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Screening of the catalysts for the fructose dehydration into 5-hydroxymethylfurfural in biphasic conditions at low temperature

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Abstract

The extended use of fossil resources for the production of chemicals and as a fuel poses several environmental problems. Biomass can be used as substitute renewable raw material for petrochemical resources to produce molecules similar to those from the petrochemistry. The objective of this master thesis is to investigate the potential acidic catalysts for the fructose dehydration into hydroxymethylfurfural (HMF) in a biphasic MIBK:H_2O system at temperatures suitable for enzymes. The obtention of such catalyst would allow the preparation of a bifunctional chemo-enzymatic catalyst to directly transform glucose into HMF in one-step. The benefit of doing the transformation in one-step is to avoid the recovery and purification costs between different reactions.

Using a Glucose Isomerase enzyme allows to obtain fructose from glucose with high selectivity. Glucose is the most available and abundant monomer obtainable from biomass. Hydroxymethylfurfural (HMF) is a platform chemical that can be obtained from biomass and further transformed into many different molecules such as monomers, fine chemicals or even fuels.

In this work, the catalysts for the fructose dehydration in biphasic conditions at relatively low temperatures have been investigated. The most efficient catalysts identified is the ion exchange resin Amberlyst-15. This work also showed the impact of both the acidity of the catalyst and the hydrophobicity of its surface. For the acidity, both the number of acid sites and the strength of these sites seems to have a positive impact on the efficiency of the catalyst. A higher hydrophobicity allowed a better extraction of the HMF in the organic phase of the system after its production leading to higher selectivities.

However, none of the investigated catalysts have shown sufficiently high performances to be used with an enzyme and moreover, a negative impact of the Amberlyst-15 on the enzyme has been detected.

The knowledge gained from this work thus allows to restraints the following researches to the investigation of other strongly acidic resins such as Nafion-117 as well as the screening of different reaction conditions such as the use of THF in place of MIBK.

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INTRODUCTION

1. Context

1.1 Fossil Resources Issues

The environmental impact of fossil fuels as well as their growing scarcity is an issue that has to be addressed. Fossil resources such as oil, natural gas and coal are used everywhere, they are a source of energy, a fuel for the transports and a raw material for the production of synthetic monomers. These synthetic monomers are used to produce many materials used every day such as nylon, polyesters or Teflon.

The global energy consumption in the world is mostly based on fossil resources; the fossil resources accounts for 87% of the energy consumption in the world [1]–[4]. Furthermore, fossil resources are also the most used raw materials for the production of common monomers such as ethylene, propylene or benzene. Indeed, 90% of these monomers were produced using crude oil or natural gas [5]. This dependency of the energy sector and the monomer industry to the fossil resources may cause major issues in the next decades.

The environmental considerations are becoming more and more important and efforts are made to reduce carbon dioxide emissions. Indeed, carbon dioxide acts as a greenhouse gas in our atmosphere and increasing its concentration leads to an increase of the global temperature on Earth [6]. In this perspective of carbon dioxide emission reduction, the non-renewability of the fossil resources is a major issue concerning the environmental crisis. While biomass can refill its stocks quite rapidly capturing and storing carbon dioxide to grow through photosynthesis, fossil resources take millions of years to refill. Even if a carbon dioxide in the atmosphere has the same impact whatever its origin, a carbon dioxide from biomass is part of a cycle between the atmosphere and the biomass while a carbon dioxide from fossil resources adds up to the amount of carbon dioxide in the cycle leading to an increasing in the carbon dioxide of the atmosphere.

Moreover, these fossil resources are finite. This means that the total amount remaining on Earth cannot be extended and that the stocks are not able to refill themselves as fast as they are consumed. The proved reserves of oil and natural gas are only enough to ensure our consumption for the next 5 decades (Figure 1) [4]. This is considering a constant production of oil and natural gas over the period as well as no new reserves discovery and no new technology implementation. The reserves could thus be partially extended but the limited amount existing on our planet will still be a problem that mankind will have to face quite rapidly.

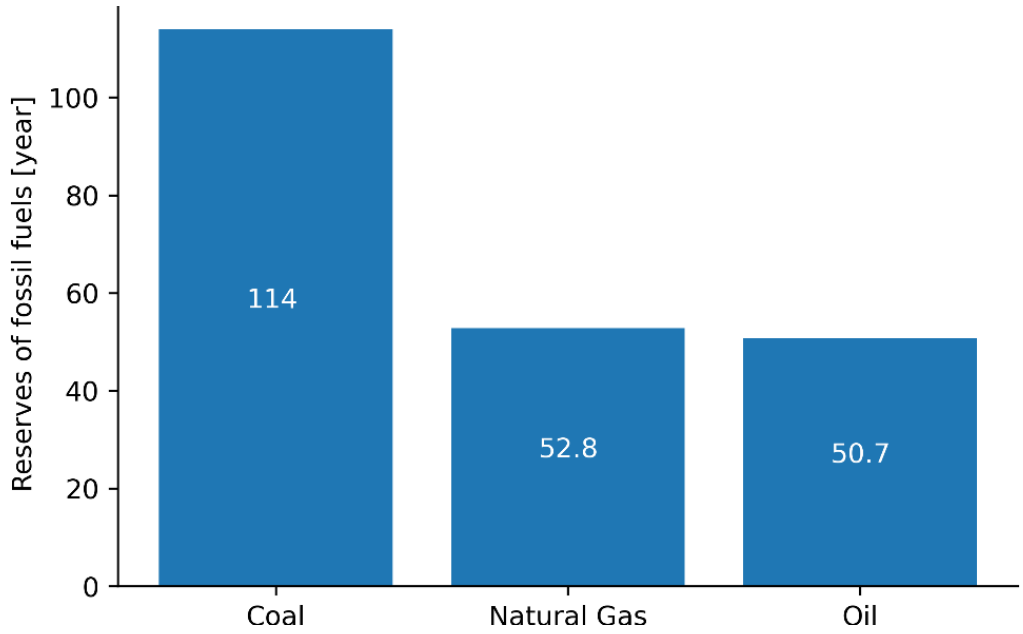

Figure 1 – Years of fossil fuel reserves left (adapted from Ritchie et al. (2020) [4])

A solution of growing interest is the use of biomass as a renewable raw material for the production of monomers and biofuels to replace the petrochemical industry. This replacement is not an easy task since the starting molecules are very different. On the one hand, coal, natural gas and mineral oil are mostly composed of saturated alkanes which contain reduced carbon atoms due to the absence of oxygen and other heteroatoms (heteroatoms are in organic chemistry any atom that is not a carbon or a hydrogen). On the other hand, biomass is mostly lignocellulose that can be separated into cellulose, hemicellulose and lignin. Cellulose and hemicellulose are polymers made of saccharides and lignin is a polymer made of various phenolic molecules. The biomass thus contains more oxidised carbons.

Having such different raw materials induces that the syntheses to obtain specific monomers are also very different: the petrochemical synthesis needs to add some oxygenated functions through oxidation processes while the biorefineries needs to remove some oxygen atoms through reactions such as dehydrations, hydrogenations or decarboxylations. The biorefineries thus have very different needs than the petrochemical industry and the knowledge we have from the use of fossil resources for decades is not useful for the biomass valorisation.

In the emerging bio-based chemical industry, some intermediate molecules are very interesting because they can be the starting point of a wide range of syntheses. These molecules are called the “Platform Chemicals”. One of them is hydroxymethylfurfural.

1.2 Hydroxymethylfurfural

5-(hydroxymethyl)furfural also called hydroxymethylfurfural or HMF is an organic compound which is a white solid at room temperature but with a melting point slightly above 30°C [7]. HMF is constituted of 6 carbon atoms arranged into a cycle containing 4 carbons and 1 oxygen (furanic ring) as well as two oxygenated functions: a primary alcohol and an aldehyde (Figure 2).

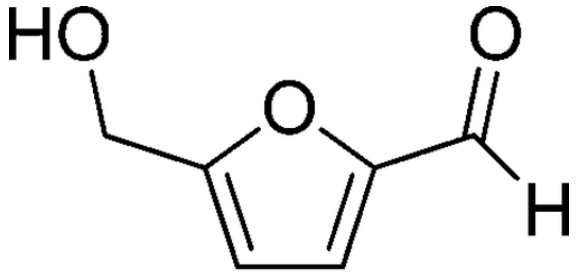

Figure 2 – Molecule of 5-hydroxymethylfurfural (HMF)

As a multifunctional molecule, HMF can be used in many different synthesis pathways and can thus be the starting point for the production of a wide range products. Some of the various possible uses of HMF (**1** in the Figure 3) as a platform chemical are presented in Figure 3:

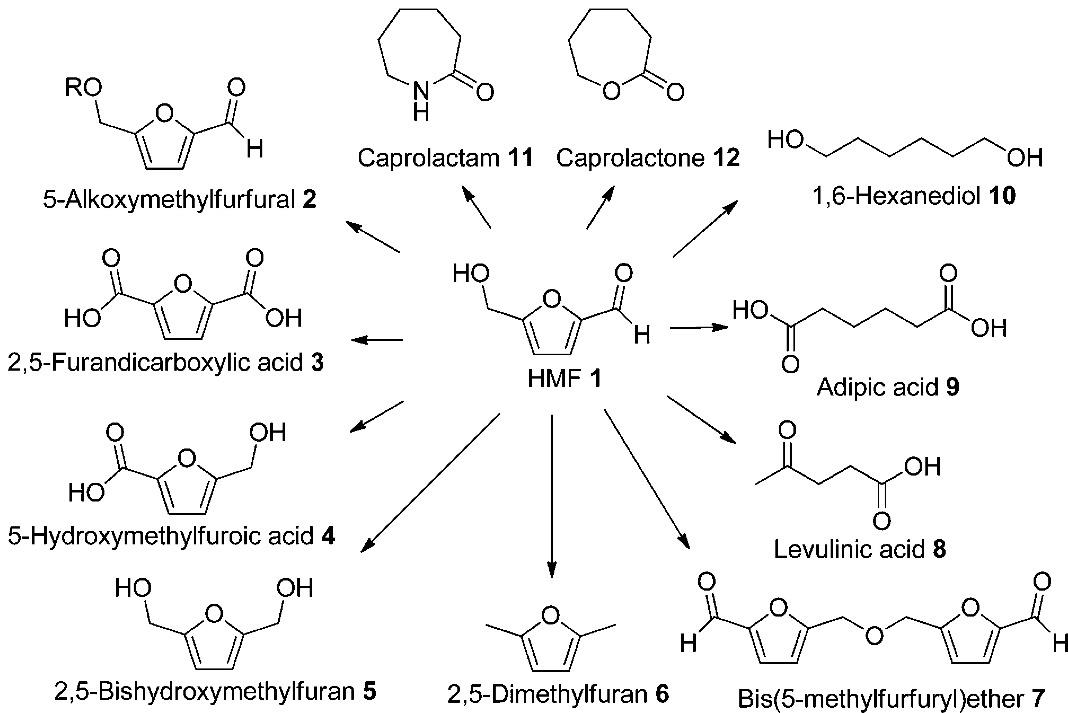

Figure 3 – Chemicals obtainable from HMF (from van Putten et al. (2013) [8]).

First, HMF can be used in the production of monomers such as diols such (e.g. 2,5-bishydroxymethylfuran, **5** in Figure 3). This 2,5-bishydroxymethylfuran can be further transformed into heat insulating material, resins, crown esters or polymers with interesting properties (shape-memory and self-healing) [9]. Among the diol monomers, 2,5-furandicarboxylic acid (FDCA, **3** in the Figure 3) – that can be used in the synthesis of succinic acid – and the caprolactam (**11** in the Figure 3) – the monomer used for the synthesis of Nylon 6 – are other monomers obtainable from HMF.

Also, HMF can be used for the production of fine chemicals such as to produce flavours, macrocycles, heterocycles, agrochemicals and even pharmaceutical compounds due to the modification possibilities induced by the alcohol and aldehyde functions. For example, the 5-amino levulinic acid is an agrochemical used as herbicide that can be synthetized from levulinic acid (LA, **8** in the Figure 3) which can be obtained from HMF. [8], [10] Moreover, levulinic acid also being a platform chemical [11], its obtainability from HMF creates a path to synthetize many other molecules.

Finally, even if HMF cannot directly be used as fuel since it is a solid with poor fuel blend properties, some furan derivatives such as dimethylfuran (DMF, **6** in Figure 3) presents high energy content and are therefore interesting biofuels candidates [10]. Moreover, furans could be further transformed into linear alkanes that could be used as diesel or jet fuel [8].

An economic analysis conducted by Bhaumik and Deppe (2015) shown that while lignocellulosic biomass could be purchased for around 50$ per ton, its derivative glucose could be purchased around 500$ per ton and HMF around 300 000$ per ton. Another updated price comparison based on the Sigma-Aldrich online catalogue is presented in Table 1 [12]. The comparison has been conducted on the 1kg pack size of the products with over 99% purity.

Table 1 – Price comparison of the HMF intermediates based on the Sigma-Aldrich catalogue (updated May 2022) [12]

Product	**Price [$/kg]**
Glucose	57
Fructose	84
Hydroxymethylfurfural	4 500

As it can be seen, the prices from Sigma-Aldrich are much higher than those presented by Bhaumik and Deppe (2015) [13]. This is probably due to the use of the 1kg pack size for the Sigma-Aldrich comparison. Moreover, the purity of the products may be varying between the comparisons and thus impact the price. However, the huge price increase between glucose and HMF shown by both Bhaumik and Deppe (2015) and the Table 1 clearly indicates the economic interest of HMF.

1.3 Hydroxymethylfurfural synthesis

Biomass that has been mentioned above as a potential solution to replace the fossil resources can be used as raw material for HMF production. According to Pang (2016), biomass can be defined as "matter originating from living plants, including tree stems, branches, leaves as well as residues from agricultural harvesting and processing of seeds or fruits" [14]. This matter is composed of a wide variety of complex molecules [15] and can be divided into edible biomass (fruits, cereals,…) and lignocellulosic biomass (grass, crop wastes, roots, …) [13]. While edible biomass is considered as the first-generation raw material for the production of biofuels (production of ethanol through the fermentation of glucose for example) [16], the use of edible biomass as a feedstock to produce biofuel may threaten human food supplies [17] and biodiversity [18]. The use of human food production by-products such as crop wastes, roots and other non-edible biomass is thus more reasonable and is known as second-generation raw material for the production of biofuels.

This non-edible biomass also known as lignocellulosic biomass is made of three main components: cellulose (around 45%), hemicellulose (around 25%) and lignin (around 20%) [19]. These 3 components may be separated using either physical or chemical methods [20] and then used for the synthesis of value-added chemicals such as sugars (e.g. D-Fructose or D-Glucose) (see Figure 4). These sugars obtained from lignocellulosic biomass can then be used for the production of biofuels (ethanol production by the fermentation of glucose) or for the production of other interesting chemicals, one of them being hydroxymethylfurfural.

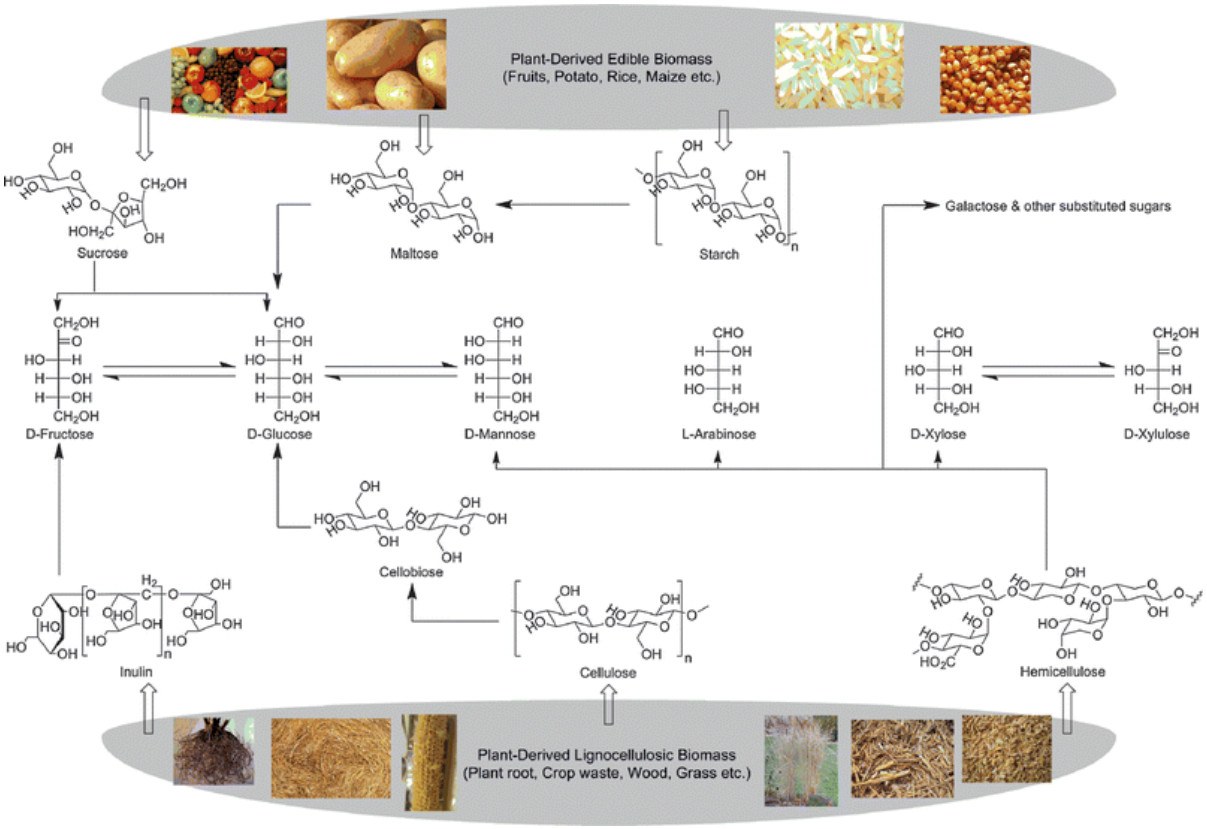

Figure 4 – Possible Pathways to produce Sugars from Biomass (from Bhaumik and Dhepe (2015) [13])

HMF can be obtained directly from fructose through successive dehydrations. Fructose which is obtainable from both edible and lignocellulosic biomass can thus be used as raw material for HMF production.

Fructose used for HMF production, is present in the biomass but only in small quantities. Fructose can be obtained from glucose which is more abundant and more accessible in the biomass. Whatever the type of biomass used (edible or lignocellulosic), the intermediate for the production of fructose is thus glucose.

1.3.1 From Biomass to Glucose

A first reaction pathway to obtain glucose is by using starch. Indeed, starch which is a branched glucose polysaccharide can be transformed in glucose monomers through hydrolysis reactions (addition of one molecule of water to break the glycosidic link between two monomers) [13]. This link cleavage can be catalysed by acids such as sulfuric acid or hydrochloric acid [21] or by the presence of enzymes such as α-amylase and glucoamylase [22], [23]. The production of glucose from starch is easier than its production from cellulose or hemicellulose due to the reactivity of the starch polymer compared to the two others [24] but as starch is an edible biomass, its use for the production of chemicals instead of human food or animal feed can be questionable.

To avoid using edible biomass and starch as a raw material, another reaction to obtain glucose from lignocellulosic biomass exists. As previously said, lignocellulosic biomass is mainly composed of cellulose, hemicellulose and lignin, the rest being inorganic salts [25]. Glucose can be obtained from cellulose and hemicellulose [25]. The first step for the production of glucose from lignocellulosic biomass is a pre-treatment removing lignin as well as weakening the crystalline structure [26]. This pre-treatment step that facilitates the following steps can be achieved through several different methods (Figure 5) that can be chemical (acid or alkali treatment, deep eutectic solvents), physical (milling or extrusion) [27] or physicochemical (supercritical fluids, ammonia fibre explosion, co-solvent enhanced fractionation) [20], [28], [29].

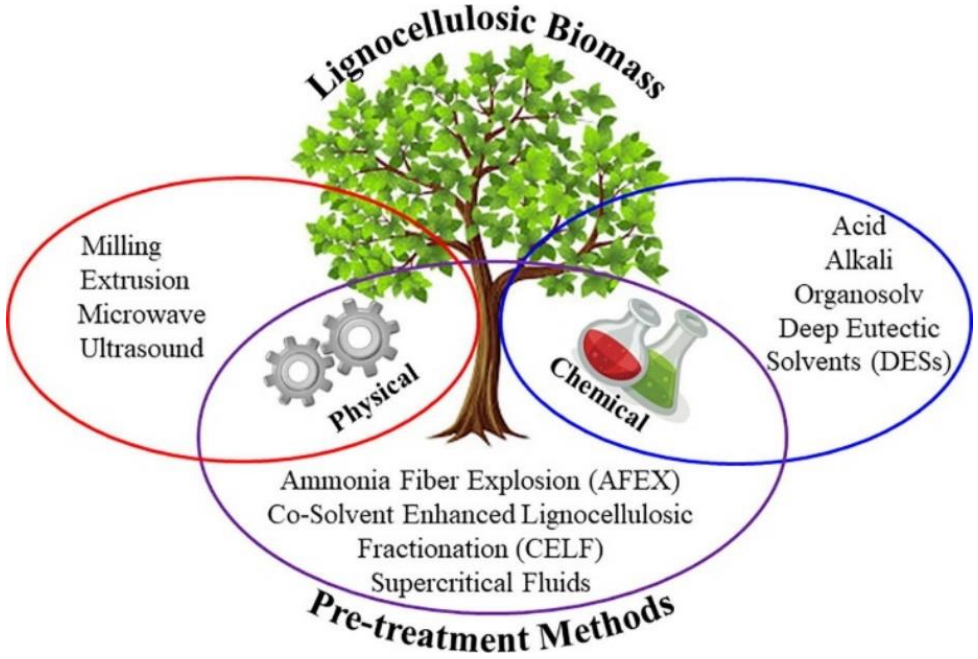

Figure 5 – Lignocellulosic Biomass Pre-treatment Methods (from Mankar et al. (2021) [28])

After the pre-treatment, cellulose can be converted to glucose through hydrolysis catalysed by either homogeneous (in the same phase than the reaction) acid catalysts (e.g. sulfuric acid or hydrochloric acid) or heterogeneous (in a different phase than the one of the reaction) acid catalysts (e.g. H-form zeolites, heteropolyacids, ion exchange resins or SO_3H bearing supports) [30]–[32]. Hemicellulose can also be used for the production of glucose using homogeneous acid catalyst such as formic acid [33] or heterogeneous catalysts such as CuO [34].

1.3.2 Glucose to Fructose Transformation

After the production of glucose, it is still needed to convert it to fructose. This reaction from glucose to fructose is an isomerization known as the Lobry–de Bruyn–van Ekenstein transformation [35], [36]. It can be promoted by either heterogeneous or homogeneous

catalysts. This reaction needing either Lewis basicity or Lewis acidity as active sites, the catalysts may vary a lot.

Lewis acidity can be brought by homogeneous catalysts such as $CrCl_3$ [37], $AlCl_3$ [38] or aluminium complexes [39]. Some other existing catalysts are heterogeneous catalysts which are mostly zeolites containing metals as active sites. Typically used metals are tin (Sn) [40]–[42], iron (Fe) [43] or titanium (Ti) [44] incorporated in a β-zeolite framework [40]–[44].

Lewis basic sites can also be used as catalysts for the isomerization of glucose to fructose [35], [42], [45], [46]. One of the basic sites containing heterogeneous catalysts used for the isomerization is the Mg-Al hydrotalcite [35]. Hydrotalcite is a magnesium-aluminium hydroxide that presents a layered crystalline structure [47] and that contains bicarbonate (HCO_3^-) groups on its surface [35], [48].

The main issue with the use of such catalysts is their poor selectivity towards fructose which leads to high amounts of by-products and requires the use of more glucose to obtain a same quantity of fructose. Moreover, the presence of by-products can also reacts during the following steps thus creating a complex mixture containing glucose and fructose as expected but also many other unwanted compounds. To avoid such complexity, separation and purification steps are required to obtain a solution mostly composed of the molecules of interest.

A possibility to avoid the formation of by-products is through the use of enzymes. Enzymes are proteins that can act as biological catalysts in living organisms. One enzyme is generally able to increase the speed of only one very specific reaction with a very high selectivity. For the isomerization of glucose to fructose, the glucose isomerase (GI) enzyme can be used as catalyst [22], [49], [50]. This enzyme is already widely used in industry for the production of high-fructose syrup (aqueous solution with high glucose and fructose concentrations used in de food industry) [51]. In addition to being a more selective catalyst than the chemical catalysts presented before, glucose isomerase, as other enzyme, is environmental friendly [51] due to the fact that enzymes are biodegradable and are non-toxic for the environment [52], [53].

Enzymes sometimes need to have co-factor to have a better activity. The glucose isomerase, requires co-factors that are divalent metal ions such as cobalt or magnesium [50] but that can vary depending on the organism at the source of the enzyme [49].

Enzymes are proteins synthetised by living organisms. They thus have been created to function in an aqueous media. The change of solvent can have an impact on the activity of the enzyme as well as its stability. Furthermore, many enzymes require the presence of

cofactors to work properly. In the case of the Glucose Isomerase, the cofactors are bivalent cations such as Mg^{2+} or Co^{2+} [49], [50], [54]. These cofactors thus have to be present in the solvent to ensure the activity of the enzyme.

Enzymes have an optimal temperature where their activity is maximal. Working at lower temperature will lead to a reduction of the activity. At a higher temperature, the activity will also be reduced and a too high temperature can even lead to a denaturation of the enzyme which irreversibly loses its 3-dimensional structure and thus loses all its catalytic activity. The optimal temperature for the classical Glucose Isomerase is around 30°C [55] but some GI from thermophilic organisms have their optimum around 60°C [55] and sometimes up to 90°C [54].

The pH impact on the enzymes is due to the change of the charges of the amino acids composing the enzyme. This charge change will lead to a change in the interactions between the amino acids and the conformation of the amino acid chain will thus be impacted modifying at the same time the catalytic activity of the enzyme. In the case of glucose isomerase, the optimal pH is between 6.0 and 8.5 [49], [55], [56]. The pH optimum may also vary a little depending on other parameters such as temperature or buffer solution. For example, Srih-Belghith and Bejar (1998) showed that the optimal pH of the GI from a *Streptomyces* was 6.0 at 60°C and shifted to 6.4 at 90°C [54].

Finally, the presence of salt in the solution can affect the enzyme. Indeed, an increase in salt concentration will lead to an increase in ionic strength leading to a lower amount of water molecule to interact with the charges present on the enzyme. Above a certain salt concentration, enzymes will precipitate and thus will not have a catalytic activity anymore. This precipitation of the enzymes due to high salt concentration is reversible meaning that if the concentration of salt decreases, enzymes will be able to solubilise again and recover their catalytic activity.

1.3.3 Fructose Dehydration to HMF

Now that the production of glucose from biomass and its transformation into fructose have been discussed, the remaining reaction is the conversion of fructose to HMF. This last step is as shown on the Figure 6, a succession of three dehydration reactions of the fructose molecule.

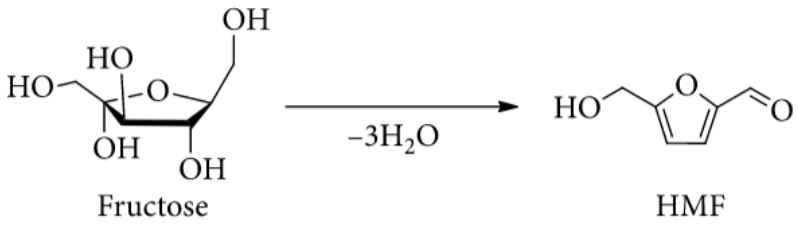

Figure 6 – Fructose to HMF reaction (from Zhang et al. (2019) [57])

Brønsted acids (containing at least one hydrogen atom that can leave as a proton) are known to be efficient catalysts for these dehydrations. Even though the mechanism through which these dehydrations occur depends on the conditions (nature of the solvent or solvents, nature of the catalyst), a mechanism proposed by Testa et al. (2020) is composed of two steps of 1,2-elimination followed by one 1,4-elimination. These 3 steps follow a E1 mechanism (reaction is facilitated through the loss of a leaving group) and are catalysed in this case by the acidic hydrogen present on the hydroxyl group (-OH) of the sulfonic acid (-SO_3H) function (Figure 7).

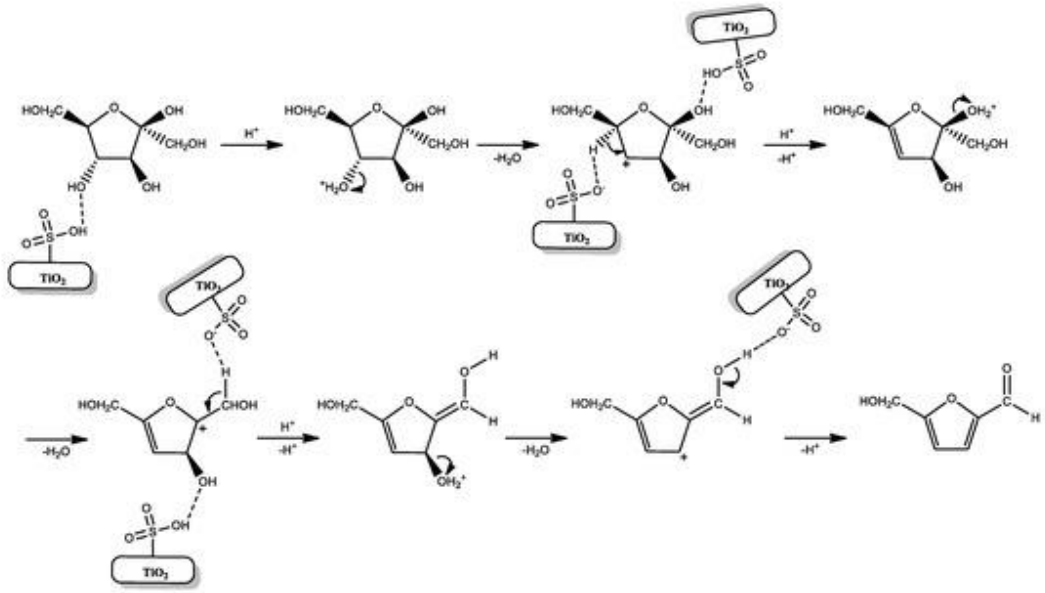

Figure 7 – Reaction mechanism proposition for the fructose dehydration to HMF (from Testa et al. (2020) [58])

Many different conditions have been used for the production of HMF from fructose. First, several solvent systems exist from the most simple monophasic aqueous system to more complex biphasic systems using high salt concentrations. Moreover, many catalysts are used. Also the reaction temperature as well as many other parameters such as the initial reactant concentration, the solvents ratio and the reaction duration are varying parameters. Table 1 presents results obtained in some of these conditions. The different solvent systems and catalysts observed in this Table are discussed in the following sections.

Table 2 – Survey of reported catalysts and conditions for the fructose dehydration to HMF in different solvent systems

	Solvent	Catalyst	Temperature [°C]	Time [min]	Fructose Conversion [%]	Selectivity [%]	HMF Yield [%]	Reference
1	H_2O	Acetic acid	200	20	91	64	58	[59]
2	H_2O	p-Toluenesulfonic acid	88	240	53	47	25	[60]
3	H_2O	H_2SO_4	200	5	92	25	23	[61]
4	H_2O	HCl	95	24	63	48	30	[62]
5	H_2O	HCl	130	5	100	28	28	[63]
6	H_2O	HCl	180	3	49	51	25	[64]
7	H_2O	$YbCl_3$	140	120	60	40	24	[65]
8	H_2O	Fe-vanadyl phosphate	80	60	71	84	60	[66]
9	H_2O	ZrP_2O_7	100	120	53	81	43	[67]
10	H_2O	Titanium-phosphate	100	120	57	69	39	[67]
11	H_2O	NiP_2O_7	100	180	51	59	30	[68]
12	H_2O	Zirconium-phosphate	240	2	81	61	49	[69]
13	H_2O	H_3PO_4-treated niobic acid	100	30	29	98	28	[70]
14	H_2O	Precipitated niobium acid	110	360	90	12	11	[71]
15	H_2O	Nb_2O_5	165	180	76	75	57	[72]
16	H_2O	TiO_2	200	5	98	22	22	[61]
17	H_2O	ZrO_2	200	5	90	17	15	[61]
18	H_2O	β zeolite (Si/Al = 12.5)	120	120	17	6	1.1	[73]
19	H_2O	ZSM-5 zeolite (Si/Al = 25)	130	360	52	16	8	[74]
20	H_2O	Dowex 50wx8-100	150	30	54	62	33	[75]

	Solvent	Catalyst	Temperature [°C]	Time [min]	Fructose Conversion [%]	Selectivity [%]	HMF Yield [%]	Reference
21	DMF	$LaCl_3$	100	240	/	/	92	[76]
22	DMSO	$LaCl_3$	100	240	/	/	95	[76]
23	DMSO	$AlCl_3$	140	5	/	/	69	[77]
24	DMF	Amberlyst-15	100	60	100	90	90	[78]
25	DMSO	Amberlyst-15	120	120	100	76	76	[79]
26	DMSO	β-zeolite (Si/Al = 12)	120	120	100	51	51	[79]
27	DMSO	SiO_2-SO_3H	100	4	95	66	63	[80]
28	MIBK:H_2O	$AlCl_3$	130	5	/	/	61	[77]
29	MIBK:H_2O	HCl	180	3	75	73	55	[64]
30	THF:H_2O	H_3BO_3	150	75	75	68	51	[81]
31	MIBK:H_2O	Nb-P/SBA-15	130	120	53	90	48	[82]
32	MIBK:H_2O	DIAION ® RCP160M	120	30	92	100	91	[83]
33	MIBK:H_2O	p-Toluenesulfonic acid functionalized graphite	140	1440	90	58	52	[84]
34	MIBK:H_2O	Pyrochlore	150	120	99	60	59	[85]
35	THF:H_2O	$CrPO_4$	140	15	99	84	83	[86]
36	MIBK:H_2O	Mordenite zeolite (Si/Al = 12)	165	390	64	66	42	[87]

1.4 Existing Solvent Systems

1.4.1 Monophasic Aqueous Systems

As presented in the Table 2, the most commonly used solvent is water since it is widely available and non-toxic for the environment (lines **1-20**). But since water is a product of the dehydration reaction, the presence of water in high quantities shifts the reaction equilibrium towards the reactants thus leading to lower HMF productions. Moreover, the stability of HMF in aqueous solution is low because of the possible reactions in which HMF can be consumed (Figure 8). These reactions are humins production by condensation of HMF with sugars and the HMF degradation into levulinic acid (LA) and formic acid (FA) [88]. Finally, León and collaborators have demonstrated that the produced HMF stays on the surface of the dehydration catalysts thus preventing the arrival of new substrate molecules and their transformation to HMF (poisoning by the product of the catalyst) [89].

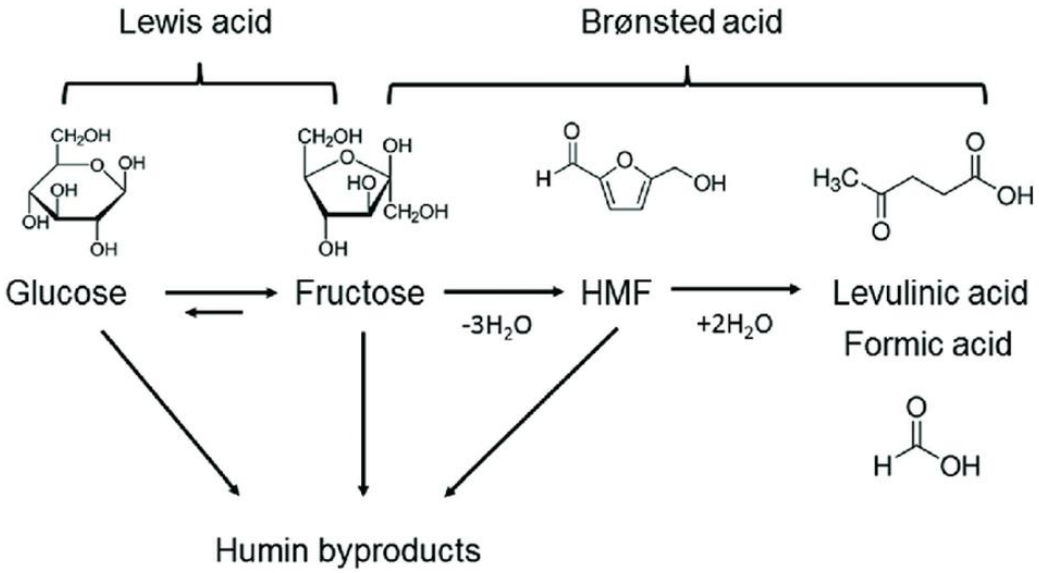

Figure 8 – Potential side-reactions during the production of HMF (from Zhang et al. (2016) [88])

A possibility to decrease these side reactions is to use an organic solvent. This organic solvent can be used in either a monophasic or a biphasic system.

1.4.2 Monophasic Organic Systems

In the case of the use of an organic solvent in a monophasic system (Table 2 lines **21-27**), the solvent must allow to solubilise high fructose concentration. Indeed, fructose is a very polar molecule that is also an H-bond donor and acceptor. These two properties make fructose a very hydrophilic molecule. Only some polar solvents such as dimethylsulfoxide (DMSO) or dimethylfuran (DMF) are able to solubilise fructose less than water but still up to significant concentrations (e.g. up to 36g/L for DMSO).

These solvents have shown a good results and a catalytic activity of DMSO for the fructose dehydration has even been proposed [90]. One of the problems of DMSO is that since this solvent has a good affinity towards HMF, its separation is hard and requires either large extraction solvent amounts or a high energy consumption [8], [91]. This is incompatible with the development of a new catalyst in the field of green chemistry where the savings of energy, reactants and solvents are a priority [92].

1.4.3 Biphasic Systems

Another possibility to use organic solvent is by using biphasic systems (Table 2, lines **28-36**). In a biphasic system, two phases are present in the same reactor and consists of an aqueous phase where fructose can be solubilised easily [84] and where the reaction occurs [93] and an organic phase that allows extracting the produced HMF directly after its production. The organic phase of such systems has to be immiscible with water and have a high affinity towards HMF to ensure an efficient extraction. The use of this kind of system has shown a better stability of HMF due to its extraction in the organic phase thus leading to a reduction in the side reactions that were previously occurring in the aqueous phase [94], [95]. The reduced rate of side-reaction thus increases the selectivity of the dehydration of fructose into HMF. Moreover, the HMF extraction also helps removing the HMF adsorbed on the surface of the catalyst [89]. The adsorption of HMF on the catalyst leads to a reduction of its activity (poisoning by the product) and thus extracting the HMF adsorbed to the organic phase leads to a clearing of the catalytic sites and thus to a higher activity compared to the catalyst with product adsorbed on its surface. This clearing is possible through a good mixing of the reactor to ensure the contact of the catalyst with the organic phase.

The most common organic solvents used for the biphasic systems is methyl isobutyl ketone (MIBK) [96]. MIBK is immiscible in water [84] and thus a MIBK-water mixture produces a biphasic system. This organic solvent has a partition coefficient (R) of HMF of between 0.8 and 1 [87], [97], [98]. The partition coefficient is the ratio of the concentration of HMF in the organic phase to the concentration of HMF in the aqueous one. This R value of 1 means that the concentrations in both organic and aqueous phase are identical. Another commonly used organic solvent is tetrahydrofuran (THF) [8]. Unlike MIBK, THF is soluble in water and needs to be used with highly saline aqueous solutions. Indeed, the addition of salt such as NaCl increases the ionic strength of the aqueous phase and leads the separation of an organic phase mostly composed of THF and an aqueous phase containing mostly the saline solution.

Salting-out

The addition of salt to biphasic systems also has an impact on the extraction of HMF. The polarity of HMF being low, the increase in the ionic strength of the aqueous solution favours the extraction of HMF to the organic phase (higher HMF partition coefficient) [99], [100]. This better extraction leads to a better selectivity due to the reduction of the side reactions in the aqueous phase as well as a better conversion [100].

1.4.4 Specific Case of Ionic Liquids and Deep Eutectic Solvents

To avoid some issues caused by the solvents, Ionic Liquids (ILs) that are salts of ions liquid at a temperature below 100°C have also been studied because they have the advantage of reducing the rehydration reaction of HMF to FA and LA as well as reducing the production of humins by having a high selectivity towards HMF and allowing a high solubility of fructose compared to organic solvents [91]. They can be used with or without catalyst and some results are shown in the Table 3:

Table 3 – Production of HMF in Ionic Liquids

Solvent	Catalyst	Temperature [°C]	Time [h]	HMF Yield	Reference
[MIm]Cl[a]	/	90	0.75	92%	[101]
[BMIm]Cl[b]	$CrCl_3$	100	6	96%	[102]
[BMIm]Cl[b]	WCl_6	50	4	63%	[103]
[BMIm]Cl[b]	HCl	23	24	72%	[104]

[a] [MIm] stands for 1-H-3-methyl imidazolium, [b] [BMIm] stands for 1-butyl-3-methylimidazolium

As it can be seen, the reaction temperatures are mostly lower than those required for the catalysts previously mentioned. Even if they have several advantages such as easy product recovery, high selectivity, low reaction temperature and good reusability, ILs have high costs and could have negative impacts on the environment [105], [106].

Another type of interesting solvents are the Deep Eutectic Solvents (DESs) since they have similar properties compared to the ILs but without having negative environmental impacts. Indeed, they have a higher biodegradability as well as lower toxicity [106]–[108].

Table 4 – Production of HMF in Deep Eutectic Solvents

Solvent	Catalyst	Temperature [°C]	Time [h]	HMF Yield	Reference
[Choline]Cl/Citric Acid	/	80	1	91%	[109]
[Choline]Cl	$CrCl_3$	100	4	75%	[110]
[Choline]Cl	HCl	100	4	90%	[110]
[Choline]Cl	H_2SO_4	100	4	83%	[110]
[Choline]Cl	Maleic acid	90	1	71%	[111]

The results presented in the Table 4 are similar to those observed with the ILs (Table 3) since in both cases, high yields (above 70%) are observed at low temperatures (below 100°C).

1.5 Existing Catalysts

The dehydration reaction of fructose to produce HMF can be enhanced by a catalyst. A catalyst allows to accelerate the reaction rate. Moreover, the catalysts are not consumed by the reaction and can thus be recycled an infinite number of times, in theory. A good catalyst can thus lead to a higher production or to a reduction of the energy demand by reducing the required temperature or the required pressure.

1.5.1 Homogeneous Catalysts

Homogeneous catalysts are catalysts that are present in the same phase as the reaction. In this case, the dehydration reaction occurs in a liquid phase, the homogeneous catalysts are thus soluble compounds.

For this reaction, some of the existing homogeneous catalysts are presented in the Table 2. As it can be seen, in a monophasic aqueous system, the catalysts used can be organic acids (such as oxalic acid or toluene sulfonic acid, lines **1-2**), inorganic acids (such as H_2SO_4 or HCl, lines **3-6**) or metal chlorides (e.g. Ytterbium Chloride $YbCl_3$ line **7**). These three different types of catalysts can be separated in two different classes. First, the Brønsted acids composed of both the organic and inorganic acids. Their acidity is due to their property of being proton donors. Secondly, the Lewis acid-based catalyst such as $YbCl_3$ that have acidic properties due to their capacity to accept an electron pair in an empty orbital of the molecule.

As it can be seen in Table 2, homogeneous catalysts based on Lewis acidity (such as $YbCl_3$, line **7**) used in aqueous systems can also be used monophasic organic solvent systems

(such as $LaCl_3$ or $AlCl_3$, lines **21-23**). In biphasic systems, both Lewis ($AlCl_3$, line **28**) and Brønsted (inorganic acids such as HCl and H_3BO_3 lines **29-30**) acid catalysts can be used.

The issue of the homogeneous catalyst is that since they are in the same phase as the reaction, they are hardly recovered from the solvent system. It is thus needed to add fresh catalyst at the start of every new reaction. Moreover, since the catalysts stays in the solvent, some specific treatment steps may be needed to avoid the dispersal of catalyst in the environment. An easy solution to this problematic is the use of heterogeneous catalysts.

1.5.2 Heterogeneous Catalysts

Heterogeneous catalysts are catalysts that are present in the system in another phase than the one where the reaction occurs. In the case of the fructose dehydration to HMF, the reaction occurs in the liquid phase and the heterogeneous catalysts are thus solids.

As presented in Table 2, many different types of catalysts for the fructose dehydration into HMF exist. They can be metal phosphates (lines **8-12, 35**), niobium based (lines **13-15**), metal oxides (lines **15-17**), zeolites (lines **18-19, 26, 36**) as well as ion exchange resins (noted IER, line **20, 24-25, 32**). All these different compounds contain acid sites that can be either from Brønsted or Lewis type. All the catalyst types presented have been found to be active in the different systems. For example, IER are used in aqueous (line **20**), organic (lines **24-25**)as well as biphasic systems (line **32**).

1.6 One-Pot Reactions

A possibility to increase the yield and reduce the amount of resources used for the production of HMF is to couple several steps into one such as the direct production of HMF from glucose in one-pot.

This way, the separation steps needed to recover fructose as intermediate are removed thus reducing the need for extracting solvent and energy. Moreover, since the products of the first reaction are directly used as the reactants for the second one, the equilibrium of the first reaction is shifted toward the products leading to a higher yield.

To perform both reactions at the same time, either two catalysts or one bifunctional catalyst with the two needed active sites that are active in the same reaction conditions have to be used. Most of the time, an heterogeneous catalyst is used for the isomerization and is either transformed into a bifunctional catalyst or working with an inorganic acid able to perform the dehydration reaction [112]. The two reactions occurring at the same time, it diversifies the compounds presents in the reaction medium. If the specificity of the catalyst is not good enough, this would lead to the formation of by-products.

Enzymes can be used to avoid this specificity issue. But since enzymes are not easily recovered, they need to be fixed on a support. The latter can be a simple carrier. Interestingly, the enzyme support can also have an intrinsic catalytic activity. Using a zeolite has the support for the enzyme could fulfil these two functions [113]. The use of bifunctional catalyst brings some difficulties. The first difficulty is that both catalysts have to be active in the same conditions (solvent system, temperature, …). Then, the preparation of the bifunctional catalyst has to use methods that do not negatively impact the activity of any catalysts.

2. Objectives

This work is a part of the PhD thesis of Marty Kinnaer. The general objective of his PhD is to investigate the potential bifunctional chemo-enzymatic catalysts for the transformation of glucose into HMF in a one-pot reaction.

This work focuses on the investigation of acidic heterogeneous catalysts that could be used for the second step of the reaction: the dehydration of fructose into HMF. The main objective of this work is to find the catalysts with the highest performances for this specific reaction. Moreover, this work will also investigate the possibilities to use the catalysts at lower temperatures trying to match the operating temperature of the enzyme.

3. Strategy

Seeing the side reactions issues in aqueous system, the extraction problems in organic solvents such as DMSO and the potential toxicity of Ionic Liquids in the environment, this project will focus on the screening of catalysts in biphasic conditions.

3.1 Mild conditions

The final objective of the PhD thesis being the preparation of a bifunctional chemo-enzymatic catalyst, the presence of water was considered as mandatory to ensure the stability of the enzyme. Moreover, the presence of high salt concentration was considered as a potential risk for the enzyme (that could precipitate). Finally, the temperatures investigated have been chosen to be relatively low (between 80°C and 130°C). Even if these temperatures are most likely to be too high for the enzyme, this allows to first observe the activity of the catalyst to determine the most promising ones before attempting to reduce the temperature and match the enzyme stability.

3.2 Solvent system of interest

The organic solvent chosen for this screening is MIBK. It has been identified has one of the best solvents for HMF production [96]. Moreover, it allows to work in biphasic conditions without requiring to use high salt concentrations. Also, MIBK allows an extraction of the HMF thus reducing the side reactions, reducing the quantity of adsorbed HMF potentially blocking the active sites of the catalyst [89] as well as allowing an easier extraction compared to the DMSO [91].

3.3 Catalysts of interest

The acidity of the catalyst has been identified has an important factor for the fructose dehydration into HMF. The catalysts chosen for this screening thus have acidic sites and can sometimes be modified to tune the number of acid sites as well as their acidic strength.

3.3.1 Zeolites

Zeolites are aluminosilicates based on a silica structure SiO_4 where a portion of silicon atoms have been replaced by aluminium atoms leading to a material with a given Si/Al ratio. This ratio has an important impact on the surface properties of the zeolites because since silicon has 4 valence electrons and aluminium only 3, the aluminium atoms will be charged negatively. Zeolites thus have naturally a negative surface that will be compensated by cations. These cations can undergo ionic exchanges to obtain a surface with chosen cations. Due to this ion exchange property, zeolites are called natural ion exchangers.

Several factors are important. First, the cations present at the surface have an impact on the catalytic activity. The presence of protons on the surface as cations leads to Brønsted acid sites and thus to potential catalytic sites for the fructose dehydration into HMF. Moreover, the Si/Al ratio determines the quantity of negative charges at the surface and thus the amount of cations that will be present to compensate. The lower the Si/Al ratio, the higher the amount of cations. This Si/Al ratio also has an impact on the hydrophilicity of the zeolite. Indeed, a low Si/Al ratio leads to a higher number of charges at the surface and thus to a more polar environment which is more hydrophilic.

Also, zeolites are tuneable catalysts that can act as a support for interesting groups that can bring interesting properties such as acidity.

3.3.2 Ion Exchange Resins

Ion Exchange Resins or IER are constituted of a polymer of styrene with side-chains containing ion-active groups [114]. The interesting ion-active groups in the case of this study are Brønsted acids. The different IER presented in the Table 2 are containing sulfonic acid groups (lines **20, 24-25, 32**) which are very acidic sites with a pKa below 0 [115].

EXPERIMENTALS

4. Materials and Methods

4.1 Catalysts Preparation

4.1.1 H-β zeolite Si/Al = 12

H-β (12) zeolite was prepared via the ionic exchange (Section 4.1.10) of a commercial β zeolite from Zeolyst (CP814E). The obtained zeolite was then calcined (Section 4.1.11) to obtain the H-form.

4.1.2 H-β nanocrystalline zeolite Si/Al = 12

First, 2.0425g of aluminium isopropoxide (98%, Acros Organics) was added to 29mL of tetraethylammonium hydroxide (20% aqueous solution, Sigma-Aldrich). The solution was stirred for 1 hour at room temperature to ensure the good dissolution of the aluminium isopropoxide. Then, 6mL of deionised water and 18.78g of colloidal silica (Ludox AS-40, Sigma-Aldrich) were added to the solution. The mixture was stirred for 2 hours at room temperature before being placed in a Teflon autoclave at 160°C for 160 hours. Finally, the obtained solid was washed using deionised water and centrifugated at 14000 rpm for 45 minutes. Five washes using deionised water followed by centrifugation were performed before drying at 120°C overnight and calcinating the solid using the protocol presented in Section 4.1.11.

4.1.3 MCM-22 zeolite

This zeolite was prepared in our lab before the start of this work following the protocol from Wang et al. (2020) [116].

4.1.4 H-ZSM-5 zeolite Si/Al = 12

This zeolite was prepared in our lab before the start of this work following a protocol adapted from the one proposed by Shang et al. (2019) [117]. Typically, 0.255g of sodium aluminate (technical anhydrous, Sigma-Aldrich) was added to a solution made of 4.1496g of deionised water and 4.2916g of tetrapropylammonium hydroxide (40% solution in water, Sigma-Aldrich). The mixture was then stirred 30 minutes at room temperature. Then, 6.7531g of tetraethyl orthosilicate (≥99.0%, Sigma-Aldrich) was added dropwise into the solution. After stirring 30 minutes at room temperature, the mixture was heated to 80°C during 1 hour under constant stirring. The mixture was finally stirred 20 more hours at room temperature before being transferred in a Teflon autoclave an treated 48 hours at 180°C. The solid was collected by 20 minutes of centrifugation at 10000rpm and then washed several times using deionised water to obtain a neutral pH. After being dried at 120°C overnight, the obtained

product was treated by ion exchange and then calcined to obtain the H-form zeolite (using the protocols from Sections 4.1.10 and 4.1.11).

4.1.5 H-ZSM-5 zeolite Si/Al = 30

This catalyst was prepared using the same protocol as for the H-ZSM-5 zeolite with a Si/Al ratio of 12 (Section 4.1.4) but with adapted reactant quantities. The adapted quantities for 0.255g of sodium aluminate are 10.3744g of deionised water, 10.7289g of tetrapropylammonium hydroxide and 16.8826g of tetraethyl orthosilicate.

4.1.6 H-ZSM-5 zeolite doped with Nb_2O_5 (5% wt.)

This modified zeolite was prepared in our lab before the start of this work following a protocol adapted from the one proposed by Barros et al. (2008) [118]. Ammonium niobium (V) oxalate (99.99%, Sigma-Aldrich) in aqueous solution was mixed with the ZSM-5 parent zeolite using 120mg of the ammonium niobium (V) oxalate precursor per 1g of zeolite. The system was then stirred at 80°C until all water had evaporated. Then, the recovered solid was dried at 100°C to remove the remaining solvent from the pores. Finally, the solid was calcinated in a muffle furnace using ambient air at 450°C for 8hours using a temperature ramp of $10K.min^{-1}$.

4.1.7 H-ZSM-5 zeolite treated with phosphoric acid (10% wt.)

This protocol is adapted from the one proposed by Pande et al. (2018) using a H-ZSM-5 (12) zeolite (Section 4.1.4) in place of an H-USY zeolite [119]. Typically, 1g of zeolite was added to an aqueous solution of 10% weight phosphoric acid (>85%, Merck). The mixture was then aged 2 hours at 100°C under constant stirring before being stirred at room temperature for 1 hour. The product was recovered through centrifugation at 14000rpm for 15 minutes and then washed three times with deionised water and recovered by centrifugation. The obtained product was then dried at 120°C overnight and then calcined using the protocol presented above.

4.1.8 Phenyl Sulfonic Acid modified silica

This protocol is adapted from Cano-Serrano et al. (2003) [120] for the impregnation step and from Wang et al. (2008) for the sulfuric acid treatment step [121]. First, 1g of silica (Aerosil® 380) was impregnated with pure trimethoxyphenylsilane solution (97%, Sigma-Aldrich) until incipient wetness (around 3.2mL). The mixture was then kept 24 hours at room temperature. Then, 12.43g of concentrated sulfuric acid (96%, Carl-Roth) was added and the mixture was stirred at 80°C for 24 hours. Finally, 80mL of deionised water were added to the mixture before filtration of the solution using a Durapore PVDF Membrane Filter (0.22µm

pore size, Sigma-Aldrich). The product was washed three times with 40mL of deionised water and the dried at 60°C during 24 hours.

4.1.9 Silica treated with sulfuric acid

This silica has been prepared following the same protocol as the one presented at Section 4.1.8 except that the trimethoxyphenylsilane precursor solution was replaced with deionised water.

4.1.10 Na^+ for NH_4^+ Ionic Exchange

Zeolites were treated 3 times with 10mL of an ammonium nitrate 1mol.L^{-1} aqueous solution for 1g of zeolite. The solution was stirred 3 hours at 80°C before being centrifugated at 14000rpm for 10 minutes.

4.1.11 Calcination

The NH_4-zeolites were calcinated under static air in a muffle furnace to obtain the corresponding H-form zeolite by the volatilisation of ammoniac molecules. These calcinations were performed under static air at 550°C for 6 hours using a temperature ramp of 3 hours (increase of 3 K.min^{-1}).

4.2 Catalytic performances evaluation

4.2.1 Standard tests in autoclave

The catalytic activity was tested in Teflon or glass flasks placed in a sealed autoclave with temperature and agitation control. Classical reactions were conducted with a headspace of 30% of the total volume of the reactor. The liquid phases were constituted of 50mL MIBK (≥98.5%, Sigma-Aldrich) and 20mL deionised water (volume ratio of 5:2 MIBK:H_2O). 0.2000g of fructose (≥99%, Sigma-Aldrich) was added in the reactor to obtain a starting concentration of 10g.L^{-1} in the aqueous phase and the catalyst was weighed to obtain a loading of 1:1 g_{cat}:$g_{fructose}$. Finally, 200µL of n-Dodecane (liquid, 99%, Sigma-Aldrich) were added as internal standard.

One sample from each phase was taken before the start of the reaction, filtered using a syringe filter (PTFE, 0.2µm pore size, VWR) and stored in a vial before being analysed in HPLC for the aqueous phase or GC for the organic phase. The volumes taken were 1mL of the aqueous phase and 2.5mL of the organic phase to keep the volume ratio constant. For the tests of the IER, the quantity of catalysts added at the start was reduced to match the absence of the IER in the sample taken before the reaction and thus keep the catalyst loading constant (IER being small beads they are not taken by the syringe used). For all the other tests, the sampling was performed just after the stop of the agitation and the concentration of the

catalyst in the two phases was thus considered homogeneous (the concentration of catalyst before and after the sampling is thus assumed to be constant in these cases).

The reactions were conducted for 6 hours using a constant temperature between 80°C and 130°. At the end of the reaction, the reactor was quenched in tap water for 15 minutes before the sampling of one sample from each phase. As for the sampling at the start of the reaction, the samples were filtered and stored before analysis.

4.2.2 Standard tests in glass bottle

These tests followed the same protocol as the one explained above for the tests using autoclaves except that the glass bottle was placed in an oil bath with agitation and temperature control to be heated.

The second difference is that samples before the reaction were taken after the temperature had already reached 80°C. After the sampling, the system was heated to the desired temperature.

4.2.3 One-Pot reactions at fixed temperature

Two solutions were prepared before starting the experiment. A Tris buffer solution was prepared by adding a Tris Buffered Saline tablet (Sigma-Aldrich) in 500mL of deionised water. To obtain a concentration of 0.01 $mol.L^{-1}$ of Mg^{2+}, 0.4761g of magnesium chloride (≥98.5%, Carl-Roth) was added to the Tris buffer solution. The resulting solution will be called Tris-Mg solution hereafter. The second solution was prepared by adding 0.1190g of cobalt (II) chloride hexahydrate (≥99%, Carl-Roth) in 10mL of deionised water to obtain a 0.05 $mol.L^{-1}$ Co^{2+} solution.

The catalytic tests were conducted as such: 12mL of Tris-Mg solution was added in a 100 mL glass bottle (Laboratory bottles, narrow neck, with screw cap, VWR). From this solution, 240µL were removed twice. The first 240µL removed were replaced with 240µL of the cobalt solution. Then, 0.1200g of glucose (99.5%, Sigma-Aldrich) and 0.0600g of sorbitol as internal standard (99%, Sigma-Aldrich) were added to obtain aqueous concentrations of $10g.L^{-1}$ and $5g.L^{-1}$ respectively. Also, 0.1120g of the IER catalyst were added to obtain a loading of $1g_{cat}$:$1g_{glucose}$ after the sampling. To obtain an organic to aqueous ratio of 5 to 2, 30mL of MIBK are added in the bottle and finally, 120µL of n-dodecane are added as internal standard. The system was then heated to 80°C in an oil bath before the addition of 240µL of a 100mU of Glucose Isomerase (replacing the second 240µL removed earlier).

After stirring, a 2mL sample from the organic phase and a 0.8mL sample from the aqueous phase were taken. The aqueous sample was added to 0.8mL of 0.01$mol.L^{-1}$

hydrochloric acid (prepared from hydrochloric acid 37%, VWR) to stop the enzyme activity. Both samples were then filtered and stored in vials before analysis.

The system was then heated to the chosen temperature (80 or 90°C) to start the reaction. Samples were taken after 1, 2, 4 and 8 hours following the procedure explained just above.

Table 5 – Concentrations in the aqueous phase before and after the initial sampling

	Before the sampling	**After the sampling**
Glucose	10 $g.L^{-1}$	10 $g.L^{-1}$
Sorbitol	5 $g.L^{-1}$	5 $g.L^{-1}$
Tris-HCl	0.5 $mol.L^{-1}$	0.5 $mol.L^{-1}$
NaCl	0.15 $mol.L^{-1}$	0.15 $mol.L^{-1}$
Mg^{2+}	0.01 $mol.L^{-1}$	0.01 $mol.L^{-1}$
Co^{2+}	0.001 $mol.L^{-1}$	0.001 $mol.L^{-1}$
Glucose Isomerase	2 mU	2 mU
Amberlyst-15	9.333 $g.L^{-1}$	10 $g.L^{-1}$

Table 5 presents the different concentrations in the aqueous phase before and after the initial sampling. As it can be seen, the quantity of Amberlyst-15 before the sampling is lower than the quantity of glucose but after the intake of 0.8mL of the aqueous phase, the concentration of Amberlyst-15 is equal to the one of glucose thus leading to a 100% weight Amberlyst-15 loading. This loading will however not be maintained after the following samplings at 1, 2 and 4 hours. After 8 hours, the system was quenched 15 minutes in tap water before taking the last sample.

4.2.4 One-Pot reactions with temperature step

This reaction was performed exactly as those conducted at constant temperature (Section 4.2.3) starting with a temperature of 80°C. After the start of the reaction, samples were taken after 1 and 4 hours before stopping the reaction timer and rising the system temperature to 120°C. After reaching that temperature, new samples were taken and the reaction was continued for 4 more hours. After 8 hours of reaction (4 at 80°C and 4 at 120°C), similarly to the reactions at a constant temperature, the system was quenched before the last sampling.

4.2.5 Gas Chromatography (GC)

GC analysis of the organic samples was carried out on a Bruker SCION 456-GC. The system was equipped with a Agilent DB-5 column (30m x 0.32mm x 1µm), a split/splitless injector (split ratio of 1 to 20) set a temperature of 250°C and an automatic sampler injecting 10µL. The detector used was a FID detector at a temperature of 250°C using 300mL.min^{-1} of air, 30 mL.min^{-1} of hydrogen and 25 mL.min^{-1} of helium as make-up gas. The system was kept at a constant pressure of 10psi. The oven followed a temperature program starting at 100°C and rising to 220°C in 6 minutes (ramp of 20K.min^{-1}). The temperature of 220°C was then kept constant for 3 minutes (Figure 9).

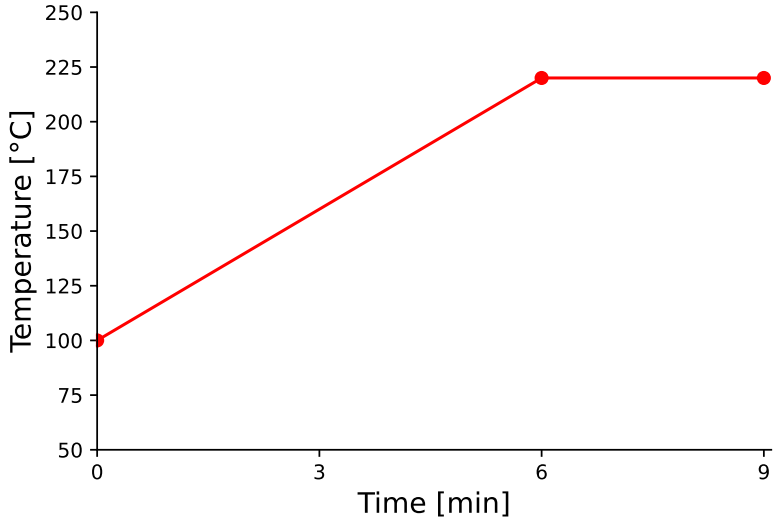

Figure 9 – Temperature profile of the GC oven during an analysis

GC calibration

To quantify the concentration of HMF in the organic phase, a calibration curve has been produced. First, 100µL of n-dodecane were added to 25mL of MIBK to produce a stock solution of organic solvent (n-dodecane concentration of 3g.L^{-1}). Then, 0.0500g of HMF were weighed and 5mL of the organic solution were added to obtain a HMF stock solution of 10g/L. 2mL of this solution were then diluted with 2mL of the MIBK/n-dodecane stock solution to obtain a 5g/L HMF solution. This dilution step was performed four more times to obtain solution of 2.5, 1.25, 0.625 and 0.3125g/L. Finally, 1mL of the last solution (0.3125g/L) was added to 3mL of the MIBK/n-dodecane stock solution to obtain an MIBK solution of 0.078125g/L concentration.

These solutions were produced thrice for three different starting HMF stock solutions and three different MIBK/n-dodecane solutions.

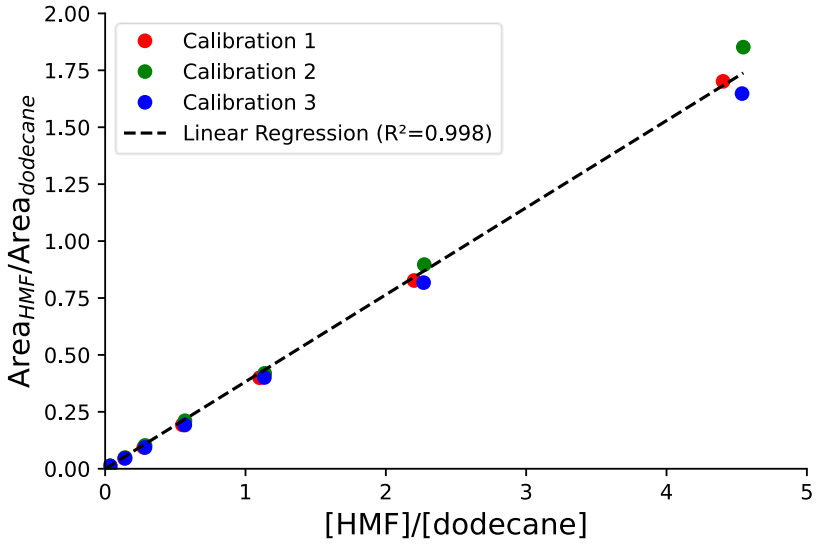

Figure 10 – Calibration of the GC: variation of the area ratio compared to the concentration ratio

Since the ratio of the areas is a linear function of the ratio of the concentrations :

$$\frac{[HMF]}{[dodecane]} = \frac{CR_{HMF}}{CR_{dodecane}} * \frac{Area_{HMF}}{Area_{dodecane}}$$

With the HMF and n-dodecane concentrations being expressed in g.L^{-1} and $\frac{CR_{HMF}}{CR_{dodecane}}$ being the ratio of the response coefficient. Figure 10 allows to determine the ratio of the response coefficient $\frac{CR_{HMF}}{CR_{dodecane}}$ using a linear regression that gives a value of 0.3823. The R^2 value obtained for this linear regression being above 0.99, the confidence about this value is high.

Quantification of HMF concentration in the organic phase

Since the areas of HMF and n-dodecane are measured and the concentration of n-dodecane is known, the HMF concentration in the organic phase in g.L^{-1} can be calculated and is equal to :

$$[HMF] = 0.3823 * \frac{Area_{HMF}}{Area_{dodecane}} * [dodecane]$$

4.2.6 High Performance Liquid Chromatography (HPLC)

HPLC analysis of the aqueous samples was carried out on a Waters 1525 Binary HPLC Pump equipped with a Aminex® HPX-87C (300mm x 7.8mm, Bio-Rad) and an automatic sampler injecting 25µL precisely. The detector used was a Waters 2414 Refractive Index Detector. The analysis were conducted with a column temperature of 85°C, a detector temperature of 30°C using milli-Q water as mobile phase with a flow of 0.5 $mL.min^{-1}$. The results were analysed using the Breeze 2 software to obtain the retention times and peak areas.

HPLC calibration

The calibration of the HPLC has been carried out to enable the quantification of both fructose and glucose concentrations in the aqueous phase. For both glucose and fructose, a first 10$g.L^{-1}$ solution was prepared by adding 100mg of glucose or fructose into 10mL of deionised water. A 5$g.L^{-1}$ was obtained via a dilution of the initial 10$g.L^{-1}$ solution. Then, a 2$g.L^{-1}$ solution was prepared by adding 200mg of glucose or fructose into 100mL of deionised water. Two successive dilutions of the 2$g.L^{-1}$ solution allowed to obtain solution of 1$g.L^{-1}$ and 0.5$g.L^{-1}$ respectively. Finally, a 0.1$g.L^{-1}$ solution was obtained through the addition of 1 volume of the 0.5$g.L^{-1}$ solution into 4 volumes of deionised water.

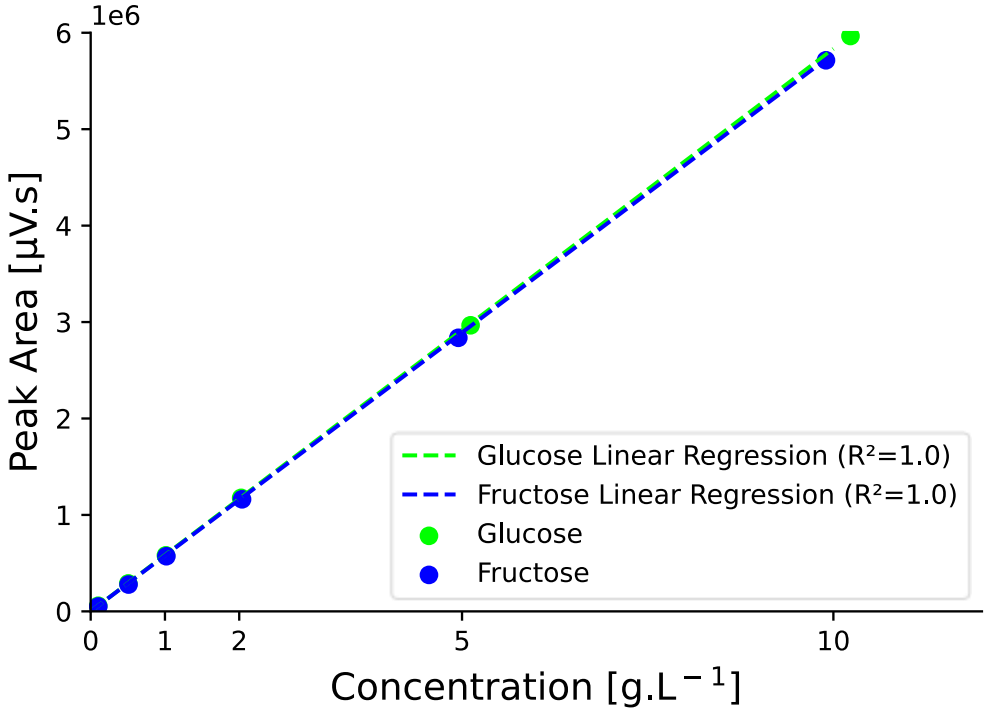

Figure 11 – Calibration of the HPLC: variation of the area compared to the concentration for both glucose and fructose

As for the GC calibration, the area measured follows linearly the increase in the concentration (Figure 11):

$$Area_x = CR_x * [x]$$

With *x* being either glucose or fructose. Using a linear regression, the response coefficients can be determined: $CR_{glucose}$ = 583352 and $CR_{fructose}$ = 578301. Once again, both R^2 values are equal to 1 meaning that the linear regression is accurate.

Quantification of sugars in the aqueous phase

After the measurement of the glucose and fructose areas using the HPLC, their concentration can be determined using the equation presented above and their respective response coefficient.

4.2.7 Determination of the partition coefficients

To obtain the total quantity of a molecule present in a biphasic system, the concentration of the molecule in both phases has to be determined. This can be done through the analysis of the two phases or by the analysis of one phases and the use of the partition coefficient. The partition coefficient is the ratio of the concentration of a molecule in the organic phase to the concentration of the same molecule in the aqueous phase.

Since HMF coeludes with MIBK in HPLC, the determination of the HMF area in HPLC was impossible and the determination of the HMF concentration in the aqueous phase has been done using its partition coeffiecient.

Partition coefficient of HMF

To determine the partition coefficient of HMF between MIBK and water, three solutions containing 5mL MIBK, 2mL deionised water, 20µL of n-dodecane and different HMF masses (50mg, 20mg and 5mg) have been prepared. After mixing, a sample of the organic phase was taken to be analysed. The concentration of HMF in the organic phase was then determined using the calibration presented before (Section 4.2.5). Since the total amount of HMF was known and the HMF present in the organic phase was measured, the quantity of HMF remaining in the aqueous phase could be determined as well as its concentration.

For each solution, the partition coefficient has been calculated and the average values of 0.89 has been used.

Partition coefficient of fructose

The partition coefficient of fructose has been determined by adding 0.1400g of fructose in a mixture containing 5mL MIBK and 2mL deionised water. After stirring, a sample of the aqueous phase was analysed by HPLC and the fructose concentration was determined using the calibration presented in Section 4.2.6. The fructose quantity observed in the aqueous phase being bigger than 98% of the total quantity, the fructose concentration in the organic phase was considered negligible and all the fructose was thus considered as being in the aqueous phase.

4.2.8 Determination of the measurements variability

GC Variability

The variability of the GC analyses has been performed by three successive measurements of the same sample. The variation of the ratio between the HMF area and the IST area has been calculated and was below 1% (around 0.6%).

HPLC Variability

The variability of the HPLC analyses has been investigated by analysing multiple times a reference solution containing 10g.L^{-1} of glucose and 10g.L^{-1} of fructose. The variation coefficient calculated was a slightly above 1% in each case (1.4% for the glucose and 1.1% for the fructose).

4.2.9 Calculation of the catalytic performances

HMF yield

The HMF yield after *t* hours of reaction was calculated using the following equation :

$$Y_{HMF} = 100 * \frac{n_{HMF,\ t} - n_{HMF}}{n_{fructose,\ 0}}$$

With Y_{HMF} the HMF yield being calculated in %, $n_{HMF,\ 0}$ and $n_{HMF,\ t}$ being the HMF molar quantities in the whole system at the start and after t hours of reaction and $n_{fructose,\ 0}$ being molar quantity of fructose at the start of the reaction. The HMF quantities were obtained using the GC measurements while the fructose quantity was known through HPLC measurements.

Fructose yield

The fructose yield after *t* hours of reaction was calculated using a formula similar to the one used for the HMF yield but by replacing the HMF quantities by the fructose concentrations in g.L^{-1} obtained through the HPLC measurements.

Fructose conversion

The fructose conversion after a t hours of reaction was calculated using the following equation:

$$C_{fructose} = 100 * \frac{[fructose]^0 - [fructose]^t}{[fructose]^0}$$

With $C_{fructose}$ being calculated in % and $[fructose]^0$ and $[fructose]^t$ being the fructose concentrations in g.L^{-1} at the start of the reaction and after t hours of reaction respectively. These fructose concentrations were determined through HPLC analysis.

Glucose conversion

The glucose conversion was calculated using a formula comparable to the one used for the fructose conversion but with the replacement of the fructose concentrations by the glucose concentrations also determined using HPLC analysis.

Selectivity

The selectivity towards a product P was calculated using the general formula for the transformation of a reactant R into a product P :

$$S_P = 100 * \frac{Y_P}{C_R}$$

With S_P the selectivity in %, Y_P the product P yield in % and C_R the reactant R conversion also expressed in %.

4.3 Characterization techniques

4.3.1 X-Ray Diffraction

The crystallinity of the prepared catalysts was verified using X-Ray Diffraction (XRD). XRD allows the identification of crystalline phases based on the diffusion of photons through crystalline phases. The diffractometer used was a Druker-D8 Advance with a Bragg-Brentano geometry. A copper anode under 40 kV and 30mA was producing the X-ray radiation with a Kα of 0.154nm. The Bruker detector was using a LynxEye XE-T technology and was recording values obtained with a 2θ value between 5° and 80° with 2θ increments of 0.015° and an increase rate of 5.93°/min. The diffractograms obtained were analysed with the Highscore software and using the ICDD-PDF2-2004 database. In practice, sample powder was dispersed on a sample holder coated with Nivea cream.

4.3.2 NH_3 Temperature Programmed Desorption

The NH_3 Temperature Programmed Desorption (NH_3-TPD) is used to characterize the acidity of a sample by adsorbing ammoniac molecules onto the acid sites. Measuring the temperature at which the NH_3 molecules are desorbed gives information about the strength and number of acid sites. NH_3-TPD analyses were performed using a Hidden CATLAB-PCS microreactor coupled with a mass spectrometer equipped with a quadrupole separator.

Practically, between 50 and 100mg of the samples were placed in the microreactor. The NH_3-TPD was composed of several steps (Figure 12). First, the sample was degassed by increasing its temperature from 50°C to 500°C at a rate of 10K.min^{-1} under a flow of 60mL.min^{-1} of Argon. The temperature was kept for 60 minutes before being reduced to 100°C always under a 60 mL.min^{-1} Argon flow. The second step was the adsorption of ammoniac. This step was conducted at a constant temperature of 100°C using a flow of 20mL.min^{-1} of Argon and 10mL.min^{-1} of Helium with 5% NH_3 during 60 minutes. The sample was then flushed at 100°C using 60mL.min^{-1} of Argon during 90 minutes. The last step was the NH_3 desorption: under a 30mL.min^{-1} Argon flow, the sample was heated at a rate of 10K.min^{-1} until 750°C. The sample was finally kept at 750°C for 30 minutes.

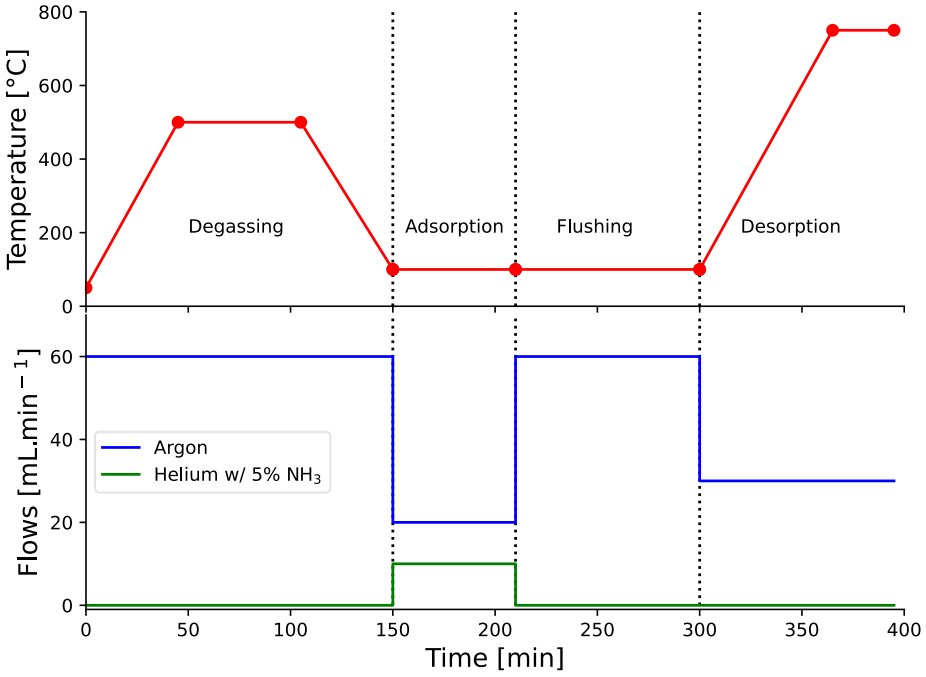

Figure 12 – Summary of the temperature program and flows program of the NH_3-TPD analysis

RESULTS AND DISCUSSION

5. Results and Discussion

5.1 Catalytic Tests

5.1.1 Screening of the previous catalysts

Before the start of this work, several catalysts for the fructose dehydration in aqueous conditions had already been tested in our lab. Due to the low HMF yield observed, it has been decided to change the conditions and to use a biphasic reactor with both water to solubilise the sugars and MIBK to extract HMF after its production. The first experiment carried out with these new conditions is the screening of the catalysts that were already prepared.

These catalysts are two different zeolites: H-ZSM-5 and MCM22 as well as a ZSM-5 zeolite impregnated with Niobium Oxide (Nb_2O_5). The reaction was conducted in the conditions previously used for the catalytic tests in a single phase aqueous reactor: a temperature of 100°C, a duration of 6 hours, 10g/L_{liquid} of fructose, 10% weight of catalyst loading and a headspace of 30% of the total reactor volume. The results obtained are shown on Figure 13:

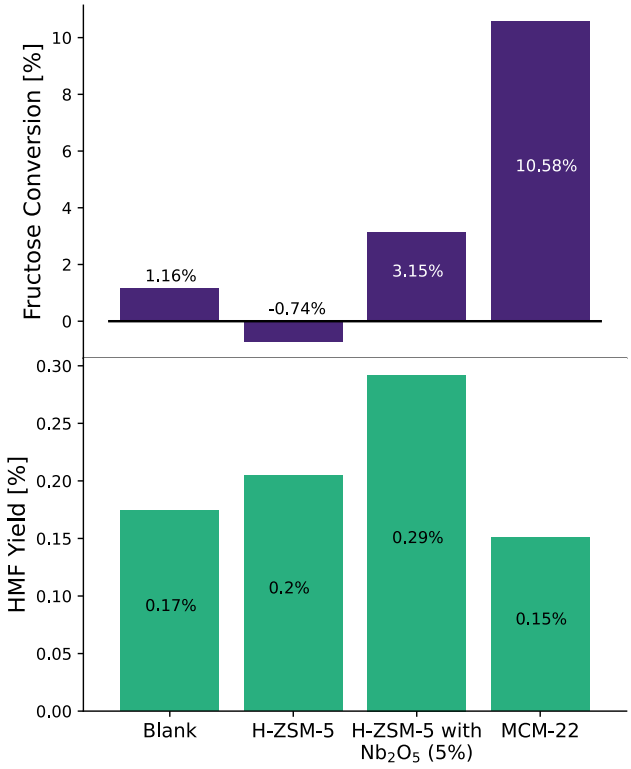

Figure 13 – Fructose conversion and HMF yield obtained with the first catalysts

As it can be seen on the Figure 13Figure 13, the conversion and selectivity of these catalysts are really low leading to tiny values of yield. Moreover, the observed negative conversion of the H-ZSM-5 is questioning. The possibility of an increase in the fructose

concentration during the reaction leading to a negative conversion is impossible because the reactor only contains water, MIBK, fructose and the H-ZSM-5 and none of these compounds can react to form fructose. The observed negative conversion is thus probably due to experimental error. It has to be noted that the positive yield observed for this same H-ZSM-5 zeolite is due to the use of another method to quantity the HMF concentration (based on the GC analysis). Since a positive yield is observed, fructose has to be converted.

The only yield difference that can be noticed is the higher HMF production of the ZSM-5 doped with Nb_2O_5 (0.29% against a maximum value of 0.20% for the others).

Seeing the results obtained by these 3 zeolites, it has been decided to not further analyse the performances of the MCM-22. Indeed, this zeolite seems to have the lowest selectivity (less than 2%). This means that even if it has a high activity to convert fructose, the products obtained are mostly not the one that is wanted. Even if the products have not been identified, the unwanted by-products are probably humins as well as levulinic and formic acids. The HMF produced thus represents only a very small fraction of them and the use of such zeolite for the catalytic dehydration of fructose to HMF is not useful since most of the reactant used will be converted into waste products. This low selectivity towards the compound of interest leads to a waste of reactant and is incompatible with Green Chemistry [92].

Also, it has been decided to work with the non-doped ZSM-5 for screening experiments. Indeed, due to the slight difference between the two yields obtained and since the preparation of the zeolite doped with Niobium Oxide (Nb_2O_5) is much more complicated than the preparation of the non-doped ZSM-5 zeolite, the use of the doped zeolite requires extra costs and results in no significant improvements.

After this first set of experiments, several mistakes and imprecisions have been detected and some corrections have thus been made for the next experiments:

First, the fructose concentration that was calculated in order to have a $10g/L_{liquid}$ concentration in the whole system has been reduced to obtain a fructose concentration of $10g/L_{water}$ (in the aqueous phase). Indeed, since fructose is not soluble in the MIBK phase, the theoretical concentration of $10g/L_{liquid}$ was divided in two different concentrations in the reactor: a concentration of $35g/L_{water}$ in the aqueous phase and a concentration of $0g/L_{MIBK}$ in the organic phase.

Also, to allow a better observation of the catalytic activity of the zeolite, it has been decided to increase the catalyst loading (in $g_{cat}/g_{fructose}$) from 10% to 100% in weight. This increase still stays in the range of loadings existing in the literature that usually vary between

10% [74], [122] to 100% [123] for the heterogeneous catalysts. Furthermore, since the catalyst is not consumed by reaction and is most of the time recyclable, the use of more catalyst is thus just representing higher economical cost and environmental impact only at the start of the production.

Impact of the first changes

Due to the changes in the fructose concentration as well as the catalyst loading, the yields obtained in the same conditions (temperature and duration of the reaction as well as the same solvent ratio) have also changed. As it can be seen on the Figure 14, the yields obtained are around 3 times higher with the new conditions. It can also be noticed that the ratio between the H-ZSM-5 HMF yield and the Blank HMF yield is nearly conserved in both conditions (1.176 for the 1st Experiment and 1.192 after the changes). This indicates that the modifications have not induced major changes in the system.

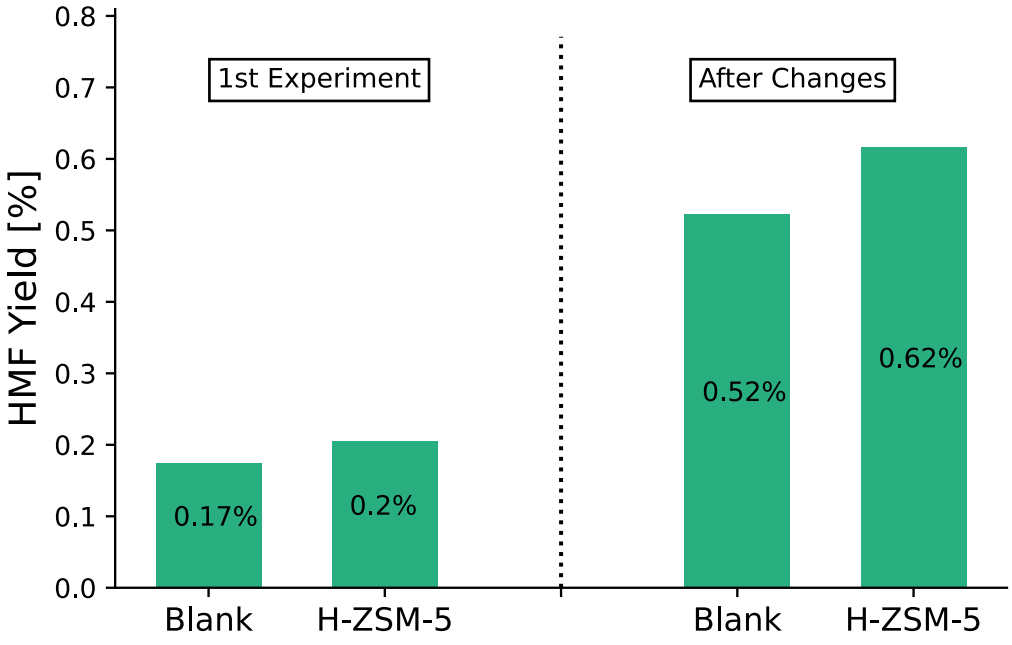

Figure 14 – Impact of the changes in the reaction setup on the yields obtained

5.1.2 Impact of the temperature on the zeolites

Since the yield observed after 6 hours of reaction were really low at a temperature of 100°C, it has been decided to increase the temperature to accelerate the reaction and thus observe higher yields.

Moreover, the impact of the temperature on the selectivity is also important because most of the time, when the temperature increases, side-reactions (catalysed or not) also occur thus leading to a lower selectivity.

H-ZSM-5 zeolite

To study the impact of the temperature on the dehydration reaction, the H-ZSM-5 zeolite previously tested at 100°C has also been used as the catalyst in biphasic systems at 110, 120 and 130°C. The results obtained are shown in the Figure 15.

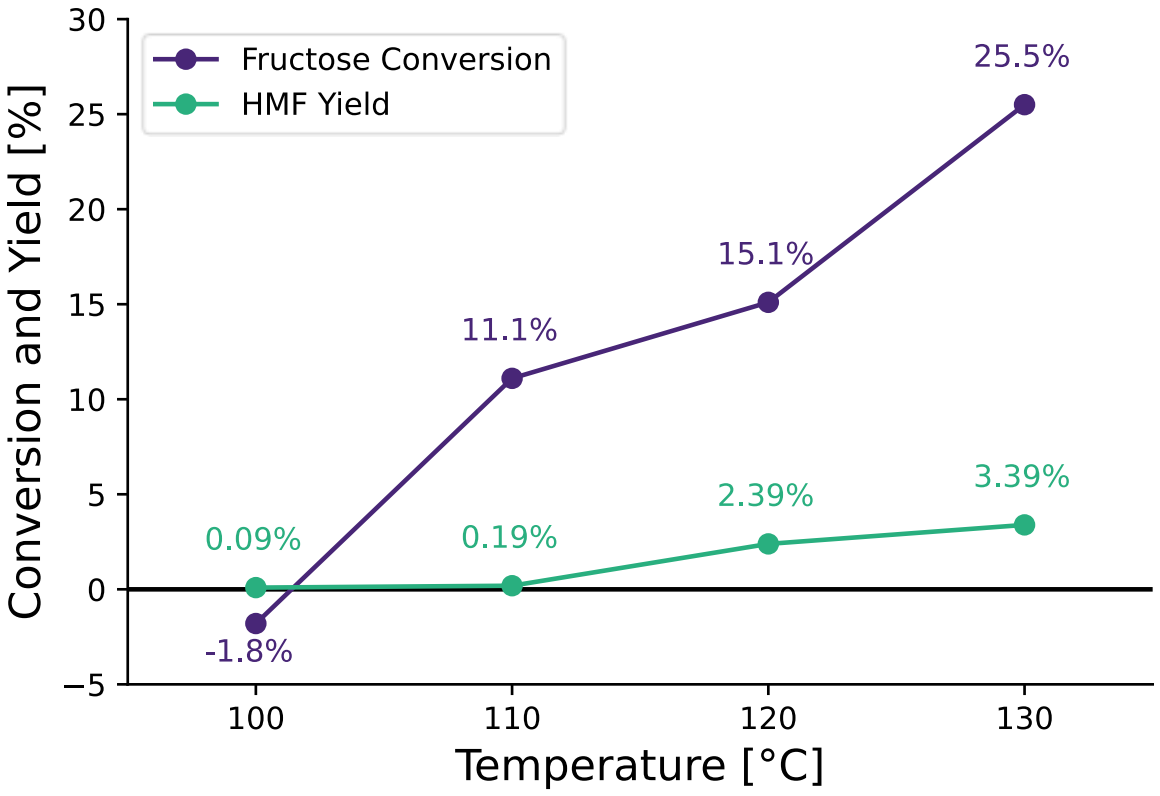

Figure 15 – Temperature impact on the fructose conversion and HMF yield of the H-ZSM-5 zeolite

As expected, the catalytic activity of the H-ZSM-5 zeolite increases with the temperature for both conversion and yield. However, it can be noticed that the increase does not follow an exponential growth. First, the negative conversion at 100°C is again just due to the variability and should be a positive value. Also, the HMF yield observed increases with the temperature between 100°C and 130°C as expected [124]. Even if the relation does not really corresponds to an exponential, the increasing trend is conserved.

The selectivities are presented in the Table 6, they have been calculated for each temperature except 100°C. Indeed, the conversion being negative, the selectivity would also be negative which makes no sense.

Table 6 – Selectivity of the H-ZSM-5 at different temperatures

	100°C	**110°C**	**120°C**	**130°C**
Selectivity [%]	/	2%	16%	13%

As it can be noticed, the selectivity does not seem to decrease with the temperature, the very low selectivity at 110°C is also questionable. This could be explained by the very low concentrations observed and the variability of the system.

In 2013, Lucas and collaborators observed a HMF yield of 28% after 1 hour at 165°C using a H-ZSM-5 zeolite (Si/Al = 23) [125]. Even if the results observed in this work are much lower, the temperature is probably the factor that has the most important impact. Since the only results existing for H-ZSM-5 are at higher temperature [45], [99], [125], the results presented in this work can also be compared to those presented by Lima et al. (2021) that showed a HMF yield of 2.4% and a selectivity of 17% in an aqueous system at 120°C after 2 hours using a commercial ZSM-5 zeolite with a Si to Al ratio of 12 [73]. Even if the results obtained in this work are a bit lower, they are in the same range. However, other results observed in aqueous conditions are higher than those presented before. Indeed, Rac et al. (2013) showed 8% yield after 6 hours at 130°C using a ZSM-5 with Si/Al = 25 [74]. This difference is surprising since the acidity of a zeolite with higher Si/Al ratio is presumed to be lower. The hydrophobicity of the surface is thus maybe the important factor since a higher hydrophobicity could lead to a better expulsion of water molecules from surface.

H-β *zeolite*

The impact of the temperature increase on the fructose dehydration has then been tested using another zeolite, the H-β as heterogeneous catalyst. This β type zeolite has been used by many researchers as a potential catalyst for this dehydration reaction [73], [74]. Alike the ZSM-5, the β zeolite has Brønsted acid sites due to the presence on its surface of protons.

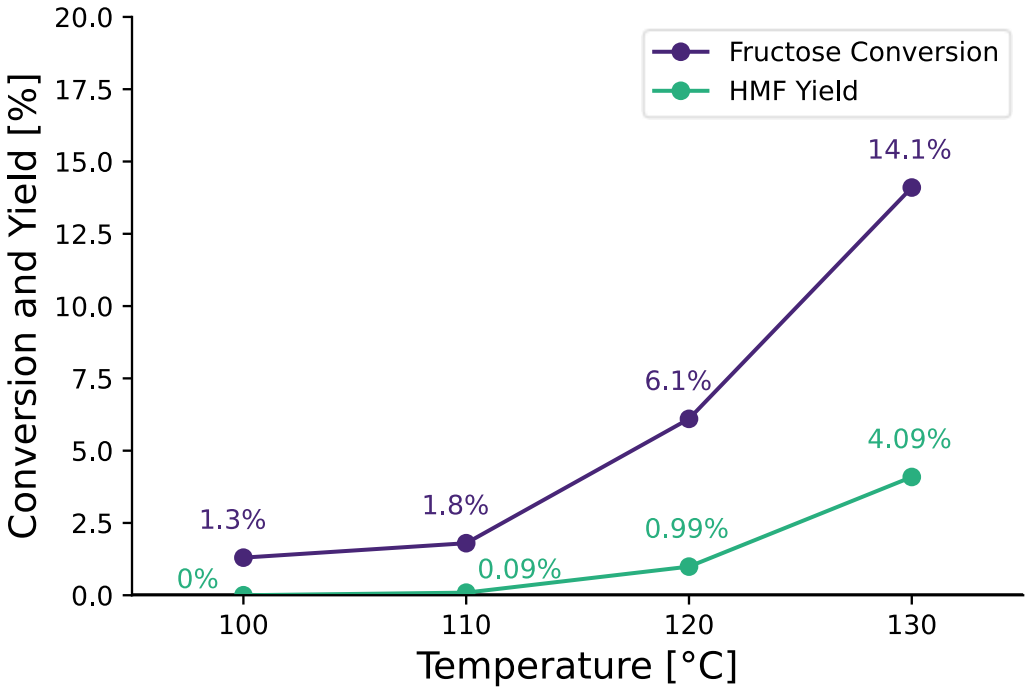

Figure 16 – Temperature Impact on the Conversion and Yield of the H-β zeolite

In Figure 16, it can clearly be seen that the temperature impacts both the conversion and the yield as an exponential relation. The selectivity of the reaction has also been calculated and is presented in the Table 7:

Table 7 – Selectivity of the H-β zeolite at different temperatures

	100°C	**110°C**	**120°C**	**130°C**
Selectivity [%]	0%	5%	16%	29%

The selectivity of the H-β clearly increases with the temperature between 100°C and 130°C. This could be due to a higher activation energy of the side reactions leading to a higher increase in the reaction rate of the fructose dehydration compared to the reaction rate of the other reactions involving fructose or HMF.

The results observed in this work could once again be compared to results obtained at higher temperatures [125] but since the temperature has a too high impact on the results, such comparison do not give more information and is not really useful.

ZSM-5 and β zeolites comparison

The comparison of the catalytic activities of the two tested zeolites is presented in Figure 17. It can be seen that even if the yield seems to be nearly equal at each tested temperature, the conversions appear to be very different. Except for the negative value obtained at 100°C, the H-ZSM-5 zeolite has a higher conversion than the H-β. The selectivity

of the H-β zeolite is around two times higher than the selectivity of the H-ZSM-5 meaning that H-ZSM-5 is more likely to produce other compounds than HMF such as degradation products (levulinic and formic acids) or condensation products (humins) [88].

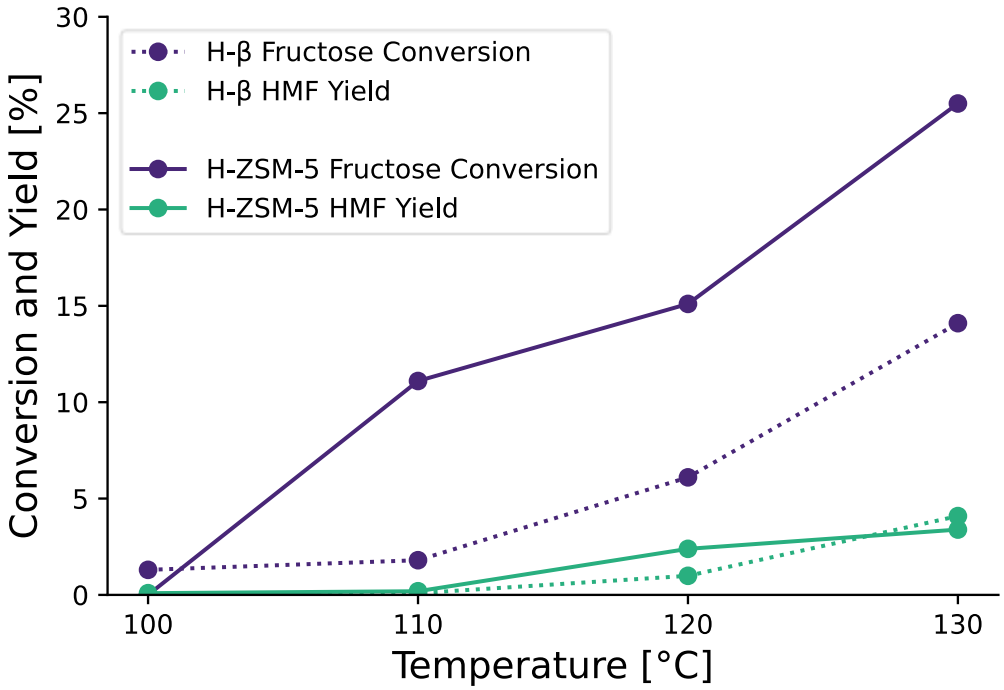

Figure 17 – Comparison of the catalytic activities of the H-ZSM-5 (solid line) and the H-β (dotted line)

The results obtained by these first experiments showed that the catalytic activity of the two zeolites were the highest at the highest temperature as it was expected. Moreover, the activities were quite similar in terms of yield at temperatures between 100 and 130°C but the conversion and selectivity were quite different in the tested range.

To fulfil the objective of working with an enzyme to first isomerize glucose to fructose, the activity of the catalyst has to be as high as possible at a temperature suitable for the enzyme. All the temperatures tested in this experiment are already too high to ensure the survival of the enzyme while not presenting high enough HMF productions. Trying to obtain higher catalytic activity, several zeolite modifications have been tested and will be presented in the next section.

At the end of this experiments, several changes have been made on the reaction setup. To avoid having a negative conversion, the addition of a sampling of both reaction phases at the start of the reaction has been added to the experimental protocol. This sampling before the start of the reaction allows to know exactly the quantity of the reactant added in the system and thus avoid potential errors that could have occurred before. Also, the temperature has been raised from 100°C to 120°C as it is the first temperature where the

reaction rate seems to increase by a significative extent. Even if this temperature is too high for the subsequent use of an enzyme, the first objective here is to obtain a catalyst for the fructose dehydration that can produce HMF selectively and in high quantities.

5.1.3 Tested zeolite modifications

H_3PO_4 treatment of a ZSM-5 zeolite

In 2018, Pande and collaborators reported HMF yields up to 65% from fructose at 120°C for 5 hours in a biphasic water/MIBK system. The catalyst was a commercial H-USY zeolite (Si/Al = 30) modified using either sulfuric acid (H_2SO_4) or phosphoric acid (H_3PO_4). The best result being obtained with the modification using a 10% weight solution of H_3PO_4.

In this work, the same treatment was applied but on a different zeolite. The chosen parent zeolite was a commercial ZSM-5 with a silicon over aluminium ratio of 12 and the obtained modified zeolite is called H-ZSM-5-10P hereafter.

The measured catalytic performances can be compared with the activities obtained with the parent H-ZSM-5 in the same conditions (Table 8) :

Table 8 – Comparison of the catalytic performances of the H-ZSM-5-10P and parent H-ZSM-5 after 6hours at 120°C

	Fructose Conversion	**Selectivity**	**HMF Yield**
H-ZSM-5-10P	1.4%	92%	1.3%
H-ZSM-5	11%	8%	0.9%

As it can be seen, the fructose conversion obtained with the modified zeolite is nearly 10 times lower than the one obtained with the unmodified zeolite. This very low conversion is questioning since the base structure of the catalyst is the same and could thus be due to very important changes in the zeolite structure (such as a loss of porosity) after the treatment with the phosphoric acid. Unlike the conversion, the yield obtained with the modified zeolite is slightly higher than the one of the parent. Pande and collaborators (2018) explain the better performance of the H_3PO_4 treated zeolite by the presence of Al-O-P bonds that present a high acidity which is useful for the fructose dehydration [119].

However, compared to the results obtained by Pande et al. (2018) that presented the phosphoric acid treated USY zeolite as a good catalyst for HMF production, the results obtained in this work are different. Indeed, in their work, Pande et al. showed that the conversion, the selectivity and the yield increased with the treatment (1.5 times higher for the conversion and two times higher for the yield) [119]. In our case, the yield increase slightly while the conversion dropped drastically (nearly 8 times lower) leading to a huge selectivity

increase. This could be due the HPLC measurements variation, the conversion value being not really higher than 1%, an error on the HPLC measurement lead to bigger changes.

Since the results obtained are very different from the one presented in the article and no other sources mention such kind of treatment and the benefits of the Al-O-P bondings, it has been decided to first try other modifications before coming back to this one if needed.

ZSM-5 zeolite with higher Si/Al ratio

MIBK being a solvent of relatively low polarity compared to the water, its accessibility to a very acidic and hydrophilic surface seems complicated. This difficulty to reach the surface could lead to a lower extraction ability of the HMF adsorbed on the surface thus leading to a potential poisoning of the catalyst by the HMF staying adsorbed on the active sites. The idea to use a zeolite with a higher Si/Al ratio to increase the hydrophobicity and thus allow the MIBK to reach the surface more easily and extract HMF has thus been tested.

To avoid reducing the number of acid sites too much, the new zeolite has been prepared with a Si/Al ratio of 30. As the zeolite chosen for this experiment was a ZSM-5 type framework, the newly prepared catalyst will be called H-ZSM-5 (30) in this work.

Also to verify if the solvent filling the pores of the catalyst at the start of the reaction was important or not, the reaction has been conducted with the H-ZSM-5 (30) by adding the catalyst either into the aqueous phase or added in the MIBK phase (before starting the reaction in the biphasic mixture, under intense stirring). The results are compared to the ones obtained with the previously used H-ZSM-5 with a Si/Al ratio equal to 12.

Table 9 – Comparison of the conversion, selectivity and yield of the H-ZSM-5 with different Si/Al ratios after 6 hours at 120°C

	Fructose Conversion	**Selectivity**	**HMF Yield**
H-ZSM-5 (30)[a]	4.9%	29%	1.4%
H-ZSM-5 (30)[b]	5.7%	21%	1.2%
H-ZSM-5 (12)[b]	11%	8%	0.9%

[a]: catalyst added in the organic phase (MIBK), [b]: catalyst added in the aqueous phase

In the results presented in the Table 9, several things can be observed. First, the medium in which the catalyst is added does not seem to have an important impact on the activity of the catalyst since both conversion and yield differences are within the range of error (around 1% for the conversion and around 0.5% for the yield, Section 4.2.8). This means that whatever the solvent filling the pores of the catalysts at the start of the experiment, the pores of the catalyst will rapidly be filled by the same solvent.

However, the comparison with the classical H-ZSM-5 (12) shows important variations: the conversion obtained with this zeolite is nearly two times higher while the yield is slightly lower than the one obtained in the two other experiments. The conversion difference can be explained by the lower amount of acidic sites in the H-ZSM-5 (30) zeolite due to the lower amount of aluminiums replacing silicons. The yield difference can be explained by the better extraction of HMF into the organic solvent due to the higher hydrophobicity of the surface. With this better extraction, the active sites will also be more frequently available to dehydrate a fructose molecule. This results shows that the variation of the Si/Al ratio (and thus the acidity and hydrophobicity variations) appears to be a relevant option to increase the catalytic performances of the zeolites.

Nanocrystalline β-zeolite

Another tested modification is the use of nano-β zeolites. These zeolites have crystals that are smaller than the ones of the commercial H-β. This implies that the active sites present in the crystals of the nano-catalyst can be reached through shorter diffusion times. If the diffusion of the molecules in the porosity of the zeolite is shorter, the molecules could be in contact with less active sites during their diffusion and thus undergo less unwanted reactions. This modification could thus lead to a increase in the selectivity.

To compare the nanocrystalline zeolite with the previously synthetised β zeolite, the preparation of the nano-β has been conducted to have a Si/Al ratio similar to the previously tested H-β zeolite: 12.

Table 10 – Comparison of the conversion, selectivity and yield obtained with the nano-β and H-β zeolites after 6 hours at 120°C

	Fructose Conversion	**Selectivity**	**HMF Yield**
nano-β (12)	5.3%	28%	1.5%
H-β (12)	9.4%	9%	0.9%

In Table 10, it can be seen that despite having the same framework and silicon to aluminium ratio, the two zeolites have different activities: the nanocrystalline zeolite has a conversion nearly two times lower than the H-β but its HMF yield is much higher. This higher selectivity could be explained by a shorter diffusion time of the molecules from the solution to the active sites in the nano-β compared to the H-β. The molecules diffusing in the nano-β are thus less in contact with potentially active sites and are thus less likely to be transformed in unwanted products resulting in a higher selectivity.

Summary of the different zeolite modifications

The results obtained by the different modifications presented in the previous sections are summarized in the Figure 18 below:

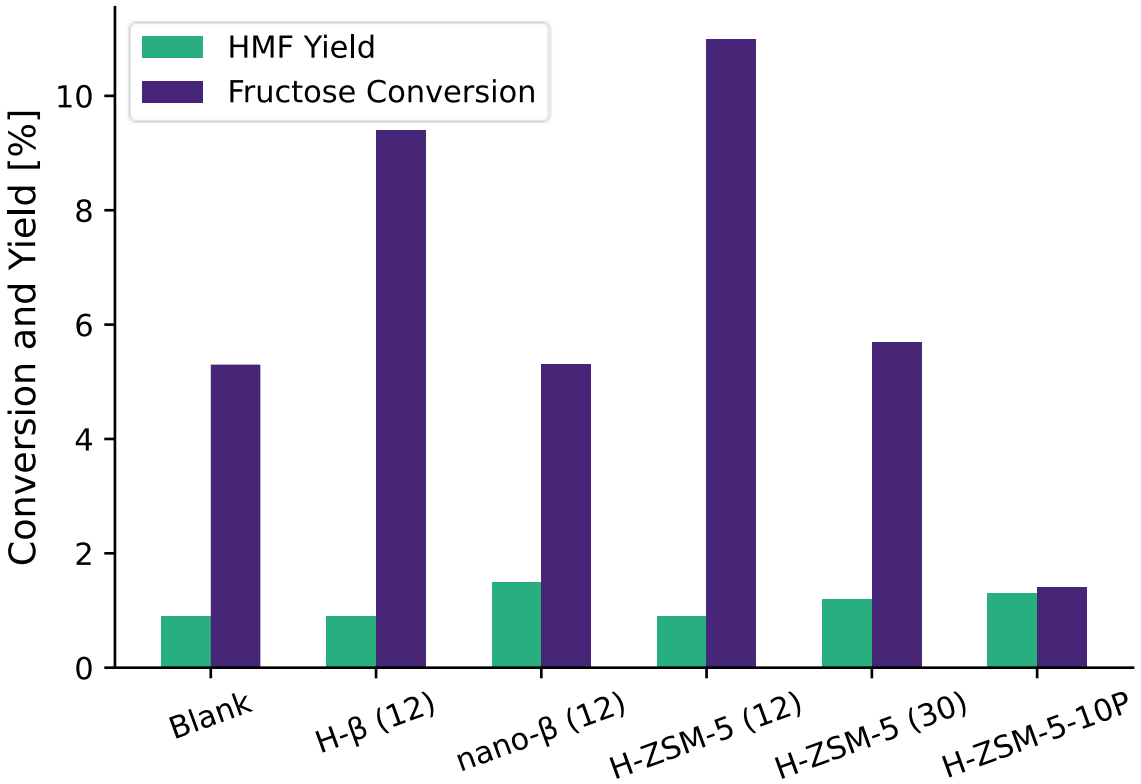

Figure 18 – Comparison of the catalytic performances obtained by the different catalysts

As it can be seen, most of the catalyst are not really better than the blank reaction in the same conditions. Moreover, none of the tested catalyst presents interesting results at the temperature of 120°C. since this temperature is already much higher than the temperature range at which the enzyme is stable. Seeing that none of the modification changed significative the activity that the “classic” catalyst had on the fructose dehydration, another solution has to be investigated.

The next section will discuss the use of the Ion Exchange Resins as catalysts for the fructose dehydration.

5.1.4 Ion Exchange Resins

As explained before, IER are constituted of a polymer of styrene with side-chains containing ion-active groups [114] that can be Brønsted acids (e.g. sulfonic acid). Several different IER have been used in the literature for the HMF production from fructose in a biphasic MIBK-water system. Amberlyst-15 [35], [112], DIAION RCP®160M [83], Nafion 117 [126] are some of them.

In this work, two resins have been tested: the Amberlite IRC120 and the Amberlyst-15 that are noted IRC120 and Amb15 respectively.

Comparison of the IERs

Both selected resins have been tested in the standard conditions to be compared by the catalysts presented in the previous section. The catalytic performances observed are shown in Figure 19:

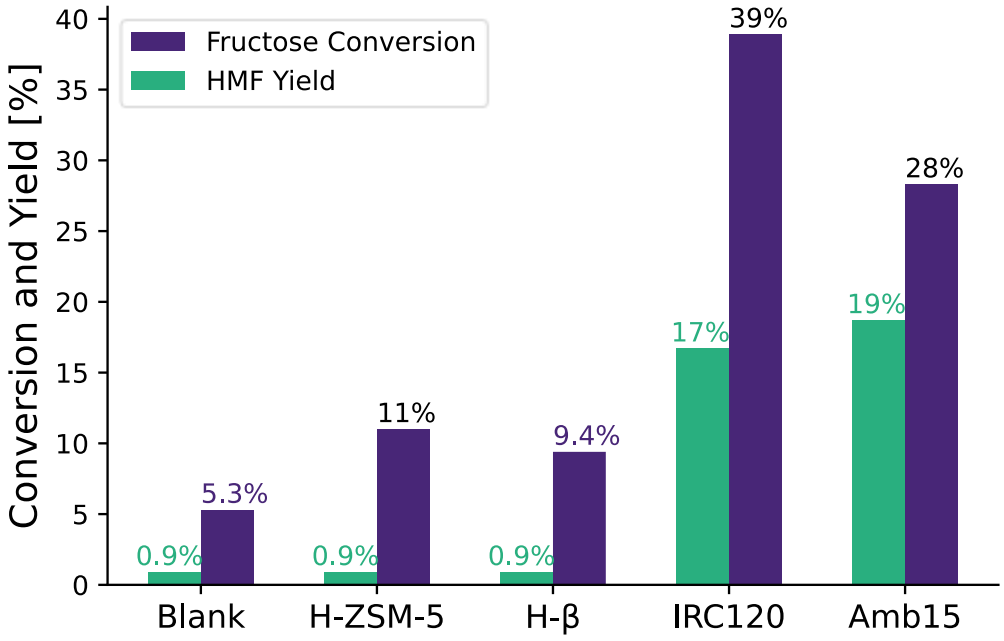

Figure 19 – Comparison of the catalytic performances of IERs and zeolites at 120°C for 6hours

Figure 19 clearly shows a difference in terms of fructose conversion and HMF yield between the previous catalysts (H-ZSM-5 and H-β) and the two tested resins. First, the yields of both resins are around 20 times higher than the ones obtained with the H-ZSM-5 or the H-β. Also, even if the fructose conversion obtained with the IER is bigger than the one obtained with the ZSM-5 and β zeolites, the increase of the conversion is less important than for the yields. This implies a higher selectivity towards HMF with the IERs than with the zeolites (Table 11):

Table 11 – Comparison of the selectivities of the IERs and zeolites after 6 hours at 120°C

	Blank	**H-ZSM-5**	**H-β**	**IRC120**	**Amb15**
Selectivity	17%	8%	10%	44%	68%

A significative difference in the selectivity of the resin compared to the selectivities observed with the zeolites can be noted. The increased performance observed for the ion exchange resins are probably due to a higher concentration of acid sites as well as the high acidic strength of these sites. Moreover, these high performances could also be due to the high hydrophobicity of the resin backbone which is made of styrene and divinyl benzene monomers [127] and thus highly hydrophobic.

Due to its better performance in terms of yield and selectivity, the Amberlyst-15 has been chosen as the best IER among the two to be used as the catalyst of the reaction in the next experiments.

Even if the fructose dehydration results obtained in this work using the Amberlyst-15 seems really good, they are much lower than the results obtained by Sonsiam et al. (2019) that observed a yield of 92% in 30 minutes. This difference could be explained by the use of a different IER, the DIAION® RCP160M and by the use of a biphasic system composed of H_2O:NMP:MIBK in proportion 3:7:40 (NMP being 1-methyl-2-pirrolidinonne) [83].

Impact of the temperature on the Amberlyst-15

As it was done for the H-ZSM-5 and H-β zeolites (page 47 and page 48), the Amberlyst-15 has been tested at various temperature. As its activity is bigger than the ones observed for the zeolites, the temperature range has been started at 80°C (in place of 100°C). Moreover, due to the maximal operating temperature of the resin, the maximal temperature tested was 120°C [127], [128].

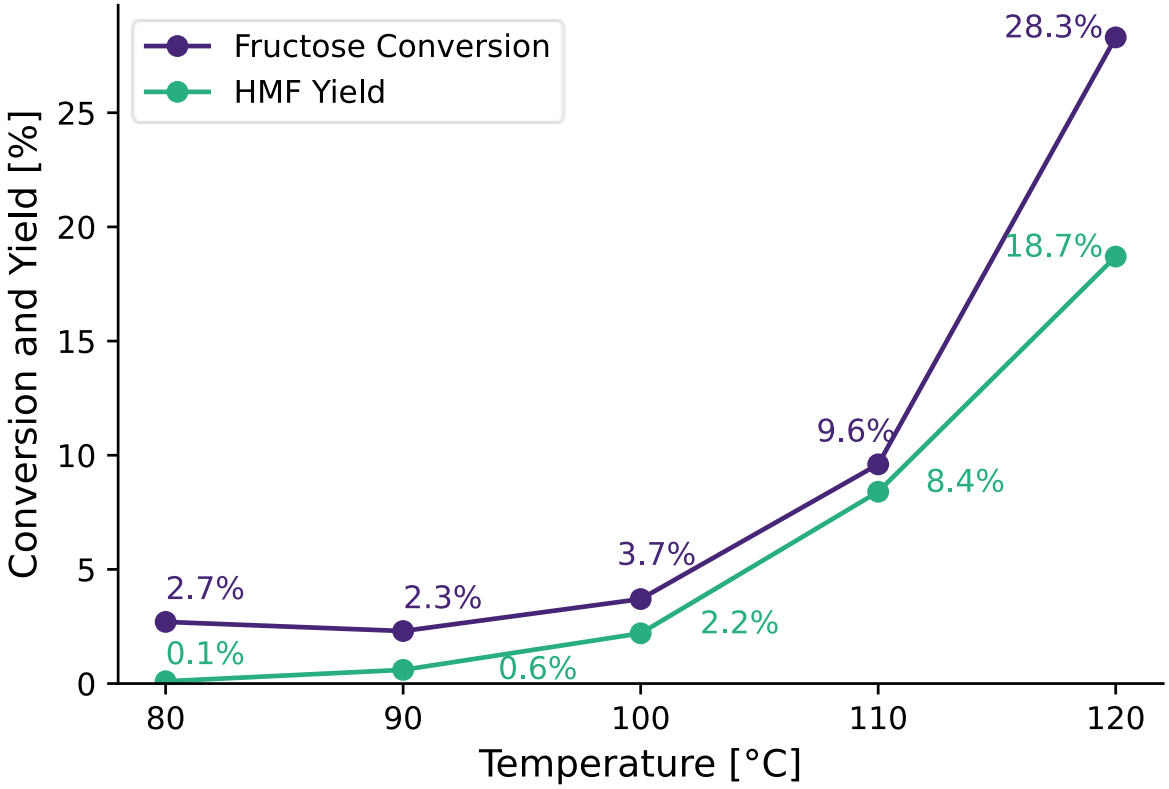

Figure 20 – Temperature impact on the performances of the Amberlyst-15 resin

As for the H-ZSM-5 and H-β zeolites, the performances of the Amb15 increase with the temperature. But unlike the two zeolites, this IER already has a significative HMF yield at 90°C and the results obtained at a temperature of 100°C are already better than the ones obtained with all the zeolites at 120°C.

Seeing this relatively high activity (compared to the zeolites) even at temperature as low as 90°C, the possibility to use the Amberlyst-15 and the Glucose Isomerase in the same system to perform the transformation of glucose to HMF in one-pot is interesting.

5.1.5 One-Pot reactions

The objective of the cascade reaction is to perform the direct conversion of glucose to HMF by using in the same system an enzyme for the glucose isomerisation to fructose and the Amberlyst-15 for the fructose dehydration into HMF. After verifying the activity of the enzyme in biphasic conditions, three different cascade reactions are presented in the following sections.

Activity of the Enzyme in biphasic conditions

For the isomerization of the glucose, several enzymes have been studied in the lab. Since the temperature range used for the fructose dehydration reaction is most of the time higher than the one of the stability of the enzyme, the best enzyme has been chosen as the one able to work at the highest temperature. Previous research in the lab showed that the best Glucose Isomerase was stable up to 80°C and could work at 90°C maximum during 1 hour (unpublished results).

The activity and stability of the enzyme being known in water but not in MIBK:H_2O biphasic systems, the first experiment was the use of the enzyme as glucose isomerisation catalyst in the biphasic system at 80°C. Figure 21 presents the activity of the enzyme in biphasic conditions compared its activity in a monophasic aqueous system.

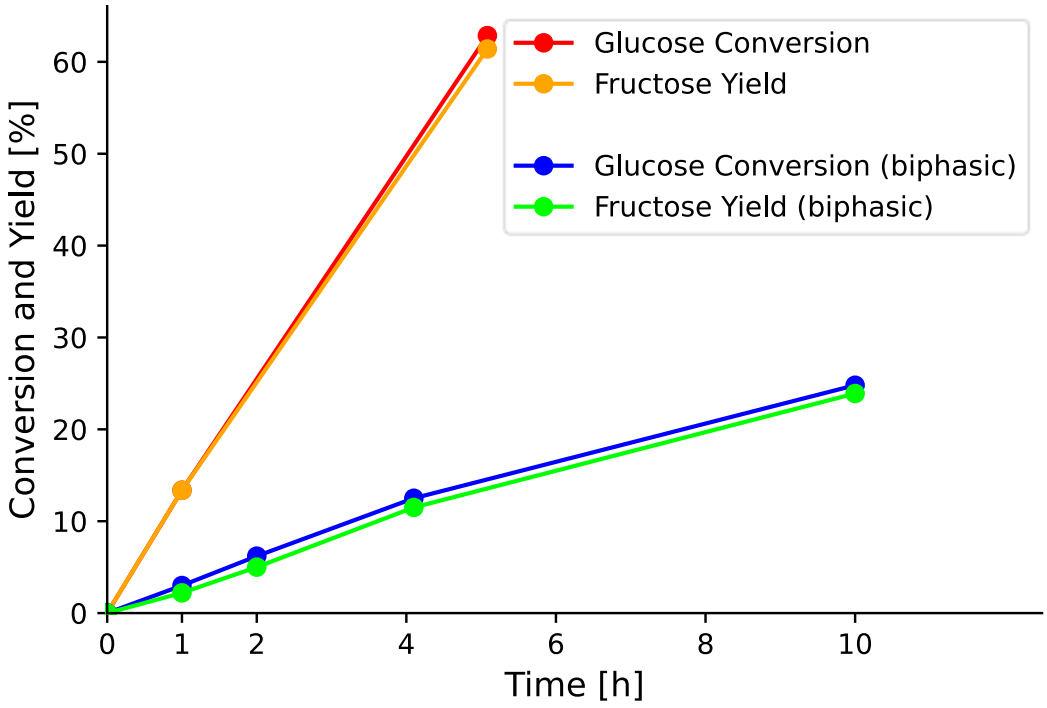

Figure 21 – Glucose Conversion and Fructose Yield observed for the GI at 80°C in monophasic aqueous and biphasic systems

As it can be observed in the Figure 21, the activity of the enzyme in biphasic conditions is much lower than the one that was obtained in the monophasic aqueous system. This is probably due to the fact that enzymes are produced by living organisms and are thus normally working in aqueous conditions. However, the presence of MIBK has not totally suppressed the activity of the enzyme and after 10 hours 20% of the glucose initially present has been transformed into fructose in the biphasic conditions.

It can be seen that the enzyme has a high selectivity towards fructose since the fructose yield observed is always very close to the glucose conversion. The selectivities observed during this experiment are indeed always higher than 70%. The very small difference observed between the glucose reacted and the fructose produced seems to be unvarying with the reaction duration. This could be due to a systematic underestimation of the fructose quantity

One-Pot Reaction at 90°C

As the Amb15 already displays some catalytic activity as low 90°C and that the enzyme could normally survive up to one hour at this temperature, it has been tried to use both catalysts in a single flask to directly produce HMF from glucose using the catalytic activity of both catalysts at the same time.

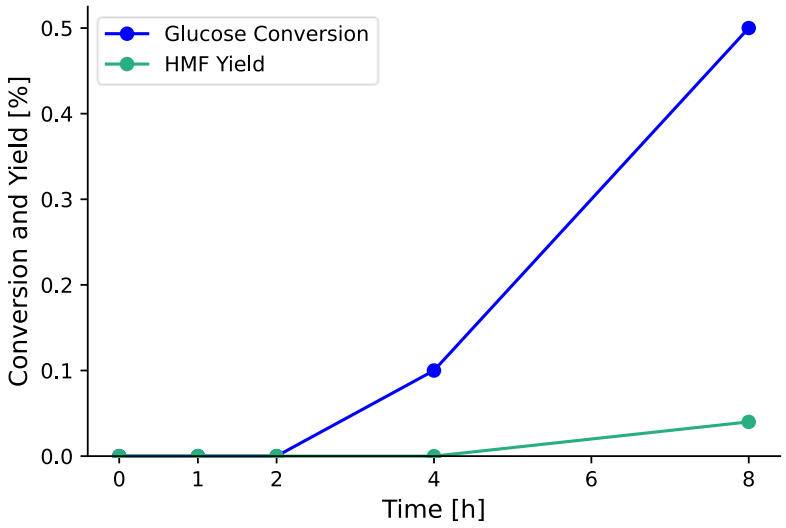

Figure 22 – Glucose conversion and HMF yield obtained with the GI and Amb15 catalysts at 90°C for 8 hours

As shown in Figure 22, the glucose conversion is really low and only reaches 0.5% after 8hours of reaction. Moreover, a positive glucose conversion is only measured after 2hours of reaction. As mentioned above, the enzyme is normally not active longer than one hour at a temperature of 90°C. The glucose conversion is thus probably only due to the glucose isomerisation to fructose without the impact of a catalyst. The inactivity of the enzyme cannot

be due to the biphasic conditions because as shown above (Figure 21), the enzyme is active during at least 10 hours in these biphasic conditions. This inactivity can be explained by a too high temperature or an negative impact of the Amberlyst-15 on the enzyme affecting its activity.

One-Pot Reaction at 80°C

To investigate the inactivity of the enzyme observed at a temperature of 90°C, the same reaction has been performed at a temperature of 80°C even if we know that the IER does not have a catalytic activity at that temperature.

The analysis of the samples taken during and after the reaction showed no production of HMF in the organic phase. Moreover, no fructose was detected in any of the samples and the glucose conversion appeared to be null. The inactivity of the enzyme is quite surprising. Since the GI was working well in the biphasic medium as showed before (Figure 21), this inactivity is probably due to the presence of the Amb15 in the system. One possibility is that the strongly acidic sites impacted the stability of the enzyme. Another possibility is a potential affinity of the enzyme for the IER (for either the acidic or the polystyrene backbone) leading to a strong adsorption and a concomitant modification of the 3 dimensional shape of the enzyme and a loss of its activity.

Temperature step One-Pot reaction

The last one-pot reaction that has been tested using the combination of the GI and the Amb15 has been conducted starting with 4 hours at 80°C followed by 4 hours at 120°C. These two temperatures have been chosen so that the enzyme would be able to isomerize glucose into fructose during the first 4 hours and then, the Amb15 would be able to perform the transformation of fructose into HMF. This reaction conditions allows to use each catalyst at its optimal temperature. Due to analysis delay, the inactivity of the enzyme in the presence of Amb15 was discovered after the completion of all the one-pot reactions. The addition of Amb15 already at the start of the reaction is thus a problem since it will inactive the enzyme. The reaction should thus have been conducted differently.

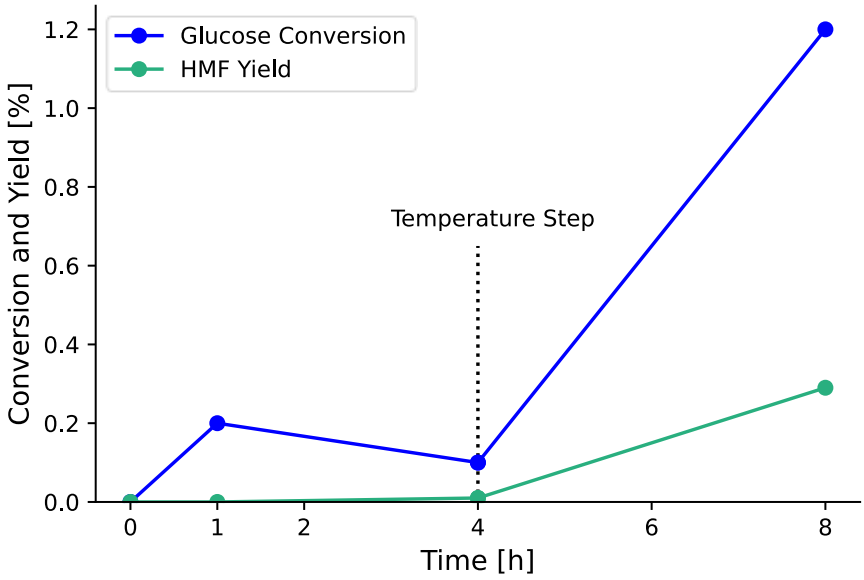

Figure 23 – Glucose conversion and HMF yield obtained using the GI and the Amb15 at 80°C for 4 hours followed by 4 hours at 120°C

It can be seen in the Figure 23 that the glucose conversion is really low until the 4th hour of reaction. This conversion being really low (below 1%), it cannot be differentiated from the experimental variation and it thus confirms the inactivity of the enzyme that was observed in the one-pot reaction at a constant temperature of 80°C.

The increase of the glucose conversion between 4 and 8 hours of reaction could be due to the non-catalytic isomerization of the glucose since a small yield (0.1%) of fructose is observed after 8 hours but this glucose conversion is most likely to be due to unwanted side-reactions consuming it.

As expected, no HMF is produced before the temperature increase due to both the inactivity of the Amb15 and the absence of fructose produced. At the end of the reaction, after 4 hours at 120°C, a small yield of HMF is detected (0.3%) showing that Amb15 catalyses the dehydration of small amounts of fructose produced in the first stages of the reaction or the direct dehydration of glucose.

Summary of the One-Pot reactions

The three one-pot reactions performed using the GI and the Amb15 have shown that even if both catalysts can be efficient in biphasic conditions, a reaction system containing both of them at the same time leads to a complete loss of the enzyme activity. This loss of activity is due to the presence of the Amberlyst-15 in the system since the enzyme is able to isomerize glucose for at least 8 hours in the absence of IER in the same conditions (biphasic system at 80°C).

A possibility to produce HMF directly from glucose in one-pot is to use the enzyme at 80°C during 4 hours to produce fructose and then add the Amb15 and rise the temperature to 120°C for 4 hours to transform the fructose into HMF. This one-pot but two-step reaction should lead to an HMF production but also to a destruction of the enzyme used. This destruction of the enzyme due to the Amb15 is not a real problem in this case since the heating at 120°C for 4 hours already denatures the enzyme after the first 4 hours.

5.1.6 Addition of phenyl sulfonic acid on a silica support

Since the IERs have very low porosity as well as a low surface area (around $9m^2.g^{-1}$) [129], the use of another support to hold the acidic sites has been investigated.

A commercial silica (Aerosil® 380) possessing a specific surface area of more than $300m^2.g^{-1}$ has been chosen as the support for the addition of phenyl sulfonic acid groups since the natural acidity of the zeolite is not required due to the addition of the phenyl sulfonic acid groups. Moreover, Aerosil® 380 has a well-known high specific surface area of $380m^2.g^{-1}$ thus proposing a high exchange surface for the impregnation of the PTMS precursor.

The prepared A380 silica impregnated to obtain phenyl sulfonic acid sites (A380-PSA) have been compared to the previously presented zeolites. Moreover, to verify the impregnation of the PTMS precursor onto the silica, an A380 silica without the PTMS impregnation step but with the sulfuric acid treatment (A380-H_2SO_4) has also been tested .

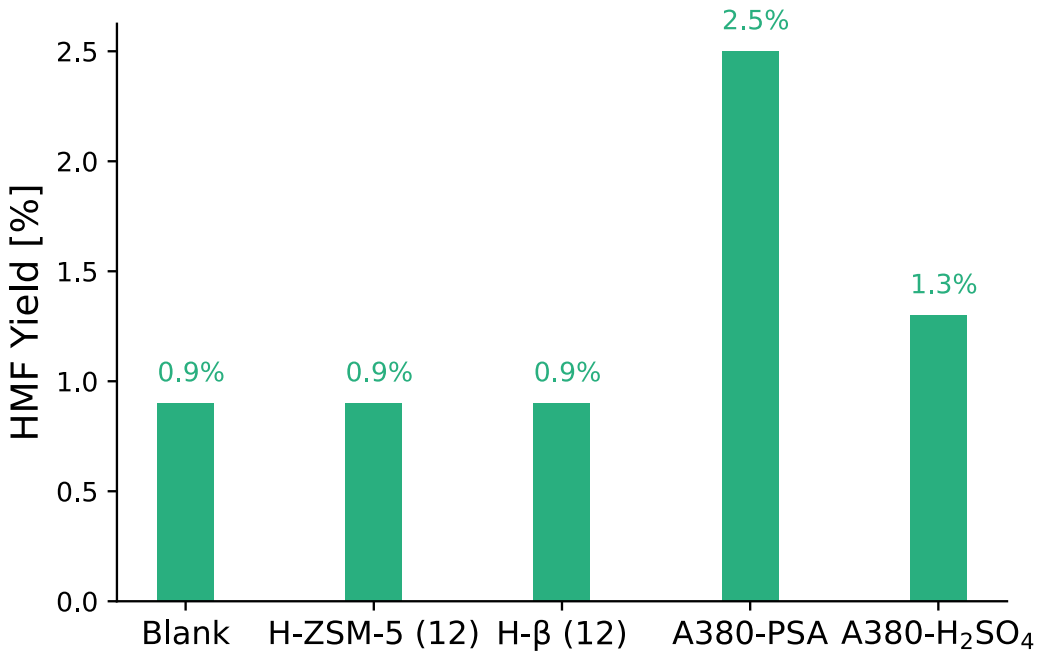

Figure 24 – HMF yield obtained at 120°C for 6hours with ZSM-5 and β zeolites compared to the treated A380 silica

As it can be seen, A380-H_2SO_4 silica is slightly more active than the zeolites discussed above. More interestingly, the A380-PSA has a much higher yield. This indicates that the PTMS impregnation onto the silica worked correctly and that the increased catalytic activity observed for the two catalysts that have been treated with sulfuric acid is not due to sulfuric acid molecules remaining on the catalyst even after the washes. The conversion values measured for the two treated silica were aberrant (negative conversions) and are thus not shown on the Figure 24 and cannot be discussed. These values are probably due to a problem in the HPLC measurements. The yields observed can however be used since their values come from the GC measurements.

The catalyst obtained with this PTMS and H_2SO_4 treatments is however clearly not as efficient as the Amberlyst-15 which was the origin of the phenyl sulfonic acid modification. Indeed, at 120°C, in the same conditions, the A380-H_2SO_4 showed an HMF yield of 2.5% while the Amb15 obtained 19% of HMF yield. This huge difference could be due to different factors: reduced amount of acid sites, different acid sites onto the silica compared to the IER, higher hydrophilicity of the A380-H_2SO_4 compared to the Amb15 backbone thus leading to a lower extraction of the HMF staying on the catalytic sites after being produced.

Even if the modified silica showed improved performances compared to the other catalysts, the activity observed is clearly lower than the one of the Amb15 in the same conditions. Since it has been shown that the Amb15 was not active below 90°C (Figure 20) and that the enzyme is only stable up to 80°C (unpublished results), the modification of the silica is clearly not sufficiently effective to be used.

5.2 Characterization Results

5.2.1 X-Ray Diffraction (XRD)

Zeolites are crystalline materials. To verify that the synthesis of the zeolites had been well performed, XRD analysis was performed on each prepared zeolite to verify the crystallinity (Figure 25).

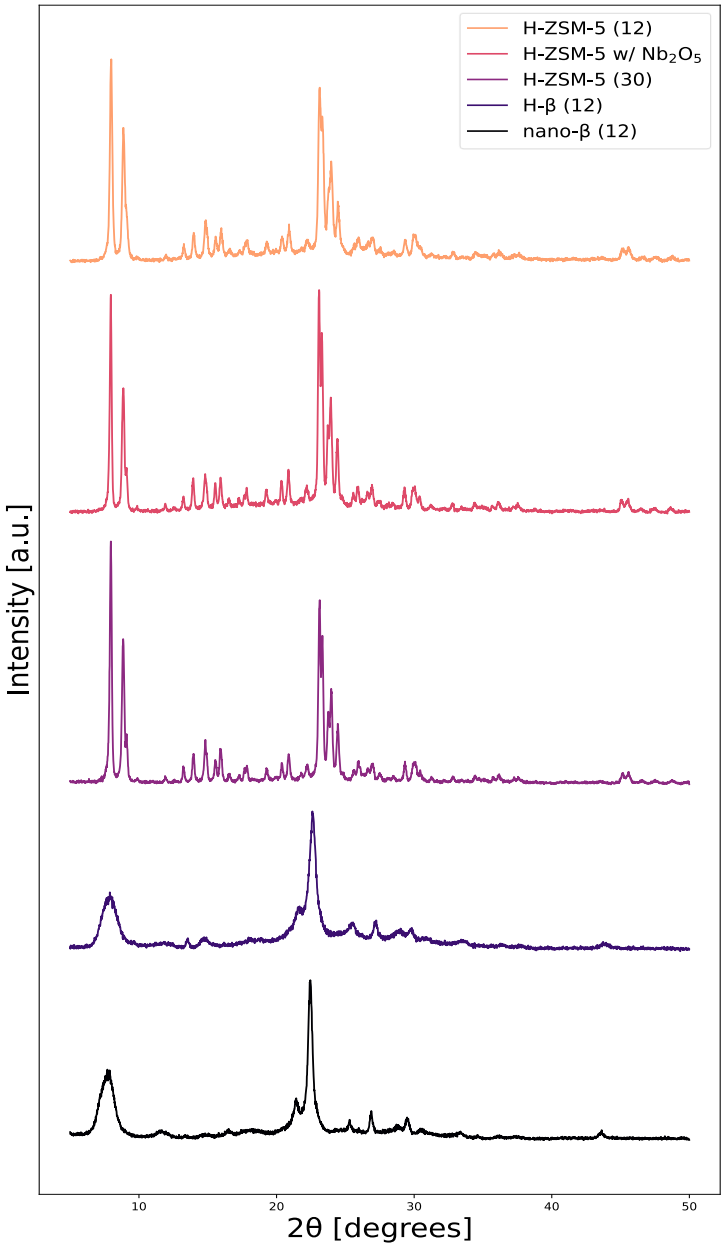

Figure 25 – Diffractograms of the different prepared zeolites

As it can be seen, all the analysed materials possess crystalline phases and it was thus assumed that the synthesis worked correctly to produce a zeolite. It can also be seen that the different zeolite frameworks (ZSM-5 and β) effectively have different diffractograms.

5.2.2 NH_3 Temperature Programmed Desorption (NH_3-TPD)

The acidity of different ZSM-5 zeolites has been measured through NH_3-TPD. The results obtained are presented in the Figure 26 below:

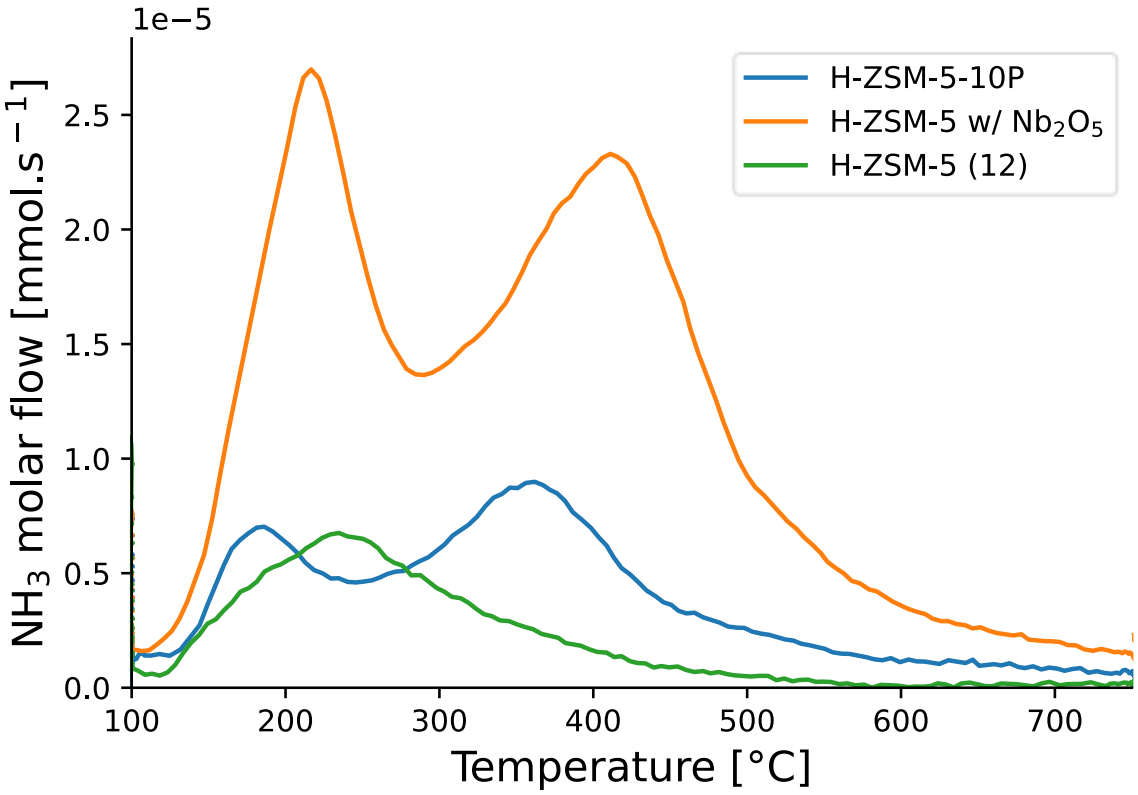

Figure 26 – Comparison of the NH_3-TPD results obtained for different ZSM-5 zeolites

A first observation that can be make is that the ZSM-5 zeolite containing niobium oxide contains much more acid sites than the other zeolites (Figure 26). Indeed, as presented in the Table 12, this zeolite has a much bigger calculated specific acidity (0.64 $mmol.g^{-1}$) than the two other ZSM-5 zeolites (0.13 $mmol.g^{-1}$ and 0.20 $mmol.g^{-1}$ for the H-ZSM-5 (12) and the H-ZSM-5-10P respectively). This acidity difference explains the higher yield that was observed in Section 5.1.1. However, the difference between the yields of the H-ZSM-5 (12) (0.2% of HMF yield after 6 hours at 100°C) and the H-ZSM-5 with Nb_2O_5 (0.29% in the same conditions) is much lower than the one observed for the specific acidities. This difference could be explained by a difficulty for the fructose molecules to access the acid catalytic sites. Some sites of the zeolite impregnated with niobium are thus maybe accessible only to ammoniac molecules and not to fructose leading to a higher specific activity detected by the NH_3-TPD but only to a slightly higher HMF yield.

Moreover, the zeolite impregnated with niobium also has stronger (peak above 300°C) and weaker (peak below 200°C) acid sites than the other zeolites. The increased activity cannot be associated to the specific increase of only of the two peaks since there is no other zeolite with a similar weak or strong acid peak.

Table 12 – Specific acidities of the ZSM-5 zeolites

ZSM-5 Zeolite	**Specific Acidity [mmol.g^{-1}]**
H-ZSM-5 (12)	0.13
H-ZSM-5 with Nb_2O_5 (5%)	0.64
H-ZSM-5-10P	0.20

The HMF yield observed in Section 5.1.3 for the H-ZSM-5-10P (1.3% after 6 hours at 120°C) was a bit higher than the one observed for the H-ZSM-5 (12) (0.9% in the same conditions). This corresponds to the increased specific acidity of the zeolite treated with phosphoric acid compared to the untreated one. Also, the increase in the specific acidity of the treated zeolite seems to be more due to an increase in the number of strong acid sites (Figure 26) than to an increase in the number of the weak ones. This result seems to indicate that the presence of stronger acid sites is more interesting in the case of fructose dehydration into HMF. Furthermore, it matches well with the good results observed with the IERs that possesses very strong acid sites [115].

The IERs could not be analysed with NH_3-TPD due to the instability of the IERs above 120°C but according to several sources, the specific acidity of the Amb15 is around 4.6mmol.g^{-1} [127], [130]. This very high amount of acid sites is probably one of the reasons explaining the very high catalytic activity of the IER compared to the zeolites presented.

5.3 Discussion

Figure 13 showed that at a temperature of 100°C, none of the tested unmodified zeolite had interesting results in the scope of chemo-enzymatic bifunctional catalysis since the observed yields were not really higher than the blank. Only the ZSM-5 impregnated with Nb_2O_5 showed a slightly higher performances 0.29% yield compared to 0.20% for the parent ZSM-5 zeolite. Moreover, the impact of the temperature on the activity (Figure 17) showed that for both H-ZSM-5 and H-β zeolites, the temperatures had to be raised to at least 120°C to significative HMF yields. These temperatures are too high for an enzyme to survive [54], [55]. This catalysts thus cannot be used as such as fructose dehydration catalysts in a context of chemo-enzymatic bifunctional catalysts.

The zeolite treated with phosphoric acid has shown a slightly better activity (Table 8) which is probably due to a higher quantity of acidic sites as well as a higher strength of these sites as presented in the Section 5.2.2.

The more hydrophobic H-ZSM-5 (30) zeolite also showed slightly better performances in terms of HMF yield (Table 9) that could be due to easier contact between MIBK and the catalyst surface thus leading to a better extraction of the HMF after its production on the catalytic sites. This extraction may allow to reduce to quantity of HMF adsorbed on the active sites. This leads to a clearing of the active sites and thus to an increase of the catalytic activity [89] but it also avoid further transformation of the HMF thus enhancing the selectivity. The lower conversion observed is probably due to the decrease in the number of acid sites due to the presence of less aluminium atoms [131].

The more specific activity of the nano-β zeolite compared to the commercial zeolite (29% compared to 8%, Table 10) shows the impact of the crystal size. With smaller crystals, molecules will diffuse less in the porosity to reach the active sites and are thus less likely to undergo side-reactions. The selectivity is thus bigger for the nanocrystalline catalyst.

As presented in the Figure 18, none of the modified zeolites (H_3PO_4 treatment, higher Si/Al, nanocrystalline catalyst) showed interesting performances at an already quite high temperature (120°C), these modifications are thus not efficient enough to produce dehydration catalyst for a bifunctional catalyst using an enzyme.

Ion Exchange Resins have been tested and allowed to obtain much higher yields compared to the other catalysts (24% after 6 hours at 120°C, Figure 19) with a catalytic activity for the fructose dehydration starting around 90°C. As explained, the very high HMF yields observed are probably due to the high number of acid sites as well as the strength of these sites [115], [127]. Indeed, Amberlyst-15 contains 4.6mmol.g^{-1} of acidic sites while the H-ZSM-5 (12) contains 0.13mmol.g^{-1} and the phosphoric acid treated ZSM-5 contains 0.20mmol.g^{-1} (Section 5.2.2). The strength of the acid sites of the Amb15 is also really high since it is know that phenyl sulfonic acid as a pKa below 0. Besides the acidity of the IER, the hydrophobicity of its surface probably also has a important impact on its selectivity. Indeed, as discussed before, the hydrophobicity allows a better extraction of HMF thus leading to higher selectivities. The backbone of the IER being a polymer of styrene and divinylbenzene, the resins is thus very hydrophobic.

Seeing the interesting results obtained with the Amberlyst-15 until temperatures around 90°C (Figure 20), one-pot reactions have been tested using Glucose Isomerase and Amberlyst-15 to directly transform glucose into HMF. It has been shown in Section 5.1.5 that even if the enzyme was active at 80°C in biphasic conditions during at least 10 hours (Figure

21), the presence of Amberlyst-15 in the reaction system drastically impacts the performances of the enzyme thus leading to the impossibility to use the soluble enzyme with the Amberlyst-15 in a one-pot reaction. A possibility to obtain HMF from glucose in one-pot is by starting with the enzyme at 80°C for 4 hours and then adding the Amb15 and rising the temperature to 120°C. This should lead to a production of HMF since the enzyme is active at 80°C in absence of Amb15 (Figure 21) and the Amb15 added later would thus have fructose to produce HMF.

The modification of a silica to obtain similar acid sites as the one present on the Amberlyst-15 has shown better results than the other zeolites in similar conditions Figure 24. These results can be attributed to the grafting of trimethoxyphenylsilane followed by the sulfuric acid treatment since the catalytic activity of the same silica treated with sulfuric acid with no trimethoxyphenylsilane showed a yield of HMF nearly two times lower. However, these results are still much lower than those observed with the Amberlyst-15. This difference could be due to a lower quantity of acidic sites as well as a more hydrophilic support. This modification is not reported in the literature and the protocol used was thus an adaptation of two different articles. A better protocol could lead to a catalyst with better performances however, even if the activity becomes comparable to the one of the Amb15, the minimal temperature required for the catalyst to be active would be 90°C which is already a too high temperature for the enzyme. Even if this modification could lead to interesting catalyst, it would not be efficient enough at low temperature to be used with an enzyme.

CONCLUSION AND OUTLOOKS

6. Conclusion and prospects

After the end of this master thesis, we confirmed the hypothesis that the acidity of the catalyst (composed of both the specific acidity and the acidic strength of the sites) has an important impact on the fructose dehydration into HMF. Furthermore, the impact of the hydrophobicity that was not really considered at the start of this master thesis is thus now better understood and taken into consideration as a very important parameter to enhance the selectivity by promoting the extraction of the HMF.

Ion Exchange Resins have clearly shown the best catalytic performances for the fructose dehydration into HMF in biphasic conditions. However, one-pot reactions using these catalysts is not possible due to a negative impact on the enzyme as well as a too low activity at temperature suitable for the enzyme. The use of more acidic and more hydrophobic Ion Exchange Resins such as Nafion-117 or DIAION® RCP160M could be an interesting possibility to reduce the temperature at which the IER is active and thus match the reaction window of the enzyme.

The modification of a silica could also be investigated further. Investigation could be made using different silica with different hydrophobicities and different porosities but also by improving the functionalization protocol or by trying different precursors than the trimethoxyphenylsilane such as (3-mercaptopropyl)trimethoxysilane (MPTMS) or 1,3-propane sultone. Moreover, the characterization of such modified silica would be very important to verify the exact modifications that happened during the different steps of the impregnation.

The exploration of different conditions and modifications of the system could also be a very interesting since many different conditions are used in the literature. These modifications can be an increased organic to aqueous ratio (up to 10:1), the addition of salts or change of organic solvent using for example tetrahydrofuran (with high salt concentration) or dimethylfuran.

With the proposed upgrades presented above and among which the use of a Nafion-117 in highly saline MIBK:H_2O or THF:H_2O systems are the most promising in my opinion, it can be hoped to find an active dehydration catalyst working at temperatures as low as 80°C and thus potentially usable with an enzyme in a one-pot reaction. It would then be also useful to test the recyclability of the catalysts. Such tests have not been performed during this work due to the absence of catalyst showing high performances during most of the time. Recyclability tests are very important since the catalyst has to be used several times. Such kind of experiment will thus be mandatory whatever the catalyst used.

References

[1] D. A. Simonetti and J. A. Dumesic, 'Catalytic Strategies for Changing the Energy Content and Achieving C–C Coupling in Biomass-Derived Oxygenated Hydrocarbons', *ChemSusChem*, vol. 1, no. 8–9, pp. 725–733, Sep. 2008, doi: 10.1002/cssc.200800105.

[2] J. C. Serrano-Ruiz, R. M. West, and J. A. Dumesic, 'Catalytic Conversion of Renewable Biomass Resources to Fuels and Chemicals', *Annu. Rev. Chem. Biomol. Eng.*, vol. 1, no. 1, pp. 79–100, Jun. 2010, doi: 10.1146/annurev-chembioeng-073009-100935.

[3] V. Smil, *Energy transitions: global and national perspectives*, Second edition. Santa Barbara, California: Praeger, an imprint of ABC-CLIO, LLC, 2017.

[4] H. Ritchie, M. Roser, and P. Rosado, 'Energy', *Our World in Data*, Nov. 2020, Accessed: Mar. 31, 2022. [Online]. Available: https://ourworldindata.org/energy

[5] W. Keim, 'Petrochemicals: Raw material change from fossil to biomass?', *Pet. Chem.*, vol. 50, no. 4, pp. 298–304, Jul. 2010, doi: 10.1134/S0965544110040079.

[6] T. Stocker, Ed., *Climate change 2013: the physical science basis: Working Group I contribution to the Fifth assessment report of the Intergovernmental Panel on Climate Change*. New York: Cambridge University Press, 2014.

[7] PubChem, '5-Hydroxymethylfurfural'. https://pubchem.ncbi.nlm.nih.gov/compound/237332 (accessed Mar. 31, 2022).

[8] R.-J. van Putten, J. C. van der Waal, E. de Jong, C. B. Rasrendra, H. J. Heeres, and J. G. de Vries, 'Hydroxymethylfurfural, A Versatile Platform Chemical Made from Renewable Resources', *Chem. Rev.*, vol. 113, no. 3, pp. 1499–1597, Mar. 2013, doi: 10.1021/cr300182k.

[9] T. Wang, J. Zhang, W. Xie, Y. Tang, D. Guo, and Y. Ni, 'Catalytic Transfer Hydrogenation of Biobased HMF to 2,5-Bis-(Hydroxymethyl)Furan over Ru/Co3O4', *Catalysts*, vol. 7, no. 12, p. 92, Mar. 2017, doi: 10.3390/catal7030092.

[10] A. A. Rosatella, S. P. Simeonov, R. F. M. Frade, and C. A. M. Afonso, '5-Hydroxymethylfurfural (HMF) as a building block platform: Biological properties, synthesis and synthetic applications', *Green Chem.*, vol. 13, no. 4, p. 754, 2011, doi: 10.1039/c0gc00401d.

[11] G. C. Hayes and C. R. Becer, 'Levulinic acid: a sustainable platform chemical for novel polymer architectures', *Polym. Chem.*, vol. 11, no. 25, pp. 4068–4077, 2020, doi: 10.1039/D0PY00705F.

[12] Sigma-Aldrich, 'Merck | Belgium'. https://www.sigmaaldrich.com (accessed May 23, 2022).

[13] P. Bhaumik and P. L. Dhepe, ‘Chapter 1. Conversion of Biomass into Sugars’, in *Green Chemistry Series*, D. Murzin and O. Simakova, Eds. Cambridge: Royal Society of Chemistry, 2015, pp. 1–53. doi: 10.1039/9781782622079-00001.

[14] S. Pang, ‘Fuel flexible gas production’, in *Fuel Flexible Energy Generation*, Elsevier, 2016, pp. 241–269. doi: 10.1016/B978-1-78242-378-2.00009-2.

[15] C. Bonechi *et al.*, ‘Biomass’, in *Bioenergy Systems for the Future*, Elsevier, 2017, pp. 3–42. doi: 10.1016/B978-0-08-101031-0.00001-6.

[16] R. A. Lee and J.-M. Lavoie, ‘From first- to third-generation biofuels: Challenges of producing a commodity from a biomass of increasing complexity’, *Animal Frontiers*, vol. 3, no. 2, pp. 6–11, Apr. 2013, doi: 10.2527/af.2013-0010.

[17] Y. Dahman, C. Dignan, A. Fiayaz, and A. Chaudhry, ‘An introduction to biofuels, foods, livestock, and the environment’, in *Biomass, Biopolymer-Based Materials, and Bioenergy*, Elsevier, 2019, pp. 241–276. doi: 10.1016/B978-0-08-102426-3.00013-8.

[18] Y. Dahman, K. Syed, S. Begum, P. Roy, and B. Mohtasebi, ‘Biofuels’, in *Biomass, Biopolymer-Based Materials, and Bioenergy*, Elsevier, 2019, pp. 277–325. doi: 10.1016/B978-0-08-102426-3.00014-X.

[19] H. Yang, R. Yan, H. Chen, C. Zheng, D. H. Lee, and D. T. Liang, ‘In-Depth Investigation of Biomass Pyrolysis Based on Three Major Components: Hemicellulose, Cellulose and Lignin’, *Energy Fuels*, vol. 20, no. 1, pp. 388–393, Jan. 2006, doi: 10.1021/ef0580117.

[20] M. Nauman Aftab, I. Iqbal, F. Riaz, A. Karadag, and M. Tabatabaei, ‘Different Pretreatment Methods of Lignocellulosic Biomass for Use in Biofuel Production’, in *Biomass for Bioenergy - Recent Trends and Future Challenges*, A. El-Fatah Abomohra, Ed. IntechOpen, 2019. doi: 10.5772/intechopen.84995.

[21] A. L. Woiciechowski, S. Nitsche, A. Pandey, and C. R. Soccol, ‘Acid and enzymatic hydrolysis to recover reducing sugars from cassava bagasse: an economic study’, *Braz. arch. biol. technol.*, vol. 45, no. 3, pp. 393–400, Sep. 2002, doi: 10.1590/S1516-89132002000300018.

[22] W. Douglas Crabb and C. Mitchinson, ‘Enzymes involved in the processing of starch to sugars’, *Trends in Biotechnology*, vol. 15, no. 9, pp. 349–352, Sep. 1997, doi: 10.1016/S0167-7799(97)01082-2.

[23] N. Haren, ‘Properties and applications of starch-converting enzymes of the a-amylase family’, *Journal of Biotechnology*, p. 19, 2002.

[24] C.-H. Zhou, X. Xia, C.-X. Lin, D.-S. Tong, and J. Beltramini, ‘Catalytic conversion of lignocellulosic biomass to fine chemicals and fuels’, *Chem. Soc. Rev.*, vol. 40, no. 11, p. 5588, 2011, doi: 10.1039/c1cs15124j.

[25] S. Kang, J. Fu, and G. Zhang, 'From lignocellulosic biomass to levulinic acid: A review on acid-catalyzed hydrolysis', *Renewable and Sustainable Energy Reviews*, vol. 94, pp. 340–362, Oct. 2018, doi: 10.1016/j.rser.2018.06.016.

[26] F. Brienza, K. Van Aelst, K. Thielemans, B. F. Sels, D. P. Debecker, and I. Cybulska, 'Enhancing lignin depolymerization *via* a dithionite-assisted organosolv fractionation of birch sawdust', *Green Chem.*, vol. 23, no. 9, pp. 3268–3276, 2021, doi: 10.1039/D1GC00503K.

[27] A. Barakat, C. Mayer-Laigle, A. Solhy, R. A. D. Arancon, H. de Vries, and R. Luque, 'Mechanical pretreatments of lignocellulosic biomass: towards facile and environmentally sound technologies for biofuels production', *RSC Adv.*, vol. 4, no. 89, pp. 48109–48127, 2014, doi: 10.1039/C4RA07568D.

[28] A. R. Mankar, A. Pandey, A. Modak, and K. K. Pant, 'Pretreatment of lignocellulosic biomass: A review on recent advances', *Bioresource Technology*, vol. 334, p. 125235, Aug. 2021, doi: 10.1016/j.biortech.2021.125235.

[29] P. Kumar, D. M. Barrett, M. J. Delwiche, and P. Stroeve, 'Methods for Pretreatment of Lignocellulosic Biomass for Efficient Hydrolysis and Biofuel Production', *Ind. Eng. Chem. Res.*, vol. 48, no. 8, pp. 3713–3729, Apr. 2009, doi: 10.1021/ie801542g.

[30] Y.-B. Huang and Y. Fu, 'Hydrolysis of cellulose to glucose by solid acid catalysts', *Green Chem.*, vol. 15, no. 5, p. 1095, 2013, doi: 10.1039/c3gc40136g.

[31] L. Hu, L. Lin, Z. Wu, S. Zhou, and S. Liu, 'Chemocatalytic hydrolysis of cellulose into glucose over solid acid catalysts', *Applied Catalysis B: Environmental*, vol. 174–175, pp. 225–243, Sep. 2015, doi: 10.1016/j.apcatb.2015.03.003.

[32] J. Wang, J. Xi, and Y. Wang, 'Recent advances in the catalytic production of glucose from lignocellulosic biomass', *Green Chem.*, vol. 17, no. 2, pp. 737–751, 2015, doi: 10.1039/C4GC02034K.

[33] K. Dussan, B. Girisuta, M. Lopes, J. J. Leahy, and M. H. B. Hayes, 'Conversion of Hemicellulose Sugars Catalyzed by Formic Acid: Kinetics of the Dehydration of D -Xylose, L -Arabinose, and D -Glucose', *ChemSusChem*, vol. 8, no. 8, pp. 1411–1428, Apr. 2015, doi: 10.1002/cssc.201403328.

[34] X. Yang, J. Zhao, J. Liang, and J. Zhu, 'Efficient and Selective Catalytic Conversion of Hemicellulose in Rice Straw by Metal Catalyst under Mild Conditions', *Sustainability*, vol. 12, no. 24, p. 10601, Dec. 2020, doi: 10.3390/su122410601.

[35] A. Takagaki, M. Ohara, S. Nishimura, and K. Ebitani, 'A one-pot reaction for biorefinery: combination of solid acid and base catalysts for direct production of 5-hydroxymethylfurfural from saccharides', *Chem. Commun.*, no. 41, p. 6276, 2009, doi: 10.1039/b914087e.

[36] J. C. Speck, 'The Lobry De Bruyn-Alberda Van Ekenstein Transformation', in *Advances in Carbohydrate Chemistry*, vol. 13, Elsevier, 1958, pp. 63–103. doi: 10.1016/S0096-5332(08)60352-5.

[37] V. Choudhary *et al.*, 'Insights into the Interplay of Lewis and Brønsted Acid Catalysts in Glucose and Fructose Conversion to 5-(Hydroxymethyl)furfural and Levulinic Acid in Aqueous Media', *J. Am. Chem. Soc.*, vol. 135, no. 10, pp. 3997–4006, Mar. 2013, doi: 10.1021/ja3122763.

[38] C. B. Rasrendra, I. G. B. N. Makertihartha, S. Adisasmito, and H. J. Heeres, 'Green Chemicals from d-glucose: Systematic Studies on Catalytic Effects of Inorganic Salts on the Chemo-Selectivity and Yield in Aqueous Solutions', *Top Catal*, vol. 53, no. 15–18, pp. 1241–1247, Sep. 2010, doi: 10.1007/s11244-010-9570-0.

[39] Z. Ju, Y. Zhang, T. Zhao, W. Xiao, and X. Yao, 'The Mechanism of Glucose-Fructose Isomerization over Aluminum-based Catalysts in Methanol Media', p. 28.

[40] W. N. P. van der Graaff *et al.*, 'Competitive Adsorption of Substrate and Solvent in Sn-Beta Zeolite During Sugar Isomerization', *ChemSusChem*, vol. 9, no. 22, pp. 3145–3149, Nov. 2016, doi: 10.1002/cssc.201600800.

[41] Y. Román-Leshkov, M. Moliner, J. A. Labinger, and M. E. Davis, 'Mechanism of Glucose Isomerization Using a Solid Lewis Acid Catalyst in Water', *Angewandte Chemie International Edition*, vol. 49, no. 47, pp. 8954–8957, Nov. 2010, doi: 10.1002/anie.201004689.

[42] E. Nikolla, Y. Román-Leshkov, M. Moliner, and M. E. Davis, '"One-Pot" Synthesis of 5-(Hydroxymethyl)furfural from Carbohydrates using Tin-Beta Zeolite', *ACS Catal.*, vol. 1, no. 4, pp. 408–410, Apr. 2011, doi: 10.1021/cs2000544.

[43] S. Xu, L. Zhang, K. Xiao, and H. Xia, 'Isomerization of glucose into fructose by environmentally friendly Fe/β zeolite catalysts', *Carbohydrate Research*, vol. 446–447, pp. 48–51, Jun. 2017, doi: 10.1016/j.carres.2017.05.006.

[44] M. Moliner, Y. Román-Leshkov, and M. E. Davis, 'Tin-containing zeolites are highly active catalysts for the isomerization of glucose in water', *Proc. Natl. Acad. Sci. U.S.A.*, vol. 107, no. 14, pp. 6164–6168, Apr. 2010, doi: 10.1073/pnas.1002358107.

[45] R. Otomo, T. Tatsumi, and T. Yokoi, 'Beta zeolite: a universally applicable catalyst for the conversion of various types of saccharides into furfurals', *Catal. Sci. Technol.*, vol. 5, no. 8, pp. 4001–4007, 2015, doi: 10.1039/C5CY00719D.

[46] F. Liang, D. Chen, H. Liu, W. Liu, M. Xian, and D. Feng, 'One-Pot Synthesis of 5-Hydroxymethylfurfural from Glucose by Brønsted Acid-Free Bifunctional Porous Coordination Polymers in Water', *ACS Omega*, vol. 4, no. 5, pp. 9316–9323, May 2019, doi: 10.1021/acsomega.9b00882.

[47] G. Wypych, *Handbook of UV degradation and stabilization*, 2nd edition. Toronto: ChemTec Publishing, 2015.

[48] D. Tichit *et al.*, 'Textural Properties and Catalytic Activity of Hydrotalcites', *Journal of Catalysis*, vol. 151, no. 1, pp. 50–59, Jan. 1995, doi: 10.1006/jcat.1995.1007.

[49] K. H. Nam, 'Glucose Isomerase: Functions, Structures, and Applications', *Applied Sciences*, vol. 12, no. 1, p. 428, Jan. 2022, doi: 10.3390/app12010428.

[50] Y. B. Tewari' and R. N. Goldberg, 'Thermodynamics of the conversion of aqueous glucose to fructose', p. 25.

[51] R. Huang, W. Qi, R. Su, and Z. He, 'Integrating enzymatic and acid catalysis to convert glucose into 5-hydroxymethylfurfural', *Chem. Commun.*, vol. 46, no. 7, pp. 1115–1117, 2010, doi: 10.1039/B921306F.

[52] D. F. Othmer and R. E. Kirk, *Encyclopedia of chemical technology*, 5th ed. Hoboken (N. J.): Wiley-Interscience, 2007.

[53] W. Soetaert and E. J. Vandamme, Eds., *Industrial Biotechnology: Sustainable Growth and Economic Success*, 1st ed. Wiley, 2010. doi: 10.1002/9783527630233.

[54] K. Srih-Belghith and S. Bejar, 'A thermostable glucose isomerase having a relatively low optimum pH: Study of activity and molecular cloning of the corresponding gene', *Biotechnology Letters*, vol. 20, no. 6, pp. 553–556, 1998, doi: 10.1023/A:1005393510435.

[55] S. H. Bhosale, M. B. Rao, and V. V. Deshpande, 'Molecular and industrial aspects of glucose isomerase', *Microbiol Rev*, vol. 60, no. 2, pp. 280–300, Jun. 1996, doi: 10.1128/mr.60.2.280-300.1996.

[56] A. Mishra and M. Debnath (Das), 'Effect of pH on Simultaneous Saccharification and Isomerization by Glucoamylase and Glucose Isomerase', *ABAB*, vol. 102–103, no. 1–6, pp. 193–200, 2002, doi: 10.1385/ABAB:102-103:1-6:193.

[57] Q. Zhang *et al.*, 'Catalytic Transfer of Fructose to 5-Hydroxymethylfurfural over Bimetal Oxide Catalysts', *International Journal of Chemical Engineering*, vol. 2019, pp. 1–6, Apr. 2019, doi: 10.1155/2019/3890298.

[58] M. L. Testa, G. Miroddi, M. Russo, V. La Parola, and G. Marcì, 'Dehydration of Fructose to 5-HMF over Acidic TiO2 Catalysts', *Materials*, vol. 13, no. 5, p. 1178, Mar. 2020, doi: 10.3390/ma13051178.

[59] Y. Li, X. Lu, L. Yuan, and X. Liu, 'Fructose decomposition kinetics in organic acids-enriched high temperature liquid water', *Biomass and Bioenergy*, vol. 33, no. 9, pp. 1182–1187, Sep. 2009, doi: 10.1016/j.biombioe.2009.05.003.

[60] H. E. van Dam, A. P. G. Kieboom, and H. van Bekkum, 'The Conversion of Fructose and Glucose in Acidic Media: Formation of Hydroxymethylfurfural', *Starch/Stärke*, vol. 38, no. 3, pp. 95–101, 1986, doi: 10.1002/star.19860380308.

[61] M. Watanabe *et al.*, 'Glucose reactions with acid and base catalysts in hot compressed water at 473K', *Carbohydrate Research*, vol. 340, no. 12, pp. 1925–1930, Sep. 2005, doi: 10.1016/j.carres.2005.06.017.

[62] B. F. M. Kuster, 'The influence of water concentration on the dehydration of d-fructose', *Carbohydrate Research*, vol. 54, no. 2, pp. 177–183, Apr. 1977, doi: 10.1016/S0008-6215(00)84807-7.

[63] T. S. Hansen, J. M. Woodley, and A. Riisager, 'Efficient microwave-assisted synthesis of 5-hydroxymethylfurfural from concentrated aqueous fructose', *Carbohydrate Research*, vol. 344, no. 18, pp. 2568–2572, Dec. 2009, doi: 10.1016/j.carres.2009.09.036.

[64] Y. Román-Leshkov, J. N. Chheda, and J. A. Dumesic, 'Phase Modifiers Promote Efficient Production of Hydroxymethylfurfural from Fructose', *Science*, vol. 312, no. 5782, pp. 1933–1937, Jun. 2006, doi: 10.1126/science.1126337.

[65] K. Seri, Y. Inoue, and H. Ishida, 'Catalytic Activity of Lanthanide(III) Ions for the Dehydration of Hexose to 5-Hydroxymethyl-2-furaldehyde in Water', *BCSJ*, vol. 74, no. 6, pp. 1145–1150, Jun. 2001, doi: 10.1246/bcsj.74.1145.

[66] C. Carlini, P. Patrono, A. M. R. Galletti, and G. Sbrana, 'Heterogeneous catalysts based on vanadyl phosphate for fructose dehydration to 5-hydroxymethyl-2-furaldehyde', *Applied Catalysis A: General*, vol. 275, no. 1–2, pp. 111–118, Nov. 2004, doi: 10.1016/j.apcata.2004.07.026.

[67] F. Benvenuti *et al.*, 'Heterogeneous zirconium and titanium catalysts for the selective synthesis of 5-hydroxymethyl-2-furaldehyde from carbohydrates', *Applied Catalysis A: General*, vol. 193, no. 1–2, pp. 147–153, Feb. 2000, doi: 10.1016/S0926-860X(99)00424-X.

[68] C. Carlini, M. Giuttari, A. Maria Raspolli Galletti, G. Sbrana, T. Armaroli, and G. Busca, 'Selective saccharides dehydration to 5-hydroxymethyl-2-furaldehyde by heterogeneous niobium catalysts', *Applied Catalysis A: General*, vol. 183, no. 2, pp. 295–302, Jul. 1999, doi: 10.1016/S0926-860X(99)00064-2.

[69] F. S. Asghari and H. Yoshida, 'Dehydration of fructose to 5-hydroxymethylfurfural in sub-critical water over heterogeneous zirconium phosphate catalysts', *Carbohydrate Research*, vol. 341, no. 14, pp. 2379–2387, Oct. 2006, doi: 10.1016/j.carres.2006.06.025.

[70] T. Armaroli, G. Busca, C. Carlini, M. Giuttari, A. M. Raspolli Galletti, and G. Sbrana, 'Acid sites characterization of niobium phosphate catalysts and their activity in fructose dehydration to 5-hydroxymethyl-2-furaldehyde', *Journal of Molecular Catalysis A: Chemical*, vol. 151, no. 1–2, pp. 233–243, Feb. 2000, doi: 10.1016/S1381-1169(99)00248-4.

[71] M. T. Reche *et al.*, 'Niobic acid nanoparticle catalysts for the aqueous phase transformation of glucose and fructose to 5-hydroxymethylfurfural', *Catal. Sci. Technol.*, vol. 6, no. 19, pp. 7334–7341, 2016, doi: 10.1039/C6CY01129B.

[72] E. I. García-López, F. R. Pomilla, B. Megna, M. L. Testa, L. F. Liotta, and G. Marcì, 'Catalytic Dehydration of Fructose to 5-Hydroxymethylfurfural in Aqueous Medium over Nb2O5-Based Catalysts', *Nanomaterials*, vol. 11, no. 7, p. 1821, Jul. 2021, doi: 10.3390/nano11071821.

[73] J. P. V. Lima, P. T. A. Campos, M. F. Paiva, J. J. Linares, S. C. L. Dias, and J. A. Dias, 'Dehydration of Fructose to 5-Hydroxymethylfurfural: Effects of Acidity and Porosity of Different Catalysts in the Conversion, Selectivity, and Yield', *Chemistry*, vol. 3, no. 4, pp. 1189–1202, Oct. 2021, doi: 10.3390/chemistry3040087.

[74] V. Rac, V. Rakić, D. Stošić, O. Otman, and A. Auroux, 'Hierarchical ZSM-5, Beta and USY zeolites: Acidity assessment by gas and aqueous phase calorimetry and catalytic activity in fructose dehydration reaction', *Microporous and Mesoporous Materials*, vol. 194, pp. 126–134, Aug. 2014, doi: 10.1016/j.micromeso.2014.04.003.

[75] X. Qi, M. Watanabe, T. M. Aida, and R. L. Smith, Jr., 'Catalytic dehydration of fructose into 5-hydroxymethylfurfural by ion-exchange resin in mixed-aqueous system by microwave heating', *Green Chem.*, vol. 10, no. 7, p. 799, 2008, doi: 10.1039/b801641k.

[76] K. Seri, Y. Inoue, and H. Ishida, 'Highly Efficient Catalytic Activity of Lanthanide(III) Ions for Conversion of Saccharides to 5-Hydroxymethyl-2-furfural in Organic Solvents', *Chem. Lett.*, vol. 29, no. 1, pp. 22–23, Jan. 2000, doi: 10.1246/cl.2000.22.

[77] S. De, S. Dutta, and B. Saha, 'Microwave assisted conversion of carbohydrates and biopolymers to 5-hydroxymethylfurfural with aluminium chloride catalyst in water', *Green Chem.*, vol. 13, no. 10, p. 2859, 2011, doi: 10.1039/c1gc15550d.

[78] M. Ohara, A. Takagaki, S. Nishimura, and K. Ebitani, 'Syntheses of 5-hydroxymethylfurfural and levoglucosan by selective dehydration of glucose using solid acid and base catalysts', *Applied Catalysis A: General*, vol. 383, no. 1–2, pp. 149–155, Jul. 2010, doi: 10.1016/j.apcata.2010.05.040.

[79] K. Shimizu, R. Uozumi, and A. Satsuma, 'Enhanced production of hydroxymethylfurfural from fructose with solid acid catalysts by simple water removal methods', *Catalysis Communications*, vol. 10, no. 14, pp. 1849–1853, Aug. 2009, doi: 10.1016/j.catcom.2009.06.012.

[80] Q. Bao, K. Qiao, D. Tomida, and C. Yokoyama, 'Preparation of 5-hydroymethylfurfural by dehydration of fructose in the presence of acidic ionic liquid', *Catalysis Communications*, vol. 9, no. 6, pp. 1383–1388, Mar. 2008, doi: 10.1016/j.catcom.2007.12.002.

[81] T. S. Hansen, J. Mielby, and A. Riisager, 'Synergy of boric acid and added salts in the catalytic dehydration of hexoses to 5-hydroxymethylfurfural in water', *Green Chem.*, vol. 13, no. 1, pp. 109–114, 2011, doi: 10.1039/C0GC00355G.

[82] L. Zhu *et al.*, 'Preparation of the Nb-P/SBA-15 catalyst and its performance in the dehydration of fructose to 5-hydroxymethylfurfural', *Journal of Fuel Chemistry and Technology*, vol. 45, no. 6, pp. 651–659, Jun. 2017, doi: 10.1016/S1872-5813(17)30034-8.

[83] C. Sonsiam, A. Kaewchada, S. pumrod, and A. Jaree, 'Synthesis of 5-hydroxymethylfurfural (5-HMF) from fructose over cation exchange resin in a continuous flow reactor', *Chemical Engineering and Processing - Process Intensification*, vol. 138, pp. 65–72, Apr. 2019, doi: 10.1016/j.cep.2019.03.001.

[84] G. Delgado Martin *et al.*, 'Fructose dehydration reaction over functionalized nanographitic catalysts in MIBK/H2O biphasic system', *Catalysis Today*, vol. 366, pp. 68–76, Apr. 2021, doi: 10.1016/j.cattod.2020.03.016.

[85] S. F. Mayer *et al.*, 'Dehydration of fructose to HMF in presence of (H3O)xSbxTe(2-x)O6 (x = 1, 1.1, 1.25) in H2O-MIBK', *Molecular Catalysis*, vol. 481, p. 110276, Feb. 2020, doi: 10.1016/j.mcat.2018.12.025.

[86] S. Xu, X. Yan, Q. Bu, and H. Xia, 'Highly efficient conversion of carbohydrates into 5-hydroxymethylfurfural using the bi-functional $CrPO_4$ catalyst', *RSC Adv.*, vol. 6, no. 10, pp. 8048–8052, 2016, doi: 10.1039/C5RA23716E.

[87] V. V. Ordomsky, J. van der Schaaf, J. C. Schouten, and T. A. Nijhuis, 'Fructose Dehydration to 5-Hydroxymethylfurfural over Solid Acid Catalysts in a Biphasic System', *ChemSusChem*, vol. 5, no. 9, pp. 1812–1819, Sep. 2012, doi: 10.1002/cssc.201200072.

[88] X. Zhang *et al.*, 'Maleic acid and aluminum chloride catalyzed conversion of glucose to 5-(hydroxymethyl) furfural and levulinic acid in aqueous media', *Green Chem.*, vol. 18, no. 19, pp. 5219–5229, 2016, doi: 10.1039/C6GC01395C.

[89] M. León, T. D. Swift, V. Nikolakis, and D. G. Vlachos, 'Adsorption of the Compounds Encountered in Monosaccharide Dehydration in Zeolite Beta', *Langmuir*, vol. 29, no. 22, pp. 6597–6605, Jun. 2013, doi: 10.1021/la401138g.

[90] A. S. Amarasekara, L. D. Williams, and C. C. Ebede, 'Mechanism of the dehydration of d-fructose to 5-hydroxymethylfurfural in dimethyl sulfoxide at 150°C: an NMR study', *Carbohydrate Research*, vol. 343, no. 18, pp. 3021–3024, Dec. 2008, doi: 10.1016/j.carres.2008.09.008.

[91] T. Ståhlberg, W. Fu, J. M. Woodley, and A. Riisager, 'Synthesis of 5-(Hydroxymethyl)furfural in Ionic Liquids: Paving the Way to Renewable Chemicals', *ChemSusChem*, vol. 4, no. 4, pp. 451–458, Apr. 2011, doi: 10.1002/cssc.201000374.

[92] D. P. Debecker *et al.*, 'Shaping Effective Practices for Incorporating Sustainability Assessment in Manuscripts Submitted to *ACS Sustainable Chemistry & Engineering* : Catalysis and Catalytic Processes', *ACS Sustainable Chem. Eng.*, vol. 9, no. 14, pp. 4936–4940, Apr. 2021, doi: 10.1021/acssuschemeng.1c02070.

[93] L. Zhu, B. Song, and Z. Wang, 'Developing an orbitally shaken bioreactor featuring a hollow cylinder vessel wall', *Journal of Chemical Technology and Biotechnology*, vol. 94, no. 7, pp. 2212–2218, 2019, doi: 10.1002/jctb.6005.

[94] B. Velaga, R. P. Parde, J. Soni, and N. R. Peela, 'Synthesized hierarchical mordenite zeolites for the biomass conversion to levulinic acid and the mechanistic insights into humins formation', *Microporous and Mesoporous Materials*, vol. 287, pp. 18–28, Oct. 2019, doi: 10.1016/j.micromeso.2019.05.049.

[95] G. Lv, L. Deng, B. Lu, J. Li, X. Hou, and Y. Yang, 'Efficient dehydration of fructose into 5-hydroxymethylfurfural in aqueous medium over silica-included heteropolyacids', *Journal of Cleaner Production*, vol. 142, pp. 2244–2251, Jan. 2017, doi: 10.1016/j.jclepro.2016.11.053.

[96] J. Esteban, A. J. Vorholt, and W. Leitner, 'An overview of the biphasic dehydration of sugars to 5-hydroxymethylfurfural and furfural: a rational selection of solvents using COSMO-RS and selection guides', *Green Chem.*, vol. 22, no. 7, pp. 2097–2128, 2020, doi: 10.1039/C9GC04208C.

[97] S. Mohammad, C. Held, E. Altuntepe, T. Köse, and G. Sadowski, 'Influence of Salts on the Partitioning of 5-Hydroxymethylfurfural in Water/MIBK', *J. Phys. Chem. B*, vol. 120, no. 16, pp. 3797–3808, Apr. 2016, doi: 10.1021/acs.jpcb.5b11588.

[98] V. V. Ordomsky, J. van der Schaaf, J. C. Schouten, and T. A. Nijhuis, 'The effect of solvent addition on fructose dehydration to 5-hydroxymethylfurfural in biphasic system over zeolites', *Journal of Catalysis*, vol. 287, pp. 68–75, Mar. 2012, doi: 10.1016/j.jcat.2011.12.002.

[99] M. Moreno-Recio, J. Santamaría-González, and P. Maireles-Torres, 'Brönsted and Lewis acid ZSM-5 zeolites for the catalytic dehydration of glucose into 5-hydroxymethylfurfural', *Chemical Engineering Journal*, vol. 303, pp. 22–30, Nov. 2016, doi: 10.1016/j.cej.2016.05.120.

[100] Y. Román-Leshkov and J. A. Dumesic, 'Solvent Effects on Fructose Dehydration to 5-Hydroxymethylfurfural in Biphasic Systems Saturated with Inorganic Salts', *Top Catal*, vol. 52, no. 3, pp. 297–303, Apr. 2009, doi: 10.1007/s11244-008-9166-0.

[101] C. Moreau, A. Finiels, and L. Vanoye, 'Dehydration of fructose and sucrose into 5-hydroxymethylfurfural in the presence of 1-H-3-methyl imidazolium chloride acting both as solvent and catalyst', *Journal of Molecular Catalysis A: Chemical*, vol. 253, no. 1–2, pp. 165–169, Jul. 2006, doi: 10.1016/j.molcata.2006.03.046.

[102] G. Yong, Y. Zhang, and J. Y. Ying, 'Efficient Catalytic System for the Selective Production of 5-Hydroxymethylfurfural from Glucose and Fructose', *Angewandte Chemie*, vol. 120, no. 48, pp. 9485–9488, Nov. 2008, doi: 10.1002/ange.200803207.

[103] J. Y. G. Chan and Y. Zhang, 'Selective Conversion of Fructose to 5-Hydroxymethylfurfural Catalyzed by Tungsten Salts at Low Temperatures', *ChemSusChem*, vol. 2, no. 8, pp. 731–734, Aug. 2009, doi: 10.1002/cssc.200900117.

[104] L. Lai and Y. Zhang, 'The Effect of Imidazolium Ionic Liquid on the Dehydration of Fructose to 5-Hydroxymethylfurfural, and a Room Temperature Catalytic System', *ChemSusChem*, vol. 3, no. 11, pp. 1257–1259, Nov. 2010, doi: 10.1002/cssc.201000201.

[105] M. C. Bubalo, K. Radošević, I. R. Redovniković, I. Slivac, and V. G. Srček, 'Toxicity mechanisms of ionic liquids', *Archives of Industrial Hygiene and Toxicology*, vol. 68, no. 3, pp. 171–179, Sep. 2017, doi: 10.1515/aiht-2017-68-2979.

[106] S. Körner, J. Albert, and C. Held, 'Catalytic Low-Temperature Dehydration of Fructose to 5-Hydroxymethylfurfural Using Acidic Deep Eutectic Solvents and Polyoxometalate Catalysts', *Front. Chem.*, vol. 7, p. 661, Oct. 2019, doi: 10.3389/fchem.2019.00661.

[107] H. Huang *et al.*, 'Tandem Catalytic Conversion of Glucose to 5-Hydroxymethylfurfural with an Immobilized Enzyme and a Solid Acid', *ACS Catal.*, vol. 4, no. 7, pp. 2165–2168, Jul. 2014, doi: 10.1021/cs500591f.

[108] E. L. Smith, A. P. Abbott, and K. S. Ryder, 'Deep Eutectic Solvents (DESs) and Their Applications', *Chem. Rev.*, vol. 114, no. 21, pp. 11060–11082, Nov. 2014, doi: 10.1021/cr300162p.

[109] S. Hu *et al.*, 'Conversion of fructose to 5-hydroxymethylfurfural using ionic liquids prepared from renewable materials', *Green Chem.*, vol. 10, no. 12, p. 1280, 2008, doi: 10.1039/b810392e.

[110] M. Zuo *et al.*, 'Green process for production of 5-hydroxymethylfurfural from carbohydrates with high purity in deep eutectic solvents', *Industrial Crops and Products*, vol. 99, pp. 1–6, May 2017, doi: 10.1016/j.indcrop.2017.01.027.

[111] T. Istasse, V. Lemaur, G. Debroux, L. Bockstal, R. Lazzaroni, and A. Richel, 'Monosaccharides Dehydration Assisted by Formation of Borate Esters of α-Hydroxyacids in Choline Chloride-Based Low Melting Mixtures', *Front. Chem.*, vol. 8, p. 569, Jul. 2020, doi: 10.3389/fchem.2020.00569.

[112] P. Zhou and Z. Zhang, 'One-pot catalytic conversion of carbohydrates into furfural and 5-hydroxymethylfurfural', *Catal. Sci. Technol.*, vol. 6, no. 11, pp. 3694–3712, 2016, doi: 10.1039/C6CY00384B.

[113] R. A. Sheldon and S. van Pelt, 'Enzyme immobilisation in biocatalysis: why, what and how', *Chem. Soc. Rev.*, vol. 42, no. 15, pp. 6223–6235, Mar. 2013, doi: 10.1039/C3CS60075K.

[114] T. Yoshida, 'Stimuli-sensitive polymers for drug delivery and diagnostic systems interacting with biosurfaces', in *Switchable and Responsive Surfaces and Materials for*

Biomedical Applications, Elsevier, 2015, pp. 235–258. doi: 10.1016/B978-0-85709-713-2.00010-9.

[115] M. Marczewski *et al.*, 'Acid strength measurements of Amberlyst 15 resin, p-xylene-2-sulfonic acid and chlorosulfonic and sulfuric acid treated SiO2, Al2O3, TiO2 and MgO', *Reac Kinet Mech Cat*, vol. 126, no. 2, pp. 1081–1096, Apr. 2019, doi: 10.1007/s11144-019-01551-7.

[116] Z. Wang *et al.*, 'Controllable direct-syntheses of delaminated MWW-type zeolites', *Chinese Journal of Catalysis*, vol. 41, no. 7, pp. 1062–1066, Jul. 2020, doi: 10.1016/S1872-2067(20)63545-8.

[117] C. Shang, Z. Wu, W. D. Wu, and X. D. Chen, 'Chemical Crosslinking Assembly of ZSM-5 Nanozeolites into Uniform and Hierarchically Porous Microparticles for High-Performance Acid Catalysis', *ACS Appl. Mater. Interfaces*, vol. 11, no. 18, pp. 16693–16703, May 2019, doi: 10.1021/acsami.9b01681.

[118] I. C. L. Barros *et al.*, 'Effects of niobium addition on ZSM-5 studied by thermal and spectroscopy methods', *Microporous and Mesoporous Materials*, vol. 109, no. 1–3, pp. 485–493, Mar. 2008, doi: 10.1016/j.micromeso.2007.05.050.

[119] A. Pande, P. Niphadkar, K. Pandare, and V. Bokade, 'Acid Modified H-USY Zeolite for Efficient Catalytic Transformation of Fructose to 5-Hydroxymethyl Furfural (Biofuel Precursor) in Methyl Isobutyl Ketone–Water Biphasic System', *Energy Fuels*, vol. 32, no. 3, pp. 3783–3791, Mar. 2018, doi: 10.1021/acs.energyfuels.7b03684.

[120] E. Cano-Serrano, G. Blanco-Brieva, J. M. Campos-Martin, and J. L. G. Fierro, 'Acid-Functionalized Amorphous Silica by Chemical Grafting−Quantitative Oxidation of Thiol Groups', *Langmuir*, vol. 19, no. 18, pp. 7621–7627, Sep. 2003, doi: 10.1021/la034520u.

[121] Y. Wang, D. Yang, X. Zheng, Z. Jiang, and J. Li, 'Zeolite beta-filled chitosan membrane with low methanol permeability for direct methanol fuel cell', *Journal of Power Sources*, vol. 183, no. 2, pp. 454–463, Sep. 2008, doi: 10.1016/j.jpowsour.2008.06.003.

[122] Y. Shi *et al.*, 'Zeolite microspheres with hierarchical structures: formation, mechanism and catalytic performance', *J. Mater. Chem.*, vol. 21, no. 40, p. 16223, 2011, doi: 10.1039/c1jm11669j.

[123] X. Li, K. Peng, X. Liu, Q. Xia, and Y. Wang, 'Comprehensive Understanding of the Role of Brønsted and Lewis Acid Sites in Glucose Conversion into 5-Hydromethylfurfural', *ChemCatChem*, vol. 9, no. 14, pp. 2739–2746, Jul. 2017, doi: 10.1002/cctc.201601203.

[124] A. Visan and R. G. H. Lammertink, 'Fructose dehydration to hydroxyl-methylfurfural in an immobilized catalytic microreactor', *J Flow Chem*, vol. 10, no. 2, pp. 461–468, Jun. 2020, doi: 10.1007/s41981-020-00087-5.

[125] N. Lucas, G. Kokate, A. Nagpure, and S. Chilukuri, 'Dehydration of fructose to 5-hydroxymethyl furfural over ordered AlSBA-15 catalysts', *Microporous and Mesoporous Materials*, vol. 181, pp. 38–46, Nov. 2013, doi: 10.1016/j.micromeso.2013.07.015.

[126] Z. Huang, W. Pan, H. Zhou, F. Qin, H. Xu, and W. Shen, 'Nafion-Resin-Modified Mesocellular Silica Foam Catalyst for 5-Hydroxymethylfurfural Production from D - Fructose', *ChemSusChem*, vol. 6, no. 6, pp. 1063–1069, Jun. 2013, doi: 10.1002/cssc.201200967.

[127] 'Amberlyst 15 dry 39389-20-3'. http://www.sigmaaldrich.com/ (accessed Jul. 07, 2022).

[128] M. Wang *et al.*, 'Remarkable acceleration of the fructose dehydration over the adjacent Brønsted acid sites contained in an MFI-type zeolite channel', *Journal of Catalysis*, vol. 319, pp. 150–154, Nov. 2014, doi: 10.1016/j.jcat.2014.08.008.

[129] B. Török, C. Schäfer, and A. Kokel, 'Solid catalysts for environmentally benign synthesis', in *Heterogeneous Catalysis in Sustainable Synthesis*, Elsevier, 2022, pp. 23–80. doi: 10.1016/B978-0-12-817825-6.00013-6.

[130] B. M. Matsagar, M. K. Munshi, A. A. Kelkar, and P. L. Dhepe, 'Conversion of concentrated sugar solutions into 5-hydroxymethyl furfural and furfural using Brönsted acidic ionic liquids', *Catal. Sci. Technol.*, vol. 5, no. 12, pp. 5086–5090, 2015, doi: 10.1039/C5CY00858A.

[131] Y. Gao, B. Zheng, G. Wu, F. Ma, and C. Liu, 'Effect of the Si/Al ratio on the performance of hierarchical ZSM-5 zeolites for methanol aromatization', *RSC Adv.*, vol. 6, no. 87, pp. 83581–83588, 2016, doi: 10.1039/C6RA17084F.

Screening of the catalysts for the fructose dehydration into 5-hydroxymethylfurfural in biphasic conditions at low temperature

Presented by Noé Laloux

The extended use of fossil resources for the production of chemicals and as a fuel poses several environmental problems. Biomass can be used as substitute renewable raw material for petrochemical resources to produce molecules similar to those from the petrochemistry. The objective of this master thesis is to investigate the potential acidic catalysts for the fructose dehydration into hydroxymethylfurfural (HMF) in a biphasic MIBK:H_2O system at temperatures suitable for enzymes. The obtention of such catalyst would allow the preparation of a bifunctional chemo-enzymatic catalyst to directly transform glucose into HMF in one-step. The benefit of doing the transformation in one-step is to avoid the recovery and purification costs between different reactions.

Using a Glucose Isomerase enzyme allows to obtain fructose from glucose with high selectivity. Glucose is the most available and abundant monomer obtainable from biomass. Hydroxymethylfurfural (HMF) is a platform chemical that can be obtained from biomass and further transformed into many different molecules such as monomers, fine chemicals or even fuels.

In this work, the catalysts for the fructose dehydration in biphasic conditions at relatively low temperatures have been investigated. The most efficient catalysts identified is the ion exchange resin Amberlyst-15. This work also showed the impact of both the acidity of the catalyst and the hydrophobicity of its surface. For the acidity, both the number of acid sites and the strength of these sites seems to have a positive impact on the efficiency of the catalyst. A higher hydrophobicity allowed a better extraction of the HMF in the organic phase of the system after its production leading to higher selectivities.

However, none of the investigated catalysts have shown sufficiently high performances to be used with an enzyme and moreover, a negative impact of the Amberlyst-15 on the enzyme has been detected.

The knowledge gained from this work thus allows to restraints the following researches to the investigation of other strongly acidic resins such as Nafion-117 as well as the screening of different reaction conditions such as the use of THF in place of MIBK.

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