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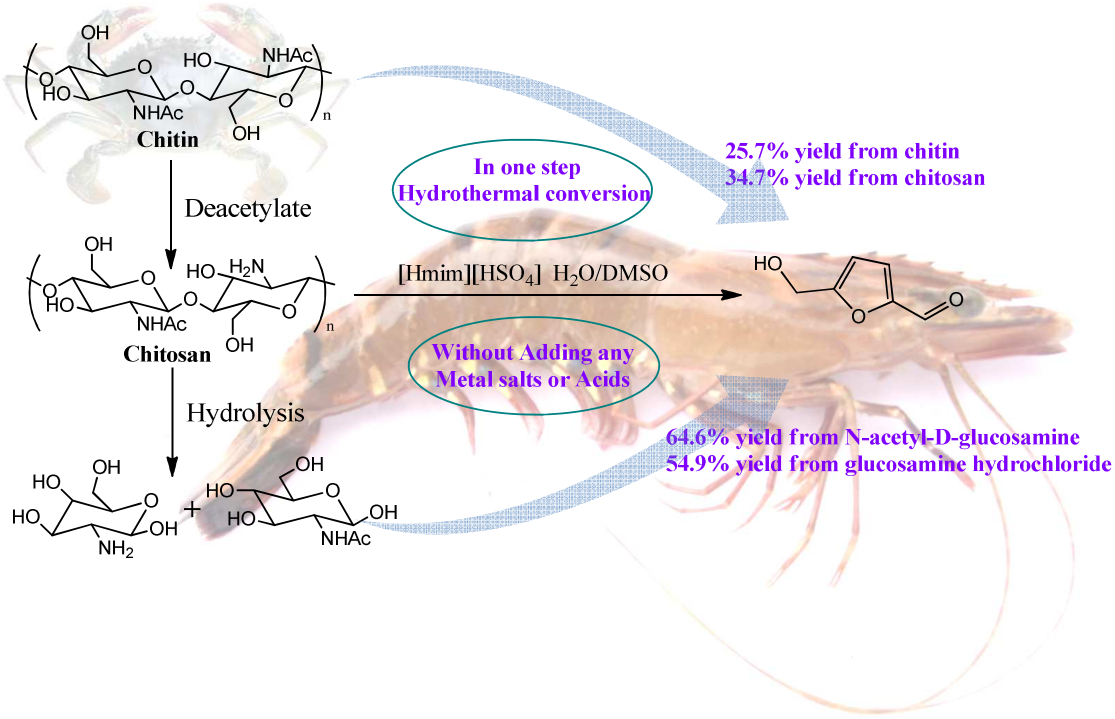

In one step
Hydrothermal conversion

Without Adding any
Metal salts or Acids

25.7% yield from chitin
34.7% yield from chitosan

64.6% yield from N-acetyl-D-glucosamine
54.9% yield from glucosamine hydrochloride

Hydrothermal Conversion of *N*-acetyl-ᴅ-glucosamine to 5-Hydroxymethylfurfural Using Ionic Liquid as a Recycled Catalyst in a Water-Dimethyl Sulfoxide Mixture

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ABSTRACT

Here, *N*-acetyl-ᴅ-glucosamine (GlcNAc), the monomer composing the second most abundant biopolymer, chitin, was efficiently converted into 5-hydroxymethylfurfural (5-HMF) using ionic liquid (IL) catalysts in a water/dimethyl sulfoxide (DMSO) mixture solvent. Various reaction parameters, including reaction temperature and time, DMSO/water mass ratios and catalyst dosage were optimized. A series of ILs with different structures were analyzed to explore their impact on GlcNAc conversion. The substrate scope was expanded from GlcNAc to ᴅ-glucosamine, chitin, chitosan and monosaccharides, although 5-HMF yields obtained from polymers and other monosaccharides were generally lower than those from GlcNAc. Moreover, the IL N-methylimidazolium hydrogen sulfate ([Hmim][HSO_4]) exhibited the best catalyst performance (64.6% yield) when GlcNAc was dehydrated in a DMSO/water mixture at

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180°C for 6 h without the addition of extra catalysts. To summarize, these results could provide knowledge essential to the production of valuable chemicals that are derived from renewable marine resources and benefit biofuel-related applications.

Key words: 5-Hydroxymethylfurfural, N-Acetyl-D-glucosamine, Ionic liquid, Dehydration, Hydrothermal Conversion

1. Introduction

The decrease in fossil resources has caused serious energy issues. As the most abundant, green, and renewable resource in the world, biomass can be considered a suitable alternative to fossil fuels and can be used for the production of fuels and various chemicals.[1] The biomass relates mainly to cellulose, hemicellulose, lignin and chitin, the catalytic conversion of cellulose and glucose has been comprehensively studied.[2] Treating cellulose and glucose over acid catalysts yields a series of dehydration products, such as 5-hydroxymethylfurfural (5-HMF) and levulinic acid (LeA).[3-5] 5-HMF has been recognized as important versatile platform compound for the synthesis of a broad range of new products as well as for the replacement of fossil resources-derived fuels and chemicals, including 2,5-diformylfuran, 2,5-furandicarbaldehyde, 2,5-furandicarboxylic acid, and importantly, 2,5-dimethylfuran.[6,7]

Aside from cellulose and glucose, chitin biomass (in the text, this refers to chitin, chitosan, and their corresponding monomers and derivatives) is also a suitable starting material for furan derivatives such as 5-HMF. However, there are few reports on the conversion of chitin biomass into furan derivatives. Recently, Yan and Chen [8] proposed the concept of shell refinery, whereby crustacean shells are separated into different fractions, and each fraction is upgraded or transformed into value-added products. Chitin is the second most plentiful biopolymer on earth, which is generated at a rate of about 100 billion tons every year.[9] Therefore, efficient methods to convert chitin biomass into valuable compounds are of great importance. Recently, $SnCl_4 \cdot 5H_2O$ was found to effectively catalyze the chitosan conversion into 5-HMF 10.0 wt.% yield in water under microwave irradiation.[10] A limitation was that the 5-HMF yield was very low, whereas no 5-HMF was obtained from chitin. An alternative transformation strategy was proposed by Hou and co-workers who utilized concentrated $ZnCl_2$ solution as the reaction solvent. After optimization,[11] 5-HMF could be obtained from chitin biomass ($GlcNH_2$ 21.9%, GlcNAc 2.8%, Chitin 9.0%, Chitosan-1K 12.8%, Chitosan-5K 12.2%, Chitosan-50K 8.0%, Chitosan-100K 8.6%, and Chitosan–COOH 9.2%) using a concentrated $ZnCl_2$ aqueous solution, and this result indicating Zn^{2+} promoted 5-HMF formation occurred by interaction with the amino group on the substrate. Under hydrothermal conditions, chitosan was converted into 5-HMF in diluted H_2SO_4,[7] obtaining a 12.1 wt% yield at 174 ^oC in 2.2 wt% H_2SO_4 solution after 37 min. Chen et al.[12] reported that GlcNAc, as chitin monomer, can be converted into 3-acetamido-5-acetylfuran through pyrolysis at high temperatures and microwave irradiation, obtaining 2% and 62% yields, respectively. Wang et al.[13] reported that

GlcNAc and D-glucosamine can be degraded to 5-HMF in subcritical water. These studies showed that chitin biomass has the potential to be a renewable feedstock for 5-HMF. However, the catalysts used in these studies were poisonous and the 5-HMF yield was very low. Therefore, efforts should be applied to investigate efficient ways to transform chitin biomass into 5-HMF.

Very recently, our team screened nine acidic ILs with different cations and anions; the acidity, hydrogen-bonding capacity and steric hindrance of ILs exhibited combined influences on the reaction. N-Methyl imidazolium hydrogen sulfate ([Mim]HSO4) afforded the highest 5-HMF yield of 29.5% from chitosan and 19.3% from chitin at 180 ^{o}C after 5 h.[14] The 5-HMF yield was the highest from chitin and chitosan among literatures reported to date. The IL [Hmim][HSO_4], used as both a green solvent and catalyst, exhibited good solubility and catalytic performance for the conversion of chitosan and chitin. These studies demonstrated the feasibility of converting chitin and chitin derivatives into 5-HMF. However, the highest 5-HMF yield directly from chitin was 19.3% is still low. Continued research is hence required in order to develop an efficient and economically feasible 5-HMF production process from chitin biomass.

Dehydration of hexoses in an aqueous solution leads to excessive solids formation.[15,16] It is believed that the solids are in the literature known as ‘humins’.[15] The solids behave and look like tar, a black oily mass that adheres to surfaces, and avoiding precipitation and formation of these is crucial for industrialization. Solvents such as DMSO can reduce humin formation drastically by protecting the hexose from degradation. Thus, DMSO, which has been previously added to reaction systems to suppress undesired side reactions, can be used as both a dehydrating agent and as a solvent. Román-Leshkov et al.[17] showed that DMSO both suppressed the formation of condensation by-products and hampered 5-HMF rehydration by lowering the overall water concentration. However, the presence of water in this reaction system is also essential. Cao et al.[18] reported that an enzyme mimicking an ammonium polymer could be used as a single catalyst in the dehydration reaction of glucose to 5-HMF. Their study showed that the presence of water in the system can block the pathway for anhydrosugar formation and push the reaction toward 5-HMF formation. Moreover, the presence of water in the system also suppressed the side reaction, resulting in the formation of 2,5-diformylfuran (DFF) and FA. In a DMSO/water solvent mixture, the dipolar aprotic solvent dramatically broke hydrogen bonds—results that pointed to a promising binary mixture solvent.[19]

Based on the aforementioned results, mixtures of DMSO and water are used as reaction solvent. We investigated whether similar transformations would be able to produce 5-HMF from chitin/chitosan monomers. We explored the correlation between monomer and copolymer degradation during Hydrothermal conversion (HTC) processes as a helpful tool for screening appropriate catalysts for chitin biomass degradation.[7] GlcNAc was chosen for the study of this conversion process because it is the monomer composing chitin. Efficient conversion of chitin/chitosan monomers to 5-HMF is a key step for using chitin/chitosan to produce liquid fuels and value-added chemicals.

Accordingly, this contribution presents a full account of our study towards the above central objective.

2. Materials and Methods

2.1. Materials

GlcNAc and N-methylimidazole were purchased from Nanjing Xiezun Chemical Co., LTD (Nanjin, China). 5-HMF (purity > 97%) was purchased from Heowns Biochem Technologies LLC (Tianjin, China). Methanol (HPLC grade) and ethyl acetate (AR grade) were purchased from Tianjin Kermel Chemical Reagent Co., Ltd. Vitriolic acid, phosphoric acid, hydrochloric acid, and nitric acid were purchased from Tianjin chemical reagent No. 5 plant (Tianjin, China). All other chemicals were supplied by local suppliers and used without further purification.

2.2. Synthesis of ILs

Brønsted acidic [Hmim][HSO_4], [Hmim][H_2PO_4], [Hmim][NO_3], and [Hmim][Cl] were synthesized in our laboratory via a neutralization reaction and developed on the basis of a previous report.[20-22] Sulfuric acid (50% w/w) was added in a 1:1 molar ratio with 1-methylimidazole over a period of 30 min with stirring and cooling to maintain the temperature at 0°C. The reaction mixture was stirred for an additional period of 2 h. Then, water was removed under reduced pressure to yield the colorless liquid [Hmim][HSO_4]. The crude product was washed several times with diethyl ether to remove non-ionic residue and then vacuum dried for 24 h under 80°C. [Hmim][H_2PO_4], [Hmim][NO_3], and [Hmim][Cl] were synthesized using similar procedures. Additionally, 4,5-dimethylthiazole hydrosulfate ([TM][HSO_4]) and 2-isobutylthiazole hydrosulfate ([TB][HSO_4]) were prepared by neutralization reactions. Then 4,5-dimethylthiazole (or 2-isobutylthiazole) was combined with sulfuric acid (50% w/w) in a 1:1 molar ratio and refluxed for 12 h. ^{SO3H}[TB] HSO_4 was synthesized in our laboratory and developed on the basis of a previous report.[23] These ILs are air-stable, hydrophilic, and their physicochemical properties have been studied.

2.3. Classical procedure for the catalytic conversion of GlcNAc into 5-HMF

GlcNAc (100 mg, 0.452 mmol) was added into a mixed solvent composed of DMSO (8 g) and deionized water (12 g) in a 50 mL stainless steel vessel with a Teflon lining and sealed by a screw cap. Different amounts of ILs with different structures, used as catalysts, were loaded into the reactor. Then, the reactor was then immersed into a preheated oil bath, and the reaction mixture stirred for a given time. Time zero was recorded when the reactor was immersed into the preheated oil bath. The clear solution darkened gradually over time. After the scheduled time, the reactor was taken out from the oil bath and immediately submerged in an ice-water bath to quench the reaction. Then, the reaction mixture was taken out and filtered with filter paper to remove insoluble humin polymer. Afterwards, 1 mL of this reaction mixture was diluted with 5 mL of methanol in a volumetric flask. This diluted solution was then taken out, filtered through a 0.22 μm PTFE filter, and injected into a glass tube. The 5-HMF yield was determined by high performance liquid chromatography (HPLC) of these aqueous solutions, using a standard curve (Fig.S1, Supplementary material) in order to quantify the amount. 5-HMF yields were calculated as shown below:

5-HMF yield [%] = Mole amount of 5-HMF/Mole amount of starting GlcNAc × 100

All experiments were performed at least in triplicates; the range of experimental errors for the HPLC analysis was ±1%.

2.4. Analysis of the products

Quantitative and qualitative analyses of 5-HMF were performed by HPLC and gas chromatography and mass spectrometry (GC-MS). The concentration of 5-HMF was analyzed using HPLC instruments (LC3000, Beijing Chuangxin Tongheng Science and Technology Co., Ltd.), equipped with a reversed phase C18 column (250 mm × 4.6 mm) and an ultraviolet detector at 284 nm. The mobile phase consisted of methanol and water (23:77 v/v) with a flow rate of 0.5 mL/min. Column temperature was maintained at 30 °C with an injection of 2 μL. Additionally, we used GC-MS to determine the structure of the product. The GC–MS analysis was performed using the Bruker SCIONSQ/436-GC system equipped with a 30 m × 0.25 mm × 0.25 μm HP-5 MS capillary column. Helium was used as the carrier gas at a linear velocity of 1.0 mL/min. The injector temperature was maintained at 220 ˚C, and the oven temperature was programmed to start at 50˚C (2 min), increasing in intervals of 15˚C/min until a temperature of 230 ˚C was obtained. This temperature was then maintained for 6 min. Mass spectrometric measurements were performed using electron impact ionization at 70 eV and a scan range of m/z 50-500, at a rate of 1 scan/s. GC-MS analysis result is shown in Fig.1.

5-HMF was separated by silica gel column chromatography with eluent of petroleum ether and ethyl acetate with proportion of 1:1. ^1H and ^{13}C NMR spectra of the isolated 5-HMF was identified. The ^1H and ^{13}C NMR spectra of the isolated 5-HMF are given in Supplementary material.

3. Results and discussion

3.1 The characterization of Ionic liquids

The ^1H NMR spectra and HPLC-MS spectra images of ionic liquids are given in Supplementary material.

1-methylimidazolium hydrosulfate, [Hmim][HSO_4], ^1H NMR (400 MHz, D_2O, ppm) δ8.55 (s, 1H, CH), δ 7.33 (s, 2H, CH), δ 3.82 (s, 3H, CH_3). Anal. Calcd. for $C_4H_8O_4N_2S$: C 26.66; H 4.48; N 15.55; S 17.80; Found: C 26.63; H 4.50; N 15.51; S 17.84.

1-methylimidazolium dihydric phosphate, [Hmim][H_2PO_4], ^1H NMR (400 MHz, D_2O, ppm) δ8.56 (s, 1H, CH), δ 7.36 (s, 2H, CH), δ 3.84 (s, 3H, CH_3). Anal. Calcd. for $C_4H_9O_4$ N_2P: C 26.68; H 5.04; N 15.55; Found: C 26.71; H 5.02; N 15.54.

1-methylimidazolium nitrate, [Hmim][NO_3], ^1H NMR (400 MHz, D_2O, ppm) δ8.60 (s, 1H, CH), δ 7.39 (s, 2H, CH), δ 3.88 (s, 3H, CH_3). Anal. Calcd. for $C_4H_7O_3N_3$: C 33.11; H 4.86; N 28.96; Found: C 33.14; H 4.85; N 28.92.

1-methylimidazolium hydrochloride, [Hmim][Cl], ^1H NMR (400 MHz, D_2O, ppm) δ8.59 (s, 1H, CH), δ 7.37 (s, 2H, CH), δ 3.85 (s, 3H, CH_3). Anal. Calcd. for $C_4H_7N_2Cl$: C 40.52; H 5.95; N 23.63. Found: C 40.53; H 5.97; N 23.61.

4,5-dimethylthiazolium hydrosulfate, [TM] HSO_4, ^1H NMR (400 MHz, D_2O, ppm) δ9.47 (s, 1H, CH), δ2.35 (s, 3H, CH_3), δ2.33 (s, 3H, CH_3). Anal. Calcd. for $C_5H_9O_4NS_2$: C 28.43; H 4.29; N 6.63; S 30.36; Found: C 28.41; H 4.27; N 6.70; S 30.31. MS (ESI, m/z):114.0385 [M^+ - HSO_4^-]

2-isobutylthiazolium hydrosulfate,[TB] HSO_4, ^1H NMR (400 MHz, D_2O, ppm) δ7.92 (d, *J* = 4 Hz, 1H, CH), δ7.79 (d, *J* = 4 Hz, 1H, CH), δ3.05 (d, *J* = 4 Hz, 2H, CH_2), δ3.05 (d, *J* = 4 Hz, 2H, CH_2), δ1.94-2.04 (m, 1H, CH), δ0.823 (d, *J* = 6.8 Hz, 6H, CH_3). Anal. Calcd. for $C_7H_{13}O_4NS_2$: C 35.13; H 5.48; N 5.85; S 26.80; Found: C 35.10; H 5.49; N 5.83; S 26.82. MS (ESI, m/z):142.0708 [M^+ - HSO_4^-]

4,5- dimethyl-3-(4-sulfonic acid butyl)thiazolium hydrosulfate , ^{SO3H}[TB] HSO_4, ^1H NMR (400 MHz, D_2O, ppm) δ9.51 (s, 1H, CH), δ4.33 (t, *J*=7.2Hz,2H,CH_2), δ2.83 (t, *J* = 7.6 Hz, 2H, CH_2), δ2.34 (s, 3H, CH_3), δ2.33 (s, 3H, CH_3), δ1.89-1.97 (m, 2H, CH_2), δ1.63-1.71 (m, 2H, CH_2). Anal. Calcd. for $C_9H_{17}O_7NS_3$: C 31.11; H 4.93; N 4.03; S 27.69; Found: C 31.12, H 4.90, N 4.03, S 27.66.

3.2 Catalytic conversion of GlcNAc into 5-HMF by various ILs

In the present study, we studied the effects of different ILs, including imidazolium-type and thizolium-type ILs on GlcNAc conversion. Seven different ILs were used in combination with various cations and anions, that is, [Hmim][HSO_4], [Hmim][H_2PO_4], [Hmim][NO_3], [Hmim][Cl], [TM][HSO_4], [TB][HSO_4], and ^{SO3H}[TB][HSO_4]. The control experiment was carried out in DMSO/water without a catalyst, where a 10.1% 5-HMF yield was observed (Table 1, entry 1). When sulfuric acid (equal molar amounts of GlcNAc) was used as a catalyst, a 23.7% yield of 5-HMF was obtained. As shown in Table 1, ILs showed remarkable effects on the conversion of GlcNAc into 5-HMF. Different types of ILs have a significant influence on the 5-HMF yield (Table 1, entries 4-10). [Hmim][HSO_4] was found to have the best catalytic performance on the conversion of GlcNAc with 5-HMF (45.2% yield) (Table 1, entry 4). Compared to the findings for sulfuric acid, it was observed that the [Hmim] cation promotes the conversion of GlcNAc into 5-HMF.

The anions in the IL were also found to have a profound effect on reactivity. The incorporation of an HSO_4 counter ion (within the IL) proved to be necessary in order to obtain significant quantities of 5-HMF. Low yields of 5-HMF were obtained when phosphate, nitrate, or chloride ILs were used as counter ions (Table 1, entries 5-7). When the reaction was catalyzed by using excess sulfuric acid and ^{SO3H}[TB][HSO_4] as catalysts, there was no formation of 5-HMF (Table 1, entries 3,10). Additionally, results show that the acidity of the reaction system may also have a remarkable effect on the yield of 5-HMF. Addition of acid facilitates formation of 5-HMF and increases selectivity, the ratio between product and by-products is improved due to higher yield of product; However, 5-HMF rapidly degrades as the acidity of the solution increases, the yield is decreased due to decomposition of 5-HMF. For this reason, the ionic liquid [Hmim][HSO_4] was employed for subsequent experiments.

3.3 Catalytic conversion of GlcNAc into 5-HMF under various reaction conditions

Various reaction parameters such as reaction temperature and time, DMSO/water mass ratio, and catalyst dosage showed a remarkable effect on the dehydration of GlcNAc to 5-HMF.

3.3.1 Effect of the different mass ratio of the DMSO/water on the conversion of GlcNAc into 5-HMF

As shown in Fig. 2, we found that differences in DMSO/water mass ratio had a significant influence on 5-HMF yields. In the absence of DMSO, 5-HMF yields in water were found to be 35.8%. However, when 40 wt.% of DMSO was used, 5-HMF yields increased from 35.8% to 52.4%. When the reaction was carried out only in DMSO, 5-HMF yields dropped to 8.9%. This suggests that the mixture of DMSO/water plays a key role in the process of conversion of GlcNAc into 5-HMF. Our results were consistent with previous results, where it was also found that appropriate water content in the system had a remarkable effect on 5-HMF yields.[24] It would be helpful to elucidate the mechanism underlying the positive effects of water and DMSO on the transformation of GlcNAc into 5-HMF. On one hand, the presence of water in this system blocks dehydration of GlcNAc and pushes the reaction toward 5-HMF formation in the deamination of GlcNAc.[18] On the other hand, the existence of DMSO in the reaction system can also inhibit undesired side reactions. Similar studies have indicated that DMSO favorably shifts the equilibrium of the rate-determining step of 5-HMF production and inhibits acyclic reaction sequences that may lead to undesirable intermediates.[17] Interestingly, it was observed that 5-HMF yields can decrease on increase in the DMSO content in water (Fig.2). Previous research had revealed that

DMSO exhibits its maximum association with water molecules when its content in solution is 66-70%.[25] However, our results showed the best DMSO/water mass ratio was 8:12 for an effective conversion of GlcNAc into 5-HMF.

3.3.2 Effect of the reaction temperature on the conversion of GlcNAc into 5-HMF

The effects of reaction temperature on substrate conversion and 5-HMF yields were evaluated. The conversion reaction of GlcNAc to 5-HMF was more effective at 180°C than at 150°C, 160°C, 170°C, 190°C, and 200°C (Fig. 3). 5-HMF yields increased gradually before 180°C and then slowly decreased. There is evidence suggesting that the activation energy for the formation of 5-HMF is higher than the activation energy for 5-HMF disappearance;[15] therefore, it is expected that 5-HMF concentration would increase with increase in temperature. On the other hand, temperature increases will generate more by-products and insoluble humins. The results showed that 180°C was the most appropriate temperature for the conversion of GlcNAc to 5-HMF. Based on these results, the reaction temperature was maintained at 180 °C in order to further optimize the reaction conditions.

3.3.3 Effect of the reaction time on the conversion of GlcNAc into 5-HMF

We studied the relationship between reaction time and 5-HMF yields, which are presented in Fig.4. Experiments were carried out at 3, 4, 5, 6, 7, and 8 h. As shown in Fig.4, reaction times showed remarkable effects on the conversion of GlcNAc into 5-HMF. 5-HMF yields increased gradually before 6 h and then slowly decreased. Maximum 5-HMF yields (52.4%) were obtained at 6 h; the percentage slightly decreased to 48% after 8 h. 5-HMF yields decreased from 6 h to 8 h, indicating that 5-HMF was not stable at 180 °C for prolonged periods of time. In this catalytic system, 6 h appears to be the most appropriate reaction time to obtain significant 5-HMF yields.

3.3.4 Effect of amount of ionic liquid and hydrothermal conditions on the conversion of GlcNAc into 5-HMF

Under the same reaction temperature and times, the effect of IL dosage on the conversion of GlcNAc into 5-HMF was investigated. Fig. 5 shows that variations in the concentration of [Hmim][HSO_4] affect the conversion of GlcNAc into 5-HMF. IL dosage also showed a significant effect on 5-HMF yields. 5-HMF yields increased with increases in [Hmim][HSO_4]/GlcNAc molar ratios, varying from 5 to 30. A 32.6% yield was obtained within 6 h at 180 °C when the [Hmim][HSO_4]/GlcNAc molar ratio was 5. Furthermore, 5-HMF yields increased to 52.2%, 56.7%, and 64.6% when using 10, 15, and 20 of [Hmim][HSO_4]/GlcNAc molar ratios, respectively. This increase in 5-HMF yields with increasing catalyst dosages (at the same reaction time points) can be attributed to increases in the availability and number of catalytically active sites. However, 5-HMF yields decreased with increasing amounts of [Hmim][HSO_4], ranging from 20 to 30 [Hmim][HSO_4]/GlcNAc molar ratios. One possibility is that high catalyst loading not only accelerates the conversion of GlcNAc into 5-HMF but also promotes other side reactions such as the rehydration of 5-HMF into LA and cross-polymerization reactions,[15] which result in lower 5-HMF yields. In the present investigation, LA was not observed.

In addition, the effect of hydrothermal conditions was studied. Under the same reaction parameters (reaction time and temperature, catalyst loading, and solvent), the reaction was refluxed in a preheated oil bath without hydrothermal conditions (Table 2, entry 1). During refluxing at atmospheric pressure, we put a thermometer into boiling flask-3-neck and the thermometer was placed below the liquid surface, under these conditions, a low yield of 3% was obtained. However, when the reaction was carried out in a 50 mL stainless steel vessel with a Teflon lining and sealed by a screw cap, a 44% yield was obtained (Table 2, entry 2). This result shows that reaction pressure is also a critical factor in the conversion of GlcNAc into 5-HMF.

3.4 [Hmim][HSO$_4$] catalyzed the conversion of other carbohydrates into 5-HMF

Other chitin biomass substrates such as glucosamine hydrochloride (GlcNH$_2$·HCl), chitin, and chitosan, in addition to several carbohydrates, were also tested in this ionic catalytic system to determine 5-HMF conversion yields (Table 3). The direct preparation of 5-HMF from these less-expensive and easily available biopolymers is essential for expanding the substrate scope. Under the same conditions, GlcNH$_2$·HCl conversion to 5-HMF produced a 54.9% yield. It stands to reason that monomers (GlcNAc and GlcNH$_2$) are easier to convert into 5-HMF than copolymers (chitosan and chitin). This may be due to strong intra- and intermolecular hydrogen bonds between –OH, –NH$_2$, and –NHAc groups found within chitin and chitosan, thereby hindering chitin and chitosan dissolution and subsequent conversion into 5-HMF. The IL [Hmim][HSO$_4$] is not an effective catalyst for the dissolution of the glycosidic bonds found within chitin and chitosan. As a result, 5-HMF yields roughly decreased as the molecular weight of substrates increased. Table 3 compares the results of 5-HMF production from chitosan, chitin, $GlcNH_2$, and GlcNAc. This study was able to achieve high 5-HMF yields derived from chitin biomass under optimal conditions.

Other carbohydrates (glucose, D-fructose, rhamnose, lactose, D-galactose, D-mannose) were also tested (Fig. 6). D-fructose produced a 57.7% yield of 5-HMF. Comparing the results for glucose and fructose showed that the decreases in 5-HMF yields were presumably due to slower glucose conversion as compared with fructose conversion.[26]

3.5 A possible reaction pathways for GlcNAc dehydration in binary systems

Reaction pathways for the dehydration of GlcNAc into 5-HMF using [Hmim][HSO_4] IL as catalyst in DMSO/water mixture systems attracted our attention. To obtain a better understanding of GlcNAc dehydration pathways, HPLC-MS spectra were used to monitor this process. As shown in Fig.S4, Supplementary material. At t = 1 h, a -NHAc group was removed from the cyclic form of GlcNAc, forming an enol-intermediate (M = 162.05). At 3 h, 5-HMF (M = 126.03, 127.04 - H^+) was observed. When the reaction proceeded for 5 h, the HPLC-MS spectrum showed the complete disappearance of the enol-intermediate (M = 162.05) peak. A very small amount of GlcNAc was still exist, 4-hydroxy-5-hydroxymethyl-4,5-dihydrofuran-2-carbaldehyde was the major by-product in reaction. In addition, the compounds with high molecular weight were not observed in aqueous solution. During this time, the 5-HMF peaks became increasingly stronger.

In previous studies, Khokhlova et al.[27] developed an efficient NMR approach with characterizing molecular transformations of the conversion of carbohydrates to 5-hydroxymethylfurfural in IL systems. A detailed study of the key sugar units involved in the biomass conversion process has shown that the simple dissolution of fructose in the ionic liquid 1-butyl-3-methylimidazolium chloride significantly changes the anomeric composition and favors the formation of the open fructoketose form. Their results reveal previously inaccessible mechanistic details of native-state IL systems at the molecular level. It is likely that the mechanism for this reaction (Fig. 7) has much in common with previously studied fructose and glucose dehydration processes. As the first step, dissolution of GlcNAc in this catalyst system leads to a disruption of hydrogen bonds between sugar molecules, and new hydrogen bonds are formed though the coordination of H^+ in HSO_4^- and imidazolium cations of IL with –OH groups. Then, H^+ and electron-rich aromatic imidazolium cations facilitate the ring-opening reaction to form the open chain aldose. In the second step, the enol-intermediate is formed by isomerization. Next, the formation of a five-membered ring and cyclic compounds, which are key intermediates in the conversion process, are obtained. The third step is the removal of a -NHAc group from the cyclic compounds, forming the enol-intermediate (M = 162.05) once again. Finally, 5-HMF is formed through the acidic hydrolysis from 4-hydroxy-5-hydroxymethyl-4,5-dihydrofuran-2-carbaldehyde.

The usual byproducts observed in this biomass conversion, i.e. LeA and FA, were not detected by HPLC-MS. The HPLC-MS provided evidence to sustain the proposed mechanism.

3.6 Recycling experiments

Catalyst recycling is an important goal in terms of green and sustainable chemistry. Thus, the reusability of the catalyst [Hmim][HSO_4] was studied (Fig. 8). The conversion of GlcNAc into 5-HMF was used as the model reaction; experiments were carried out at 180°C for 6 h in a DMSO/water mixture and using [Hmim][HSO_4] as the catalyst. After the reaction, most of the 5-HMF in the aqueous solution was removed by ethyl acetate extraction until no 5-HMF was detected in the ethyl acetate. The water found in the aqueous phase was completely removed through vacuum evaporation. The remaining [Hmim][HSO_4] and DMSO were used directly in the next run by adding a fresh GlcNAc sample and water under the same reaction conditions. This processes was repeated 5 times, obtaining 5-HMF yields of 63.6%, 58.8%, 57.4%, 54.5%, and 51.8%, respectively. The loss of catalytic activity was possibly due to mass loss during the recycling procedure. Therefore, it can be concluded that the catalyst was stable in this system, and has potential applications for large-scale industrial synthesis.

4. Conclusion

For the first time, direct conversion (producing high yields) of GlcNAc into 5-HMF was achieved via hydrothermal synthesis in an acidic IL aqueous solution. The conversion method depends on a DMSO/water mixture catalyzed by [Hmim][HSO_4].

GC-MS and HPLC analyses showed 5-HMF as the main product, with undetectable levels of byproducts such as LeA (except humins), highlighting high yields and selective reaction. This is a proof-of-principle study that GlcNAc can be hydrolyzed to obtain useful chemical building blocks. The catalytic system was effectively recycled five times. This system has great potential for large-scale 5-HMF production. The method described herein should be valuable to facilitate cost-effective conversion of renewable marine resources into biofuels and bio-based products.

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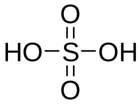
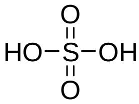
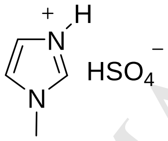
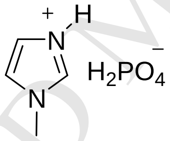
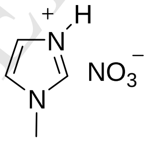
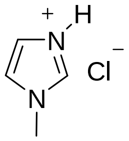
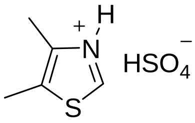
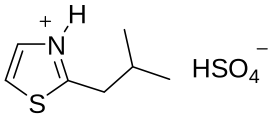
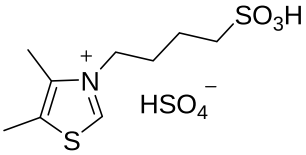
Table 1

Effect of sulfuric acid and different ionic liquids on the conversion of the GlcNAc into 5-HMF under hydrothermal conditions ^{a}

Entry	catalyst	structure	5-HMF yield [%]
1	No catalyst		10.1±0.9
2	H_2SO_4(44.31mg)		23.7±1.3
3	H_2SO_4(443.02mg)		trace
4	[Hmim][HSO_4]		45.2±2.9
5	[Hmim][H_2PO_4]		19.6±2.2
6	[Hmim][NO_3]		15.1±3.3
7	[Hmim][Cl]		5.5±1.3
8	[TM][HSO_4]		19.2±2.2
9	[TB][HSO_4]		28.7±1.2

10	^{SO3H}[TB] HSO_4		trace

[a] The reaction conditions: GlcNAc (100 mg), the ILs with GlcNAc in a 10:1 molar ratio, distilled water, 12g; DMSO, 8g; reaction temperature, 180 °C; reaction time, 5 h.

Table 2

The effect of reaction pressure on the conversion of GlcNAc into 5-HMF[a]

Entry	Solvent		Temperature(˚C)	Time(h)	$R_{Catalyst}$	5-HMF yield [%]
1[b]	Water 16g	DMSO 4g	180	6	10	3.0±1.3
2	Water 16g	DMSO 4g	180	6	10	44.0±4.4

[a] Reaction conditions: GlcNAc, 100 mg; [Hmim][HSO_4], 813mg ; reaction temperature, 180 °C, reaction time, 6 h. $R_{catalyst}$= the molar ratio of [Hmim][HSO_4] / GlcNAc

[b] It was immersed in a preheated oil bath heated at 180 ˚C and carried out atmospheric pressure reflux for 6h.

Table 3

Comparison of 5-HMF production from other chitin biomass substrates such as chitin, chitosan D-fructose and GlcNAc

Materials	Reaction conditions	$Y_{5\text{-HMF}}$	
		Reference	This work[a]
Chitin	microwave irradiation , 100 mg chitosan in 15 mL water, 0.12 mmol $SnCl_4 \cdot 5H_2O$,200 °C, 30 min	ND [10]	25.7mol%
Chitosan		10.0 wt% [10]	34.7 mol%
$GlcNH_2 \cdot HCl$	1 g substrate in 30 g 67 wt.% $ZnCl_2$ solution, 120°C, 90 min	21.9 mol% [11]	54.9 mol%
GlcNAc		2.8 mol% [11]	64.6 mol%

ND not detected

[a] Reaction conditions: carbohydrate (100 mg),the [Hmim][HSO_4] with carbohydrate in a 20:1 molar ratio, distilled water, 12g; DMSO, 8g; reaction temperature, 180 °C; reaction time, 6 h.

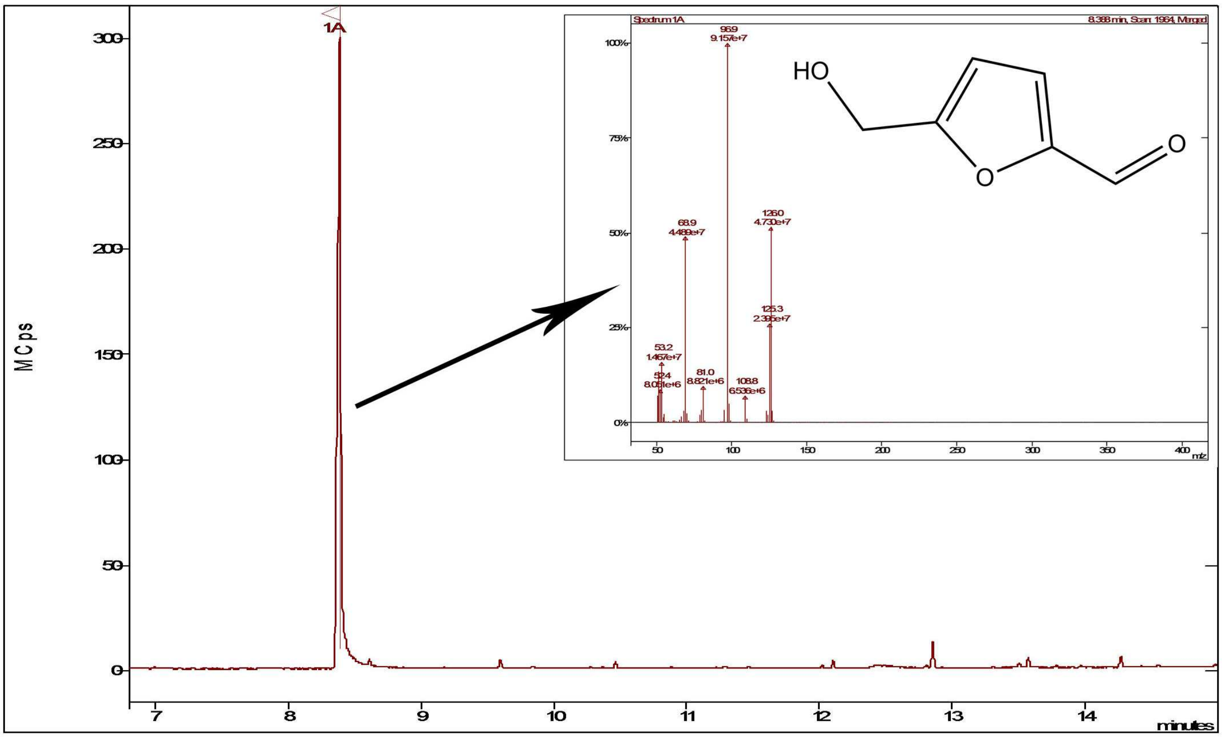


Fig.1. Experiment GC-MS of the 5-HMF

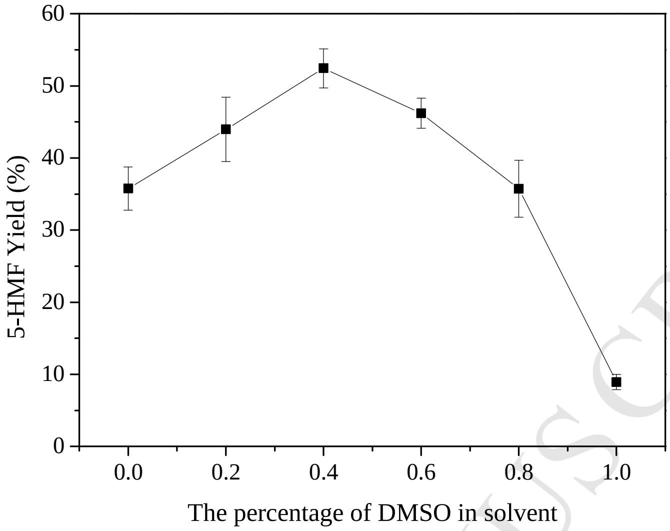


Fig.2. Effect of the different mass ratio of the DMSO/water on the conversion of GlcNAc into 5-HMF under hydrothermal conditions. Reaction conditions: GlcNAc, 100 mg; [Hmim][HSO_4], 4.516mmol ; reaction temperature, 180 °C.

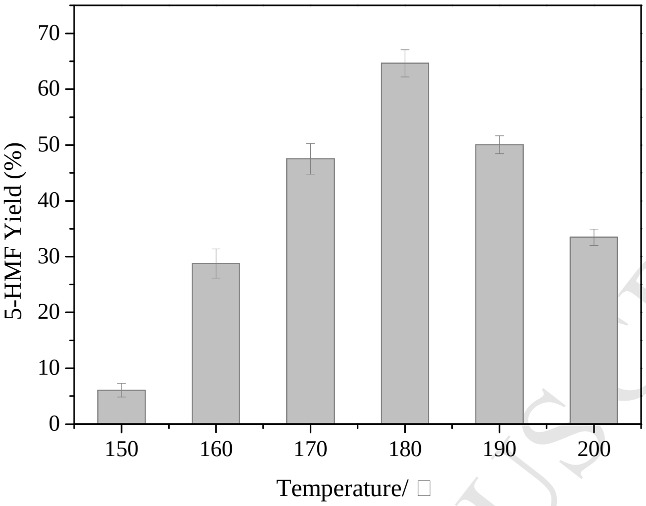


Fig.3. Effect of reaction temperature on 5-HMF production under hydrothermal conditions. Reaction conditions: GlcNAc, 100 mg; distilled water, 12g; DMSO, 8g; [Hmim][HSO_4], 9.040mmol; reaction time, 6 h.

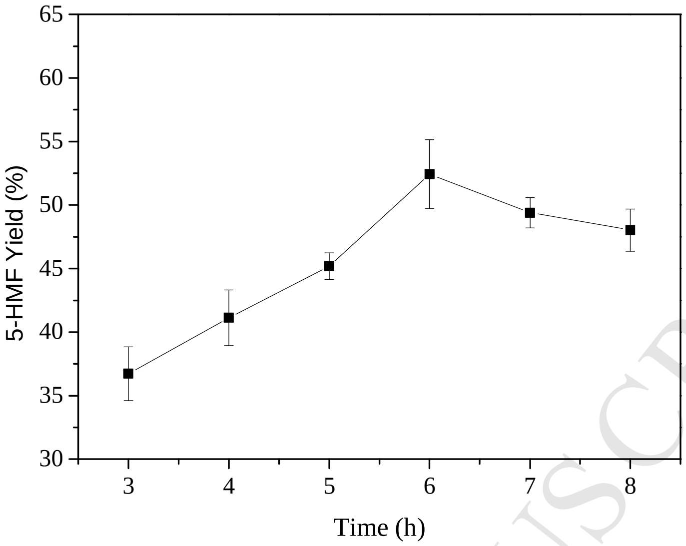


Fig.4. Effect of reaction time on 5-HMF production under hydrothermal conditions. Reaction conditions: GlcNAc, 100 mg; distilled water, 12g; DMSO, 8g; [Hmim][HSO_4], 4.516mmol; reaction temperature, 180 °C.

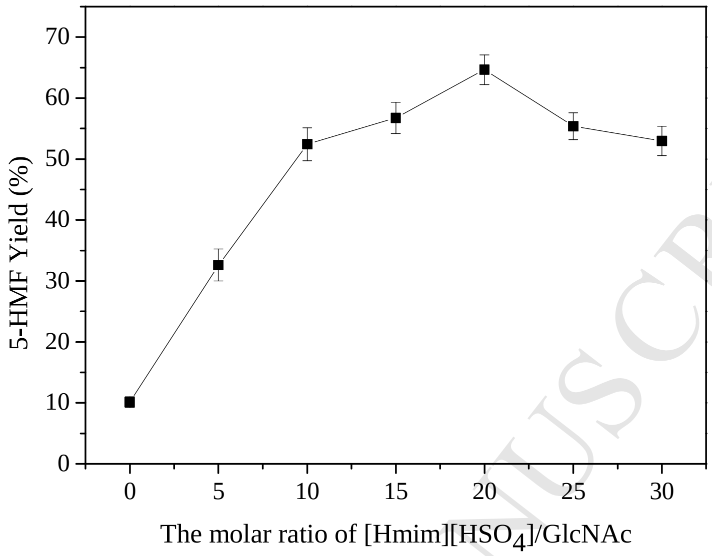


Fig.5. Effect of the ionic liquid dosage on the conversion of GlcNAc into 5-HMF under hydrothermal conditions. Reaction conditions: GlcNAc, 100 mg; distilled water, 12g; DMSO, 8g; reaction temperature, 180 °C, reaction time, 6 h.

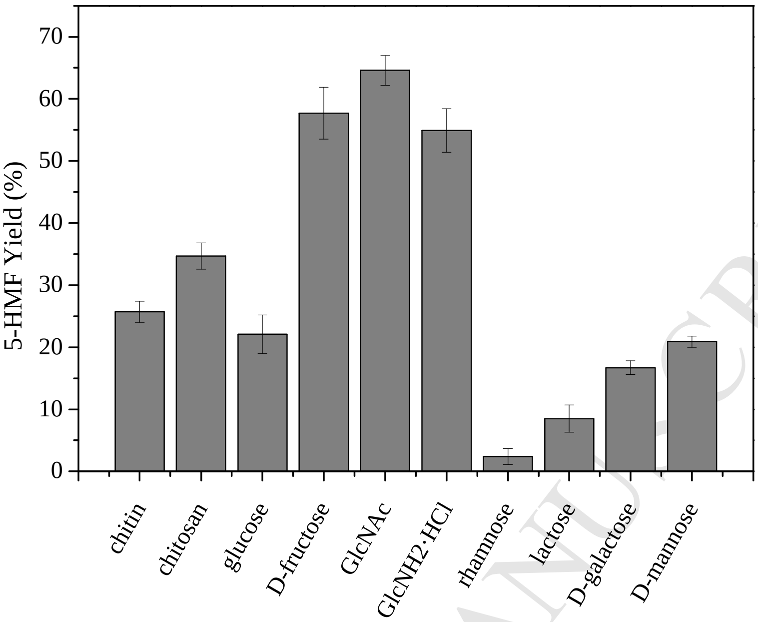
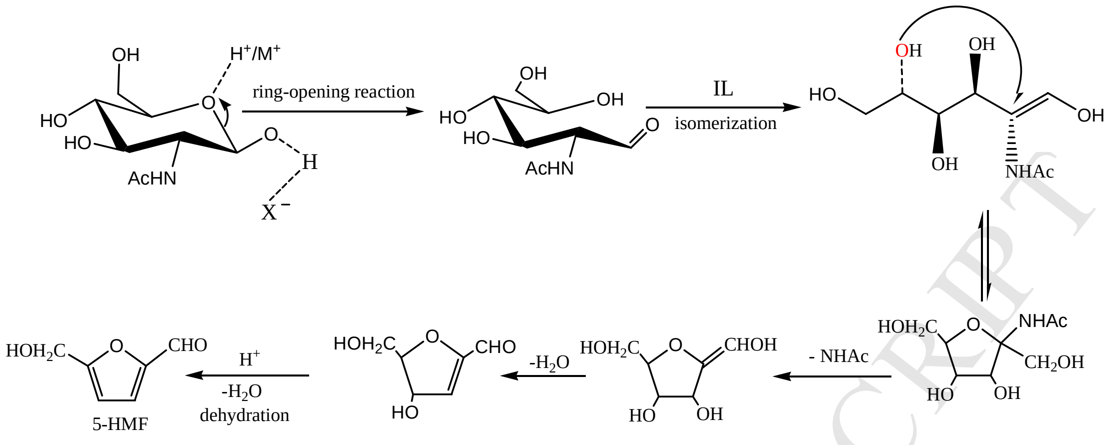


Fig.6. Conversion of several carbohydrate into 5-HMF use [Hmim][HSO_4] as catalyst. Reaction conditions: carbohydrate,100 mg; the [Hmim][HSO_4] with carbohydrate in a 20:1 molar ratio, distilled water, 12g; DMSO, 8g; reaction temperature, 180 °C; reaction time, 6 h.



M:$[HMIM]^+$;   X:HSO_4^-

Fig.7. Proposed mechanism of IL promoted conversion of GlcNAc into 5-HMF.

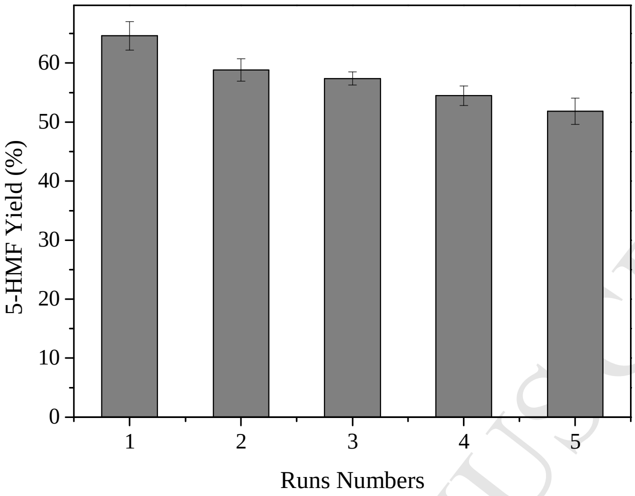


Fig.8. Recycling of [Hmim][HSO_4] for the synthesis of 5-HMF from GlcNAc under hydrothermal conditions. Reaction conditions: GlcNAc, 100 mg; [Hmim][HSO_4], 9.040mmol; distilled water, 12g; DMSO, 8g; reaction temperature, 180 °C; reaction time, 6 h.

Highlights

- Effective conversion of amino sugars to 5-HMF catalyzed by ionic liquid was realized.
- High 5-HMF yield of 35.8% was obtained from *N*-acetyl-D-glucosamine in water.
- The yield improved to 64.6% on using a water-dimethyl sulfoxide mixture solvent.
- This catalysis system can be recycled at least five times.