



Synthesis of renewable monomer 2, 5-bishydroxymethylfuran from highly concentrated 5-hydroxymethylfurfural in deep eutectic solvents

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ABSTRACT

2, 5-Bishydroxymethylfuran (BHMF) has been currently emerged as a promising biomass-derived monomer. It is highly desirable to proceed a chemical process at a high substrate concentration, by which a facile and cost-effective separation of products can be expected. Herein, we report for the first time on the hydrogenation of highly concentrated 5-hydroxymethylfurfural (HMF) in deep eutectic solvents (DESs), giving a near quantitative selectivity towards BHMF in ChCl-glycerol DES at 25 °C in 3 h using NaBH₄ as the H-donor. DES is hailed as a new class of green solvent, in which HMF/BHMF could be stabilized by the strong hydrogen-bond interaction, and allowed the selective hydrogenation of HMF at high concentration up to 40 wt%. Notably, the resulting BHMF could be readily separated by extraction with ethyl acetate, and then high purity of BHMF with a desirable isolated yield around 80% was obtained after removing of ethyl acetate. Additionally, the reaction efficiency of HMF hydrogenation in DESs was verified to be strongly associated with the viscosity of DESs and the *p*K_a value of hydrogen-bonding donor. © 2019 The Korean Society of Industrial and Engineering Chemistry. Published by Elsevier B.V. All rights reserved.

Introduction

Biomass resources are considered as preferable raw materials with the features of renewability, wide-distribution and large-scale production in the world [1–3]. 5-Hydroxymethylfurfural (HMF), which can be readily formed by acid-catalyzed dehydration of bio-based carbohydrates, is put forward as an all-purpose platform molecule for the production of materials, chemicals, and fuels [4,5]. Multiple functionalities, including C=C, C=O, and O–H, enable flexible catalytic valorization of HMF into a wide range of products by hydrogenation, hydrogenolysis, oxidation or etherification, etc. [6–9]. Thereinto, 2, 5-bishydroxymethylfuran (BHMF) derived from the hydrogenation of HMF is a versatile diol that can be used as a building-block for the synthesis of crown ethers, artificial fibers and resins [10]. Moreover, electron-donating hydroxy groups allowed BHMF to produce self-healing polymeric materials by Diels–Alder reaction between furan and maleimide groups [10].

In recent years, numerous reports focused on the selective hydrogenation of HMF to BHMF and the representative works are enumerated in Table S1 based on H-donors and solvents used. H₂ is the most common hydrogen source and could give desirable BHMF yields from HMF in conventional solvents, such as H₂O, methanol, 1-butanol, tetrahydrofuran (THF), over various heterogeneous catalysts [11]. However, the vast majority of catalytic systems containing molecular H₂ are limited by relatively low HMF concentrations (<6.0 wt%). It is highly desirable to proceed a chemical process at a high substrate concentration, by which a facile and cost-effective separation of products can be expected. Up to now, only two works focused on the formation of BHMF at a relatively high HMF concentration in the presence of molecular H₂ in water or methanol [12,13]. For example, Cu/SiO₂ gave a BHMF yield of 97.0% from HMF with an initial concentration of 20.0 wt% in methanol at 100 °C for 8 h (Table S1, entry 3) [12]. Under milder reaction conditions (35 °C, 2 h, 8 bar H₂), a comparable BHMF yield of 98.9% was gained from HMF (20.0 wt%) in water over Pt/MCM-41 (Table S1, entry 4) [13]. Besides that, alcohols or formic acid also can be used as in-situ hydrogen source to replace gaseous hydrogen for the catalytic transfer hydrogenation (CTH) of HMF [10]. However, relatively low HMF

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concentrations (lower than 6.0 wt%) were still required for the CTH route to minimize by-reactions at relatively high reaction temperature or in the presence of acidic catalysts. HMF could also be converted to an equimolar mixture of BHMF and 5-hydroxymethylfuranic acid (HMFA) by Cannizzaro reaction [14]. Notably, the additional separation of BHMF and HMFA was needed in this case. In addition, electrocatalytic hydrogenation of HMF to BHMF was studied, which also suffered from the low initial HMF concentration (<0.6 wt%) [15]. Recently, NaBH₄ was employed as a efficient reducing agent for the formation of BHMF from HMF with high concentrations (around 20 wt%) in methanol, ethanol or THF; however, relatively low BHMF yields (55%–88%) with excessive amounts of NaBH₄ (>30.0 wt%, relative to HMF) were required in these cases [16]. At this point, quantitative conversion of highly concentrated HMF to BHMF with a marginal amount of NaBH₄ is highly desirable.

HMF contains various active functionalities, such as hydroxyl and aldehyde groups, which could readily result in the transformation of HMF to humins by aldol addition/condensation reactions [17]. Hence, the conversion of highly concentrated HMF to BHMF requires solvents that are capable of stabilizing HMF and/or BHMF during the reaction. In this context, deep eutectic solvents (DESs) possess great application potential and were successfully employed in the acid-catalyzed dehydration of highly concentrated carbohydrates to HMF [18]. DESs have sprung up as a new family of green solvents that are liquid eutectic mixtures formed by hydrogen-bonding interaction of two or more safe and biodegradable components, such as choline chloride (ChCl), carbohydrates, and glycerol [19,20]. Our group also studied the formation of value-added chemicals, such as 5-brominemethylfurfural, 5-ethoxymethylfurfural, and 5-chloromethylfurfural from biomass-derived carbohydrates in ChCl-based DESs [21–23]. Encouraged by previous works, we studied the conversion of highly concentrated HMF to BHMF in DESs in this work.

Herein, we investigated the selective hydrogenation of highly concentrated HMF to BHMF in the presence of NaBH₄ in various ChCl-based DESs, including ChCl-urea, ChCl-ethylene glycol and ChCl-glycerol DESs. Generally, ChCl and another component in these DES systems act as hydrogen-bonding acceptor (HBA) and hydrogen-bonding donor (HBD), respectively [20]. Interestingly, HMF with a concentration as high as 40.0 wt% in ChCl-glycerol DES could be quantitatively converted to BHMF at 25 °C in 180 min. Notably, a marginal amount of NaBH₄ of 10.0 wt% or 48.5 mol% relative to HMF was sufficient for the hydrogenation of HMF in this case. The separation/purification of BHMF from DES and the recycling of DES were also performed. These findings clearly indicate that DES is a promising medium for the treatment of HMF at high concentrations.

Materials and methods

Materials

2, 5-Bishydroxymethylfuran (BHMF, 95%) was supplied by BePharm Co. Ltd. (Shanghai, China). 5-Hydroxymethylfurfural (HMF, 98%) was obtained from Shanghai Energy Chemical Industrial Co. Ltd. (Shanghai, China). Glycerol, ethylene glycol and methyl isobutyl ketone (MIBK) were purchased from Xilong Chemical Co. Ltd. (Guangzhou, China). Choline Chloride (ChCl) and D-glucitol were provided by Aladdin Chemical Technology Co. Ltd. (Shanghai, China). All the other chemicals were supplied by Sinopharm Chemical Reagent Co. Ltd. (Shanghai, China). All reagents were of analytical grade and used without further purification.

Synthesis of DESs

In this study, ChCl was chosen as HBA for all DESs. Urea, ethylene glycol or glycerol was employed as HBD. The preparation of DES was

carried out in a round-bottomed flask. HBA and HBD were mixed at a certain molar ratio (mostly 1:2) and then heated at 80 °C to give a transparent melting mixture. The viscosity of the prepared DESs was measured using a Brookfield DV-C Digital Viscometer.

Typical reaction for BHMF formation from highly concentrated HMF

In a typical procedure for BHMF preparation in ChCl-glycerol DES, 1.85 g (14.7 mmol) of HMF and 0.18 g (4.8 mmol) of NaBH₄ were added into the DES (ChCl: 1.20 g, glycerol: 1.58 g). The resulting mixture was then added into a stainless steel reactor and was stirred with a magnetic bar at 25 °C for a certain time. After, 8 g of ethanol was added into the reaction mixture to disturb the DES and all products were dissolved in ethanol, followed by analysis with GC-MS and GC methods, respectively.

Separation of BHMF and recycling of DES

After the reaction, the DES was dissolved in 2 mL of water and BHMF in the mixture was then extracted with 8 mL of ethyl acetate for 5 times. About 40 mL of extract was subsequently evaporated at 45 °C under reduced pressure to remove the organic solvent (ethylene acetate) and then gave white solid product (BHMF). The obtained BHMF was characterized by ¹H NMR and ¹³C NMR, respectively (Figures. S1–S2). ¹H NMR (600 MHz, D₂O): δ 6.24 (2 H), 4.44 (4 H); ¹³C NMR (151 MHz, D₂O): δ 153.64(=C-O), 109.07(=C-H), 55.82(-CH₂-). In addition, the possible residual atoms (Na, B, Cl) in the separated BHMF product were detected by energy dispersive spectrometer (EDS) and inductively coupled plasma optical emission spectroscopy (ICP-OES). The remaining aqueous phase was also evaporated at 65 °C under reduced pressure to remove water and then offered viscous spent DES, which was reused in the next run under the same reaction conditions.

Product analysis

The qualitative analysis was performed by a GC-MS instrument (Thermo Trace 1300 and ISQ LT) that equipped with a TR-5MS column (15 m × 0.25 mm × 0.25 μm). The quantitative analysis of HMF and BHMF was conducted by an Agilent 7890 series (GC) using a DB-WAXETR column. The concentration of BHMF and HMF in liquid product was calculated by using a standard curve based on known concentration of these compounds. HMF conversion (X_{HMF}, %), BHMF selectivity (S_{BHMF}, %), BHMF yield (Y_{BHMF}, %) were calculated according to Eqs. 1–3:

$$X_{\text{HMF}} (\text{mol } \%) = (1 - M_{\text{HMF}}/M_{\text{HMF}_0}) \times 100\% \quad (1)$$

$$Y_{\text{BHMF}} (\text{mol } \%) = M_{\text{BHMF}}/M_{\text{HMF}_0} \times 100\% \quad (2)$$

$$S_{\text{BHMF}} (\text{mol } \%) = Y_{\text{BHMF}}/X_{\text{HMF}} \times 100\% \quad (3)$$

where M_{HMF}, M_{HMF₀} and M_{BHMF} stand for the final molar weight of HMF, the initial molar weight of HMF and the final molar weight of BHMF, respectively.

Results and discussion

Hydrogenation of HMF to BHMF in different DESs

In this study, ChCl acted as a HBA was mixed with a HBD (e.g. urea, ethylene glycol, glycerol) at a molar ratio of 1:2. These above HBA and HBD were cheap, biodegradable, renewable and/or non-toxic compounds [19]. In the first set of our experiments, a 13.0 wt%

Table 1
The hydrogenation of HMF to BHMF in different DESs.^a

Entry	HBD	t (min)	Conv. ^b (%)	Selec. (%)	Yield ^c (%)
1	Urea	30	55.7	73.4	40.9
2	Urea	60	75.7	68.3	51.7
3	Urea	120	98.4	71.1	70.0
4	Ethylene glycol	5	83.6	81.1	67.8
5	Ethylene glycol	10	95.2	90.8	86.4
6	Ethylene glycol	20	98.4	94.5	93.0
7	Ethylene glycol	30	98.7	94.4	93.2
8	Ethylene glycol	40	98.5	95.0	93.6
9	Glycerol	5	98.4	85.4	83.1
10	Glycerol	10	100.0	96.0	96.0
11	Glycerol	20	100.0	>99.9	>99.9

^a Reaction conditions: 3.3 mmol HMF, 1.6 mmol NaBH₄ (10 wt% or 48.5 mol% relative to HMF), 8.6 mmol HBA (ChCl), the molar ratio of HBA (ChCl) to HBD = 1:2, 25 °C.

^b GC conversion.

^c GC yield.

of HMF (3.3 mmol) with 1.6 mmol NaBH₄ was employed for the BHMF formation at 25 °C. As presented in Table 1, both HMF conversion and BHMF yield increased with the reaction time in all ChCl-based DESs. For example, an HMF conversion of only 55.7% with a BHMF yield of 40.9% was obtained in ChCl-urea DES for 30 min (Table 1, entry 1). If the reaction time was prolonged to 120 min, HMF conversion and BHMF yield gradually increased to 98.4% and 70.0%, respectively (Table 1, entry 3). Notably, BHMF yields of 93.6% and 99.9% were achieved in ChCl-ethylene glycol DES within 40 min and in ChCl-glycerol DES within 20 min, respectively (Table 1, entries 8 and 11). Repeatability tests were also conducted in different DESs, which provided stable HMF conversions and product distributions (Table S2), indicating that the data provided in this study are highly reliable. The above results demonstrate that the conversion of concentrated HMF towards BHMF with a high selectivity is feasible in DESs.

Notably, the obvious gap between HMF conversion and BHMF selectivity was observed in all the experiments conducted in ChCl-urea DES (Table 1). For example, a HMF conversion of 98.4% with a BHMF selectivity of only 71.1% was achieved at 25 °C in 120 min in ChCl-urea DES (Table 1, entry 3). Interestingly, the difference between HMF conversion and BHMF selectivity reduced in ChCl-ethylene glycol or ChCl-glycerol DES. As shown in Table 1, a HMF conversion of 98.5% with a BHMF selectivity of 95.0% was achieved at 25 °C in 40 min in ChCl-ethylene glycol DES (Table 1, entry 8). However, no other by-products derived from HMF were detected by GC or ¹H/¹³C NMR analysis in these cases (Figures S1–S3). Previous literature reported that ChCl could act as a ligand to form complex with HMF in aqueous solution [24], similar complex probably formed in ChCl-based DESs, which is undetectable by GC analysis. Note that changes in chemical shift of the protons of HMF were clearly observed in all ¹H NMR spectra with the addition of DESs, which will be deeply discussed later (Section “The hydrogen-bonding interaction between HMF and DESs”).

Table 2
Measurement of recovery rate of HMF or BHMF in different DESs without NaBH₄.^a

Entry	HBA	HBD	HMF recovery ^b (%)	BHMF recovery ^b (%)
1	ChCl	Urea	65.3	95.0
2	ChCl	Ethylene glycol	69.2	91.8
3	ChCl	Glycerol	87.9	96.9
4	ChCl	/	96.6	/
5	/	Urea	95.0	/

^a Reaction conditions: 0.6 mmol HMF, 2.1 mmol HBA (ChCl), the molar ratio of HBA to HBD = 1:2.

^b The ratio of HMF initial mass to HMF measured mass.

To verify the above assumption, the recovery rate of HMF or BHMF in DESs was measured by GC method without NaBH₄. Specifically, 0.6 mmol HMF or BHMF (around 13.0 wt%) was mixed with DESs (HBA:HBD = 1:2) at 25 °C without NaBH₄. Excessive ethanol was then added into the above mixtures and gave transparent ethanol solution for GC analysis. As expected, only 65.3% or 69.2% of the initial HMF was detected in the case of ChCl-urea or ChCl-ethylene glycol DES, whereas HMF recovery of 87.9% was obtained in the case of ChCl-glycerol DES (Table 2, entries 1–3). In comparison, BHMF recovery greater than 90% was obtained from these DESs under the same conditions. It follows that undetectable HMF-derived complex could form in DESs, especially in ChCl-urea DES, which should be responsible for the difference between HMF conversion and BHMF selectivity (Table 1). Notably, the formation of the HMF-derived complexes could be a reversible process, especially in ChCl-glycerol DES. As shown in Table 1, BHMF selectivity improved from 85.4% to 99.9% with reaction time increasing from 5 min to 20 min in ChCl-glycerol DES, whereas HMF conversion only increased slightly from 98.4% to 100% (Table 1, entries 9–11), implying that additional free HMF from HMF-derived complexes was probably further hydrogenated to form BHMF with the reaction time. Nevertheless, BHMF selectivity kept around 70% even after a prolonged reaction time of 120 min in ChCl-urea DES (Table 1, entry 3), probably because the decomposition of HMF-derived complex was suppressed by the relatively stronger hydrogen-bond interaction in this system (discussed in Section “The hydrogen-bonding interaction between HMF and DESs”).

The influence of DES components on the HMF recovery was further investigated individually. Unexpectedly, HMF recovery of greater than 95% was achieved in the presence of either ChCl or urea alone (Table 2, entries 4–5), implying that almost no HMF-derived complex formed with ChCl or urea alone in ethanol. It is known that there is strong hydrogen-bonding interaction between HBAs and HBDs in DESs [19], which could be responsible for the formation of undetectable HMF-derived complex in the presence of ChCl and urea in ethanol.

The hydrogen-bonding interaction between HMF and DESs

To investigate the hydrogen-bonding interaction between HMF and DESs, ¹H NMR tests were conducted for the mixture of HMF and DESs. HMF (3.3 mmol) was mixed with different DESs followed by the addition of D₂O for ¹H NMR tests. It is commonly acknowledged that the signal peak of the active hydrogen in hydroxyl functional group could shift easily, or even directly disappear in ¹H NMR spectrum. Therefore, the change of chemical shift for the proton in hydroxyl group was not discussed in this work. As shown in Fig. 1, all the signal peaks of protons in HMF shift to low field in the presence of DESs, which could be attributed to the deshielding effect caused by the hydrogen-bonding interaction between HMF and DES [25]. The maximum offsetting of HMF in ¹H NMR spectra is observed in ChCl-urea DES, indicating the strongest hydrogen-bonding interaction and deshielding effect in ChCl-urea DES. Too strong hydrogen-bonding interaction between HMF and DES could result in considerable decrease in the reaction activity of HMF during the reaction, and also led to the formation of undetectable and stable HMF-derived complexes. Therefore, ChCl-urea DES offered a relatively low reaction efficiency and BHMF selectivity for HMF hydrogenation as compared to ChCl-ethylene glycol or ChCl-glycerol DES (Table 1). On the other hand, it is known that the condensation reactions of HMF to by-products usually occur at carbonyl and hydroxy groups in HMF [17], which could be considerably minimized by hydrogen-bonding interaction between carbonyl or hydroxy group in HMF and DES. Hence, the selective hydrogenation of highly concentrated HMF to form BHMF can be largely facilitated in DESs.

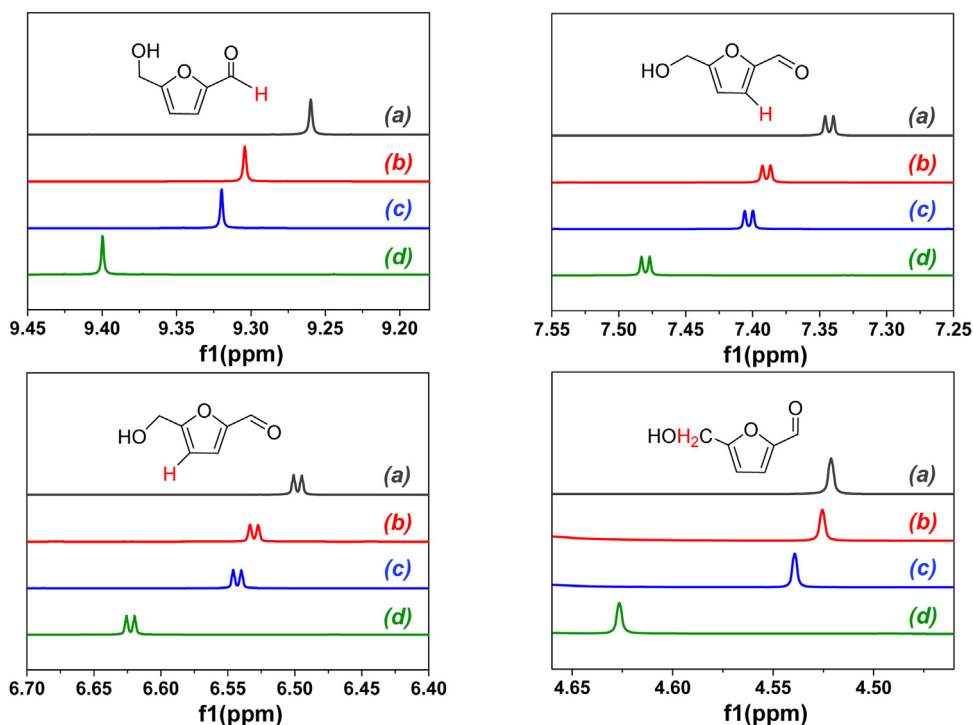


Fig. 1. ^1H NMR spectra (D_2O) of HMF in the presence of different DESs (a) HMF only, (b) HMF with ChCl-glycerol DES, (c) HMF with ChCl-ethylene glycol DES, (d) HMF with ChCl-urea DES.

Hydrogenation of HMF at low loading of NaBH_4

It is highly desirable to reduce the loading amount of NaBH_4 for the hydrogenation of HMF in DESs from the perspective of atom economy. In this light, the hydrogenation of HMF to BHMF in DESs was further investigated at a low NaBH_4 loading (7.5 wt% or 36.4 mol% relative to HMF) in this study (Table 3). In ChCl-glycerol DES, a HMF conversion of 89.2% with a BHMF yield of 82.1% was still achieved at 25 °C in 5 min (Table 3, entry 1). By prolonging the reaction time to 30 min, both HMF conversion and BHMF yield gradually increased to 94.4% and 90.2%, respectively (Table 3, entry 4). Similar trend was also observed in ChCl-ethylene glycol DES (Table 3, entries 5–9). It follows that a relatively low loading of NaBH_4 could also offer desirable BHMF yield from HMF hydrogenation in DESs. Notably, 36.4 mol% is so far the lowest NaBH_4 loading for the hydrogenation of concentrated HMF to BHMF, which is considerably lower than those applied in traditional solvents (100 mol%–203 mol%) [16,26–28]. This finding reinforces

the fact that DESs are promising media for the conversion of HMF at high concentration.

Influence of viscosity of DESs and pK values of HBDs

Generally, DESs have relatively high viscosity as compared to traditional solvents, such as methanol, THF [29]. It is known that high viscosity of solvent has negative effect on the mass transfer [30], which encourages us to study the influence of the viscosity of DESs on HMF hydrogenation at a high concentration. The viscosity of DES is strongly related to its composition, and thus the viscosity of DESs with varied HBDs was measured. As shown in Table 4, the viscosity of ChCl-based DESs at a HBA/HBD ratio of 1:2 decreased in the order of glucitol (2890 cP) > urea (975 cP) > glycerol (338 cP) > ethylene glycol (25 cP), based on the diversity of HBDs. However, the conversion of HMF did not increase with the decrease of the viscosity of these DESs. For example, ChCl-glucitol DES with the highest viscosity (2890 cP) gave a desirable HMF conversion of 85.7%, whereas ChCl-ethylene glycol DES with the lowest viscosity (25 cP) only offered a HMF conversion of 69.2% under the same conditions (Table 4, entries 2 and 4). The maximum HMF conversion of 92.3% was achieved in ChCl-glycol DES with a moderate viscosity (Table 4, entry 3). The similar phenomenon was also observed in DESs with a HBA/HBD ratio of 1:3 (Table 4, entries 5–7).

The viscosity of DESs is also associated with their HBA/HBD ratios. For ChCl-ethylene glycol DES, its viscosity reduced from 25 cP to 13 cP with the decrease of HBA/HBD ratio from 1:2 to 1:3 (Table 4, entries 2 and 5). In comparison, the viscosity of ChCl-glycol DES increased from 338 cP to 395 cP with the decrease of HBA/HBD ratio from 1:2 to 1:3 (Table 4, entries 3 and 6). It is clear that HMF conversion increased with the decrease of the viscosity of DESs consisting of the same HBA and HBD. For instance, ChCl-ethylene glycol DES with the HBA/HBD ratio of 1:3 provided a HMF conversion of 81.1%, which is higher than that obtained in ChCl-ethylene glycol DES with the HBA/HBD ratio of 1:2 (Table 4, entries 2 and 5). The above findings imply that HMF conversion is not only influenced by the viscosity of DESs.

Table 3
The hydrogenation of HMF to BHMF in DESs at low loading of NaBH_4 .^a

Entry	HBD ^b	t (min)	Conv. ^b (%)	Selec. (%)	Yield ^c (%)
1	Glycerol	5	89.2	92.0	82.1
2	Glycerol	10	92.3	94.7	87.4
3	Glycerol	20	93.1	95.3	88.7
4	Glycerol	30	94.4	95.6	90.2
5	Ethylene glycol	5	64.7	53.9	34.9
6	Ethylene glycol	10	69.2	73.1	50.6
7	Ethylene glycol	20	95.9	74.4	71.4
8	Ethylene glycol	30	96.6	83.1	80.3
9	Ethylene glycol	60	97.2	82.3	80.0

^a Reaction conditions: 3.3 mmol HMF, 1.2 mmol NaBH_4 (7.5 wt% or 36.4 mol% relative to HMF), 8.6 mmol HBA (ChCl), the molar ratio of HBA (ChCl) to HBD = 1:2, 25 °C.

^b GC conversion.

^c GC yield.

Table 4The viscosity of different DESs and pK_a values of its HBD.^a

Entry	HBD	HBA:HBD	Viscosity (cP)	pK_a^b	Conv. ^c (%)	Yield ^d (%)
1	Urea	1:2	975	14.43	49.7	12.2
2	Ethylene glycol	1:2	25	14.13	69.2	50.6
3	Glycerol	1:2	338	13.68	92.3	87.4
4	D-glucitol ^e	1:2	2890	13.14	85.7	41.6
5	Ethylene glycol	1:3	13	14.13	81.1	67.3
6	Glycerol	1:3	395	13.68	91.2	82.1
7	1, 4-butylene glycol	1:3	46	14.73	27.3	8.0

^a ChCl was used as HBA, and the viscosity of DESs was detected at 25 °C; reaction conditions: 3.3 mmol HMF, 1.2 mmol NaBH₄ (7.5 wt% or 36.4 mol% relative to HMF), 8.6 mmol HBA (ChCl), 25 °C, 10 min.

^b The pK_a values of HBDs were provided by SciFinder, which were measured in aqueous solution of these HBDs.

^c GC conversion.

^d GC yield.

^e The viscosity of ChCl-D-glucitol DES or the reactions in ChCl-D-glucitol DES was detected at 65 °C due to its extremely high viscosity.

On the other hand, the rate of the reduction of carbonyl in the presence of NaBH₄ is strongly associated with pK_a values of reaction solvents. To be specific, the nucleophilic attack of hydride or borohydride ion on carbonyl can be greatly facilitated in the solvents with low pK_a values [31]. Therefore, it is necessary to investigate the interrelation between HMF conversion and the pK_a values of DESs. However, DESs are eutectic mixtures and their pK_a values are not available. Instead, we found that pK_a values of HBDs of DESs showed a clear negative correlation to HMF conversion obtained in corresponding DESs. As shown in Table 4, the pK_a value of HBD in DESs with a HBA/HBD ratio of 1:2 decreased in the order of urea (14.43) > ethylene glycol (14.13) > glycerol (13.68), resulting in HMF conversion increased with the decrease of pK_a value of HBD (Table 4, entries 1–3). The similar trend was also observed in the DESs with a HBA/HBD ratio of 1:3 (Table 4, entries 5–7). For example, 1, 4-butylene glycol had the highest pK_a value of 14.73, and ChCl-butylene glycol DES offered the lowest HMF conversion of 27.3% (Table 4, entry 7). However, ChCl-glycerol DES was an exception in DESs with a HBA/HBD ratio of 1:2, because D-glucitol with the lowest pK_a value failed to give the highest HMF conversion even at a higher reaction temperature of 65 °C (Table 4, entry 4). The relatively low HMF conversion in ChCl-glycerol DES is probably attributed to its extremely high viscosity of 2890 cP, which is eight times higher than that of ChCl-glycerol DES (Table 4, entries 3–4). These above findings clearly indicate that the reaction rate of HMF hydrogenation in DESs is influenced by both the viscosity of DESs and the pK_a values of HBDs.

Separation and purification of BHMF

In view of the outstanding performance of DESs in the hydrogenation of HMF, the concentration of HMF was further increased to 40.0 wt%, which is so far the highest HMF concentration for the formation of BHMF. As shown in Table 5, BHMF yield of 78.5% or 89.5% was still achieved from 40.0 wt% HMF in ChCl-ethylene glycol or ChCl-glycerol DES at 25 °C with a low NaBH₄ loading of 24.5 mol% relative to HMF (Table 5, entries 1–2). These above BHMF yields are comparable to those obtained from the hydrogenation of 13.0 wt% HMF with a higher NaBH₄ loading of 36.4 mol% (Table 3, entries 4 and 9). Excitingly, almost quantitative conversion of HMF to BHMF was observed in ChCl-glycerol DES if the NaBH₄ loading increased to 32.7 mol% at 25 °C for 180 min (Table 5, entry 3).

In this study, a facile separation/purification of BHMF from ChCl-glycerol DES was also conducted. As shown in Fig. 2, water was first added to dissolve the resulting DES and BHMF mixture, and ethyl acetate was then added to extract BHMF from the aqueous solution (Detailed procedure is provided in Experimental Section). BHMF product was easily obtained by the removal of ethyl acetate and then

Table 5The formation and separation of BHMF from HMF at a concentration of 40.0 wt% in DESs.^a

Entry	t(min)	Conv. (%)	Yield (%)	Selec. (%)	Isolated rate ^d (%)
1	60	88.9	78.5	88.3	–
2	30	92.1	89.5	97.2	–
3	180	100	>99.9	>99.9	79.1
4 ^b	180	–	–	–	87.5
5 ^c	180	–	–	–	85.7

^a Reaction conditions: 14.7 mmol HMF (40 wt% relative to DES), 3.6 mmol NaBH₄ (24.5 mol% relative to HMF, entries 1–2), 4.8 mmol NaBH₄ (32.7 mol% relative to HMF, entries 3–5), 8.6 mmol HBA (ChCl), the molar ratio of HBA (ChCl) to HBD = 1:2, HBD: ethylene glycol (entry 1), HBD: glycerol (entries 2–5), 25 °C.

^b The first recycle of ChCl-glycerol DES.

^c The second recycle of ChCl-glycerol DES.

^d Isolated rate (%) = $\frac{\text{the extracted molar weight of BHMF}}{\text{the initial molar weight of HMF}}$ (%).

gave a desirable isolated yield of 79.1% (Table 5, entry 3), which indicates that near 20% BHMF still kept in the aqueous solution. This part of BHMF in the aqueous solution cannot be regarded as a loss, because the spent DES system with the remaining BHMF can be recycled. At this point, the regeneration of ChCl-glycerol DES was performed by the removal of water at 65 °C in vacuum (Fig. 2). Interestingly, the regenerated ChCl-glycerol DES could be reused twice, and offered high isolated yield of BHMF of 87.5% or 85.7% for the first or second recycling test, respectively (Table 5, entries 4–5). Notably, the isolated yields of BHMF from the recycling tests of

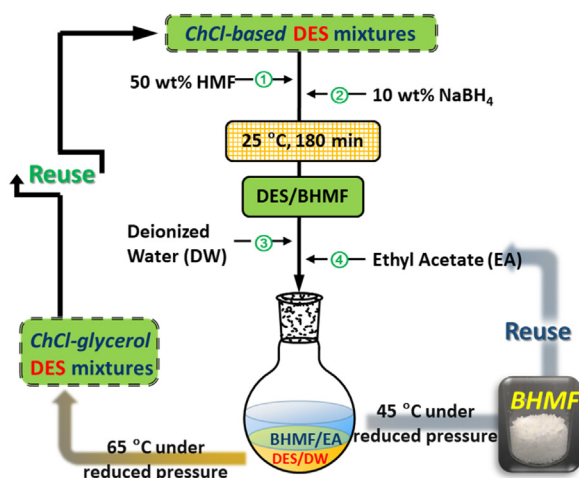


Fig. 2. Schematic representation of separation of BHMF and the recycling of ChCl-glycerol DES.

ChCl-glycerol DES were higher than that obtained from the fresh DES (Table 5, entry 3), because the remaining BHMF in the used DES could also be extracted out by ethyl acetate during the recycling test. As a result, direct BHMF yield from the recycling tests was not provided in Table 5. Therefore, DESs can be employed as recyclable solvents for the catalytic upgrading of HMF at high concentrations.

Furthermore, the high purity of BHMF was characterized by energy dispersive spectrometer (EDS), Inductively Coupled Plasma Optical Emission Spectrometer (ICP-OES) and $^1\text{H}/^{13}\text{C}$ NMR. The results of EDS and ICP-OES indicated that only C and O were detected in the BHMF sample, and the content of Na or B is negligible (Tables S3–S6). $^1\text{H}/^{13}\text{C}$ NMR spectra of the BHMF sample suggested that only trace amount of residual HMF or glycerol was observed (Figure S1–S2).

Conclusion

In this contribution, DESs were confirmed as outstanding media for HMF hydrogenation to BHMF, in which a quantitative selectivity towards BHMF from highly concentrated HMF up to 40.0 wt% with low NaBH_4 loading (32.7 mol% relative to HMF) was achieved. The resulting BHMF could be facilely separated by extraction with ethyl acetate, giving high purity of BHMF with a desirable isolated yield of around 80%. The hydrogen-bonding interaction between HMF/BHMF and DES was confirmed by ^1H NMR characterization, which enables the selective hydrogenation of HMF at high concentration in DESs. In addition, the reaction efficiency of HMF hydrogenation in DESs was verified to be strongly associated with the viscosity of DESs and the pK_a values of hydrogen-bonding donors. Therefore, DESs hold great promise as green and effective media in the catalytic upgrading of HMF.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jiec.2019.08.057>.

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