Green Chemistry

Microwave assisted conversion of carbohydrates and biopolymers to 5-hydroxymethylfurfural with aluminium chloride catalyst in water[†]

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The common Lewis acid AlCl₃ has efficiently produced 5-hydroxymethylfurfural (HMF) from carbohydrate and biopolymer substrates in water, DMSO, and water–methylisobutylketone biphasic solvents under microwave irradiation. The yield of HMF in different solvents follows an increasing order from water to water–MIBK biphasic solvent to DMSO. The yield of HMF increased with an increase in catalyst loading whereas it remains unchanged upon increase of the carbohydrate concentration. In most reactions, the maximum yield of HMF is recorded within 2 min of reaction time. The mechanism of the AlCl₃ catalyzed glucose dehydration reaction is proposed to proceed through the isomerization of glucopyranose to fructofuranose, followed by a proton assisted transformation of fructofuranose to HMF.

1. Introduction

Irreversible consumption of carbon sources by humankind resulted in diminishing reserves of fossil fuels and global warming by CO₂ emission.¹ This issue has prompted a shift of economy to replace fossil-based resources with renewable and sustainable ones.² In this context 5-hydroxymethylfurfural (HMF) has received significant attention as a platform chemical for synthesizing a broad range of chemicals and liquid transportation fuels.³ Carbohydrates constitute 75% of the world's renewable biomass and cellulose.4 The dehydration of fructose and glucose serve as model reactions for the synthesis of HMF from biomass-derived carbohydrates since the conversion to HMF always involves these sugars in the final reaction sequence.5 Recently, fructose and glucose have been converted to HMF in high yields with Cr(II) or Cr(III) halide catalysts in imidazolium ionic liquids.6 In recent years, research efforts for developing sustainable methods of HMF production from various carbohydrates with Lewis acid catalysts have been limited to the use of ionic liquid solvents. Among these efforts, HMF synthesis from carbohydrates, including glucose, was accomplished by various catalytic systems. A catalytic system consisting of Cr(II) or Cr(III)-chlorides and bulky N-heterocyclic carbene ligands produced high yields of HMF from fructose and glucose.⁷ A SnCl₄ catalyzed dehydration reaction of glucose produced 60% HMF in 1-ethyl-3-imidazolium tetrafluroborate

([EMIM]BF₄) at 100 °C.⁸ Tungsten salts (WCl₄, WCl₆) acted as Lewis acid catalysts for glucose conversion in 1-butyl-3imidazolium chloride [BMIM]Cl solvent and produced 72% HMF at mild reaction conditions (50 °C).9 In more recent studies, GeCl₄ in [EMIM]BF₄ catalytic system produced 92.1% HMF from fructose at 100 °C.10 The catalytic conversion of fructose to HMF with boric acid (B(OH)₃) has been reported to produce 46% HMF in biphasic water-methylisobutylketone (MIBK) solvent at 150 °C.11 The lanthanide salt-based catalytic systems have been reported to produce 24% HMF yield at 140 °C in 6 h from glucose.12 In limited cases, the synthesis of HMF using mixed Brønsted and Lewis acid catalysts13 and the microwave-assisted14 reactions from cellulose and sugar derivatives were reported to be successful. Among the reports on the microwave (MW) assisted green synthesis of HMF, concentrated HCl catalyzed dehydration of fructose produced 63% HMF in water. However, the selectivity of HMF decreased when the reaction was carried out for more than 1 min.^{14a} Microwave assisted glucose dehydration with butyl-3-imidazolium chloride [BMIMCl]/CrCl₃ (10 mol%) catalyst produced 71% HMF in 0.5 min. The yield of HMF decreased to 67% upon continuing the reaction for 1 h.^{14d} However, potential drawbacks of these methods using ionic liquids is that ionic liquids are expensive and hence probably not suitable candidates for developing an economically favourable and scalable HMF production method.

Therefore, it is beneficial to replace expensive ionic liquid solvents with aqueous and/or mixed aqueous biphasic and highly polar aprotic organic solvents for the sustainable synthesis of HMF from carbohydrates. Regardless of recent developments of metal salt catalyzed synthetic methods for HMF production, it remains highly challenging to develop a sustainable route for HMF production from carbohydrates and biopolymers in environmentally benign solvents. In a continuation of our

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Scheme 1 The microwave assisted transformation of fructose or starch to HMF with AlCl₃ catalyst.

ongoing research program in developing Lewis acid and metal salt catalyzed dehydration of biomass derived sugars and cellulosic biomass, we have studied the microwave (MW) assisted technique of HMF synthesis from various sugar derivatives with a strong Lewis acid catalyst. AlCl₃ is known as an effective Lewis acid catalyst for HMF synthesis in ionic liquid ([BMIMCl]).9 However, the catalytic effectiveness of AlCl₃ for HMF synthesis has not been reported in aqueous or mixed aqueous solvents under microwave irradiation. The present paper describes the transformation of carbohydrates (fructose, glucose, sucrose) and biopolymers (inulin, starch) into HMF in environmentally benign solvents with anhydrous and hydrated AlCl₃, and AlBr₃ Lewis acid catalysts (Scheme 1).

Experimental 2.

Materials and experimental methods 2.1

Substrates (fructose, glucose, sucrose, starch and inulin) and solvents (DMSO, MIBK) were purchased from Sigma Aldrich and used without further purification. The starch sample, was dried under vacuum at 100 °C for 24 h before use. Anhydrous and hydrated AlCl₃, AlBr₃, and Yb(OTf)₃ were purchased from Sigma Aldrich and used without further purification. SnCl₄ was purchased from Spectrochem, India and used without further purification. Unless otherwise mentioned, distilled water was used as the aqueous phase and anhydrous AlCl₃ was used as catalyst for all reactions. The catalytic conversion of carbohydrates to HMF was performed in a CEM Matthews WC Discover Microwave reactor, (model: Discover System, no. 908010 DV9068) at the standard operating frequency of a microwave synthesis reactor (2.45 GHz, power 300 Watt). ¹H NMR spectra were recorded on a JEOL JNM ECX-400 P 400 MHz instrument and NMR data were processed with JEOL DELTA program version 4.3.6. Progress of the reaction was monitored by ¹H NMR spectroscopy in limited cases. HMF yields were measured by both UV-visible spectrophotometric (UV-SPECORD 250 analytikjena) and NMR spectroscopic techniques.

HMF production

Dehydration of carbohydrate using microwave irradiation

The dehydration reactions of carbohydrates, ca. D-fructose, glucose, sucrose and biopolymer substrates, were carried out by charging substrates, solvent and catalyst in a microwave tube under the reaction conditions mentioned in Tables 1 and 2. The microwave tube was then inserted into the microwave reactor pre-set at the desired temperature and reaction time.

Upon completion of the reaction for the set reaction time, the reactor was opened. The temperature of the reaction mass was cooled down to room temperature before analyzing the product using NMR spectroscopic and UV-Visible spectrophotometric techniques.

In the case of the DMSO solvent mediated reaction, HMF was isolated from the reaction mixture by distilling out DMSO at reduced pressure and then extracting the residue as the organic layer with diethyl ether after adding water into the DMSO separated residue. The organic layer was collected in a preweighed empty vial and dried under vacuum. After drying off the solvent, the weight of the vial was recorded. The yield of isolated HMF was determined by subtracting the weight of the HMF-containing vial from that of empty vial.

Dehydration of carbohydrates using oil-bath heating. The synthesis of HMF from carbohydrates was also carried out in a round bottom flask by oil-bath heating. For oil bath heating, a glass round bottom flask was charged with substrate, solvent and catalyst, and then refluxed in an oil bath. After completion of reaction, the reaction mixture was cooled down to room temperature and analyzed by UV-Visible spectrophotometric and ¹H NMR spectroscopic techniques.

Catalyst life-time study

The life-time of the catalyst was studied by recycling the reaction mixture containing the spent catalyst. Prior to recycling for the next run, the HMF component was extracted from the reaction mixture with diethyl ether and fresh substrate was added into the reaction mixture. Fresh AlCl₃ catalyst was not added to compensate any loss of the catalyst in the prior runs.

Determination of HMF yield

The yield of HMF was determined by both 1H NMR and UV-Visible spectrophotometric techniques. For ¹H NMR spectroscopic analysis, HMF was extracted from the reaction mixture with diethyl ether. Pale yellow oily HMF was obtained after removing the solvent in vacuum at room temperature.

¹H NMR method. For quantifying the yield of HMF using ¹H NMR spectroscopic technique, a known concentration of mesitylene (internal standard) was added into the HMF product solution in DMSO- d_6 . The percentage of HMF yield was calculated by using the integrated values of the aldehyde proton (δ = 9.58 ppm) of HMF and three aromatic ring protons of mesitylene ($\delta = 6.79$ ppm) (Fig S1[†]). First, a standard HMF solution of 99% purity was analyzed for correlating the percentage of actual and calculated amount of HMF.

						HMF Yield (%)		
Entry	Fructose (wt%)	AlCl ₃ (mol%)	Solvent	<i>T</i> (°C)	t (min)	¹ H NMR	UV-Vis	Isolated
1	5	50	Water/MIBK	130	5	60.1	61.2	
2ª	5	50	Water/MIBK	130	5	61.6	63.3	61.0
3	5	50	Water	120	5	51.4	53.9	50.2
4	5	40	Water	120	5	50.6	51.5	
5	5	25	Water	120	5		40.9	
6	5	50	Water	120	15	_	55.1	
7	5	50	Water	120	10	_	54.6	
8	5	50	Water	120	2	_	52.3	
9	5	50	Water	120	20	53.3	55.7	52.7
10	5	50	DMSO	100	5	_	42.9	
11	5	50	DMSO	140	5	70.1	71.3	69.4
12	5	_	DMSO	100	5	_	3.5	
13	5	_	DMSO	140	5	21.4	22.0	
14	5	50	Water	120	5	54.8	55.3	
15	15	50	Water	120	5	51.0	52.6	50.1
16	30	50	Water	120	5	51.4	52.1	50.8
17 ^a	5	50	Water/THF	100	5	57.9	59.0	
18	5	50	Water	120	0.5		47.8	
19	5	40	Water	120	2		55.1	_
20	5	40	Water	120	15	45.7	47.0	45.5
21	5	25	Water	120	2		38.0	_
22	5	25	Water	120	10		42.3	_
23	5	25	Water	120	15	42.8	43.4	
24	10	50	Water	120	5	51.2	53.5	51.9
25	5	_	Water	120	5		0.8	_
^a NaCl (50	(mg) For hinhasic solve	nte aqueque : organic	$r = 1 \cdot 2$ volume ratio ((mL) was used				

Table 1 The AlCl₃ catalyzed dehydration of fructose to HMF under microwave irradiation

Table 2	Conversion	of fructose to	HMF	catalyzed by	AlCl ₃	under	oil-bath	heating
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				HMF Yield (%)			
Entry	Fructose (wt%)	AlCl ₃ (mol%)	Solvent	¹ H NMR	UV-Vis	Isolated	
1	5	50	Water/MIBK (2/8)	32.2	33.4	_	
2ª	5	50	Water/MIBK (2/8)	33.5	36.1	33.4	
3	5	50	Water	13.0	14.1		
4	5	50	DMSO		30.7		

Once a good correction was established, the extracted HMF product samples were run and the percentage of HMF yield was calculated.

UV-Visible spectrophotometric method. The UV-Visible spectrum of pure HMF solution (Fig. S2[†]) has a distinct peak at 284 nm with a corresponding extinction coefficient (ε) value of 1.66 × 10⁴ M⁻¹ cm⁻¹. The percentage of HMF in each of the reaction products, as tabulated in Table 1, was calculated from the measured absorbance values at 284 nm and the extinction coefficient value. Repeated measurement of the same solution showed the percentage of error associated with this measurement was $\pm 3\%$. The yield of HMF obtained from two different methods (1H NMR and UV-Visible) for the same reaction product agreed very well and the result was within $\pm 5\%$ error (Table 1).

Results and discussion 3.

Several experiments were designed for studying the catalytic dehydration of carbohydrates to HMF under various experimental

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conditions, such as the nature of solvents, catalysts, catalyst concentrations, nature of substrates, substrate concentrations, reaction time etc. The purpose for designing these experiments are: (i) identification of an effective substrate for the synthesis of HMF in an aqueous medium and (ii) optimization of reaction conditions for maximizing HMF yield. The effect of several reaction parameters on HMF yield and catalysts effectiveness are described below.

3.1 Effect of solvents on HMF yield

The dehydration reactions of carbohydrates (fructose, glucose, sucrose) with the AlCl₃ catalyst were carried out in water, DMSO and water-MIBK biphasic solvents under microwave irradiation to investigate the effect of different solvents on HMF yield. Details of reaction conditions and the corresponding HMF yields are summarized in Tables 1 and 2. Under identical reaction conditions, water, water-MIBK and DMSO solvent mediated fructose dehydration reactions produced 53.9%, 61.2% and 71.3% HMF (entries 1, 3, 11 in Table 1), respectively. The higher

Entry	AlCl ₃ (mol%)	Solvent	<i>T</i> (°C)	<i>t</i> (min)	HMF yield (%)
1	50	Water	120	5	37.3
2ª	50	Water/MIBK	130	5	43.7
3	50	Water/MIBK	130	5	43.0
4	50	DMSO	140	5	6.4
5	50	DMSO	140	5	52.4
6	50	Water	120	2	35.1
7	50	Water	120	10	39.0
8	50	Water	120	15	39.8
9	50	Water	120	20	40.3
10	33	Water	120	5	30.2
11	33	Water	120	15	33.6
12	20	Water	120	5	25.4
" NaCl (50 mg	g), Glucose = 5 wt%.				

Table 3 Results of glucose dehydration catalyzed by AlCl₃ under MW irradiation

HMF yield in DMSO solvent in comparison to that in aqueous medium for all carbohydrate substrates can be attributed to the (i) higher microwave absorbing ability of DMSO, as measured by the higher tangent value of DMSO (tan δ 0.825) than water (tan δ 0.123),¹⁵ (ii) avoidance of the side reactions in DMSO that occur in aqueous medium¹⁶ and (iii) catalytic ability of DMSO in converting fructofuranose to HMF *via* a 5-membered cyclic mechanism at a higher temperature (150 °C) without any added catalyst.¹⁷ These positive characteristics of DMSO accounted for its use as a solvent so that a comparison of HMF yields in different solvents can be drawn. The lower HMF yield in water is due to the rehydration of HMF and the formation of levulinic and formic acids as side-products.

On the other hand, the higher HMF yield in water–MIBK biphasic solvent than in water is due to the driving force of the biphasic mixture in which HMF accumulates in the organic phase after its formation in the aqueous phase. This method of HMF synthesis in a biphasic solvent also produced pure HMF, as evidenced from the clean ¹H NMR spectrum of the HMF product collected from the MIBK layer (Fig. S3[†]).

It is reported that the salting-out effect¹⁸ has a positive influence in increasing HMF yield in a biphasic solvent mediated dehydration reaction. This effect was observed in boric acid catalyzed fructose dehydration in aqueous-organic biphasic medium upon addition of NaCl and similar alkali metal salts.¹¹ To check the salting-out effect in the present study, the dehydration reactions of 5 wt% fructose and 5 wt% glucose were carried out with an AlCl₃ catalyst in biphasic aqueous-MIBK solvent using NaCl salt. The results as tabulated in Table 1 (entries 1 and 2), Table 2 (entries 1 and 2) and Table 3 (entries 2 and 3) suggested that the effect of NaCl on HMF yields was insignificant. A comparison of the results between entry 2 of Table 1 and entry 2 of Table 2 also revealed that HMF formation from the oil bath heating experiment for the optimized reaction time was significantly lower (36%) than that of microwave assisted heating (63%) experiment. To further check the salting-out effect, additional experiments were performed for a 30% fructose dehydration reaction with an AlCl₃ catalyst in the presence of Na2SO4, NaBr, and NaNO3 salts. The results confirmed no significant effect of these salts on HMF yield in biphasic aqueous-MIBK solvent.

 Table 4
 Results of 30 wt% fructose dehydration with AlCl₃ catalyst at variable catalyst loading

a	Fructose (wt%)	AlCl ₃ (mol%)	HMF yield (%)
1	30	50	52.1
2	30	40	48.6
3	30	33	46.0
4	30	25	38.8
5	30	20	35.8

Solvent = water (2 mL), $T = 120 \degree \text{C}$, $t = 5 \min$, MW.

3.2 Effect of the starting fructose concentration on HMF yield

The literature report suggests that HMF yield and selectivity depend on the starting fructose concentrations. Humin is one of the side reaction products of the fructose dehydration reaction. The percentage of humin formation is reported to increase with an increase in starting fructose concentrations, and thereby lower the desired HMF yield. The formation of humin can be as high as 35% for 18 wt% fructose solution and 20% for 4.5 wt% fructose solution in water.19 Therefore, a significant loss of HMF yield has been reported in aqueous medium. To study this effect, the starting fructose concentrations were varied from 5 wt% to 30 wt%. Under identical reaction conditions of 50 mol% of AlCl₃ and at 120 °C in water, the yield of HMF changed from 53.9% to 52.1% (Fig. 1(a)). Thus, HMF yield remain unchanged upon increase in fructose concentrations from 5 wt% to 30 wt%. Additional experiments for the dehydration of highly concentrated fructose (30 wt%) at 120 °C under microwave assisted heating (Table 4) showed an appearance of insoluble brown material in the solution. Attempts were made to analyze the brown material using ¹HMR spectroscopy; however, due to poor solubility of this brown material in most deuterated solvents, signals were not intense (Fig. S4[†]). Inspection of the ¹H NMR spectrum in DMSO-d₆ confirms the presence of signals corresponding to two furan ring protons and a -CHO group proton (δ 9.50 ppm). This brown insoluble material is believed to be humin as mentioned in the literature.²⁰ Thus, the probability of loss of HMF to the form of humin may be high when the reaction starts with concentrated fructose solution (ca. 30 wt%) in aqueous medium.20



Fig. 1 (a) The effect of HMF yields on (a) fructose concentrations at fixed AlCl₃ loading (50 mol%), and (b) AlCl₃ catalyst dosage for 5 wt% fructose dehydration in water at 120 $^{\circ}$ C MW heating for 5 min.

3.3 Effect of the catalyst dosage on HMF yield

The dehydration reaction of fructose to HMF was studied at variable catalyst concentrations for optimizing the reaction conditions and maximizing the HMF yield. The concentrations of AlCl₃ were varied from 20 mol% to 50 mol% while other reaction parameters were constant at [fructose] = 5 wt%, T =120 °C, reaction time = 5 min and solvent = water. As shown in Fig. 1(b), the yield of HMF increased from 37.2% to 53.9% with an increase in AlCl₃ concentration from 20 mol% to 50 mol%. The high catalyst loaded experiments improved HMF yield, meaning that the kinetic of fructose dehydration is fast in the case of higher catalyst loading. It has been shown in section 3.2 that HMF yields remain unchanged upon increase in starting fructose concentration from 5 wt% to 30 wt%. This prompted us to further study the catalyst variation experiments using concentrated fructose solution (ca. 30 wt%). The results, as tabulated in Table 4, show the yield of HMF increased from 35.8% to 52.1% upon increase in catalyst loading from 20 wt% to 50 wt% (Table 4). Thus, the trend of HMF formation against AlCl₃ loading for 30 wt% fructose dehydration was similar to that obtained for 5 wt% fructose dehydration.

3.4 Effect of reaction time on HMF yield

The reaction time of the dehydration reaction was varied to study the rate of HMF formation as a function of time. As plotted in Fig. 2, the yield of HMF improved from 47.8% to 52.3% upon increasing the duration of the reaction from 30 s to 2 min for AlCl₃ catalyzed dehydration of fructose at 120 °C. Further increase in reaction time to 20 min under similar conditions resulted in 55.7% HMF yield. Thus, the kinetics of HMF formation are rapid in first 0.5 min followed by a slow reaction. This behavior of increasing HMF yield with an increase in reaction time agreed well with the trend observed for fructose dehydration in water and water–DMSO solvent using mineral acid and an ion-exchange resin catalyst under MW heating.^{14a,21} A similar trend of slow HMF yield after 0.5 min of reaction time was observed for AlCl₃ catalyzed dehydration of glucose and sucrose as well. Under comparable reaction conditions, glucose



Fig. 2 The effect of reaction time on HMF yield for the conversion of carbohydrates (fructose, glucose, sucrose) to HMF in water under microwave heating at 120° . The concentrations of carbohydrate and AlCl₃ are 5 wt% and 50 mol%, respectively.

and sucrose dehydration reactions showed 5% and 7% increase in HMF yield during 2–20 min of reaction time, respectively.

It is important to note that the color of the reaction mixture gradually turned to deep brown from pale yellow when the dehydration of fructose was continued for a longer time (20 min). Perhaps, the color change of the reaction mixture is associated with the decomposition of the product HMF into side products. To further investigate the HMF decomposition and end product, the reaction mixture was analyzed by ¹H NMR spectroscopy. A ¹H NMR spectral analysis of the vacuum dried reaction mixture in chloroform-d₁ confirmed the formation 5chloromethylfurfural (CMF)²² and levulinic acid as side products (Fig. 3). The formation of levulinic acid can be explained by the rehydration of HMF.^{20,23} The self-polymerization of HMF molecules or cross-polymerization of HMF with fructose is also possible, particularly due to the fact that the HMF yield is not significantly increased upon prolonged reaction.²⁰ Although HMF rehydration can be suppressed in non-aqueous solvents, considerable rehydration of HMF is possible in aqueous or mixed aqueous solvents. This hypothesis supports the literature data where a lower HMF yield has been reported in aqueous



Fig. 3 A representative ¹H NMR (CDCl₃) spectrum of the reaction product obtained from the dehydration reaction of 5 wt% fructose with 50 mol% AlCl₃ in water under microwave heating at T = 120 °C for 15 min reaction time.

medium than in biphasic solvent.²⁴ The integration of proton signals corresponding to the -CHO group in ¹H NMR spectra (Fig. 3) of the reaction mixture suggests the formation of CMF occurs in a 1:2 molar ratio of CMF: HMF in water. The formation of CMF can be attributed to the ability of AlCl₃ to chlorinate the intermediate species formed during the dehydration of fructose.

As discussed above, detection of levulinic acid as a by-product in the ¹H NMR spectrum of the reaction mixture in the water mediated reaction suggested the formation of formic acid as well. However, the signal for the –COOH group proton of formic acid (δ 8.05 ppm) was too small in comparison to the levulinic acid signal. This could be due to the fact that the –COOH proton signal of formic acid did not resolve well in a reaction mixture or disappeared due to its consumption in undefined side reactions.

In order to investigate the role of formic acid in fructose dehydration, a control experiment was performed for the dehydration of 5 wt% fructose with 0.56 mmol formic acid at $120 \,^{\circ}$ C for 5 min under microwave-assisted heating. This control experiment with formic acid did not produce HMF, which precludes the possibility of the participation of a formic acid by-product as a catalyst in the fructose dehydration reaction.

3.5 Effect of other aluminium catalysts

The dehydration reaction of fructose to HMF was also investigated with two other commercially available aluminium salts, AlBr₃ and hydrated aluminium chloride AlCl₃·6H₂O. The results (Fig. 4) show that AlBr₃ is a less active catalyst for HMF production, which produced 35.1% HMF in 5 min as compared to 53.9% with the anhydrous AlCl₃ catalyst. Under comparable reaction conditions, the hydrated aluminium chloride catalyst



Fig. 4 The effect of aluminum catalysts and reaction time on HMF yields for the dehydration of 5 wt% fructose with 50 mol% catalysts in water under microwave heating at 120 $^{\circ}$ C.

produced about 2–7% less HMF than its anhydrous analogue (Fig. 4), which could be due to the contribution of extra water from the hydrated salt.

3.6 Conversion of glucose and sucrose

Although fructose has been the preferred feedstock for HMF production, its occurrence in nature is limited. This drives the attention to utilize more abundant carbohydrates, glucose and sucrose, as raw materials for HMF synthesis. A recent study demonstrates that the conversion of glucose to HMF is likely to proceed *via* consecutive steps, namely, mutarotation and isomerization of glucose into fructose followed by dehydration



Scheme 2 The proposed mechanism for glucose dehydration to HMF with the AlCl₃ catalyst in water.

Entry	AlCl ₃ (mg)	Solvent	$T(^{\circ}C)$	t (min)	HMF yield (%)
1	50	Water	120	5	30.0
2	50	Water	120	10	30.4
3	50	DMSO	140	5	4.6
4	50	DMSO	140	5	42.5
5	50	Water	120	2	26.7
6	50	Water	120	15	31.7
7	50	Water	120	20	33.2
8	33	Water	120	5	26.0
9	33	Water	120	15	27.8
10	20	Water	120	5	20.6
Sucros	e = 5 wt%				

of fructose to HMF.⁶ In the present study, the conversion of glucose and sucrose to HMF was carried out with anhydrous AlCl₃ catalyst in water at 120 °C and in DMSO at 140 °C under MW heating. The yield of HMF was monitored as a function of reaction time in the range of 2–20 min. The results, as shown in Tables 3 and 5, reveal the maximum HMF yield from glucose and sucrose are 52.4% (entry 5 in Table 3) and 42.5% (entry 4 in Table 5), respectively, in DMSO at 140 °C for 5 min reaction time. Under similar conditions, the HMF yields in water are 37.3% and 30.0% from glucose and sucrose, respectively. The glucose dehydration reaction in water–MIBK biphasic solvent produced 43% HMF as compared to 37.3% in water.

To understand the mechanism of glucose dehydration reaction, a ¹H NMR study of a reaction mixture of glucose and AlCl₃ in DMSO-d₆ was carried out at room temperature. It shows a line broadening of –OH proton signals of glucose in the range of δ 4–5 ppm. This line broadening of –OH protons indicates a H-bonding interaction between a Cl atom of AlCl₃ and the –OH protons of glucose forming an AlCl₃–glucose adduct. The line broadening of the –OH protons corresponding –H····Cl– interaction completely disappeared at 100 °C (Fig. S5(d)†) and a new signal appeared at δ 9.49 ppm in the ¹H NMR spectra after heating the reaction mixture at 100 °C for 40 min. The new signal at δ 9.49 ppm corresponds to the –CHO proton of HMF. This experiment suggests that the dehydration of glucose in DMSO occurs *via* the formation of an intermediate species between the –OH proton and the Cl atom of AlCl₃.

The dehydration reaction is believed to be initiated by the hydrolysis of AlCl₃. The hydrolysis of AlCl₃ in water under microwave irradiation forms a cationic species $[Al(OH)(H_2O)_5]^{2+}$. This active form of the catalyst, $[Al(OH)(H_2O)_5]^+$ acts as a potential electrophile that reacts with α -glucopyranose to form the intermediate **A** (Scheme 2). Intermediate **A** is possibly converted to ketohexose **B** *via* a hydride transfer, which forms fructofuranose through cyclization. This proposed mechanistic route for the formation of ketohexose **B** is similar to the mechanism described by Davis *et al.* using a SnCl₄ catalyst.²⁵

The mechanism of HMF formation from fructose has been a topic of debate over the years. In our case, the transformation of fructofuranose to intermediate compound **E** occurs *via* a cyclic

mechanism assisted by a proton that is generated during AlCl₃ hydrolysis. It is of note that the possibility of Cl⁻ acting as a base was taken into account for abstracting the proton from the oxonium ion forming structure **D** (path A), as proposed by Raines *et al.*²⁶ In path B, Cl⁻ functions as both the nucleophile and base to form intermediate **D**. The cyclic intermediate **E** has been identified recently by NMR study,¹⁷ which supports our proposed mechanism for the formation of **E** (Scheme 2). A similar mechanism involving intermediate **E** *via* a cyclic pathway was also proposed by Riisager *et al.*²⁶ In the formation of **E** then releases a water molecule to form the final product HMF.

This proposed mechanism was similar to a mechanism previously described for SnCl₄ catalyzed dehydration of glucose in mixed $[EMIM]BF_4$ (EMIM = 1-ethyl-3-methylimidazolium) and DMSO-d₆ solvents (9:1 w/w).8 Nevertheless, to understand the role of other cations in the present reaction, a mechanistic investigation for glucose (5 wt%) dehydration with SnCl₄ catalyst (20 mol%) was carried out in DMSO-d₆ (0.5 mL). ¹H NMR spectra revealed the formation of HMF upon heating at 80 °C for 45 min, when the signals of -OH proton corresponding -H...Cl- interactions (interaction between -OH proton and Cl atom of SnCl₄) disappeared. (see supporting information, Fig. S6[†]). Further heating at 120 °C for 30 min ensured significant conversion of glucose to HMF, as revealed from ¹H NMR (Fig. S6(d)[†]). Attempts were made to investigate the mechanism of glucose dehydration with a lanthanide cation, Yb(OTf)₃ (Tf = trifluromethanesulfonate) as a catalyst in DMSO-d₆. ¹H NMR investigation confirmed the low conversion of glucose into HMF in the presence of Yb(OTf)₃ at 120 °C for 1 h (Fig. S7[†]). This result is consistent with a previously reported Yb(OTf)₃ catalyzed glucose dehydration reaction in ionic liquid solvent [BMIM]Cl (BMIM = 1-butyl-3-methylimidazolium) where a maximum 24% HMF yield was realized at 140 °C for 6 h.12

3.7 Catalyst life-time in water medium

The life-time of the AlCl₃ catalyst was studied for fructose dehydration reaction in aqueous medium by recycling the reaction mixture containing the spent catalyst. The life time study of the catalyst was carried out with 5 wt% fructose and 50 mol% AlCl₃ in water at 120 °C for 5 min under microwave heating. Prior to recycle for the next run, HMF component was extracted from the reaction mixture with diethyl ether and fresh

fructose was added into the reaction mixture. Fig. 5 shows that the loss of activity of the catalyst in terms of HMF yield is only 10% after five cycles (53.9% in first cycle *versus* 44% in fifth cycle).



Fig. 5 Catalyst recyclability study for dehydration of fructose with AlCl₃ catalyst in water. Reaction conditions: fructose = 5 wt%, AlCl₃ = 50 mol%, T = 120 °C, t = 5 min.

3.8 Conversion of starch and inulin

The synthesis of HMF from biopolymers, such as starch and inulin, was carried out using an anhydrous AlCl₃ catalyst under microwave irradiation. Table 6 shows details of reaction conditions for HMF synthesis from biopolymers. However, prerequisite for successful dehydration of starch to HMF is the facile depolymerization of biopolymeric units. The depolymerization of the biopolymeric unit is reported to follow firstorder kinetics with respect to catalyst concentration.²⁴ In the present work, we used AlCl₃ to hydrolyze the glycosidic linkages between monomeric unit. AlCl₃ is believed to be effective for hydrolysis of glycosidic linkages because of its strong Lewis acidic character. As shown in Table 6, a maximum 29.6% HMF was obtained from dehydration of starch with AlCl₃ catalyst in DMSO at 140 °C under MW heating. The same reaction in aqueous solvent produced about 21% HMF, which is clearly less than that obtained in DMSO. The effect of solvent on the HMF yield has been discussed in section 3.1. The dehydration of starch to HMF has been reported in the literature

Table 6 Results of starch and inulin dehydration catalyzed by AlCl₃ under MW irradiation

Entry	Substrate (5 wt%)	AlCl ₃ (mol%)	Solvent	<i>T</i> (°C)	t (min)	HMF yield (%)
1	Starch	50	Water	120	2	19.6
2	Starch	50	Water	120	5	21.1
3	Starch	50	Water/MIBK	130	5	24.1
4	Starch	50	DMSO	140	5	30.6
5	Starch	50	Water	120	10	21.3
6	Starch	50	Water	120	5	14.0
7	Starch	50	Water	120	10	15.2
8	Inulin	50	Water	120	5	29.4
9	Inulin	50	Water	120	10	31.0
10	Inulin	50	Water/MIBK	130	5	32.5
11	Inulin	50	DMSO	140	5	39.2

Aqueous: organic = 1:2 volume (mL)

with SnCl₄ and CrCl₂ catalysts in 1-ethyl-3-methylimidazolium chloride ([EMIM]Cl) and 1-octyl-3-methylimidazolium chloride ([OMIM]Cl]) solvent, respectively. These reported reactions produced 47% and 73% HMF with SnCl₄ and CrCl₂ catalysts, respectively²⁸ Although the yield of HMF in water is less than that reported in ionic liquid with different Lewis acid catalysts, but our reaction in water is more sustainable in terms of avoiding the use of expensive ionic liquid solvents.

The direct synthesis of HMF from inulin occurs *via* hydrolysis of inulin to fructose followed by dehydration of fructose. The synthesis of HMF from inulin was carried out with an anhydrous AlCl₃ catalyst in three different solvents (water, water–MIBK and DMSO) using 1:1 molar ratio of inulin: AlCl₃ for 5 min microwave heating. The inulin dehydration reaction produced maximum 39% and 31% HMF in DMSO and water, respectively (Table 6). In an earlier report, Amberlyst 70 catalyst promoted hydrolysis and dehydration of inulin produced 60% HMF at 110 °C in [BMIM]Cl/glycerol carbonate (10:90).²⁹ Although yield of HMF in aqueous solvent is less, but it is more sustainable and environmentally friendly process.

3.8 Substrate scope of AlCl₃ catalyst

From the experimental results demonstrated above, we sought to explore the substrate scope of AlCl₃ catalyst and an estimation of comparative yields of HMF under microwave heating. This analysis for all substrates showed a trend of decrease in HMF yield from 53.9% to 21.1% in aqueous medium at 120 °C for 5 min reaction duration. A similar decreasing trend of HMF yield is also noted in DMSO for the dehydration reaction of fructose, glucose, sucrose, inulin and starch (Fig. 6). The yields of HMF from starch and inulin were comparatively lower than those obtained from fructose and glucose. However, the direct synthesis of HMF from starch and inulin certainly is a promising alternative route to HMF production. Nevertheless, the AlCl₃ catalyst is shown to be effective to convert less-expensive and easily available biopolymers (starch and inulin) to HMF in aqueous medium under microwave irradiation. This indeed expands the substrate scope of the catalyst and sustainability.





4. Conclusions

In summary, we have demonstrated that AlCl₃ is an excellent catalyst for the rapid conversion of carbohydrates and biopolymers into HMF in water, DMSO and water-MIBK biphasic solvents under microwave irradiation. The yield of HMF remains unchanged upon varying the starting fructose concentrations from 5 wt% to 30 wt%. The optimized reaction conditions were developed to maximize HMF yield by varying catalyst loading, reaction time, aluminium salts etc. Satisfactory results were obtained when glucose, sucrose, starch, and inulin were used as the substrates. The mechanism of the AlCl₃ catalyzed glucose dehydration reaction is proposed to proceed through the isomerization of glucopyranose to fructofuranose followed by a proton assisted transformation of fructofuranose to HMF. Finally, the Lewis acidic catalyst AlCl₃ deserves further investigation in less expensive ionic liquids to facilitate sustainable conversions of cellulosic materials to value added products.

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References

- 1 (a) A. J. Ragauskas, C. K. Williams, B. H. Davidson, G. Britovsek, J. Cairney, W. J. Frederick, J. P. Hallett, D. J. Leak, C. L. Liotta, J. R. Mielenz, R. Murphy, R. Templet and T. Tschaplinski, *Science*, 2006, 311, 484; (b) G. Stephanopoulos, *Science*, 2007, 315, 801.
- 2 Y. Román-Leshkov, C. J. Barrett, Z. Y. Liu and J. A. Dumesic, *Nature*, 2007, 447, 982.
- 3 (a) G. W. Huber, J. N. Chheda, C. J. Barrett and J. A. Dumesic, Science, 2005, 308, 1446; (b) J. N. Chheda, G. W. Huber and J. A. Dumesic, Angew. Chem., Int. Ed., 2007, 46, 7164; (c) A. Boisen, T. Christensen, W. Fu, Y. Gorbanev, T. Hansen, J. Jensen, S. Klitgaard,S. Pedersen, A. Riisager, T. Ståhlberg and J. Woodley, Chem. Eng. Res. Des., 2009, 87, 1318.
- 4 A. Corma, S. Iborra and A. Velty, Chem. Rev., 2007, 107, 2411.
- 5 T. Ståhlberg, W. Fu, J. M. Woodley and A. Riisager, *ChemSusChem*, 2011, 4, 451.
- 6 H. Zhao, J. E. Holladay, H. Brown and Z. C. Zhang, *Science*, 2007, 316, 1597.
- 7 G. Yong, Y. Zhang and J. Y. Ying, *Angew. Chem., Int. Ed.*, 2008, **47**, 9345.
- 8 S. Hu, Z. Zhang, J. Song, Y. Zhou and B. Han, *Green Chem.*, 2009, 11, 1746.
- 9 J. Y. Gerentt and Y. Zhang, ChemSusChem, 2009, 2, 731.
- 10 Z. Zhang, Q. Wang, H. Xie, W. Liu and Z. K. Zhao, *ChemSusChem*, 2011, **4**, 131.
- 11 T. S. Hansen, J. Mielby and A. Riisager, Green Chem., 2011, 13, 109.
- 12 T. Stahlberg, M. G. Sorensen and A. Riisager, *Green Chem.*, 2010, **12**, 321.
- 13 S. Zhao, M. Cheng, J. Li, J. Tian and X. Wang, *Chem. Commun.*, 2011, 47, 2176.
- 14 (a) T. S. Hansen, J. M. Woodley and A. Riisager, *Carbohydr. Res.*, 2009, 344, 2568; (b) Z. Zhang and Z. K. Zhao, *Biores. Tech.*, 2010, 101, 1111; (c) C. Z. Li, Z. H. Zhang and Z. B. K. Zhao, *Tetrahedron Lett.*, 2009, 50, 5403; (d) X. Qi, M. Watanabe, T. M. Aida and R. L. Smith Jr., *ChemSusChem*, 2010, 3, 1071.
- 15 D. Dallinger and C. O. Kappe, Chem. Rev., 2007, 107, 2563.
- 16 X. Tong and Y. Li, ChemSusChem, 2010, 3, 350.
- 17 A. S. Amarasekara, L. D. Williams and C. C. Ebede, *Carbohydr. Res.*, 2008, **343**, 3021.
- 18 Y. Román-Leshkov and J. A. Dumesic, Top. Catal., 2009, 52, 297.
- 19 B. F. M. Kuster, Starch/Staerke, 1990, 42, 314.

- 20 X. Qi, M. Watanabe, T. M. Aida and R. L. Smith Jr., *Green Chem.*, 2009, **11**, 1327.
- 21 X. Zi, M. Watanabe, T. M. Aida and R. L. Smith Jr., *Green Chem.*, 2008, **10**, 799.
- 22 M. Brasholz, K. von Känel, C. H. Hornung, S. Saubern and J. Tsanaktsidis, *Green Chem.*, 2011, **13**, 1114.
- 23 F. S. Asghari and H. Yoshida, Ind. Eng. Chem. Res., 2007, 46, 7703.
- 24 (a) R. Rinaldi, R. Palkovits and F. Scüth, *Angew. Chem., Int. Ed.*, 2008, **47**, 8047; (b) R. Rinaldi, N. Meine, J. vom Stein, R. Palkovits and F. Scüth, *ChemSusChem*, 2010, **3**, 266.
- 25 Y. Román-Leshkov, M. Moliner, J. A. Labinger and M. E. Davis, Angew. Chem., Int. Ed., 2010, 49, 8954.
- 26 J. B. Binder and R. T. Raines, J. Am. Chem. Soc., 2009, 131, 1979.
- 27 T. Ståhlberg, S. Rodriguez-Rodriguez, P. Fristrup and A. Riisager, *Chem.-Eur. J.*, 2011, **17**, 1456.
- 28 J.-A. Chun, J.-W. Lee, Y.-B. Yi, S.-S. Hong and C.-H. Chung, *Starch/Staerke*, 2010, 62, 326.
- 29 M. Benoit, Y. Brissonnet, E. Guelou, K. D. Oliveira Vigier, J. Barrault and F. Jerome, *ChemSusChem*, 2010, **3**, 1304.