic study of zinc chloride hydrates in the catalytic valorisation of cellulosic biomass†

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3.3. Towards furfural from the reaction of cellulosic biomass in zinc chloride hydrate solvents

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Towards furfural from the reaction of cellulosic biomass in zinc chloride hydrate solvents

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ABSTRACT

Cellulosic biomass is abundant and is readily accessible for the renewable production of industrially useful chemicals. In the present study, we develop a method for the selective synthesis of furfural directly from native lignocellulose and algal biomass employing acidic zinc chloride hydrate solvents. To do this, we first optimise the conversion of xylans (hemicellulose) and separately of cellulose, to find an optimum compromise between the reaction conditions. The acidic inorganic media, along with the solvent-extractant anisole, enable simultaneous transformation of xylans and glucans into significantly value added furfural under mild processing conditions. This unique process affords substantial progress towards the valorisation of native carbohydrates into furfural, compared to existing methods based on the reactions of simple pentoses or pentosans. It enables the direct processing or raw, unrefined bulk biomass.

1. Introduction

The production of biobased organic building block chemicals (platform molecules) from non-edible cellulosic biomass is a key step towards sustainable chemical industrial development (Bodachivskyi et al., 2018; Dusselier et al., 2014). Among various platform molecules, furfural (FF) is a pivot from which to generate a range of renewable bulk and fine chemicals (Hoydonckx et al., 2007; Mariscal et al., 2016; Peleteiro et al., 2016). For example, FF can be turned into liquid hydrocarbon fuel, into derivative monomers for plastics, or into food additives and pharmaceuticals (Hoydonckx et al., 2007; Mariscal et al., 2016; Peleteiro et al., 2016). FF is commercially obtained by the hydrolysis-conversion of pentosans, found in the hemicellulosic portion of lignocellulose, under the action of acidic catalysts in reactions in aqueous media (Hoydonckx et al., 2007; Peleteiro et al., 2016). Most technologies afford modest yields of furanoids (45–55%, based on pentosan content in biomass) and employ somewhat forcing reaction conditions (commercial units often operate at 150–220 °C), which are accompanied by the formation of undesirable by-products (Hoydonckx et al., 2007; Peleteiro et al., 2016). Additional complexities arise because the isolation of FF involves energy demanding distillation of the aqueous media, or steam stripping, leading to unavoidable losses of the product (Agirrezabal-Telleria et al., 2013; Hoydonckx et al., 2007; Peleteiro et al., 2016). To circumvent these difficulties, current methods often employ alternative (to water) reaction systems, such as ionic liquids (ILs) (Bodachivskyi et al., 2018; Peleteiro et al., 2016). ILs bring substantial improvements to the outcomes of FF, relative to reactions in water. A typical restriction of most current practices is that they are effectively applied only for the conversions of purified saccharides (e.g., xylose or xylans), and for processes under microwave irradiation (Bodachivskyi et al., 2018; Peleteiro et al., 2016; Zhang et al., 2013a). The need to refine biomass, along with cost implications associated with the use of ILs in conjunction with microwave reactors at large scale, requires the development of new robust methods that are capable of providing high yields of desirable furanoid products *directly* from native substances and under mild reaction conditions.

Zinc chloride hydrate solvents with molecular formula $ZnCl_2{\cdot}nH_2O$ (this system is a true IL with the molecular formula $[Zn(OH_2)_6][ZnCl_4]$ in the case of $n = 3$ (Sen et al., 2016)) have been employed as inexpensive and recyclable solvent-catalyst media for the valorisation of cellulose (Bodachivskyi et al., 2019a, 2019b, 2018; Sen et al., 2016; Yang et al., 2011; Zhang et al., 2016). Such ILs possess intrinsic Lewis acidity along with Lewis acid-assisted Brønsted acidity; these permit direct reactions in the neat solvent under mild processing parameters (Bodachivskyi et al., 2019a, 2019b). These ILs are thermally stable up to and including 150 °C (and are likely stable at higher temperatures too, Zhang et al., 2016). As a matter of interest, in some instances, inorganic solvents enable the unusual reaction of glucans into FF and

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furyl hydroxymethyl ketone (FHK) as principal products (glucose polymers normally convert into 5-(hydroxymethyl)furfural, HMF) (Bodachivskyi et al., 2019a, 2019b; Yang et al., 2011). There exists the potential to enable the simultaneous conversion of native pentosans and other cellulosic polysaccharides in favour of FF by performing the processing in zinc chloride hydrate systems. This paper explores this potential, by optimising conversion of xylan polymers and separately of glucan polymers, and culminates in the use of crude, raw, bulk biomass.

2. Experimental

Cellulosic biomass (63, 53, 86, 75, 75, 250 or 217 mg, corresponding to 50 mg of polysaccharides) of corn husk-derived xylans, microcrystalline cellulose (MCC), corn husk, corncob, wood chips, *Chlorella vulgaris*, or *Porphyridium cruentum*, respectively, and $ZnCl_2{\cdot}nH_2O$ (5.0 g) were introduced to a round bottom flask equipped with a condenser, thermometer, and magnetic follower and the mixture was heated and agitated at 80 °C for 2.5 h (step 1). After step 1, the reaction system was heated and stirred at 120 °C for 1 h (step 2). In some instances, preheated organic solvent-extractant (120 °C, 40.0 mL) was added to the reactor when performing the second step in the biphasic solvent systems. After completion of the process, the reaction media were cooled and the IL was diluted with deionised water (5.0 mL). A small amount of the diluted IL (0.25 mL) was neutralised with aqueous sodium bicarbonate (0.75 mL, 1 M), centrifuged (20,000 × g for 10 min) to remove water insoluble zinc salts, and decanted. The recovered solution was diluted with a known volume of deionised water and analysed to provide the results detailed in the main text. Recovery of the organic solvent phase for chromatography-analysis included centrifugation and decantation of the organic solvent (20,000 × g for 10 min). Details of the materials and analytical methods are provided in the Supporting Information.

3. Results and discussion

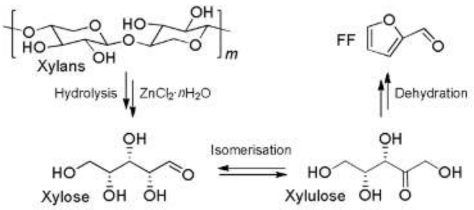
We initially probed the two-step one-pot processing of xylans isolated from corn husk, in $ZnCl_2{\cdot}nH_2O$ ($n = 2.5–4.5$) solvents by conducting the dissolution of the substrate at moderate temperature (80 °C, 2.5 h), and then the hydrolytic conversion at elevated temperature under homogeneous conditions (120 °C, 1 h). This approach facilitates dissolution with some conversion into low molecular weight components, followed by optimum solution phase catalytic transformation into target derivative products, to enhance yields and selectivity to product. Table 1 demonstrates that the dissolution process yielded a mixture of xylans, xylose, xylulose and FF after the first step, which convert predominantly into the furanoid product at elevated temperature during the second step. Chromatographic analysis of the product mixture after step 2 showed only trace amounts of saccharides to be present, indicating very high conversions of the saccharide content into other products. The small specific suite of products, i.e. xylose, xylulose and FF, suggests that conversion of xylans in ILs occurs through an acid-catalysed cascade of reactions involving sequential hydrolysis of the xylan into monomer xylose, followed by xylose-xylulose isomerisation, and dehydration of xylulose into FF (Scheme 1), as has been discussed in the literature (Bodachivskyi et al., 2019b; Yang et al., 2012).

Evidently, the various reactions proceed at appreciably different rates during step 1 for the various inorganic systems, likely related to the acidity of $ZnCl_2{\cdot}2.5–4.5H_2O$ solvents. This intrinsic acidity is known to be reduced in response to the growing hydration number (Bodachivskyi et al., 2019b). The least hydrated solvent, $ZnCl_2{\cdot}2.5H_2O$ (the most acidic (Bodachivskyi et al., 2019b)), was the most active solvent-catalyst medium at moderate temperature (step 1, 80 °C, total monosaccharide yield 23 wt% based on xylans input, FF yield 26 mol% based on anhydroxylose units present in the xylans, Table 1), in the step intended simply to dissolve the xylans. This points to the high reactivity of the xylans under these reaction conditions.

Table 1
Two-step acid-catalysed reaction of xylans in $ZnCl_2{\cdot}nH_2O$[a].

Solvent-catalyst	Solvent-extractant	Step 1 Yield xylose (wt%)	Step 1 Yield xylulose (wt%)	Step 1 Yield FF (mol %)	Step 2 Yield FF (mol %)
$ZnCl_2{\cdot}2.5H_2O$	none	14	9	26	47
	anisole	—	—	—	65[b]
$ZnCl_2{\cdot}3.0H_2O$	none	15	5	18	48
	anisole	—	—	—	68[b]
	m-xylene	—	—	—	65[b]
	tert-butylbenzene	—	—	—	51[b]
	4-methylanisole	—	—	—	52[b]
	1,2-dimethoxybenzene	—	—	—	14[b]
$ZnCl_2{\cdot}3.5H_2O$	none	13	3	8	47
	anisole	—	—	—	71[b]
$ZnCl_2{\cdot}4.0H_2O$	none	11	2	5	46
	anisole	—	—	—	71[b]
$ZnCl_2{\cdot}4.5H_2O$	none	8	1	4	45
	anisole	—	—	—	71[b]

[a] Yields are specified in wt% based on xylans input for carbohydrates and in mol% based on anhydroxylose units present in the substrate for FF. Reaction conditions: xylans (50 mg), solvent-catalyst (5.0 g), 80 °C, 2.5 h (step 1), then 120 °C, 1 h (step 2). [b] Reaction conditions: xylans (50 mg), solvent-catalyst (5.0 g), 80 °C, 2.5 h (step 1), then addition of the solvent-extractant (40.0 mL), 120 °C, 1 h (step 2).



Scheme 1. Acid-catalysed reaction of xylans in zinc chloride hydrate solvents. m = integer. n = hydration number.

At elevated temperature (120 °C, step 2), the changes in acidity were less determinative, and the FF yield hovered around 45–48 mol% for all inorganic solvents (Table 1). This also points to the high propensity of the xylans and derivative monosaccharides to succumb to hydrolysis-conversion reactions. The reactions at higher temperature were accompanied by the formation of dark brown colour solid by-product humins (a condensation product of saccharides and furans) (Bodachivskyi et al., 2019c). The presence of humins signifies side reactions involving the furan derivative in the acidic medium-catalyst. To avoid these side reactions, and to improve the outcomes towards FF, we performed the continuous extraction of the unstable furanoid into the organic solvent phase by the addition of anisole from the start of the step 2. The organic solvent formed a second phase which separated FF from the acidic inorganic acid-solvent (Bodachivskyi et al., 2019a), effectively separating the furanoid products from the acidic medium and the saccharide content therein. This approach very significantly improved the FF yield to 71 mol%, and is especially highlighted by the combination of $ZnCl_2{\cdot}3.5–4.5H_2O$ and anisole. Less hydrated $ZnCl_2{\cdot}2.5–3.0H_2O$ solvents afforded slightly lower yields after step 2 (Table 1). These yields are comparable to those obtained in imidazolium-based ILs under microwave irradiation (70–85 mol%) (Peleteiro et al., 2016; Zhang et al., 2013a). Other organic solvent-extractants, namely *m*-xylene, *tert*-butylbenzene, 4-methylanisole, and 1,2-dimethoxybenzene led to lower yields of FF (65, 51, 52, and 14 mol%, respectively) after step 2 when using $ZnCl_2{\cdot}3.0H_2O$ (Table 1). This is likely related to a combination of the miscibility between these solvents and the zinc chloride hydrate, lower partition coefficients of the reactive product in the organic solvent phase, as disclosed in our recent work (Bodachivskyi et al., 2019a), and, possibly, the ability of 1,2-dimethoxybenzene to chelate to the zinc cation.

The cellulosic portion of native biomass usually comprises of both hemicellulose (mostly pentosans) and cellulose (β-linearly linked glucan) (Bodachivskyi et al., 2018; Dusselier et al., 2014). It was our intention to devise a chemical method that provides an optimum outcome for the reactions of both types of substrates, with the view to ultimately apply the optimised method to whole, raw cellulosic materials. However, given the structural differences between these two saccharide polymers, their individual reactivity can be reasonably expected to vary in the solvent-catalyst. Indeed, we found that cellulose is largely resistant to conversion to any products during the dissolution process in the inorganic solvent at 80 °C (2.5 h, $ZnCl_2{\cdot}2.5–4.5H_2O$). Only trace amounts were detected of low molecular weight saccharides and furanoids as degradation products of the cellulosic material (Bodachivskyi et al., 2019b). This is in contrast to the appreciable yields of such substances obtained during the dissolution of xylans (Table 1), as discovered in the present study, especially in the more acidic (lower hydration number) zinc chloride hydrates. After dissolution of the cellulose, its reactive conversion was conducted at elevated temperature (120 °C, 1 h) in the presence of anisole. Our previous work shows that the biphasic system $ZnCl_2{\cdot}3H_2O$/anisole favours reactions of glucans towards furanoids (Bodachivskyi et al., 2019a). We now wished to learn whether the changes of the hydration number of the inorganic media influence their yields and selectivity. FF was most efficiently produced in less hydrated $ZnCl_2{\cdot}2.5–3.5H_2O$ (more acidic) solvents (yield 10 mol%, based on anhydroglucose units present in cellulose, Fig. 1), along with FHK (yield up to 18 mol%, Fig. 1), another valuable furan derivative. HMF appeared in very small amounts (yield 1 mol%, Fig. 1) and only in the most highly hydrated $ZnCl_2{\cdot}4.5H_2O$ solvent. As we previously noted for single phase processes (Bodachivskyi et al., 2019b), the unusual reaction of glucans towards FF and FHK, in preference to HMF, is more favourable in zinc chloride systems with low hydration number (n = 2.5–3.0), owing to the higher acidity of such media. Similarly, the production of FF and FHK from MCC is more prevalent in $ZnCl_2{\cdot}2.5–3.0H_2O$/anisole in the present study. In contrast to cellulose, reactions of xylans in less hydrated solvents led to diminished yields of FF (Table 1). The preferential reaction conditions are therefore mutually exclusive for the two different classes of polysaccharides. Of the solvents investigated, $ZnCl_2{\cdot}3.0H_2O$/anisole would appear to provide optimum yields of desirable products from *both* types of polysaccharide, i.e., from xylans and glucans. Therefore, this system was employed in subsequent processes, with raw, bulk cellulosic substrates (Table 2).

Finally, we applied the optimised reaction system to the conversion of native terrestrial (corn husk, corncob and softwood chips) and marine (microalgae *Chlorella vulgaris* and *Porphyridium cruentum*) biomass employing two-step processing in $ZnCl_2{\cdot}3.0H_2O$. Table 2 highlights that the dissolution processes at low temperature caused an appreciable measure of depolymerisation-conversion of native biomass into low molecular weight derivative hexoses (glucose and fructose, total yield up to 29 wt%, based on glucan content, Table 2), pentoses (xylose and xylulose, total yield up to 40 wt%, based on xylan content, Table 2) and FF (FF yield up to 5 wt%, based on total carbohydrate content); FHK was identified in only low trace amounts after step 1. This is consistent with the highly branched and heterogeneous nature of the cellulosic portion of these substrates (Brandt et al., 2013;Höfer and Höfer, 2015). Only softwood chips resisted hydrolytic conversion at low temperature, likely due to the rigid molecular structure of the timber substrate, in comparison with the other sources (Brandt et al., 2013). The second step at elevated temperature and in the presence of anisole enabled the selective production of FF and FHK from the reaction of all substrates including the softwood (FF yield up to 42 wt%, based on total carbohydrate content, FHK yield up to 13 mol% based on glucan content, Table 2) with no accumulation of sugars. It is notable with our special solvent systems that both glucans and xylans were convertible into FF, delivering higher yields of the desirable furanoid product than other common processes based on the reaction of pentosan-rich substrates (i.e. most processes enable the production of FF from pentosans such as xylans, but not from hexosans such as glucans). For comparison, reactions of native corn stalk, corncob, pine wood, or grass, in 1-butyl-3-methylimidazolium chloride in the presence of acidic catalyst under microwave irradiation provide FF yields in the range 4–31 mol%, based on pentosan content in the substrate (Zhang et al., 2013b; Zhang and Zhao, 2010). These values would be greatly reduced if based on the total carbohydrate content, as we do in the present work. In addition and besides FF, our process in $ZnCl_2{\cdot}3.0H_2O$/anisole yielded FHK (up to 13 mol%, Table 2). This molecule is usually only produced during the conversion of refined cellulose (e.g., MCC or cotton fibre), not raw biomass, in slightly higher yields (12–24 mol%) than realised in the present study (Bodachivskyi et al., 2019a; Yang et al., 2011).

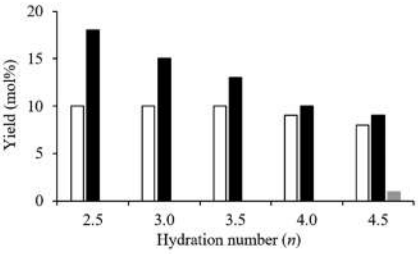


Fig. 1. Production of FF from microcrystalline cellulose in the biphasic system $ZnCl_2{\cdot}2.5–4.5H_2O$/anisole. Reaction conditions: microcrystalline cellulose (50 mg), zinc chloride hydrate (5.0 g), 80 °C, 2.5 h (step 1), then addition of anisole (40.0 mL), 120 °C, 1 h (step 2). Yields are specified in mol% based on ahydroglucose unit. □ = yield of FF. ■ = yield of FHK. ▨ = yield of HMF.

Table 2
Acid-catalysed valorisation of cellulosic biomass in the biphasic system $ZnCl_2{\cdot}3.0H_2O$/anisole[a].

Biomass	Step 1 Yield hexoses (wt%)	Step 1 Yield pentoses (wt%)	Step 1 Yield FF (wt%)	Step 2 Yield FF (wt%)	Step 2 Yield FHK (mol%)
Corn husk	25	40	5	26	12
Corncob	29	38	5	23	10
Softwood	0	0	1	16	13
C. vulgaris	28	3	2	20	3
P. cruentum	14	6	4	42	4

[a] Yields are specified in wt% based on total glucan or xylan content in biomass for hexoses (glucose and fructose), or pentoses (xylose and xylulose), respectively. Yields are specified in wt% for FF, based on the total carbohydrate content in substrate because both xylans and glucans are convertible into FF. Yields are specified in mol% for FHK based on the glucan content. Reaction conditions: polysaccharides (50 mg), $ZnCl_2{\cdot}3.0H_2O$ (5.0 g), 80 °C, 2.5 h (step 1), then addition of anisole (40.0 mL), 120 °C, 1 h (step 2).

4. Conclusions

In this study we demonstrate the functionality and potential of zinc chloride solvents for the direct catalytic valorisation of cellulosic biomass into FF. The unique activity of the inorganic solvent-catalyst medium offers simultaneous conversion of both xylans and glucans into the targeted furanoid product. This level of selectivity stands out from many common methods that are usually based on the reaction of pentosan-rich substrates. Although this study realises some advancement towards higher yields and selectivities of FF, the technology itself requires further improvement. The yields of furans varied for various substrates, leaving a need to optimise reaction conditions for the targeted biomass. In particular, optimisation of the recovery of reactive furanoid products is a high priority, and we are currently investigating efficient methods for recovery of the products and solvents.

CRediT authorship contribution statement

Iurii Bodachivskyi: Conceptualization, Data curation, Formal analysis, Investigation, Writing - original draft. **Unnikrishnan Kuzhiumparambil:** Formal analysis, Methodology, Resources, Funding acquisition. **D. Bradley G. Williams:** Conceptualization, Funding acquisition, Project administration, Supervision, Writing - original draft.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.indcrop.2020.112179.

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Declaration, author contributions and copyright information

This section is a peer-reviewed published article (DOI: 10.1016/j.indcrop.2020.112179). Iurii Bodachivskyi (graduate research student) developed the methodology, conducted research, including experimental work, data collection and data analysis, and drafted the manuscript. Prof. D. Bradley G. Williams (principal supervisor) and Dr Unnikrishnan Kuzhiumparambil (co-supervisor) supervised Iurii Bodachivskyi's research activities, provided conceptual advice and revised the manuscript.

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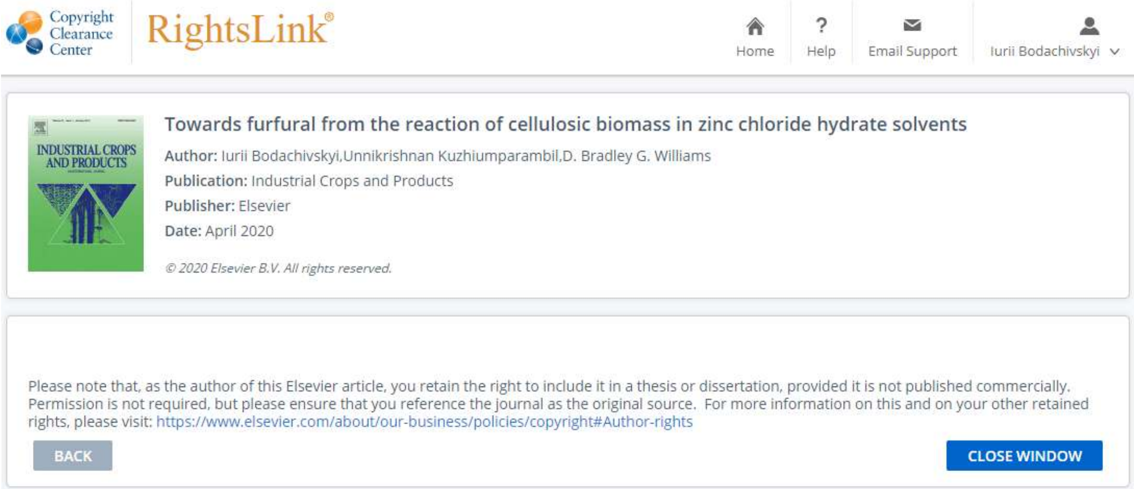

Towards furfural from the reaction of cellulosic biomass in zinc chloride hydrate solvents

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3.4. High yielding acid-catalysed hydrolysis of cellulosic polysaccharides and native biomass into low molecular weight sugars in mixed ionic liquid systems

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High Yielding Acid-Catalysed Hydrolysis of Cellulosic Polysaccharides and Native Biomass into Low Molecular Weight Sugars in Mixed Ionic Liquid Systems

Iurii Bodachivskyi,[a] Unnikrishnan Kuzhiumparambil,[b] and D. Bradley G. Williams*[a]

Ionic media comprising 1-butyl-3-methylimidazolium chloride and the acidic deep eutectic solvent choline chloride/oxalic acid as co-solvent-catalyst, very efficiently convert various cellulosic substrates, including native cellulosic biomass, into water-soluble carbohydrates. The optimum reaction systems yield a narrow range of low molecular weight carbohydrates directly from cellulose, lignocellulose, or algal saccharides, in high yields and selectivities up to 98%. Cellulose possesses significant potential as a renewable platform from which to generate large volumes of green replacements to many petrochemical products. Within this goal, the production of low molecular weight saccharides from cellulosic substances is the key to success. Native cellulose and lignocellulosic feedstocks are less accessible for such transformations and depolymerisation of polysaccharides remains a primary challenge to be overcome. In this study, we identify the catalytic activity associated with selected deep eutectic solvents that favours the hydrolysis of polysaccharides and develop reaction conditions to improve the outcomes of desirable low molecular weight sugars. We successfully apply the chemistry to raw bulk, non-pretreated cellulosic substances.

1. Introduction

Biomass is the principal renewable resource for sustainable industrial production of high-volume and high-value chemicals.[1,2] Within natural sources, cellulose is the most abundant substrate with the scale to reduce reliance on fossil fuel-derived bulk chemicals.[3] There is an intense effort to efficiently transform polysaccharides into small organic building block molecules (platform chemicals) generating a source of renewable replacements to crude oil-based products.[3–5] In the presence of an acid catalyst, cellulose hydrolyses into low molecular weight glucans and monomer glucose, which are convertible into a range of value added molecules with high potential for manufacturing applications (Scheme 1). Platform chemicals are readily accessible on industrial scale but the present production is mostly based on refined edible sugars (such as glucose, fructose, sucrose, or starch). This reliance undermines the sustainability of the biorefinery and becomes a source of controversy and public concern.[3–5] Cellulose-derived low molecular weight sugars can potentially provide an inexhaustible source of substrates for useful chemicals (Scheme 1). Cellulose is composed of monomer units suitable for conversion into platform chemicals but cellulose has an intractable structure which renders challenging the direct transformation thereof into platform chemicals. The synthesis of platform chemicals directly from cellulose thus remains mostly industrially unviable.[3,6,7] The ongoing major challenge relates to the efficient depolymerisation of cellulose and its concomitant hydrolysis into low molecular weight water-soluble saccharides under green processing conditions.

An excellent example of the direct transformation of biomass into platform chemicals is the Biofine Process.[8] High temperature reaction of cellulosic biomass with dilute mineral acids yields levulinic acid, formic acid, furfural and biochar. Stage 1 processing of a high cellulose-content substrate at 210 °C affords low molecular weight saccharides and 5-(hydroxymethyl)furfural (HMF), while Stage 2 reaction at below 200 °C converts the sugars into levulinic and formic acids as major products.[8] Importantly, the procedure requires the pre-processing of the lignocellulosic raw material to remove hemicellulose and generate the high cellulose-content feed for the reactors. Equally importantly, the two-stage process requires the hydrolytic formation of low molecular weight sugars from cellulose, which are converted into the desired platform products. The hydrolysis of cellulose is therefore a critical step in the chemical transformation of this substance.[2,3,8]

Ionic liquids (ILs) are efficient solvents for reactions of cellulosic materials.[9a] These ionic media can fully dissolve polysaccharides, and thereby can promote chemical transformations into highly desirable products under mild reaction conditions; in contrast, common aqueous media cannot dissolve cellulose and require forcing processing conditions to

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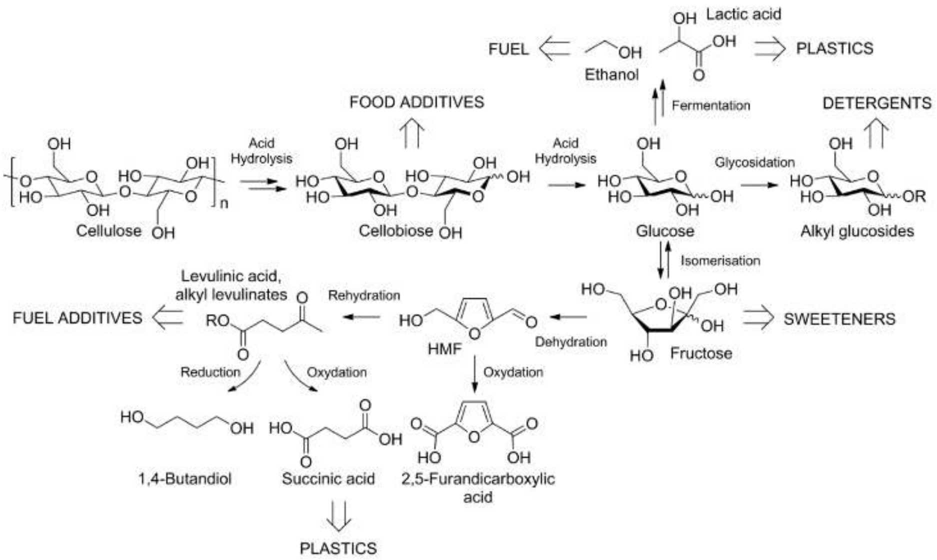


Scheme 1. Catalytic conversion of cellulose into value added molecules. n = integer, R = H, or alkyl.

promote catalytic reactions.[3,9b,c] In particular, mineral acids (e.g., hydrochloric, sulfuric or phosphoric acids) or solid acid catalysts (e.g., acidic resins or carbonaceous acids) in imidazolium-based ILs have been heavily explored in the hydrolysis of microcrystalline cellulose (MCC) to low molecular weight reducing sugars and sometimes for its conversion directly into platform chemicals such as HMF.[10–12] In some instances the imidazolium quaternary salts possess acidic functional groups, which avoids the need to add catalysts.[13] Importantly, ionic solvents and saccharides can be fully recovered after catalytic processing by potentially scalable methods.[14a]

The low molecular weight sugars so produced are amenable to fermentation into alcohols.[14] Much of the work presented in the current literature relating to the hydrolysis of cellulose employs pretreated cellulose such as MCC, obtained by the treatment of cellulose with mineral acids, or ball-milled cellulose.[9b,c,10,11,13,15,16] Some works present the use of unfractionated biomass. However, many chemical treatments detailed in the literature have not been demonstrated on native- or raw biomass, or even the type of cellulose that is available via the large volume cellulose refining technologies applied in the paper and pulp industry.[3,14]

While common imdazolium-based systems present some advantages in the processing of cellulose, deep eutectic solvents (DESs) are somewhat overlooked in this arena. DESs are alternative media (to common ILs) usually formed from eutectic mixtures of Lewis or Brønsted acids and bases under solvent-free conditions.[3] These solvents can be produced from inexpensive plant-based substances and many DESs are considered to be environmentally benign reaction systems for the processing of carbohydrates.[17,18] Especially, the combinations of choline chloride (ChCl) with organic acids prove to be useful green media for chemical conversions of some poly- and oligosaccharides.[18] The intrinsic acidity of such DESs facilitates the transformation of inulin and hemicellulose into monomer sugars and ultimately into furan-type molecules in a single solvent system.[19,20] Despite the promising characteristics of DES systems, cellulose largely resists dissolution in DES. The optimum conditions deliver solutions containing a maximum of 6.5 wt% cellulose. In this instance, a specific cotton linter pulp with a low degree of polymerisation is used and the observations are not generalised (this material is known as a dissolving pulp, which is soluble in aqueous solutions of mineral bases).[18,21,22] If native cellulose can be dissolved and selectively chemically transformed in the presence of DESs then substantial progress would have been made in the processing of biomass into useful products, offering an area with significant scope for exploration.

The present work uncovers and demonstrates the functionality of DESs as reactive (catalyst) co-solvents in imidazolium-based solvents for the conversion of cellulose and native biomass into low molecular weight carbohydrates under green processing conditions. It researches the chemistry associated with catalytic reactions of polysaccharides, and develops novel acidic systems for their effective employment in biorefinery settings. Most importantly, we successfully apply the optimised conditions to the hydrolysis of raw bulk cellulosic substrates of terrestrial and marine origin, including an example of an agricultural waste product. Many current state-of-the-art systems employ vigorous pretreatment methods such as extensive ball milling.[9b,c] Such energy intensive techniques are more suited to scientific studies than to large scale industrial manufacture. In contrast to most related studies which typically report for glucose, we track the formation of $(glucose)_n$

saccharides for n=1–4 by LC-MS, thereby improving our understanding of the course of the hydrolysis chemistry.

2. Results and Discussion

To explore the course of the hydrolytic reaction of cellulose in various ILs, we investigated the conversion of MCC and of typical low-molecular-weight sugars that commonly appear during the hydrolysis of cellulose (i.e., cellobiose, glucose, fructose; Scheme 1). Reactions were conducted in 1-butyl-3-methylimidazolium chloride ([C_4mim]Cl) or in DESs based on ChCl and oxalic or citric acids, or on ChCl and TsOH, at 120 °C for 2 h (Table 1 and in Table S1). Neither the imidazolium IL nor the DES systems were suited to the task, for different reasons. While MCC is freely soluble in [C_4mim]Cl, it does not hydrolyse notably in this solvent under our conditions, and the masses of the input and recovered cellulose were practically identical (Table 1, entry 1). Within the low molecular weight saccharides, cellobiose was hydrolysed into glucose in [C_4mim]Cl in only low yield (8 wt%), while glucose or fructose provided a little HMF (up to 6 mol%), but were otherwise unchanged (Table S1). The imidazolium-based solvent clearly possesses some Brønsted acidity which catalyses certain reactions to a limited extent (e.g., hydrolysis of glycosidic bonds, dehydration into HMF), but this solvent-derived acidity is insufficient to catalyse the transformation of cellulose into products.[3] On the other hand, DES systems based on ChCl/oxalic acid or ChCl/TsOH promoted more comprehensive transformation of MCC under the selected reaction conditions (conversion up to 46%, Table 1, entries 2 and 4) but mostly into undesirable high molecular weight humins (even though MCC remained as a suspension in the DES). Humins are thought to form by the condensation of intermediate sugars and aldehydes.[23,24] Similarly, low molecular weight carbohydrates in ChCl/oxalic acid DES were almost completely transformed (total conversion to product of 96, 97, and 99% for cellobiose, glucose, and fructose, respectively, Table S1) into a bulk of undesirable humins and small amounts of HMF (yields up to 11 mol%). The results clearly suggest that neither imidazolium-based solvent nor the acidic DESs are suitable reaction media under our conditions, due to a) the low acidity of [C_4mim]Cl which fails to promote the catalytic conversion of cellulose and b) the high acidity of DESs inducing the formation of by-products. These drawbacks are likely to be mutually exclusive and a combined solvent system based on [C_4mim]Cl and acidic DESs should favour the more selective transformation of cellulose into desirable low molecular weight sugars.

To test this hypothesis, the transformation of MCC was conducted in mixed [C_4mim]Cl/DES systems, in which the intention was to employ the acidic DES to catalyse the hydrolysis (Table 1, entries 5–7, 9–14). A combination of [C_4mim]Cl and ChCl/oxalic acid 10:1 w/w showed high selectivity towards low molecular weight carbohydrates (total selectivity is 81% for the products glucose, cellobiose, cellotriose, and cellotetraose) after reaction of MCC at 120 °C for 2 h (Table 1, entry 5). This mixed solvent readily dissolves cellulose and, based on observation, has lower viscosity than neat

Table 1. Acid-catalysed conversion of cellulose in single and combined ILs.[a]

Entry	IL	Time [h]	*X* [%]	*S* [%]	Yield glucose [wt%]	Yield cellobiose [wt%]	Yield cellotriose [wt%]	Yield cellotetraose [wt%]	Yield HMF [mol%]
1	[C_4mim]Cl	2	4	0	0	0	0	0	0
2	ChCl/oxalic acid	2	43	0	0	0	0	0	2
3	ChCl/citric acid	2	10	0	0	0	0	0	2
4	ChCl/TsOH	2	46	0	0	0	0	0	2
5	[C_4mim]Cl/ChCl/oxalic[b]	2	31	81	3	1	7	14	0
6	[C_4mim]Cl/ChCl/citric[b]	2	3	33	0	0	0	1	0
7	[C_4mim]Cl/ChCl/TsOH [b]	2	68	0	0	0	0	0	8
8	[C_4mim]Cl/oxalic acid [c]	2	23	74	0	1	4	12	0
9	[C_4mim]Cl/ChCl/oxalic [b]	4	80	89	12	8	20	31	0
10		6	85	98	16	16	20	31	2
11		8	87	92	21	12	20	27	3
12		12	90	79	28	11	16	16	5
13		16	94	46	26	5	7	5	7
14		20	96	30	23	2	2	2	9

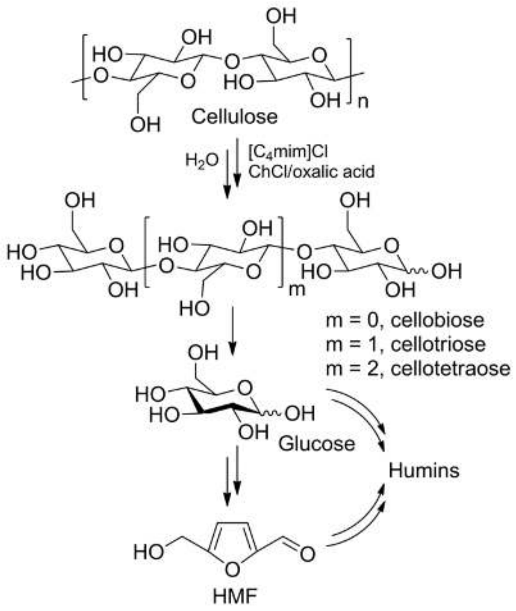
[a] Yields are specified in wt% based on input of cellulose for carbohydrates and in mol% based on anhydroglucose units present for HMF; '0' means that product was identified in trace amounts based on HPLC analysis; X = conversion; S = total selectivity of carbohydrates (glucose, cellobiose, cellotriose, and cellotetraose). Reaction conditions: MCC (50 mg), IL or DES (1.000 g), 120 °C. [b] Reaction conditions: MCC (50 mg), [C_4mim]Cl (1.000 g), DES (0.100 g), 120 °C. [c] Reaction conditions: MCC (50 mg), [C_4mim]Cl (1.000 g), oxalic acid dihydrate (48 mg), 120 °C.

$[C_4mim]Cl$, which alleviates one of the downsides attributed to the use of imidazolium-based ILs.[25] Other DESs based on citric acid or TsOH, combined with $[C_4mim]Cl$, are less effective for the hydrolysis of cellulose under similar conditions (Table 1, entries 6 and 7). Possibly, the solvent system with ChCl/citric acid possesses insufficient acidity to catalyse the hydrolysis under the prevailing conditions (see Table 2 below, for pH measurements and the discussion relating thereto), while the higher acidity of ChCl/TsOH caused the formation of HMF and humins. It is worth noting that the combined solvent $[C_4mim]Cl$/ChCl/oxalic acid provided higher yield and selectivity for sugars than $[C_4mim]Cl$/oxalic acid (Table 1, entries 5 and 8). The hydrolysis of MCC in $[C_4mim]Cl$/ChCl/oxalic acid showed very high conversions of polysaccharide (up to 96%) and selectivity to low molecular weight reducing sugars (up to 98%, Table 1). Cellotriose and cellotetraose appeared as major products in the range 2–8 h (Table 1, entries 5, 9–11), while extended reaction times (12 h, Table 1, entry 12) favoured the production of glucose. These results show that cellulose hydrolyses predominantly into 'chunks' rather than directly to glucose, i.e., low molecular weight oligosaccharides (cellotetraose, cellotriose and cellobiose) from which glucose emerges. The longest reactions (16 and 20 h, Table 1, entries 13 and 14) led to the formation of HMF and by-product humins, which reduced the overall selectivity. HMF likely derives from fructose, the isomerisation product of glucose, while humins form by condensation of sugars and HMF.[23,24] Scheme 2 summarises the findings.

Table 2. pH readings of ionic liquids and single acids.[a]

Source	pH/0.15 M
ChCl	4.89
Oxalic acid	1.58
ChCl/oxalic acid	1.37
Citric acid	2.03
ChCl/citric acid	1.87
TsOH	1.29
ChCl/TsOH	1.28
$[C_4mim]Cl$	7.15
$La(OTf)_3$	7.43
$La(OTf)_3$/oxalic acid	1.52[b] 1.39[c]
$La(OTf)_3$/ChCl/oxalic acid	1.33[b] 1.29[c]

[a] pH readings were performed in triplicate in water at room temperature. The molar concentration of DES solutions and combined acid solutions is calculated based on the content of the Brønsted acid comonent. OTf = trifluoromethanesulfonate. [b] The molar ratio of oxalic acid and $La(OTf)_3$ is 12:1. [c] The molar ratio of oxalic acid and $La(OTf)_3$ is 1:1.



Scheme 2. Acid-catalysed conversion of cellulose in solvent system $[C_4mim]Cl$/ChCl/oxalic acid.

We sought to better understand the origins of the catalyst activity in the ChCl systems. pH readings of dilute aqueous solutions of the DES systems and of their parent acids revealed that the ionic solvents possess enhanced Brønsted acidity compared to the parent acids, in the cases of the organic acids (Table 2). All readings were performed at the same concentration of the components being measured and are therefore a measure of acid strength. ChCl, which is considered to be a Lewis acid, apparently forms a Lewis acid-assisted Brønsted acid complex[26,27] with oxalic acid; this complexation assists to deliver the higher acidity of the DES (Scheme S1). Most likely, the complex so formed consists of choline cation and oxalate anion, as proposed in Scheme S1. Interestingly, the induced Brønsted acidity catalyses the esterification[28] of oxalic acid with ChCl (Scheme S1). The esterification of carboxylic acids with ChCl in molten media, especially with added hydrochloric acid, has been previously noticed by Florindo et al.[29] In our hands, ^{13}C NMR analysis of ChCl/oxalic acid (1:1 mixture, dissolved in deutero acetonitrile) demonstrates three chemical shifts associated with the carboxylic groups of oxalic acid (one peak associated with free oxalic acid at 160.2 ppm, and two new peaks at 158.9 and 158.7 ppm that are consistent with the formation of the ester, Figure S1), along with six chemical shifts assigned to the carbon atoms of choline cation (three peaks associated with free ChCl at 68.5, 56.5 and 54.7 ppm, and three new peaks assigned to the ester at 64.8, 60.5, and 54.6 ppm, Figure S1). Integration of the peaks in the ^1H NMR spectrum of ChCl/oxalic acid diluted in deuterated solvents (CD_3CN or D_2O, Figure S2) or using neat DES (with DMSO-d_6 for external lock employing a coaxial insert tube, Figure S2), showed the ester and ChCl to be present in a ratio 1:10. The FTIR spectrum of the DES indicates a band at 1723 cm^{-1} characteristic of the asymmetrical C=O stretching mode and a band at 1185 cm^{-1} corresponding to asymmetrical vibration of C–C(=O)–O (Figure S3).[30] Free oxalic acid or ChCl do not provide these vibrations, which we propose to be associated with the ChCl/oxalic acid ester.

Now with reference to the experimental results (Table 1) and the pH measurements (Table 2), while Table 2 shows only incremental differences between the various acidic systems, there are distinct experimental outcomes associated with the different reaction media (Table 1). Of the media probed, the acidity secured through ChCl/oxalic acid is optimal for the conversion of cellulose into water-soluble low molecular weight carbohydrates. Other DESs showed either high Brønsted acid activity leading to the rapid conversion of cellulose into by-products, or too low acidity for the effective hydrolysis of glycosidic bonds. The experimental data point to a need for sufficient acidity to cause the hydrolysis but for a tight balancing act such that the acidity is not so high as to cause secondary reactions under the conditions.

Although cellulose-derived oligoglucans (such as those produced as described above: cellobiose, cellotriose, cellotetraose) are valuable products, glucose is usually considered to be *the* desired product of the hydrolysis of polysaccharides.[9,31] Metal triflates are efficient green Lewis acidic catalysts for a range of chemical transformations, including the processing of cellulose, especially when mixed with Brønsted acids to form Lewis acid-assisted Brønsted acid complexes.[3,32,33] Because DESs possess intrinsic Brønsted acidity as shown above (Table 2, Scheme S1), in theory, it is possible to advantage the conversion of cellulose in favour of glucose by modifying solvent/catalyst system with Lewis acid. Accordingly, the activity of metal triflates ($Al(OTf)_3$, $Y(OTf)_3$, AgOTf, $In(OTf)_3$, $Sn(OTf)_2$, $La(OTf)_3$, $Yb(OTf)_3$ and $Hf(OTf)_4$) in mixed ionic solvent [C_4mim]Cl/ChCl/oxalic acid was investigated for the conversion of MCC. Table 3 presents that metal triflates, specifically AgOTf, $In(OTf)_3$, $Sn(OTf)_2$, $La(OTf)_3$, and $Yb(OTf)_3$, promote the rapid hydrolysis of cellulose into low molecular weight sugars. Those that afford higher acidity ($Al(OTf)_3$, $Y(OTf)_3$ and $Hf(OTf)_4$) favour the formation of HMF and the unwanted by-product humins. $La(OTf)_3$ possessed the highest activity to catalyse the transformation of MCC directly into desired monomer glucose in high yield (35 wt% based on cellulose), and in shorter reaction time compared to the process without metal triflate catalysts. $La(OTf)_3$ and oxalic acid formed a Lewis acid-assisted Brønsted acid in the DES, improving the overall activity of the catalytic media for hydrolysis of glycosidic bonds. The addition of $La(OTf)_3$ leads to slightly higher acidity (Table 2). This is caused by complexation of the La to the oxalic acid, thereby providing a complementary form of Lewis acid-assisted Brønsted acidity. This complexation was unambiguously demonstrated by FTIR analyses of [C_4mim]Cl ionic liquid solutions of $La(OTf)_3$ mixed with oxalic acid and separately $La(OTf)_3$ mixed with ChCl/oxalic acid (Figure S4). Both mixtures showed the appearance of an asymmetrical stretching band at 1620–1600 cm^{-1} of the carboxylate anion[30] confirming the complexation. As we have already discussed for the $La(OTf)_3/H_3PO_4$ system,[23,27,34] La holds a special place relating to Lewis acid-assisted Brønsted acidity, providing a complex acid system with exceptional catalyst activity in several different chemical transformations. pH readings of the mixed acid systems ($La(OTf)_3$ + oxalic acid) show the increased acidity, albeit that it too appears incremental in dilute solution. Notwithstanding this incremental change to the pH, the experimental results (Table 3) provide strong evidence for the benefits brought by the addition of the Lewis acid, leading to 73% conversion of cellulose within two hours into 69% low molecular weight saccharides (w/w based on the input cellulose) and 95% selectivity for such saccharides. Care needs to be taken with reaction times, though. The heightened activity of the reaction media with $La(OTf)_3$ is detrimental after extended periods due to the transformation of glucose into HMF and ultimately into humins (Table 3, Scheme 2).

The hydrolytic conversion of cellulose in ILs is more efficient in the presence of water, favouring the formation of glucose.[10,14,15] We therefore conducted the transformation of MCC in the mixed ionic solvent [C_4mim]Cl / ChCl/oxalic acid at 120 °C with the addition of water (Figure 1). MCC was first dissolved in the ionic solvent at 100 °C for 2 h, after which the temperature was raised to 120 °C to cause the reaction, and water was added to the reaction media after 0.5 h (water content 20 wt% based on IL) and 1 h (water content 30 wt% based on IL) of reaction time. The glucose yield is dramatically enhanced in the presence of water. Recall that in the absence of added water, cellulose yielded (with a maximum at 12 h) 28 wt% glucose, along with 43 wt% oligosaccharides consisting of 11, 16 and 16 wt% of cellobiose, cellotriose and cellotetraose,

Table 3. Acid-catalysed conversion of MCC in [C_4mim]Cl / ChCl/oxalic acid in the presence of metal triflates.[a]

Catalyst	Time [h]	*X* [%]	*S* [%]	Yield glucose [wt%]	Yield cellobiose [wt%]	Yield cellotriose [wt%]	Yield cellotetraose [wt%]	Yield HMF [mol%]
none	2	31	81	3	1	7	14	0
$Al(OTf)_3$	2	66	5	3	0	0	0	10
$Y(OTf)_3$	2	65	15	10	0	0	0	10
AgOTf	2	76	89	13	8	18	29	1
$In(OTf)_3$	2	79	85	15	8	18	26	1
$Sn(OTf)_2$	2	60	70	6	4	8	24	0
$La(OTf)_3$	1	71	92	14	7	17	27	1
	2	73	95	35	6	10	18	4
	4	75	21	16	0	0	0	10
	6	76	8	6	0	0	0	11
$Yb(OTf)_3$	2	69	41	17	10	1	0	8
$Hf(OTf)_4$	2	65	0	0	0	0	0	9

[a] Yields are specified in wt% based on input of cellulose for carbohydrates and in mol% based on anhydroglucose units present for HMF; '0' means that product was identified in trace amounts based on HPLC analysis; *X* = conversion; *S* = total selectivity of carbohydrates (glucose, cellobiose, cellotriose, cellotetraose); HMF = 5-(hydroxymethyl)furfural; OTf = trifluoromethanesulfonate. Reaction conditions: MCC (50 mg), [C_4mim]Cl (1.000 g), DES (0.100 g), catalyst (10 mol% based on anhydroglucose unit present), 120 °C.

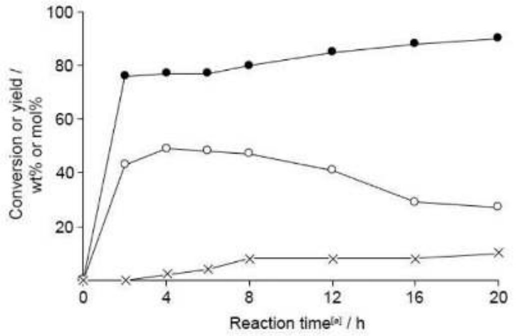


Figure 1. Acid-catalysed conversion of MCC in $[C_4mim]Cl$/ChCl/oxalic acid with gradually added water. ● conversion, ○ glucose yield (wt% based on MCC), × HMF yield (mol% based on anhydroglucose units present). [a] Dissolution of MCC (50 mg), $[C_4mim]Cl$ (1.000 g), DES (0.100 g), 100 °C, 2 h. Reaction of cellulose: $T=120\,^{\circ}C$; addition of water in two steps (step 1: 0.220 mL, water content 20 wt%, based on IL, $t=0.5$ h; step 2: 0.110 mL, total water content 30 wt%, based on IL, $t=1$ h).

respectively (Table 1, entry 12). In contrast, in the presence of water, glucose was the major product (maximum at 4 h, 49 wt %, Figure 1), with only little accumulation of oligosaccharides (maximum at 2 h, 8, 9, 7 wt% of cellobiose, cellotriose and cellotetraose, respectively). These results suggest that added water improved the rates of hydrolysis of glucans. Other studies also note that water suppresses the conversion of glucose into HMF in ILs, most likely related to the reduced acidity of the diluted media.[14,15] Longer reaction times nonetheless led to diminished yields of glucose by the formation of HMF and humins (Figure 1).

All of the reactions performed to this stage had been conducted using MCC as a substrate. MCC is a polysaccharide obtained after the acid-catalysed depolymerisation of native cellulose and is a commodity product for many industries.[35] However, the conversion of non-pretreated substrates is desirable. A subsequent set of reactions was performed employing non-pretreated cellulose of various origins (cotton linter, cellulose extracted from eucalyptus and *Pinus*, microalgal biomass, macroalgal biomass). Processing of non-pretreated bulk cellulose in the co-solvent system $[C_4mim]Cl$ / ChCl/oxalic acid at 120 °C for 6 h afforded lower yields of low molecular weight reducing sugars compared to MCC (Table 4, entries 1, 3, 5, 8, 10), showing the difficulties experienced when working with native biomass, and the need to improve and modify reaction conditions. Depolymerisation of bulk cellulose requires more forcing conditions compared with MCC, and therefore the overall rate of hydrolysis is lower.[36] The addition of $La(OTf)_3$ slightly improved the transformation of cellulose extracted from eucalyptus to glucose (yield 20 wt%, Table 4, entry 6), but the effect of the Lewis acid is less prominent, when compared to the conversion of MCC under identical reaction conditions (glucose yield 35 wt%, Table 3). Similar to the processing of MCC, longer reactions were accompanied by the formation of humins. Pleasingly, the addition of water in two steps as before, improved the hydrolysis of polysaccharides, affording excellent yields of glucose (45–50 wt%, based on substrate, Table 4, entries 4, 7, 9, 11). This is an efficient process for the conversion of a range of non-pretreated cellulosic substrates into glucose, involving environmentally benign solvent-catalyst media. The results compare favourably with outcomes in the literature where mineral acids or zeolites are employed as catalysts for cellulose hydrolysis in $[C_4mim]Cl$ (Table 4, entries 21–23).[11,15]

The conversion of native cellulosic biomass is a significant challenge, and we applied our hydrolysis protocols to biomass derived from terrestrial (chips obtained from softwood or corncob) and marine sources (macroalgae *Ulva lactuca* and microalgae *Porphyridium cruentum*), respectively. Optimal conditions for each source of cellulose or biomass and the reaction outcomes are given in Table 4, entries 12–20. The direct processing of biomass is inherently difficult because native cellulose is usually entangled into plant cell walls with other polysaccharides (e.g., hemicellulose, polymannosides, glycoproteins, etc.) and aromatic polymers (e.g., lignin) forming a rigid polymer system.[3,6] In our hands, the transformation of softwood chips (Table 4, entry 13) in the mixed solvent $[C_4mim]Cl$/ChCl/oxalic acid yielded low molecular weight carbohydrates (glucose + glucosyl oligosaccharides) in a respectable 38 wt% yield based on the glucan content in the biomass. This required processing of wood chip biomass at 120 °C for 6 h, followed by further processing for 4 h after the addition of water (30 wt% of water, based on solvent, added as detailed in Table 4, entry 13). Under these conditions, the xylans (part of the hemicellulose) were hydrolysed into monomer xylose in 25 wt% yield (based on xylan content in the biomass), demonstrating the hydrolysis of both linear and branched polysaccharides (Table 4, entry 13). Most likely, the lower yields of low molecular weight carbohydrates are caused by complicated depolymerisation of wood biomass in ILs. Nevertheless, higher yields of glucose (25 wt%) and xylose (30 wt%, Table 4, entry 14) were attainable after somewhat extended processing of the wood chips (120 °C, 12 h) before addition of water and further heating. In distinct contrast to softwood, the conversion of corncob provided excellent yields of glucose (54 wt%) and xylose (35 wt%) under milder processing conditions before the dilution (100 °C, 2 h, Table 4, entry 16), likely due to the less rigid molecular structure and larger amount of structurally branched polysaccharides present (e.g., hemicellulose and starch).[37] For the same reason,[38–40] marine cell walls were more amenable to hydrolysis. For example, the conversion of the seaweed *Ulva lactuca* in $[C_4mim]Cl$ / ChCl/oxalic acid at 120 °C for 6 h, followed by addition of water (30 wt% of water) and further heating at 120 °C for 4 h, provided glucose in 40 wt% yield (based on the glucan content, Table 4, entry 17). This yield can reach 43 wt% when adding water at the 4 h mark (instead of at 6 h, Table 4, entry 18). The experimental data confirm that the branched saccharides which are predominant in marine plant cell walls require less forcing reaction conditions for selective conversion into desirable low molecular weight saccharides. In a remarkable example, the direct processing of microalgae *P. cruentum*, as raw biomass, in $[C_4mim]Cl$ / ChCl/oxalic acid, yielded 55 wt% of glucose and 40 wt% of xylose (based on the content of glucans and xylans in biomass, respectively, Table 4, entry 20),

Table 4. Acid-catalysed conversion of bulk cellulose and cellulosic biomass in [C_4mim]Cl / ChCl/oxalic acid.[a]

Entry	Substrate	X [%]	S [%]	Yield xylose [wt%]	Yield glucose [wt%]	Yield cellobiose [wt%]	Yield cellotriose [wt%]	Yield cellotetraose [wt%]	Yield HMF [mol%]
1	MCC	85	98	–	16	16	20	31	2
2[b]		91	73	–	37	9	11	9	6
3	Cotton linter	93	73	–	19	8	19	22	3
4[b]		95	60	–	45	7	8	5	6
5	Eucalyptus cellulose	85	64	–	11	7	16	20	1
6[c]		68	85	–	20	8	14	16	4
7[b]		91	74	–	48	7	7	5	4
8	*Pinus* cellulose	82	73	–	11	8	17	24	5
9 [b]		92	77	–	50	7	8	6	6
10	*Pinus* cellulose (unbleached)	80	73	–	12	7	16	23	1
11[b]		91	80	–	46	9	10	8	4
12	Wood chips (softwood)	36	–	1	8	4	9	12	0
13[b]		65	–	25	20	5	7	6	0
14[d]		75	–	30	25	5	6	4	2
15 [b]	Corncob	73	–	2	18	0	0	0	10
16[e]		74	–	35	54	0	0	0	10
17[b]	*Ulva lactuca*	86	–	3	40	2	3	2	0
18[f]		83	–	4	43	5	4	4	0
19[b]	*P. cruentum*	99	–	3	16	0	0	0	0
20[e]		98	–	40	55	0	0	0	0
21[g,11]	Sigmacell	–	–	–	38	–	–	–	–
22[h,11]		–	–	–	21	–	–	–	–
23[i,15]	MCC	–	–	–	50 (mol%)	5 (mol%)	–	–	24

[a] Yields are specified in wt% based on input of cellulose for carbohydrates and in mol% based on anhydroglucose units present for HMF; yields of glucose, cellobiose, cellotriose and cellotetraose obtained from lignocellulose, or algal biomass, are specified in wt% based on the glucans content in substrate; yields of xylose are specified based on the xylans content in biomass; '0' means that product was identified in trace amounts based on LC analysis; X = conversion; S = total selectivity of carbohydrates (glucose, cellobiose, cellotriose, cellotetraose). Reaction conditions: substrate (50 mg), [C_4mim]Cl (1.000 g), DES (0.100 g), 120 °C, 6 h. [b] Reaction conditions: substrate (50 mg), [C_4mim]Cl (1.000 g), DES (0.100 g), 120 °C, 6 h, then addition of water in two steps (step 1: 0.220 mL, water content 20 wt%, based on IL, $t=0$; step 2: 0.110 mL, water content 30 wt%, based on IL, $t=0.5$ h), 120 °C, 4 h. [c] Reaction conditions: substrate (50 mg), [C_4mim]Cl (1.000 g), DES (0.100 g), La(OTf)$_3$ (10 mol% based on anhydroglucose unit present), 120 °C, 2 h. [d] Reaction conditions: substrate (50 mg), [C_4mim]Cl (1.000 g), DES (0.100 g), 120 °C, 12 h, then addition of water in two steps (step 1: 0.220 mL, water content 20 wt%, based on IL, $t=0$; step 2: 0.110 mL, water content 30 wt%, based on IL, $t=0.5$ h), 120 °C, 4 h. [e] Reaction conditions: substrate (50 mg), [C_4mim]Cl (1.000 g), DES (0.100 g), 100 °C, 2 h, then temperature increase to 120 °C and gradual addition of water in two steps (step 1: 0.220 mL, water content 20 wt%, based on IL, $t=0$; step 2: 0.110 mL, water content 30 wt%, based on IL, $t=0.5$ h), 4 h. [f] Reaction conditions: substrate (50 mg), [C_4mim]Cl (1.000 g), DES (0.100 g), 120 °C, 4 h, then addition of water in two steps (step 1: 0.220 mL, water content 20 wt%, based on IL, $t=0$; step 2: 0.110 mL, water content 30 wt%, based on IL, $t=0.5$ h), 120 °C, 4 h. [g] Sigmacell is a commodity cellulose that typically consist of cotton linters. Reaction conditions: substrate (0.32 g), [C_4mim]Cl (4.0 g), H_2SO_4 (98 wt%, 0.184 g), water (0.063 g), 100 °C, 45 min.[11] [h] Reaction conditions: substrate (0.32 g), [C_4mim]Cl (4.0 g), HCl (36 wt%, 0.285 g), water (0.063 g), 100 °C, 11 min.[11] [i] Reaction conditions: substrate (0.1 g), [C_4mim]Cl (2.0 g), 130 °C, to complete dissolution, then addition of HY-zeolite (11 mol%) and water in three steps (step 1: water content 5 wt %, based on IL, $t=0$; step 2: water content 20 wt%, based on IL, $t=0.5$ h; step 3: water content 33 wt%, $t=60$ min), 130 °C, 2 h.[15]

giving 98% conversion of the biomass. These experimental outcomes shine light on the exquisite promise held by the direct conversion of biomass into significantly higher value and useful monosaccharides. One persistent drawback is the need to employ large volumes of the IL solvent, and this challenge remains to be solved. Nevertheless, the results serve as a springboard towards scalable processes to manufacture sustainable and renewable chemicals (Scheme 1).

3. Conclusions

The combined ionic liquid mixture of [C_4mim]Cl/ChCl/oxalic acid is an excellent solvent-catalyst system for the high yielding and selective conversion of cellulose and native biomass, of terrestrial and marine origin, into the low molecular weight saccharides glucose, cellobiose, cellotriose, cellotetraose and xylose. We demonstrate that the acid-catalysed transformation of cellulose in mixed solvents occurs predominantly into glucan oligomer 'chunks' (cellotetraose, cellotriose and cellobiose) from which glucose emerges. The conversion into glucose can be improved by modifying the natural acidity of the DES with added Lewis acid, producing a Lewis acid-assisted Brønsted acid complex, or by the addition of water during the course of the reaction. Importantly, the mixed system avoids the need for pretreatment of the native cellulosic materials. While efficient in this process, the need for large volumes of the ionic system remains to be solved.

Experimental Section

Materials

Reagents and metal trifluoromethanesulfonate (metal triflate) catalysts (Al(OTf)$_3$, Y(OTf)$_3$, AgOTf, In(OTf)$_3$, Sn(OTf)$_2$, La(OTf)$_3$, Yb(OTf)$_3$, or Hf(OTf)$_4$) were used as supplied from commercial sources. Cotton linter, and cellulose extracted from eucalyptus and *Pinus* (unbleached and bleached, BKT, Kinleith, New Zealand) were a generous gift from Dr Simon Hinkley, The Ferrier Research Institute, Victoria University of Wellington (New Zealand). Lignocellulose (softwood chips and corncob) was sourced from local growers (Australia). Macroalgae *Ulva lactuca* was provided as a generous gift by Dr Wayne O'Connor, Department of Primary Industries Fisheries, Port Stephens Fisheries Institute (Australia). Microalgae *Porphyridium cruentum* was grown and supplied by Climate Change Cluster (C3), University of Technology Sydney (Australia). Biomass for acid-catalysed reactions was vacuum oven-dried (60 °C, 12 h). Compositional analysis of biomass was performed using standard analytical procedures: NREL/TP-510-42618[41] for lignocellulose, NREL/TP-5100-60957[42] for algal biomass. The total amount of carbohydrates in the given biomass is specified in the Supporting information Table S2. [C_4mim]Cl was prepared according to reference,[43] while ChCl/acid (1:1 molar ratio for oxalic acid dihydrate or *p*-toluenesulfonic acid monohydrate, respectively; 1:0.5 for citric acid monohydrate, respectively) solvents were prepared according to reference.[44]

High Performance Liquid Chromatography

Carbohydrates were analysed using liquid chromatography-mass spectrometry (LC/MS) on a Shimadzu LCMS-8060 instrument with electrospray ionisation source in negative ion mode. The separation was conducted on a Supelco apHera NH2-Polymer analytical column (150 mm × 4.6 mm, 5 μm) using a mixture of acetonitrile and water (65:35 v/v) as the mobile phase at a flow rate 0.6 mL min^{-1} and a run time of 18 min. Five transitions *m/z* 149.10→89.05 (fragmentor voltage 12 V, collision energy 7 eV), *m/z* 178.85→89.15 (fragmentor voltage 19 V, collision energy 8 eV), *m/z* 341.30→161.20 (fragmentor voltage 16 V, collision energy 8 eV), *m/z* 503.35→161.20 (fragmentor voltage 24 V, collision energy 13 eV) and *m/z* 665.25→503.10 (fragmentor voltage 26 V, collision energy 12 eV) were monitored for detection of xylose, glucose, cellobiose, cellotriose and cellotetraose, respectively. A representative chromatogram is shown in Figure S5. HPLC analysis of HMF was performed using an Agilent 1290 LC instrument equipped with an Agilent Zorbax Eclipse XDB-C18 analytical column (150 mm × 4.6 mm, 3 μm) and Agilent 1260 DAD VL+ detector (detection wavelength: 278 nm). The mobile phase was a mixture of methanol and water (15:85 v/v) at a flow rate of 1.1 mL min^{-1} with a run time of 20 min. Quantitative analysis was performed with the use of a standard curve plotted with analytical standards. The standard curves were generated using measured HPLC-peak area at appropriate concentration of the analytical standard; all figures provided linear correlation coefficient > 0.99.

NMR Spectroscopy

NMR spectra of the products were recorded on an Agilent 500 MHz NMR spectrometer using deuteroacetonitrile-d_3 (CD_3CN), or deuterium oxide (D_2O) as solvents. 2D NMR spectroscopy (HSQC and COSY) were used to unambiguously assign the peaks. Samples were dissolved in the selected solvents in a 5 mm NMR tube and the spectra were collected at 25 °C with chemical shifts referenced relative to residual solvent for samples recorded in CD_3CN (^{1}H: $\delta = 1.96$ ppm; ^{13}C: $\delta = 118.2$ ppm), or to deuterated sodium 3-trimethylsilylpropionate ([D_4]TMSP, ^{1}H, ^{13}C: $\delta = 0.00$ ppm) for samples recorded in D_2O. NMR spectra of the neat DESs were collected at 25 °C in a 5 mm NMR tube equipped with coaxial inserts containing deuterodimethyl sulfoxide ([D_6]DMSO, ^{1}H: $\delta = 2.49$ ppm; ^{13}C: $\delta = 39.7$ ppm) as an external lock.

IR Spectrometry

IR spectra were collected using a thin film on a Thermo Scientific Nicolet 6700 spectrometer in a range 4000–450 cm^{-1}.

pH Readings

pH Readings were recorded at room temperature (22–23 °C) using a Mettler Toledo pH meter adapted with a standard glass electrode with prior calibration by two buffer solutions (pH = 4.00, pH = 7.00). Measurements were performed in triplicate and the average values are presented.

Acid-Catalysed Conversion of Cellulosic Substrates

MCC, cellobiose, glucose, or fructose (50 mg) and solvent ([C_4mim]Cl, or DES, 1.000 g) were loaded to a glass pressure tube equipped with a magnetic follower and the reactor was sealed. The mixture was heated and stirred at 120 °C for 2 h. After completion of the process, the reaction mixture was cooled and diluted with deionised water (9.00 mL) to precipitate any unreacted cellulose. The mixture was centrifuged (10,000 × g for 15 min) and decanted. The recovered solids were washed with deionised water (3 × 10 mL), vacuum oven-dried (60 °C, 1 mbar, 12 h) and weighed to calculate the conversion of cellulose. The decanted liquid phase was quenched by the addition of an aqueous solution of sodium hydrogen carbonate (1.00 mL, 0.05 M) and centrifuged (10,000 × g for 15 min). The recovered solutions were diluted with a known volume of deionised water, if required, and analysed by HPLC. To recover HMF from the diluted and neutralised ILs (50.0 mL, combined aqueous phases after conversions of carbohydrates), an extraction with ethyl acetate (3 × 100 mL) was performed. The ethyl acetate layers were combined and dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was subjected to flash column chromatography (hexane/ethyl acetate, 60:40 v/v) to isolate HMF, which gave satisfactory analytical data.[23]

For the conversions in mixed ionic solvent, cellulose (50 mg), [C_4mim]Cl (1.000 g) and DES (0.100 g), and in some instances metal triflate catalyst ($Al(OTf)_3$, $Y(OTf)_3$, AgOTf, $In(OTf)_3$, $Sn(OTf)_2$, $La(OTf)_3$, $Yb(OTf)_3$, or $Hf(OTf)_4$, 10 mol% based on the number of anhydroglucose units present in cellulose), were introduced to a glass pressure tube equipped with a magnetic follower and the reactor was sealed. The mixture was heated and stirred at the predetermined temperature for a fixed period of time. The products were recovered and analysed as detailed above.

For the conversions with gradually added water, cellulosic substrate (cellulose, lignocellulose, or algal biomass, 50 mg), [C_4mim]Cl (1.000 g) and DES (0.100 g) were charged to a glass pressure tube equipped with a magnetic follower and the reaction mixture was heated and agitated for a fixed amount of time. After this fixed period of time (which varied from case to case), deionised water was added (0.220 mL, water content 20 wt%, based on IL) followed by heating, and 30 minutes later a second portion was added (0.110 mL, total water content 30 wt%, based on IL) and the reaction system was additionally heated and stirred for a fixed period of time. The products were recovered and analysed as detailed above.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: biomass · carbohydrates · ionic liquids · acid catalysis · green chemistry

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Iurii Bodachivskyi (graduate research student) developed the methodology, conducted research, including experimental work, data collection and data analysis, and drafted the manuscript. Prof. D. Bradley G. Williams (principal supervisor) and Dr Unnikrishnan Kuzhiumparambil (co-supervisor) supervised Iurii Bodachivskyi's research activities, provided conceptual advice and revised the manuscript.

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Principal supervisor	Production Note: Signature removed prior to publication.	Prof. D. Bradley G. Williams
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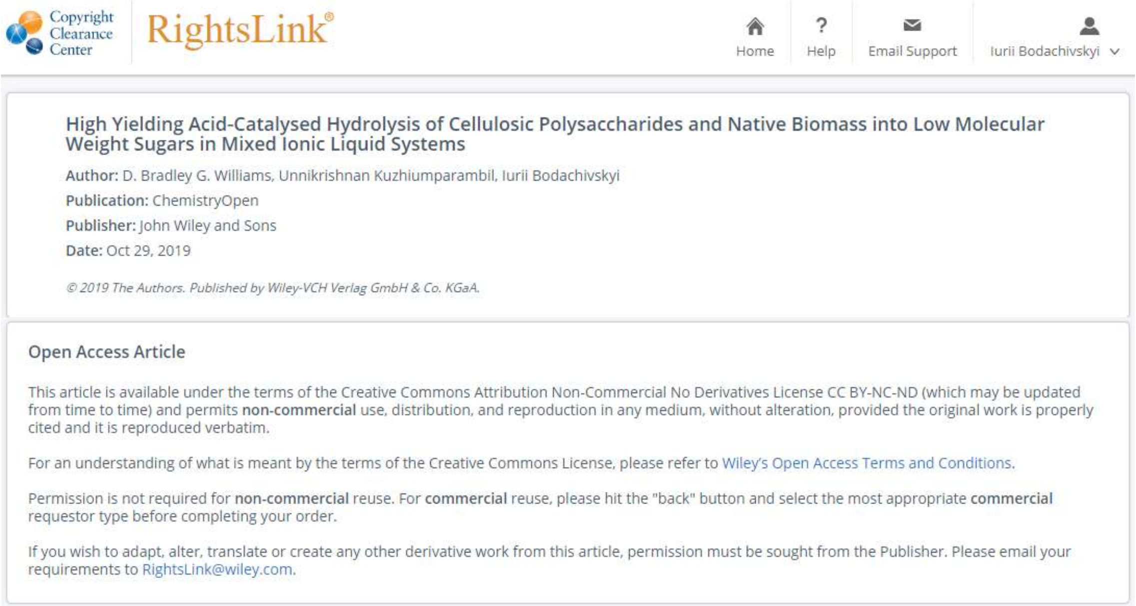

High Yielding Acid-Catalysed Hydrolysis of Cellulosic Polysaccharides and Native Biomass into Low Molecular Weight Sugars in Mixed Ionic Liquid Systems

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3.5. Catalytic valorisation of native biomass in a deep eutectic solvent: a systematic approach towards high yielding reactions of polysaccharides

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Catalytic Valorization of Native Biomass in a Deep Eutectic Solvent: A Systematic Approach toward High-Yielding Reactions of Polysaccharides

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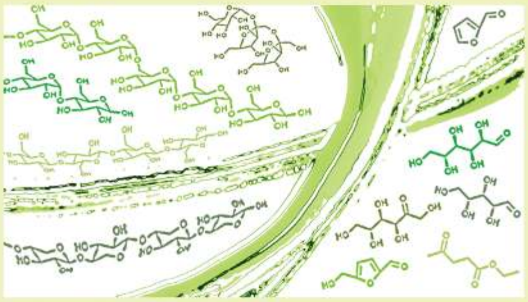
Supporting Information



ABSTRACT: This work investigates catalytic reactions of raw, bulk, native biomass (poly)carbohydrates in the choline chloride/oxalic acid deep eutectic solvent. In particular, we systematically explore the reactivity of native glucans, fructans, and xylans in model transformations of refined substrates and unrefined cellulosic materials in the catalyst−solvent. We show that α-linked glucose polymers, fructans, and xylans are all amenable to hydrolytic processing, and only the linear polysaccharide cellulose remains rather intractable under our conditions. Improved fundamental understanding of the chemistry permits tuning the reaction parameters toward high yielding conversion of undervalued terrestrial and marine biomass into significantly value-added glucose (yield up to 68 wt %), fructose (yield up to 60 wt %), xylose (yield up to 73 wt %), 5-(hydroxymethyl)furfural (yield up to 14 mol %), or furfural (yield up to 72 mol %). Under these optimized conditions, cellulose remains as an unreacted portion, which could be recovered and very effectively beneficiated, delivering additional useful chemicals in high yields from the biomass and optimizing toward total use of the biomass. We realize efficient conversions of polysaccharides of the biomass into high yields of useful small molecules.

KEYWORDS: *biomass, carbohydrates, deep eutectic solvents, acid catalysis, green chemistry*

■ INTRODUCTION

Biomass is a large-scale alternative source (to fossil-derived materials) of substrates for the large volume production of carbon neutral fuels and chemicals.[1−3] Terrestrial cellulosic biomass, including undervalued or waste streams of non-food-competitive polysaccharides, possesses the scale and general ease of accessibility to set the foundation for sustainable industrial chemistry.[1−4] There is substantial and growing interest in the acid-catalyzed valorization of cellulosic substances into value-added organic building block chemicals (platform molecules), as effective petrochemical replacement products.[1−7] However, the catalytic valorization of cellulosic biomass into platform molecules is inherently difficult due to macromolecular structures that are challenging for chemical processing.[3,4,7−9] This chemistry is plagued by low selectivity and, often, suffers significant energy implications during preprocessing steps. To circumvent these difficulties, laboratory scale methods are commonly based on refined individual polysaccharides (e.g., microcrystalline cellulose or dissolving pulp)[a] or even edible low molecular weight carbohydrates (e.g., fructose or sucrose). The use of such substances reduces the overall benefit and impact of the biorefinery.[3,5,6,10] It is, therefore, essential to develop and employ sustainable methods for the catalytic valorization of less refined, or raw, biomass into platform molecules, and this problem remains to be solved.

With widespread application of ionic liquids in chemical processes, there has been an intense effort to valorize cellulosic biomass in such media.[11] In distinct contrast to common aqueous or organic solvents, ionic liquids are able to dissolve polysaccharides, enabling significant progress toward milder reaction conditions and better yields of desirable products.[11−13] While common imidazolium salts have shown to be efficient for the processing of cellulose, their high cost, along with challenging recovery of ionic media, remains a concern for industrial practices.[3,14] Alternatively, deep eutectic solvents (DESs) show promise to avoid some of these downsides. DESs are inexpensive and recoverable media for the fractionation of biomass and in rare instances also for the conversion of mono- and oligosaccharides into value-added products.[15−17] However, there is only little information relating to the direct transformation of biomass into platform

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chemicals in DESs. In our former studies, we discovered that the fully renewable mixture of choline chloride and oxalic acid dihydrate (ChCl/oxalic acid) is a highly functional deep eutectic system for the pretreatment of bulk cellulose, such as wood pulp.[18] The work has shown that this DES can be recycled without loss of activity.[18] We have also shown that ChCl/oxalic acid is an optimal catalyst, relative to other acidic DESs, for the hydrolysis of cellulose into low-molecular weight saccharides in a co-solvent system with 1-butyl-3-methylimidazolium chloride ([C$_4$mim]Cl).[19] There is presently no efficient transformation of unrefined lignocellulose in DESs under known conditions,[18,19] seemingly a consequence of the complex chemical composition of native polysaccharides and their varied reactivities. In one instance,[18] the processing of the softwood biomass in ChCl/oxalic acid solvent led to substantial formation of byproducts. In the second,[19] the effective conversion of lignocellulose in the co-solvent system, comprising [C$_4$mim]Cl and ChCl/oxalic acid, is compromised by the complicated depolymerization of the unrefined wood. The problem of the sustainable valorization of biomass is presently essentially unsolved, and the present study addresses this topical issue. Here, in distinct contrast to earlier works, we create new information relating to the relative reactivity of the different polysaccharides and optimized conditions to be employed during their valorization reactions. To start, we investigate and characterize the activity of ChCl/oxalic acid as a solvent−catalyst system in reactions of various purified forms of (poly)carbohydrate substances and with the macromolecular portion of unrefined corn husk. With unrefined biomass, we monitor the progress of conversion of each polysaccharide individually, thereby providing deeper insights to the reactivity of native carbohydrates in the catalytic solvent. The improved fundamental understanding of the chemistry enabled the development of optimized reaction conditions permitting the high-yielding direct transformation of low value bulk cellulosic substrates obtained from terrestrial or aquatic sources into high value low-molecular weight saccharides, furan derivatives, and into refined cellulose. We then show how to selectively convert the recovered cellulose into platform chemicals, providing a scenario for multistage sustainable biorefinery. The approach maximizes use and beneficiation of the input biomass.

■ MATERIALS AND METHODS

Materials. ChCl, oxalic acid, corn starch, inulin, low-molecular weight carbohydrates, organic solvents, zinc chloride (anhydrous), yttrium(III) trifluoromethanesulfonate, hydrochloric acid (32 wt % aqueous solution), and phosphoric acid (85 wt % aqueous solution) were used as supplied from commercial sources. Lignocellulose (corn husk, corncob, and softwood chips) was sourced from local growers (Australia). The macroalga *Ulva lactuca* was provided as a generous gift by Dr Wayne O'Connor, Department of Primary Industries Fisheries, Port Stephens Fisheries Institute (Australia). The microalgae *Porphyridium cruentum* was grown and supplied by Climate Change Cluster (C3), University of Technology Sydney (Australia). Cellulose and hemicellulose were extracted from corn husk by treatment with aqueous NaOH using a known method, details of which are given in the Supporting Information.[20] Vacuum oven-dried (60 °C, 1 mbar, 12 h) cellulosic materials were used for acid-catalyzed reactions. The carbohydrate content in the cellulosic biomass was established by standard analytical methods: NREL/TP-510-42618[21] for lignocellulose, NREL/TP-5100-60957[22] for algal biomass (Table S1). ChCl/oxalic acid solvent (1:1 molar ratio) was prepared according to the literature;[23] a 1:1 molar ratio between ChCl and oxalic acid is considered to be optimal for this deep eutectic system.[23] [C$_4$mim]Cl was synthesized according to a known method.[24] Zinc chloride hydrate solvent was prepared by mixing the anhydrous salt with the appropriate amount of deionized water to attain the molecular formula $\mathrm{ZnCl_2 \cdot 4.25H_2O}$.[25] Details of the analytical methods are provided in the Supporting Information.

Acid-Catalyzed Conversion of Cellulosic Substances. For the model conversions of refined (poly)saccharides, the substrate (starch, cellulose, inulin, hemicellulose, cellobiose, maltose, sucrose, glucose, fructose, or xylose, 50 mg) and ChCl/oxalic acid solvent (4.0 g) were introduced to a round-bottom flask equipped with a condenser, thermometer, and magnetic follower and the mixture was heated and stirred at the predetermined temperature for a fixed period of time. After completion, the reaction mixture was cooled and diluted with deionized water (4.00 mL). A small amount of the aqueous phase (0.50 mL) was retained for chromatographic analysis, as detailed in the Supporting Information, to provide the results detailed in the main text. Work-up of the aqueous phase before analysis included addition of aqueous sodium hydrogen carbonate (0.50 mL, 1 M), followed by centrifugation (20 000*g* for 10 min) and decantation. The recovered solutions were diluted with a known volume of deionized water, for analysis. The remaining reaction mixture was diluted with aqueous ethanol (30.0 mL, 95%) to precipitate the unreacted polysaccharides. The recovered solids were washed with aqueous ethanol (3 × 25.0 mL, 95%), vacuum oven-dried (60 °C, 1 mbar, 12 h), and weighed. The conversion of substrates was established based on the weight of the recovered and vacuum-dried substrate for polysaccharides and by chromatographic analysis for mono- and disaccharides. Recovery of furanoid products for characterization comprised extraction thereof from the diluted aqueous ChCl/oxalic acid (25.0 mL, combined aqueous phases achieved after processing in ChCl/oxalic acid solvent) with ethyl acetate (3 × 50.0 mL). The resulting ethyl acetate fractions were combined and dried over $\mathrm{MgSO_4}$, and the solvent was removed under reduced pressure (30 °C, 50 mbar). The crude mixture was subjected to flash column chromatography (hexane/ethyl acetate, 1.5:1 v/v mixture) to isolate 5-(hydroxymethyl)furfural (HMF) and furfural (FF), which gave satisfactory analytical data (Figures S1−S4).[14,26]

For conversion of cellulosic biomass in the DES, substrate (200 mg) and ChCl/oxalic acid solvent (4.0 g) were introduced to a round-bottom flask equipped with a condenser, thermometer, and magnetic follower and the mixture was heated and agitated at the predetermined temperature for a fixed period of time. The reaction mixture was cooled and diluted with deionized water (4.00 mL). The reaction media were recovered, as detailed above, and analyzed, as detailed in the SI. The recovered and vacuum oven-dried solid residues were analyzed according to the method in NREL/TP-510-42618[21] to identify the individual conversions of glucans, fructans, and xylans detailed in the main text.

For conversions in the DES/organic solvent biphasic systems, native biomass (corn husk, corncob, softwood chips, *U. lactuca*, or *P. cruentum*, 200 or 300 mg), ChCl/oxalic acid solvent (4.0 g), and organic solvent−extractant [methyl isobutyl ketone (MIBK), anisole, 1,2-dimethoxybenzene, 8.0 or 12.0 mL] were introduced to a round-bottom flask equipped with a condenser, thermometer, and magnetic follower and the mixture was heated and stirred at the predetermined temperature for a fixed period of time. The conversion with ethyl acetate as a solvent−extractant was conducted in a sealed glass pressure vessel equipped with a magnetic follower (CAUTION: risk of glass rupture due to elevated pressure). Work-up of the reaction media included dilution of the DES with water (4.00 mL), followed by agitation of the biphasic system at room temperature for 5 min. The resulting emulsion was transferred to a conical tube and centrifuged (2000*g* for 10 min) to separate the aqueous and organic phases. Recovery of the aqueous phase and analysis of the products was performed as detailed above. In one instance, the aqueous phase was subjected to extraction with ethyl acetate (2 × 8.0 mL) before analysis, to assess the recovery of furanoids from the diluted reaction media. Recovery of the organic phase before analysis comprised dilution with a known amount of anisole, followed by centrifugation and decantation (20 000*g* for 10 min).

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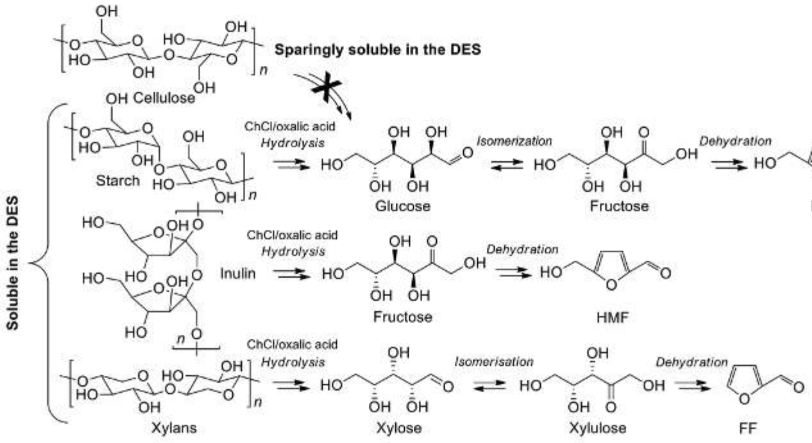
Scheme 1. Acid-Catalyzed Transformation of (Poly)Carbohydrates in the ChCl/Oxalic Acid Solvent, with an Emphasis on the Solubility of Substrates[a]



[a] n = integer.

Table 1. Catalytic Conversion of Cellulosic Substances in ChCl/Oxalic Acid Solvent[a]

entry	substrate	T (°C)	t (h)	conv glucans (wt %)	conv fructans (wt %)	conv xylans (wt %)	yield glucose (wt %)	yield fructose (wt %)	yield xylose (wt %)	yield HMF (mol %)	yield FF (mol %)
1	corn husk	60	1	28	99	51	26	60	24	10	0
2		60	2	30	99	62	25	12	35	12	0
3		60	4	36	99	75	25	0	62	14	1
4		60	6	37	99	79	25	0	63	14	1
5		60	8	38	99	87	22	0	67	14	3
6		80	1	46	99	89	20	0	63	14	4
7		80	2	55	99	92	18	0	65	12	10
8		80	4	59	99	97	16	0	55	9	19
9		80	6	60	99	98	14	0	51	8	22
10		80	8	63	99	99	14	0	44	6	28
11		100	1	52	99	99	14	0	24	8	32
12		100	2	65	99	99	11	0	20	7	35
13		100	4	65	99	99	10	0	7	5	34
14		100	6	66	99	99	8	0	0	4	34
15		100	8	67	99	99	5	0	0	4	31
16[b]	starch	60	1	30			5	0	0	0	0
17[b]		80	1	99			45	0	0	1	0
18[b]		100	1	99			36	0	0	10	0
19[b]	cellulose	60	1	2			0	0	0	0	0
20[b]		80	1	10			0	0	0	0	0
21[b]		100	1	15			1	0	0	1	0
22[b]	inulin	60	1		98		0	24	0	35	0
23[b]		80	1		99		0	0	0	37	0
24[b]		100	1		99		0	0	0	32	0
25[b]	hemicellulose	60	1			64	0	0	12	0	0
26[b]		80	1			99	0	0	66	0	8
27[b]		100	1			99	0	0	25	0	46

[a] Conversions are specified in wt % based on glucan, fructan, and xylan contents in the substrate, respectively. Yields are specified in wt % for carbohydrates, based on glucan, fructans and xylan content in the substrate, respectively. Yields are specified in mol % for HMF based on the total hexosan content in the substrate because both glucans and fructans are convertible into HMF. Yields are specified in mol % for FF, based on the xylan content in the substrate. T = processing temperature; t = processing time. Reaction conditions: corn husk (200 mg), ChCl/oxalic acid (4.0 g), 60−100 °C, 1−8 h. [b] Reaction conditions: substrate (50 mg), ChCl/oxalic acid (4.0 g), 60−100 °C, 1−8 h.

Conversions of softwood-derived cellulose in $ZnCl_2 \cdot 4.25H_2O$,[27] co-solvent system comprising $[C_4mim]Cl$ and ChCl/oxalic acid,[19] or in ethanol (water content < 0.2%)[18] were performed according to the respective references.

■ RESULTS AND DISCUSSION

The catalytic transformation of polysaccharides is a complex cascade of reactions, in which the direction and rate are determined by the nature of the acidic catalyst and processing conditions.[3] Because the selected solvent ChCl/oxalic acid is naturally acidic, this reaction medium is a budding candidate for the direct valorization of cellulosic substances.[19] We modeled the reactivity of (poly)carbohydrates in the DES system by performing conversions of representative disaccharides (maltose, cellobiose, and sucrose) and monosaccharides (glucose, fructose, and xylose) in ChCl/oxalic acid solvent (Table S2). The selected carbohydrates are structural units of carbohydrate polymeric substances. Therefore, studies relating to their transformations under specific reaction conditions may provide deeper insights into prospective reactions of native polysaccharides. It became clear that maltose, formed from two units of glucose with an $\alpha(1 \rightarrow 4)$ glycosidic bond, is more susceptible to hydrolysis into monomer glucose in DES media at lower temperatures than its $\beta(1 \rightarrow 4)$-linked isomer cellobiose (Table S2, entries 1−6). Sucrose, which consists of glucose and fructose units with $\alpha(1 \rightarrow 2)\beta$ glycosidic bond type, was even more reactive providing glucose (yield up to 85 wt %, Table S2, entry 7) and HMF (yield up to 16 mol %, Table S2, entry 8) as major products with little or no accumulation of fructose (yield only up to 2 wt %, Table S2, entry 7−9); HMF is a dehydration product derived from fructose (Scheme 1).[3] We subsequently performed transformations of monosaccharides in ChCl/oxalic acid solvent, confirming that fructose transforms rapidly into HMF in the acidic media (HMF yield up to 45 mol %, Table S2, entry 14). In distinct contrast, glucose and xylose required higher temperatures to promote their conversion into furan derivatives (Table S2, entries 10−12, 16−18). This shift in reactivity is apparently associated with a need towards aldose−ketose isomerization for glucose or xylose (into fructose or xylulose, respectively) before dehydration into the corresponding furanoid product (Scheme 1).[3] For comparison, fructose dehydrates directly into HMF (Scheme 1), without the need for prior isomerization. All processes with mono- or disaccharides were persistently accompanied by the formation of dark-brown-colored high-molecular weight byproduct humins (a condensation product of furans and carbohydrates).[26,28] The formation of humins under these conditions most likely relates to the intrinsic acidity of the reaction media that catalyze both desirable and side reactions, in combination with the extended contact between the furan products and carbohydrates in the presence of the acidic system.

To investigate catalytic reactions of native polysaccharides in the DES, we conducted the conversion of corn husk (small oven-dried flakes, comprising polyglucans, -fructans, and -xylans) and various individual polysaccharides (starch, cellulose, inulin, and hemicellulose) in the ChCl/oxalic acid solvent at various reaction temperatures (60−100 °C) and times (1−8 h, Table 1). As opposed to common imidazolium salts in which cellulosic substrates can be fully soluble,[29] lignocellulose appeared to be only partially soluble in the DES in our hands. Nonetheless, this acidic medium was sufficiently active to promote the conversion of native lignocellulose into low-molecular weight carbohydrates such as glucose, fructose, and xylose, and furan derivatives, such as HMF and FF (Table 1). This range of products suggests that polymeric sugars hydrolyze into their respective monomers in the DES medium, followed by dehydration into furan derivatives, as pictorially represented in Scheme 1. This view is consistent with current research,[3,11,26,27] and with the results of our model reactions in the present study (Table S2). However, these conversions occur at appreciably different rates for each polysaccharide substrate, thereby influencing the portfolio of major products during the course of the processing. The native glucans that comprise starch [a mixture of $\alpha(1 \rightarrow 4)$ linearly linked glucose polymer amylose and branched α-glucose polymer amylopectin] and cellulose [$\beta(1 \rightarrow 4)$ linearly linked glucose polymer] are presumably both transformed into glucose followed by its conversion into HMF, that is, they follow similar reaction pathways to the product. Table 1 shows glucose accumulation in various amounts, up to a maximum of 26 wt % (entry 1) based on the glucan content. HMF reaches a maximum of 14 mol % (entries 3−6) based on the hexosan content. The starch extracted from corn showed that α-linked glucans are soluble in the DES and are amenable to hydrolysis into glucose with little formation of HMF (Table 1, entries 16−18). In contrast, cellulose ($\beta(1 \rightarrow 4)$-linked glucan) was recalcitrant under these conditions in the acidic media, likely associated with its limited solubility in the ionic solvent (cellulose remained essentially insoluble in the DES at all tested temperatures, Table 1, entries 19−21). Difficulties processing cellulose in DESs have been reported in other studies.[17,19] These two instances exemplify the defining influence that the structure of the polysaccharide may have on the rate and outcome of these reactions. Chromatographic analysis of the aqueous diluted reaction media from cellulose (see experimental details above and in the Supporting Information) identified only trace amounts of monosaccharides and oligosaccharides (we are capable of detecting and quantifying di-, tri-, and tetrasaccharides, and could identify only trace amounts thereof). The incomplete conversion of corn husk-derived glucans (Table 1, entries 1−15) may be similarly explained by the resistance of the cellulosic portion to the present processing conditions. This result correlates with model reactions of disaccharides in the DES, during which we established that $\beta(1 \rightarrow 4)$-linked glucans possess lower reactivity than $\alpha(1 \rightarrow 4)$-linked analogues (Table S2, entries 1−6). In contrast to glucans, and similarly to the reaction of sucrose (a proxy for native inulin, Table S2, entries 7−9), the fructan inulin (inulin is a $\beta(1 \rightarrow 2)$ linearly linked fructose polymer with occasional chain-terminating glucose units) was found to be fully soluble and rapidly convertible into fructose and HMF in ChCl/oxalic acid at lower temperatures (yields 24 wt % and 35 mol % based on the fructan content, respectively, Table 1, entry 22). Higher temperatures promoted the transformation of the fructan into byproduct humins reducing the overall yield and selectivity of the processes (Table 1, entry 23, 24). The conversion of inulin into HMF and humins has been previously noted in various DESs.[15,17] The data suggest that, at low temperatures, HMF is produced from the fructan component of the biomass rather than the glucan component. The sluggish reaction of the glucans is likely associated with a need for aldose−ketose isomerization for glucose, as was noted for model reactions of low molecular weight saccharides (Table S2). This isomerization is not required for fructans, which produce the ready-made saccharide intermediates that do not require isomerization en route to furanoids. Extended processing and elevated temperatures promoted undesired reactions toward humins, accounting for losses of the desired products.

Table 2. Catalytic Conversion of Cellulosic Biomass in ChCl/Oxalic Acid Solvent[a]

entry	substrate	solvent−extractant	conv glucans (wt %)	conv fructans (wt %)	conv xylans (wt %)	yield glucose (wt %)	yield fructose (wt %)	yield xylose (wt %)	yield HMF (mol %)	yield FF (mol %)
1	corn husk	ethyl acetate	70	99	97	9	0	33	13	37
2		MIBK	69	99	99	27	0	22	9	52
3		anisole	72	99	99	20	0	25	6	52
4		1,2-dimethoxy-benzene	66	99	99	17	0	24	7	50
5	corncob	MIBK	73	99	98	25	0	21	11	41
6[b]		MIBK	73	99	99	0	0	0	9	51
7	softwood	MIBK	25		99	1	0	14	1	36
8[b]		MIBK	26		99	0	0	0	1	53
9[c]		MIBK	26		99	0	0	0	1	55
10	*U. lactuca*	MIBK	86		99	51	0	0	7	60
11	*P. cruentum*	MIBK	99		99	68	0	13	9	44
12[b]		MIBK	99		99	32	0	0	5	72
13[d]		none	98		99	42	0	73	1	25

[a] Conversions are specified in wt % based on glucan, fructan, and xylan contents in the substrate, respectively. Yields are specified in wt % for carbohydrates, based on glucan, fructan, and xylan contents in the substrate, respectively. Yields are specified in mol % for HMF based on the total hexosan content in the substrate because both glucans and fructans are convertible into HMF. Yields are specified in mol % for FF, based on the xylan content in the substrate. Reaction conditions: substrate (200 mg), ChCl/oxalic acid (4.0 g), solvent−extractant (8.0 mL), 100 °C, 2 h. The outcome of the unreacted material is specified in wt % based on the substrate. [b] Reaction conditions: substrate (200 mg), ChCl/oxalic acid (4.0 g), MIBK (8.0 mL), 100 °C, 4 h. [c] Reaction conditions: substrate (300 mg), ChCl/oxalic acid (4.0 g), MIBK (12.0 mL), 100 °C, 5 h. [d] Reaction conditions: substrate (200 mg), ChCl/oxalic acid (4.0 g), 80 °C, 2 h.

Hemicellulose (a native polysaccharide often made of structurally branched xylose units) dissolves in the DES and transforms into monomer xylose at moderate temperatures (yields up to 67 wt % based on the xylan content, Table 1, entries 3−7, 26) and FF under more forcing conditions (yields up to 46 mol % based on the xylan content, Table 1, entries 11−15, 27). As was the case for starch and inulin, as well as mono- and disaccharides, longer residence times in the reaction media and higher temperatures, were detrimental to the conversion of xylans leading to the formation of byproducts.

We have previously shown that dilute aqueous solutions of ChCl/oxalic acid possess higher acidity relative to the solution of oxalic acid alone: the pH of a 0.15 M solution of ChCl/oxalic acid is 1.37 while that of a 0.15 M aqueous solution of oxalic acid is 1.58.[19] The enhanced acidity of the DES is attributed to the complexation of ChCl and oxalic acid through a Lewis acid-assisted Brønsted acidity mechanism.[30,31] To further probe this DES, especially in the context of the current set of reactions, we conducted a study of the binding of the DES to mesityl oxide as a proxy for carbohydrate substrates, employing ^{13}C NMR spectroscopy to define the activity of the neat solvent system.[32] Mesityl oxide is known to form complexes (Lewis or Brønsted type complexes) with acids. The binding produces changes in the chemical shifts of the α and β carbons ($\Delta\delta$) of the unsaturated ketone, and the induced $\Delta\delta$ value provides a measure of acidity (a greater $\Delta\delta$ value corresponds to a stronger acid).[32−34] This method has been previously employed to evaluate the acid strength of various ionic solvents[27,34] and so is known to be appropriate for the task. In the present study, the $\Delta\delta$ value for ChCl/oxalic acid was found to be 78.0 (the reading was taken in the neat DES, with DMSO-d_6 as external lock employing a coaxial insert tube). This measure is equivalent to strong Brønsted acids such as aqueous sulfuric acid ($\Delta\delta$ is 78.0 for a 89.8 wt % H_2SO_4 solution) or trifluoromethanesulfonic acid ($\Delta\delta$ is 81.9).[32] This result highlights a strong predilection of ChCl/oxalic acid to form complexes with O-containing bases (this may occur by protonation or by the interaction with Lewis acidic choline cation[32,33]), such as mesityl oxide or carbohydrates, and immediately explains the high activity of the DES in acid-catalyzed reactions (Scheme 1, Tables 1 and S2).

When considering the combined experimental data, the following emerges:

1 The reactivity of the saccharides in the DES media depends on the nature of their glycosidic linkages: α-linked glucans (e.g., maltose and starch), $\beta(1 \rightarrow 2)$-linked fructans (e.g., sucrose and inulin), and branched saccharides (e.g., hemicellulose) are more susceptible to hydrolytic conversion than $\beta(1 \rightarrow 4)$-linked glucans, such as cellulose (Tables 1 and S2);

2 Aldoses such as glucose and xylose require more forcing conditions for the dehydration thereof into derivative furanoids, relating to the requisite aldose−ketose isomerization step before dehydration takes place (Table S2);

3 Polysaccharides that are soluble in the ChCl/oxalic acid system, such as starch, fructans, and hemicellulose, are all fully convertible into the corresponding monosaccharides, furans, and byproduct humins, while cellulose, an insoluble glucan, is not sufficiently reactive under the action of the acidic DES (Table 1);

4 The high acid strength of the solvent promotes reactions of low-molecular weight products into condensation byproduct humins, reducing selectivity and yields of the catalytic processes.

The losses of desirable products and the occurrence of unwanted humins are a rather frequent problem during the acid-catalyzed valorization of cellulosic substances in aqueous solvents or ionic liquids.[3] The current literature suggests that continuous extraction of reactive nonpolar furans from the acidic reaction media by organic solvents can improve the selectivity of the products, preventing byproduct forma-

Table 3. Production of Value-Added Molecules from Reaction of Cellulosic Biomass[a]

entry	substrate	yield glucose (wt %)	yield fructose (wt %)	yield oligosac-charides (wt %)	yield furans (wt %)	yield ELev (wt %)	refs
1[b]	softwood	26	0	0	22;[c] 11[d]		27
2[b]	softwood cellulose	33	14	0	24;[c] 6[d]		this work
3[e]	softwood	20	0	5;[f] 7;[g] 6[h]	0		19
4[c]	softwood cellulose	30	0	7;[f] 13;[g] 15[h]	2		this work
5[i]	softwood	0	0	0	0	52	18
6[i]	softwood cellulose	0	0	0	0	62	this work

[a]Yields are specified in wt % for carbohydrates and for HMF based on glucan content in the substrate. Yields are specified in wt % for FF and ELev based on the total content of carbohydrates in the substrate. Softwood cellulose means cellulose obtained after processing in ChCl/oxalic acid (Table 3, entry 9). [b]Reaction conditions: polysaccharide (50 mg), $ZnCl_2 \cdot 4.25H_2O$ (5.0 g), HCl (0.03 mmol), 80 °C, 5 h, then 120 °C, 1 h.[27] [c]Yields of HMF. [d]Yields of FF. [e]Reaction conditions: substrate (50 mg), $[C_4mim]Cl$ (1.0 g), ChCl/oxalic acid (0.100 g), 120 °C, 6 h; then, addition of water in two steps (step 1: 0.220 mL, water content 20 wt %, based on IL, $t = 0$; step 2: 0.110 mL, water content 30 wt %, based on IL, $t = 0.5$ h), 120 °C, 4 h.[19] [f]Yields of cellobiose. [g]Yields of cellotriose. [h]Yields of cellotetrose. [i]Reaction conditions: substrate (50 mg), ethanol (4.00 mL), yttrium triflate (0.05 mmol), H_3PO_4 (0.05 mmol), 180 °C, 2 h.[18]

tion.[3,6,14] To test this proposal, we performed the conversion of corn husk in the biphasic solvent system ChCl/oxalic acid solvent/organic solvent–extractant at 100 °C for 2 h (Table 2). Dimethylsulfoxide and γ-valerolactone were miscible with the DES and therefore unsuitable for use, while 2-*sec*-butylphenol formed dark-colored viscous substances, and *n*-butanol reacted with oxalic acid forming dibutyl oxalate. In turn, organic solvents such as ethyl acetate, MIBK, anisole, and 1,2-dimethoxybenzene formed a second phase and favored the acid-catalyzed transformation of lignocellulose into a small suite of valuable products (glucose yield up to 27 wt %, xylose yield up to 33 wt %, HMF yield up to 13 mol %, FF yield up to 52 mol %, Table 2, entries 1–4). Among them, MIBK afforded optimal yields of glucose, xylose, HMF, and FF (yields 27 wt %, 22 wt %, 9 mol % and 52 mol %, respectively, Table 2, entry 2). MIBK is an acceptable "green" solvent for chemical processing.[35] Importantly, the yields of FF achieved in the DES-based biphasic solvent systems compare favorably with commercialized processes that are typically performed in water under forcing reaction conditions (most commercial units are operated at a temperature of 150–220 °C, with a typical FF yield of 50%, based on the pentosan content).[36] Equally importantly, the extraction of FF into the organic phase during processing serves for immediate isolation of this product, posing some advantages over commercialized processes that frequently involve energy demanding distillation of the aqueous media or steam stripping.[36] In our hands, MIBK contained 85 mol % of the FF produced and 33 mol % of HMF produced, based on total yields of these products after processing. The residual furans, found in the ionic liquid phase, can be fully separated by secondary extraction with ethyl acetate, as was confirmed by chromatography analysis of the recovered reaction media. The recovery of monosaccharides form the DES remains to be investigated.

The ultimate goal of our study was to translate the findings into conversions of complex raw (lingo)cellulosic biomass into valuable platform products. Accordingly, we turned our attention to the conversion of these types of substrates in ChCl/oxalic acid/MIBK, including terrestrial lignocellulose (corncobs and softwood chips), marine macroalgae (*U. lactuca*), and microalgae (*P. cruentum*, Table 2). Corncob yielded somewhat similar outcomes of saccharides to corn husk, after a 2 h reaction at 100 °C, namely, glucose in 25 wt % yield and xylose in 21 wt % yield (corncob, Table 2, entry 5), compared to a glucose yield of 27 wt % and xylose in a yield of 22 wt % (corn husk, Table 2, entry 2). However, the yield of FF was slightly lower (yield 41 mol %, Table 2, entry 5). Nevertheless, a higher yield of FF was attainable after longer processing in the DES-based biphasic solvent system (4 h, FF yield 51 mol %, Table 2, entry 6). The complex lignocellulose that was less reactive than the other substrates employed in this study was unmistakable. Acceptable conversion of softwood chips required longer reaction times to achieve good yields of furaldehyde (100 °C, 4 h, yield 53 mol %, Table 2, entry 8; 55 mol %, Table 2, entry 9). The softwood glucans are less convertible compared to other substrates (conversion up to 26 wt %, Table 2, entries 7–9), caused by the prevalence of cellulose, which is less reactive in the acidic DES (Table 1), leaving a finely powdered unreacted cellulosic residue with IR spectra consistent with microcrystalline cellulose (Figure S5).[b] On the other hand, algal biomass showed excellent reactivity toward derivative low-molecular weight carbohydrates or furans (glucose yield up to 68 wt %, xylose yield up to 73 wt %, HMF yield up to 9 mol %, FF yield up to 72 mol %, Table 2, entries 10–15). The optimal conditions varied for each substrate and provided differing portfolios of products. The conversion of *U. lactuca* at 100 °C for 2 h afforded high yields of glucose (yield 51 wt %, Table 2, entry 10) and FF (yield 60 mol %, Table 2, entry 10). Interestingly, the reaction of *P. cruentum* could be targeted toward specific major products. When employing optimal reaction parameters for each targeted product, *P. cruentum* yielded impressive yields, respectively, of glucose (100 °C, 2 h, yield 68 wt %, Table 2, entry 11), FF (100 °C, 4 h, yield 72 mol %, Table 2, entry 12), and xylose (80 °C, 2 h, yield 73 wt %, Table 2, entry 13). These results reveal that the glucan polysaccharides in terrestrial substrates are more resistant to the reaction conditions than those present in marine sources (where conversions of up to 99 wt % were realized, Table 2, entries 10–15). This observation reflects the prominence of structurally branched glucans in algal materials,[37–39] which are fully convertible in the acidic solvent (Tables 1 and 2).

As part of our broader efforts toward the catalytic valorization of cellulose, we have developed methods to directly convert cellulose into industrially useful monosaccharides and furan-type molecules in zinc chloride hydrate solvent,[27] or into low-molecular weight carbohydrates in co-solvent system $[C_4mim]Cl$/ChCl/oxalic acid,[19] or into ethyl levulinate (ELev) in ethanol under the action of acidic metal triflates.[18] While these methods were applicable to refined cellulose, in no case did the processing afford the productive valorization of native softwood in ionic liquids or ethanol.

Those processes are persistently accompanied by the formation of humins and losses of target products. As mentioned above, catalytic processing of the softwood with the DES afforded a finely powdered cellulosic residue (recovered after the processing in DES/MIBK at 100 °C for 5 h, Table 2, entry 9). This residue could be subjected to catalytic processing in the DES, under more forcing conditions, which are unsuitable to optimal yields of the products listed in Table 2. Pleasingly, the conversion of this cellulose residue obtained from softwood enabled substantial improvements to the yield of desirable products (Table 3, entries 2, 4 and 6), relative to the conversion of the crude biomass under identical conditions (Table 3, entries 1, 3, and 5), importantly avoiding the undesirable formation of humins. This two-step process enables maximum use of the raw, bulk, softwood input material, and its conversion into valorized products, neatly avoiding losses and the production of secondary waste streams. The initial valorization of the native softwood biomass in the DES, followed by transformation of the unreacted cellulosic portion into significantly value added low-molecular weight saccharides, furans, or ELev. In total, we are able to fully convert native softwood xylans, yielding 55 mol % of FF (based on the xylan content in the softwood, Table 3, entry 9) and to convert up to 88 wt % of native cellulose into 58 wt % of useful chemicals (based on the glucan content in the softwood), after the two-step processing of native softwood and softwood-derived cellulose.

CONCLUSIONS

This work demonstrates the catalytic valorization of low-value raw, native bulk cellulosic biomass into significantly value-added platform molecules in the DES based on ChCl and oxalic acid. Its power is demonstrated by effecient conversions of polysaccharides of crude and previously untreated raw biomass, leading to high yields of useful small molecule derivatives. Model reactions of refined (poly)carbohydrates improved our fundamental understanding toward the processing of native lignocellulose and algal biomass. We show that the acidic DES promotes transformations of structurally branched glucans, fructans, or xylans, into glucose (yield up to 68%), fructose (yield up to 60%), xylose (yield up to 73%), HMF (yield up to 14%), or FF (yield up to 72%). The studies allow a definition of optimum conditions to favor the conversion of selected native biomass into derivative products. Cellulose, a *β*-linearly linked glucose polymer, is less reactive under our conditions but can be recovered after the processing of softwood and converted into useful chemicals, creating additional value from the input materials.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acssuschemeng.9b06528.

> Supporting tables and figures, analytical and general methods, and IR and NMR spectra (PDF)

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The authors all contributed to the drafting of the manuscript, acquiring and processing the data, and/or intellectually to the conceptualization and management of the project.

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ABBREVIATIONS

DES,deep eutectic solvent; ChCl,choline chloride; $[C_4mim]$-Cl,1-butyl-3-methylimidazolium chloride; HMF,5-(hydroxymethyl)furfural; FF,furfural; DMSO-d_6,deuterated dimethylsulfoxide; MIBK,methyl isobutyl ketone; ELev,ethyl levulinate

ADDITIONAL NOTES

[a] Microcrystalline cellulose is a polysaccharide obtained by treatment of native cellulose with aqueous solution of mineral acids,[9] while dissolving pulp is a refined cotton linter pulp with a low degree of polymerization.[40]

[b] With softwood, the recovered and dried unreacted portion of the substrate (yield 52 wt % based on the substrate) was a fine cellulosic material (cellulose content 80 wt %) with some residual lignin (19 wt %). Such cellulose can potentially be a valuable substrate for large volume cellulose refining technologies, such as paper manufacturing or fiber production, as well as for the synthesis of platform chemicals.

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Declaration, author contributions and copyright information

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Iurii Bodachivskyi (graduate research student) developed the methodology, conducted research, including experimental work, data collection and data analysis, and drafted the manuscript. Prof. D. Bradley G. Williams (principal supervisor) and Dr Unnikrishnan Kuzhiumparambil (co-supervisor) supervised Iurii Bodachivskyi's research activities, provided conceptual advice and revised the manuscript.

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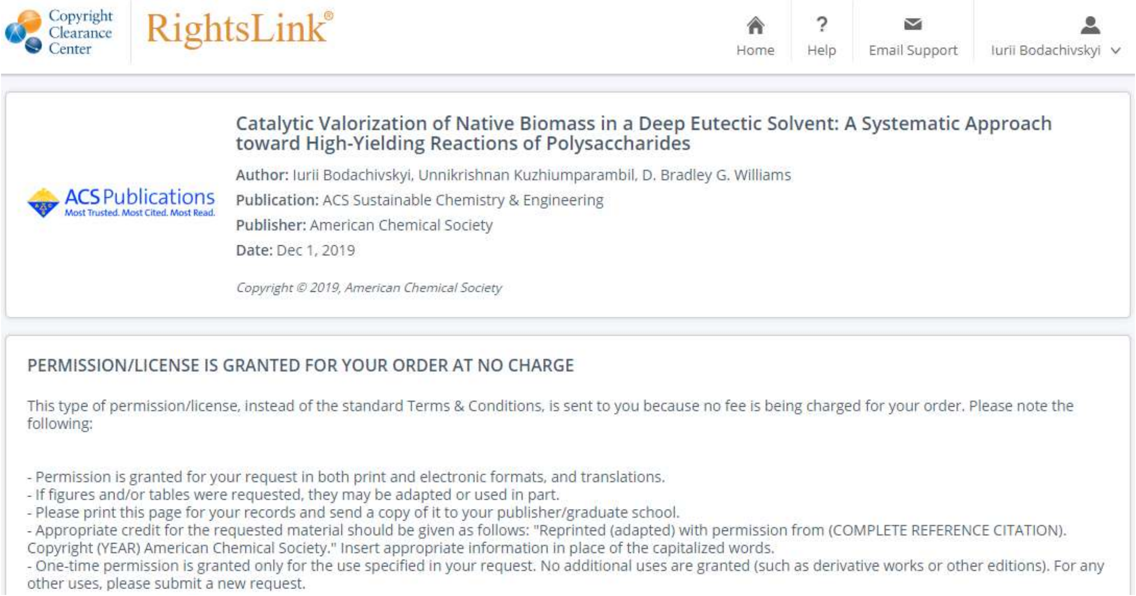

Catalytic Valorization of Native Biomass in a Deep Eutectic Solvent: A Systematic Approach toward High-Yielding Reactions of Polysaccharides

Author: Iurii Bodachivskyi, Unnikrishnan Kuzhiumparambil, D. Bradley G. Williams
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Chapter 4:

Dissolution of cellulose: are ionic liquids innocent or non-innocent solvents?

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Research Article

Dissolution of Cellulose: Are Ionic Liquids Innocent or Noninnocent Solvents?

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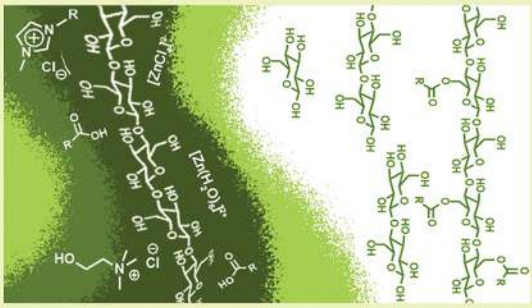

ABSTRACT: Cellulose is a naturally abundant and readily accessible substrate for large scale biorefinery technologies. There has been a significant focus on ionic liquids as alternative solvents for the valorization of cellulosic substances. Ionic liquids dissolve cellulose in varying degrees, facilitating ready chemical transformations. However, there is no self-contained set of knowledge and information on the influence (or not) of the simple dissolution process on the cellulose molecule. Herein, we detail the dissolution, recovery, and characterization of cellulose in various classes of ionic solvents in a systematic study. This provides a view of the stability of cellulose in each solvent. We consider the major classes of ionic liquids commonly employed for cellulose chemistry, the dissolution in zinc chloride hydrate systems, quaternary ammonium salts, and deep eutectic solvents under varied processing conditions. We regenerate cellulosic material from the solvent and characterize the polymer employing gravimetric analysis, IR spectroscopy, and size exclusion chromatography. Surprisingly, most ionic liquids employed caused reduction in the MW of the cellulose.

KEYWORDS: *Biomass, Cellulose, Cellulose solvents, Ionic liquids, Deep eutectic solvents*

INTRODUCTION

Cellulose is a linear β-(1 → 4) linked glucose polymer which forms a major portion of the cell walls of terrestrial plants.[1] Cellulosic substances are realistic alternative substrates (to crude oil) for the renewable production of bulk and fine chemicals,[1−3] given their global prevalence on a large scale, mostly as inexpensive (wood) or no value (waste streams such as from agricultural or horticultural) feedstocks. The chemical processing of cellulosic substances is challenging due to the strong intramolecular and intermolecular interactions, making them virtually insoluble in common aqueous or organic solvents.[3,4] To disrupt supramolecular structures, many processing technologies use specialty solvent systems that enable dissolution and subsequent processing of the polysaccharide.[5−7] Accordingly, there has been significant interest in the discovery and exploitation of solvents for cellulose to perform the many demanding tasks associated with cellulose refining industries.[5] Such specialty solvents are employed in the shaping of fibers and membranes, the synthesis of functionalized polysaccharides, such as cellulose esters, ethers, and graft copolymers, and in the hydrolysis-conversion of cellulosic materials into low molecular weight organic building block chemicals (platform molecules).[3,5,7,8]

The selection of solvents appropriate to a specific task remains a major prerequisite for cellulose-based technologies.[7] Reaction media that are suitable for some tasks may be deleterious for others: some solvents convert cellulose into soluble derivatives during dissolution by chemically reacting with the cellulose (known in the literature as derivatizing solvents). Others are presumed to retain the chemical composition of cellulose (known in the literature as nonderivatizing solvents).[6,7,9] The use of derivatizing solvents is typically restricted to a few commercialized processes. One is the Viscose process which relies upon the derivatization of cellulose into cellulose xanthate in an aqueous sodium hydroxide/carbon disulfide system.[5,7] Another example is the CarbaCell process where cellulose is derivatized into cellulose carbamates in concentrated aqueous urea solution.[5,7] Mixtures of organic acids and mineral acids are used in the commercial production of cellulose esters, and these systems are also considered to be derivatizing media.[7] The term not so innocent has also been applied to ionic liquids.[10,11] In this instance, the ionic liquid in question was derivatizing, in that it

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Table 1. Dissolution and Recovery of Cellulose in/from Zinc Chloride Solvents[a]

entry	solvent	cellulose	T (°C)	t (h)	recovered material (wt %)	M_w (g mol^{-1})	M_n (g mol^{-1})
1	$ZnCl_2 \cdot 2.5H_2O$	MCC	80	1	69	66800	46200
2			100		25	66500	41800
3	$ZnCl_2 \cdot 3.0H_2O$	MCC	80	1	96	14700	14100
4			100		73	12700	11700
5	$ZnCl_2 \cdot 3.5H_2O$	MCC	80	1	99	28100	14900
6			100		44	19800	12500
7		cotton linter	80	1.5	99	26700	24700
8		eucalyptus			79	45300	30000
9		*Pinus* (bleached)			91	14700	13600
10		*Pinus* (unbleached)			90	169000	149000
11	$ZnCl_2 \cdot 4.0H_2O$	MCC	80	1	99	36800	31900
12			100		52	38800	27400
13	$ZnCl_2 \cdot 4.5H_2O$	MCC	80	1	99	50200	44900
14			100		75	39200	32300
15	none	MCC				64800	58200
16		cotton linter				343000	321000
17		eucalyptus				363000	310000
18		*Pinus* (bleached)				442000	394000
19		*Pinus* (unbleached)				496000	375000

[a] The amount of the recovered material is specified in wt % based on input of cellulose. T = processing temperature; t = processing time; M_w = weight-average molecular weight; M_n = number-average molecular weight. Processing conditions: cellulose (100 mg) and solvent (5.0 g).

produced an adduct with the cellulose. In this paper we use the term derivatizing only when the solvent chemically reacts with the cellulose to form an adduct. We apply the term noninnocent to encapsulate all types of reactions, not only adduct formation, and innocent to mean that it does not cause or participate in any reactions with cellulose. This is to avoid the potential confusion between cellulose that has become derivatized by chemical adduct formation with the solvent, as compared to other types of modifications that do not involve adduct formation with the solvent (e.g., hydrolysis). The hydrolysis of cellulose, for example, while not an example where cellulose is derivatized, will be regarded as a non-innocent system rather than a derivatizing system.

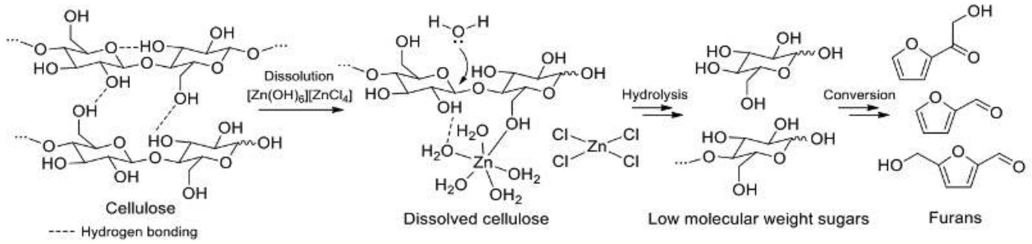
There is a high degree of interest in innocent solvents for the fractionation of native cellulosic biomass, production of cellulose fibers, or targeted chemical processing and functionalization of polysaccharides.[6,8,12] Aqueous solutions of metal-amino complexes and strong bases, inorganic molten salt hydrates, amine oxides, or solutions of strong electrolytes in organic aprotic solvents are the most frequent representatives of innocent solvents for cellulose.[5,7]

In other studies, ionic liquids (ILs) have drawn significant interest as a class of solvents for cellulose.[6,7,13−16] ILs are especially promising systems for sustainable biorefinery processes, owing to their benign nature and extremely low vapor pressure.[3,17] Many studies imply that ILs are innocent media.[7,8,16] However, many commonly applied systems, such as zinc chloride hydrate with a molecular formula $ZnCl_2 \cdot nH_2O$ (this system is considered to be an IL with the molecular formula $[Zn(OH_2)_6][ZnCl_4]$ in the case of n = 3),[18,19] imidazolium salts, or choline chloride-based deep eutectic solvents (DESs), have been shown to promote the transformation of polysaccharides into low molecular weight derivatives.[3,19−22] Separately, Welton and co-workers[10] have conducted some elegant studies showing that imidazolium carboxylate ILs are derivatizing, forming adducts with reducing sugars, and Laborie[23] also showed that similar ILs acetylate polysaccharides. Welton[10,24] also demonstrated that such ILs do not affect the degree of polymerization of the cellulose, compared to untreated substrate, employing gel permeation chromatography in LiCl/N,N-dimethylacetamide (LiCl/DMAC), also demonstrating that imidazolium chloride ILs are unreactive concerning the derivatization of cellulose. Several works[25−29] mention the depolymerization of cellulose in varied dialkylimidazolium salts. Imadazolium chlorides are included in this list, in conflict with Welton's report, indicating inconsistency in the literature based on existing data.

There have been a number of studies relating to the dissolution processes of cellulose in ILs and subsequent structural analysis of the recovered cellulose (mainly, determination of crystallinity or surface analysis)[4,19,30−32] but with little or no information providing an accurate quantitative measure of cellulose integrity in such solvents. Additionally, most studies scrutinize one or limited series of ionic solvents under differing processing parameters (loading of cellulose, temperature and time of the dissolution) thereby limiting or altogether preventing correlations to be made within the available information. What is lacking is a consolidated understanding of the influence of the various ILs on the molecular weight of the polysaccharide based on a systematic study. Rather, previous studies have focused on the functionalization/derivatization of the polysaccharides. However, the molecular weight of the cellulose can play a key role in the properties of derivatives thereof, as we have shown in film-forming ester derivatives of cellulose.[33]

In the present article, we systematically probe various classes of ILs, namely zinc chloride hydrate solvents ($ZnCl_2 \cdot nH_2O$, with n = 2.5–4.5), quaternary ammonium salts and DESs, as applied to the dissolution and recovery of cellulose, and provide the extent of the polymer stability for each solvent class. We provide practical recommendations for the use of this series of solvents. The aim of the present study is not to comprehensively cover a wide range of solvents and qualitatively analyze cellulosic substances recovered after the processing but rather to generate sufficient data to streamline the selection of ILs to the specific needs of a cellulose refinery.

Scheme 1. Dissolution and Conversion of Cellulose in Zinc Chloride Hydrate Solvents



■ MATERIALS AND METHODS

For the dissolution study, we used vacuum-oven-dried microcrystalline cellulose (MCC), cotton linter, and cellulose extracted from eucalyptus and *Pinus* (60 °C, 1 mbar, 12 h). The oven drying was conducted to minimize the influence of the variable water content present in the substrate on the tests. It has been shown that 1 wt % water content causes imidazolium-based ILs to lose their ability to dissolve cellulose, ostensibly because of competitive hydrogen of the water to the cellulose, inhibiting the disruptive hydrogen bonding between the anion of the IL and the cellulose hydroxyl groups.[34] Conversely, systems employing tetrabutylammonium chloride appear relatively insensitive to the presence of water up to 10 wt %.[35] Anhydrous zinc chloride and all ammonium salts were also carefully dried before the preparation of ionic solvents or their use for cellulose dissolution (120 °C, 1 mbar, 6 h for $ZnCl_2$; 80 °C, 1 mbar, 6 h for imidazolium salts; 22−24 °C, 0.01 mbar, 24 h for tetrabutylammonium chloride (TBAC)). We employed size-exclusion chromatography with multiangle laser light scattering analysis to determine molecular weight distributions of the cellulosic materials (details of the method are given in the Supporting Information; data for the feedstock substrates are given in Tables 1−3). Data are represented as the weight-average molecular weight (M_w) and the number-average molecular weight (M_n; MW as used in this text denotes generically either or both of M_w and M_n) and are shown to three significant figures only (Tables 1−3). Chromatographic analysis was conducted using DMAC containing LiCl as a modifier for both sample preparation and as the eluent, as has been established in the literature.[36,37] The LiCl/DMAC organic electrolyte solution system is considered innocent, rendering it suitable for the present study.[27,28,32,37−39]

Infrared spectroscopy (IR) and gravimetric analysis were used to compare gross structural features and mass recoveries, respectively, for cellulose recovered from ionic solvents, relative to the initial substrates.

Details of materials and analytical methods are given in the Supporting Information.

For the dissolution, cellulose (100 mg) and ionic solvent (5.0 g) were introduced to a round-bottom flask equipped with a magnetic follower and the reactor was sealed. The mixture was heated and stirred at the predetermined temperature for a fixed period of time, resulting in a transparent solution or a turbid suspension. After completion of the process, the system was cooled to ambient temperature (18 °C).

For the regeneration of cellulose from $ZnCl_2 \cdot nH_2O$, the resulting cooled mixture was diluted with aqueous hydrochloric acid (0.01 M, 40.0 mL) to precipitate polysaccharide, which was recovered, washed with deionized water (4 × 40.0 mL), vacuum oven-dried (60 °C, 1 mbar, 12 h), and weighed to calculate the percentage of the recovered material.

For the regeneration of cellulose from imidazolium salts, the resulted mixture was diluted with acetonitrile (40.0 mL) to precipitate polysaccharide, which was recovered, washed with acetonitrile (4 × 40.0 mL), vacuum oven-dried (60 °C, 1 mbar, 12 h), and weighed to calculate the percentage of the recovered material.

For the regeneration of cellulose from TBAC and DESs, the resulted mixture was diluted with deionized water (40.0 mL) to precipitate polysaccharide, which was recovered, washed with deionized water (4 × 40.0 mL), vacuum oven-dried (60 °C, 1 mbar, 12 h), and weighed to calculate the percentage of the recovered material.

■ RESULTS AND DISCUSSION

Zinc Chloride Hydrate Solvents. Although zinc chloride hydrate solvents are commonly employed as nonderivatizing media for the fractionation of native biomass or functionalization of individual polysaccharides,[6,19,40,41] depolymerization of cellulosic substances has been noted in such media but without substantive studies relating to this specific point.[20,42,43] They are likely, therefore, noninnocent. We sought to understand a little better the influence of zinc chloride hydrate solvents on cellulose, using systems with the molecular formula $ZnCl_2 \cdot nH_2O$ (n = 2.5−4.5). Accordingly, MCC and bulk cellulose (cotton linter, eucalyptus, and *Pinus*) were subjected to dissolution under various processing conditions followed by cooling to room temperature. Recovery of the cellulosic material was effected by precipitation thereof with aqueous hydrochloric acid (0.01 M) at ambient temperature (Note: precipitation of the cellulose with neat water causes coprecipitation of insoluble zinc salts),[6] washing with water and drying. All solvents tested but one ($ZnCl_2 \cdot 4.5H_2O$), permitted dissolution of MCC under the applied loadings of cellulose and dissolution conditions (Table 1, entries 1−12). The exception solvent, $ZnCl_2 \cdot 4.5H_2O$, partially dissolved the cellulose, forming a suspension (Table 1, entries 13 and 14). As proposed by Martin and colleagues,[19] the dissolution takes place through the disruption of hydrogen-bonding network between carbohydrate polymers by the direct coordination of hydroxyl groups to Zn^{2+} or to the water in the first hydration shell of the ion $[Zn(OH_2)_6]^{2+}$ (Scheme 1). With highly hydrated $ZnCl_2 \cdot 4.5H_2O$, the coordination most likely occurs through the second hydration shell, restricting effective interactions between cellulose and zinc ion, ultimately leading to incomplete solubilization. The solvent−substrate interactions may be also negatively influenced by the increased heterogeneity of the substrate. As detailed in the present study, dissolution of native cellulose (cotton linter, eucalyptus, and *Pinus* cellulose, examples of specimens with "increased heterogeneity") required slightly longer processing times (1.5 h) compared with MCC, owing to its more rigid molecular structure (i.e., higher molecular weight and often stronger supramolecular bonding between polymers) and larger physical size (Table 1).[44]

As is evident from Table 1, the dissolution process caused mass losses of cellulose to varying degrees, as measured by the

Scheme 2. Dissolution and Hydrolysis of Cellulose in Dialkylimidazolium Chlorides, R = Alkyl

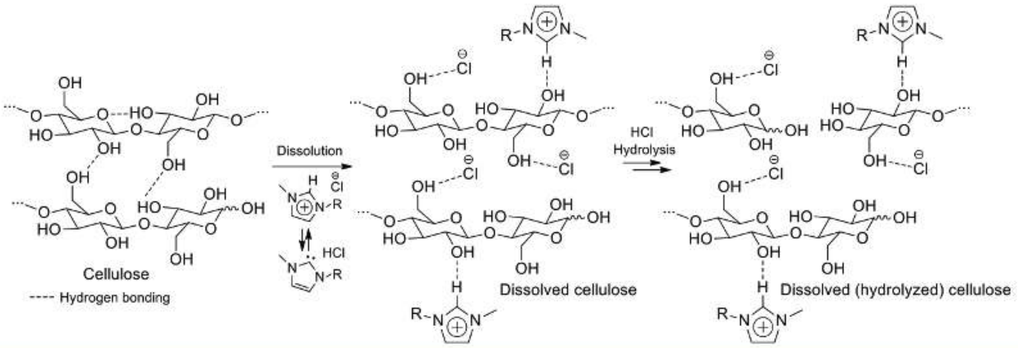


Table 2. Dissolution and Recovery of Cellulose in/from Quaternary Ammonium Salts[a]

entry	solvent	cellulose	T (°C)	t (h)	recovered material (wt %)	M_w (g mol^{-1})	M_n (g mol^{-1})
1a	[C_4 mim]Cl	MCC	100	1	96	73 200	69 500
1b						63 400[b]	55 800[b]
2a			120	1	94	104 000	98 000
2b						37 300[b]	31 300[b]
3a		cotton linter	100	6	109	135 000	131 000
3b						107 000[b]	97 400[b]
4a		eucalyptus	100	6	107	211 000	196 000
4b						106 000[b]	94 000[b]
5a		*Pinus* (bleached)	100	6	107	490 000	448 000
5b						212 000[b]	149 000[b]
6a		*Pinus* (unbleached)	100	6	99	197 000	187 000
6b						297 000[b]	234 000[b]
7a	[C_6 mim]Cl	MCC	100	1	99	77 600	73 100
7b						48 300[b]	41 300[b]
8a	[C_8 mim]Cl	MCC	100	1	100	98 700	92 600
8b						37 400[b]	32 100[b]
9a	TBAC	MCC	100	1	92	62 400	57 000
9b						40 100[b]	35 000[b]
10	none	MCC				64 800	58 200
11		cotton linter				343 000	321 000
12		eucalyptus				363 000	310 000
13		*Pinus* (bleached)				442 000	394 000
14		*Pinus* (unbleached)				496 000	375 000

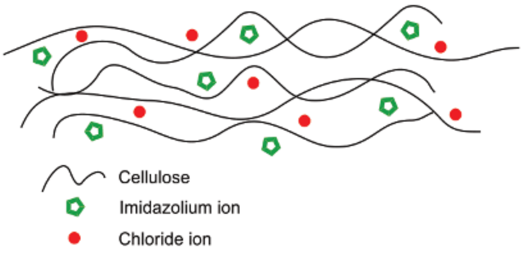
[a] The amount of the recovered material is specified in wt % based on input of cellulose. T = processing temperature; t = processing time; M_w = weight-average molecular weight; M_n = number-average molecular weight; [C_4 mim]Cl = 1-butyl-3-methylimidazolium chloride; [C_6 mim]Cl = 1-hexyl-3-methylimidazolium chloride; [C_8 mim]Cl = 1-octyl-3-methylimidazolium chloride. Processing conditions: cellulose (100 mg), solvent (5.0 g). [b] M_w and M_n were determined by the direct analysis of the diluted ionic liquid solutions, without regeneration of the dissolved cellulose.

mass recovered. As a general observation, the lower the water content in the zinc chloride hydrate, the higher the losses of cellulose and the lower the molecular weight of the recovered solids relative to the input MCC (Table 1, entries 3−6, 11−15). The values stabilized to a certain degree in response to the growing hydration number. This is fully consistent with the increasing acidity of the zinc chloride hydrate with reducing levels of water present.[43,45] Increased acidity leads to more rapid hydrolysis of the cellulose, forming water-soluble di-, tri- and short chain oligosaccharides, that will not precipitate with aqueous HCl (Scheme 1).[20,43,45]

Bulk cellulose (cotton linter, eucalyptus, and *Pinus* cellulose) was also susceptible to MW reductions, during dissolutions in $ZnCl_2 \cdot 3.5H_2O$ at 80 °C for 1.5 h (Table 1, entries 7−10 and 16−19). The unbleached *Pinus* cellulose was somewhat resistant to hydrolysis, consistent with the lesser degree of processing that would maintain the cross-linked native molecular structure to a greater extent and afford a substrate of greater heterogeneity. A second general observation is that, for dissolutions conducted at 80 °C, more of the cellulose was retained. At 100 °C (Table 1, entries 2, 4, 6, 12, and 14), the hydrolysis processes are accelerated, as is evident from the mass losses. These more substantial mass losses are accompanied by lower M_w and M_n of the recovered material. At the elevated temperature, hydrolysis of the cellulose is likely accompanied by the conversion of the low molecular weight water-soluble saccharides into furans (Scheme 1).[20,43,45] The hydrolysis is associated with the induced Brønsted acidity, caused by Lewis acid-assisted Brønsted acidity, which affords systems with pH 0.5 to 1.1 depending on the Zn/H_2O ratio, while the onward reaction to produce furanoids depends on both Lewis and Brønsted acidity.[20,43,45] The unusually high apparent molecular weight of the recovered material from $ZnCl_2 \cdot 2.5H_2O$ warrants comment. The recovered material was brown in color, likely caused by the formation of humins (high molecular weight condensation products formed by the reaction of saccharides and furans).[46] This is consistent with observations noted in the literature.[42] IR analysis of the regenerated material demonstrated the broadening of the O−H stretching mode of cellulose and the occurrence of two new peaks at 3490 and 3438 cm^{-1}, relating to the intramolecular bonding between the OH groups,[32] as well as a new C−O vibration mode at 995 cm^{-1}, that could reasonably be attributed to humins adsorbed on the cellulose surface (Supporting Information, Figure S1).[32,47,48] There was also a decrease in the intensity of characteristic vibrations for MCC at 2989−2943 cm^{-1} (CH_2 antisymmetric stretch), 1428 cm^{-1} (CH_2 scissor vibration), and 1103 cm^{-1} (ring asymmetric stretch), consistent with reduced cellulose content in the recovered material (Figure S1).[32,47,48] It is therefore possible that the formation of cellulosic-humin composites in $ZnCl_2 \cdot 2.5H_2O$ is responsible for the high MW of the regenerated material (Table 1, entries 1 and 2), incidentally coinciding with the MW recorded for MCC (Table 1, entry 15). With $ZnCl_2 \cdot 3.0–4.5H_2O$ and for the processes at lower temperature (80 °C), negligible amounts of humins were noted (by observation; Table 1, entries 3, 5, 11, and 13).

Quaternary Ammonium Salts. Quaternary ammonium salts are another class of ILs that have gained widespread acceptance as nonderivatizing solvents for biorefinery practices.[7,8] Among them, dialkylimidazolium salts are the most commonly employed.[21] It is considered that the concerted action of imidazolium cations and their counterions, such as chloride or acetate anions, orient the hydroxyl groups of cellulose and disrupt the hydrogen bonding between cellulosic aggregates ultimately achieving full dissolution in the ionic media (Scheme 2);[49,50] however, the exact mechanism remains to be established.[50] As mentioned above, some recent work has shown that not all classes of imidazolium-based ionic liquids are nonderivatizing or innocent media.[10,29] To better understand this class of ILs with a focus on imidazolium chloride systems, we performed the processing of cellulose in 1-butyl-3-methylimidazolium chloride ($[C_4 mim]Cl$), 1-hexyl-3-methylimidazolium chloride ($[C_6 mim]Cl$), or 1-octyl-3-methylimidazolium chloride ($[C_8 mim]Cl$) under various conditions, followed by recovery of the cellulose. With this class of ILs, MCC is freely soluble in the solvent media under our conditions, but care must be taken during the precipitation of cellulose. The precipitation and washing of cellulose was performed with acetonitrile; dilution with protic solvents, such as water or low molecular weight alcohols, caused the formation of gel-like substances that were difficult to purify.[51] Cellulose recovered from solutions of MCC in the ILs demonstrated higher MW values than the substrate, also showing higher MW with increasing length of the alkyl substituent of the imidazolium ring, and in response to elevated temperature (Table 2, entries 1a, 2a, 7a, 8a, and 10). An increase of the apparent degree of polymerization of Avicel cellulose after dissolution in $[C_4 mim]Cl$ was previously reported, but with no rationalization of the observed data.[25,30] Other studies have identified the interaction of the reducing-end group of cellodextrins and 1-methyl-3-ethylimidazolium acetate. If this were the only interaction present, changes to the MW would be rather small.[10,29,52] It is possible that the results of size-exclusion chromatography are in response to the lasting adsorption of imidazolium-based ILs on the surface of cellulose (Schemes 2 and 3). This would serve to increase the observed MW of the polymer due to its increased apparent physical size.[53,54] Interrogation of the IR spectra of the substrate and the recovered cellulose showed new C−H stretching vibrations at 2988 and 2960 cm^{-1} consistent with methyl groups, likely corresponding to the alkyl chains of the IL (Supporting Information, Figure S2).[55] In addition, the specific solvent−solute interactions are evidenced by a decrease of characteristic bands for cellulose at 1428 (CH_2 scissors vibration), 1335 (OH in-plane deformation), 1315 (CH_2 tip vibration), and 1103 cm^{-1} (ring antisymmetric stretch).[32,47] In contrast to MCC, the dissolution of bulk cellulose required extended processing times (6 h). These extended dissolution times potentially enable the acid-catalyzed hydrolysis of the polysaccharides into derivatives with lower MW.[56−58] This was indeed found to be the case, based on the MW of the cellulose regenerated from solution (Table 2, entries 3−5). Notwithstanding the lower MW, the amount of recovered cotton linter, eucalyptus, and *Pinus* (bleached) cellulose was above 100 wt % after processing (Table 2, entries 3a−5a). These gravimetric results support the notion that the IL remains associated with the polymer after recovery (Scheme 3). To confirm this, the regenerated cotton linter was allowed to swell in deuterodimethyl sulfoxide-d_6 at room temperature for 12 h in an attempt to leach some of the residual IL into the deuterated solvent. Follow up ^{1}H NMR spectroscopy-analysis of the decanted liquid phase identified a small amount of $[C_4 mim]Cl$ (approximately 4 wt %, based on the regenerated cellulose; Figure S3), providing definitive evidence for the presence of residual IL in the polymer matrix. These results, supported by both the recovered mass and NMR spectroscopy, are in contrast to previous work which indicated the regenerated cellulose to be free from IL.[59]

Scheme 3. Cartoon Proposal for the Structure of the Regenerated Cellulose from Dialkylimidazolium Chlorides



To avoid the putative adsorption of imidazolium salts to the cellulose, and the confounding influence thereof on the analytical results, we conducted size-exclusion chromatography analysis of ionic liquid solutions of cellulose without regeneration of the polymer (Table 2). Recall that in the first set of experiments the cellulose was regenerated by precipitation thereof from the IL solution using acetonitrile as antisolvent. In the present instance, the direct analyses were performed by dilution of the cellulosic solutions with LiCl/DMAC to the desired concentration, followed directly by size-exclusion chromatography analysis. This approach has been

Table 3. Dissolution and Recovery of Cellulose in/from DESs[a]

entry	solvent (molar ratio)	cellulose	T (°C)	recovered material (wt %)	M_w (g mol^{-1})	M_n (g mol^{-1})
1	ChCl/oxalic (1:1)	MCC	100	83	61 800	57 100
2			120	57	394 000	178 000
3		cotton linter	100	75	126 000	99 000
4		eucalyptus	100	80	64 900	58 000
5		*Pinus* (bleached)	100	78	75 500	69 400
6		*Pinus* (bleached)	100	67	126 000	115 000
7	ChCl/citric (1:0.5)	MCC	100	100	68 900	62 400
8			120	93	122 000	101 000
9	ChCl/malic (1:1)	MCC	100	96	75 700	65 900
10			120	91	101 000	86 800
11	Gly/malic (1:1)	MCC	100	98	146 000	107 000
12			120	109	205 000	134 000
13	Pro/malic (3:1)	MCC	100	91	78 100	71 400
14			120	111	92 700	82 600
15	ChCl/imidazole (3:7)	MCC	100	99	65 000	59 000
16			120	99	78 800	75 500
17	none	MCC			64 800	58 200
18		cotton linter			343 000	321 000
19		eucalyptus			363 000	310 000
20		*Pinus* (bleached)			442 000	394 000
21		*Pinus* (unbleached)			496 000	375 000

[a] The amount of the recovered material is specified in wt% based on input of cellulose. T = processing temperature; M_w = weight average molecular weight; M_n = number average molecular weight; ChCl = choline chloride; Gly = glycine; Pro = proline. Processing conditions: cellulose (100 mg), solvent (5.0 g), 2 h.

previously employed by Welton and colleagues.[24] Our results demonstrate that [C_4 mim]Cl is effectively innocent toward MCC at 100 °C (Table 2, entry 1b) but reduces its MW at higher temperature (Table 2, entry 2b), likely due to the acid-catalyzed hydrolysis of the polysaccharides. At elevated temperature, the ionic solvent is known to decompose into transient *N*-heterocyclic carbene and hydrochloric acid (Scheme 2).[24,56−58] The latter would catalyze the hydrolysis of glycosidic linkages in cellulose, reducing the MW of the polymer.[58] This outcome is repeated with imidazolium salts with longer alkyl substituents, such as [C_6 mim]Cl and [C_8 mim]Cl (Table 2, entries 7b and 8b), becoming slightly enhanced with the latter systems.

With regenerated bulk cellulose, we observed a decrease of MW (Table 2, entries 3a−6a), relative to the substrates (Table 2, entries 11−14), with the exception of *Pinus* bleached cellulose (Table 2, entry 5a), which gave slightly higher MW values. However, when cellulose was dissolved and then analyzed directly without regeneration, a reduction of MW was observed for all instances (Table 2, entries 3b−6b), supporting the notion that the IL becomes adsorbed to the cellulose during the regeneration process. This also provides a much clearer picture of the noninnocent nature of the IL.

We also attempted dissolution of cellulose in tetrabutylammonium chloride (TBAC), another IL with a growing interest in the field.[35,60] Cellulose is not fully soluble in TBAC and even after extended processing we observed a turbid suspension. Although the chloride anion is an excellent candidate for hydrogen bonding and thus for hydrogen bond disruption, the symmetrical and sterically hindered ammonium cation is less suited to the task,[61] accounting for the low solubility of cellulose in this solvent. The recovery of cellulose included dilution and washing with water. With TBAC, the mass of the recovered MCC and its MW were both diminished, possibly due to hydrolysis of the polysaccharide into soluble derivatives (Table 2, entry 9a and 9b). While the exact mechanism of hydrolysis is unknown for this IL, the presence of high activity chloride ion (nonsolvated) is implicated in strong hydrogen bonding[34] and serves to accelerate hydrolysis reaction.[62,63] IR analysis revealed no significant qualitative changes of the recovered cellulose, indicative of essentially identical specimens throughout (Figure S2).

Deep Eutectic Solvents. Finally, we turned our attention to the processing of cellulose in DESs. These systems are a class of green and sometimes fully renewable ILs, in which there is significant promise for cellulose biorefinery.[64] DESs have been employed in the fractionation of native lignocellulose into individual macromolecules, production of cellulose nanofibers and nanocrystals, and in the synthesis of various macromolecular and low molecular weight cellulose derivatives.[3,22,64−66] Some DES systems are known to solubilize polysaccharides, while others chemically transform cellulosic materials into derivative substances.[64−68] In the present study we systematically probe a selected set of DESs for the dissolution of cellulose.

To do this, the processing of cellulose was conducted in deep eutectic systems based on choline chloride (ChCl) in combination with oxalic, citric or malic acids (ChCl/xx acid), on ChCl and imidazole (ChCl/imidazole), on glycine combined with malic acid (Gly/malic), or on the mixture of proline and malic acid (Pro/malic), all of which have been previously applied to the dissolution or conversion of polysaccharides.[64] At a loading of 2 wt % cellulose based on the solvent, all DES systems provided only partial solubility of the polymer, resulting in turbid dispersions after processing at 100 °C, or 120 °C, for 2 h (Table 3). More highly concentrated solutions of cellulose in DES (up to 6.48 wt %) have been detailed in the literature only with pretreated cotton linter pulp, while the dissolution of nonpretreated

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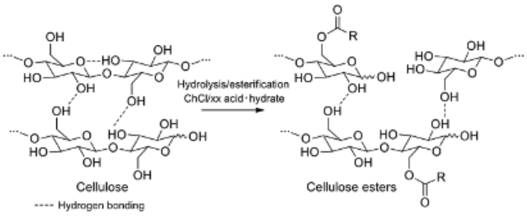
materials has largely been restricted to concentrations below 0.8 wt %.[67−70] The recovery of cellulose from DES systems was performed by precipitation and washing of the precipitated cellulose with water. Gravimetric analysis of the recovered materials established substantial mass losses for MCC and bulk cellulose samples processed in ChCl/xx acid solvents (Table 3, entries 1−10), likely due to the acid-catalyzed hydrolysis of cellulose into water-soluble derivatives, such as oligosaccharides or their esters (with low degree of substitution). At 120 °C, the MW of the recovered cellulosic samples was noted to increase. We considered that this outcome potentially relates to the esterification of the polysaccharides by the organic acid (Scheme 4). IR analysis revealed a stretching vibration at 1730 cm^{-1}, corresponding to the ester C = O stretch (Figure S3).[55] This is consistent with our recent observations relating to the production of ethyl levulinate from saccharides performed in the presence of ChCl/oxalic acid and ethanol, where the production of some ethyl oxalate was noted.[71] We observed similar C = O stretching vibrations in the region 1740−1710 cm^{-1} for cellulose processed in amino acid−based solvents Gly/malic acid and Pro/malic acid (Table 3, entries 11−14, and Figure S3).[55] There were also notable increases in the weight percentage of the recovered polymer after the processing at 120 °C, for 2 h (Table 3, entries 12 and 14), correlating with esterification of the cellulose backbone. With ChCl/imidazole, we did not identify significant changes to the cellulose, based on IR and chromatography analyses, despite a modest increase of the MW after the processing at elevated temperature (Table 3, entries 15 and 16, and Figure S3).

Scheme 4. Processing of Cellulose in ChCl/xx Acid Systems, R = Organyl



CONCLUSION

This work details the dissolution of cellulose in various classes of ILs and provides valuable measures of the polymer integrity, based on results of gravimetric analyses, IR spectroscopy and size-exclusion chromatography. Although it is generally accepted (with some exceptions) that ILs are nonderivatizing and innocent media, our results highlight that this commonly held opinion is not necessarily valid and, in certain instances, is quite the opposite. Zinc chloride hydrate solvents were noted to transform cellulose into low molecular weight derivatives,[20,43] and this tendency strongly depended on the levels of hydration of ionic systems and rather determinatively on the processing conditions. Dialkylimidazolium chlorides resisted desorption from cellulosic substances during the recovery step and also promoted the hydrolysis of bulk cellulose during the extended processing time. In fact, only [C$_4$ mim]Cl was found to be essentially innocent and only at 100 °C. In all other cases, reduced MW was noted. While not especially significant, slight decreases of the molecular weight were also apparent during the processing of cellulose in tetrabutylammonium chloride. Third, deep eutectic solvents caused chemical reactions of the cellulose, such as hydrolysis, and became more directly involved through esterification reactions. This study highlights the reactivity of ionic media toward cellulose and demonstrates the need for the judicious selection of the processing conditions (type of cellulose, solvent, temperature, and time) to enable the selective production of desirable cellulose-derived materials. In particular, the recovery and purification of the targeted products must be carefully considered, especially when employing inorganic solvents or imidazolium salts.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acssuschemeng.0c02204.

Supporting figures, materials, analytical methods, and scheme (PDF)

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Author Contributions

The authors all contributed to the drafting of the manuscript, acquiring and processing the data, and/or intellectually to the conceptualization and management of the project.

Notes

The authors declare no competing financial interest.

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ABBREVIATIONS

IL, ionic liquid; DES, deep eutectic solvent; MCC, microcrystalline cellulose; MW, molecular weight; M_w, weight-average molecular weight; M_n, number-average molecular weight; DMAC, dimethylacetamide; [C$_4$ mim]Cl, 1-butyl-3-methylimidazolium chloride; [C$_6$ mim]Cl, 1-hexyl-3-methylimidazolium chloride; [C_8 mim]Cl, 1-octyl-3-methylimidazolium chloride; TBAC, tetrabutylammonium chloride; ChCl, choline chloride; Gly, glycine; Pro, proline

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Iurii Bodachivskyi (graduate research student) developed the methodology, conducted research, including experimental work, data collection and data analysis (except for size exclusion chromatography-analysis), and drafted the manuscript. Prof. D. Bradley G. Williams (principal supervisor) and Dr Unnikrishnan Kuzhiumparambil (co-supervisor) supervised Iurii Bodachivskyi's research activities, provided conceptual advice, and revised the manuscript. Charlotte J. Page, Dr Simon F. R. Hinkley and Dr Ian M. Sims (co-investigators) performed size exclusion chromatography-analysis and revised the manuscript.

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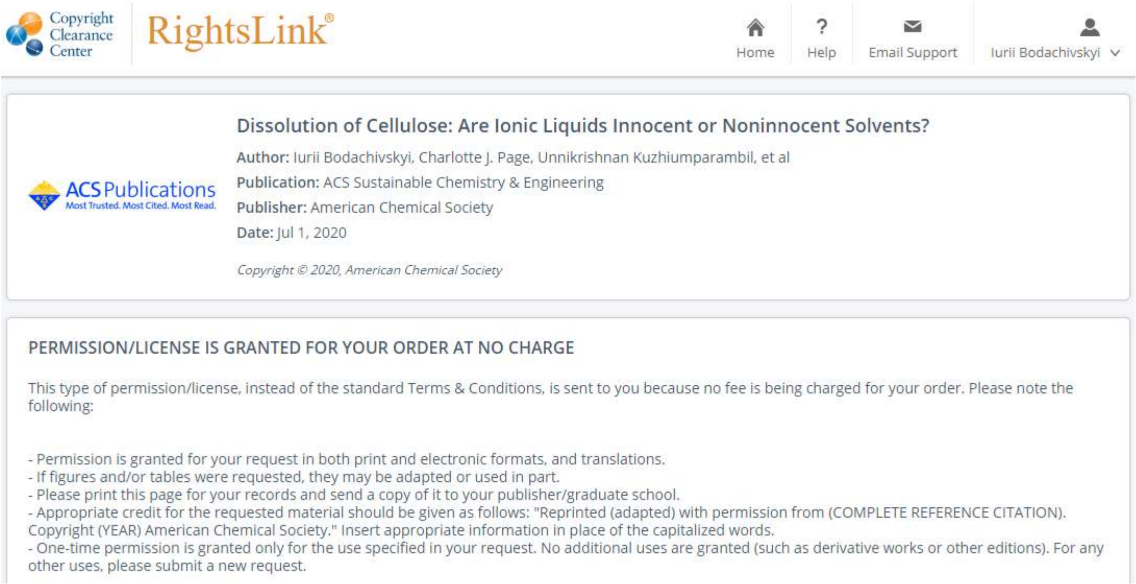

Dissolution of Cellulose: Are Ionic Liquids Innocent or Noninnocent Solvents?

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Chapter 5:

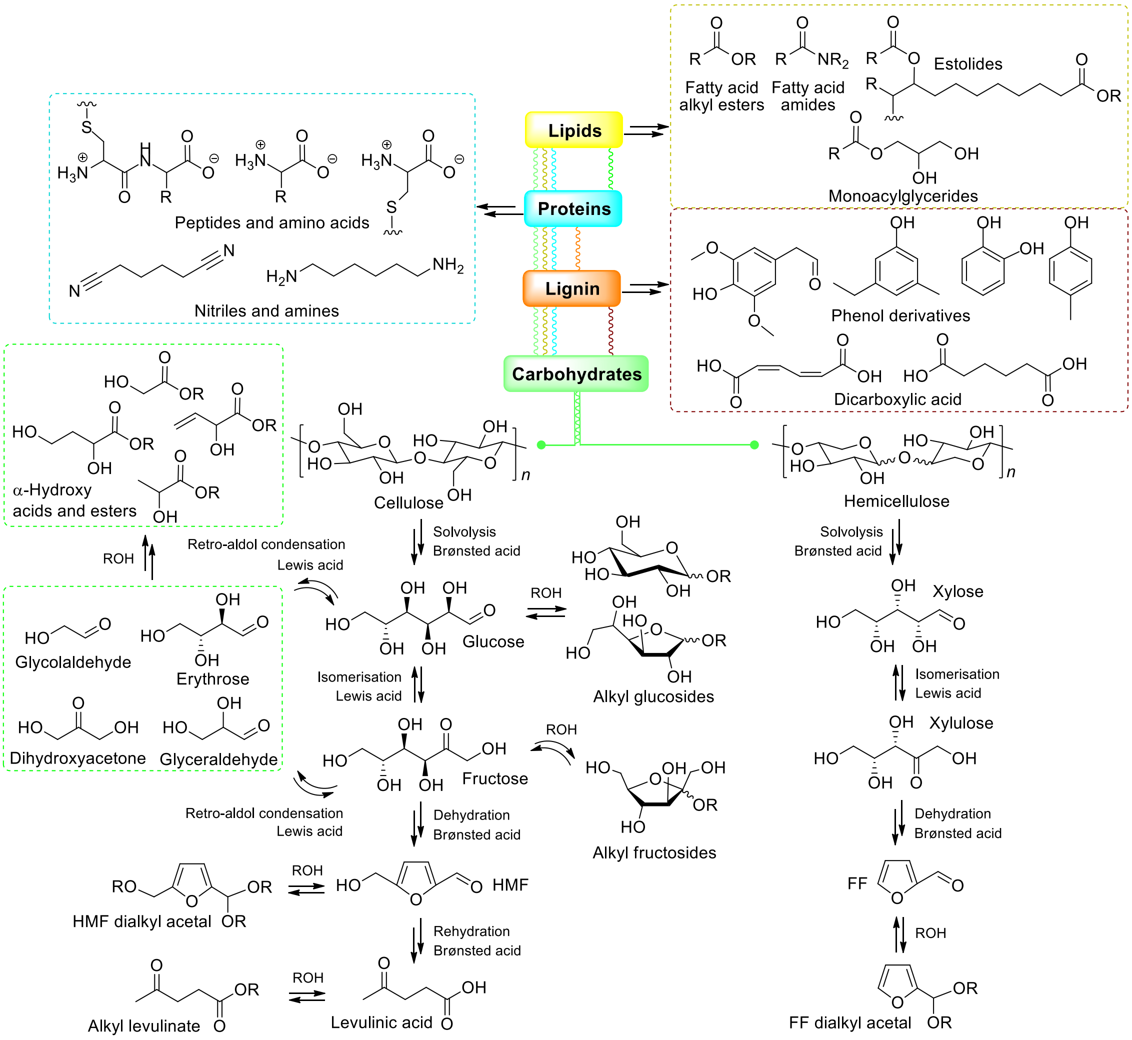
Account of this thesis, conclusions and future directions

5.1. Account of the conducted chemical research

5.1.1. Introduction

Biomass is a plant or animal material comprising one or more high molecular weight carbohydrates, lignin (aromatic polymers), lipids and proteins, and is naturally or artificially produced for food and energy needs.[1,10–12] Additionally, and alternatively to fossil-derived materials, macromolecular constituents of biomass show promise for the industrial synthesis of a large range of organic building block molecules (platform chemicals) as low-carbon or carbon-neutral replacement products (Scheme 5.1).[1,10–15] For example, polysaccharides are convertible into low molecular weight fermentable sugars, or into functional acids and esters.[1,10,12,16] Chemical or biochemical processing of lignin is known to form a suite of phenolic monomers, and sometimes dicarboxylic acids.[15,17–19] Lipids, such as triacylglycerides, can be transformed into manifold fatty acid derivatives, while the proteinaceous portion of biomass can be hydrolysed into amino acids for the further transformation into nitriles or amines.[10,11,20–24] In their own right, these many derivative molecules are useful speciality chemicals that can be further subjected to secondary valorisation into renewable fuel, plastics, detergents, lubricants, and other commodity products.[1,10,14,20,24,25] This makes the biorefinery a topic of significant current scientific, societal, and political interest. Herein, the key to success is catalysis on which the above-mentioned transformations rely.

Despite public attention across the globe and a growing number of research and commercial projects on the subject, there is still no solution for this problem. Most successful laboratory or pilot-scale methods are based on catalytic conversions of refined edible substrates, including low molecular weight saccharides, vegetable oils, or proteins.[1,10] At the industrial scale, these materials become food-competitive, undermining sustainability impacts relating to the use of renewable biomass. The ideal substrates for sustainable industrial chemical processing should be non-food-competitive, inexpensive, easily accessible (i.e., physical accessibility to natural resources), and be available in sizeable amounts.[1,10]



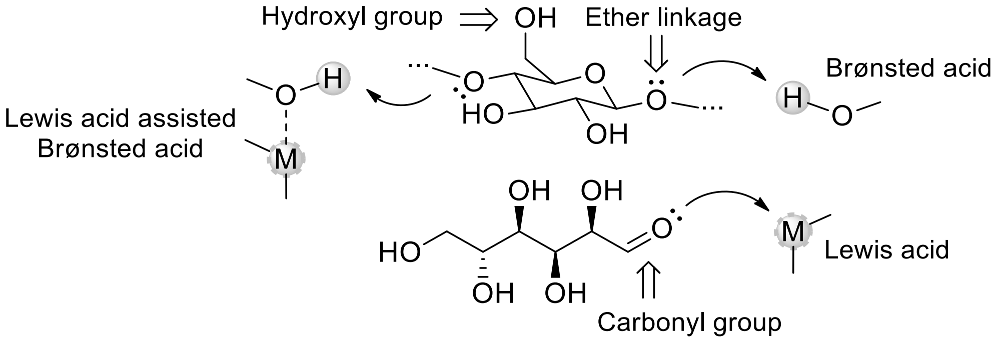
Scheme 5.1. Catalytic valorisation of biomacromolecules. R = H or alkyl; HMF = 5-(hydroxymethyl)furfural; FF = furfural.

Among various non-edible resources, terrestrial plant cell walls (lignocellulose) is the most naturally abundant material with the estimated net output of 150–170 billion tons per year.[26] Even with a poor mass balance of the biorefinery, the existing scale would significantly exceed the needs of materials for the total annual production of chemicals worldwide (ca. 1.2 billion tons per year).[26] In addition, there has been a ready and poised supply chain of lignocellulosic feedstock as zero or negative cost residues delivering by agriculture and food manufacturing, forestry, horticulture, paper, and cardboard recycling industries. Other promising high-volume sources of cellulosic biomass are non-food-competitive streams of marine and freshwater algae aquaculture.[1,10]

Notwithstanding the scale and availability of substrates, the chemocatalytic valorisation of lignocellulose generally remains industrially unviable for different reasons. In the first, it pertains to the rigid (supra)molecular structure of native plant cell walls, formed by inter- and intramolecular bonding of cellulosic polysaccharides and lignin, and sometimes other macromolecules.[27] These structures are virtually insoluble in most common aqueous or organic solvents and require forcing conditions to promote catalytic reactions. In the second, the efficient valorisation is compromised by the different reactivity of native polymers that are differentially dependent on the nature of the catalyst present and processing parameters. These conditions are often mutually exclusive for carbohydrates and lignins. For example, polysaccharides, such as cellulose ($\beta(1\rightarrow4)$ linearly linked glucose polymer) and hemicellulose (carbohydrate polymers often made of structurally branched xylose units), require the action of acid catalysis for the direct transformation into value added chemicals.[1,16] Conversely, lignins are the most efficiently converted via reductive or oxidative catalysis and typically in the basic reaction media.[17,18,28] A common strategy to circumvent these difficulties is to separate cellulosic and lignin polymers.[29] Despite widely commercialised pulping processes providing refined cellulose and lignin derivatives (these processes are known to alter the structure of lignin),[10,29] fractionation of biomass can be performed by the selective catalytic hydrogenolysis of aromatic polymers into low molecular weight phenolic substances retaining the carbohydrate portion.[10,29,30] This makes polysaccharides the most readily accessible feedstock for the development of biorefinery processes at present.

With a view of the dominance of polysaccharides in nature over other macromolecules and large volumes of available cellulose provided by existing manufactories, the principal focus of the present doctoral project is on the catalytic valorisation of cellulosic carbohydrates into value added chemicals. This involves systematic research of acid-catalysed transformations of purified sugar monomers and polymers under varied catalytic conditions, followed by the translation of the improved knowledge and optimised reaction systems into the valorisation of industrially available native cellulose and cellulosic biomass.

Chemocatalytic conversion of polysaccharides into value added molecules is considered to be a complex cascade of Brønsted acid-catalysed and Lewis acid-promoted reactions, as detailed in Scheme 5.1.[1] Mechanistically, Brønsted acids (protic acids) activate substrates by protonation of their reactive centres with hydrogen ion (typically $H_{13}O_6^+$ in dilute aqueous solutions).[1,2] Lewis acids catalyse reactions through the bonding of their electron-deficient centre with Lewis basic site on the substrate. The site and strength of the bonding may be predicted based on Pearson's HSAB principles,[31,32] which consider that hard Lewis acids interact preferentially with hard Lewis bases and soft with soft. When it comes to carbohydrates, the major active sites are O-containing hard Lewis bases, such as glycosidic linkages, hydroxyl, and carbonyl groups, and so, in theory, they should mainly be activated by hard Lewis acids.[10] It is worth noting that HSAB principles predict the hydrogen ion to be a hard Lewis acid.[31,32] Thus, the activation by Brønsted acids principally occurs at similar hard Lewis basic sites of carbohydrates, but not all protonation steps lead to chemical reactions. Sometimes the specific catalyst activity (Brønsted or Lewis) may be manifested by a combination of two Brønsted acids (Brønsted acid-assisted Brønsted acid catalysts), two Lewis acids (Lewis acid-assisted Lewis acid catalysts), or Brønsted and Lewis acids (Brønsted acid-assisted Lewis acid catalysts, or Lewis acid-assisted Brønsted acid catalysts) via assisted acidity mechanism.[33,34] This phenomenon should not be confounded with deactivation/decomposition of Lewis acids in protic media leading to the formation of Brønsted acids. A pictorial representation of various reactive centres of carbohydrates and possible ways of their activation by Brønsted and Lewis acid catalysis is given in Scheme 5.2.



Scheme 5.2. Types of acid catalysts and acid-catalysed activations. H = hydrogen ion; although Brønsted acids are conventionally denoted as H^+, the hydrogen ion is known to form Lewis acid–Lewis base complexes, for instance, $H_{13}O_6^+$ in aqueous solutions.[1,2] M = electron deficient centre of Lewis acid catalyst.

The entry point of carbohydrate refineries is solvolysis of cellulosic polymers into derivative aldohexoses and aldopentoses.[16] This transformation typically relies on the Brønsted acid catalysis (Scheme 5.1 and 5.2).[1,10] Lewis acids can further catalyse the isomerisation of aldoses into respective ketoses,[1,2,35] or facilitate retro-aldol condensation of monosaccharides (both aldoses and ketoses) into C_2–C_4 sugars, from which α-hydroxy acids are produced.[36–38] On the other hand, Brønsted acids can promote dehydration of ketoses into furan-type molecules, such as 5-(hydroxymetyl)furfural (HMF) and furfural (FF), and rehydration thereof into levulinic acid under more forcing conditions.[1,2,35] Alcohols, which are often employed as solvents for catalytic reactions of cellulosic materials, typically convert monosaccharides, aldehydes and acids into respective glycosides, acetals and esters (Scheme 5.1).[2] Selectivity towards one or another product, is often determined by the nature of the acid catalyst present and the process conditions. Some of these reactions are catalysed by Brønsted acidity, such as solvolysis, dehydration, and rehydration, while others require Lewis acidity, including isomerisation and retro-aldol condensation (Scheme 5.1 and 5.2).[1,2,10] Despite targeted conversions of cellulosic substances into value added molecules, acid catalysis may also promote unfavourable transformations into high molecular weight byproduct humins that are generally considered to be condensation products of saccharides and furans, which has a limited scope of applications at present.[39,40] The ongoing challenge is to define optimum catalytic systems and processing conditions, enabling desired reactions with maximum selectivity into the targeted product(s).

5.1.2. Acid-catalysed transformations in aqueous and alcohol media: identifying the essential challenge for sustainable cellulose refinery

To detail the course of catalytic processing of polysaccharides, the present study starts from the model reactions of purified substrates (glucose and microcrystalline cellulose (MCC)) in the presence of catalytic metal trifluoromethanesulfonates (metal triflates), including their analogous Brønsted acid-assisted and Brønsted base-modified systems, in aqueous and alcohol media. Metal triflates are known to be stable in protic solvents and to deliver both Lewis acid activity and Brønsted acid activity through Lewis acid-assisted Brønsted acidity (not solvolysis into Brønsted acid, Scheme 5.2).[2,3,34,41,42] As mentioned, both types of acid activities (Brønsted and Lewis) are required for the catalytic transformation of carbohydrates into platform chemicals, making triflates ideal candidates for the present research study. The initial screening of various metal triflates (LiOTf, $Al(OTf)_3$, AgOTf, $In(OTf)_3$, $Sn(OTf)_2$, $Y(OTf)_3$, $La(OTf)_3$, or $Hf(OTf)_4$, where OTf = trifluoromethanesulfonate), Brønsted acids (H_3PO_4 or TsOH), and combined Lewis/Brønsted acids ($La(OTf)_3/H_3PO_4$ or $La(OTf)_3$/TsOH) in the transformation of glucose in water under solvent reflux at atmospheric pressure showed only slight conversion into fructose (yields up to 9 mol%), which is an anticipated product under these conditions.[2] In the presence of hard Lewis acids, such as $Al(OTf)_3$,

$In(OTf)_3$, $Sn(OTf)_2$ or $Hf(OTf)_4$, the transformations were also accompanied by the formation of unwanted dark-brown byproduct humins. In turn, soft Lewis acids (LiOTf and AgOTf) showed no catalytic activity, underscoring the weak complexation of these catalysts with the hard Lewis basic reactive centres of glucose (Scheme 5.2). Instead of fructose and humins, Brønsted acids or Lewis acid-assisted Brønsted acids catalysed the transformation of glucose into isomaltose (major disaccharide product) and other di-, tri- and oligosaccharides. The self-condensation process may become an exciting alternative to the commercial enzymatic production of isomaltose,[43] but it is typically overlooked in sugar platform refineries. In this work,[2] the conversion into di- and oligosaccharides was the most efficiently promoted by the combined acid system $La(OTf)_3/H_3PO_4$ in concentrated aqueous solutions (30 wt% glucose in water) and prolonged reaction time (12 h, conversion 43 wt%, isomaltose yield 18 mol%, total oligosaccharides yields 42 wt%, based on the substrate, Table 5.1). The improved activity of the catalyst is explained by high Brønsted acidity of $La(OTf)_3/H_3PO_4$ in aqueous media (this catalyst is established to be the strongest Brønsted acid in the given series of catalysts), as defined by pH readings of aqueous acidic solutions.[2] This highlights that the self-condensation of glucose is a typical Brønsted acid-catalysed reaction.

Aldose-ketose isomerisation was reported to be more efficient in alcohols than in water,[44–46] and this general knowledge was confirmed in the present research.[2] Among the abovementioned catalysts, $Al(OTf)_3$ was found to possess optimum activity for the isomerisation reaction.[2] In methanol, this catalyst promoted almost complete conversion of glucose into a combination of methyl glucosides (methyl glucofuranosides and methyl glucopyranosides (*non-isomerisation product*)) and methyl fructofuranosides (methyl fructofuranosides and methyl fructopyranosides (*isomerisation product*)) under mild reaction conditions (solvent reflux at atmosphere pressure, 1 h). The subsequent solvent exchange with water and additional processing in aqueous media (solvent reflux at atmosphere pressure, 1 h) let to obtain glucose, fructose, and methyl glucopyranosides (MG, 1:1 mixture of α- and β-anomers) (Table 5.1). Note that MG appeared somewhat stable to hydrolysis, relative to methyl glucofuranosides or methyl fructofuranosides, and therefore are among major products. Given that the conversion into methyl glucosides is favoured by Brønsted acidity and that the isomerisation into fructose is favoured by Lewis acidity,[2] it is possible to improve the conversion into ketose by selectively inhibiting Lewis acid-assisted Brønsted acidity associated with the catalyst. This task can be accomplished by the addition of 2,6-di-*tert*-butyl-4-methylpyridine (TBP) as Brønsted base (3:1 based on $Al(OTf)_3$)) that is known to exclusively neutralise hydrogen ions, preventing interactions with any larger cations, such as Al^{3+}, due to steric hindrance exerted by the *tert*-butyl-groups.[2,34] This approach improved the yield and selectivity of fructose after the two-step transformation in methanol and water, simultaneously reducing Brønsted acid-catalysed production of methyl glucosides (Table 5.1). The achieved yields of the desired ketose (47 mol%, based on the substrate) under mild reaction conditions compare very favourably with industrial methods based on the isomerase enzymes (42%), or with bench-scale chemocatalytic methods that typically require forcing processing parameters (< 55%).[1,46]

To promote other catalytic reactions of glucose (Scheme 5.1), further work attempted acid-catalysed conversions in methanol at elevated temperature (120 °C) and longer reaction time (12 h) before the hydrolysis step in water (solvent reflux at atmosphere pressure, 1 h).[2] Under these conditions, metal triflates and various Brønsted acid catalysts enabled highly selective transformations of glucose into derivative MG or methyl levulinate (MLev). Hard Lewis acids, such as $Al(OTf)_3$, $In(OTf)_3$, $Sn(OTf)_2$ or $Hf(OTf)_4$, delivered excellent outcomes of MLev (Table 5.1). In these examples, chromatography-analysis of the reaction mixture also identified trace amounts of HMF and 5-(methoxymethyl)furfural, as prospective reaction intermediates towards MLev (Scheme 5.1). Conversely, Brønsted acid catalysts (H_3PO_4 or TsOH) or Lewis acid-assisted Brønsted acids ($La(OTf)_3/H_3PO_4$ or $La(OTf)_3$/TsOH) and soft Lewis acids ($Y(OTf)_3$, AgOTf or $La(OTf)_3$) promoted the transformation of glucose into MG, with no or minimum conversion into MLev (Table 5.1). One exception was soft Lewis acidic LiOTf that mostly yielded fructose (fructose yield 8 mol%, Table 5.1), likely associated with weak induced Brønsted acidity to catalyse *O*-glycosidation or dehydration/rehydration reactions. Evidently, only hard Lewis acids can effectively transform glucose into rehydration products through the entire cascade of reactions, while softer Lewis acids or combined acids are less suited for this task under applied conditions. Table 5.1 demonstrates the results of several instances, as discussed above.

Table 5.1. Conditions and results of the acid-catalysed processing of (poly)carbohydrates in aqueous and alcohol media [a]

Substrate	Reaction media	Catalyst	Conv (%)	Yield isomaltose (%)	Yield fructose (%)	Yield MG (%)	Yield alkyl levulinates (%)
Glucose	water	$Al(OTf)_3$	12 [b]	0 [b]	5 [b]	–	–
		$La(OTf)_3$	13 [c]	6 [c]	1 [c]	–	–
		H_3PO_4	23 [c]	2 [c]	0 [c]	–	–
		$La(OTf)_3/H_3PO_4$	43 [c]	18 [c] (42 wt%)[c,d]	0 [c]	–	–
Glucose	methanol	$Al(OTf)_3$	42 [e]	–	24 [e]	5 [e]	–
			99 [f]	–	0 [f]	10 [f]	59 (MLev)[f]
		$Al(OTf)_3$/TBP	64 [g]	–	47 [g]	1 [g]	–
		$Sn(OTf)_2$	90 [f]	–	0 [f]	46 [f]	43 (MLev)[f]
		$La(OTf)_3$	99 [f]	–	0 [f]	89 [f]	9 (MLev)[f]
		TsOH	93 [f]	–	0 [f]	93 [f]	0 (MLev)[f]
		LiOTf	13 [f]	–	8 [f]	0 [f]	0 (MLev)[f]
MCC	ethanol	$Al(OTf)_3$	74 [h]	–	–	–	32 (ELev)[h]
		$Sn(OTf)_2$	50 [h]	–	–	–	23 (ELev)[h]
		$Y(OTf)_3$	15 [h]	–	–	–	0 (ELev)[h]
		H_3PO_4	12 [h]	–	–	–	0 (ELev)[h]
		$Y(OTf)_3/H_3PO_4$	78 [h]	–	–	–	68 (ELev)[h]
			85 [i]	–	–	–	75 (ELev)[i]
Pinus cellulose	ethanol	$Y(OTf)_3/H_3PO_4$	81 [i]	–	–	–	68 (ELev)[i]
Wood pulp (*Pinus*)	ethanol	$Y(OTf)_3/H_3PO_4$	64 wt% [i]	–	–	–	53 wt% (ELev)[i]
Softwood	ethanol	$Y(OTf)_3/H_3PO_4$	77 wt% [i]	–	–	–	52 wt% (ELev)[i]

[a] Yields and conversions are specified in mol% (in some instances also in wt%) based on the substrate. '0' = not detected, or detected in trace amounts; MG = methyl glucopyranosides; MLev = methyl levulinate; ELev = ethyl levulinate; OTf = trifluoromethanesulfonate; TBP = 2,6-di-*tert*-butyl-4-methylpyridine; TsOH = *p*-toluenesulfonic acid; MCC = microcrystalline cellulose. [b] Reaction conditions: glucose (50 mg), water (2.00 mL), catalyst (20 mol% based on glucose), reflux at atmosphere pressure, 2 h.[2] [c] Reaction conditions: glucose (500 mg), water (1.65 mL), catalyst (20 mol% based on glucose), reflux at atmosphere pressure, 12 h.[2] [d] Total yield of di-, tri-, and oligosaccharides. [e] Reaction conditions: glucose (50 mg), methanol (2.00 mL), catalyst (20 mol% based on glucose), reflux at atmosphere pressure, 1 h, then solvent exchange with water (2.00 mL), reflux at atmosphere pressure, 1 h.[2] [f] Reaction conditions: glucose (50 mg), methanol (2.00 mL), catalyst (20 mol% based on glucose), 120 °C, 8 h, then solvent exchange with water (2.00 mL), reflux at atmosphere pressure, 1 h.[2] [g] Reaction conditions: glucose (50 mg), methanol (2.00 mL), $Al(OTf)_3$ (20 mol% based on glucose), TBP (60 mol% based on glucose), reflux at atmosphere pressure, 36 h, then solvent exchange with water (2.00 mL), reflux at atmosphere pressure, 1 h.[2] [h] Reaction conditions: MCC (50 mg), ethanol (4.00 mL), catalyst (0.05 mmol; 0.05 mmol each acid for combined catalysts), 160 °C, 4 h.[3] [i] Reaction conditions: substrate (50 mg), ethanol (4.00 mL), $Y(OTf)_3$ (0.05 mmol), H_3PO_4 (0.05 mmol), 180 °C, 2 h.[3]

The following goal was to employ acidic metal triflates to the reaction of cellulosic polysaccharides.[3] In these instances, methanol was replaced with ethanol, to provide fully renewable content in the anticipated products (ethanol may be produced by fermentation of cellulosic carbohydrates).[47] The processing was performed under more forcing parameters (160 °C, 4 h), to facilitate depolymerisation of cellulose. In ethanol, the acid-catalysed conversion of MCC yielded ethyl levulinate (ELev) as a principal product (Table 5.1). Similar to transformations of glucose, the conversion of cellulose into ELev was predominantly catalysed by hard Lewis acids ($Al(OTf)_3$, $In(OTf)_3$, $Sn(OTf)_2$, or $Hf(OTf)_4$), even though in moderate yields (Table 5.1). These processes yielded only trace amounts of ethyl glucosides (solvolysis products), or other reaction intermediates towards ELev, but resulted in the formation of byproduct humins, accounting for the poor selectivity of the process.[3] Soft Lewis acids ($Y(OTf)_3$, AgOTf, $La(OTf)_3$, or $Yb(OTf)_3$) or Brønsted acids (H_3PO_4 or TsOH) delivered no transformation into the targeted ester, nor into solvolysis products (Table 5.1). However, the combinations of soft Lewis acids and Brønsted acids formed active catalyst systems through a Lewis acid-assisted acidity mechanism, providing the improved conversion into ELev (Table 5.1). Among tested combined acid catalysts, the mixture $Y(OTf)_3/H_3PO_4$ offered superb yields and selectivity of ELev, which could be further increased in reactions at slightly elevated temperature (ELev yield 75 mol%, 180 °C, 2 h, Table 5.1).[3]

Despite the promising results for the processing of refined MCC, the direct conversion of bulk, raw cellulose obtained from (eucalyptus cellulose, bleached and unbleached *Pinus* cellulose), wood pulp and softwood chips was less efficient under similar conditions. Apparently, the large particle size and molecular weight of bulk materials, along with their rigid heterogeneous structure, reduced the number of effective substrate-catalyst interactions during the processing. The increased heterogeneity of reaction systems also led to the excessive formation of humins, reducing the selectivity of targeted reactions.[3] To ameliorate these confounding issues, many laboratory methods opt for the use of refined cellulose, such as MCC (a medium value product formed by the treatment of native cellulose with dilute aqueous mineral acids) and dissolving pulp (cotton linter pulp with a low degree of polymerisation), or involve energy-demanding pretreatment processes, such as ball-milling.[1,3,10,48] These approaches add unwanted complexities to biorefining technologies and restrict the use of largely available native cellulosic biomass. Therefore, the problem of the direct catalytic valorisation of raw, unrefined substrates remains essentially unsolved in all but few isolated cases. This account will return to this problem once it has identified an acceptable solution.

5.1.3. Ionic liquids are enablers for efficient transformation of cellulosic biomass

The rates of chemical reactions often improve if they can be performed under homogeneous conditions.[10] As mentioned, cellulosic materials are insoluble in most common aqueous and organic media, and appear somewhat recalcitrant to chemical conversion in heterogeneous systems. In contrast, ionic liquids (ILs) in their many accessible forms are potentially key to improved chemical transformations of cellulosic materials. Many classes of ionic solvents, such as inorganic molten salt hydrates, quaternary ammonium salts and deep eutectic solvents (DESs), are able to fully dissolve cellulosic polysaccharides, enabling significant progress towards milder reaction conditions and better yields of some targeted products.[49–51] In addition, some ionic media are naturally acidic and are reported to promote acid-catalysed transformations of carbohydrates into platform chemicals.[1,51,52] These make ILs outstanding reaction systems for the catalytic valorisation of cellulosic biomass. Accordingly, the next task of the present work was to interrogate various classes of ionic solvents, including inorganic molten salt hydrates, imidazolium salts, and acidic DESs, for dissolution and chemocatalytic processing of cellulosic polysaccharides into value added derivatives.

The research was initially oriented towards the use of zinc chloride hydrate solvents, with the molecular formula $ZnCl_2 \cdot nH_2O$ (hydration number $n = 2.5–4.5$), as acidic solvent-catalyst systems for valorisation processes. Historically, these solvents have obtained widespread application as non-derivatising media in cellulose refining technologies, and more recently as useful processing systems for the production of cellulose aerogels, or sugar alcohols.[53–55] In this work, the dissolution of MCC and bulk cellulose (cotton linter, eucalyptus, and *Pinus* cellulose) showed that $ZnCl_2 \cdot 2.5–4.25H_2O$ systems freely solubilise this polymer at low temperatures (80 °C for 1–1.5 h), while more hydrated $ZnCl_2 \cdot 4.5H_2O$ formed a suspension thereof in the IL medium.[5,9] Additionally, gravimetric analysis and size exclusion chromatographic determination of the molecular weight of the regenerated materials revealed that cellulose depolymerises during processing in $ZnCl_2 \cdot 2.5–4.5H_2O$.[5,9] As a general observation, the lower the hydration levels in the zinc chloride hydrate, the higher the losses of cellulose and the lower the molecular weight of the recovered solids relative to the input. This correlation between the degree of the depolymerisation and hydration number of $ZnCl_2 \cdot nH_2O$ was established to be related to the acidity of the reaction media, which diminishes with rising n, as was shown by pH readings and NMR spectroscopy.[5]

The dissolution of cellulose and following hydrolytic processing at elevated temperature (120 °C, 1 h) demonstrated that the differing acid activity of $ZnCl_2{\cdot}2.5–4.5H_2O$ influences the course of the catalytic reactions of cellulose (Figure 5.1).[5] It is consequently possible to adjust the selectivity of the process by manipulating the hydration levels of the solvent.[4–6] Less hydrated media, $ZnCl_2{\cdot}2.5–3.0H_2O$, favour the transformation of cellulose into furans, namely HMF, furyl hydroxymethyl ketone (FHK), and FF (Figure 5.1).[5] FHK and FF are unusual major dehydration products and their formation is accordingly seldom recorded for the reactions of cellulose. FHK is considered to originate by the dehydration of the intermediate ketohexose (isomerisation product derived from fructose), while FF is thought to form from fructose via an intermediate pentose (e.g., arabinose), as shown in Scheme 5.3.[4,10] Interestingly, the selectivity to these unusual furanoids may be significantly improved when performing reactions in the biphasic system $ZnCl_2{\cdot}3.0H_2O$/anisole (Table 5.2).[4,6] This biphasic system is especially useful for the production of FF from native biomass, due to the simultaneous conversion of both cellulose and hemicellulose into targeted furaldehyde (yield up to 42 wt% based on cellulose and hemicellulose content in biomass, Table 5.2).[6] In distinct contrast to less hydrated solvents, highly hydrated molten salts $ZnCl_2{\cdot}4.0–4.5H_2O$ transform cellulose predominantly into HMF (yield up to 21 mol%, based on anhydroglucose units present in the substrate) and low molecular weight saccharides (total yield up to 48 wt%, based on the substrate, Figure 5.1).[5] After optimising the process, high yields of HMF (up to 35 mol%), FF (up to 29 wt%), and sugars (up to 61 wt%, based on the cellulose content in biomass) are achievable by performing the conversion of native lignocellulose (corncob or softwood) and algal biomass (macroalga *Ulva lactuca*, or microalga *Porphiridium cruentum*) in $ZnCl_2{\cdot}4.25H_2O$ under relatively mild conditions (Table 5.2).[5] In these instances, the processing required slightly prolonged solubilisation of biomass at lower temperature (80 °C, 5 h) and the addition of hydrochloric acid as co-catalyst.[5] However, not all types of biomass were efficiently subjected to the valorisation. For example, native softwood is less amenable for the catalytic conversion in the inorganic solvent (Table 5.2). Additionally, economical methods to recover products and solvents warrant further investigations.

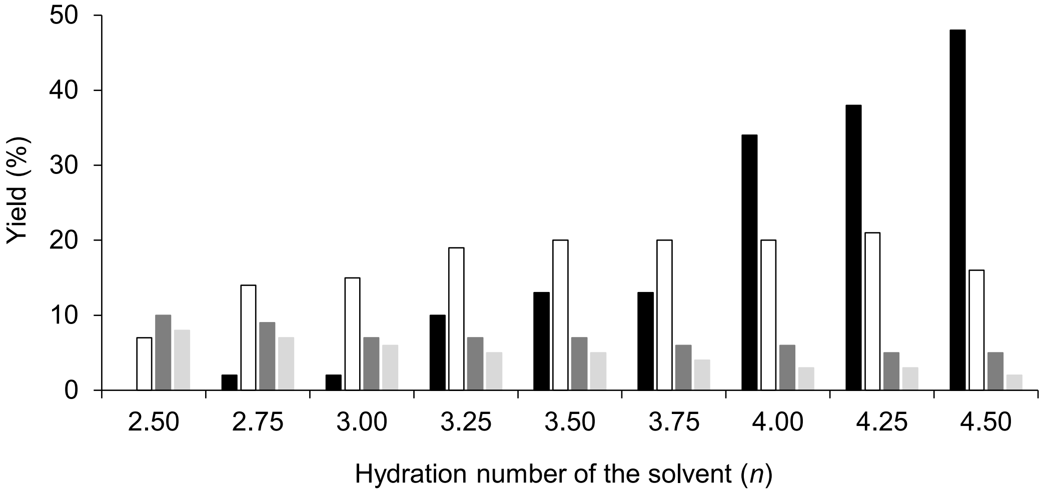
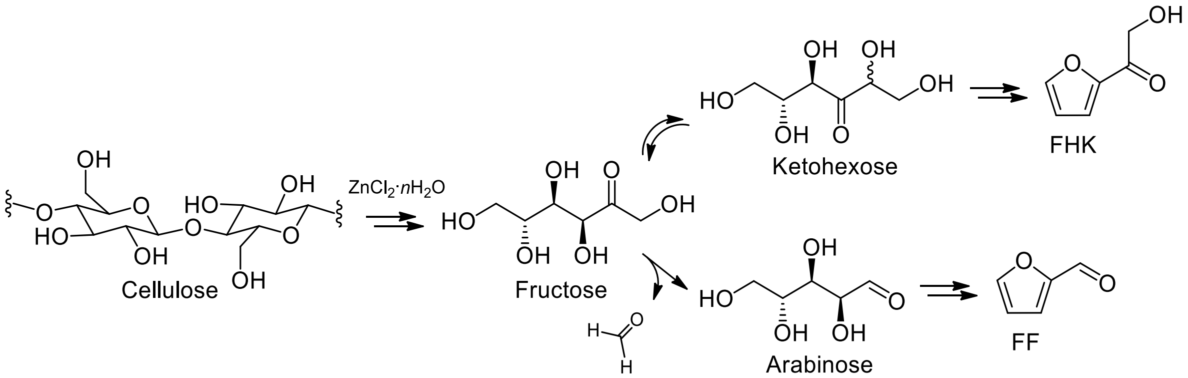


Figure 5.1. Acid-catalysed transformation of cellulose into low molecular weight molecules in $ZnCl_2 \cdot nH_2O$. The figure specifies combined yields of mono-, di-, tri- and tetrasaccharides in wt% and yields of furans in mol %. Reaction conditions: MCC (50 mg), solvent-catalyst (5.000 g), 80 °C, 2.5 h, then 120 °C, 1 h.[5] ■ : saccharides; □ : 5-(hydroxymethyl)furfural; ▨ : furyl hydroxymethyl ketone; ░ : furfural.



Scheme 5.3. Unusual acid-catalysed transformations of cellulose in zinc chloride hydrate solvents into furan type molecules.[4,10] n = integer.

Table 5.2. Conditions and results of the acid-catalysed processing of cellulosic biomass in ionic solvents [a]

Substrate	Reaction media	Yield oligosaccharides (%)	Yield glucose (%)	Yield xylose (%)	Yield HMF (%)	Yield FHK (%)	Yield FF (%)
Corn husk	$ZnCl_2\cdot 3.0H_2O$ / anisole	–	–	–	–	12 [b]	26 wt% [b]
P. cruentum		–	–	–	–	4 [b]	42 wt% [b]
Corncob	$ZnCl_2\cdot 4.25H_2O$ / HCl	–	61 wt% [c]	–	30 [c]	–	22 wt% [c]
Softwood		–	26 wt% [c]	–	22 [c]	–	11 wt% [c]
Ulva lactuca		–	52 wt% [c]	–	25 [c]	–	15 wt% [c]
P. cruentum		–	49 wt% [c]	–	35 [c]	–	29 wt% [c]
MCC	[C_4mim]Cl / ChCl/oxalic / La(OTf)$_3$	34 wt% [d]	35 wt% [d]	–	4 [d]	0 [d]	0 [d]
MCC	[C_4mim]Cl / ChCl/oxalic / H_2O	4 wt% [e]	49 wt% [e]	–	2 [e]	0 [e]	0 [e]
Pinus cellulose		21 wt% [f]	50 wt% [f]	–	6 [f]	0 [f]	–
Softwood		15 wt% [f]	25 wt% [f]	30 wt% [f]	2 [f]	0 [f]	0 [f]
Corncob		0 [e]	54 wt% [e]	35 wt% [e]	10 [e]	0 [e]	0 [e]
P. cruentum		0 [e]	55 wt% [e]	40 wt% [e]	0 [e]	0 [e]	0 [e]
P. cruentum	ChCl/oxalic	0 [g]	42 wt% [g]	73 wt% [g]	1 [g]	0 [g]	25 [g]
P. cruentum	ChCl/oxalic/ MIBK	0 [h]	32 wt% [h]	0 [h]	5 [h]	0 [h]	72 [h]
Softwood	ChCl/oxalic/ MIBK	0 [i]	0 [i]	0 [i]	1 [i]	0 [i]	55 [i]

[a] Yields are specified in mol% (in some instances also in wt%) based on the carbohydrate content in the substrate. Yield oligosaccharides means combined gains of di-, tri- and tetrasaccharides. '0' = not detected, or detected in trace amounts; HMF = 5-(hydroxymethyl)furfural; FHK = furyl hydroxymethyl ketone; FF = furfural; MCC = microcrystalline cellulose; OTf = trifluoromethanesulfonate; [C_4mim]Cl = 1-butyl-3-methylimidazolium chloride; ChCl = choline chloride; MIBK = methyl isobutyl ketone. [b] Reaction conditions: polysaccharides (50 mg, calculated based on carbohydrate content in the substrate), solvent (5.0 g), 80 °C, 2.5 h, then addition of anisole (40.0 mL), 120 °C, 1 h.[6] [c] Reaction conditions: polysaccharide (50 mg, calculated based on carbohydrate content in the substrate), $ZnCl_2\cdot 4.25H_2O$ (5.000 g), HCl (0.03 mmol), 80 °C, 5 h, then 120 °C, 1 h.[5] [d] Reaction conditions: MCC (50 mg), [C_4mim]Cl (1.000 g), ChCl/oxalic acid (0.100 g), La(OTf)$_3$ (10 mol% based on anhydroglucose unit present), 120 °C, 2 h.[7] [e] Reaction conditions: substrate (50 mg), [C_4mim]Cl (1.000 g), ChCl/oxalic acid (0.100 g), 100 °C, 2 h, then temperature increase to 120 °C and gradual addition of water in two steps (step 1: 0.220 mL, water content 20 wt%, based on IL, t = 0; step 2: 0.110 mL, water content 30 wt%, based on IL, t = 0.5 h), 4 h.[7] [f] Reaction conditions: substrate (50 mg), [C_4mim]Cl (1.000 g), ChCl/oxalic acid (0.100 g), 120 °C, 6 h (12 h for softwood), then addition of water in two steps (step 1: 0.220 mL, water content 20 wt%, based on IL, t = 0; step 2: 0.110 mL, water content 30 wt%, based on IL, t = 0.5 h), 120 °C, 4 h.[7] [g] Reaction conditions: *P. cruentum* (200 mg), ChCl/oxalic acid (4.0 g), 80 °C, 2 h.[8] [h] Reaction conditions: *P. cruentum* (200 mg), ChCl/oxalic acid (4.0 g), MIBK (8.0 mL), 100 °C, 4 h.[8] [i] Reaction conditions: softwood (300 mg), ChCl/oxalic acid (4.0 g), MIBK (12.0 mL), 100 °C, 5 h.[8]

Since the seminal work of Rogers and colleagues exploring the dissolution of cellulose in imidazolium-based ILs,[49] there has been a significant and growing interest to apply quaternary ammonium salts to biorefining technologies. Various imidazolium derivatives, tetraalkylammonium chlorides, and ammonium salt-containing DESs have been attempted to the conversion of cellulosic materials under homogeneous conditions, substantially improving analogous heterogeneous processes in water or aqueous solvents.[1,7,10] However, most of these studies present the conversions of MCC, or ball-milled cellulose, or even edible polysaccharides, such as starch and inulin, avoiding the direct conversion of native cellulosic materials.[7] This work is focussed on the valorisation of non-food-competitive biomass, and herein the processing of cellulosic substances in imidazolium solvents and acidic DESs has been readdressed.

Similar to the majority of zinc chloride solvents, selected dialkylimidazolium chlorides (1-butyl-3-methylimidazolium chloride ([C_4mim]Cl), 1-hexyl-3-methylimidazolium chloride ([C_6mim]Cl), or 1-octyl-3-methylimidazolium chloride ([C_8mim]Cl)) were able to solubilise cellulose and to reduce its molecular weight during dissolution (100 °C, 1–6 h).[9] However, ILs with longer alkyl chains ([C_6mim]Cl and [C_8mim]Cl) were less effective for the dissolution of bulk cellulose, and thus were found less suitable for further catalytic transformations. Acidic deep eutectic systems based on choline chloride (ChCl) in combination with oxalic, citric or malic acids (ChCl/acid; 1:1 molar ratio for oxalic acid dihydrate or malic acid monohydrate, respectively; 1:0.5 for citric acid monohydrate, respectively), on glycine combined with malic acid monohydrate (1:1 molar ratio, respectively), or on the mixture of proline and malic acid monohydrate (3:1 molar ratio, respectively), were unable to afford complete solubilisation of MCC or bulk cellulose at 100 °C for 2 h, even though some of these systems were earlier reported as cellulose solvents.[56–59] Among DESs, only ChCl/oxalic acid system reduced the molecular weight of substrates, while other systems increased this parameter due to the esterification of cellulose by the organic acid, as assured by IR analysis;[9] therefore, most of the DESs (with exception of ChCl/oxalic acid) were considered unsuited for the production of platform chemicals. In the instances with ChCl/oxalic acid solvent, it was also observed that bulk, native cellulose (cotton linter, eucalyptus, *Pinus* cellulose, wood pulp) is amenable to deconstruction into fine particulate cellulosic material with particle size and structure consistent with MCC (average particle size 54–86 μm, Figure 5.2). The production of cellulosic powder from native cellulose in ChCl/oxalic acid can be achieved at lower temperature (80 °C), and in the concentrated system (up to 20 wt% of cellulose, based on the DES). Moreover, the DES can be recovered and reused without changes of activity.[3] As will be shown below, this process may become an efficient pathway for the pretreatment of native cellulose.

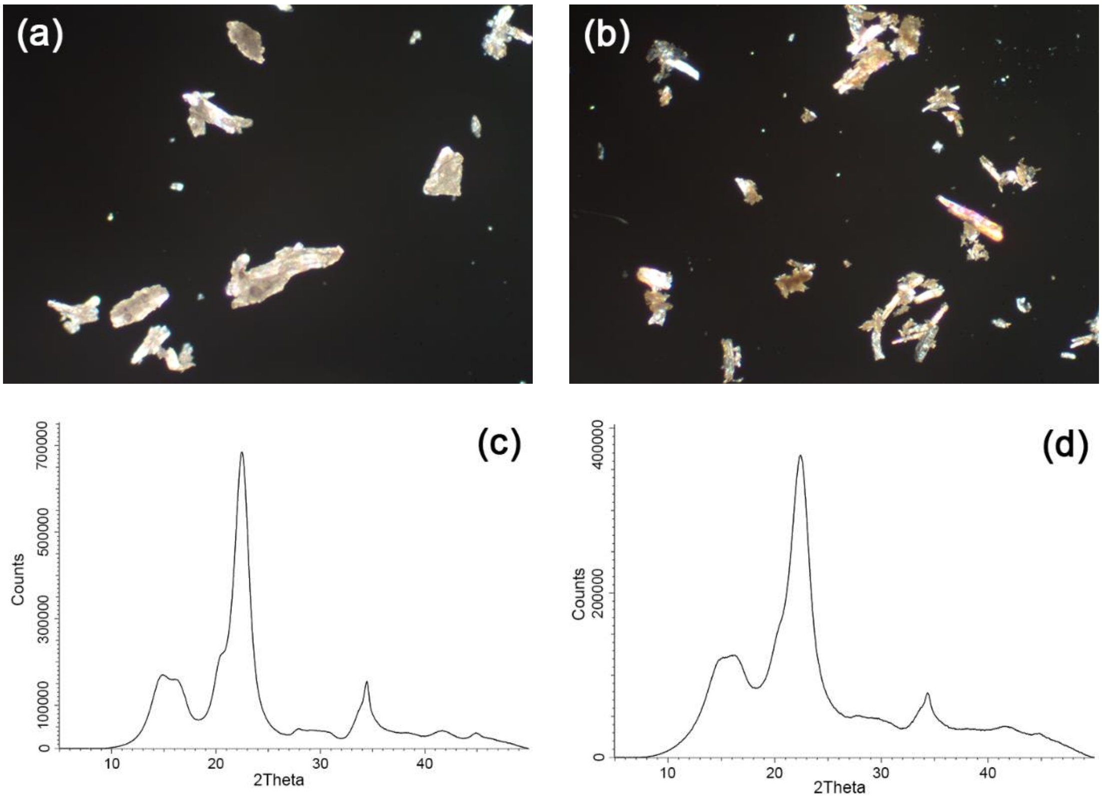
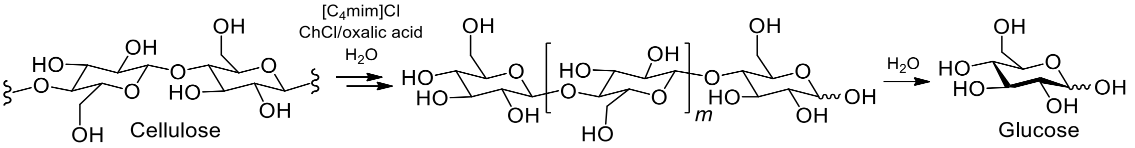


Figure 5.2. 20x Microphotographs of microcrystalline cellulose (a) and the pretreated in the ChCl/oxalic acid solvent wood pulp (b), and their respective X-ray diffraction spectra (c, d)

The subsequent exploratory conversions of MCC in the neat [C_4mim]Cl or in the ChCl/oxalic acid solvent did not provide further conversion into desired low molecular weight derivatives under more forcing conditions (120 °C, 2 h), and was followed by the formation of humins in the case with the DES.[7] However, a combination of [C_4mim]Cl and ChCl/oxalic acid (10:1 w/w, respectively) provided the selective transformation of cellulose into glucose and glucose oligomers (cellotetraose, cellotriose, and cellobiose). In this co-solvent system, [C_4mim]Cl enables dissolution of the substrate, while ChCl/oxalic acid serves as a catalyst for the hydrolytic depolymerisation.[7] The suite of products suggests that hydrolysis is not the direct process, and firstly occur into cellulose chunks and only then into terminal product glucose, as proposed in the Scheme 5.4.[7] This is also evidenced by more complete hydrolysis into glucose at extended reaction times, consequently to the subsequent hydrolysis of oligoglucans into monomer sugar (Figure 5.3). However, the longest reactions (16 and 20 h, Figure 5.3) led to the formation of byproduct humins, which reduced the overall selectivity. The conversion into glucose can be promoted by the addition of La(OTf)$_3$ to generate an *in situ* Lewis acid-assisted Brønsted acid catalytic system, or by the sequential dilution of the reaction systems with water (Table 5.2).[7] The latter process is particularly favoured, and is also known to suppress side reaction of saccharides in imidazolium-based ILs.[60] The optimised method delivered similarly excellent depolymerisation of bulk cellulose (cotton linter, eucalyptus or *Pinus* cellulose) and native biomass (corncob, *Ulva lactuca* or *P. cruentum*) into significantly value added low molecular weight saccharides.[7] With native biomass, there was an additional output of xylose due to the hydrolysis of hemicellulose (Scheme 5.1).[7] Despite this success, the co-solvent system did not afford efficient depolymerisation of wood biomass, similarly to zinc chloride hydrates (Table 5.2).



Scheme 5.4. Acid-catalysed hydrolysis of cellulose into low-molecular weight carbohydrates in the co-solvent [C_4mim]Cl / ChCl/oxalic acid. *n* = integer. *m* = 0, 1 and 2 for cellobiose, cellotriose and cellotetraose, respectively.

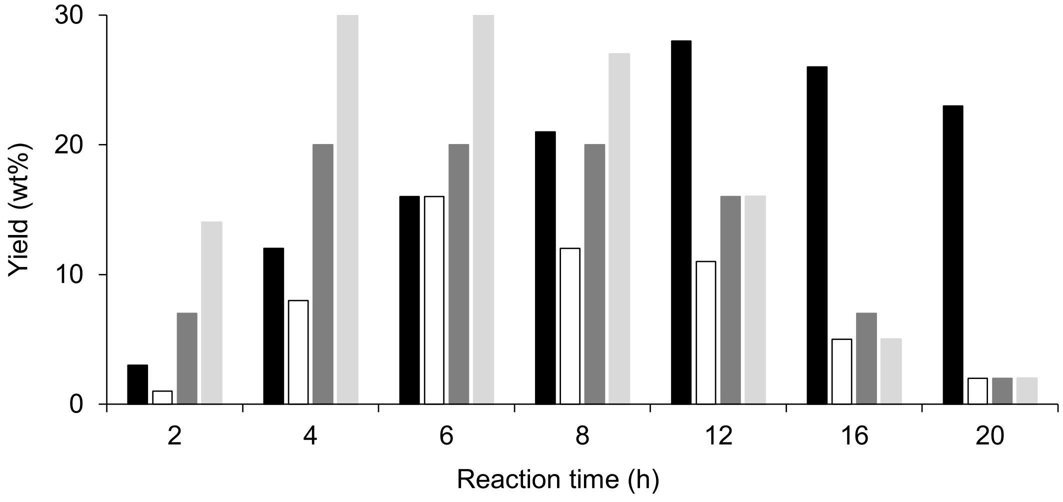


Figure 5.3. Acid-catalysed transformation of cellulose into low molecular weight saccharides in the co-solvent [C_4mim]Cl / ChCl/oxalic acid. Reaction conditions: MCC (50 mg), solvent-catalyst (5.000 g), 120 °C.[7] ■ : glucose; □ : cellobiose; ■ : cellotriose; ■ : cellotetraose.

Although the ChCl/oxalic acid system appeared rather inefficient in the previous test, likely due to poor solubility of cellulose, other natural polysaccharides may be amenable to the valorisation in this medium.[8,56] The valorisation in neat DESs is of particular interest for biorefinery. In distinct contrast to inorganic molten salts or imidazolium ILs, many DESs, including ChCl/oxalic acid solvent, may be produced from plant feedstock, implying renewability of this media.[56] A study[8] of the reactivity of several polycarbohydrates in the neat ChCl/oxalic acid solvent showed that starch (a mixture of α(1→4) linearly linked glucose polymer amylose and branched α-glucose polymer amylopectin), inulin (a β(1→2) linearly linked fructose polymer with occasional chain-terminating glucose units) and hemicellulose are all soluble and convertible into monosaccharides and furans in the DES (reaction temperature 60–100 °C, time 1 h).[8] This highlights the correlation between the solubility and reactivity of substrates: linear polymer cellulose is sparingly soluble and less convertible, relative to soluble polysaccharides, such as starch, xylans, or fructans.[8] The subsequent processing of lignocellulose (corn husk, corncobs, softwood chips) and algal biomass (*Ulva lactuca*, *P. cruentum*, *C. vulgaris*) provided conversions of native starch, fructans, and xylans into monosaccharides (glucose yield up to 68 wt%, fructose yield up to 60 wt%, xylose yield up to 73 wt%, based on respective polysaccharide content in biomass), HMF (up to 13 mol%) and FF (up to 72 mol%) in the neat DES or in the biphasic system ChCl/oxalic acid / methyl isobutyl ketone (MIBK).[8] Some of these instances are given in Table 5.2, demonstrating that the formation of specific product(s) is favourable under specific reaction conditions and for specified substrate types. The polysaccharide component of the microalgae *P. cruentum*, comprising predominantly structurally branched glucans and xylans, can be transformed into the respective monomers at modest reaction temperature, and into FF at elevated temperature and extended reaction time (Table 5.2). In contrast, the direct processing of softwood chips with high cellulose content converts only hemicellulose into FF (yield 55 mol%, Table 5.2) and leaves a fine cellulosic powder, analogous to MCC, as an unreacted portion of the biomass.

During the course of this account, there have been defined problems relating to the rigid structure of raw lignocellulosic biomass, including its physical size, molecular weight of the carbohydrate polymers present, and their strong supramolecular interactions. These altogether compromised several targeted processes in the present study and warrants a solution. In the first instance, catalytic conversions of bulk cellulose into ELev in ethanol led to reduced selectivity and to the production of byproduct humins.[3] In the second, it was woody biomass that resisted the efficient valorisation in zinc chloride hydrate solvents,[5] or in the co-solvent system [C_4mim]Cl / ChCl/oxalic acid.[7] In parallel, this research uncovered that the biobased ChCl/oxalic acid solvent is a recyclable medium for the deconstruction of bulk cellulose (Figure 5.2), or softwood biomass (Table 5.2), into fine cellulosic materials.[3,8,9] Pleasingly, the following conversion of this pretreated cellulosic residue enabled substantial improvements to the yield of ELev, low molecular weight saccharides or furan type molecules, compared with the processing of the crude (ligno)cellulose under identical conditions, avoiding side reactions towards unwanted humins (Tables 5.2 and 5.3).[3,8] Such combined technologies are valuable with a view to a multistage sustainable biorefinery, providing maximum use and beneficiation of undervalued cellulosic materials.

Table 5.3. Production of value added molecules from reaction of pretreated cellulosic biomass [a]

Substrate	Reaction media	Yield oligosaccharides (%)	Yield hexoses (%)	Yield HMF (%)	Yield FF (%)	Yield ELev (%)
Pinus cellulose	ethanol / Y(OTf)$_3$/H_3PO_4	0 [b]	0 [b]	0 [b]	0 [b]	68 mol% [b]
Pretreated *Pinus* cellulose		0 [b]	0 [b]	0 [b]	0 [b]	73 mol% [b]
Wood pulp (*Pinus*)		0 [b]	0 [b]	0 [b]	0 [b]	53 [b]
Pretreated wood pulp (*Pinus*)		0 [b]	0 [b]	0 [b]	0 [b]	62 [b]
Softwood		0 [b]	0 [b]	0 [b]	0 [b]	52 [b]
Pretreated softwood		0 [b]	0 [b]	0 [b]	0 [b]	62 [b]
Softwood	$ZnCl_2 \cdot 4.25H_2O$ / HCl	0 [c]	26 [c]	22 mol% [c]	11 [c]	–
Pretreated softwood		0 [c]	47 [c]	24 mol% [c]	6 [c]	–
Softwood	[C_4mim]Cl / ChCl/oxalic / H_2O	15 [d]	25 [d]	2 [d]	0 [d]	–
Pretreated softwood		35 [d]	30 [d]	2 [d]	0 [d]	–

[a] Yields are specified in wt% (in some instances also in mol%) based on the carbohydrate content in the substrate. *Pretreated substrate* means cellulosic material obtained after processing in ChCl/oxalic acid. Yield oligosaccharides means combined gains of di-, tri- and tetrasaccharides. Yield hexoses means combined gains of glucose and fructose. '0' = not detected, or detected in trace amounts; HMF = 5-(hydroxymethyl)furfural; FF = furfural; OTf = trifluoromethanesulfonate; [C_4mim]Cl = 1-butyl-3-methylimidazolium chloride; ChCl = choline chloride. [b] Reaction conditions: substrate (50 mg), ethanol (4.00 mL), Y(OTf)$_3$ (0.05 mmol), H_3PO_4 (0.05 mmol), 180 °C, 2 h.[3] [c] Reaction conditions: polysaccharide (50 mg, calculated based on carbohydrate content in the substrate), $ZnCl_2 \cdot 4.25H_2O$ (5.000 g), HCl (0.03 mmol), 80 °C, 5 h, then 120 °C, 1 h.[5] Reaction conditions: substrate (50 mg), [C_4mim]Cl (1.000 g), ChCl/oxalic acid (0.100 g), 120 °C, 12 h, then addition of water in two steps (step 1: 0.220 mL, water content 20 wt%, based on IL, $t = 0$; step 2: 0.110 mL, water content 30 wt%, based on IL, $t = 0.5$ h), 120 °C, 4 h.[7]

5.2. Conclusions and future directions

As a part of the global effort to establish a sustainable biorefinery, this project has researched acid-catalysed conversion of cellulosic carbohydrates into carbon-neutral replacement chemicals. It has improved current fundamental understanding of the chemistry and has applied new insights into the valorisation of widely available cellulosic materials, such as native terrestrial lignocellulose and aquatic algal biomass. While the act of creating this new knowledge was based on model transformations, it has been successfully applied in more complex systems and has advantaged the production of several commercially valuable products, such as fructose, isomaltose, and methyl glucosides. It has furthermore explored synergistic acid catalysts for the direct transformation of cellulose into ethyl levulinate. In parallel, a systematic study of various ionic liquids has demonstrated that these solvents are tuneable reaction systems for high-yielding transformations of native cellulosic biomass into significantly value added monosaccharides and furan type molecules. It has also demonstrated that a renewable deep eutectic mixture of choline chloride and oxalic acid is an excellent medium for the pretreatment of crude cellulose and woody biomass into the particulate cellulosic material for the subsequent valorisation into platform chemicals.

Despite this progress, there have been many research problems to address for further scientific and industrial developments of the biorefinery. Some of the synthesised molecules in the present research study, such as low molecular weight carbohydrates and furans, are often building blocks for use *en route* to final commodity- and performance products rather than final products themselves. This will require additional investigations of secondary and possibly tertiary transformations of platform molecules for the production of the targeted replacement chemicals. For example, the glycosidation of low molecular weight sugars with long-chain nature-derived detergent alcohols in acidic ionic solvents would permit the renewable synthesis of alkyl (poly)glucosides as biodegradable surfactants with high renewable content manufactured under sustainable practices. Redox catalytic transformations of furanoids into renewable fuel type molecules, such as (cyclo)alkanes, or into alternative monomers for plastics, such as diamines, diols and dicarboxylic acids, would be other exciting pathways for subsequent research. Ideally, such post-valorisation procedures into final products should be possible to perform using crude reaction systems, avoiding separation steps.

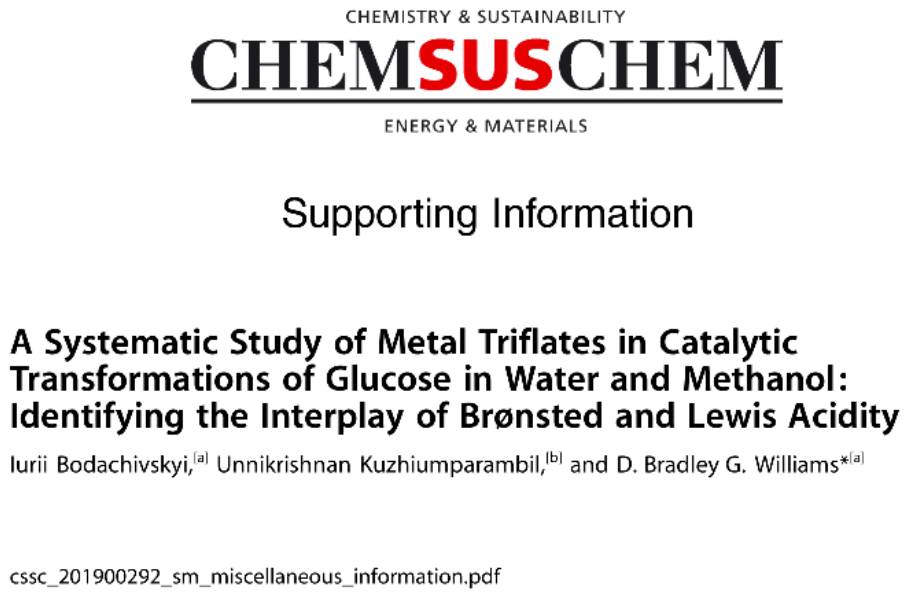
Among other exciting directions there is a retro-aldol condensation of carbohydrates and accompanying conversions into α-hydroxy acids or their respective esters. These molecules are building blocks for commodity polyesters, but their direct production from the acid-catalysed processing of polysaccharides remains less investigated, relative to other platform chemicals. It would therefore be beneficial to define the preferred acidic catalysts and suitable reaction conditions to directly convert cellulose and native cellulosic biomass into valuable α-hydroxy acids and their derivatives.

In addition, and besides reactions of carbohydrates, future studies will be likely oriented towards the chemocatalytic processing of lignins. Until recently, developments in lignin refineries have somewhat lagged behind, in comparison to the processing of carbohydrates, and, as is the case in any emerging field, it lacks a deep fundamental understanding of the chemistry. Follow up studies may involve the development of new analytical methods to detail the structure of heterogeneous aromatic polymers, along with chemical research of the reactivity of lignin model compounds under varied catalytic conditions. The defined optimum reaction systems should permit the selective transformation of commercially available lignin into value added derivatives. As opposed to current hydrocatalytic reductive processes, the future interrogations might be predominantly based on the oxidative (photo)catalytic depolymerisation of lignins.

Finally, there remain technological difficulties in translating scientific findings into commercialisable continuous processes, analogous to those that operate in petrochemical industries. These will be a combined task for scientists and engineers to develop new catalyst systems achieving highly selective reactions of polysaccharides and lignins into desired products under flow chemical conditions. The possible solution here is the engineering of orthogonal cascade processes, during which the whole lignocellulosic feedstocks will be valorised in-sequence, facilitating to effective separation of the unreacted portion of biomass, catalyst, and product after each processing stage. Of simultaneous conversions of various classes of biomacromolecules, forming complex mixtures of products and byproducts, differential selectivities of reactions would likely be the most important measure of success for continuous chemistry. For the foreseeable future, biorefineries are likely to focus on thermochemical conversions of the dissolved biomass in ionic solvents in cascades of continuous rotating bed catalytic reactors, or in flash vacuum pyrolysis settings. The ability of ionic liquids to solubilise raw biomass and to catalyse its valorisation would be an enabler for state-of-the-art industrial flow chemical processes.

Appendices

A1. Supporting information for Section 2.1



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Supporting Information

A Systematic Study of Metal Triflates in Catalytic Transformations of Glucose in Water and Methanol: Identifying the Interplay of Brønsted and Lewis Acidity

Iurii Bodachivskyi,[a] Unnikrishnan Kuzhiumparambil,[b] and D. Bradley G. Williams*[a]

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1. Results and Discussion

1.1. Acid-catalyzed conversion of glucose in water

Scheme S1 Acid-catalyzed transformation of glucose into platform molecules in water.

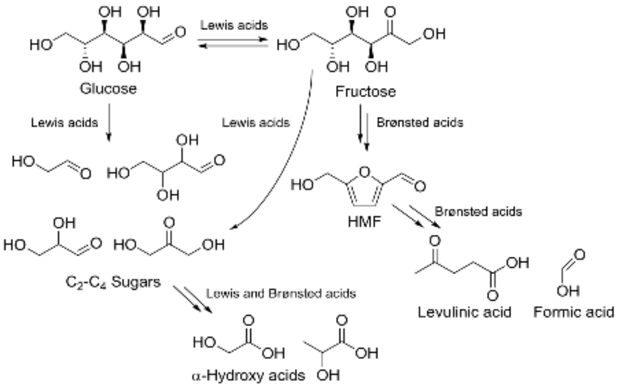


Table S1 Acid-catalyzed transformation of glucose in water[a]

Catalyst	Conversion [%]	Fructose yield [%]	Isomaltose yield [%]
$La(OTf)_3/H_3PO_4$	11 43[b]	0 0[b]	6 18 (17wt%)[b]
$Hf(OTf)_4$	38	2	0
TsOH	10 25[b]	0 0[b]	2 6[b]
H_3PO_4	9 23[b]	0 0[b]	2 2[b]
$La(OTf)_3/TsOH$	9 39[b]	0 0[b]	4 16 (15 wt%)[b]
$Sn(OTf)_2$	14	4	0
$In(OTf)_3$	22	9	0
$Al(OTf)_3$	12	5	0
AgOTf	0	0	0
LiOTf	0	0	0
$La(OTf)_3$	12 13[b]	5 1[b]	0 6[b]
$Y(OTf)_3$	7	3	0

[a] Yields and conversions are specified in mol% (in some instances also in wt% based on input glucose) based on glucose and determined on the basis of trace analysis by HPLC. Conversion means the amount of substrate consumed into any and all products. OTf = trifluoromethanesulfonate; TsOH = *p*-toluenesulfonic acid. Reaction conditions: glucose (50 mg), water (2.00 mL), catalyst (20 mol% based on glucose), reflux at atmosphere pressure, 2 h. [b] Reaction conditions: glucose (500 mg), water (1.65 mL), catalyst (20 mol% based on glucose), reflux at atmosphere pressure, 12 h.

Table S2 Results of preparative chromatographic separation of carbohydrates and comparative literature data of the condensation of glucose [a]

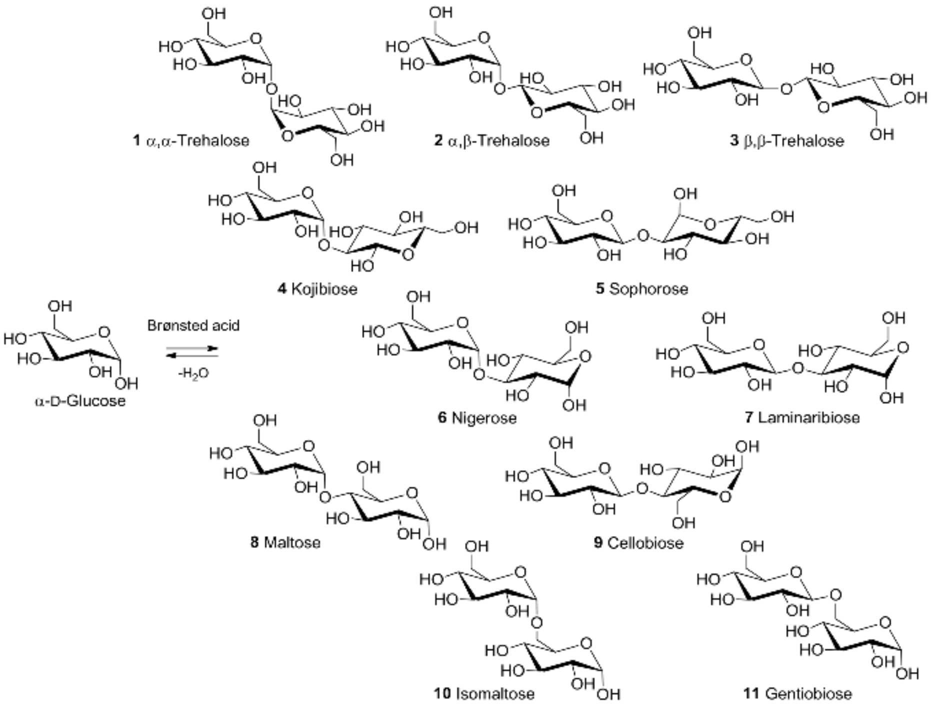
Catalyst	Monosaccharides yield [%]	Disaccharides yield [%]	Trisaccharides yield [%]	Oligosaccharides yield [%]
$La(OTf)_3/H_3PO_4$[b]	58	22	6	14
Enzyme[c]	78	18	3	1

[a] Yield is specified in wt% based on glucose. [b] Reaction conditions: glucose (500 mg), water (1.65 mL), catalyst (20 mol% based on glucose), reflux at atmosphere pressure, 12 h. Yield of disaccharides is specified as a sum of isomaltose (17%) and 'other' disaccharides (5%). [c] Yield of disaccharides is specified as a sum of isomaltose (14%) and maltose (4%). Reaction conditions: aqueous solution of glucose (40%), enzyme amyloglucosidase (10 U.g^{-1} based on glucose), 60 °C, 48h.[1]

1.2. Molecular modelling of the self-condensation of glucose

Various disaccharides that can be potentially synthesized by the self-condensation of glucose are shown in Scheme S2 and Scheme S3. A geometry optimization of various disaccharides and calculation of their Gibbs free energies of formation from α-D-glucose were conducted using methods of computational chemistry adjusted to experimental reaction parameters (solvent, reaction temperature, pressure, Table S3). This was done to determine the likely kinetic and thermodynamic products of such a reaction. The results show that disaccharides possessing α glycosidic linkage between the first and the sixth atoms of carbon of glucose (**10** and **11**) are the major thermodynamic products. They also highlight that the reaction pathway to **10** proceeds via the lowest energy protonated species between the glycosyl cation and the products (Figure S1), implying that it is the kinetic product. This correlates with experimental outcomes.

Scheme S2 Condensation of glucose into disaccharides



SUPPORTING INFORMATION

The dimerization of glucose is likely to occur through the protonation of the anomeric hydroxyl group followed by dehydration into glycosyl oxocarbenium ion (Scheme S3). This notion would, in any event, be anticipated by a global understanding of glycosidation chemistry,[2] and is supported by density-functional modeling of the reaction course as part of the present study. The appearance of dimers would be due to the nucleophilic attack of an OH group of glucose at the glycosyl cation. The last step in the process would be the removal of a hydrogen ion from the glycosidic O atom. The energy values of the structurally optimized intermediates were calculated and the values obtained support the dominant formation of the (1→6)-disaccharide isomaltose, due to the low energy of the protonated intermediate and of the final product (Figure S1).

Scheme S3 Proposed mechanism (consistent with the mechanism usually anticipated from a knowledge of saccharide chemistry) of glucose condensation into disaccharides exemplified for isomaltose. **10** H$^+$ = isomaltose with protonated glycosidic bond. **10** = isomaltose.

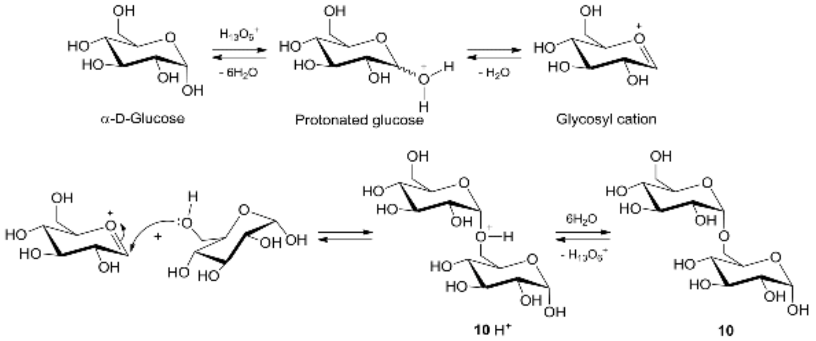


Figure S1 Progress of condensation of glucose into various disaccharides. ΔG = Gibbs free energy. Disaccharides with protonated glysosidic bond: **1** H$^+$ = α,α-trehalose, **2** H$^+$ = α,β-trehalose, **3** H$^+$ = β,β-trehalose, **4** H$^+$ = kojibiose, **5** H$^+$ = sophorose, **6** H$^+$ = nigerose, **7** H$^+$ = laminaribiose, **8** H$^+$ = maltose, **9** H$^+$ = cellobiose, **10** H$^+$ = isomaltose, **11** H$^+$ = gentiobiose. Disaccharides: **1** = α,α-trehalose, **2** = α,β-trehalose, **3** = β,β-trehalose, **4** = kojibiose, **5** = sophorose, **6** = nigerose, **7** = laminaribiose, **8** = maltose, **9** = cellobiose, **10** = isomaltose, **11** = gentiobiose.

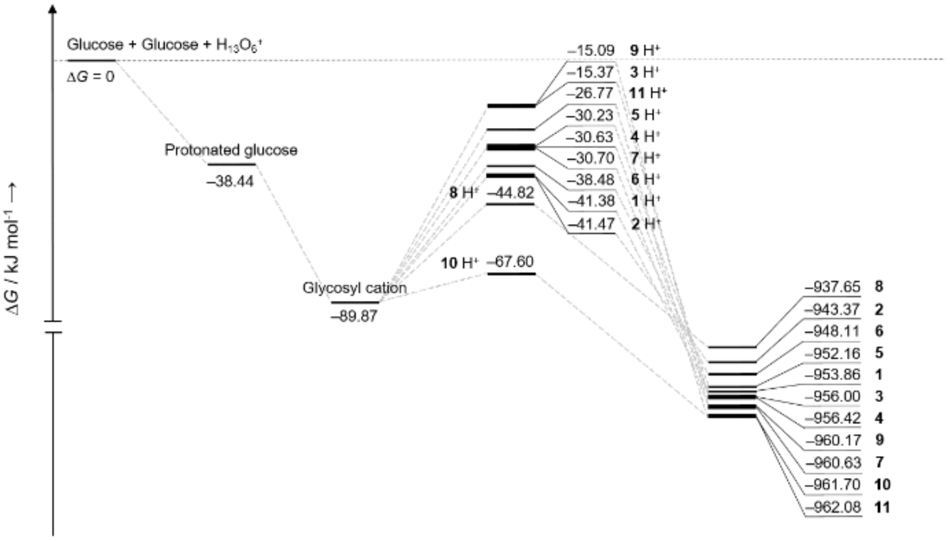
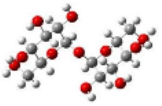
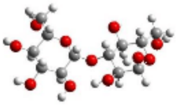
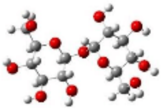
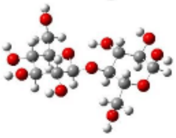
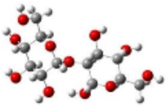
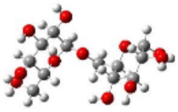
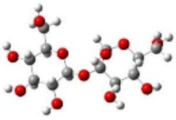


Table S3 Optimized structure of disaccharides (α-anomers) and their Gibbs free energy of formation from α-D-glucose[a]

Product	Glycosidic bond type	Optimized structure	ΔG [kJ mol^{-1}]	Product	Glycosidic bond type	Optimized structure	ΔG [kJ mol^{-1}]
α,α-Trehalose **1**	α(1→1)α		1.15	Laminaribiose **7**	β(1→3)		–5.62
α,β-Trehalose **2**	α(1→1)β		11.63	Maltose **8**	α(1→4)		17.35
β,β-Trehalose **3**	β(1→1)β		–0.99	Cellobiose **9**	β(1→4)		–5.17
Kojibiose **4**	α(1→2)		–1.41	Isomaltose **10**	α(1→6)		–6.70
Sophorose **5**	β(1→2)		2.85	Gentiobiose **11**	β(1→6)		–7.07
Nigerose **6**	α(1→3)		6.89				

[a] Geometry optimization and calculation of thermodynamic values were performed at B3LYP/6-31+g(d) level of theory considering the solvation effect of water and temperature 373.15 K. ΔG = Gibbs free energy of formation. Color of atoms: ● = hydrogen, ● = carbon, ● = oxygen.

1.3. Two-step acid-catalyzed conversion in methanol and water

Composition analyses of carbohydrates after the acid-catalyzed conversion of glucose in methanol (step 1) and water (step 2) were conducted using quantitative ^{13}C NMR and the results are presented in Figures S2–S5, S7 and S8.

Figure S2 ^{13}C NMR spectrum and ratio of carbohydrates obtained after Al(OTf)$_3$-processing in methanol (step 1) and then in water (step 2). Reaction conditions: glucose (50 mg), methanol (2.00 mL), Al(OTf)$_3$ (20 mol% based on glucose), reflux at atmosphere pressure, 1 h. then solvent exchange with water (2.00 mL). reflux at atmosphere pressure, 1 h. Parameters of NMR analysis: 50 mg sample, D$_2$O (0.60 mL), 25 °C. G$^{\alpha}$, G$^{\beta}$, MG$^{\alpha pyr}$, MG$^{\beta pyr}$, F$^{\beta fur}$, and F$^{\beta pyr}$ mean α-D-glucopyranose, β-D-glucopyranose, methyl α-D-glucopyranoside, methyl β-D-glucopyranoside, β-D-fructofuranose, and β-D-fructopyranose, respectively. The anomeric C atoms (C-1) of the various compounds are labelled on the spectrum.

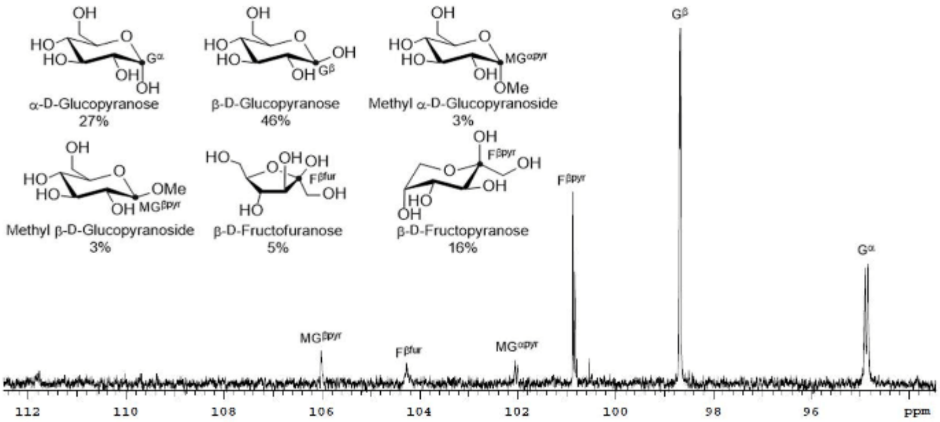


Figure S3 ^{13}C NMR spectrum and the ratio of carbohydrates obtained after La(OTf)$_3$/H$_3$PO$_4$-processing in methanol (step 1). Reaction conditions: glucose (50 mg), methanol (2.00 mL), La(OTf)$_3$ (10 mol% based on glucose), H$_3$PO$_4$ (10 mol% based on glucose), reflux at atmosphere pressure, 1 h. Parameters of NMR analysis: 50 mg sample, D$_2$O (0.60 mL), 25 °C. G$^{\alpha}$, G$^{\beta}$, MG$^{\alpha pyr}$, MG$^{\beta pyr}$, MG$^{\alpha fur}$, and MG$^{\beta fur}$ mean α-D-glucopyranose, β-D-glucopyranose, methyl α-D-glucopyranoside, methyl β-D-glucopyranoside, methyl α-D-glucofuranoside, and methyl β-D-glucofuranoside, respectively. The anomeric C atoms (C-1) of the various compounds are labelled on the spectrum.

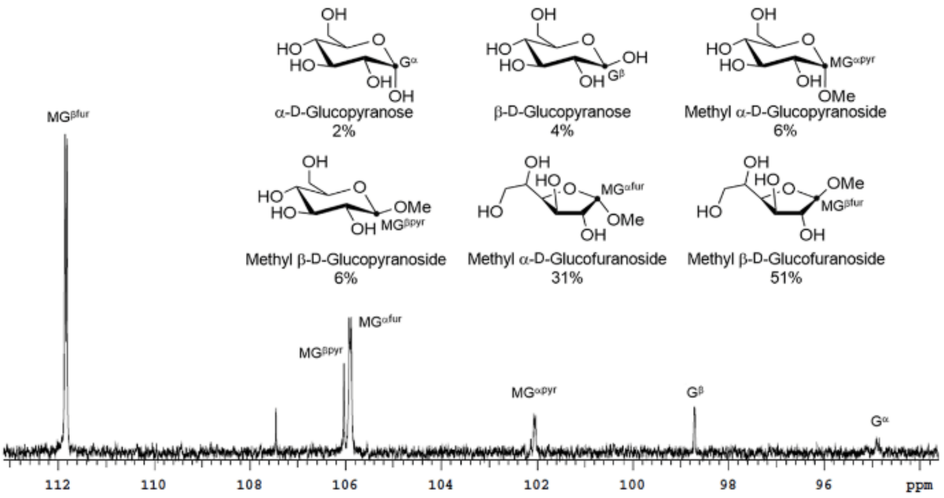


Figure S4 ^{13}C NMR spectrum and the ratio of carbohydrates obtained after Hf(OTf)$_4$-processing in methanol (step 1). Reaction conditions: glucose (50 mg), methanol (2.00 mL), Hf(OTf)$_4$ (20 mol% based on glucose), reflux at atmosphere pressure, 1 h. Parameters of NMR analysis: 50 mg sample, D$_2$O (0.60 mL), 25 °C. G$^{\alpha}$, G$^{\beta}$, MG$^{\alpha pyr}$, MG$^{\beta pyr}$, MG$^{\alpha fur}$, and MG$^{\beta fur}$ mean α-D-glucopyranose, β-D-glucopyranose, methyl α-D-glucopyranoside, methyl β-D-glucopyranoside, methyl α-D-glucofuranoside, and methyl β-D-glucofuranoside, respectively. The anomeric C atoms (C-1) of the various compounds are labelled on the spectrum.

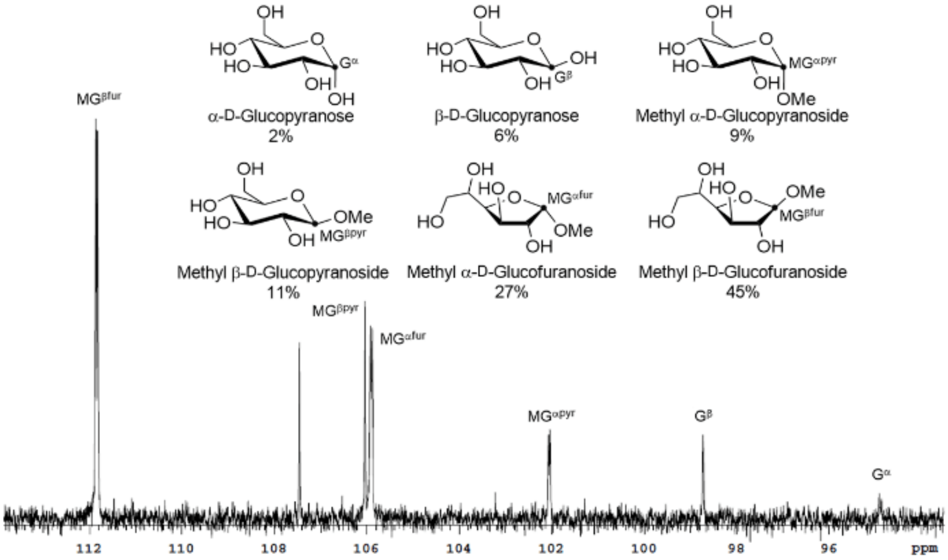


Figure S5 ^{13}C NMR spectrum and the ratio of carbohydrates obtained after La(OTf)$_3$-processing in methanol (step 1). Reaction conditions: glucose (50 mg), methanol (2.00 mL), La(OTf)$_3$ (20 mol% based on glucose), reflux at atmosphere pressure, 1 h. Parameters of NMR analysis: 50 mg sample, D$_2$O (0.60 mL), 25 °C. G$^{\alpha}$, G$^{\beta}$, MG$^{\alpha fur}$, and MG$^{\beta fur}$ mean α-D-glucopyranose, β-D-glucopyranose, methyl α-D-glucofuranoside, and methyl β-D-glucofuranoside, respectively. The anomeric C atoms (C-1) of the various compounds are labelled on the spectrum.

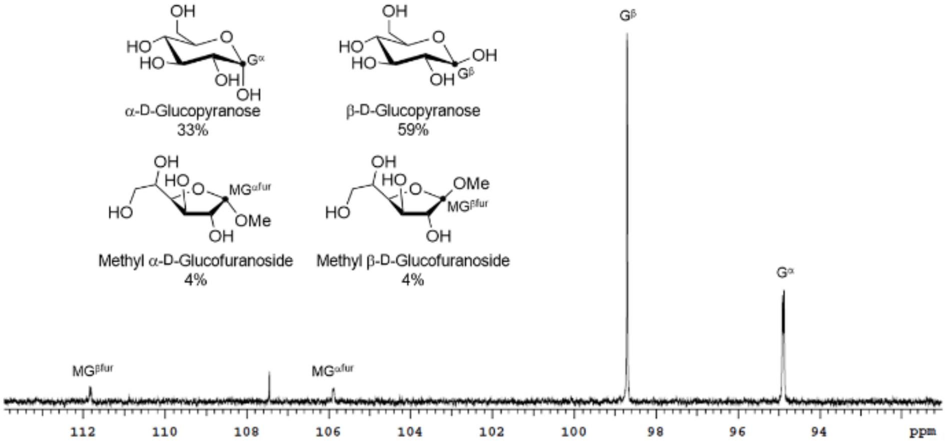


Table S4 Al(OTf)$_3$/TBP-catalyzed transformation of glucose in methanol and water[a]

TBP loading [mol%]	Time [h]	Conv [%]	Fructose yield [%]	MG yield [%]
30	1	34	20	1
30	2	39	30	4
30	4	44	32	6
60	4	27	14	1
60	8	31	22	1
60	12	36	32	1
60	24	63	41	1
60	36	64	47	1

[a] TBP = 2,6-di-*tert*-butyl-4-methylpyridine; MG = methyl glucopyranosides. TBP loading and yields of products are specified in mol% based on glucose. Reaction conditions: glucose (50 mg), methanol (2.00 mL), Al(OTf)$_3$ (20 mol% based on glucose), reflux at atmosphere pressure (reaction time of the first step is shown in Table), solvent exchange with water (2.00 mL), solvent under reflux at atmosphere pressure (1 h).

Figure S6 represents a ^{1}H NMR spectrum of the dimethyl acetal of MMF (5-(methoxymethyl)furfural) isolated after Al(OTf)$_3$-catalyzed processing of glucose in methanol (first step). This product was unstable and hydrolyzed into MMF even in deuterochloroform, likely due to trace amounts of HCl and water present in the deuterated solvent. It is worth noting that deacetalization of the acetal occurs quantitatively in aqueous solution of Al(OTf)$_3$ (0.028 M, appropriate to the loading of the catalyst used for the acid-catalyzed conversion of glucose) at room temperature (1 h), or in neat water at 80 °C (2 h), in accordance with earlier findings in deacetalization processes shown in the literature.[3]

Figure S6 ^{1}H NMR spectrum of dimethyl acetal and MMF (product of hydrolysis). Parameters of NMR analysis: 18 mg sample, CDCl$_3$ (0.50 mL), 25 °C.

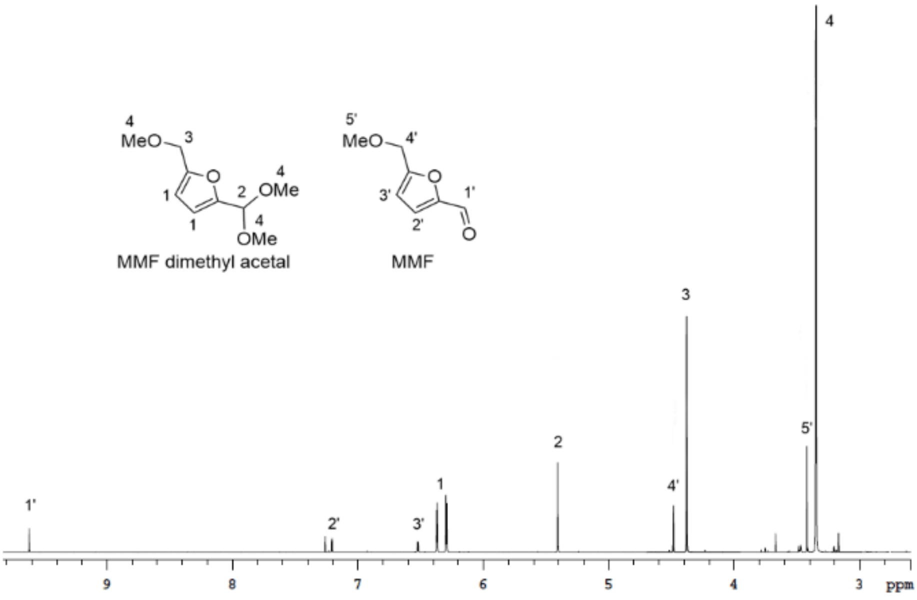


Table S5. TsOH-catalyzed conversion of fructose and HMF [a]

Substrate	Conv [%]	MMF yield [%]	MLev yield[b] [%]
Fructose	76	31	25
HMF	99	30	45

[a] Yields and conversions are specified in mol% based on the substrate and determined on the basis of trace analysis by HPLC. HMF = 5-(hydroxymethyl)furfural; MMF = 5-(methoxymethyl)furfural; MLev = methyl levulinate. Reaction conditions: substrate (50 mg), methanol (2.00 mL), catalyst (20 mol% based on the substrate), 100 °C, 1 h, then solvent exchange with water (2.00 mL), reflux at atmosphere pressure, 1 h. [b] Yield of MLev was identified immediately after the processing in methanol.

Figure S7 ^{13}C NMR spectrum and the ratio of carbohydrates obtained after TsOH-processing in methanol (step 1). Reaction conditions: glucose (50 mg), methanol (2.00 mL). TsOH (20 mol% based on glucose). 120 °C, 8 h. Parameters of NMR analysis: 50 mg sample. D_2O (0.60 mL). 25 °C. $MG^{\alpha pyr}$, $MG^{\beta pyr}$, $MG^{\alpha fur}$, and $MG^{\beta fur}$ mean methyl α-D-glucopyranoside, methyl β-D-glucopyranoside, methyl α-D-glucofuranoside, and methyl β-D-glucofuranoside, respectively. The anomeric C atoms (C-1) of the various compounds are labelled on the spectrum.

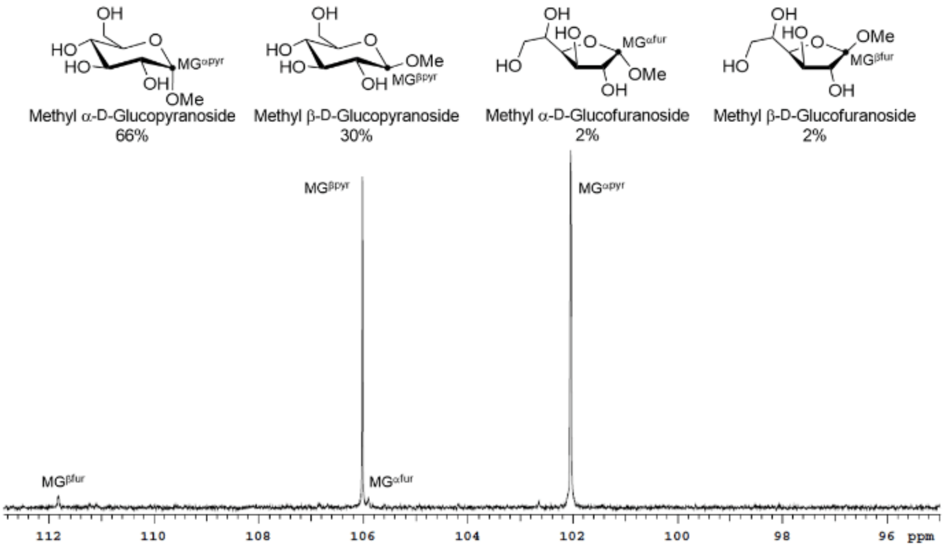
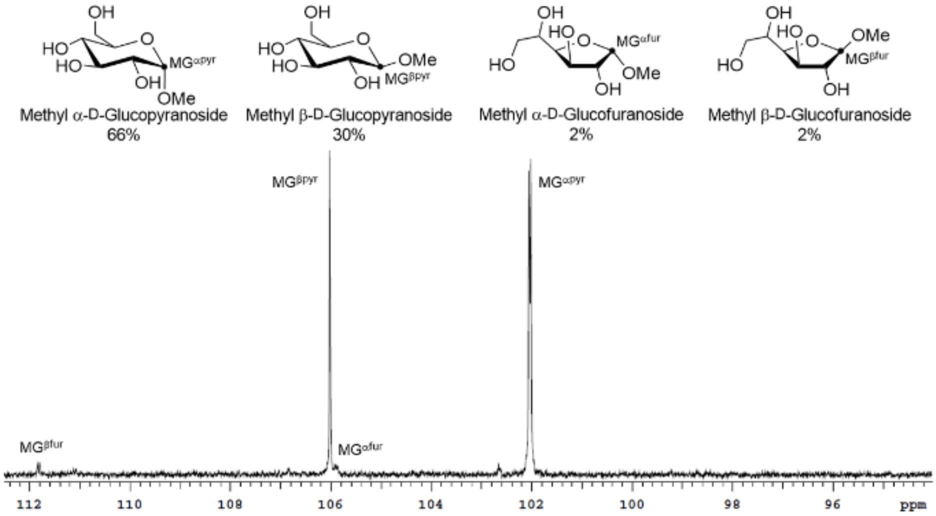


Figure S8 ^{13}C NMR spectrum and the ratio of carbohydrates obtained after $La(OTf)_3/H_3PO_4$-processing in methanol (step 1). Reaction conditions: glucose (50 mg), methanol (2.00 mL), $La(OTf)_3$ (10 mol% based on glucose), H_3PO_4 (10 mol% based on glucose), 120 °C, 8 h. Parameters of NMR analysis: 50 mg sample, D_2O (0.60 mL), 25 °C. $MG^{\alpha pyr}$, $MG^{\beta pyr}$, $MG^{\alpha fur}$, and $MG^{\beta fur}$ mean methyl α-D-glucopyranoside, methyl β-D-glucopyranoside, methyl α-D-glucofuranoside, and methyl β-D-glucofuranoside, respectively. The anomeric C atoms (C-1) of the various compounds are labelled on the spectrum.



2. Experimental Procedures

2.1. Analytical methods

2.1.1. Chromatography-analysis

Chromatographic separation and analysis of carbohydrates after acid-catalyzed transformations of glucose were performed on a Waters 2695 LC instrument connected to Erma ERC-7510 refractive index detector. The separation was performed on a Supelco apHera NH2-Polymer analytical column (150 mm × 4.6 mm, 5 µm) using a mixture of acetonitrile and water (65:35 v/v) as the mobile phase at a flow rate 0.6 mL·min^{-1} and a run time of 15 min. HPLC analysis of HMF and MMF was performed using an Agilent 1290 LC instrument equipped with an Agilent Zorbax Eclipse XDB–C18 analytical column (150 mm × 4.6 mm, 3 µm) and Agilent 1260 DAD VL+ detector (detection wavelength: 278 nm). The mobile phase was a mixture of methanol and water (15:85 v/v) at a flow rate of 1.1 mL·min^{-1} with a run time of 20 min. MLev was analyzed using an Agilent 6890 GC system coupled to an Agilent Quadrupole Mass Selective detector (5973N) using a HP-5MS fused capillary column (Agilent Technologies 5%-phenyl-methylpolysiloxane, with dimensions 30 m, 0.25 mm i.d., film thickness 0.25 µm). Helium was used as carrier gas (flow rate: 1.2 mL·min^{-1}) and the GC inlet temperature was 250 °C. A splitless mode of injection was used with a purge time of 1 min. The column temperature program was as follows: initial oven temperature of 50 °C (2 min), followed by a 4 °C/min ramp up to 220 °C, and then to 300 °C at 60 °C/min (held for 3 min). Peaks were identified by comparison of their retention times and mass spectrum with analytical standards. Quantitative analysis was performed with the use of a standard curve plotted with analytical standards.

2.1.2. NMR Spectroscopy

NMR spectra of the products were recorded on an Agilent 500 MHz NMR spectrometer using deuterium oxide (D_2O), or deuterochloroform ($CDCl_3$) as solvents. Samples (16–50 mg) were dissolved in the selected solvents (0.50–0.60 mL) in a 5 mm NMR tube and the spectra were collected at 25 °C with chemical shifts referenced relative to: deuterated sodium 3-trimethylsilylpropionate ([D$_4$]TMSP, ^{1}H, ^{13}C: δ = 0.00 ppm) for samples recorded in D_2O, and the solvent itself for samples recorded in deuterochloroform (^{1}H: δ = 7.26 ppm; ^{13}C: δ = 77.0 ppm). For quantitative ^{13}C NMR analysis of mixtures of carbohydrates, a relaxation delay of 15 s and pulse angle of 45° were employed; spectra were recorded in 2000 scans. 2D NMR spectra (HSQC, HMBC, and COSY) were used to unambiguously assign the peaks.

2.1.3. High resolution mass spectrometry

HRMS analysis was performed using an Agilent 6550 QTOF attached to an Agilent 1200 series HPLC system. The MS was operated in negative (carbohydrates, MLev), or positive (HMF, MMF) ion mode using the following conditions: nebulizer pressure 200 kPa, gas flow-rate 10 L·min^{-1}, gas temperature 300 °C, capillary voltage 4000 V, fragmentor 150 and skimmer 65 V. The instrument was operated in the extended dynamic range mode with data collected in *m/z* range 60–1000. Injection volume was 1 µL.

2.1.4. IR spectrometry

IR spectra were collected using a thin film on a Thermo Scientific Nicolet 6700 spectrometer in a range 4000–450 cm^{-1}.

2.1.5. pH Readings

pH Readings were recorded at room temperature (22–23 °C) using a Mettler Toledo pH meter adapted with a standard glass electrode with prior calibration by two buffer solutions (pH = 4.00, pH = 7.00). Measurements were performed in triplicate and the average values are presented.

2.2. Theoretical methods

Density functional computations were conducted using Gaussian 09 software.[4] Optimization of carbohydrates and reaction intermediates was conducted using the B3LYP functional and the basis set 6-31+g(d). Predictions of thermochemical properties were performed in a simulated system at 373.15 K and pressure of 101.325 kPa. The solvation effect by water was considered using a polarizable continuum model. Relevant results from the molecular modeling operations, as specified above, are given in Figure S1 and Table S3.

2.3. Preparative separation of products

2.3.1. Chromatographic separation of mono- and oligosaccharides

Preparative separation of carbohydrates after self-condensation of glucose was performed by employing charcoal-celite column chromatography that is known to differentiate between mono-, di-, tri- and oligosaccharides.[5] A glass chromatographic tube (height = 50 cm, diameter = 5 cm) was packed with a premixed charcoal (6.0 g) and celite (6.0 g) and the stationary phase was washed with deionized water (100 mL). A neutralized and centrifuged solution of carbohydrates (40 mL, centrifuged at 3,000 × g for 20 min) was added to the column and the carbohydrates were consecutively eluted with water (400 mL), 5% (v/v) aqueous ethanol solution (450 mL), 10% aqueous ethanol solution (800 mL), and 30% aqueous ethanol solution (500 mL) to isolate mono-, di-, tri-, and oligosaccharide fractions, respectively. The fractions were analyzed using HPLC analysis, as detailed above. HRMS analysis of the isolated fractions confirmed the presence of glucose in water (*m/z*: calcd for $C_6H_{11}O_6$ [M–H]$^-$: 179.0561, found: 179.0563), disaccharides in 5% ethanol (*m/z*: calcd for $C_{12}H_{21}O_{11}$ [M–H]$^-$: 341.1088, found: 341.1085), trisaccharides in 10% ethanol (*m/z*: calcd for $C_{18}H_{31}O_{16}$ [M–H]$^-$: 503.1618, found: 503.1623), oligosaccharides in 30% ethanol (*m/z*: $C_{18}H_{31}O_{16}$ $[M–H]^-$: 503.1618, found: 503.1616; $C_{24}H_{41}O_{21}$ $[M–H]^-$: 665.2146, found: 665.2142; $C_{30}H_{51}O_{26}$ $[M–H]^-$: 827.2674, found: 827.2669; $C_{36}H_{61}O_{31}$ $[M–H]^-$: 989.3202, found: 989.3193). The fractions were centrifuged (3,000 × g for 20 min), decanted and freeze-dried (–78.0 °C, 0.01 mbar, 36 h) to provide the outcomes represented in Table S2. NMR spectra for the isolated disaccharides were assigned by comparison with literature data and spectra produced from an authentic commercial sample of isomaltose (Figures S9–S16).[6–9]

2.3.2. Isolation of carbohydrates for ^{13}C NMR composition analyses

The presence of carbohydrates and the ratio between them after processing in methanol (step 1: solvent under reflux at atmosphere pressure, 1 h), or methanol and water (step 1 + step 2: solvent under reflux at atmosphere pressure, 1 h), was confirmed by quantitative ^{13}C NMR analysis (Figures S2–S5, S7, S8). Preparation of samples for NMR spectroscopy after step 1 comprised acid-catalyzed transformation (as specified in the main text), neutralization of the catalyst with aqueous solution of sodium hydrogen carbonate (2.00 mL, 0.05 M), centrifugation (20,000 × g for 10 min), evaporation of methanol under reduced pressure (30 °C, 90 mbar), then freeze-drying (–78.0 °C, 0.01 mbar, 12 h) and addition of D_2O (0.60 mL). Preparation of samples for NMR spectroscopy after step 2 consisted of acid-catalyzed transformation (step 1 + step 2, as detailed in the main text), then neutralization of the catalyst (aqueous $NaHCO_3$, 2.00 mL, 0.05 M), centrifugation (20,000 × g for 10 min), freeze-drying (–78.0 °C, 0.01 mbar, 12 h) and addition of D_2O (0.60 mL).

2.3.3. Isolation of methyl glucosides

Isolation of MG for NMR, HRMS and IR analyses was done from solution after TsOH-catalyzed conversion of glucose in methanol at a reaction temperature of 120 °C for 8 h, as detailed in the main text. This was done by evaporation of methanol under reduced pressure (30 °C, 90 mbar), dispersion by sonication of the crude product in a mixed solvent comprising ethanol/ethyl acetate (4.0 mL, ethanol/EtOAc 1:20 v/v mixture), filtration, and washing of the solid phase with the same solvent mixture (3 × 2.0 mL). The isolated MG was dried under reduced pressure (room temperature, 0.01 mbar) before analysis. NMR spectra of the recovered product are shown in Figures S17 and S18.

2.3.4. Isolation of MMF-dimethyl acetal

The presence of the dimethyl acetal of MMF after processing in methanol (step 1) was established by ^1H NMR analysis. The reaction mixture obtained after the first step of $Al(OTf)_3$-catalyzed conversion of glucose (20.0 mL, combined methanolic solutions) after evaporation of solvent was dispersed in ethanol/EtOAc mixture (10 mL, 1:20 v/v mixture) and filtered through a layer of silica gel to remove the catalyst and carbohydrates. The silica gel layer was washed with EtOAc (2 × 10.0 mL) and the resulting solutions of products were combined. The solvent was removed under reduced pressure (30 °C, 90 mbar) and the crude mixture of products was subjected to flash column chromatography (hexane/EtOAc, 1.5:1 v/v mixture, Rf = 0.760; UV, $KMnO_4$). The ^1H NMR spectrum of the isolated dimethyl acetal of MMF is shown in Figure S6.

2.3.5. Isolation of non-polar products

Recovery of non-polar products, such as HMF, MMF and MLev, for characterization comprised extraction thereof from neutralized aqueous phases (20.0 mL, combined aqueous phases achieved after $Al(OTf)_3$-catalyzed conversion of glucose) with EtOAc (4 × 30.0 mL). The resulting solutions of products in EtOAc were combined and dried over $MgSO_4$ and the solvent was removed under reduced pressure (30 °C, 50 mbar). The crude mixture was subjected to flash column chromatography (hexane/EtOAc, 1.5:1 v/v mixture) to isolate HMF, MMF and MLev. NMR spectra of the isolated products are represented in Figures S19–S24.

2.4. Two-step TsOH-catalyzed transformations of fructose and HMF in methanol and water

Two-step transformations of fructose and HMF using TsOH as catalyst were performed as follows. The substrate (50 mg), methanol (2.00 mL) and TsOH (20 mol% based on the substrate) were introduced to a glass pressure tube equipped with a magnetic follower and the reactor was sealed. The mixture was heated and stirred at 100 °C for 1 h (step 1). After cooling, the mixture was transferred to a round-bottom flask and methanol was evaporated under reduced pressure (30 °C, 90 mbar). Then water (2.00 mL) was added to the reactor (solvent exchange) and the resulting mixture was heated and stirred under reflux at atmosphere pressure for 1 h (step 2). The recovered solutions were analyzed using an HPLC system, as detailed above, and results are summarized in Table S5.

3. Copies of NMR spectra of synthesized products

Following NMR spectra of disaccharides (Figures S9–S16) are assigned according to the numbering scheme used in Scheme S4.

Scheme S4 Structure of isomaltose and indexes for α- and β-anomers.

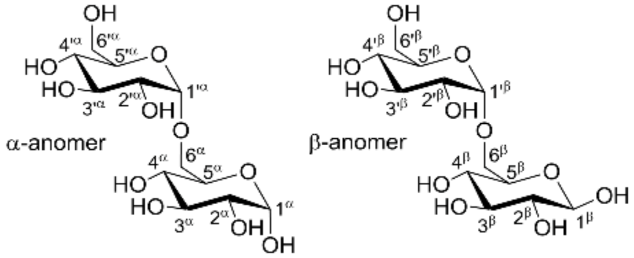


Figure S9 ^{1}H NMR spectrum of a reference sample of authentic isomaltose: 20 mg sample, D_2O (0.50 mL), 25 °C.

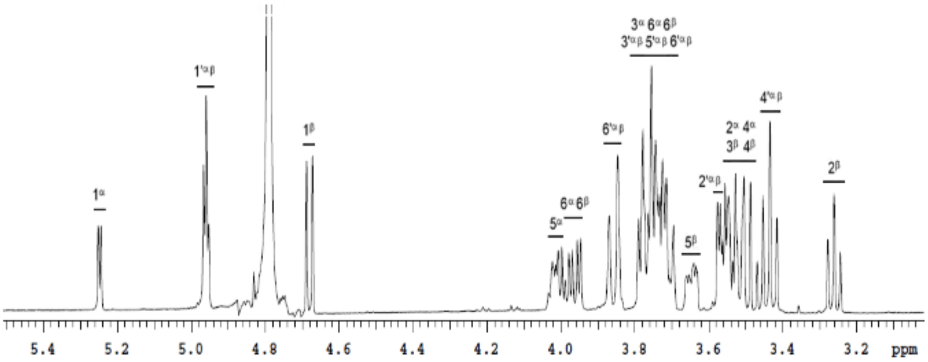


Figure S10 ^1H NMR spectrum of the isolated disaccharides: 16 mg sample, D_2O (0.50 mL), 25 °C.

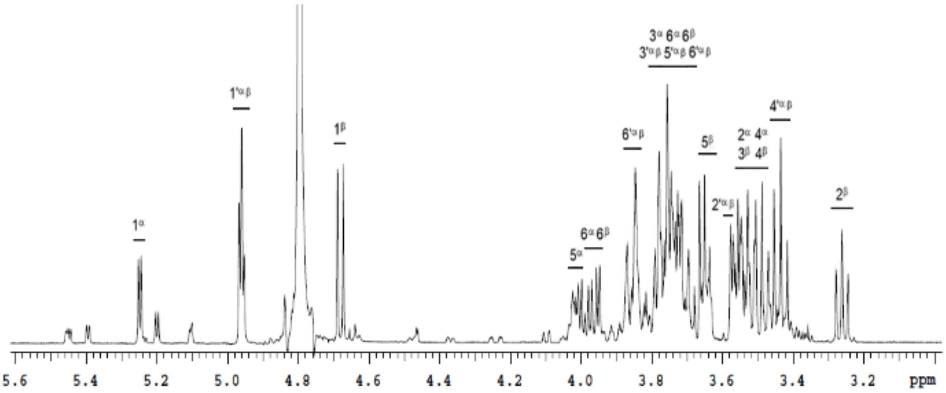


Figure S11 ^{13}C NMR spectrum of a reference sample of authentic isomaltose: 20 mg sample, D_2O (0.50 mL), 25 °C.

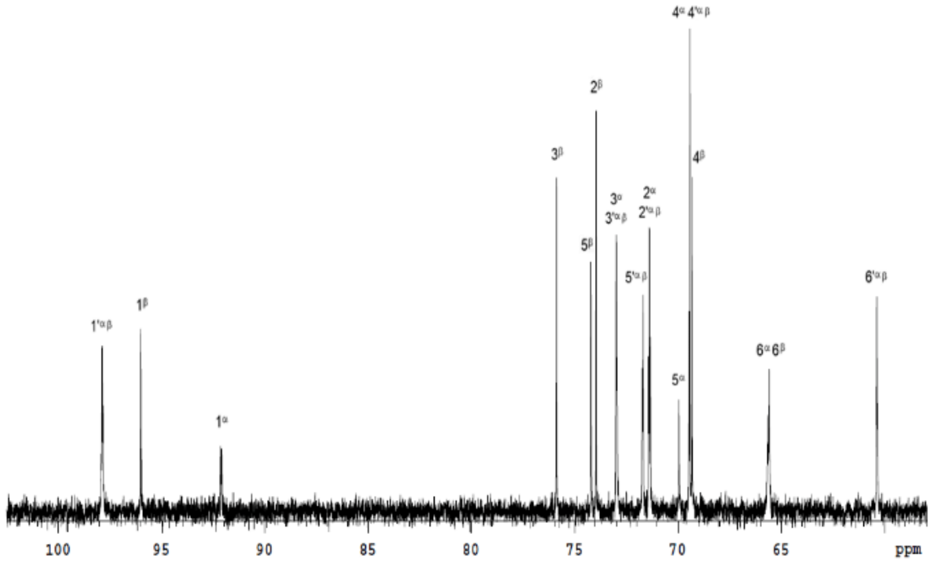


Figure S12 ^{13}C NMR spectrum of the isolated disaccharides: 16 mg sample, D_2O (0.50 mL), 25 °C.

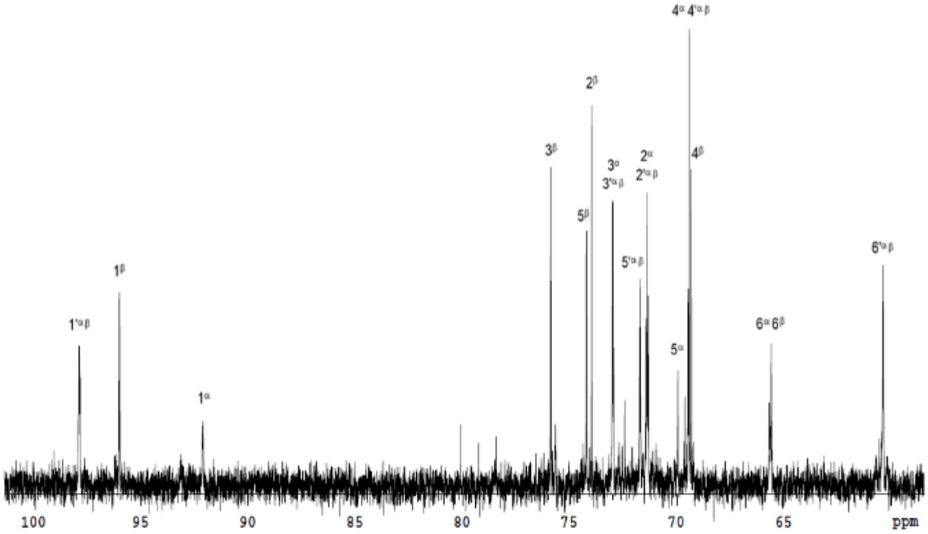


Figure S13 HSQC NMR spectrum of a reference sample of authentic isomaltose: 20 mg sample, D_2O (0.50 mL), 25 °C.

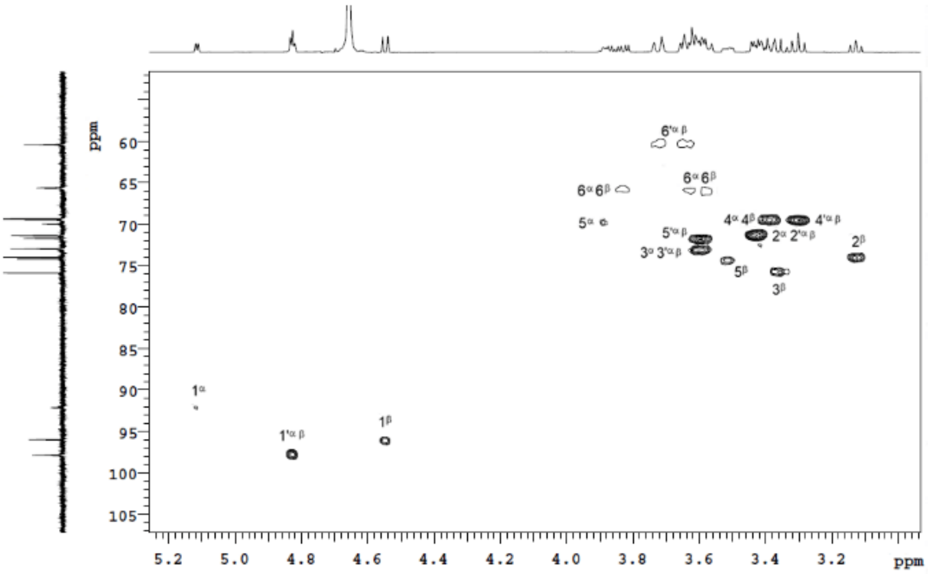


Figure S14 HSQC NMR spectrum of the isolated disaccharides: 16 mg sample, D_2O (0.50 mL), 25 °C.

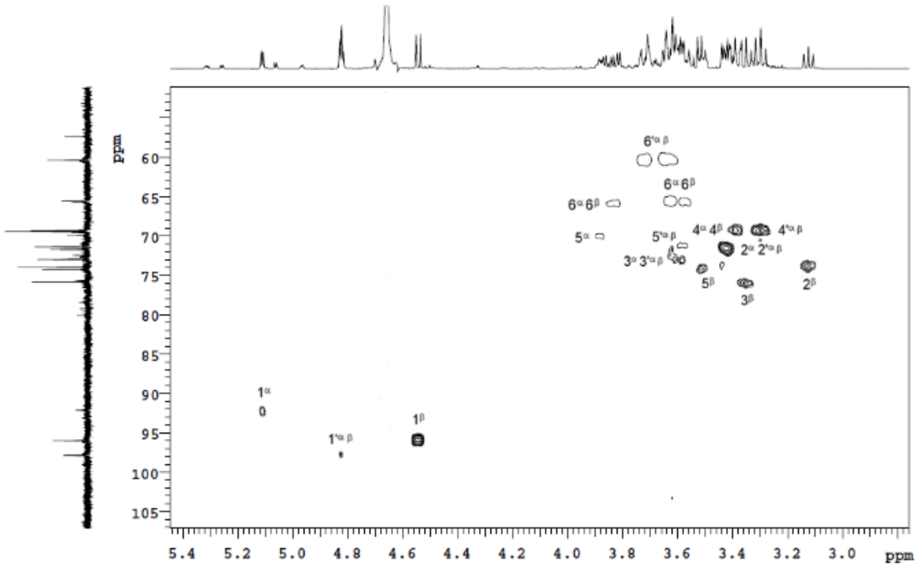


Figure S15 HMBC NMR spectrum of a reference sample of authentic isomaltose: 20 mg sample, D_2O (0.50 mL), 25 °C.

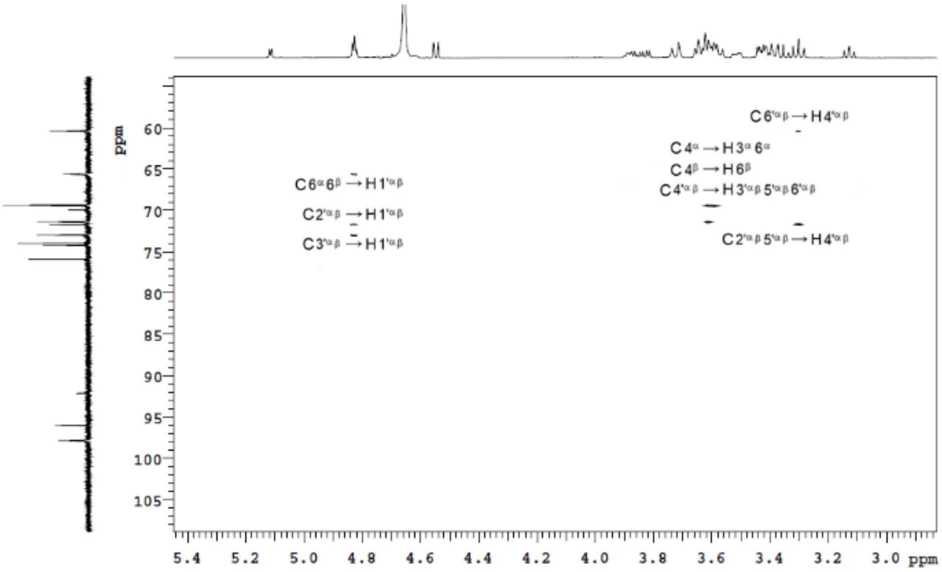


Figure S16 HMBC NMR spectrum of the isolated disaccharides: 16 mg sample, D_2O (0.50 mL), 25 °C.

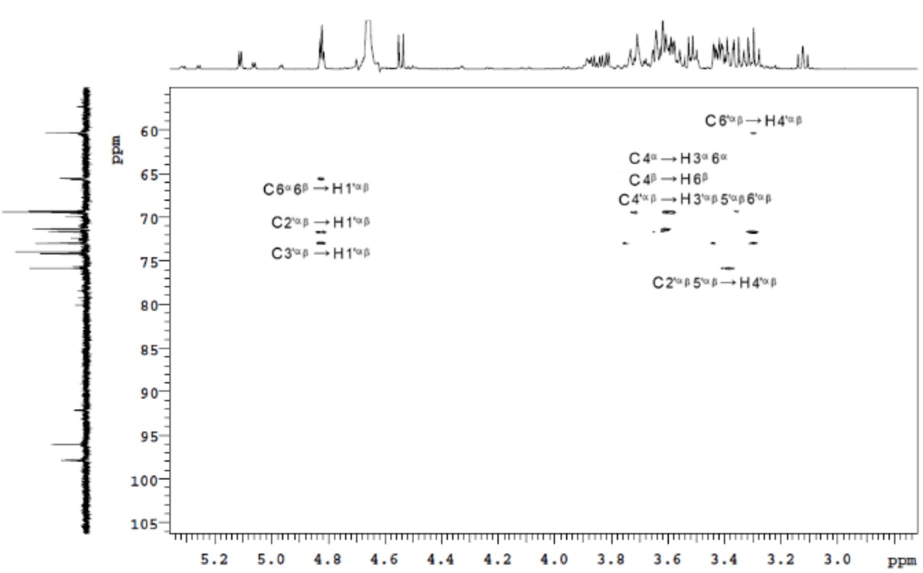


Figure S17 ^1H NMR spectrum of the isolated MG (α-anomer): 20 mg sample, D_2O (0.50 mL), 25 °C.

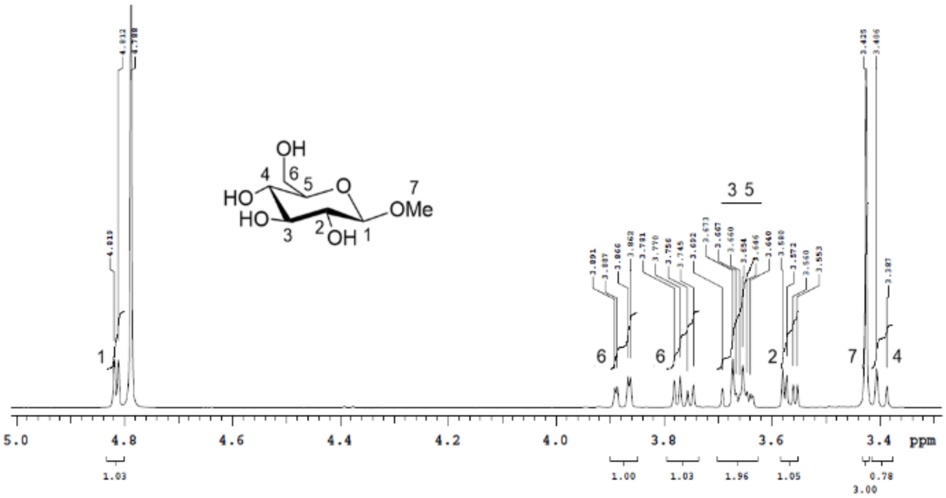


Figure S18 ^{13}C NMR spectrum of the isolated MG (α-anomer): 20 mg sample, D_2O (0.50 mL), 25 °C.

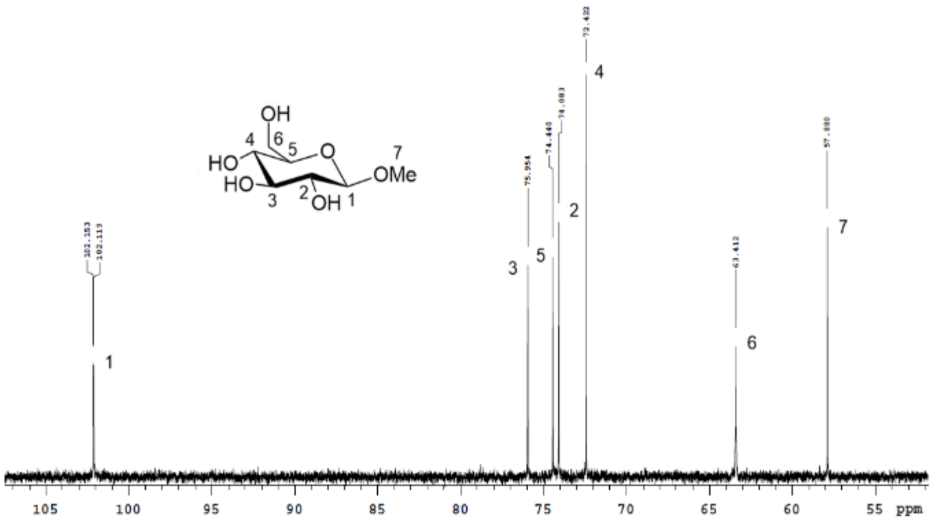


Figure S19 ^{1}H NMR spectrum of the isolated HMF: 18 mg sample, $CDCl_3$ (0.50 mL), 25 °C.

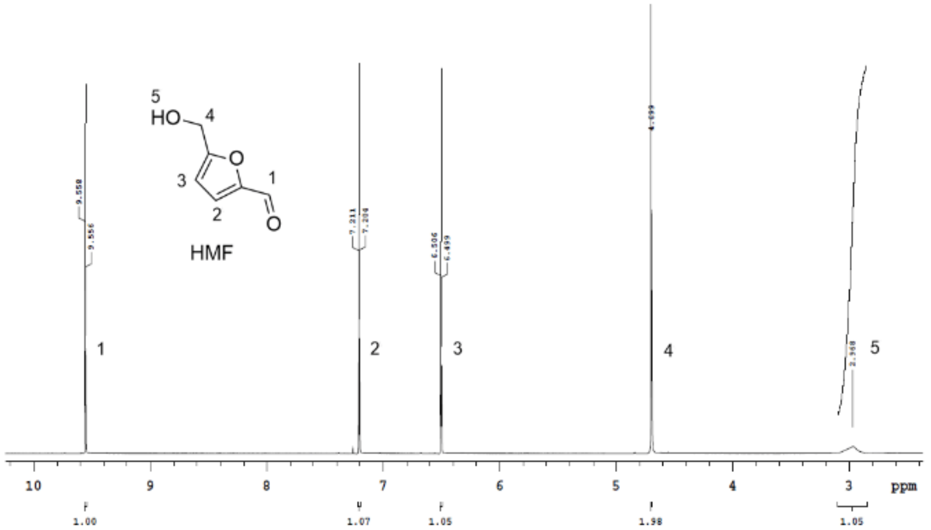


Figure S20 ^{13}C NMR spectrum of the isolated HMF: 18 mg sample, $CDCl_3$ (0.50 mL), 25 °C.

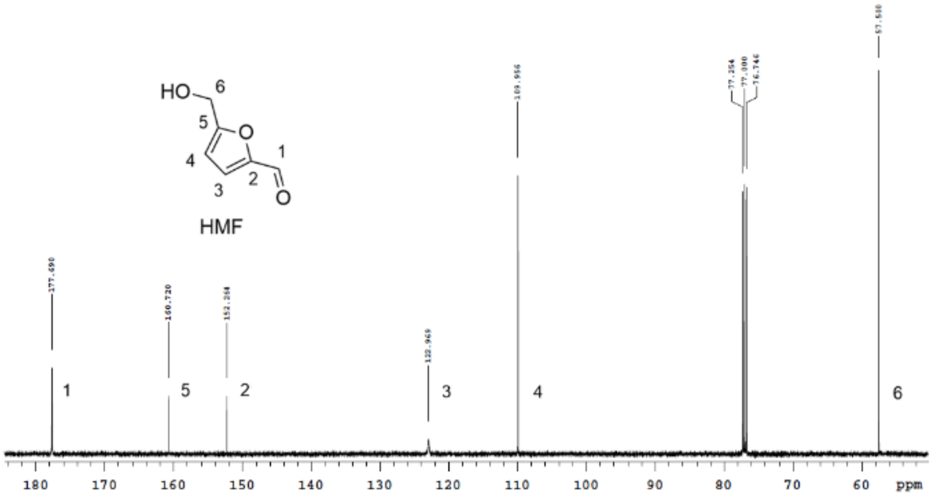


Figure S21 ^{1}H NMR spectrum of the isolated MMF: 16 mg sample, $CDCl_3$ (0.50 mL), 25 °C.

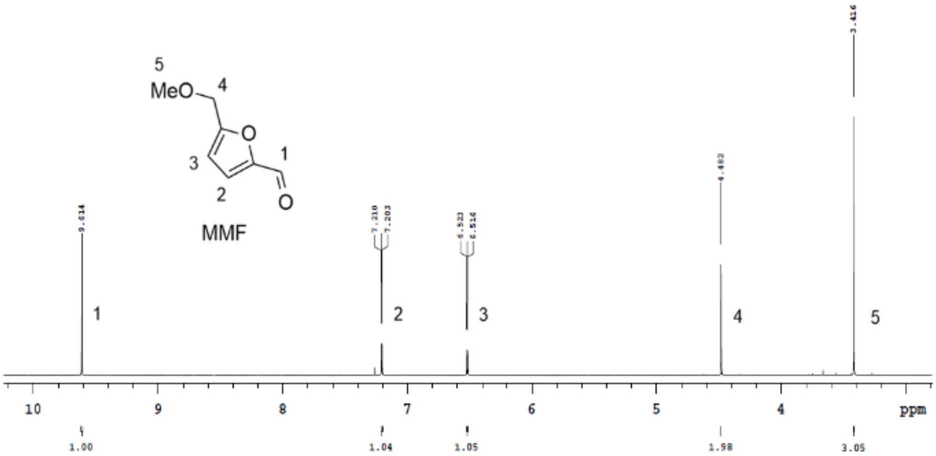


Figure S22 ^{13}C NMR spectrum of the isolated MMF: 16 mg sample, $CDCl_3$ (0.50 mL), 25 °C.

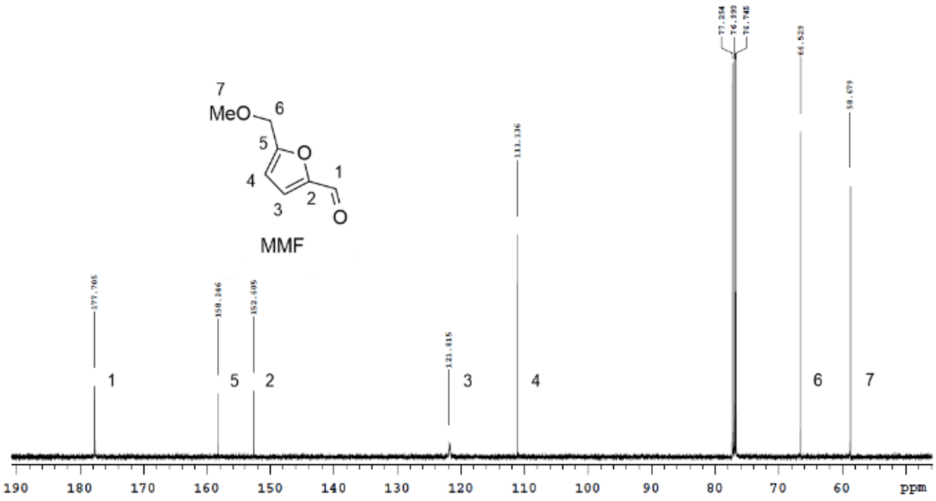


Figure S23 ^{1}H NMR spectrum of the isolated MLev: 16 mg sample, $CDCl_3$ (0.50 mL), 25 °C.

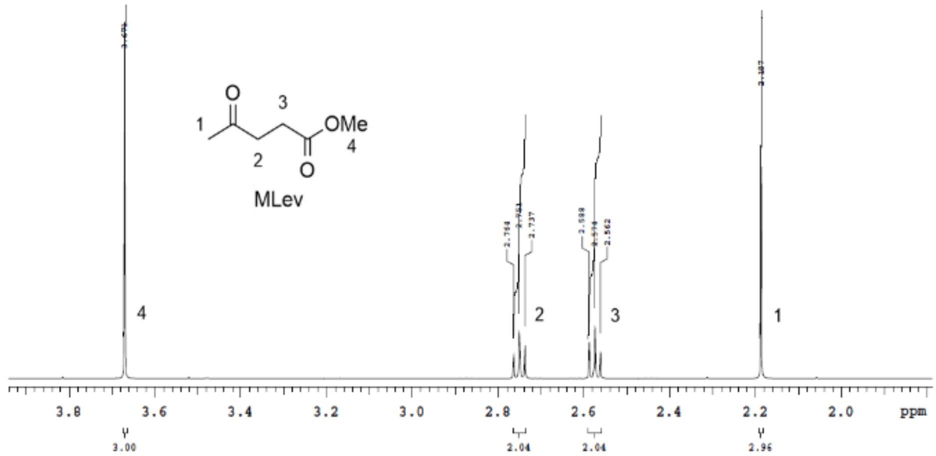
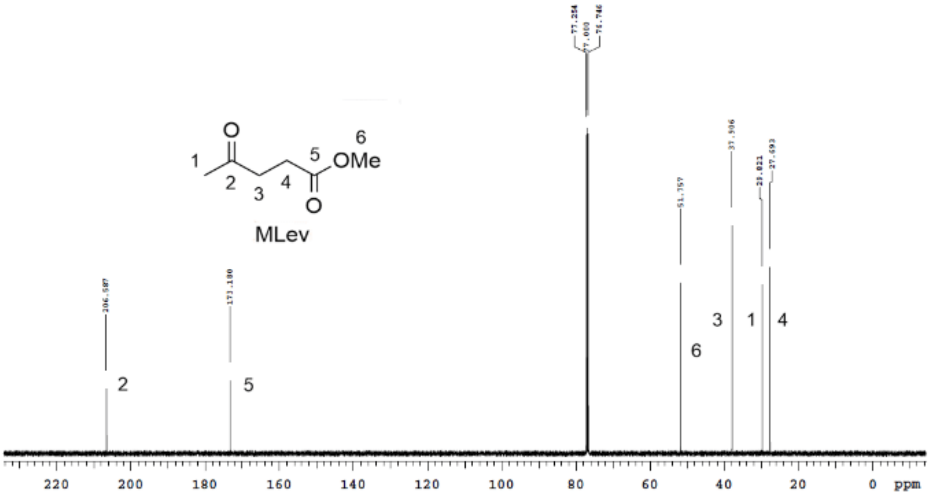


Figure S24 ^{13}C NMR spectrum of the isolated MLev: 16 mg sample, CDCl$_3$ (0.50 mL), 25 °C.



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A2. Supporting information for Section 2.2

Supporting Information

Metal triflates are tunable acidic catalysts for high yielding conversion of cellulosic biomass into ethyl levulinate

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Table of Contents

1. Supporting data

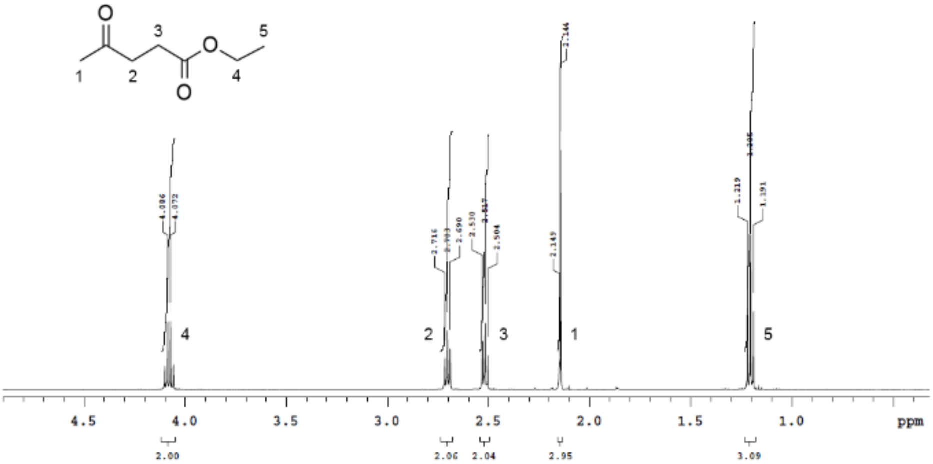

Fig. S1. ^1H NMR spectrum of the isolated ethyl levulinate recorded in $CDCl_3$.

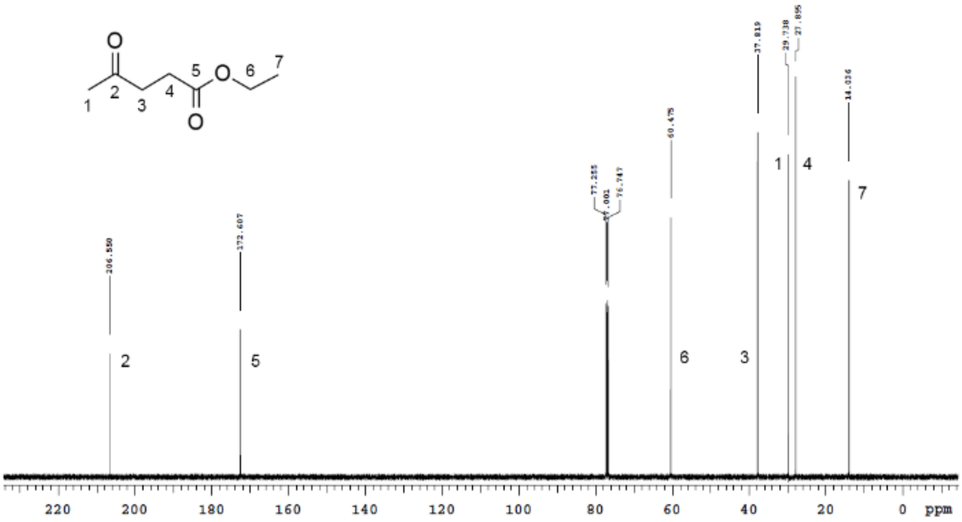

Fig. S2. ^{13}C NMR spectrum of the isolated ethyl levulinate recorded in $CDCl_3$.

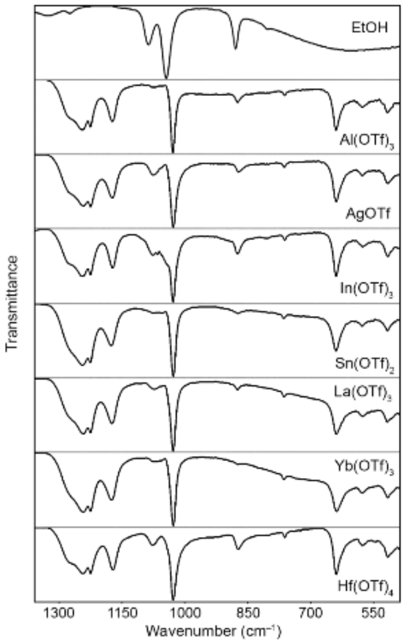

Fig. S3. IR spectra of ethanol and 0.1 M ethanolic solutions of metal triflates (ethanol peaks were subtracted from the spectra of solutions). Characteristic vibrations of triflates correspond with data reported in literature [1].

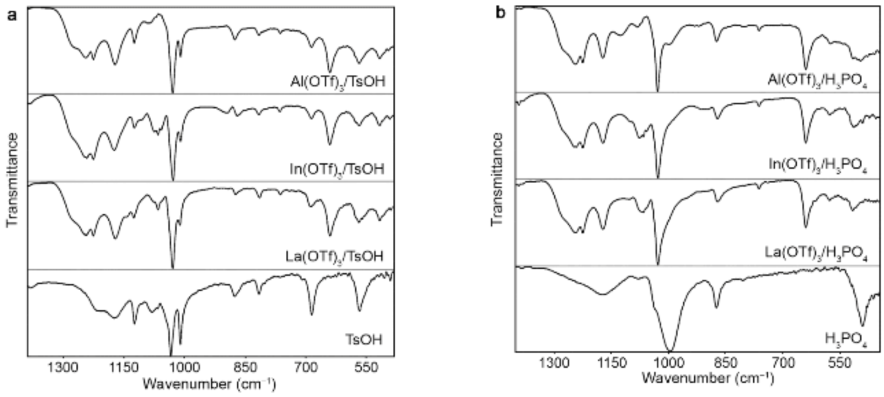

Fig. S4. IR spectra of ethanol 0.1 M solutions of mixed metal triflates with a) *p*-toluenesulfonic acid (TsOH), and b) H_3PO_4.

Table S1. Results of pretreatment of various cellulosic substrates in the deep eutectic solvent based on choline chloride and oxalic acid [a]

Substrate	Cellulose powder yield (wt%)	Average particle size (μm)	Crystallinity index [b]
Microcrystalline cellulose	–	150	90
Eucalyptus cellulose	92	60	86
Pinus cellulose	98	79	87
	96[c]	82[c]	80
	97[d]	80[d]	81
Pinus cellulose (unbleached)	93	86	86
Wood pulp (*Pinus*)	67	54	77

[a] Yield of cellulose is specified in wt% based on the dry substrate [2]. Pretreatment conditions: substrate (0.500 g), choline chloride/oxalic acid dihydrate solvent (1:1 molar ratio, 10.000 g), 80 °C, 2 h.

[b] The crystallinity index was determined from the height ratio between the intensity of the crystalline peak and total intensity [3,4].

[c,d] Values obtained after the second and third recycling of the deep eutectic solvent, respectively.

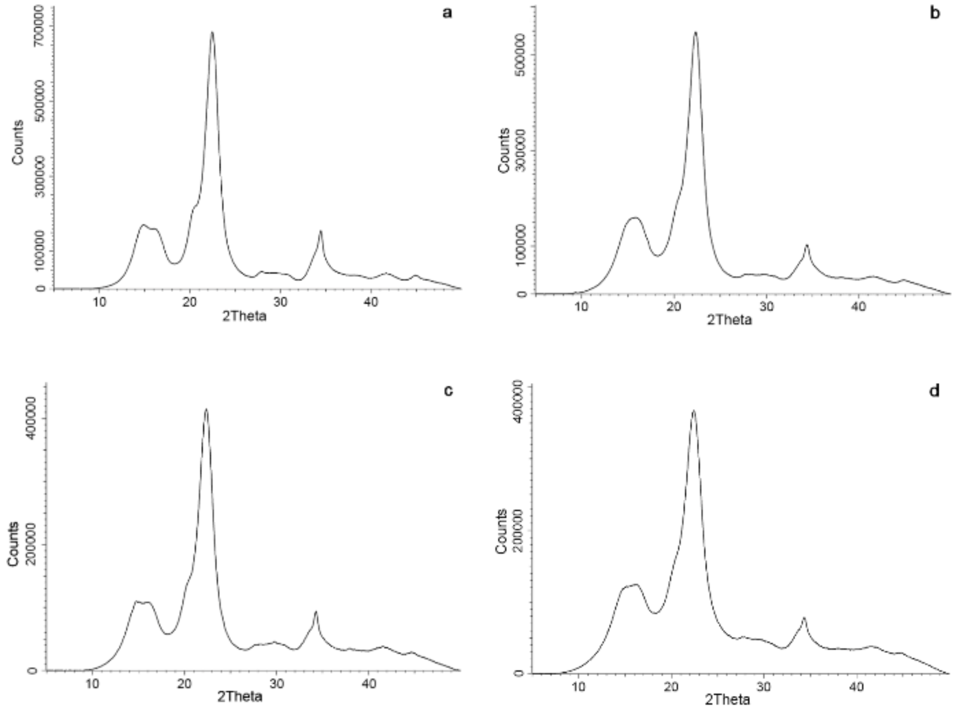

Fig. S5. X-ray diffraction spectra of microcrystalline cellulose (a), pre-treated eucalyptus cellulose, *Pinus* cellulose (bleached), and wood pulp (b, c, d, respectively). The acquired spectra of cellulose corresponds with data reported in literature [3,4].

2. Experimental Procedures

2.1. Chromatography-analysis

Ethyl levulinate was analysed on a Shimadzu GCMS-QP2020 gas chromatograph-mass spectrometer equipped with a Shimadzu AOC-20i auto injector, and a SH-Rxi-5Sil MS silica fused capillary column (30.0m x 0.25mm x 0.25µm). Helium was used as carrier gas (flow rate: 1.2 $mL.min^{-1}$) and the GC inlet temperature was 250 °C. A splitless mode of injection was used with a purge time of 1 min. The column temperature programme was as follows: initial oven temperature of 50 °C (1 min), followed by a 15 °C/min ramp to 220 °C (held for 5 min), and then to 325 °C at 60 °C/min (held for 3 min). Peaks were identified by comparison of their retention times and fragmentation patterns with analytical standards. Quantitative analysis was performed with the use of a standard curve plotted with analytical standards.

Liquid chromatography-mass spectrometry (LC-MS) trace analysis of carbohydrates was conducted on a Shimadzu LCMS-8060 instrument with electrospray ionisation source in negative ion mode (scanning *m/z* range 60–1000). The separation of sugars was conducted on a Supelco apHera NH2-Polymer analytical column (150 mm × 4.6 mm, 5 µm) using a mixture of acetonitrile and water (65:35 v/v) as the mobile phase at a flow rate 0.6 $mL.min^{-1}$ and a run time of 18 min. High performance liquid chromatography (HPLC) trace analysis of furan type aldehydes was performed employing an Agilent 1290 LC instrument equipped with an Agilent Zorbax Eclipse XDB–C18 analytical column (150 mm × 4.6 mm, 3 µm) and Agilent 1260 DAD VL+ detector (detection wavelength: 278 nm). The mobile phase was a mixture of methanol and water (15:85 v/v) at a flow rate of 1.1 $mL.min^{-1}$ with a run time of 20 min.

2.2. NMR spectroscopy

NMR spectra were recorded on an Agilent 500 MHz NMR spectrometer using deuterochloroform ($CDCl_3$) as solvent. The isolated ethyl levulinate was dissolved in the solvent in a 5 mm NMR tube and the spectra were collected at 25 °C with chemical shifts referenced relative to residual solvent (^{1}H: δ = 7.26 ppm; ^{13}C: δ = 77.0 ppm). 2D NMR spectra (HSQC and COSY) were used to unambiguously assign the peaks.

2.3. IR spectroscopy

IR spectra were collected in ATR mode by placing a drop of solution onto a diamond crystal using Thermo Scientific Nicolet 6700 spectrometer in a range 4000–450 cm^{-1}. The processing of spectra was performed using OMNIC software.

2.4. X-ray diffraction analysis of cellulose

X-ray diffraction measurements were performed on a Bruker D8 X-ray diffractometer using CuKα radiation. Scans were obtained in a range 5–50 degrees 2θ in 0.05 degree steps for 15 seconds per step. The crystallinity index was calculated from the height ratio between the intensity of the crystalline peak and total intensity using standard method [3,4].

2.5. Particle size analysis

Particle size analysis of cellulose was performed using an Olympus BH2 microscope equipped with an AmScope MU1803-HS digital camera.

2.6. pH Measurements

pH Readings were conducted at room temperature (22–23 °C) using a Mettler Toledo pH meter adapted with a standard glass electrode with prior calibration with two buffer solutions (pH = 4.00, pH = 7.00). Measurements were performed in triplicate and the average values are presented.

2.7. The isolation of ethyl levulinate

To recover ethyl levulinate, an ethanol solution of the product and the catalyst (20.0 mL, combined solutions obtained after acid-catalysed conversion of microcrystalline cellulose) was quenched with addition of aqueous sodium bicarbonate (5.0 mL, 0.05 M). The neutralised system was centrifuged (3,000 × g for 20 min), and decanted. The aqueous ethanol was removed under reduced pressure (40 °C, 10 mbar) and the crude mixture was subjected to flash column chromatography (hexane/EtOAc, 1.5:1 v/v mixture) to isolate ethyl levulinate. NMR spectra of the isolated product are demonstrated in Fig. S1 and S2.

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A3. Supporting information for Section 3.1

CHEMPLUSCHEM

Supporting Information

Acid-Catalysed Conversion of Carbohydrates into Furan-Type Molecules in Zinc Chloride Hydrate

Iurii Bodachivskyi[+], Unnikrishnan Kuzhiumparambil[+], and D. Bradley G. Williams[+]*

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Supporting data

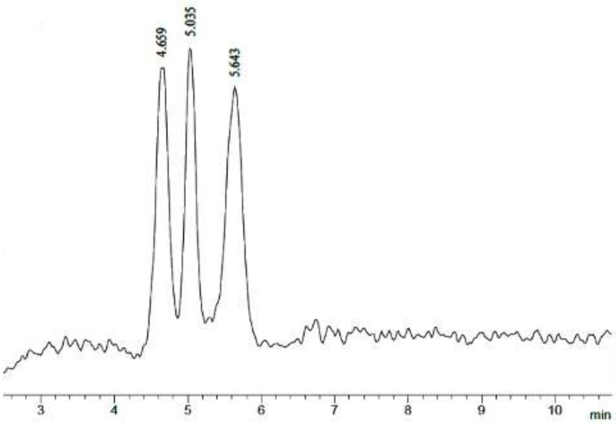


Figure S1. LC-MS analysis of the recovered aqueous phase after the conversion of cellulose in $ZnCl_2 \cdot 3H_2O$. Peaks at retention time of 4.659, 5.035 and 5.643 are consistent with an unidentified hexose sugar, fructose and glucose, respectively.

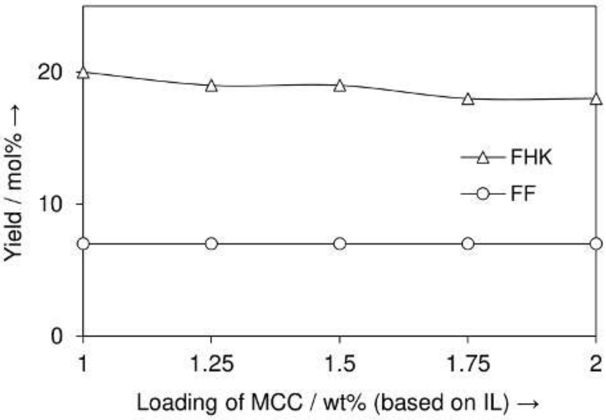


Figure S2. Production of furanoids from reaction of cellulose in the biphasic system $ZnCl_2 \cdot 3H_2O$/anisole at various loading of substrate. FHK = furyl hydroxymethyl ketone; FF = furfural. Reaction conditions: microcrystalline cellulose (MCC, 5-10 mg), $ZnCl_2 \cdot 3H_2O$ (500 mg), anisole (1.00 mL), 120 °C, 1 h.

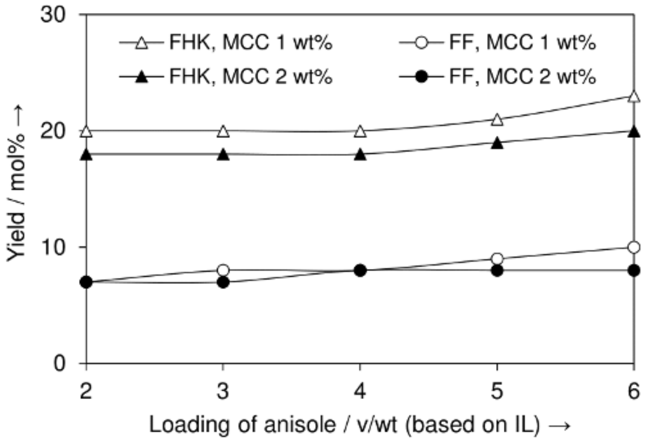


Figure S3. Production of furanoids from reaction of cellulose in the biphasic system $ZnCl_2 \cdot 3H_2O$/anisole at various loadings of organic solvent and substrate. FHK = furyl hydroxymethyl ketone; FF = furfural. Reaction conditions: MCC (5 or 10 mg), $ZnCl_2 \cdot 3H_2O$ (500 mg), 120 °C, 1 h.

Table S1 presents the results of the conversion of MCC in zinc chloride with higher ratios of water ($ZnCl_2 \cdot 3.25H_2O$ and $ZnCl_2 \cdot 3.5H_2O$), or $ZnCl_2 \cdot 3H_2O$ with added acid catalysts (*p*-toluenesulfonic acid, oxalic acid, $Al(OTf)_3$, $Hf(OTf)_4$, $Gd(OTf)_3$, $GdCl_3$, $Yb(OTf)_3$, $La(OTf)_3$, $LaCl_3$, respectively. The results show that the yields of FHK are reduced, relatively speaking, in the conversion of cellulose in zinc chloride with higher ratios of water (Entries 2 and 3). Arguably, the excess of water increases the acidity of the reaction media leading to decomposition of the ketone before its extraction. The presence of Brønsted acid or Lewis acid catalysts has a neutral or negative effect that relates to the loading of the catalyst, as well as to the Brønsted acidity of the system caused by the added acids (Entries 4-14). The addition of 1 mol% of acid (based on anhydroglucose unit equivalents in the MCC) does not influence the conversion of cellulose in $ZnCl_2 \cdot 3H_2O$ but higher loadings of some catalysts (10 and 20 mol%) diminish the yields of major products. For instance, Lewis acids such as $Gd(OTf)_3$, $GdCl_3$, $La(OTf)_3$, and $LaCl_3$ hardly influence the process, while Brønsted acids (*p*-toluenesulfonic acid, oxalic acid), or harder Lewis acids ($Al(OTf)_3$, $Hf(OTf)_4$, $Yb(OTf)_3$) tend to lower the overall yield of products. One reason for this is that Brønsted acids, or Lewis acidic metal trifluromethanesulfonates that serve to release Brønsted acidity as has been previously shown,[1–3] promote the decomposition of some products during the processing of cellulose.

Table S1. Production of furanoids from reaction of cellulose in the biphasic system $ZnCl_2 \cdot nH_2O$/anisole using various acid catalysts

Entry	Solvent	Catalyst[a]	FHK yield [mol%]	FF Yield [mol%]
1	$ZnCl_2 \cdot 3H_2O$	None	24	10
2	$ZnCl_2 \cdot 3.25H_2O$	None	20	8
3	$ZnCl_2 \cdot 3.5H_2O$	None	19	10
4	$ZnCl_2 \cdot 3H_2O$	TsOH[b]	24	10
5		TsOH[c]	22	10
6		TsOH[d]	18	9
7		$H_2C_2O_4$[d]	19	9
8		$Al(OTf)_3$[d]	20	9
9		$La(OTf)_3$[d]	23	8
10		$LaCl_3$[d]	23	8
11		$Hf(OTf)_4$[d]	16	8
12		$Gd(OTf)_3$[d]	21	9
13		$GdCl_3$[d]	21	8
14		$Y(OTf)_3$[d]	20	9

[a] TsOH = *p*-toluenesulfonic acid; $H_2C_2O_4$ = oxalic acid; OTf = trifluoromethane-sulfonate. [b,c,d] Catalyst loading 1, 10, or 20 mol% (based on anhydroglucose unit), respectively. Reaction conditions: MCC (5 mg), $ZnCl_2 \cdot nH_2O$ (500 mg), anisole (3.00 mL), 120 °C, 1.5 h.

Table S2. Preparation of zinc chloride hydrate ionic liquids.

Zinc chloride hydrate	$ZnCl_2$ [g]	H_2O [g]
$ZnCl_2 \cdot 3H_2O$	7.16	2.84
$ZnCl_2 \cdot 3.25H_2O$	7.00	3.00
$ZnCl_2 \cdot 3.5H_2O$	6.84	3.16

Analytical methods

High performance liquid chromatography (HPLC)

Chromatographic analysis of furan derivatives was performed using an Agilent 1290 LC instrument equipped with an Agilent Zorbax Eclipse XDB-C18 analytical column (150 mm × 4.6 mm, 5 µm) and an Agilent 1260 DAD VL+ detector. The mobile phase was a mixture of methanol and water (15/85 v/v) and a detection wavelength of 278 nm was used; time of a typical run was 20 minutes. Quantification of FHK, FF and HMF was conducted with the use of a standard curve set up using authentic samples. A Bio-Rad Aminex HPX-87H ion exclusion analytical column (300 mm × 7.8 mm, 9 µm) was used for the trace analysis of levulinic acid. Aqueous sulfuric acid (5 mM) was used as the mobile phase; time of a typical run was 45 minutes. Detection wavelength was 210 nm. Analysis of cellobiose, glucose and fructose after conversion in the ionic liquid was performed on a Waters 5890 LC instrument equipped with a Supelco apHera NH2-Polymer analytical column (150 mm × 4.6 mm, 5 µm) connected to Erma ERC-7510 refractive index detector. A mixture of acetonitrile and water (65/35 v/v) was used as the mobile phase; time of a typical run was 15 minutes.

To identify reaction intermediates liquid chromatography-mass spectrometry (LC-MS) analysis of the recovered aqueous media after the conversion of cellulose was conducted on a Shimadzu LCMS-8060 instrument with an electrospray ionization source in negative ion mode. The chromatographic separation of sugars was performed on a Supelco apHera NH2-Polymer analytical column (as specified above) using a mixture of acetonitrile and water (65/35 v/v) as a mobile phase; time of a typical run was 15 minutes. Two transitions (m/z 178.85 → 89.15 and m/z 178.85 → 59.10) were monitored with fragmentor voltage of 20 V and collision energy of 8 and 15 eV, respectively. Peaks were identified by comparison of their retention times with analytical standards.

NMR spectroscopy

^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were recorded on an Agilent spectrometer using $CDCl_3$ as a solvent. Samples (15–20 mg) were dissolved in the solvent (0.55–0.60 mL) in a 5 mm NMR tube and the spectra were collected at 25 °C with chemical shifts referenced relative to the solvent itself (^{1}H: δ = 7.26 ppm; ^{13}C: δ = 77.0 ppm).

FTIR Spectroscopy

IR spectra were collected in thin film using Thermo Scientific Nicolet 6700 spectrometer in a range 4000-450 cm^{-1}.

Mass spectrometry

MS analysis was performed using an Agilent 6550 QTOF attached to an Agilent 1200 series HPLC system. The MS was operated in positive mode using the following conditions: nebulizer pressure 30 psi, gas flow-rate 10 $L \cdot min^{-1}$, gas temperature 300 °C, capillary voltage 4000 V, fragmentor 150 and skimmer 65 V. Instrument was operated in the extended dynamic range mode with data collected in *m/z* range 60-660.

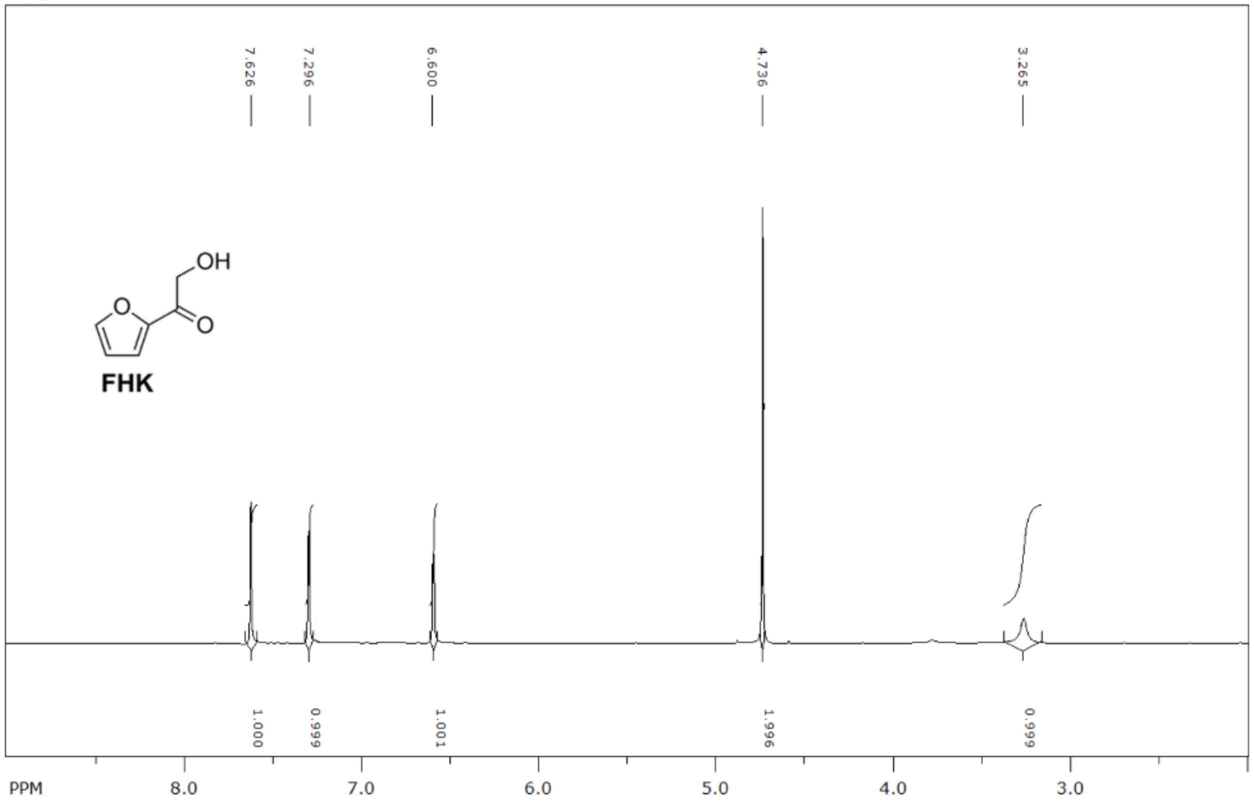
References

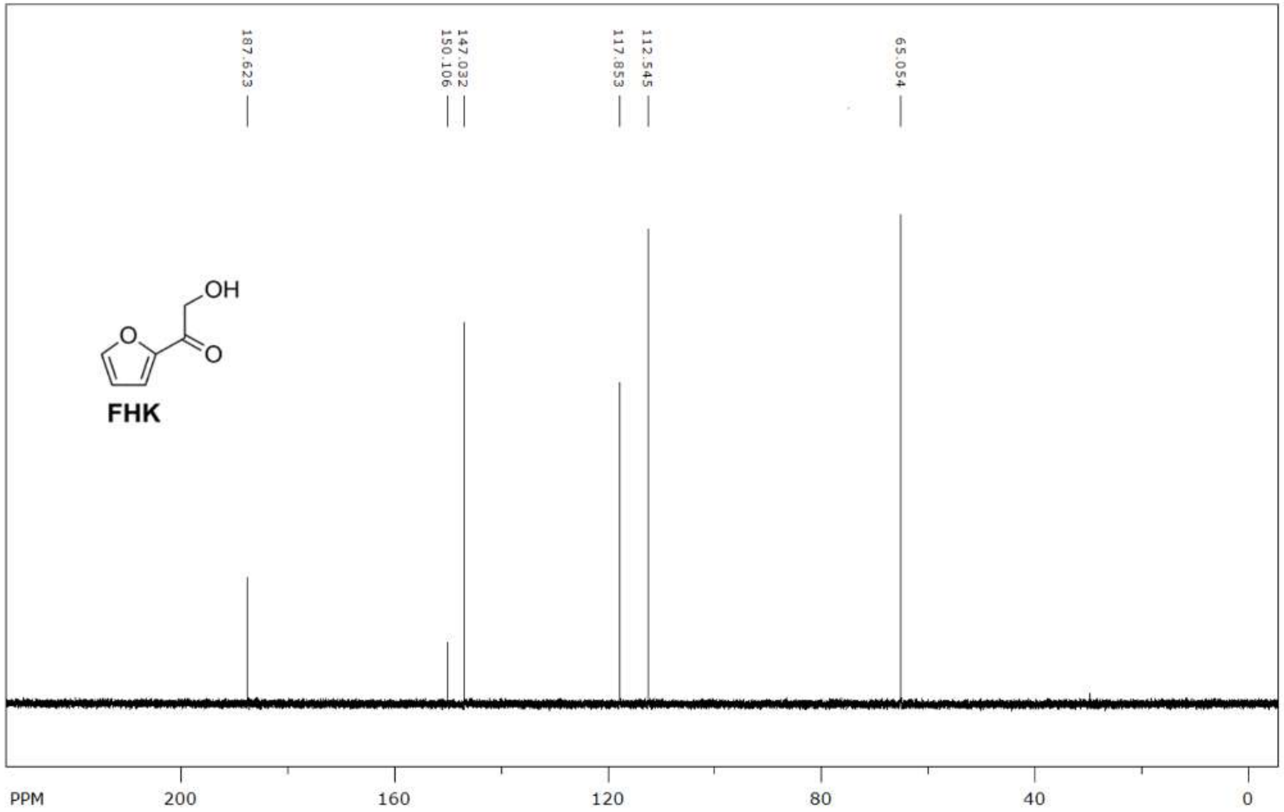
[1] D.B.G. Williams, M. Lawton, *J. Mol. Catal. A: Chem.* **2010**, *317*, 68–71.

[2] D.B.G. Williams, T. Bredenkamp, *ChemCatChem* **2012**, *4*, 206–208.

[3] D.B.G. Williams, M.S. Sibiya, P.S. Van Heerden, *Fuel Process. Technol.* **2012**, *94*, 75–79.

Copies of ^{1}H and ^{13}C NMR spectra of synthesized products

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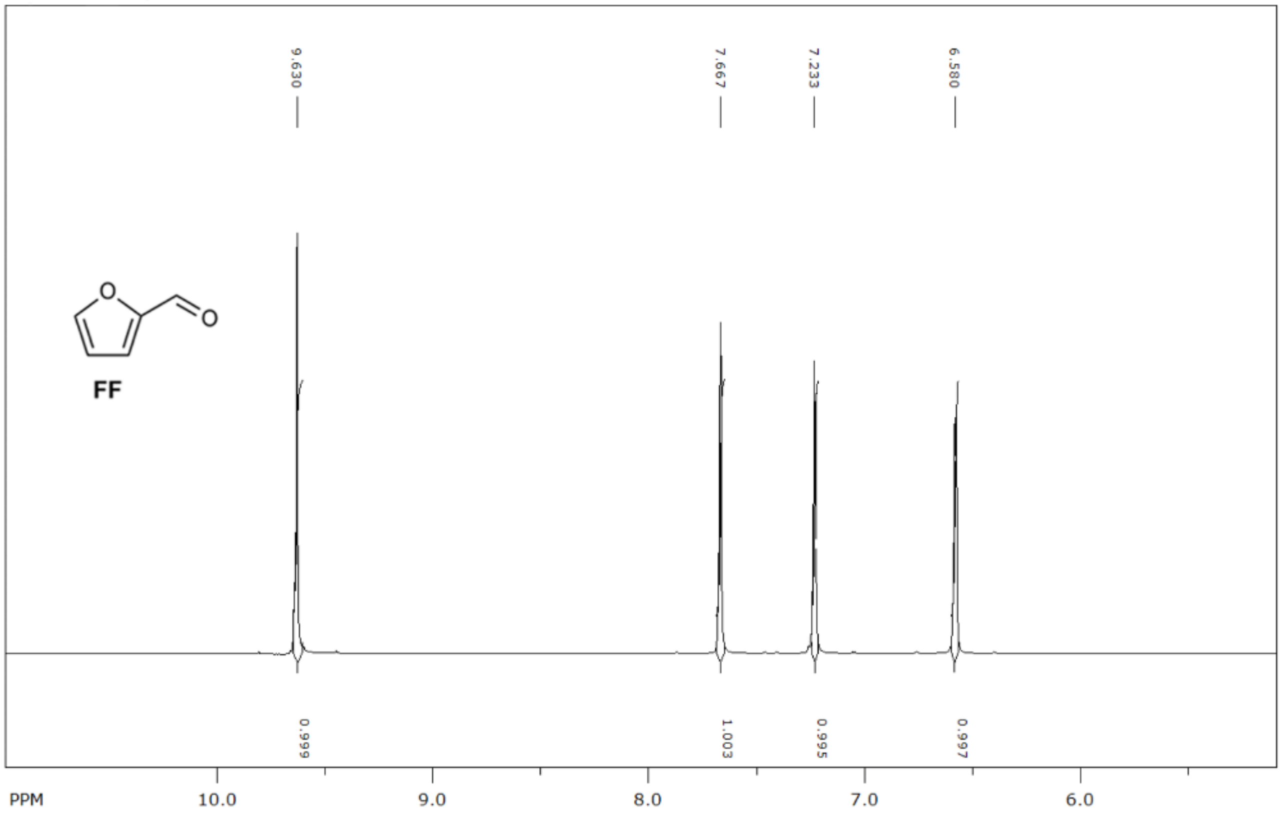
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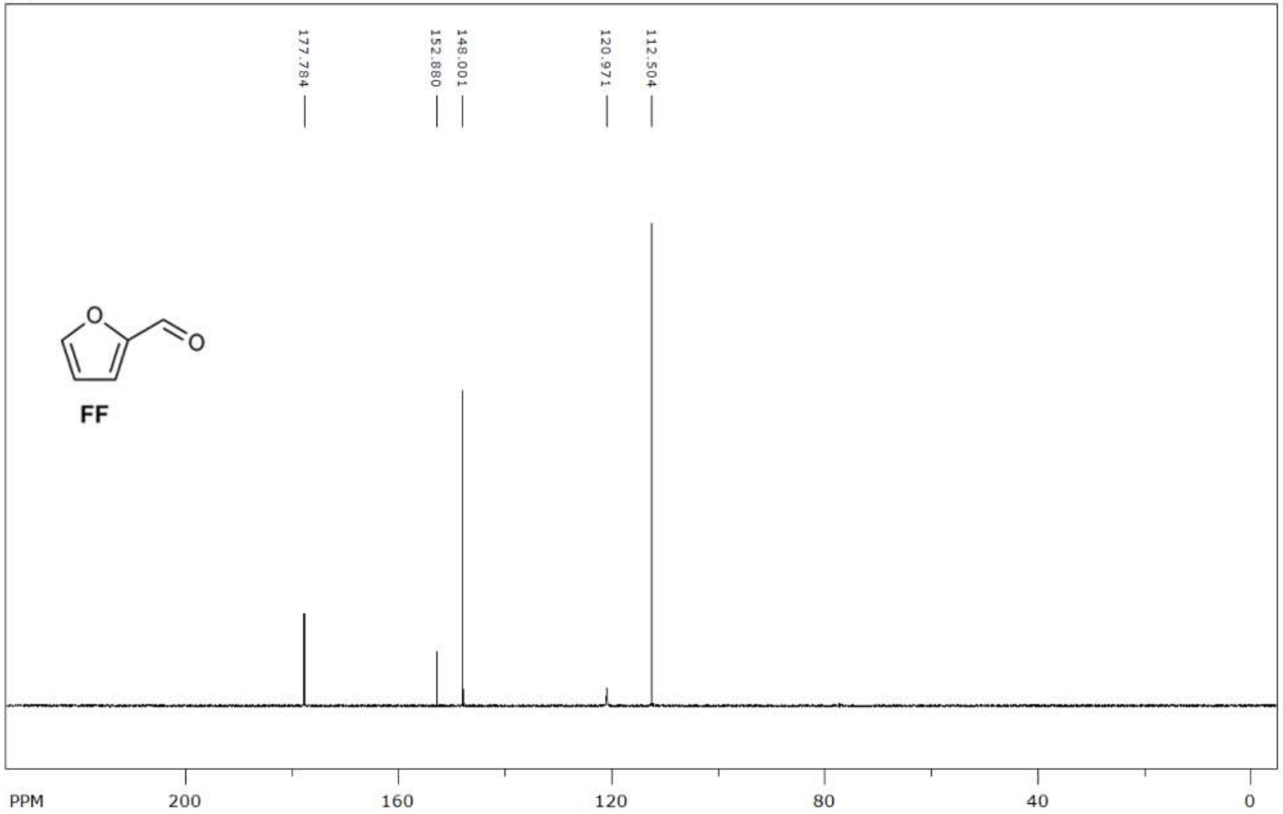
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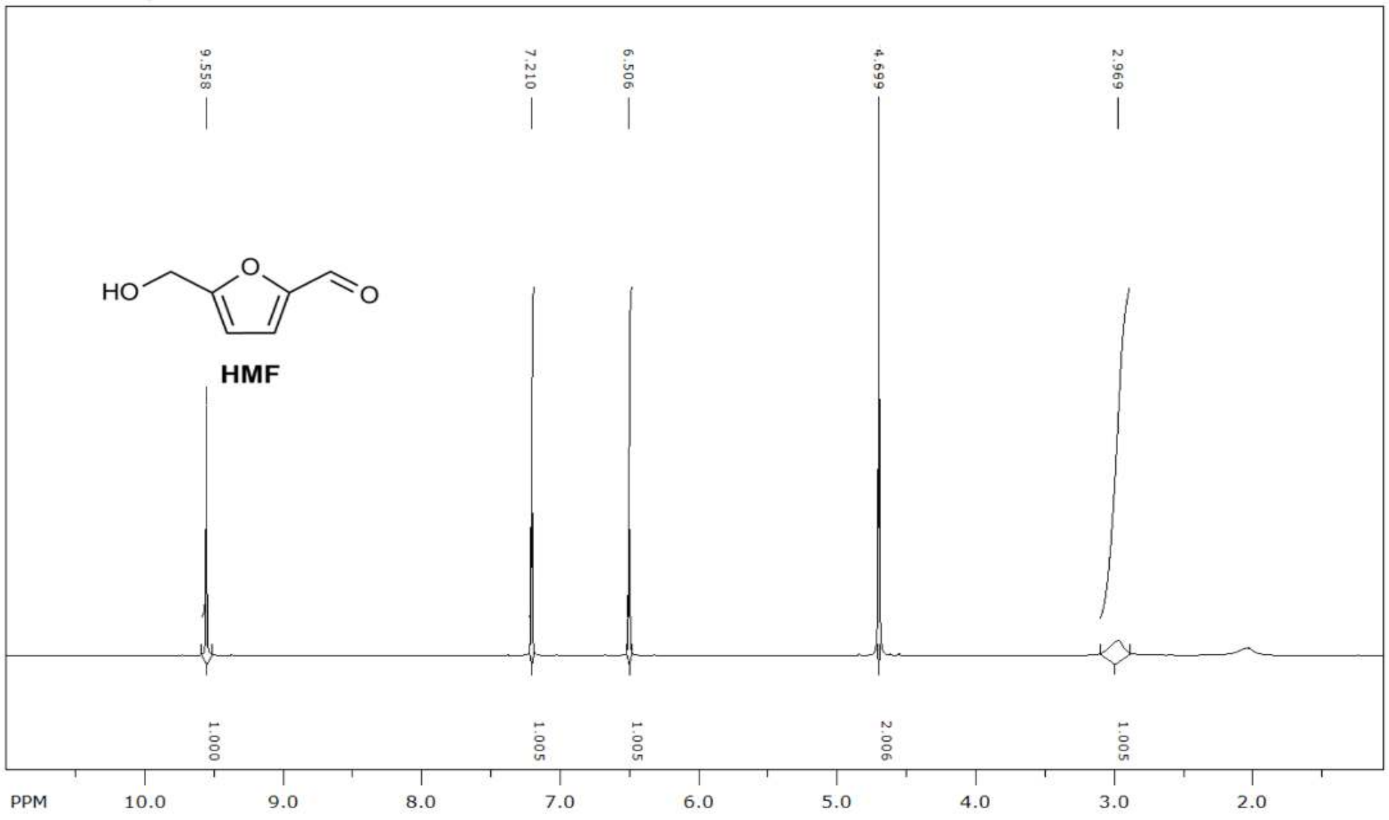
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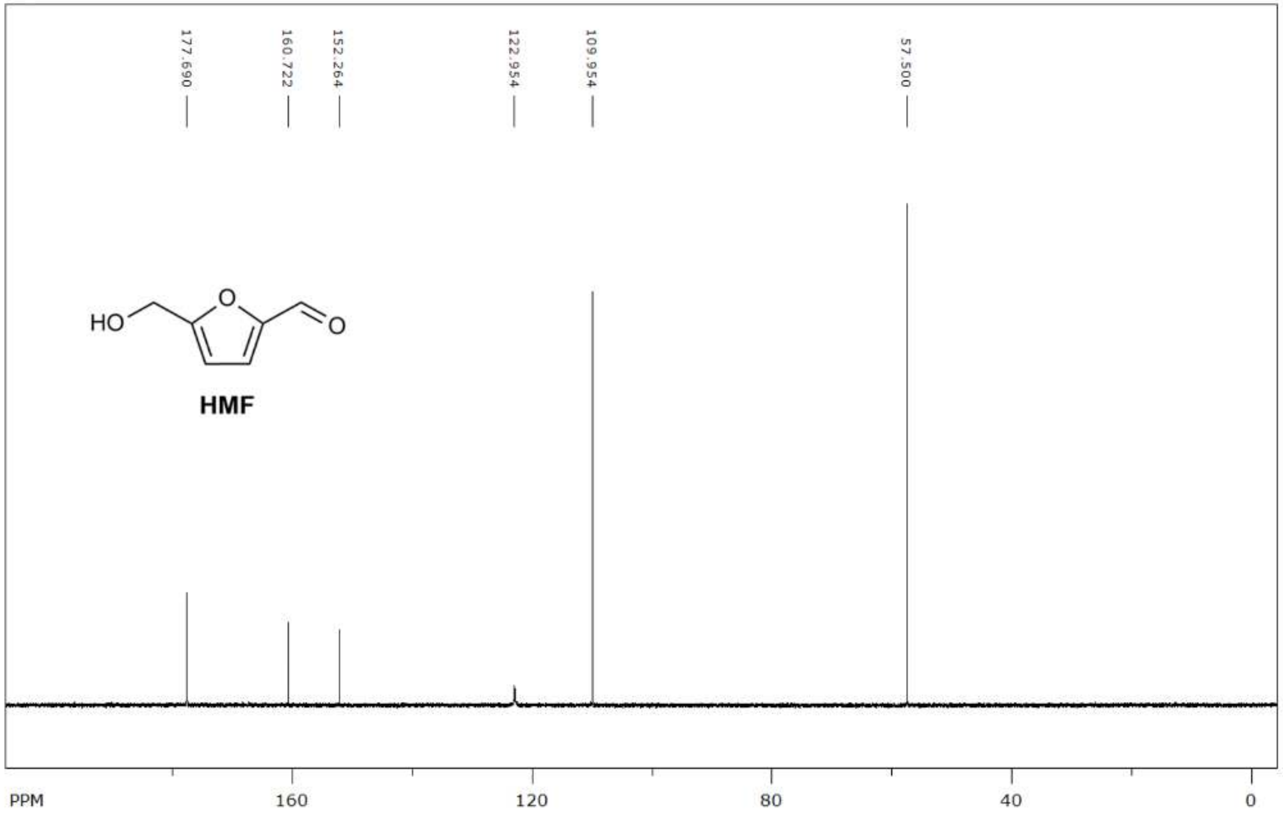
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A4. Supporting information for Section 3.2

Electronic Supplementary Material (ESI) for Catalysis Science & Technology.

Supporting Information

The role of the molecular formula of $ZnCl_2 \cdot nH_2O$ on its catalyst activity: A systematic study of zinc chloride hydrates in the catalytic valorisation of cellulosic biomass

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Abstract: The present work demonstrates a functionality of zinc chloride hydrate solvents in catalytic processing of cellulosic materials into value added small molecules. We conduct a systematic study of $ZnCl_2 \cdot nH_2O$ (n = 2.5–4.5) and its activity in varied model transformations based on refined saccharides and discover an optimal systems and conditions for the target catalytic processes. This enable the efficient and direct transformation of a range of low value substrates, such as lignocellulose and algal biomass, into significantly higher value chemicals, including small reducing saccharides, 5-(hydroxymethyl)furfural, furyl hydroxymethyl ketone and furfural.

DOI: 10.1039/x0xx00000x

Supporting data

Table S1. The content of carbohydrates in cellulosic substrates[a]

Substrate	Glucans content (wt%)	Xylans content (wt%)
Hemicellulose (obtained from Corncob)	9	60
Algal sugars (obtained from *Ulva lactuca*)	63	0
Corncob	37	29
Wood chips (softwood)	48	18
Ulva lactuca	36	5
P. Cruentum	11	12

[a] The content of carbohydrates was established by standard analytical methods and is specified in wt% based on the dry substrate.[1,2] Other polysaccharides (despite glucans and xylans) were identified in trace amounts.

Table S2. Dissolution and regeneration of microcrystalline cellulose in/from $ZnCl_2 \cdot nH_2O$ (n = 2.5–3.5) [a]

Solvent	Mass loss (wt%)
$ZnCl_2 \cdot 2.5H_2O$	18
$ZnCl_2 \cdot 2.75H_2O$	17
$ZnCl_2 \cdot 3.0H_2O$	14
$ZnCl_2 \cdot 3.25H_2O$	11
$ZnCl_2 \cdot 3.5H_2O$	5
$ZnCl_2 \cdot 3.75H_2O$	5
$ZnCl_2 \cdot 4.0H_2O$	3
$ZnCl_2 \cdot 4.25H_2O$	0
$ZnCl_2 \cdot 4.5H_2O$	0

[a] Mass loss is specified in wt% based on cellulose input. Dissolution conditions: cellulose (50 mg), $ZnCl_2 \cdot nH_2O$ (5.000 g), 80 °C, 2.5 h.

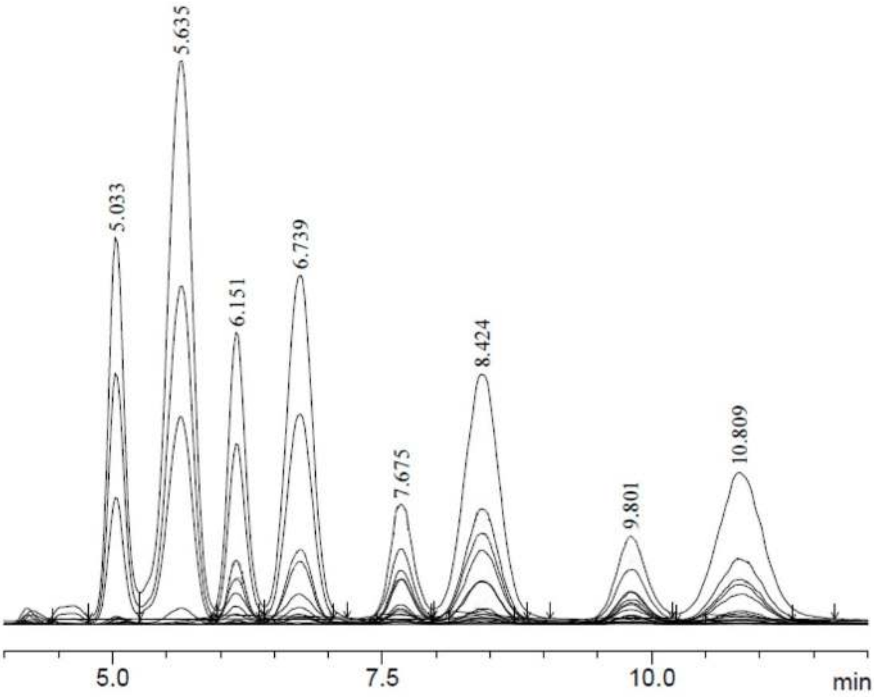

Fig. S1. LC-MS analysis of the recovered aqueous phase after the conversion of cellulose in $ZnCl_2 \cdot 4.5H_2O$ (transitions *m/z* 149.10 → 89.05, *m/z* 178.85 → 89.15, *m/z* 341.30 → 161.20, *m/z* 503.35 → 161.20 and *m/z* 665.25 → 503.10 were monitored). Peaks at retention time of 5.033, 5.635, 6.151, 6.739, 8.424 and 10.809 are appropriate to fructose, glucose, cellobiulose, cellobiose, cellotriose and cellotetraose respectively. Peaks at retention time of 7.675 and 9.801 are considered to be *keto*-isomers of cellotriose and cellotetraose, respectively.

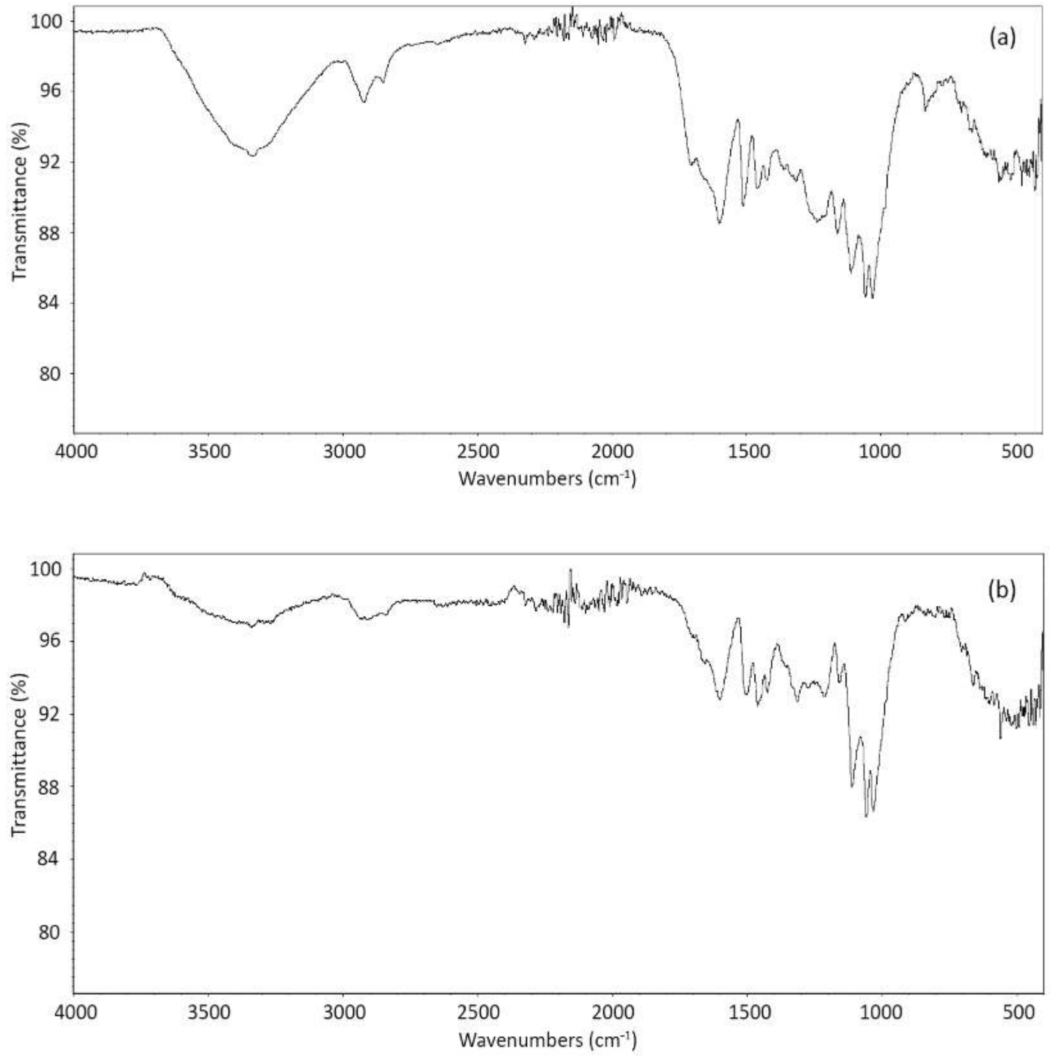

Fig. S2. IR spectra of lignin recovered after the acid-catalysed conversion of corncob (a) and softwood chips (b) in $ZnCl_2 \cdot 4.5H_2O$.

The assignment of IR spectra compares favourably with reported analytical data and is represented in Table S3.[3]

Table S3. Assignments of IR absorption bands of the recovered lignin[3]

Absorption bands for corncob lignin (cm^{-1})	Absorption bands for softwood lignin (cm^{-1})	Assignment
3335	3340	OH stretching
2922	2908	CH stretching of alkyl groups
1601, 1512, 1426	1601, 1501, 1425	Aromatic skeletal vibration
1460	1460	Aromatic methyl group vibrations
1360	1359	Aliphatic C–H stretch in CH_3
1315	1314	Syringyl ring breathing with C–O stretching
1160	1157	C–O stretch in ester groups
1111, 1056, 1031	1111, 1058, 1032	Aromatic C–H in-plane deformation

References

1 A. Sluiter, B. Hames, R. Ruiz, C. Scarlata, J. Sluiter, D. Templeton and D. Crocker, *Determination of structural carbohydrates and lignin in biomass*, NREL/TP-510-42618, US National Renewable Energy Laboratory, Golden, Colorado, 2008.

2 S. Van Wychen and L.M.L. Laurens, *Determination of Total Carbohydrates in Algal Biomass*, NREL/TP-5100-60957, US National Renewable Energy Laboratory, Golden, Colorado, 2013.

3 S. H. Ghaffar, M. Fan, *Biomass Bioenergy*, 2013, **57**, 264–279.

A5. Supporting information for Section 3.3

Supporting Information

Towards furfural from the reaction of cellulosic biomass in zinc chloride hydrate solvents

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1. Materials

Microcrystalline cellulose, $ZnCl_2$ (anhydrous) and organic solvents were obtained from commercials sources. Lignocellulosic substances (corn husk, corncob and softwood chips) were sourced from local growers (Australia). Microalgae *Chlorella vulgaris* and *Porphiridium cruentum* were grown and supplied by Climate Change Cluster (C3), University of Technology Sydney (Australia). Vacuum oven-dried (60 °C, 1 mbar, 12 h) cellulosic materials were used for acid-catalysed reactions. Xylans were extracted from corn husk using an optimised method (Stoklosa and Hodge, 2012). In brief, oven-dried biomass (5.000 g) was treated with aqueous NaOH (6 wt%, 100 mL) at 85 °C for 1 h. After cooling, the resulting mixture was filtered to remove the insoluble portion, and xylans (soluble portion) were precipitated from the filtrate by adding aqueous ethanol (95 vol%, 500 mL) (Stoklosa and Hodge, 2012). Crude xylans were recovered and bleached with 1.0 mM aqueous NaOH (250 mL) containing hydrogen peroxide (2 wt% based on solvent) at room temperature for 24 h. Xylans were precipitated from the aqueous solution by adding ethanol (95 vol%, 500 mL). The residue was recovered and washed repeatedly with ethanolic acetic acid (5 wt% acetic acid, 2 × 30 mL) and ethanol (3 × 30 mL), filtered and lyophilised to obtain purified xylans. The carbohydrate content of the substrates was determined by standard analytical procedures: NREL/TP-510-42618 (Sluiter et al., 2008) for lignocellulose, NREL/TP-5100-60957 (Van Wychen and Laurens, 2013) for algal biomass. Zinc chloride hydrate solvents ($ZnCl_2{\cdot}nH_2O$) were prepared according to reference (Sen et al., 2016).

2. Analytical Methods

Chromatography-analysis of carbohydrates and furans were performed according to the respective reference (Bodachivskyi et al., 2019). Liquid chromatography-mass spectrometry analysis of carbohydrates was conducted on a Shimadzu LCMS-8060 instrument with the electrospray ionisation source in negative ion mode. The separation was performed on a Supelco apHera NH2-Polymer analytical column (150 mm × 4.6 mm, 5 µm) using a mixture of acetonitrile and water (65:35 v/v) as the mobile phase at a flow rate 0.6 $mL.min^{-1}$ and a run time of 15 min. Two transitions *m/z* 149.10 → 89.05 (fragmentor voltage 12 V, collision energy 7 eV; detection of xylose and xylulose) and *m/z* 178.85 →

89.15 (fragmentor voltage 19 V, collision energy 8 eV; detection of glucose and fructose) were monitored. Liquid chromatography analysis of furan derivatives (furfural, furyl hydroxymethyl ketone and 5-(hydroxymethyl)furfural) was performed employing an Agilent 1290 LC instrument equipped with an Agilent Zorbax Eclipse XDB–C18 analytical column (150 mm × 4.6 mm, 3 μm) and Agilent 1260 DAD VL+ detector (detection wavelength 278 nm). The mobile phase was a mixture of methanol and water (15:85 v/v) at a flow rate of 1.1 $mL.min^{-1}$ with a run time of 20 min. Quantitation of monosaccharides and furans was conducted with the use of a standard curve based on analytical standards.

3. References

Bodachivskyi, I., Kuzhiumparambil, U., Williams, D.B.G., 2019. The role of the molecular formula of $ZnCl_2 \cdot nH_2O$ on its catalyst activity: a systematic study of zinc chloride hydrates in the catalytic valorisation of cellulosic biomass. Catal. Sci. Technol. 9, 4693–4701.

Sen, S., Losey, B.P., Gordon, E.E., Argyropoulos, D.S., Martin, J.D., 2016. Ionic liquid character of zinc chloride hydrates define solvent characteristics that afford the solubility of cellulose. J. Phys. Chem. B 120, 1134–1141.

Sluiter, A., Hames, B., Ruiz, R., Scarlata, C., Sluiter, J., Templeton, D., 2008. Determination of structural carbohydrates and lignin in biomass, NREL/TP-510-42618. US National Renewable Energy Laboratory, Golden, Colorado.

Stoklosa, R.J., Hodge, D., 2012. Extraction, recovery, and characterization of hardwood and grass hemicelluloses for integration into biorefining processes. Ind. Eng. Chem. Res. 51, 11045–11053.

Van Wychen, S., Laurens, L.M.L., 2013. Determination of total carbohydrates in algal biomass, NREL/TP-5100-60957. US National Renewable Energy Laboratory, Golden, Colorado.

A6. Supporting information for Section 3.4

Open Access
ChemistryOPEN

Supporting Information

High Yielding Acid-Catalysed Hydrolysis of Cellulosic Polysaccharides and Native Biomass into Low Molecular Weight Sugars in Mixed Ionic Liquid Systems

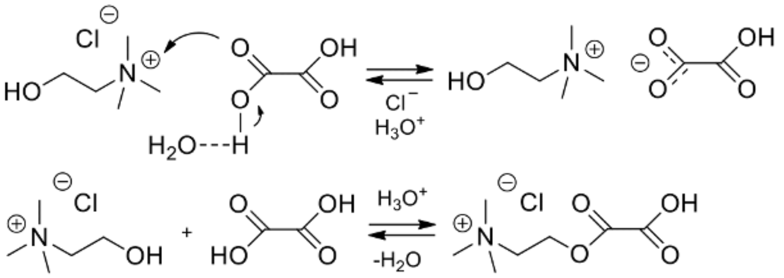
Iurii Bodachivskyi, Unnikrishnan Kuzhiumparambil, and D. Bradley G. Williams*

Supporting data

Table S1. Acid-catalysed conversion of low molecular weight saccharides in ionic liquids [a]

Substrate	Solvent	Conversion [wt%]	Yield glucose [wt%]	Yield HMF [mol%]
Cellobiose	[C_4mim]Cl	9	8	0
Glucose	[C_4mim]Cl	6	–	0
Fructose	[C_4mim]Cl	53	–	6
Cellobiose	ChCl/oxalic acid	96	0	6
Glucose	ChCl/oxalic acid	97	–	7
Fructose	ChCl/oxalic acid	99	–	11

[a] Yields are specified in wt% based on input of the substrate for glucose and in mol% for HMF; '0' means that product was identified in trace amounts based on HPLC analysis; [C_4mim]Cl = 1-butyl-3-methylimidazolium chloride; ChCl = choline chloride. Reaction conditions: substrate (50 mg), solvent (1.000 g), 120 °C, 2 h.



Scheme S1. Proposed complexation of choline chloride and oxalic acid.

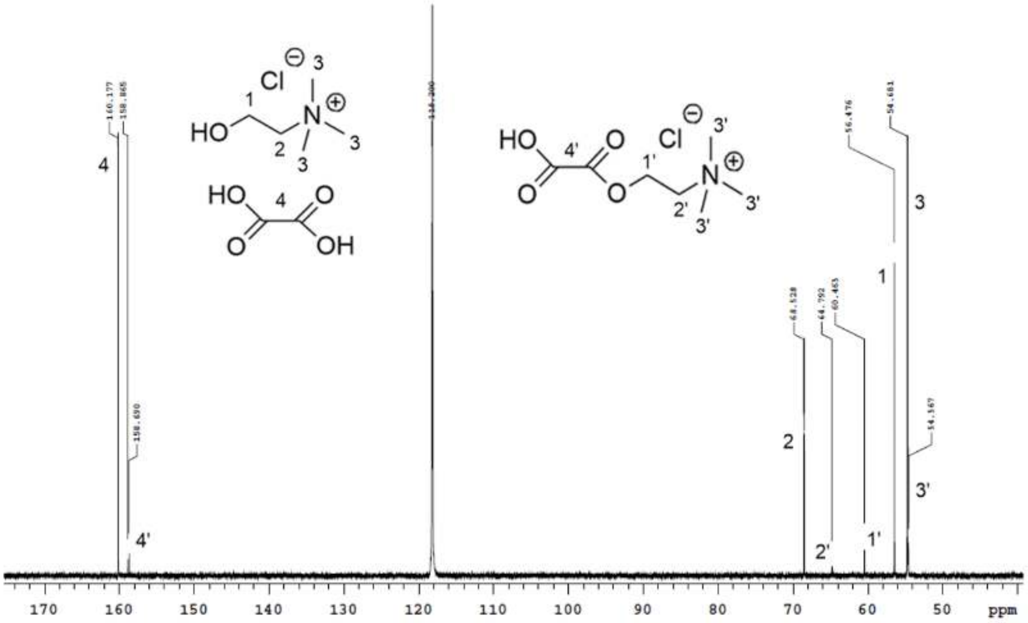
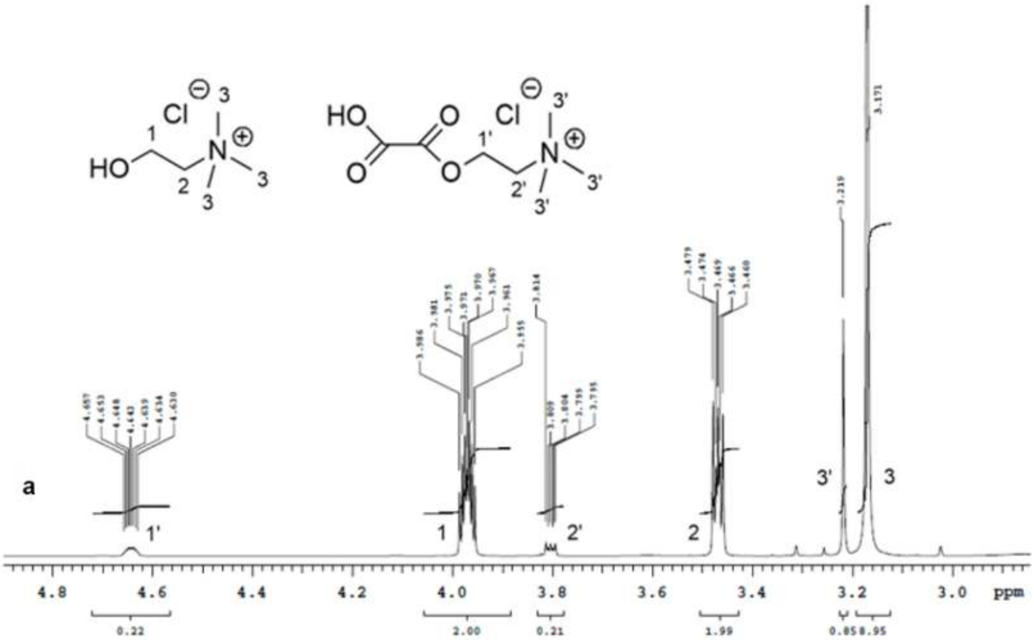


Figure S1. ^{13}C NMR spectrum of choline ChCl/oxalic acid recorded in CD_3CN.



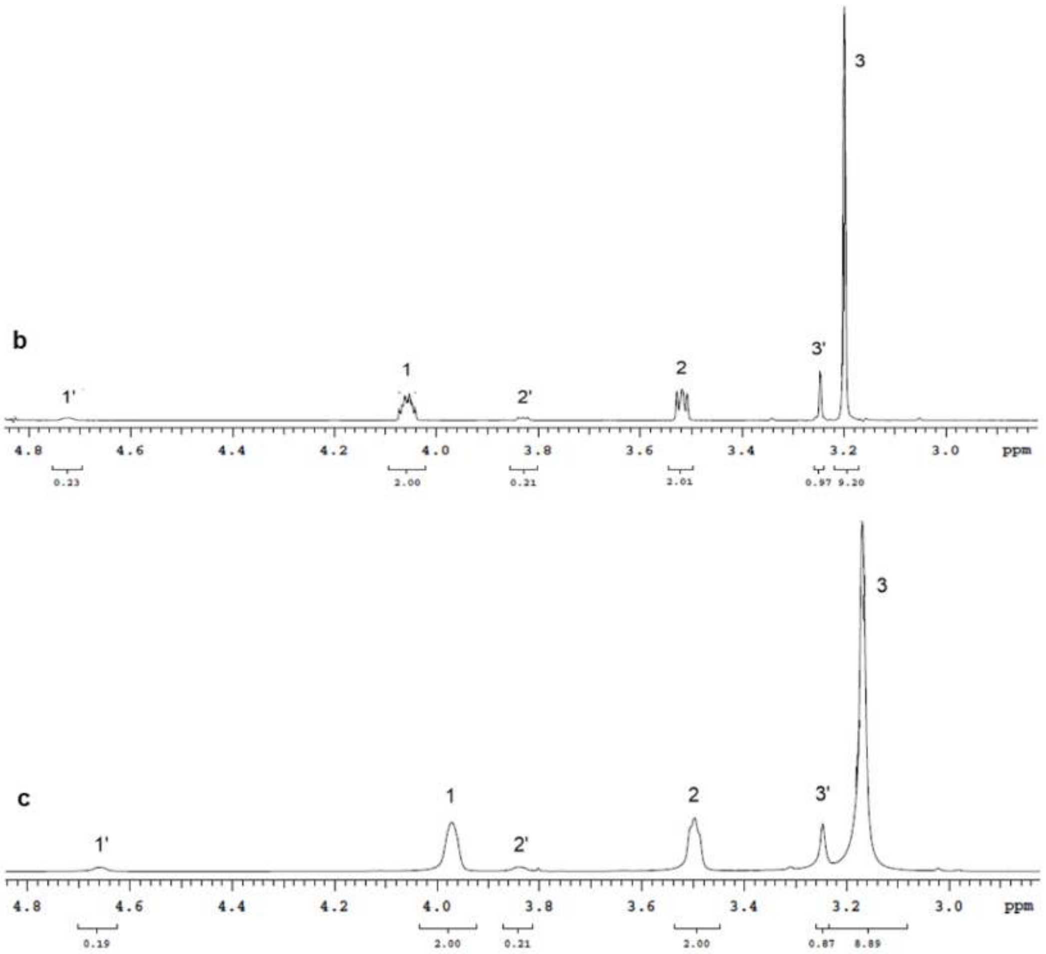


Figure S2. ^{1}H NMR spectra of ChCl/oxalic acid recorded in CD_3CN (a), D_2O (b), neat with extarnal lock [D_6]DMSO (c).

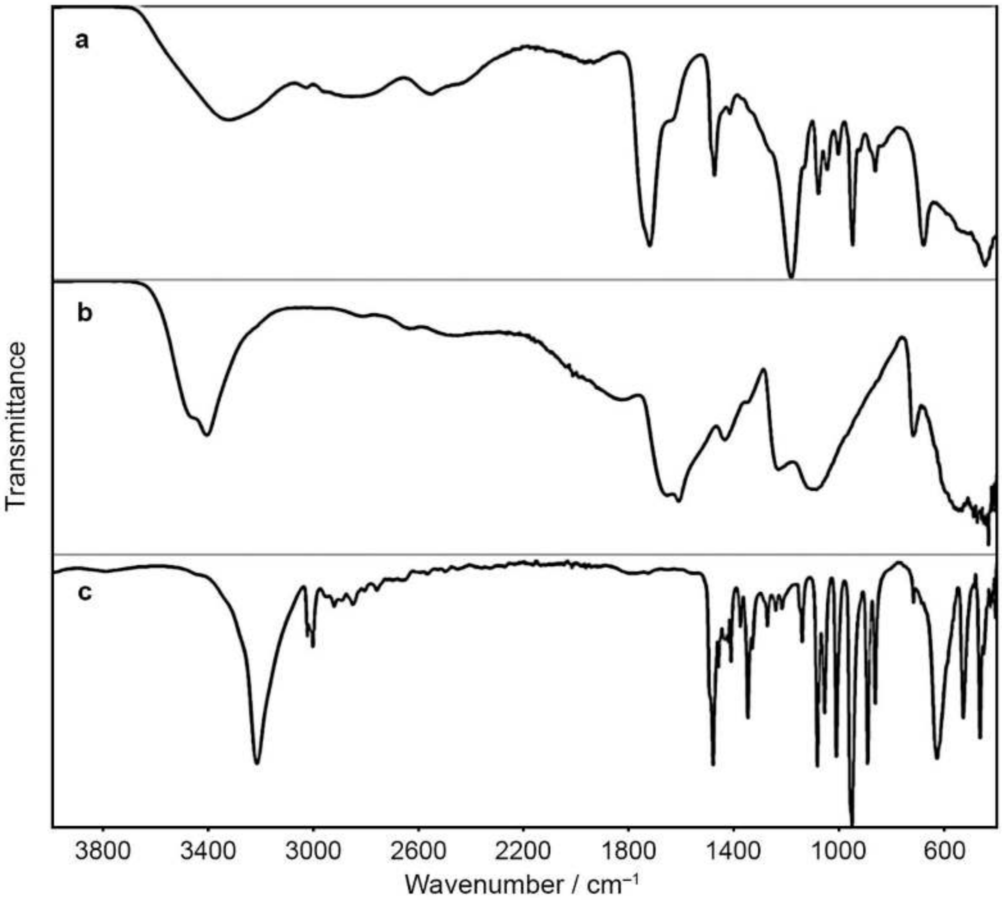


Figure S3. IR spectra of a) ChCl/oxalic acid, b) oxalic acid dihydrate and c) ChCl.

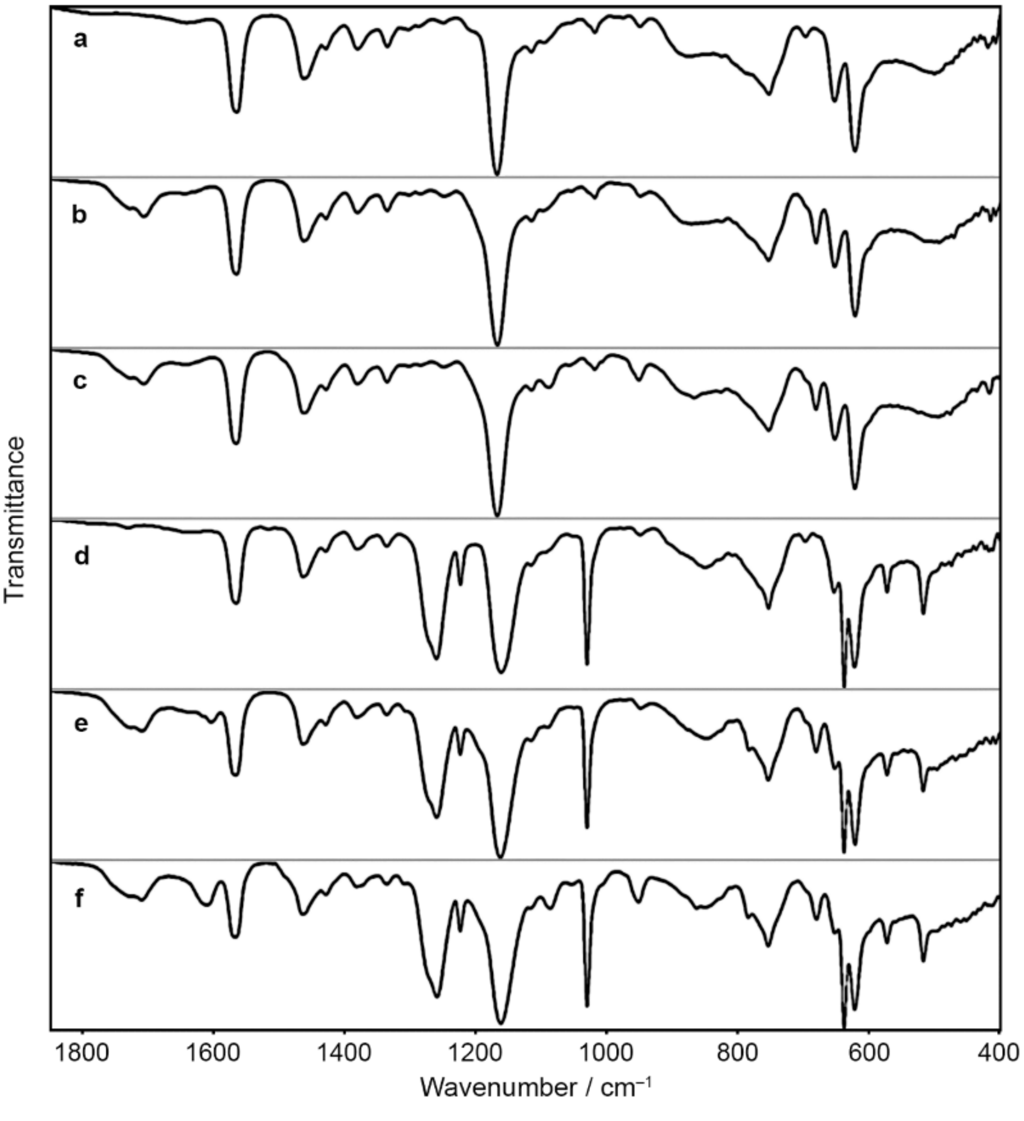


Figure S4. IR spectra of a) [C_4mim]Cl, and [C_4mim]Cl ionic liquid solutions of b) oxalic acid, c) of ChCl/oxalic acid, d) of La(OTf)$_3$, e) of mixed oxalic acid dihydrate with La(OTf)$_3$ (1 : 1 molar ratio), and f) of mixed ChCl/oxalic acid with La(OTf)$_3$ (1 : 1 molar ratio for acids).

Table S2. The content of carbohydrates in cellulosic substrates [a]

Substrate	Glucans content [wt%]	Xylans content [wt%]
Corncob	37	29
Wood chips (softwood)	48	18
Ulva lactuca	36	5
P. Cruentum	11	12

[a] Other polysaccharides (despite glucans and xylans) were identified in trace amounts.

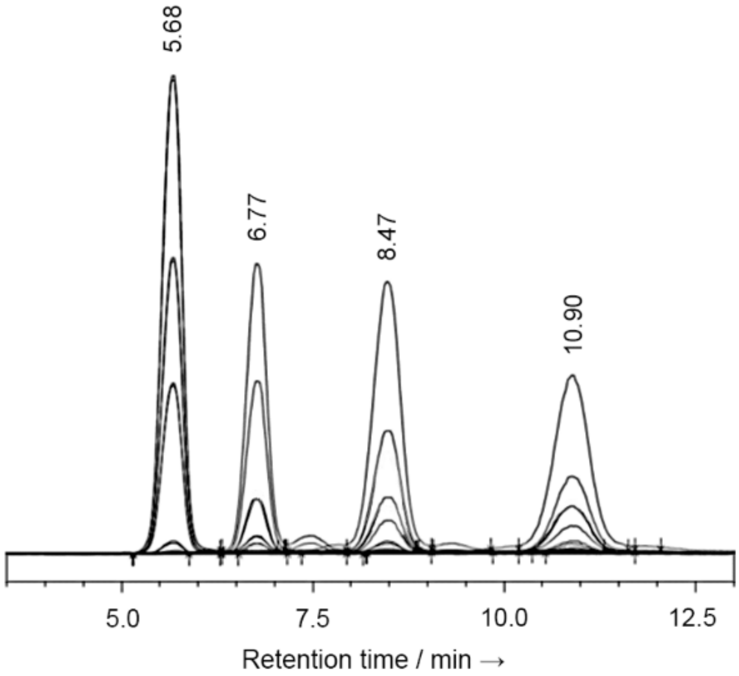


Figure S5. LC-MS analysis of the recovered aqueous phase after the conversion of cellulose in the co-solvent system [C_4mim]Cl / ChCl/oxalic acid. Peaks at retention time of 5.68, 6.77, 8.47 and 10.90 correspond with glucose, cellobiose, cellotriose and cellotetraose respectively.

A7. Supporting information for Section 3.5

Supporting Information

CATALYTIC VALORIZATION OF NATIVE BIOMASS IN A DEEP EUTECTIC SOLVENT: A SYSTEMATIC APPROACH TOWARDS HIGH YIELDING REACTIONS OF POLYSACCHARIDES

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10 Pages

2 Table

5 Figures

SUPPORTING DATA

Table S1 Saccharide content of carbohydrates in cellulosic substrates [a]

Substrate	Glucans content (wt%)	Fructans content (wt%)	Xylans content (wt%)
Cellulose (obtained from corn husk)	90	0	0
Hemicellulose (obtained from corn husk)	10	0	80
Corn husk	45	1	25
Corncob	37	2	29
Wood chips (softwood)	48	0	18
Ulva lactuca	36	0	5
P. cruentum	11	0	12

[a] The content of carbohydrates was established by standard analytical methods and is specified in wt% based on the dry substrate.[1,2] Other polysaccharides (besides glucans, fructans and xylans) were identified in trace amounts.

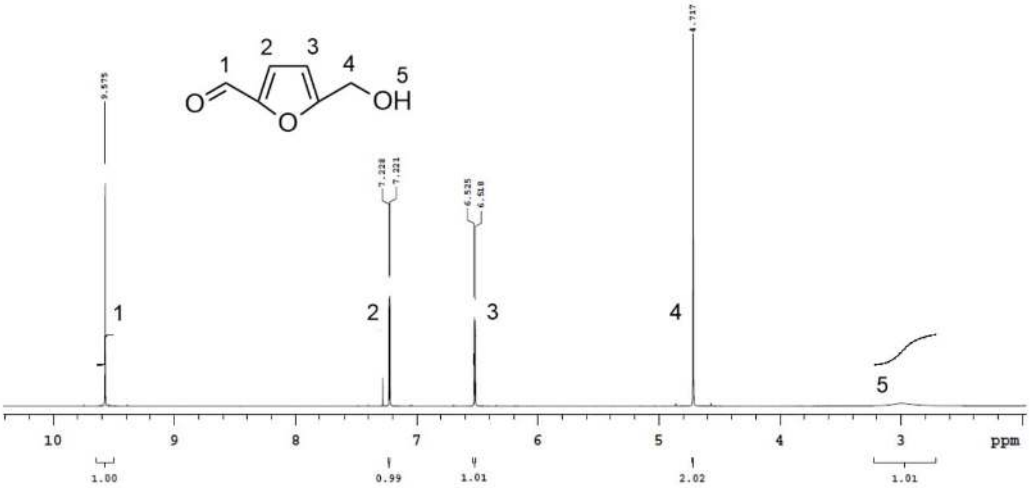

Figure S1 ^{1}H NMR spectrum of the isolated 5-(hydroxymethyl)furfural recorded in $CDCl_3$.

S2

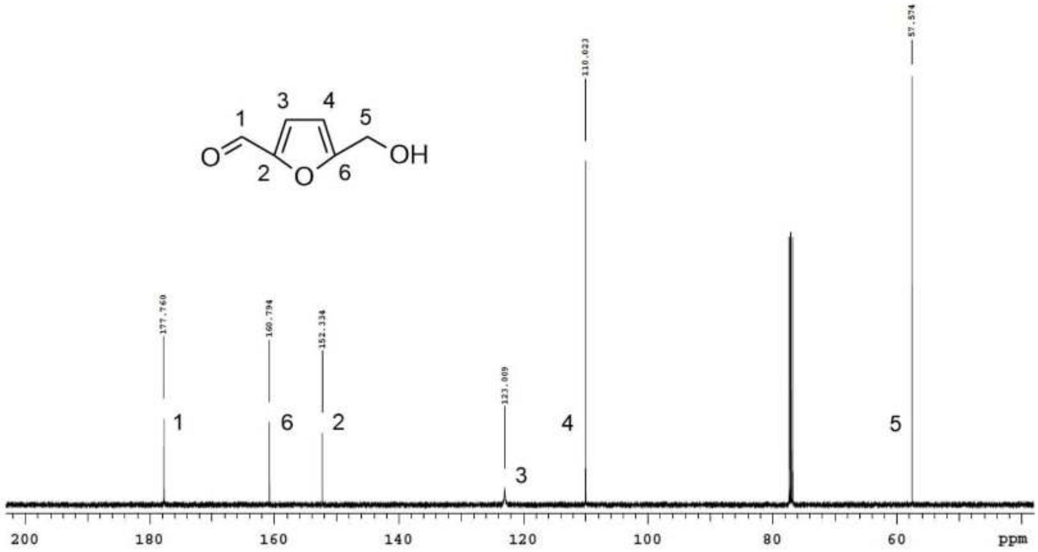

Figure S2 ^{13}C NMR spectrum of the isolated 5-(hydroxymethyl)furfural recorded in CDCl$_3$.

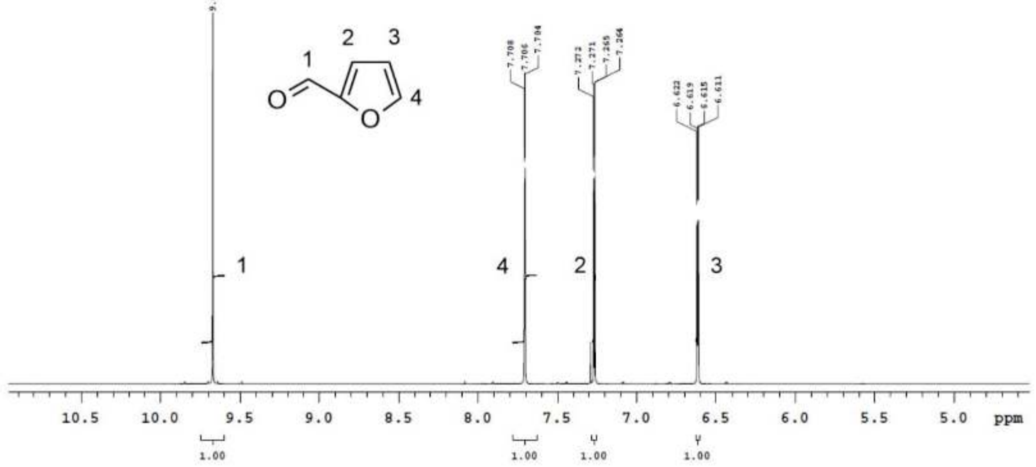

Figure S3 ^{1}H NMR spectrum of the isolated furfural recorded in CDCl$_3$.

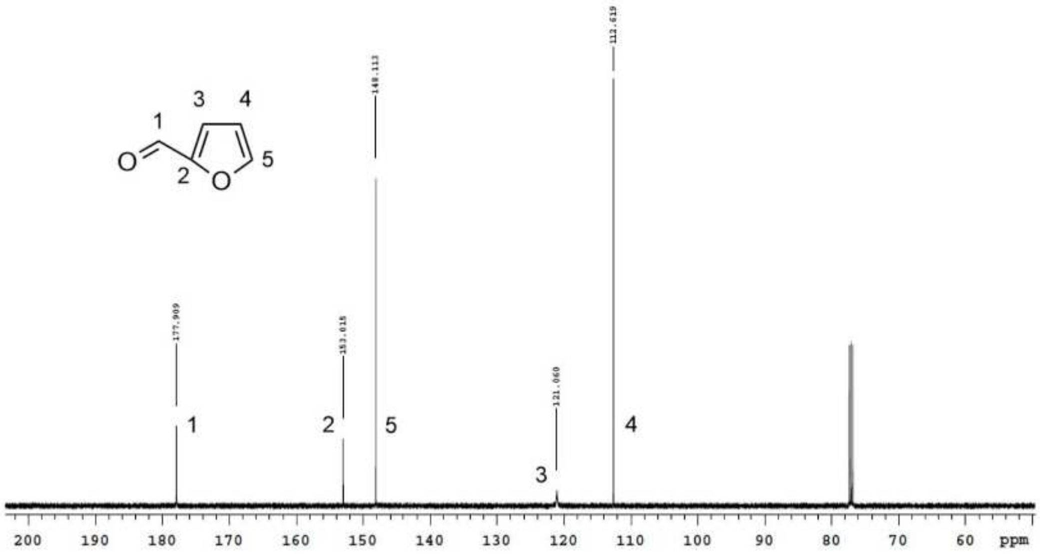

Figure S4 ^{13}C NMR spectrum of the isolated furfural recorded in $CDCl_3$.

Table S2 Catalytic conversion of low molecular weight carbohydrates in ChCl/oxalic acid solvent[a]

Entry	Substrate	Reaction temp (°C)	Conv (%)	Yield glucose (wt%)	Yield fructose (wt%)	Yield furans (mol%)
1	Maltose	60	67	24	0	0[b]
2		80	99	45	0	1[b]
3		100	99	37	0	5[b]
4	Cellobiose	60	38	10	0	0[b]
5		80	97	35	0	1[b]
6		100	99	33	0	4[b]
7	Sucrose	60	99	85	2	15[b]
8		80	99	47	0	16[b]
9		100	99	36	0	13[b]
10	Glucose	60	31	–	0	0[b]
11		80	45	–	0	2[b]
12		100	58	–	0	12[b]
13	Fructose	60	80	–	–	40[b]
14		80	99	–	–	45[b]
15		100	99	–	–	38[b]
16	Xylose	60	1	–	–	0[c]
17		80	35	–	–	10[c]
18		100	51	–	–	28[c]

[a] Conversions and yields of carbohydrates are specified in wt% based on the substrate. Yields are specified in mol% for furans based on the substrate. Reaction conditions: substrate (50 mg), ChCl/oxalic acid (4.0 g), temperature as specified in the table, 1 h. [b] Yield of HMF. [c] Yield of FF.

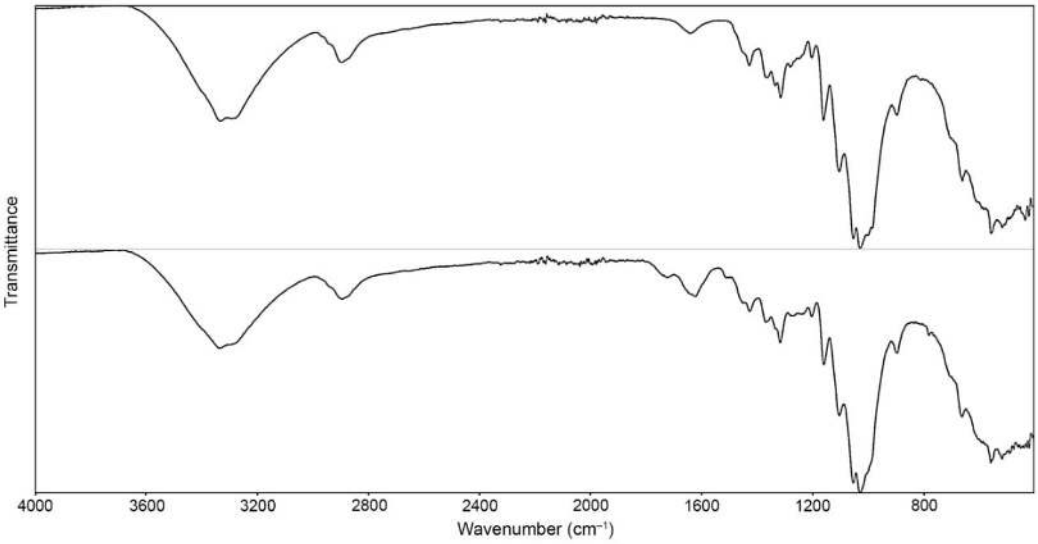

Figure S5 IR spectra of microcrystalline cellulose (top) and cellulosic residue (bottom) recovered unreacted after the acid-catalyzed conversion of softwood chips in the choline chloride/oxalic acid solvent. Characteristic vibrations of cellulose correspond with data reported in the literature.[3]

ANALYTICAL METHODS

Chromatography-analysis. Chromatography-analysis of carbohydrates,[4] furans,[4,5] and ethyl levulinate,[5] were performed according to the respective references. Liquid chromatography-mass spectrometry analysis of carbohydrates was conducted on a Shimadzu LCMS-8060 instrument with electrospray ionization source in negative ion mode. The separation was performed on a Supelco apHera NH2-Polymer analytical column (150 mm × 4.6 mm, 5 μm) using a mixture of acetonitrile and water (65:35 v/v) as the mobile phase at a flow rate 0.6 mL min^{-1} and a run time of 15 min. Five transitions *m/z* 149.10 → 89.05 (fragmentor voltage 12 V, collision energy 7 eV; detection of xylose), *m/z* 178.85 → 89.15 (fragmentor voltage 19 V, collision energy 8 eV; detection of glucose and fructose), *m/z* 341.30 → 161.20 (fragmentor voltage 16 V, collision energy 8 eV; detection of cellobiose), *m/z* 503.35 → 161.20 (fragmentor voltage 24 V, collision energy 13 eV; detection of cellotriose) and *m/z* 665.25 → 503.10 (fragmentor voltage 26 V, collision energy 12 eV; detection of cellotetraose) were monitored.[4] Liquid chromatography analysis of furan derivatives (5-(hydroxymethyl)furfural and furfural) was performed employing an Agilent 1290 LC instrument equipped with an Agilent Zorbax Eclipse XDB–C18 analytical column (150 mm × 4.6 mm, 3 μm) and Agilent 1260 DAD VL+ detector (detection wavelength 278 nm). The mobile phase was a mixture of methanol and water (15:85 v/v) at a flow rate of 1.1 mL·min^{-1} with a run time of 20 min.[4,5] Ethyl levulinate was analyzed on a Shimadzu GCMS-QP2020 gas chromatograph-mass spectrometer equipped with a Shimadzu AOC-20i auto injector, and a SH-Rxi-5Sil MS silica fused capillary column (30.0 m x 0.25 mm x 0.25 μm). Helium was used as carrier gas (flow rate: 1.2 mL min^{-1}) and the GC inlet temperature was 250 °C. A splitless mode of injection was used with a purge time of 1 min. The column temperature program was as follows: initial oven temperature of 50 °C (1 min), followed by a 15 °C/min ramp to 220 °C (held for 5 min), and then to 325 °C at 60 °C/min (held for 3 min).[5] Peaks were identified by comparison of their retention times and fragmentation patterns with analytical standards. Quantification of saccharides, furans and ethyl levulinate was conducted with the use of a standard curve plotted with analytical standards.

NMR spectroscopy. NMR spectra were recorded on an Agilent 500 MHz NMR spectrometer using deuterochloroform ($CDCl_3$) as solvent. The isolated furan derivatives were dissolved in the solvent in a 5 mm NMR tube and the spectra were collected at 25 °C with chemical shifts referenced relative to tetramethylsilane (^1H: $\delta = 0.00$ ppm; ^{13}C: $\delta = 0.0$ ppm). 2D NMR spectra (HSQC and COSY) were used to unambiguously assign the peaks.

Binding study by the ^{13}C NMR probe method. The binding ability of choline chloride/oxalic acid system to mesityl oxide was conducted using a ^{13}C NMR method according to the reference.[6] Choline chloride/oxalic acid (4.000 g) and mesityl oxide (200 mg to form a 5 wt% solution based on the solvent) were introduced to the round-bottom flask equipped with a magnetic follower and the mixture was agitated at room temperature for 2 h, resulting in a yellowish transparent solution. The solution (1.0 g) was transferred in a 5 mm NMR tube equipped with a coaxial insert containing deuterodimethyl sulfoxide-d_6 (external lock, ^{13}C: $\delta = 39.7$ ppm) and the sample was immediately analyzed by NMR spectroscopy at 25 °C.

IR spectroscopy. IR spectra were collected in ATR mode by placing cellulosic material onto a diamond crystal using Thermo Scientific Nicolet 6700 spectrometer in a range 4000–450 cm^{-1}.

GENERAL METHODS

Cellulose and hemicellulose were extracted from corn husk using a modified method.[7] Oven-dried biomass (5.000 g) was treated with aqueous NaOH (6 wt%, 100 mL) at 85 °C for 1 h. After cooling, the mixture was filtered to separate the insoluble cellulose fraction and soluble hemicellulose fraction. The recovered cellulose fraction was bleached with 1.0 mM aqueous NaOH (250 mL) containing hydrogen peroxide (2 wt% based on solvent) at room temperature for 24 h. The bleached solids were then repeatedly washed with an ethanolic solution of acetic acid (5 wt%, 2 × 30 mL) and ethanol (3 × 30 mL), filtered and lyophilized to obtain purified cellulose. The hemicellulose fraction was precipitated from the filtrate by adding aqueous ethanol (95 vol%, 500 mL). Crude hemicellulose was recovered and bleached with 1.0 mM aqueous NaOH (250 mL) containing hydrogen peroxide (2 wt% based on solvent) at room temperature for 24 h. Hemicellulose was precipitated from the aqueous solution by adding ethanol (95 vol%, 500 mL). The residue was recovered and washed repeatedly with an ethanolic solution of acetic acid (5 wt%, 2 × 30 mL) and ethanol (3 × 30 mL), filtered and lyophilized to obtain purified hemicellulose. The carbohydrate content of cellulose and hemicellulose fractions was analyzed according to the standard analytical method[2], and is specified in Table S1.

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A8. Supporting information for Chapter 4

SUPPORTING INFORMATION

DISSOLUTION OF CELLULOSE: ARE IONIC LIQUIDS INNOCENT OR NON-INNOCENT SOLVENTS?

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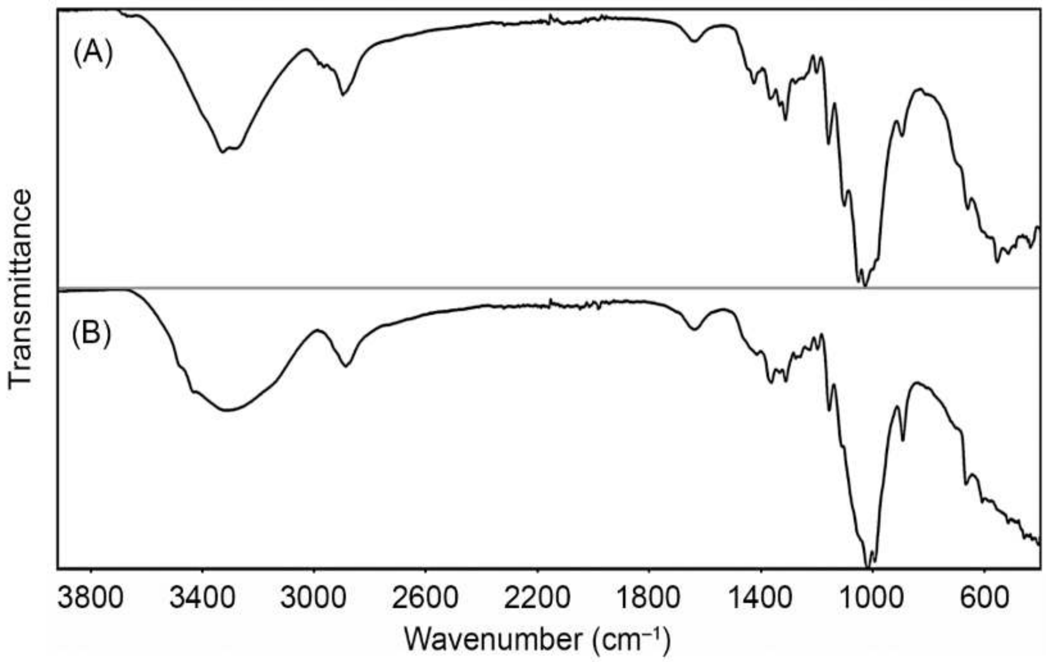

Figure S1. IR spectra of microcrystalline cellulose (A), and cellulose recovered after processing in $ZnCl_2 \cdot 2.5H_2O$ at 100 ºC, for 1 h (B).

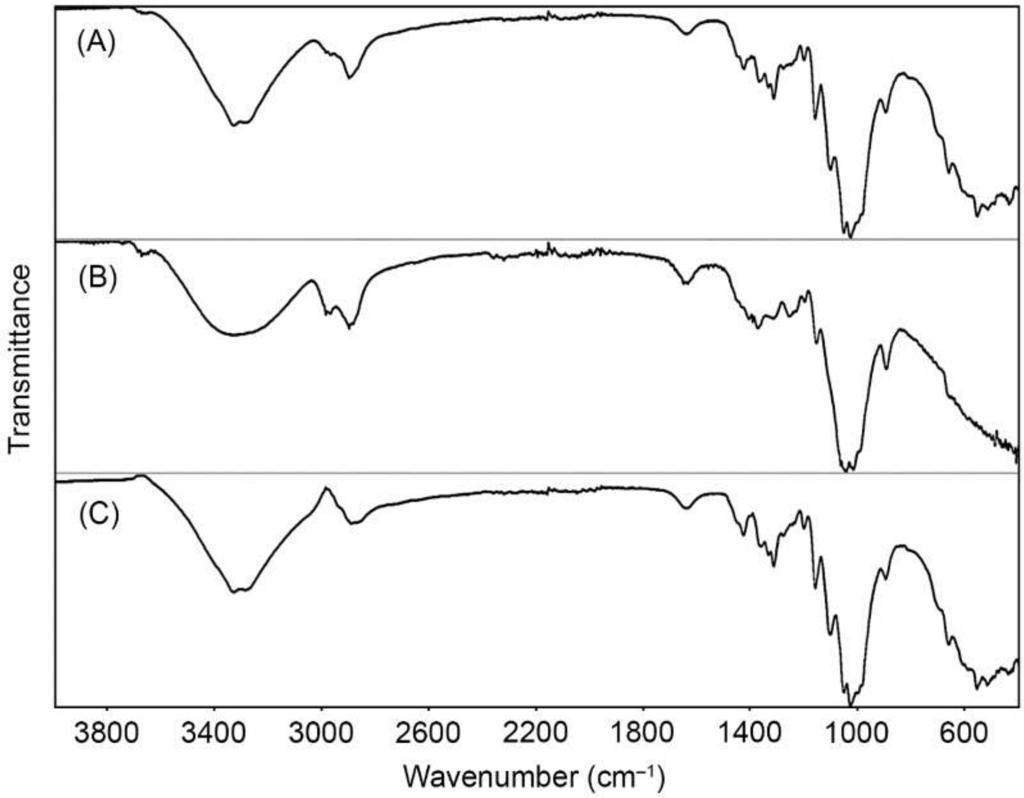

Figure S2. IR spectra of microcrystalline cellulose (A), and cellulose recovered after processing in 1-hexyl-3-methylimidazolium chloride (B) or tetrabutylammonium chloride (C) at 100 ºC, for 1 h.

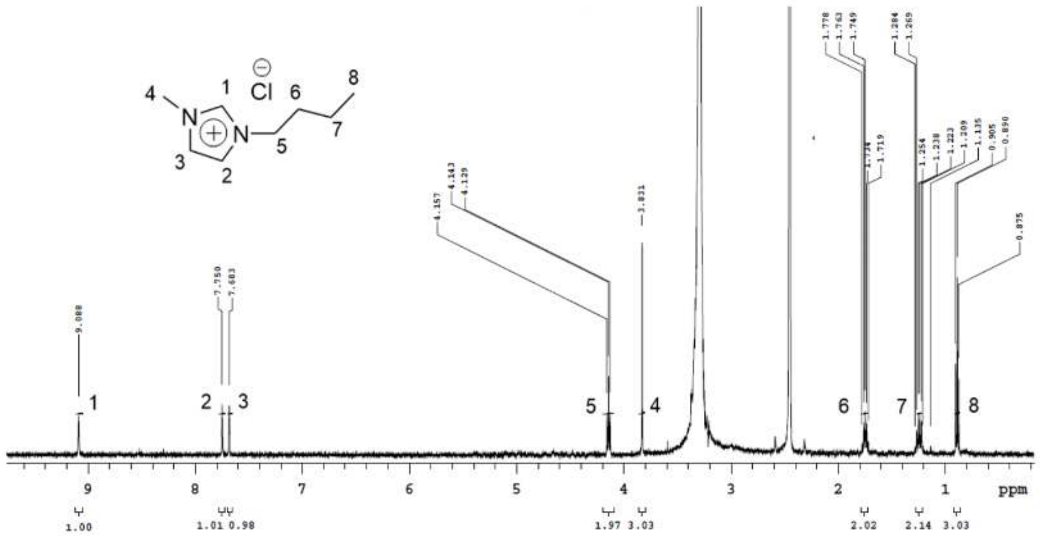

Figure S3. ^{1}H NMR spectrum of the 1-butyl-3-methylimidazolium chloride recovered after swelling of the regenerated cotton linter in deuterodimethyl sulfoxide-d_6 at room temperature for 12 h. The acquired spectrum of 1-butyl-3-methylimidazolium chloride correponds with data reported in the literature.[1]

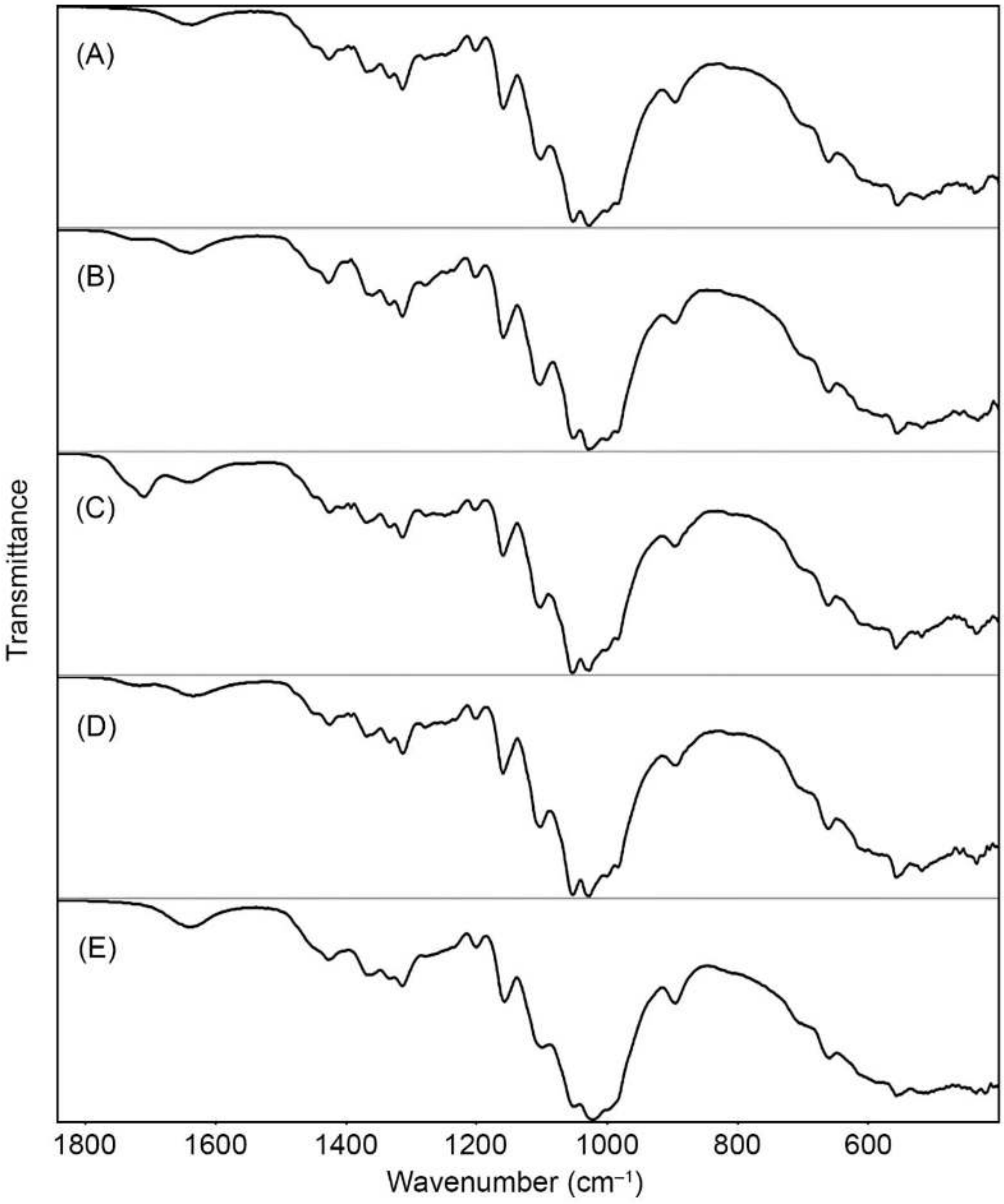

Figure S4. IR spectra of microcrystalline cellulose (A), and cellulose recovered after processing in choline chloride/malic acid (B), glycine/malic acid (C) proline/malic acid (D) or choline chloride/imidazole (E) deep eutectic systems at 120 ºC, for 2 h.

2. EXPERIMENTAL

2.1. Materials. Microcrystalline cellulose (MCC), cotton linter, eucalyptus cellulose, *Pinus* (unbleached and bleached) cellulose and other chemicals were supplied from commercial sources. Vacuum oven-dried (60 °C, 1 mbar, 12 h) cellulosic materials were employed for dissolution. Average particle size of substrates was 150 μm for MCC, and 3 mm for cotton linter, eucalyptus and *Pinus* cellulose. Analyses of the carbohydrate content of substrates using standard method[1] ensured the dominance of cellulose in samples, while other polysaccharides were absent or identified in trace amounts. Zinc chloride hydrate solvents ($ZnCl_2{\cdot}nH_2O$, $n = 2.5–4.5$),[3] imidazolium salts,[1] ChCl/acid (1:1 molar ratio for oxalic acid dihydrate or malic acid monohydrate, respectively; 1:0.5 for citric acid monohydrate, respectively),[4] ChCl/imidazole (3:7 molar ratio, respectively),[5] Gly/malic acid (1:1 molar ratio, respectively),[6] and Pro/malic acid (3:1 molar ratio, respectively)[6] solvents were prepared according to respective references. TBAC was dried under reduced pressure (22–24 °C, 0.01 mbar, 24 h) before use as a cellulose solvent.

2.2. Size-exclusion chromatography. Size-exclusion chromatography analysis of cellulosic materials was performed on an Agilent Technologies 1260 Infinity SECurity GPC System. Solutions were prepared at approximately 4 mg/mL in LiCl/DMAC (8 wt% of LiCl). The samples were heated at 70 °C for 18 h to allow the polymeric material to swell, followed by a six-hour resting period at room temperature to dissolve. This process was repeated until dissolution was observed. In some instances, when wishing to avoid the regeneration of the dissolved material, samples were prepared by dilution of the ionic liquid solutions of cellulose with LiCl/DMAC (8 wt% of LiCl) to the desired concentration. Centrifugation (3500 × g, 16 °C, for 15 min) followed by decantation into vials ensured the removal of any undissolved material. The soluble samples (100 μL) were injected and eluted from TSK-gel SuperHM-L and TSK-gel SuperHM-H columns connected in series with LiCl/DMAC (0.5 wt% LiCl, HPLC grade DMAC) at a flow rate 0.25 mL min^{-1} and at 60 °C. The eluted material was detected using a variable wavelength detector (280 nm), a multiangle laser light scattering detector (SLD7000, Polymer Standards Service GmbH, Mainz, Germany), and a refractive index monitor. The data for molecular weight determinations were analyzed with PSS WinGPC Unichrom software (version 8.2.1, Polymer Standards Service GmbH) using a dn/dc of 0.104 $\mathrm{mL.g}^{-1}$. The angular dependence of light scattering was fitted using a linear Berry plot and molecular weight data fitted using a 3rd order polynomial. The system was also calibrated with a series of monodisperse polystyrene molecular weight standards (1–1100 kDa, Tosoh Corp.).

2.3. IR spectroscopy. IR spectra were acquired in ATR mode using Thermo Scientific Nicolet 6700 spectrometer in a range 4000–450 cm^{-1}.

2.4. NMR spectroscopy. ^{1}H NMR spectrum was recorded on an Agilent 500 MHz NMR spectrometer using deuterodimethyl sulfoxide-d_6 (DMSO-d_6) as solvent at 25 °C. To prepare the sample for analysis, the regenerated cotton linter (20 mg) and DMSO-d_6 (0.5 mL) were introduced to a glass vial and the mixture was kept at room temperature for 12 h. The liquid phase was decanted and transferred in a 5 mm NMR tube and the spectrum was collected at 25 °C with chemical shifts referenced relative to residual solvent ($\delta = 2.49$ ppm). The solid phase was washed with acetone (3×1.0 mL), vacuum-oven dried (60 °C, 1 mbar, 2 h) and weighted to calculate the percentage of the recovered material.

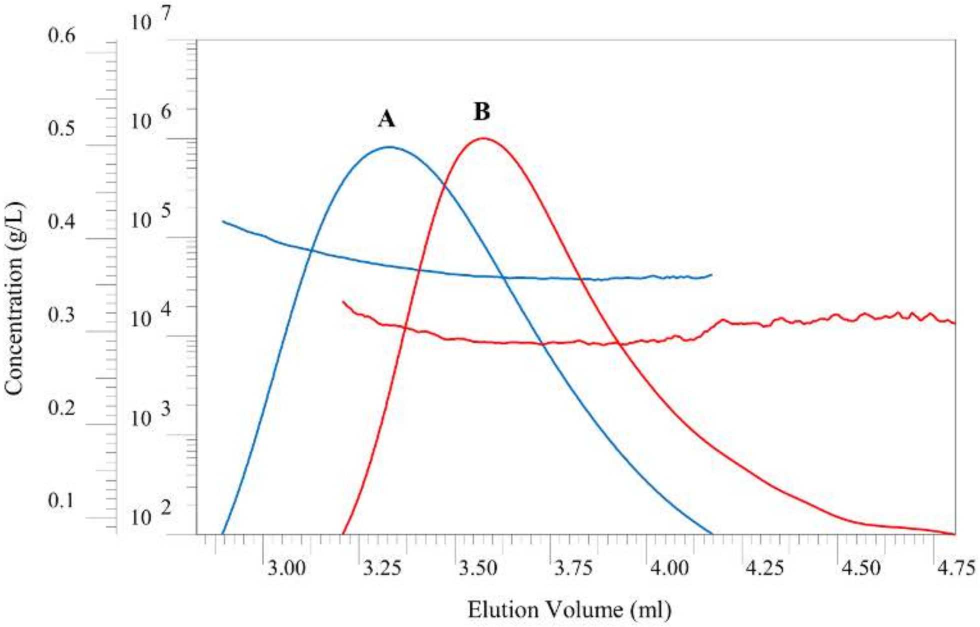

Figure S5. A representative size-exclusion chromatography spectrum of cellulose recovered after processing in choline chloride/citric acid deep eutectic system (100 ºC, 2 h; A), and in $ZnCl_2 \cdot 3.0H_2O$ (100 ºC, 1 h; B).

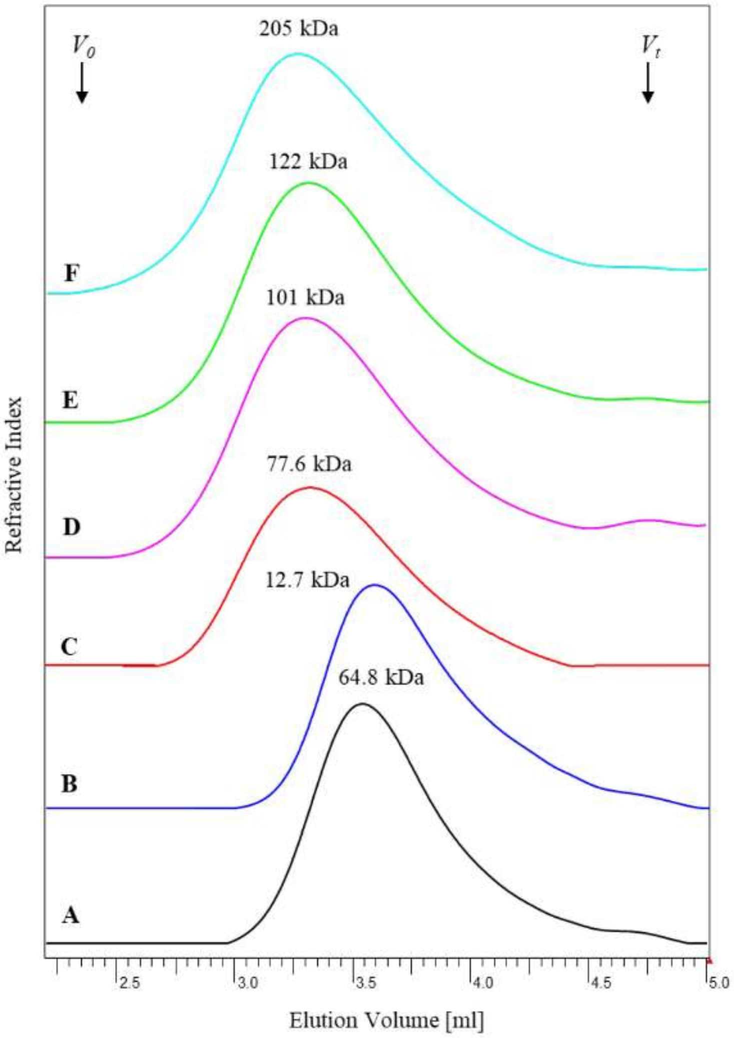

Figure S6. Size-exclusion chromatography elution profiles of microcrystalline cellulose (A) and cellulose recovered after processing in $ZnCl_2 \cdot 3.0H_2O$ (100 ºC, 1 h; B), 1-hexyl-3-methylimidazolium chloride (100 ºC, 1 h; C), and in choline chloride/malic acid (120 ºC, 2 h; D), choline chloride/citric acid (120 ºC, 2 h; E), glycine/malic acid (120 ºC, 2 h; F) deep eutectic systems. Weight average molecular weights are shown for each samples. V_0 = exclusion limit of columns; V_t = total elution volume.

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