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CRITICAL REVIEW
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Heterogeneous catalytic oxidation for lignin valorization into valuable chemicals: what results? What limitations? What trends?

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Paper

Effect of different Brønsted acids on the hydrothermal conversion of fructose to HMF

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The hydrothermal dehydration of fructose to 5-hydroxymethylfurfural (HMF), a promising platform chemical from renewable resources, is commonly known to be Brønsted acid catalysed. Despite, it was not clear, if the acids used as catalyst may have an additional effect on the reaction, besides the donation of protons. In this work, we studied the effect of different Brønsted acids on the hydrothermal conversion of fructose to HMF. Especially phosphoric acid, if present in a high concentration, leads to a significantly stronger acceleration of the reaction than it would be expected from the pH value, calculated at hydrothermal conditions. Acetic acid, on the other hand, seems to evoke an alternative reaction mechanism. The maximal HMF yield however is essentially unaffected by the pH value or the type of acid.

Introduction

As fossil resources are becoming scarce and have a significant environmental and climate impact, mankind is looking for renewable substitutes. 5-hydroxymethylfurfural (HMF) is a promising platform chemical obtained by the dehydration of biomass-derived hexoses, such as glucose or fructose. It can be further processed into intermediates of bio-based polymers or fuels.

Subcritical water has the benefits of being cheap, environmentally friendly, non-flammable and non-toxic which make it a promising solvent for industrial-scale HMF production. Hydrothermal conversion processes of hexoses however suffer from relatively low yields and selectivities due to side and subsequent reactions forming humins, levulinic acid (LA) and other organic acids.[1] Besides, a comprehensive understanding of the underlying kinetics is crucial for the development of an industrial process for the production of HMF.

Within many other studies, the dehydration reaction has been studied intensively using different mono-, di-, oligo- polysaccharides and, occasionally, biomass as starting material.[2–6] Also, various solvents, such as aprotic solvents or ionic liquids, and various catalysts, such as Brønsted and Lewis acids, have been applied.[6–10] It could be demonstrated that the pH value as well as the acid itself play a major role in the production of HMF [3]. The comparison among different catalysts is difficult, if reaction rate constants at reaction conditions were not calculated [3,11,9]. It is impossible to work out a conclusion on the actual impact of the catalyst, namely the acceleration of the reaction, if no kinetic analysis is done. What has not been investigated so far, is a possible effect of the type of Brønsted acid on the hydrothermal dehydration, *i.e.*: Does it matter, if, for instance, sulfuric or phosphoric acid is used as a catalyst, besides that they are proton donators of different strength? For this purpose, we studied the Brønsted acid catalysed hydrothermal conversion of fructose to HMF at different reaction times using phosphoric acid, sulfuric acid, hydrochloric acid, nitric acid, citric acid, glycolic acid and acetic acid as Brønsted catalysts. In some cases, identical initial pH values were used, in other cases it was varied. The reaction rate constants for every acid and initial pH value are calculated. By means of the reaction rate constants a comparison of the different acidic catalyst is possible.

The data obtained allows an estimation of the maximal yield, reaction time and selectivity as function of reaction conditions.

In addition, a deeper understanding of the role of Brønsted acids shall be created. It has to be pointed out

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here, that the properties of water, namely the ionic product changes with temperatures. As consequence, the acidity of acids in subcritical water is different from ambient water. This effect differs for different acids.[12,13]

Results

Experimental yields, conversion and selectivities

In principle, a faster fructose conversion, earlier maximum HMF yields, faster HMF degradation and higher LA yields are observed with decreasing pH. The selectivity of the HMF formation initially increases in most cases.

In order to depict product yield (Y), educt conversion (C) and selectivity (S) of the reaction within one diagram, a ternary plot was designed which we will subsequently term a CYS plot. It can be read as follows: on the left axis the amount of unreacted educt is plotted (1-C), on the right axis the yield of product (Y) and on the bottom axis the yield of by- and degradation products (C-Y), or, in other words, what is deficit to 100%. The selectivity can be found by drawing a line from the data point to the lower left edge of the triangle and identifying the intersection point with the right axis. Thus, a point laying exactly on the bottom axis would represent a selectivity of 0%, while a point on the left axis would represent 100% selectivity.

Within figure 1, left, the CYS plot of the reaction of fructose to HMF, catalysed by various acids, is depicted. For most acids investigated in our work the reaction follows the same path, even though the reaction rates differ drastically in some cases. Generally speaking, the

maximal selectivity is achieved at roughly 60% fructose conversion (*i.e.* 1-C = 40%) and the maximal HMF yield between 70% and 80% fructose conversion. A divergent behaviour, however, was observed for concentrated citric acid (pH 1.4) and acetic acid, for which initially a significantly higher and lower selectivity, respectively, was found.

Figure 1, right, shows the CYS plot of the reaction of fructose to LA, catalysed by various acids. The path that the reaction takes though the plot depends significantly on the kind of acid used and the pH value, respectively. A general observation is that only few LA is formed until a fructose conversion of 40%. From between 70% and 80% when normally the maximal HMF yield is achieved the LA formation increases, but very differently. In HCl and HNO$_3$ solution high LA yields are achieved even before fructose is converted completely, while in H$_2$SO$_4$ solution, selectivity and LA yield are lower. Still, incomplete fructose conversion does not hinder high LA yields. In H$_3$PO$_4$, pH 1.0 also very high LA yields are achieved and the reaction proceeds considerably faster. However, the LA yield does not exceed 30% before nearly all fructose is converted. Interestingly, the curves of H$_3$PO$_4$, pH 2.0 and citric acid progress similarly. In glycolic and acetic acid only low LA yields are achieved, even after a long reaction time.

Reaction rate constants

The measurement values were used to obtain the reaction rate constants by kinetic modelling as described in the method section. Within figure 2 k_1, k_2 and k_3+k_4 are plotted against the proton concentration as determined at
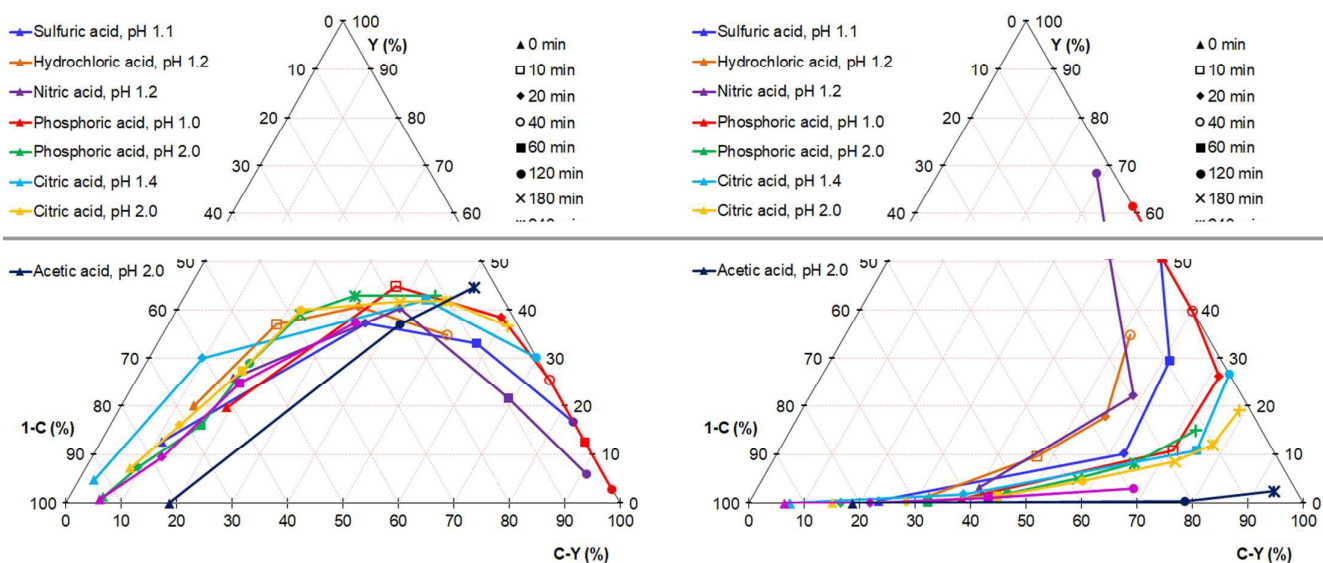

Figure 1   left: CYS plot of the reaction of fructose to HMF, catalysed by various acids. right: CYS plot of the reaction of fructose to LA, catalysed by various acids
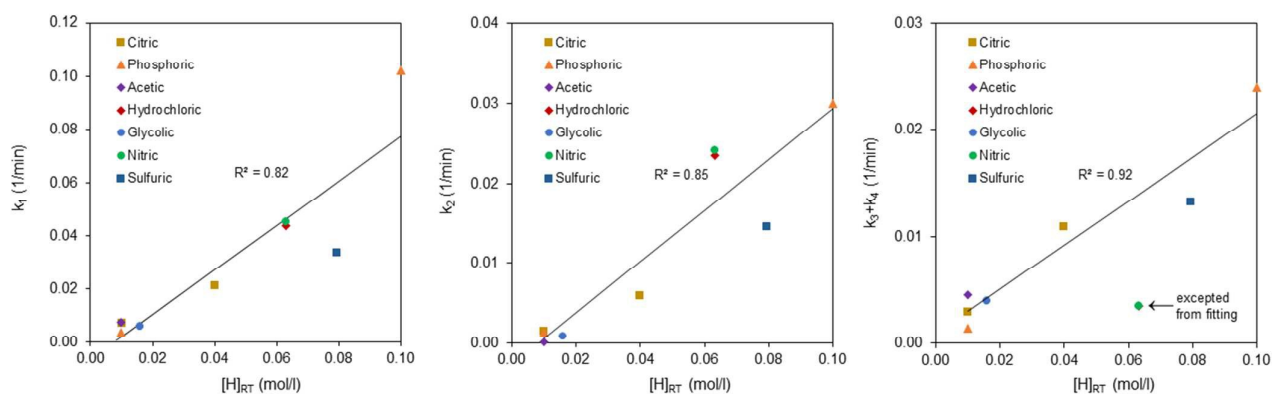
Figure 2 Plotting of the reaction rate constants against $[H]_{RT}$. In the plotting of k_3+k_4, the values of nitric and hydrochloric acid are excepted from the fitting in order to achieve a good linear correlation

room temperature ($[H]_{RT}$) yielding a more or less linear trend. However, certain deviations must be observed: $k_1(H_2SO_4, 1.1)$ is unexpectedly small. For k_3+k_4 the best linear correlation is achieved, provided that the values for nitric and hydrochloric acid are excepted from the fitting, as they deviate strongly downwards. In order to determine the effect of the actual proton concentration under hydrothermal reaction conditions, $[H]_{140°C}$ was calculated as described in the methods section.

Plotting the reaction rate constants against $[H]_{140°C}$ yields a different picture as shown in figure 3.

The linear correlation of k_1 and k_2 as function of the calculated proton concentration is better than as function of the initial pH value. However, the values for phosphoric acid at high proton concentration have to be excepted from the fitting, as they deviate significantly upwards. For k_3+k_4 no linear correlation can be identified in the plotting against $[H]_{140°C}$.

Theoretical maximum HMF yield

The analytical solutions of the kinetic model for [Frc] and [HMF] were used to calculate the theoretical

The k_1 in phosphoric acid at pH 1.0 ($k_1(H_3PO_4, 1.0)$) is substantially higher than all other k_1 values, while

maximal HMF yield (Y_{max}), the reaction time to achieve Y_{max} (t_{Ymax}), the fructose conversion and the selectivity at Y_{max} (C_{Ymax} and S_{Ymax}, respectively) for each acid as described within the method section. The results are depicted in table 1. Interestingly, Y_{max} and S_{Ymax} are very similar for each acid amounting 43% and 52%, respectively, while $C_{Y_{max}}$ varies more strongly between 75% and 95%. $t_{Y_{max}}$ in principle increases with increasing pH, however fluctuates strongly even for identical initial pH values.

Table 1 Y_{max}, t_{Ymax}, C_{ymax} and S_{Ymax} calculated from the modelled k values by using the analytical solution for *Frc* and *HMF*.

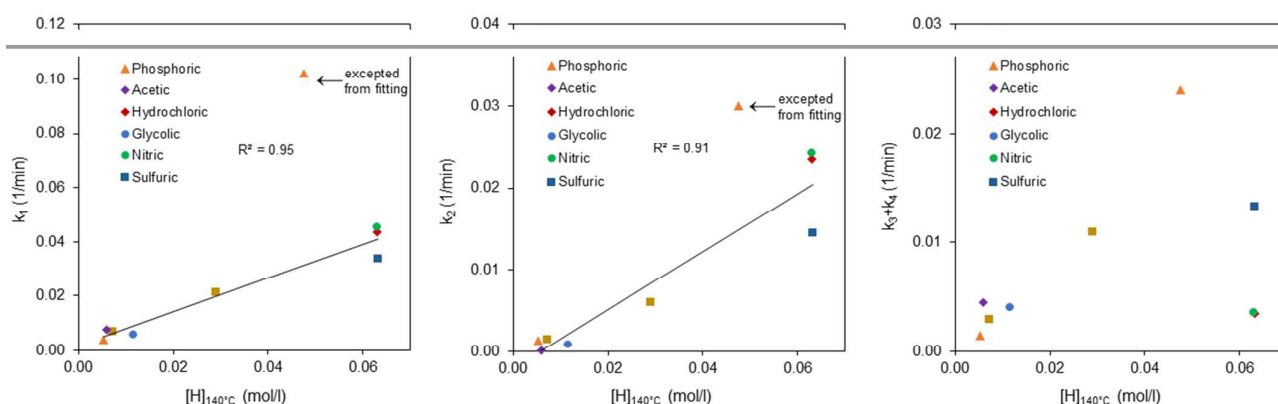| Acid	pH_{RT}	Y_{max} [%]	t_{Ymax} [min]	C_{Ymax} [%]	S_{Ymax} [%]
Phosphoric	1	45	13	87	51
Sulfuric	1.1	40	32	83	48
Hydrochloric	1.2	41	22	75	55
Nitric	1.2	40	19	76	53
Citric	1.4	42	53	78	54
Glycolic	1.8	42	224	88	48
Citric	2	43	167	77	56
Phosphoric	2	44	431	88	50

Figure 3 Plotting of the reaction rate constants against $[H]_{140°C}$. In the plotting of k_1 and k_2, the value of phosphoric acid at pH 1.0 ($[H]_{140°C} = 0.047$) is excepted in order to achieve a good linear correlation.

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Acetic	2	48	243	95	51	± 2.3%	± 6.4%	± 2.6%
average		42.6		82.9	51.5			

Discussion

Comparison of the kinetic data with literature values

A comparison with literature values seems appropriate even though it is difficult, because the reaction conditions often are not directly comparable. Besides, it must be taken into consideration that reaction rate constants usually are strongly temperature-depending. This can be a reason for alleged deviations from literature values, as different systems for temperature determination are used.

The pH values noted here have to be understood as initial pH values.

Fachri et al.[5] investigated the HMF formation from inulin at 170°C and 30 min, catalysed by different acids at their concentration of 0.006 M. They found higher HMF yields for stronger acids, which however is due to the fact that stronger acids cause a lower pH than weaker acids at the same concentration. Thus, the reason for the observed effect are different pH values and not necessarily the type of acid. Lower pH values cause an accelerated HMF formation as well as a faster HMF degradation. This is why it is difficult to interpret different HMF yields, if the reaction was studied at only one reaction time and one acid concentration.

Weiqi & Shubin[14] studied the LA formation from glucose in a mixture of H_3PO_4 and $CrCl_3$ that according to our calculation should have an initial pH of around 2 at temperatures ranging from 150 to 180°C. By extrapolating the Arrhenius graph with their data in order to estimate the rate constants at 140°C, we find that k_1 and k_3 are within the same dimension of $k(H_3PO_4$, pH 2.0), but k_2 and k_4 are significantly larger. Obviously, $CrCl_3$ increases especially the rehydration rate, which is also a basic outcome of the cited study.

The LA formation from glucose was also studied by Chang et al.[15] at 170°C and 190°C, respectively, by using 1%, 3% or 5% sulfuric acid as catalyst. They provide an empirical model to predict k as a function of the H_2SO_4 concentration and the temperature. However, if we apply our data (H_2SO_4 pH 1.1, 140°C), only the predicted value for k_2 lays within the range of our findings, while predicted k_1 and k_3 are several orders of magnitude smaller than the experimental values. Obviously, a comparison of glucose and fructose conversion is not fruitful under these conditions. At that the risks of

performing an extrapolation of temperature and H_2SO_4 concentration.

Jiang et al.[10] investigated the decomposition of glucose to HMF and LA at 140°C, catalysed by $FeCl_3$. The kinetic data they provide bases on the assumption that there is no direct conversion of glucose to HMF, but that it is isomerised to fructose first. Hence, their data is in principle way more comparable with ours as the rate constant for fructose conversion is available. $FeCl_3$ of course is a Lewis acid which however is partially hydrolysed in water yielding HCl. Thus, depending on the $FeCl_3$ concentration the initial pH in their study was 1.06 and 1.74, respectively. Assuming a linear dependency of k on [H], we can calculate the k values for pH 1.2. Although, except for k_2 these calculated values are substantially higher than our findings for HCl, pH 1.2, indicating that the different iron species formed from $FeCl_3$ in water have an additional effect on the reaction apart from the isomerisation of glucose to fructose, which is in complete accordance with the conclusion of the authors.

Swift et al.[2] studied the HMF conversion and production from fructose in HCl at pH values between 0.7 and 1.6 and temperatures ranging from 70 to 150°C. The kinetic model they take as a basis is more complex than ours in such a way that pH independent rate constants are determined by assuming that each conversion is a bimolecular reaction depending on both, the concentration of the educt and of the protons. For the conversion of fructose to HMF they take into consideration that an intermediate is formed of which consumption, not formation, is the rate-limiting step. However, they also assume that only fructo-furanose can directly be converted into this intermediate, while the partition between open-chain, pyranose and furanose fructose depends on the temperature. Attempts of calculating the rate constants for pH 1.2 and 140°C from their data in order to compare them with k(HCl, pH 1.2) yields values that are more or less in a range with ours in the case of k_1 and k_2, but not k_3 and k_4. In the work of Swift and co-workers, a divergent understanding of what k_3 and k_4 represent is applied. According to their hypothesis, humins may be formed from HMF via one path and from fructose via two paths of which one is accompanied with the formation of formic acid. In our work, k_3 and k_4 represent the formation of undefined side and degradation products which certainly comprise humins, but not exclusively. The mechanism of humin

formation from fructose or HMF, respectively, has not been fully understood, yet. Our data suggests that at least the overall formation of side and degradation products is not or not exclusively Brønsted acid catalysed. This may be an additional reason why an implication of the proton concentration into the determination of k may lead to divergent results.

Dependency of the rate constants on the type of acid

When plotting the reaction rate constants against the proton concentration as measured at room temperature ($[H]_{RT}$), a more or less linear trend can be identified for k_1, k_2, and to some extent for k_3+k_4, as it can be seen in figure 2. This would be expected for Brønsted acid catalysed reactions, as our kinetic model bases on the assumption that the reaction of an educt E to a product P is of first order with respect to E.

E → P

$$\frac{d[P]}{dt} = k_x[E] \quad (1)$$

Thus, it neglects that fact that this reaction, at least in some cases, can be homogeneously catalysed by protons which makes k_x a function of [H].

However, if we assume the common kinetic model for homogeneously catalysed reactions as:

$$E + H \underset{}{\overset{R_1}{\rightleftharpoons}} EH \overset{R_2}{\longrightarrow} P + H$$

(R_1: formation of a protonated intermediate EH; R_2: formation of P) and furthermore assume quasi-stationarity for [EH], then we can draft three ordinary differential equations (equ. 2-4):

$$\frac{d[E]}{dt} = -k'_{x1}[E][H] + k'_{x2}[EH] \quad (2)$$

$$\frac{d[EH]}{dt} = k'_{x1}[E][H] - (k'_{x2} + k'_{x3})[EH] = 0 \quad (3)$$

$$\frac{d[P]}{dt} = k'_{x2}[EH] \quad (4)$$

Equ. 3 can be formed into:

$$k'_{x1}[E][H] = (k'_{x2} + k'_{x3})[EH] \quad (5)$$

Transposing equ. 5 leads to:

$$[EH] = \frac{k'_{x1}}{k'_{x2} + k'_{x3}}[E][H] \quad (6)$$

Which can be inserted into equ. 4:

$$\frac{d[P]}{dt} = k'_{x2}\frac{k'_{x1}}{k'_{x2} + k'_{x3}}[E][H] \quad (7)$$

Equating equ. 1 and 7 and rearranging them after k_x gives:

$$k_x = \frac{k'_{x2}k'_{x1}}{k'_{x2} + k'_{x3}}[H] \quad (8)$$

From equ. 8 we learn that k_x depends linearly on [H]. So, if we assume that [H] is the only catalyst in our system and there is no effect by the type of acid, we should be able to identify one linear trend when plotting k_x against [H] for all acids.

According to this reflection, our findings confirm that especially the HMF formation from fructose (k_1) and the HMF rehydration to LA (k_2) are Brønsted acid catalysed. Furthermore, the linear correlation of the plot improves, if not the proton concentration at room temperature, but at reaction temperature is considered. This suggests that it makes sense to determine the latter one, in particular if different acids shall be compared. From the same data we can conclude that the overall formation of side and degradation products (k_3+k_4), which comprise humins, acetic acid, formic acid, furfural and others, either is not Brønsted acid catalysed or the catalytic effect is strongly superimposed by other mechanisms, as no linear trend can be identified in the k_3+k_4 plot (figure 3).

Although, considering the k_1 and k_2 plot in figure 3, certain deviations from the linear trend are observed. Especially, $k_1(H_3PO_4$, pH 1.0) and $k_2(H_3PO_4$, pH 1.0) deviate substantially upwards, which suggests that the type of acid can have an additional effect on these reactions.

In order to discuss the effect on the acid type on the dehydration reaction, we distinguish between three cases: A) acid as co-catalyst; B) acid as co-solvent; C) acid as co-reagent.

Case A comprises catalytic effects of the acid molecule or the corresponding anion, besides the donation of protons, that could be the formation of intermediate complexes with the substrate, the transfer of electrons or protons etc. For instance, sulfuric acid is a common catalyst in esterification reactions as it does not only provide protons, but also withdraws the formed water molecules by complexing them. For transesterification reactions it has been shown that the counter anion of the acid catalyst (which usually is sulfuric acid) participates in the transition state, at least if the solvent is nonpolar.[16]

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Case B comprises the possibility of the acid used to change the properties of the solvent and hence to act as a co-solvent. The effects of organic solvents in biomass conversion reactions have been reviewed by Shuai and Luterbacher[17]. Within this paragraph we will focus on the possible solvent effects of the acid on the catalyst, the reactants and the transition state. It should however be taken into consideration that solvent effects of the acid probably only appear in the case that high concentrations of these acids are used as we did for H_3PO_4 pH 1.0 (1.5 M), citric acid pH 1.4 (2.1 M), glycolic acid pH 1.8 (1.7 M) and acetic acid pH 2.0 (5.7 M). Although, only for H_3PO_4 pH 1.0 strongly deviating reaction rate constants have been identified, while the other systems rather stand out by a different reaction behaviour in terms of intermediate selectivity and yield, which we will discuss in next section.

While a possible co-catalytic effect of the acid used or especially the counterion should not be excluded, there is no doubt that the formation of HMF from fructose is catalysed by protons. In this context it is intriguing to note that the standard Gibbs free energy of the protons depends on the solvent. Thus, adding a co-solvent-like substance to the reaction medium may not only change the amount of protons, but also their activity or reactivity, respectively, which can have a significant effect on the overall reaction rate.[17]

Another effect can take place with respect to the reactant, *i.e.* the substrate which is fructose in our work. It is commonly known that hexoses appear in five different isomers that exist in an equilibrium: an *α*- and a *β*-furanose, an *α*- and a *β*-pyranose as well as an open-chain form. The ratio of these isomers does not only depend on the temperature, but also on the solvent.[18,19] Swift and co-workers[2] determined the effect of neglecting the isomer distribution on the apparent fructose dehydration rate and found a deviation by a factor of two. Hence, the isomer distribution is a relevant factor and the possible effect of the acid used on the isomer distribution should be taken into consideration.

The most obvious effect of the solvent on the reaction of a molecule arises from the fact that it always surrounds the molecule. In doing so, it affects the mobility of the molecule, the likeliness of protonation etc. In other words, the solvent has an influence on the transition state with various consequences.[17] Insofar, the co-solvent
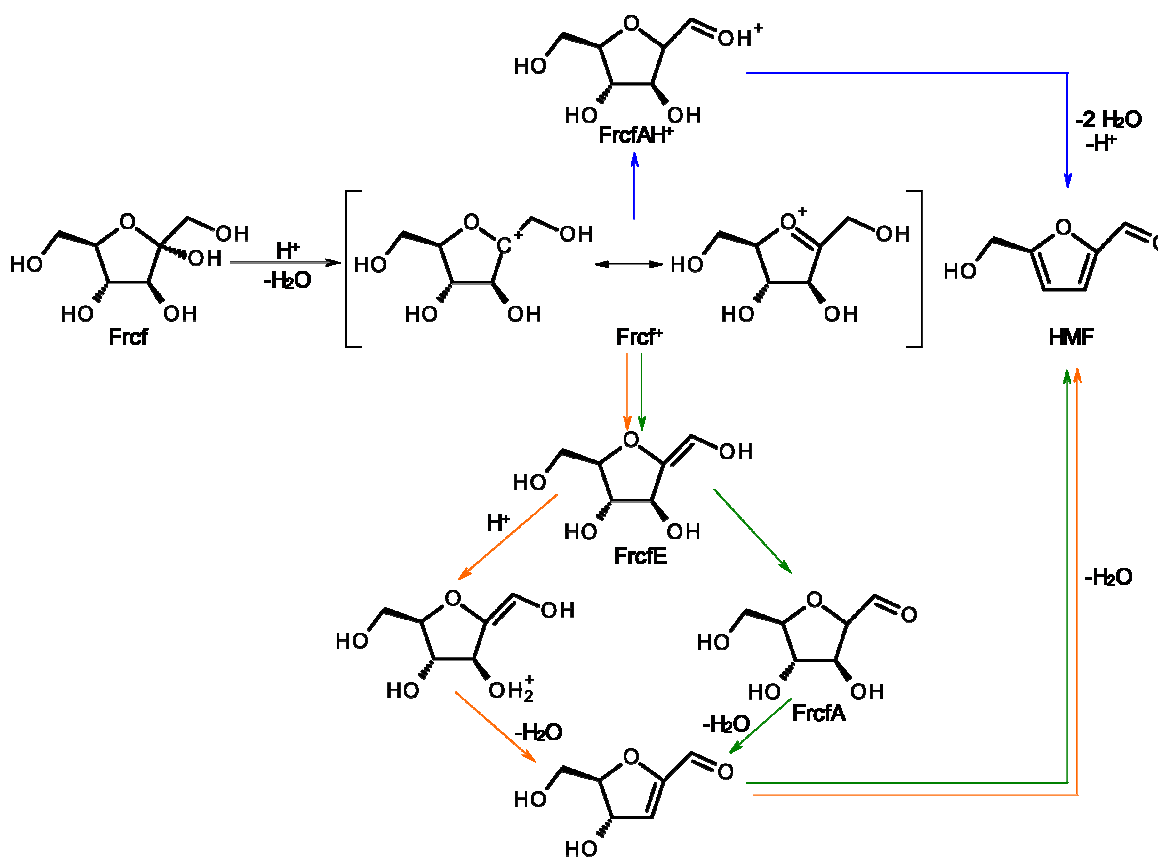

Figure 4   Different hypotheses about the HMF formation from the intermediate Frcf+ [20,21,22, 23]

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effect is comparable with a co-catalytic effect. The difference consists in that a co-catalyst is active at a low concentration due to a very specific interaction with the substrate, while a co-solvent must be present in a high amount.

Case C comprises the possibility of the acid molecule or the corresponding anion to form additional products with the substrate or intermediates that could either be dead-ends (or lead to dead-ends) of the reaction which would in particular affect the selectivity of the reaction, or that could be further intermediates of which formation can affect both, the selectivity and the velocity of the reaction.
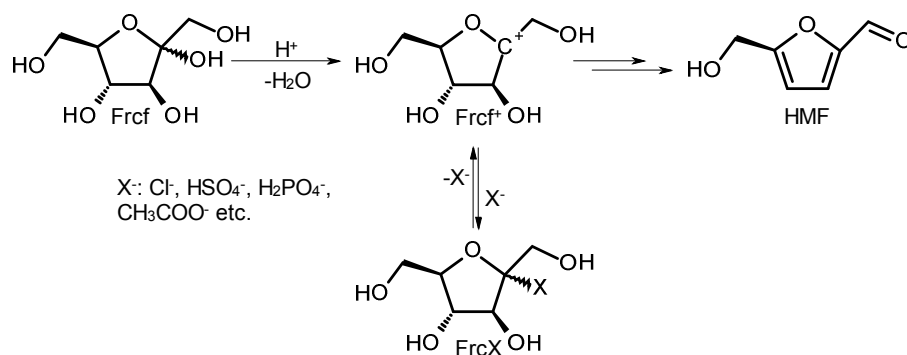

Figure 5   Possible formation of intermediate fructose derivatives by nucleophilic attack on Frcf$^+$

About the exact mechanism of the HMF formation from fructose no consensus has been reached, yet. Antal and co-workers[20] somehow ended the discussion whether it proceeds via an open-chain or a cyclic path. Since then, it is generally accepted that the first step comprises the abstraction of the hydroxyl group from C2 of fructo-furanose (Frcf) leading to a fructo-furanosyl cation (Frcf$^+$), which in the end yields HMF without any intermittent ring opening. About the further reaction of Frcf$^+$ different hypotheses exist, that are condensed in figure 4.

One assumption is that a subsequent abstraction of the proton from C1 takes place leading to an enol (FrcE) which in principle features an E_1 reaction. FrcE is then either isomerised to the corresponding aldehyde (FrcA) prior to the dehydration of the hydroxyl group from C3[20], or the dehydration from C3 takes place first, resulting subsequently in the formation of the aldehyde function[21,22]. Another assumption consists in a hydride shift taking place from C1 to C2 in Frcf$^+$ yielding somehow a protonated FrcA that is further dehydrated[23]. In an E_1 reaction, the abstraction of the leaving group usually is the rate-limiting step, while the subsequent deprotonation is fast. Swift et al.[2] studied the reaction of unlabelled fructose and fructose that is deuterated at C1. They found that both, the fructose conversion and the HMF formation proceed considerably more slowly in the case of deuterated fructose due to the kinetic isotope effect. This finding suggests that the abstraction of the proton or hydride from C1 is rate-limiting which contradicts the assumption that the first dehydration is a classic E_1 reaction. It also implicates that the formation of Frcf$^+$ is comparatively fast, which gives rise to the consideration that it may feature an attractive target for nucleophilic attacks as summarized in figure 5.

Of course, in an aqueous medium the most important nucleophile is water and, to some extent, hydroxide ions. The recombination of Frcf$^+$ with water or OH$^-$ ions, respectively, would simply yield fructose back. However, it is also imaginable that the acid used or especially the corresponding anion acts as nucleophile yielding fructose-2-phosphate or fructose-2-sulfate, for instance. Phan and co-workers[24] studied the hydrolysis of methyl glucopyranoside under non-hydrothermal conditions. They found that the hydrolysis rate constant is significantly larger in a HBr system compared with a HCl or H_2SO_4 system, even though the proton concentration should have been identically large in all three systems or even larger in the H_2SO_4 system. They attributed this finding to a direct participation of the Br$^-$ ion in the reaction. When the solvent was modified by adding 74% and 82% 1,4-dioxane, respectively, the reaction rate constants increased considerably, also in the case of the HCl system, which suggests that the nucleophilicity of chloride and bromide increases with increasing 1,4-dioxane content allowing them for a direct participation in the reaction. In the frame of a subsequent work[25], Phan et al. confirmed their assumption by demonstrating that the addition of KCl and in particular KBr to the respective system causes a further increase of

the reaction rate constant. It also increased in the case that KHSO$_4$ was added to the H$_2$SO$_4$ system, but the authors attribute this to the higher proton activity rather than to a direct participation of the anion. However, the formation of sulfated sugars is not in principle devious, as such compounds are formed to a large extent, if carbohydrates are treated with concentrated sulfuric acid[26]. Besides, numerous naturally sulfated polysaccharides such as agar, carrageenan and chondroitin sulfate are known. Also, sugar phosphates are common natural compounds whereby DNA is a prominent example. Phosphorylases produce glucose-1-phosphate from glucans via phosphorolysis. If chitin is treated with concentrated phosphoric acid, *N*-acetylglucosamine-1-phosphate is formed from an intermediate carbocation.[27] This reaction can even be used to determine the degree of *N*-acetylation in chitin/chitosan.[28] Overall, it seems permissible to assume that the acid used in the hydrothermal treatment of fructose is able to form fructose derivatives of the FrcX type. The contribution of especially halide ions in the fructose dehydration as both, nucleophile attacking on C2 and base removing the proton from C1 in order to form FrcfE, is also proposed in other works, even though non-aqueous solvents were used in those.[6,8]

The formation of FrcX ought to be understood as a S$_{N}$1 reaction, which consists of two partial steps: the dissociation of the leaving group from the molecule yielding a carbocation (Frcf$^+$ in this case), followed by the attack of a nucleophile. Normally, the first step is rate-limiting. Of course, the counterions of strong or medium strong acids are weak nucleophiles in aqueous media. However, because the second step of a S$_{N}$1 reaction is much faster than the first one, the nucleophilicity of X, does not affect the formation of RX, provided that X is available in a sufficient amount. Frcf$^+$ will literally react with the first nucleophile that comes along. Although, the nucleophilicity of X affects the stability of RX with regard to the re-dissociation, as a weak nucleophile is a good leaving group. As k$_x$ depends on [EH] (as we discussed a few pages ago), which in this case is identical with [Frcf$^+$], a change in the quasi-stationary concentration of [Frcf$^+$] has an impact on the HMF formation rate. We assume that the dissociation of FrcX into Frcf$^+$ and X$^-$ is fast, but its velocity depends on the stability of FrcX. Furthermore, we assume that the formation of FrcX is even faster, but its rate depends on the concentration of X. Eventually, we assume that the reaction of Frcf$^+$ towards HMF is slow: then the intermediate concentration of [Frcf$^+$] and hence the HMF formation rate increases with increasing amount of X and decreasing stability of FrcX. This could be the reason for

the enormously high k$_1$(H$_3$PO$_4$, pH 1.0) compared with the k$_1$ values in other systems even at higher proton concentration. Possibly, fructose-2-phosphate was formed in a significant amount, as large amounts of H$_3$PO$_4$/H$_2$PO$_4^-$ were available (the concentration of H$_3$PO$_4$ at pH 1.0 is roughly 1.5 M), which however is less stable than fructose itself. This results in a higher quasi-stationary concentration of Frcf$^+$ and thus in a higher HMF formation rate. By contrast, fructose-2-chloride and fructose-2-sulfate were not formed in a significant amount within the respective systems due to the low concentration of chloride (0.063 M) and hydrogensufate (0.060 M), respectively. This renders these systems much more close to an exclusively Brønsted acid catalysed system.

Selectivity of the HMF and LA formation from fructose

The yield and the selectivity of HMF and also of LA formation strongly depend on the reaction time which is influenced by the reaction temperature, the solvent and the catalyst. They also depend on the kind of carbohydrate used as educt[29,30], though within the frame of this work we focus on the conversion of fructose. Generally speaking, a short reaction time leads to low HMF and LA yields while the selectivity with regard to HMF might be relatively high. This is attributed to a low fructose conversion. Conversely, a long reaction time can also be the reason for low HMF yields and selectivities due to decomposition or polymerisation of the substance. In return, the LA yield increases. This ambivalent behaviour of HMF renders it difficult to classify the effect of certain reaction conditions, if only few reaction times were studied.

Asghari & Yoshida[3] investigated the effect of various acids at different pH values at 240°C and a residence time of 120 s on the formation of degradation products from fructose in water. Even though their results are not easily comparable with those in our work, as they did not only employ a higher reaction temperature, but especially do not provide any reaction rate constants, they were able to show that the HMF yield differs for different acids even at same room temperature pH. We plotted a selection of their data against the initial proton concentration in figure 6, left, where it can be seen that there are apparently large differences in HMF and LA yields within one pH value. However, if we calculate the actual proton concentrations at 240°C, similarly as we did it with our own data, and plot the yields against them, a more reasonable picture appears. As it can be seen in

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figure 6, right, the highest HMF yields are achieved at low proton concentration when only little degradation to LA has taken place. With increasing proton concentration, the HMF yield decreases while the LA yield increases. Still, there are significant differences in the HMF yield even at similar proton concentration: way better yields are achieved with H_3PO_4 than with HCl/H_2SO_4, which suggest that the HMF formation in

H_3PO_4 is either faster or more selective. At least the former assumption would be in accordance with our finding of a much larger $k_1(H_3PO_4$, pH 1.0).

The fructose dehydration has been studied in various reaction systems. In a purely aqueous system, *i.e.* without catalyst, HMF yields up to 56% were achieved with a selectivity of 78%, when 4.5 wt% fructose were
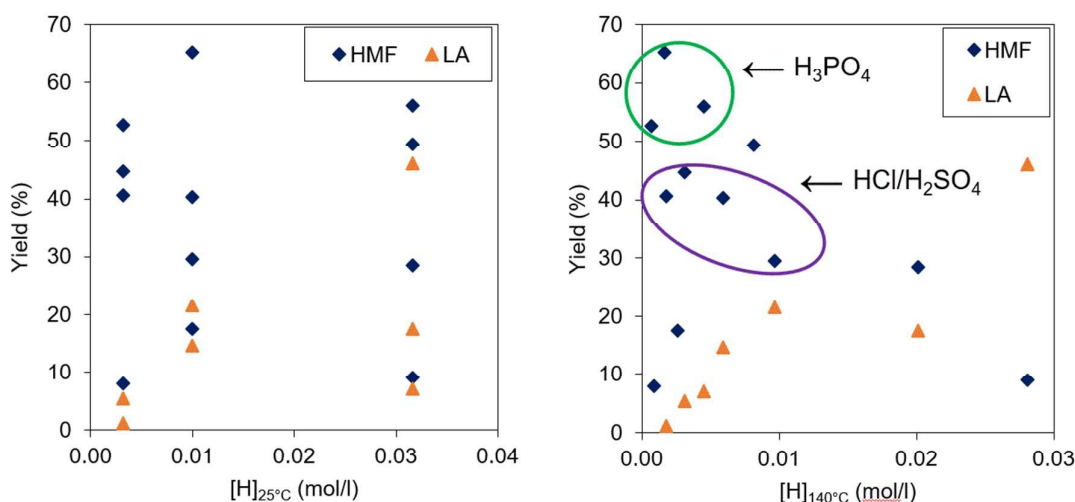

Figure 6 Data from Asghari & Yoshida[3]; HMF (blue) and LA (orange) yield plotted against [H]

dehydrated at 175°C for 1.5 h.[31] With 11 wt% fructose at 200°C for 30 min 51% HMF were achieved with a selectivity of 57%.[32] The presence of Brønsted acid catalysts seemingly tends to decrease the reaction time, which however is not necessarily favourable for the HMF yield, because the HMF rehydration which gives LA is also acid-catalysed. In 1 mM H_2SO_4 9 wt% fructose yielded 23% HMF with a selectivity of 25% after 5 min at 200°C.[11] From 4.5 wt% fructose in 16 mol% H_3PO_4 at 240°C and 4 mol% H_3PO_4 at 260°C, respectively, 40% HMF were produced.[4] At 95°C, 9 wt% fructose in 400 mol% HCl gave 26% and 30% HMF with a selectivity of 57% and 48% after 16 and 24 min, respectively.[33] An interesting effect can be stated for the use of formic and acetic acid as catalyst, because comparably high yields were achieved with 56% and 58% at a selectivity of 61% and 64% after 10 and 20 min, respectively, at 200°C and a catalyst loading of 100 wt%.[32]

In one case, even a selectivity of 100% is reported for the conversion of 4.5 wt% fructose in formic acid pH 2.7 at 175°C after 45 min. The yield was 56%.[31] Possibly, the presence of acetic and formic acid, which are degradation products, prevents side and subsequent reactions by shifting the equilibrium state. At least, a divergent

behaviour of acetic acid in the dehydration of fructose can also be concluded from our data.

The utilisation of heterogeneous catalysts in aqueous media leads to a large range of yields and selectivities, depending on the reaction conditions. However, they usually are not larger than with homogeneous catalysts. In non-aqueous, especially aprotic solvents significantly better yields and selectivities towards HMF are achieved, which can be attributed to the missing rehydration in the absence of water, among other reasons.[1]

In order to find an appropriate basis for the comparison of HMF yield and selectivity in dependence on the catalyst, The analytical solutions of the kinetic model for [Frc] and [HMF] were used to calculate the theoretical maximal HMF yield (Y_{max}), the reaction time to achieve Y_{max} (t_{Ymax}), the fructose conversion and the selectivity at Y_{max} (C_{Ymax} and S_{Ymax}, respectively) for each acid as described within the method section. As it can be seen in table 1, the highest Y_{max} is achieved in the acetic acid system while the H_2SO_4 systems gives the lowest yield. Although, the differences in Y_{max} as well as in S_{Ymax} between different systems are not significant. In this context, it has to be stressed that Y_{max} is not lower for higher pH values. It is only a matter of time when it is achieved which is an interesting finding. Swift and co-

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workers[2] found that Y_{max} depends on the reaction temperature as it was higher for higher temperatures. Obviously, an analogue effect does not take place in case of the initial pH value (at least, if it is 2 or below). t_{Ymax} expectedly increases with increasing pH value, but fluctuates strongly even for identical pH values. Also, C_{Ymax} differs for different systems such as in the acetic acid system it is possible to aim at a nearly complete fructose conversion in order to achieve Y_{max}, while in the HCl system a conversion exceeding 75% lowers the HMF yield. With regard to a technical process, the latter case is of course not favoured as it either means that a significant percentage of the substrate is dissipated or a recycling is required.

The discussion of yield, conversion and selectivity as a function of the reaction time is often hindered, because multiple diagrams must be used to depict the relation. In order to facilitate the representation of all four parameters, we developed the CYS plot which is a single diagram for an entire reaction. From the representation of the reaction of fructose to HMF within a CYS plot (figure 1) we learn that for most acids investigated in our work the reaction follows an identical path, even though the reaction rates differ drastically in some cases. The divergent behaviour of concentrated citric acid (pH 1.4) and acetic acid indicates that either a different reaction mechanism takes place in these solvents, or the relations of the elementary reaction rates differ. Especially, the behaviour of the acetic acid system might be explainable with hypotheses proposed previously: First, as a degradation product acetic acid may shift the equilibrium state preventing the degradation of fructose to other products than HMF. Second, it may act as a co-solvent influencing the transition states, for instance, as it is present in a high amount (5.7 M). Third, acetate may contribute to the dehydration of fructose by forming 2-*O*-acetlyfructose or other intermediates which, in the beginning of the reaction, causes a high fructose conversion without HMF formation what is indeed observed in our experiments. Later, these intermediates may react more selectively towards HMF, which is why in the end the highest yields were obtained with the acetic acid system.

Considering the CYS plot of the reaction of fructose to LA (figure 1), we find three types of courses: In the case of HCl, HNO₃ and H₂SO₄, high LA yields are already achieved even before all fructose is converted into HMF. In the consequence, the maximal HMF yield should be lower for these acids which in principle is true according to Y_{max} we calculated for them (table 1). On the other hand, the selectivity towards LA is high preventing side-reactions of HMF. In the case of acetic and glycolic acid,

the LA yield is low, even at high fructose conversion and after long reaction times. Interestingly, this is not reflected in the selectivity towards HMF that is not higher compared with the other systems. Obviously, the low rehydration rate is compensated by higher side-reaction rates. In the case of phosphoric and citric acid, the LA yield does not exceed 30% before nearly all fructose is converted which makes these acids more suitable catalyst for processes that strive selectively for HMF.

The curve progressions denoted here correlate perfectly with the ratio of LA formation to fructose conversion (*i.e.* $k_2/(k_1 + k_3)$) which is 0.54 and 0.53 for HCl and HNO₃, respectively, 0.31 for H₂SO₄ and 0.10 and 0.01 for glycolic and acetic acid, respectively. For phosphoric and citric acid, it fluctuates between 0.19 and 0.25. It is interesting to note that, even though k_1(H₃PO₄, ,pH 1.0) and k_2(H₃PO₄, pH 1.0) have been found to be exceptionally high, the $k_2/(k_1 + k_3)$ ratio is similar to that of citric acid and more diluted H₃PO₄.

A final important observation is that the selectivity towards HMF initially increased, especially at the higher pH values investigated. This might be unexpected when considering that the HMF formation always has to compete with the HMF degradation and polymerisation. In addition, it contradicts the outcome of other works.[2] Although, it can be attributed to the assumption that an intermediate is formed from fructose of which consumption, not formation, is rate-limiting in the HMF formation. Hence, the initial fructose consumption is faster than the initial HMF formation, which is reflected in a lower selectivity at the beginning of the reaction. However, this kind of behaviour is possibly not observed at all reaction conditions and in particular not, if the reaction proceeds fast due to a low pH value and/or a high temperature. Also, it requires that the intermediate does not occur in a quasi-stationary state, but that its concentration depends on the amount of fructose or fructose derivative, respectively.

Experimental
Material

Fructose, phosphoric acid, sulfuric acid, hydrochloric acid, nitric acid, citric acid, glycolic acid, acetic acid, methanol, acetonitrile and trifluoroacetic acid were purchased from VWR. The analytical standards levulinic acid and 5-Hydroxymethylfurural were purchased from VWR and Sigma Aldrich, respectively.

Procedure

100 g/l fructose are dissolved in the respective aqueous acid. The initial pH is determined with a pH probe. 10.6 ml of the resulting solution are filled into a stainless-steal microautoclave (total volume ≈ 15 ml) and heated up to 140°C in a modified GC oven. Reaction time (t_R) counts from reaching 139.0°C (*i.e.* t_R = 0 min), the preheating time is around 15 min. After the respective reaction time, the microautoclave is removed from the oven and quickly cooled down in a water bath. The product solution is analysed by HPLC.

Analysis

HPLC analysis was carried out in a Shimadzu Prominence System comprising a refractive index detector.

For the determination of the fructose content, a YMC-Pack Polyamine II column (250 x 4.6 mm I.D.) was used. The measurements were run isocraticly with 78:22 acetonitrile:water containing 10 mM ammonium formiate as the eluent at a flow rate of 1.0 ml/min and an oven temperature of 35°C.

For the determination of the HMF and LA content, a Luna C18 column (150 x 4.6 mm I.D.) was used. The measurements were run isocraticly with 20:80 methanol:water containing 0.1% trifluoroacetic acid as the eluent at a flow rate of 0.5 ml/min and an oven temperature of 25°C.

Prior to each measurement, the samples were filtered through a syringe filter. A dilution was not necessary. The injection volume was 30 μl per analysis.

Kinetic model

The reaction pathways in scheme 1 were used to set up a kinetic model of the reaction network (equ. 9-12).
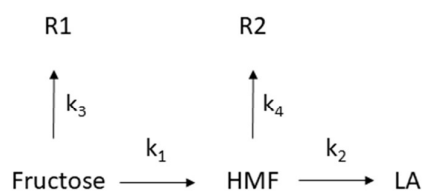
Scheme 1   Proposed reaction pathways for fructose conversion to HMF and levulinic acid. R1 and R2 are unknown decomposition products.

$$\frac{d[Frc]}{dt} = -k_1[Frc] - k_3[Frc] \tag{9}$$

$$\frac{d[HMF]}{dt} = k_1[Frc] - k_2[HMF] - k_4[HMF] \tag{10}$$

$$\frac{d[LA]}{dt} = k_2[HMF] \tag{11}$$

$$\frac{d[R_1 + R_2]}{dt} = k_3[Frc] + k_4[HMF] \tag{3}$$

With k_1, k_2, k_3, k_4 the reaction rate constants and $R_1 + R_2$ as the undefined degradation products from fructose and HMF. *[Frc], [HMF], [LA]* and *[$R_1 + R_2$]* are the molar concentrations (mol/l) of the substances.

The calculation of the reaction rate constants has been done with MATLAB R2015b by numerical integration of equations 9-12 with *ODE45* followed by an optimization with the *lsqnonlin* tool.

Determination of yield, conversion and selectivity

Product yield *Y*, educt conversion *C* and selectivity of the reaction *S* are calculated using equ. 13-15 for both, the experimental and the theoretical data.

$$Y = \frac{c_P v_E}{c_E v_P} \tag{4}$$

$$C = \frac{c_{E0} - c_E}{c_{E0}} \tag{5}$$

$$S = \frac{Y}{C} \tag{6}$$

For the calculation we used the molar concentration instead of the amount of substance, as in principle there is no volume change during the reaction on the one hand and the exact determination of the amount of substance would be more error-prone on the other hand.

Basing on the kinetic model applied (scheme 1), the analytical solutions for *[Frc]* and *[HMF]* have been identified (equ. 16 and 17).

$$[Frc] = [Frc]_0 e^{-(k_1+k_3)t} \tag{7}$$

$$[HMF] = \left(\frac{k_1[Frc]_0}{-k_1 - k_3 + k_2 + k_4} \left[e^{(-k_1-k_3+k_2+k_4)t} - 1 \right] + [HMF]_0 \right) e^{-(k_2+k_4)t} \tag{8}$$

In order to determine the theoretical maximum yield (Y_{max}) as well as C_{Ymax} and S_{Ymax}, [Frc]$_{Ymax}$ and [HMF]$_{Ymax}$ are obtained from equ. 16 and 17, respectively, by applying $t = t_{Ymax}$. t_{Ymax} is obtained by equating equ. 10 with zero.

Computational determination of the proton concentration at elevated temperature

The determination of the proton concentration at reaction temperature bases on a model developed by Helgeson[34], in which the pK_a as a function of the temperature is calculated from the free energy of dissociation. Helgeson also provides a set of parameters for different acids. Details about these calculations can be found in the supplementary information.

Conclusion

Within the frame of this work we pointed out that the effect of Brønsted acids on the hydrothermal dehydration of fructose to HMF exceeds the sole donation of catalytically active protons. In fact, there are additional effects caused by the type of acid, which can be identified as a change in the overall reaction velocity or mechanism and that become the more relevant, the higher the acid concentration is. Interestingly, the type of acid used has however only a low impact on the maximal HMF yield. Future investigations will target a better understanding of the substrate-catalyst interaction.

Acknowledgement

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