# Efficient conversion of fructose to 5-[(formyloxy)methyl]furfural by reactive extraction and in-situ esterification

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**Abstract**–5-[(Formyloxy)methyl]furfural (FMF), an analogue of 5-(hydroxymethyl)furfural (HMF) is becoming more attractive due to its superior stability and hydrophobicity, which make it easier to refineand store. In the present study, FMF was produced from fructose by one-pot approach in pure formic acid media or by a two-step approach via HMF in choline chloride (ChCl)/fructose deep eutectic solvents (DES) system. A favorable FMF yield of 63.22% was reached by two-step approach. In addition, the effects of reaction parameters, such as temperature and acidity, on preparation of FMF from fructose were systematically investigated. The dehydration of fructose into HMF was confirmed as the rate-controlling step in the consecutive reaction. Ultimately, the separation and purification procedures of FMF were put forward. The FMF with a purity of 98.8% was obtained finally. Meanwhile, the FMF purified by saturated sodium bicarbonate solution showed an excelled storage stability.

Keywords: 5-[(Formyloxy)methyl]furfural, 5-Hydroxymethylfurfural, Fructose, Deep Eutectic Solvents, Purification

## INTRODUCTION

Substantial efforts have been devoted to chemical and biological conversion of abundant lignocellulosic biomass into versatile chemicals [1]. In particular, 5-(hydroxymethyl)furfural (HMF) derived from biomass via dehydration of glucose and fructose, has been regarded as a versatile and key platform chemical for the production of a variety of important chemicals on a large scale [2-5]. Until now, numerous endeavors have been made to improve the process of HMF production and have brought some satisfying results. Ionic liquid with metal catalyst has shown high selectivity and excellent stability for the conversion of carbohydrates to HMF [6,7]. Recently, deep eutectic solvents (DES), another promising solvent system, have elicited great interest in biomass conversion, since it was first reported in 2004 [8-10]. DES has many favorable merits, such as low cost, low toxicity, recyclability and wide availability [9], which can be obtained by mixing a hydrogen-bond donor (HBD) with a hydrogen-bond acceptor (HBA). Its unique property allows us to make the best of renewably-sourced polyols or carboxylic acids as HBD [9]. Based on this, attempts to dehydrate hexoses into HMF in choline chloride (ChCl)/carbohydrate DES have been made and some satisfactory results achieved [11-13]. However, intractable challenges still remain for industrial production of HMF in view of the difficulties in separation, purification and storage. These issues are more obvious in ionic liquids, while high yields of HMF from carbohydrates can be obtained owing to their unique ability to dissolve lignocellulosic biomass [14].

Compared with HMF, another novel biomass-derived chemical,

5-[(formyloxy)methyl]furfural (FMF) shows more attractive property of stability [15]. FMF can be separated and purified more easily than HMF due to the less-hydrophilic formyloxymethyl group instead of hydroxyl group. In some researches, FMF has been detected in the process of converting lignocellulosic biomass or HMF into bio-based chemicals in the presence of formic acid (FA). FMF was observed as a byproduct in the oxidation of HMF to produce maleic anhydride and 2,5-diformylfuran (DFF) using $VO(acac)_2$ and $VOPO_4 \cdot 2H_2O$ as the catalyst, respectively [16,17]. FMF was produced via the esterification of HMF with in-situ generated FA [17]. In addition, FMF was also viewed as an important intermediate for the production of DMF from fructose and HMF in the presence of FA and catalyst Pd/C [18] or Ru/C [19]. In this process, FA served as a hydrogen donor, a deoxygenating agent and even an acid catalyst involved in the formylation of HMF. In addition, it showed that the arylation of HMF in FA proceeding via FMF was the key step to synthesize mesitylmethylfurfural (MMF), a hybrid diesel fuel precursor, from carbohydrates and petrochemicals using formic acid as a solvent [20]. A control experiment showed that FMF also could be used as substrate to produce MMF like HMF. Another analog of FMF, 5-acetoxymethylfurfural (AMF), prepared from 5-chloromethylfurfural (CMF), was converted into various promising furanic compounds, such as 2, 5-furandicarboxylic acid (FDCA), 2, 5-furandimethanol (FDM), and 5-hydroxymethyl-2-furanoic acid (HFA) with high yields [21]. Based on these facts, FMF exhibits a great potential to substitute for HMF as a promising platform chemical. Indeed, a few studies were involved in the production of FMF. Zhao obtained a 70% yield of FMF from HMF with the addition of HCl at 120 °C for 4 h, whereas the yield decreased to 21% using fructose as the substrate [20].

In our previous study, FMF was observed as a main degradation product when catalytic hydrolyzing bamboo fiber into fermentable

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sugars was performed in formic acid solution containing 4% HCl [22]. Later, one-pot conversion of cellulose into FMF in FA was also developed with a yield of 33.4% at 150 °C for 2 h, while only 33.2% yield of FMF was gained from fructose after 2.5 h in the presence of NaBr as catalyst [15]. This result was quite different from those in ILs or DES reaction system. Meanwhile, utilization of a large amount of salt catalyst NaBr resulted in high cost due to the difficulty in catalyst recovery. It is necessary to find a key factor for one-pot conversion of fructose into FMF. Based on an understanding of this process, high-yield conversion of fructose into FMF via HMF prepared from ChCl/fructose DES was developed. The effective purification process and stability of FMF were also explored.

## EXPERIMENTAL

### 1. Materials

HMF (99%) was obtained from Shanghai Energy Chemical Industrial Co. Ltd. (Shanghai, China), and levulinic acid (LA) (98%) was supplied by Sigma-Aldrich China Co. Ltd. (Shanghai, China). FMF (98%) was prepared and purified in our laboratory (see supplementary material). Choline Chloride (ChCl), fructose and formic acid (98%) were purchased from Aladdin Chemical Technology Co. Ltd. (Shanghai, China). All other chemicals were supplied by Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China) and used without further treatment.

### 2. One-pot Approach for Producing FMF from Fructose or HMF

The experiments were carried out in 100 mL stainless steel medium-pressure tank with Teflon liner. The reactor was manufactured by Yantai Keli Chemical Equipment Co., Ltd. (Shandong, China). In a typical run, the tetrafluoroethylene tank was loaded with fructose (0.27 g) or HMF (0.20 g) and FA (20 mL), and then sealed with a stainless steel sleeve. The reaction mixture was then heated to the prescribed temperature with the rate of 3 °C/min and kept for a desired reaction time. In addition, the experiments were carried out in a glass flask (50 mL) when the required reaction temperature was below 100 °C. After reaction, the reaction mixture was cooled to room temperature. Then, FA was removed by vacuum distillation and crude FMF was obtained.

### 3. Two-step Approach for Producing FMF

All reactions were in 50 mL flasks with a condenser pipe and heated by oil bath. In a typical run, 0.27 g fructose, 1.08 g ChCl and 2 μL HCl of 12 mol/L (0.024 mmol) were mixed by vibration in a reactor, and then 10 mL extractant (as in-situ extractant) was added into the mixture. After the reaction ran for the desired duration, the reaction mixture was cooled to room temperature. Then the extract was separated, and the residue was extracted with a certain volume of fresh extractant. All extracts were merged into a new flask. After adding formic acid, the second step of reaction was carried out for a certain time at a suitable temperature. After the reaction, all solvents were removed by vacuum distillation and the crude FMF was obtained.

### 4. Products Analysis

The qualitative analysis of products was determined by a Thermo-Fisher Trace 1300 & ISQ LT GC-MS instrument with a TR-5MS col-

umn (30.0 m×250 m×0.25 m). The following programmed temperature was used in the analysis: 40 °C (2 min)-10 °C/min-250 °C (2 min). The carrier gas was He with a flow rate of 1.2 mL/min and the split ratio was 1 : 100. The mass spectrometer contained an electron impact ionization (EI) with an electron energy of 70 eV and emission current of 25 A.

The products were determined on an Agilent 7890 series GC equipped with a TR-WAX capillary column (30.0 m×250 m×0.25 m) and a flame ionization detector (FID) operating at 270 °C. The carrier gas was $N_2$ with a flow rate of 1.0 mL/min. The following programmed temperature was used in the analysis: 60 °C (2 min)-10 °C/min-240 °C (5 min). FMF, HMF and LA were quantitative analyzed using the external standard. Typically, the yields of FMF, HMF and LA were calculated as follows:

$$FMF \text{ yield (mol\%)} = \frac{\text{mole of FMF}}{\text{initial mole of fructose or HMF}} \times 100 \quad (1)$$

$$HMF \text{ yield (mol\%)} = \frac{\text{mole of HMF}}{\text{initial mole of fructose}} \times 100 \quad (2)$$

$$LA \text{ yield (mol\%)} = \frac{\text{mole of LA}}{\text{initial mole of fructose}} \times 100 \quad (3)$$

## RESULTS AND DISCUSSION

### 1. One-pot Conversion of Fructose to FMF

Formic acid (FA), generated as a by-product from biomass degradation, has attracted much recent interest in the field of green chemistry because of the multifunctional roles. FA is a good solvent for fructose. FA is also a relatively strong acid with a pKa of 3.77, which makes it possible to catalyze the dehydration of fructose [20]. Hence, in the current research, FA serves as both solvent and catalyst for one-pot conversion of fructose to FMF.

1-1. Effect of Reaction Temperature

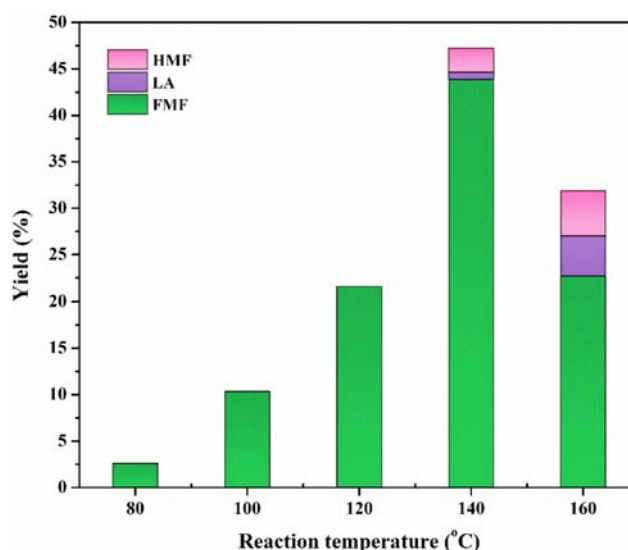Initial experiments were carried out to investigate the effect of



Fig. 1. Effect of reaction temperature on the one-pot conversion of fructose to FMF.

reaction temperature on the preparation of FMF by one-pot conversion in formic acid solvent for 2 h. As clearly shown in Fig. 1, the FMF yield was significantly influenced by reaction temperature. The reaction conducted at 80 °C for 2 h obtained a poor FMF yield of only 2.60%. Encouragingly, raising reaction temperature from 100 °C to 140 °C enhanced the yields of FMF from 10.34% to 43.92%, whereas a higher reaction temperature (160 °C) lowered the yield of FMF slightly, accompanied by the formation of colored byproducts and insoluble polymeric products named humins. The formylation was also carried out by reacting HMF with formic acid at different temperature. Temperature had an insignificant effect on the yields of FMF from HMF, when experiments were performed at temperature ranging from 25 °C to 140 °C with a suitable reaction time (Fig. S2). Based on these results, it is concluded that the poor yield of FMF from fructose at a low reaction temperature is extremely likely due to the ineffective dehydration of fructose to yield HMF in FA. More importantly, it further shows that the dehydration of fructose to HMF is the controlling step for converting fructose into FMF, rather than the esterification of HMF.

1-2. Effect of Acidity

With the anticipation that adding mineral acids to the reaction system may promote the conversion of fructose into FMF, experiments were performed by adding hydrochloric acid at 80 °C and 120 °C respectively. The results are shown in Fig. 2. Raising the concentration of HCl from 0 to 0.02 M at 80 °C improved the yields of FMF from 5.63% to 22.00%. Meanwhile, only a little levulinic acid (LA) was detected in all experiments. However, HCl concentration being more than 0.005 M, FMF yields suffered a marked drop at 120 °C, accompanied by the increasing yields of
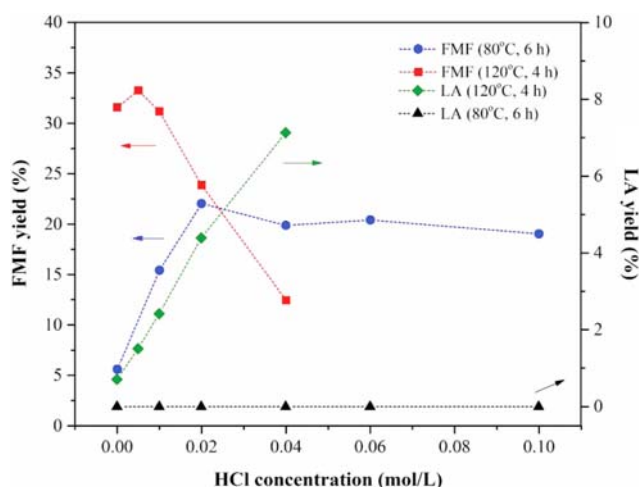


Fig. 2. Effect of HCl on the conversion of fructose into FMF.

LA. Continuously increasing the concentration of HCl to 0.04 M resulted in a poor FMF yield of only 12.56% and LA yield of 7.14%. The increasing LA yield might be ascribed to subsequent degradation of FMF and HMF. At the same time, the high concentration of HCl also promoted the formation of dark humins and unidentified soluble byproducts [23,24].

Experiments were also conducted at 40 °C and 120 °C in the presence of mineral acid to study the effects of acidity on the conversion of HMF into FMF. Results showed the reaction temperature had indeed less impact on the formylation of HMF (Table 1, entry 1, 3). However, the addition of mineral acid to formic acid

Table 1. Effect of acids on the conversion of HMF into FMF[a]

| Entry | Additive | Temperature (°C) | Conversion (%) | FMF yield (%) | LA yield (%) |
|---|---|---|---|---|---|
| 1 | Blank | 40 | 97.98 | 88.25 | 0 |
| 2 | 0.04 M HCl | 40 | 97.77 | 78.90 | 0 |
| 3 | Blank | 120 | 96.31 | 92.58 | 2.26 |
| 4 | 0.01 M H$_2$SO$_4$ | 120 | 95.25 | 58.54 | 18.03 |
| 5 | 0.02 M HCl | 120 | 94.27 | 54.22 | 13.90 |

[a]Reaction conditions: 0.20 g HMF, 20 mL formic acid, 6 h

Table 2. Effect of adding ethyl formate to formic acid solution on the FMF yield from fructose

| Entry | Solvent (v/v) | Temperature (°C) | Time (h) | FMF yield (%) | LA yield (%) | HMF yield (%) |
|---|---|---|---|---|---|---|
| 1 | FA | 140 | 2 | 43.87 | 0.76 | 2.59 |
| 2 | FA | 140 | 3 | 34.89 | 2.07 | 5.84 |
| 3 | FA : EF=2 : 1 | 140 | 2 | 33.33 | 0 | 1.34 |
| 4 | FA : EF=1 : 1 | 140 | 2 | 19.47 | 0 | 1.72 |
| 5 | FA : EF=1 : 2 | 140 | 2 | 8.95 | 0 | 0.82 |
| 6 | FA : EF=1 : 2 | 140 | 5 | 22.92 | 0 | 4.90 |
| 7 | FA | 160 | 0.5 | 24.43 | 0 | 0 |
| 8 | FA | 160 | 1 | 40.32 | 0.98 | 2.38 |
| 9 | FA | 160 | 2 | 22.68 | 4.32 | 4.88 |
| 10 | FA : EF=2 : 1 | 160 | 1 | 38.15 | 0 | 1.84 |
| 11 | FA : EF=1 : 1 | 160 | 3 | 32.43 | 0.85 | 2.79 |
| 12 | FA : EF=1 : 2 | 160 | 3 | 28.51 | 0 | 2.97 |

solution resulted in obvious decline in the yield of FMF, especially at high reaction temperature (Table 1). It may be that mineral acid in formic acid solution made HMF more unstable, forming insoluble and soluble humins [25,26]. Nevertheless, from the results of converting fructose into FMF in formic acid solution with a certain amount of HCl, it is further inferred that hydrochloric acid in FA accelerates the dehydration of fructose into HMF, thereby improving the yield of FMF. Furthermore, it seems that raising a reaction temperature is required to lower a acidity of reaction system properly. Too high a temperature and acidity also accelerates the degradation of products resulting in the drop in the yield of FMF.

To further investigate the effect of acidity at a higher reaction temperature, ethyl formate (EF) was added to the formic acid solution to lower the acidity of reaction system. As summarized in Table 2, lowering volume ratio of FA to ethyl formate gradually resulted in a significant decrease in the yields of FMF. It was essential to prolong the reaction time to recover the yield of FMF. This indicated that the acidity of FA itself was sufficient to catalyze the dehydration of fructose in the high temperature reaction. Either adding HCl to FA or raising reaction temperature promoted not only the dehydration of fructose but also the side reactions, such as the formation of humins and degradation of FMF and HMF into LA. In particular, it should be stressed that adding an appropriate amount of HCl made for the formation of FMF whatever at high or low reaction temperature.
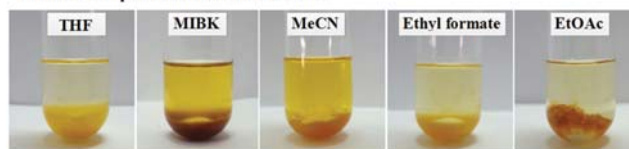
## 2. Two-step Approach for Converting Fructose into FMF

Since it is difficult to improve the FMF yield from fructose in the formic acid media, taking DES into consideration, a two-step approach for converting fructose into FMF was investigated. DES has been viewed as a novel reaction medium, which has physical properties similar to the imidazolium-based ionic liquids [8,9]. Interestingly, DES can be tolerant to a highly concentrated feedstock, which is a significant advantage for industrial application. Carbohydrates are used as both a reactant and a component of DES [9]. In our previous study, one strategy was developed to produce HMF efficiently in ChCl/fructose DES system using HCl as catalyst [27]. Herein, with the aim to gain higher yield of FMF from fructose, this strategy was adopted as the first step in the process to prepare HMF efficiently, then the resulting HMF directly reacts with formic acid to generate FMF.

### 2-1. Screening of Reaction Solvents

In the process to prepare HMF, the biphasic reaction system was established by DES and organic solvent. The organic solvent
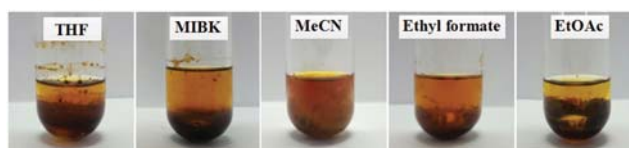


Fig. 3. The conversion of fructose in ChCl/fructose DESs with different organic aprotic solvents.

acted as an extractant of HMF during the dehydration of fructose in DES system and a reaction solvent for producing FMF. Several solvents such as tetrahydrofuran (THF), methyl isobutyl ketone (MIBK), acetonitrile (MeCN), ethyl formate and ethyl acetate (EtOAc) for screening had excellent solubility for HMF, but it was exactly opposite to DES. As shown in Fig. 3, the viscosity of DESs varied with the different solvents, resulting in different mass transport process between the two-phase interfaces. In particular, ChCl/fructose DES behaved better in MeCN, which benefited the extraction of HMF from DES. Besides, the color of MeCN phase changed to yellow quickly with less dark impurities in DES when reaction temperature reached 100 °C.

To avoid the complex purification process for HMF and lower energy consumption, after the first step in the process was finished, formic acid was added directly into the extractant separated from the biphasic reaction system without concentration. Note that the organic solvent had an effect not only on the dehydration of fructose into HMF, but on the subsequent esterification between HMF and formic acid. Besides, a combination of fructose dehydration and HMF esterification to obtain FMF required a suitable solvent which was beneficial to both steps. Results are shown in Table 3, MeCN performed better for producing HMF with the yield of 73.98%, which was in accord with our previous study [27], and led to a satisfactory FMF yield of 63.22%. However, about 30-50% yield of FMF was obtained using THF, MIBK, ethyl formate or EtOAc as reaction solvent, respectively, under the same conditions. In addition, 5.78% yield of FMF was obtained using ethyl formate as extractant in the first step of process in the presence of formic acid

Table 3. The effect of extractants on the yields of HMF and FMF in two-step approach

| Extraction solvent | Fructose to HMF[a] | HMF to FMF[b] | |
| --- | --- | --- | --- |
| | HMF yield (%) | FMF yield (%)[c] | Selectivity of FMF (%)[d] |
| THF | 49.63 | 45.29 | 91.26 |
| MIBK | 48.67 | 36.94 | 75.90 |
| MeCN | 73.98 | 63.22 | 85.46 |
| Ethyl formate | 45.66 (5.78% FMF) | 43.69 | 95.69 |
| EtOAc | 49.92 | 46.52 | 93.19 |

Reaction conditions: [a]0.27 g fructose, 1.08 g ChCl, 10 mL extraction solvent, 2 μL 36% HCl, 100 °C, 4 h; [b]13 mL reaction solvent, 7 mL FA, 100 °C, 6 h; [c]based on fructose; [d]based on HMF prepared in the first step of process

**Table 4. Effect of volume ratio of formic acid to MeCN on the conversion of HMF into FMF[a]**

| Entry | Solvent (v/v) | Temperature (°C) | Time (h) | Conversion (%) | FMF yield (%) |
|-------|---------------|------------------|----------|----------------|---------------|
| 1 | FA : MeCN (2 : 1) | 100 | 6 | 98.15 | 71.39 |
| 2 | FA : MeCN (1 : 1) | 100 | 6 | 98.46 | 80.51 |
| 3 | FA : MeCN (1 : 2) | 100 | 6 | 93.85 | 85.04 |
| 4 | FA : MeCN (1 : 2) | 100 | 5 | 97.47 | 83.34 |
| 5 | FA : MeCN (1 : 2) | 100 | 7 | 93.91 | 80.34 |
| 6 | FA : MeCN (1 : 2) | 60 | 9 | 93.01 | 85.54 |
| 7 | FA : MeCN (1 : 2) | 80 | 8 | 96.43 | 82.65 |
| 8 | FA : MeCN (1 : 2)[b] | 100 | 6 | 97.99 | 80.21 |

Reaction conditions: [a]0.2 g HMF, 20 mL mixture solvent; [b]adding 0.2 g ChCl and 2 μL 36% HCl

derived from hydrolysis of ethyl formate. Furthermore, under the same conditions, THF, ethyl formate, and EtOAc gave selectivity of FMF more than 90%, while 75.90% and 85.46% for MIBK and MeCN, respectively. Significantly, the fructose conversions for all reactions reached 98%. Considering the effect of reaction solvents on two steps, MeCN was more suitable for the two-step approach to converting fructose into FMF.

2-2. The Effect of Reaction Condition on the Second Step in Two-step Approach

In an effort to favor the formation of FMF, the reaction conditions for the second step were studied. The influence of volume ratio of formic acid to MeCN on the conversion of HMF into FMF is shown in Table 4. The yield of FMF exhibited a moderate increase from 71.39% to 85.04% with the decreasing volume ratio from 2 : 1 to 1 : 2, while no substantial change in HMF conversion was observed obviously (Table 4, entry 1-3). It was inferred that a higher amount of formic acid led to a slight drop in yield of FMF in the same conditions due to the formation of humins, as seen from the darker reaction mixture. Therefore, FA/MeCN mixture in volume ratio of 1/2 was used for further investigation. It could be found that the reaction time had a minor impact on the yield of FMF. Besides, prolonging the reaction time favored to enhance the yield of FMF at lower temperature (Table 4, entry 5-7). In the second step, choline chloride and hydrochloric acid introduced from the first step inevitably, may be slightly harmful to yield FMF (Table 4, entry 8). From the above results, it is clear that the esterification of HMF with FA was easier than the dehydration of fructose to HMF; therefore, the key of this strategy is to improve the conversion of fructose to HMF.
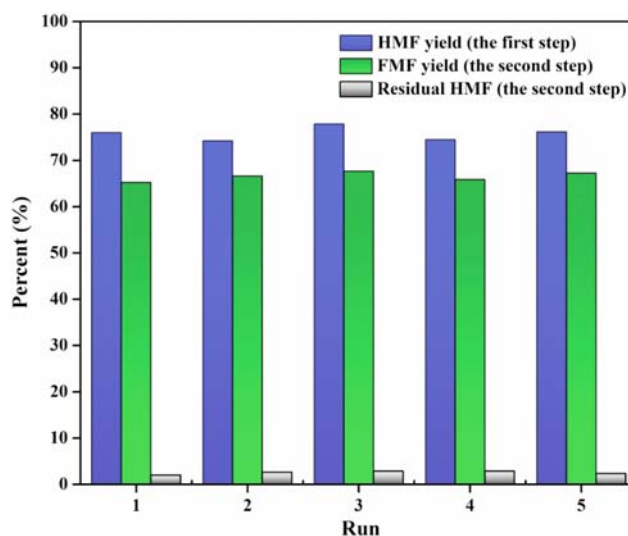
2-3. The recycling of ChCl

After the reaction mixture was cooled in the first step, needle-like choline chloride crystallized when MeCN was used as extractant. It allowed us to separate and recycle the choline chloride, just sucking the extractant out of the reaction mixture followed by adding fresh fructose to the recycled choline chloride. It can be seen from Fig. 4, the yields of HMF and FMF remained constant in the subsequent runs using recycled ChCl directly for the reaction.

Reaction conditions: 0.27 g fructose, 1.08 g ChCl, 10 mL extraction solvent, 2 μL 36% HCl, 100 °C, 4 h (the first step); 13 mL reaction solvent, 7 mL FA, 100 °C, 6.5 h (the second step).

**3. Separation and Purification of FMF**

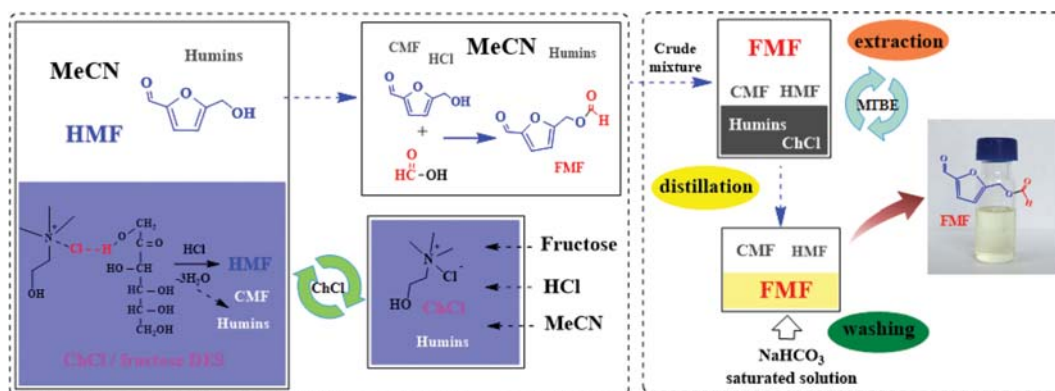Isolation/purification plays a crucial role in industrial produc-

**Fig. 4. The recycling of ChCl.**

tion. However, it is still a challenge for HMF. The reported endeavors tend to be costly and not suitable for mass production. Among the reported purification methods available, vacuum distillation is not suitable to purify heat-sensitive HMF, which results in a serious yield loss due to decomposition and polymerization. Compared with HMF, FMF with -OOCH in place of -OH, possesses lower polarity, higher stability and enhanced hydrophobicity (approximately 80 g water was needed to dissolve 1 g of FMF). Moreover, the decreased polarity of FMF brings about a lower boiling point, which ensures less energy is required for distillation at lower temperature. These properties of FMF, distinct from HMF, make an effective and practical separation and purification strategy possible. In our work, one problem for FMF production is the presence of soluble and insoluble impurities, like humins, which are soluble in many organic solvents and coexist with FMF. The impurities not only affect the appearance of the final product, but also become a tricky barrier to isolate FMF from crude mixture. Taking this issue into account, extraction was carried out to remove the most dark impurity before vacuum distillation.

The crude mixtures prepared for above two-step approaches differed in the amount of humins and the types of impurities. The one-step conversion gave a more viscous crude mixture than the

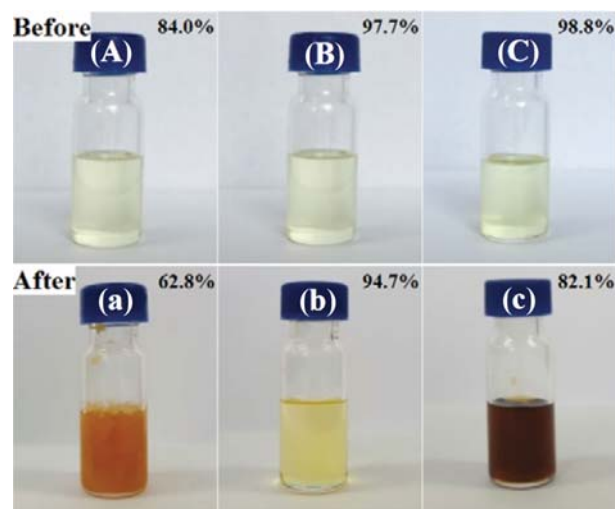**Table 5. Results of extracting FMF obtained from one-pot conversion and two-step approach**

| Extraction solvent | One-pot conversion | | Two-step approach | |
|---|---|---|---|---|
| | Extraction rate (%) | Purity (%) | Extraction rate (%) | Purity (%) |
| Ethyl acetate | >99 | 47.70 | >99 | 50.22 |
| MTBE | 66.86 | 66.27 | 82.32 | 72.00 |
| Hexane/EtOAc (4 : 1, v/v) | 34.52 | 73.18 | 76.60 | 74.73 |



**Scheme 1. The process for production and purification of FMF from fructose.**

two-step approach because of more severe fructose degradation. The large amount of dark humins hindered the extraction process (Fig. S3). As shown in Table 5, the extraction ratio of one-step process was obviously lower than that of two-step approach, although the resulting extracts have little difference in their purity.

Next, efforts were made to purify FMF from crude reaction mixture prepared by two-step approach. The separation and purification process in detail is depicted in Scheme 1. Methyl tert-butyl ether (MTBE) as extractant showed preferable extraction rate and accepted purity. After extraction and concentration, FMF(A) was easily distilled from the residue with slight loss. Pale-yellow was obtained with a purity of 84.0% (Fig. S4). Further, higher pure FMF(B) with purity of 97.7% was readily obtained by washing FMF(A) with saturated sodium bicarbonate (NaHCO$_3$) solution to remove acidic impurities and CMF (Fig. S5-S7). Residual water-soluble HMF and LA was further removed by washing FMF(B) with deionized water. After resulting FMF solution was dried with anhydrous MgSO$_4$, FMF(C) was ultimately obtained with purity of 98.8%, while HMF cannot be absolutely precluded due to hydrolysis of FMF (Fig. S8).

To investigate the storage stability of FMF prepared by two-step approach, FMF(A), FMF(B) and FMF(C) were stored at room temperature under natural light condition in the laboratory for 60 days. The change of solution color indicates that FMF(B) was more stable than FMF(A) and FMF(C). It may be due to the hydrolysis of FMF to HMF followed by further polymerizing to dark substances (Fig. S10). However, the purity of FMF(C) underwent clear deterioration with the formation of dark humins, in which 18.0% HMF was detected because of hydrolysis of FMF in the presence of residual water (Fig. S11). After 60 day storage, an unknown solid impurity appeared in FMF(a); however, the impurity, CMF, in FMF(A) strangely disappeared. Moreover, the hydrolysis of FMF



**Fig. 5. FMF with different purity stored at room temperature in the laboratory for 60 days (before store: (A), (B) and (C); after store: (a), (b) and (c)).**

to HMF also occurred (Fig. S9). Hence, it is essential to wash FMF with saturated sodium bicarbonate solution (NaHCO$_3$) after vacuum distillation.

**CONCLUSIONS**

An efficient and mild two-step approach to producing FMF from fructose was put forward. The first step involved producing HMF in ChCl/fructose system, followed by the in-situ extraction, which not only enhanced the yield of HMF, but also reduced the generation of dark humins in the presence of acid. In the subsequent

step, HMF was easily transformed into FMF by esterification without any catalysts. A favorable FMF yield of 63.22% was reached finally. The one-step conversion also was studied in formic acid reaction solution; it was found that the dehydration of fructose into HMF was the rate-controlling step for producing FMF from fructose. Either appropriate acidity by addition of mineral acid or raising reaction temperature promoted the dehydration of fructose to HMF, so as to increase the yield of FMF. However, it was essential to coordinate the reaction temperature and acidity of reaction system. In the end, an FMF yield of less than 45% was obtained by one-pot conversion.

FMF possesses hydrophobicity and improved stability due to the less-hydrophilic formyloxymethyl group instead of the hydroxymethyl group, which made the purification easier than HMF. In the purification process, washing with saturated sodium bicarbonate solution (NaHCO$_3$) was an effective measure to remove acid impurities. FMF purity of up to 98.8% was obtained ultimately. The purified FMF was stored at room temperature under natural light condition in the laboratory for 60 days with only a little decline in purity.

## ACKNOWLEDGEMENTS

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