

# A Facile and Eco-Effective Catalytic System for Synthesis of 5-Hydroxymethylfurfural from Glucose

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A facile and eco-friendly system for synthesis of 5-hydroxymethylfurfural (HMF) from glucose has been investigated with the catalyst dihydric phosphate ( $\text{H}_2\text{PO}_4^-$ ) in a methyl isobutyl ketone (MIBK)/ $\text{H}_2\text{O}$  biphasic system. The results showed that the catalyst dosage, reaction temperature, and reaction time had noticeable effects on glucose conversion and the HMF yield; more than 50% yield of HMF was achieved at the optimum conditions. In addition, this catalytic system was broadly substrate-tolerant; a satisfactory HMF yield was obtained from higher substrate concentrations and complex substrates. Furthermore, this efficient catalyst was recycled up to nine consecutive times without the loss of catalytic activity.

*Keywords:* Dihydric phosphate; Glucose; 5-Hydroxymethylfurfural; Biphasic system; Platform chemical

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## INTRODUCTION

Because of the depletion of fossil fuels and increased environmental concerns, the development of environmentally and economically viable synthetic means for producing chemicals and fuels from non-fossil fuel sources has been invigorated in recent years (Petrus and Noordermeer 2006; Alonso *et al.* 2010; Yan *et al.* 2014). In this context, 5-hydroxymethylfurfural (HMF), named as one of the “top 10 biobased chemicals” by the U.S. Department of Energy (Werpy *et al.* 2004), has received significant attention as a precursor for synthesizing a broad range of chemicals and liquid transportation fuels, such as levulinic acid, 2,5-furandicarboxylic acid, 2,5-diformylfuran, dimethylfuran, and dihydroxymethylfuran (Bozell and Petersen 2010; Teong *et al.* 2014). The demand for HMF will continue to grow with the diminishing supply of petroleum feedstock.

It is well known that excellent yields of biomass-derived HMF can be prepared *via* dehydration of the preferred feedstock, *viz.*, fructose, in the presence of an acid catalyst (such as HCl,  $\text{H}_2\text{SO}_4$ , cation exchanged resins, and others) (Rosatella *et al.* 2011; van Putten *et al.* 2013; Yan *et al.* 2013). In nature, however, fructose is not a highly prevalent carbohydrate. In contrast, the isomer of fructose, glucose, which is the monomeric unit of cellulose and the most abundant monosaccharide in nature, is a better candidate for the production of HMF. The possibility to economically convert glucose into HMF has motivated a tremendous amount of recent research (Song *et al.* 2013).

Obtaining HMF from glucose is, however, difficult because the direct synthesis of HMF from glucose usually proceeds in two steps. First, the isomerization of glucose to fructose occurs in the presence of enzyme, base, or metal chloride (Huang *et al.* 2010; Peng *et al.* 2012; Song *et al.* 2013; van Putten *et al.* 2013). Next, the fructose is dehydrated in the presence of an acid catalyst ( $\text{H}^+$ ) to yield HMF. The two-step process

for producing HMF from glucose results in a low selectivity of HMF and a high amount of humins. Hence, the ideal strategy for the catalytic conversion of glucose into HMF requires a bifunctional catalyst that would affect both the isomerization of glucose to fructose and the subsequent dehydration of fructose. In recent years, a series of novel bifunctional catalysts have been synthesized, such as *N,N'*-dimethylformamide (DMF), which combines Amberlyst-15 (a solid acid) and Mg–Al hydrotalcite (a solid base) for the one-pot synthesis of HMF from glucose (Takagaki *et al.* 2009). An HMF selectivity of 58% and a glucose conversion of 73% was achieved at 180 °C. In this catalytic system, the base acted as the catalyst for isomerizing the glucose into fructose, and the acid was the catalyst for dehydrating the fructose into HMF. In another instance, Cao *et al.* (2015) used an ammonium resin (PBnNH<sub>3</sub>Cl) as a single catalyst for the glucose and polysaccharide dehydration into HMF, with high selectivity (> 80%). This example demonstrated, through decomposing ammonium resin under the high reaction temperature, that the *in situ* formation of –NH<sub>2</sub> (PBnNH<sub>2</sub>) and H<sup>+</sup> (HCl) could act as both the isomerizing agent for glucose and the acid catalyst for the dehydration of fructose. However, the procedures for preparing bifunctional catalysts are tedious and cumbersome, although these catalysts display high catalytic performance and recyclability, and using a commercially available commodity as the bifunctional catalyst would be preferred.

Interestingly, recent breakthroughs have indicated that some metal chlorides can effectively catalyze isomerization and dehydration of glucose into HMF in ionic liquids. Zhao *et al.* (2007) were the first to report a significant HMF yield of nearly 70% from glucose by using chromium(II) chloride (CrCl<sub>2</sub>) in 1-ethyl-3-methyl-imidazolium chloride ([C<sub>2</sub>mim]Cl), at 100 °C, for 3 h. Hu *et al.* (2009) found that SnCl<sub>4</sub> could also act as the catalyst for the conversion of glucose-based feedstocks (glucose, cellobiose, and starch) into HMF with an acceptable yield. Zhang *et al.* (2011) converted glucose into HMF with a yield of 48.4% by employing GeCl<sub>4</sub> as the catalyst. Kim *et al.* (2011) developed a binary metal chlorides catalyst system, consisting of CrCl<sub>2</sub> and RuCl<sub>3</sub>, and obtained up to 60% yield from cellulose. Moreover, it has been found that some metal oxides (such as Nb<sub>2</sub>O<sub>5</sub>·*n*H<sub>2</sub>O, Cr<sub>2</sub>O<sub>3</sub>, and TiO<sub>2</sub>) (McNeff *et al.* 2010; Nakajima *et al.* 2011; Zhang *et al.* 2015) and phosphate (NbPO<sub>4</sub>, TaOPO<sub>4</sub>, Ti<sub>3</sub>(PO<sub>4</sub>)<sub>4</sub>, Sr(PO<sub>3</sub>)<sub>2</sub>, and others) (Daorattanachai *et al.* 2012; Dutta *et al.* 2012; Behera and Parida 2013; Ordonsky *et al.* 2013; Dutta *et al.* 2014; Jiménez-Morales *et al.* 2014; Atanda *et al.* 2015; Jain *et al.* 2015) could also have the capacity to convert glucose into HMF. However, these contributions still encountered problems in terms of environmental toxicity, low catalytic activity, and tedious workup procedures for catalyst preparation (Agirrezabal-Telleria *et al.* 2014; Deuss *et al.* 2014). In addition, methods like these that use ionic liquids as the solvents are expensive, and probably not suitable for developing into an economically favorable and scalable HMF production method. Developing a relatively inexpensive, low-toxicity, and high-yield catalytic system for producing HMF from glucose is still necessary and desirable.

As a continuation of an ongoing research program to develop a mild catalytic route for preparing bio-chemicals from biomass (Ma *et al.* 2012, 2015a,b), this paper reports an efficient method with an intensification strategy to produce HMF from glucose. In this method, the high efficiency was realized via selective conversion of glucose-based carbohydrates promoted by H<sub>2</sub>PO<sub>4</sub><sup>–</sup> into HMF. This occurs in an aqueous solution, which is then enriched in an organic phase (MIBK) under mild conditions. The effect of the reaction process parameters (catalyst dosage, temperature, and time) and the

extent of the substrate concentration and types are evaluated in detail. The recycle performance of the catalyst was also investigated.

## EXPERIMENTAL

### Materials

D-glucose (99%), D-fructose (99%), sucrose (98%), maltose (99%), starch (99%), cellulose (99%), and CH<sub>3</sub>OH (high-performance liquid chromatography, HPLC) were purchased from the J&K Chemical Company (Beijing, China) and used as received. Analytical graded KH<sub>2</sub>PO<sub>4</sub> (99%), K<sub>2</sub>HPO<sub>4</sub>·3H<sub>2</sub>O (99%), K<sub>3</sub>PO<sub>4</sub>·3H<sub>2</sub>O (99%), NaH<sub>2</sub>PO<sub>4</sub>·2H<sub>2</sub>O (99%), Na<sub>2</sub>HPO<sub>4</sub>·12H<sub>2</sub>O (99%), Na<sub>3</sub>PO<sub>4</sub>·12H<sub>2</sub>O (99%), B(OH)<sub>3</sub> (99%), H<sub>3</sub>PO<sub>4</sub> (85%), H<sub>2</sub>SO<sub>4</sub> (98%), HCl (36.5%), MIBK (99%), and other reagents were supplied by the Guanghua Chemical Factory Co. Ltd. (Shantou, China).

### Procedure for the Dehydration of Glucose

A 25-mL hydrothermal autoclave reactor was charged with 5 mmol (0.9 g) of glucose, 2 mmol of KH<sub>2</sub>PO<sub>4</sub>, 2 mL of H<sub>2</sub>O, and 8 mL of MIBK, and then blown with a nitrogen stream for 1 min to displace air. The autoclave reactor was capped and immersed in an oil bath that was pre-heated to the designated temperature of 160 °C for a reaction time of 2 h, while undergoing magnetic stirring of 500 rpm, and then rapidly brought to room temperature by loading it with cooling water.

### Analysis Procedure

The analysis of the reaction products was carried out by means of an HPLC apparatus. After reaction, the catalyst KH<sub>2</sub>PO<sub>4</sub> and the unconverted glucose were enriched in an aqueous phase. The formed HMF was distributed in both phases. The glucose was determined by an Agilent 1200 HPLC (Agilent Technologies, USA) equipped with a RID detector and a HPX-87H column (300 × 7.8 mm, 5 μm, 5 mM H<sub>2</sub>SO<sub>4</sub>, 0.6 mL·min<sup>-1</sup>). The HMF distributed in each phase was determined by the above HPLC using a UV detector (284 nm) with a C18 reversed-phase column (250 × 4.6 mm, 5 μm, CH<sub>3</sub>OH/H<sub>2</sub>O [v/v, 1:4], 0.6 mL·min<sup>-1</sup>). The amount of glucose and HMF were determined by comparison to standard calibration curves using commercially available standard substrates. The conversion of glucose (Conv., mol%), yield of HMF (Y<sub>HMF</sub>, mol%), selectivity of HMF (S<sub>HMF</sub>, mol%), and extraction ratio of HMF (ER<sub>HMF</sub>, mol%) were calculated according to Eqs. 1 through 4.

$$\text{Conv. (mol\%)} = \left(1 - \frac{\text{moles of glucose unreacted}}{\text{moles of starting glucose units}}\right) \times 100\% \quad (1)$$

$$Y_{\text{HMF}} \text{ (mol\%)} = \frac{\text{moles of HMF produced}}{\text{moles of starting glucose units}} \times 100\% \quad (2)$$

$$S_{\text{HMF}} \text{ (mol\%)} = \frac{Y_{\text{HMF}}}{\text{Conv.}} \times 100\% \quad (3)$$

$$\text{ER}_{\text{HMF}} \text{ (mol\%)} = \frac{\text{moles of HMF existed in organic phase}}{\text{moles of HMF produced}} \times 100\% \quad (4)$$

Recycling of catalyst was done according to the following procedures: After reaction, the MIBK phase was first isolated from the reaction mixture using a separation funnel; and then the HMF component existed in aqueous phase was extracted with MIBK (15 mL  $\times$  3). At last, the fresh glucose and MIBK were added into the residual aqueous solution for the next run. The amount of HMF in pooled MIBK was examined to represent the total HMF yield, and the total separation efficiency of HMF was approximately 95%.

## RESULTS AND DISCUSSION

### Catalytic Conversion of Glucose into HMF

A wide range of catalysts, including mineral acids ( $\text{H}_3\text{PO}_4$ ,  $\text{H}_2\text{SO}_4$ , and  $\text{HCl}$ ), dihydric phosphates ( $\text{NaH}_2\text{PO}_4$  and  $\text{KH}_2\text{PO}_4$ ), hydrogen phosphates ( $\text{Na}_2\text{HPO}_4$  and  $\text{K}_2\text{HPO}_4$ ), phosphates ( $\text{Na}_3\text{PO}_4$  and  $\text{K}_3\text{PO}_4$ ), and others ( $\text{KCl}$ ,  $\text{K}_2\text{SO}_4$ , and  $\text{B}(\text{OH})_3$ ), were screened for the production of HMF from glucose in a MIBK/ $\text{H}_2\text{O}$  biphasic system (Table 1).

**Table 1.** Dehydration of Glucose with Various Catalysts <sup>[a]</sup>

Entry	Catalysts	Conversion (%)	HMF	
			Yield (%)	Selectivity (%)
1	/	36.1	5.5	15.2
2	$\text{H}_3\text{PO}_4$	54.3	8.1	14.9
3	$\text{NaH}_2\text{PO}_4$	40.6	24.9	61.3
4	$\text{Na}_2\text{HPO}_4$	60.1	12.5	20.8
5	$\text{Na}_3\text{PO}_4$	74.5	trace	/
6	$\text{KH}_2\text{PO}_4$	41.2	25.8	62.6
7	$\text{K}_2\text{HPO}_4$	59.8	12.7	21.2
8	$\text{K}_3\text{PO}_4$	75.6	trace	/
9	$\text{KCl}$	37.7	5.3	14.1
10	$\text{K}_2\text{SO}_4$	40.9	1.2	2.9
11	$\text{B}(\text{OH})_3$	53.8	7.1	13.2
12	$\text{HCl}$	60.5	1.6	2.6
13	$\text{H}_2\text{SO}_4$	66.4	0.9	1.4
14 <sup>[b]</sup>	$\text{H}_3\text{PO}_4$	40.7	2.3	5.7
15 <sup>[b]</sup>	$\text{HCl}$	41.2	2.3	5.6
16 <sup>[b]</sup>	$\text{H}_2\text{SO}_4$	41.1	2.3	5.6

<sup>[a]</sup> Condition: 5 mmol glucose, 0.5 mmol catalyst, 2 mL  $\text{H}_2\text{O}$ , 8 mL MIBK, 160 °C for 2 h; <sup>[b]</sup> before reaction, the pH value of acid solution is equal to entry 6.

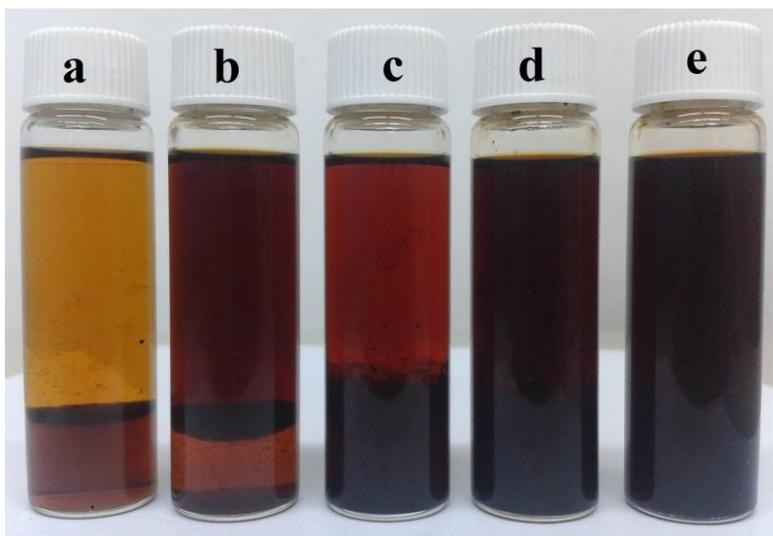
It can be seen that the HMF yield was highly dependent on the catalyst. In the absence of catalyst, the yield of HMF was only 5.5% (Table 1, entry 1). When  $\text{H}_3\text{PO}_4$  was added, the HMF yield improved to a certain degree, with a final HMF yield of 8.1% (Table 1, entry 2). Unexpectedly,  $\text{NaH}_2\text{PO}_4$  had obvious catalytic activities in the conversion of glucose and gave an HMF yield of 24.9% with 61.3% HMF selectivity (Table 1, entry 3). However, as  $\text{NaH}_2\text{PO}_4$  was replaced by  $\text{Na}_2\text{HPO}_4$  and  $\text{Na}_3\text{PO}_4$ , the conversion of glucose increased obviously while the yield of HMF declined sharply from

24.9% to trace (Table 1, entries 3-5). These results showed that the acid strength was not the only determining factor in glucose conversion, as the weak acid  $\text{NaH}_2\text{PO}_4$  had a better catalytic effect on this reaction than  $\text{H}_3\text{PO}_4$  (Table 2).

**Table 2.** pH Value of Aqueous Solution

Catalyst	$\text{H}_3\text{PO}_4$	$\text{NaH}_2\text{PO}_4$	$\text{Na}_2\text{HPO}_4$	$\text{Na}_3\text{PO}_4$
pH value <sup>[a]</sup>	1.09	4.26	9.07	12.59
<sup>[a]</sup> pH value: 0.5 mmol catalyst in 2 mL $\text{H}_2\text{O}$ at 25 °C				

Because of the instability of HMF in aqueous solution (Teong *et al.* 2014), the presence of a base catalyst accelerated the occurrence of side reactions. This increase is illustrated in Fig. 1, where the color of the reaction mixture gradually turned from pale yellow to deep brown as the base strength of the catalyst increased, and resulted in lower HMF yields in the presence of  $\text{Na}_2\text{HPO}_4$  and  $\text{Na}_3\text{PO}_4$ .



**Fig. 1.** Photographs of mixtures from different catalyst systems: (a) no catalyst, (b)  $\text{H}_3\text{PO}_4$ , (c)  $\text{NaH}_2\text{PO}_4$ , (d)  $\text{Na}_2\text{HPO}_4$ , and (e)  $\text{Na}_3\text{PO}_4$ . Reaction conditions: 5 mmol glucose, 0.5 mmol catalyst, 2 mL  $\text{H}_2\text{O}$ , 8 mL MIBK, 160 °C for 2 h

To confirm the contributions of cations and anions from  $\text{NaH}_2\text{PO}_4$ , a series of catalysts with different cations and anions were used in the reaction. It was found that  $\text{KH}_2\text{PO}_4$ ,  $\text{K}_2\text{HPO}_4$ , and  $\text{K}_3\text{PO}_4$  afforded similar catalytic activity as  $\text{NaH}_2\text{PO}_4$ ,  $\text{Na}_2\text{HPO}_4$ , and  $\text{Na}_3\text{PO}_4$ , respectively (Table 1, entries 6-8). When  $\text{KH}_2\text{PO}_4$  was used as catalyst, a 25.8% HMF yield was achieved. In addition, as expected,  $\text{KCl}$  and  $\text{K}_2\text{SO}_4$  had no obvious catalytic participation in the conversion of glucose, and gave HMF yields of less than 6% (Table 1, entries 9 and 10). Therefore, the results mentioned above demonstrated that the anion  $\text{H}_2\text{PO}_4^{-1}$  played a key role in the consecutive isomerization-dehydration reactions.

Subsequently, the well-known isomerizing agent  $\text{B}(\text{OH})_3$  was examined as the catalyst (Ståhlberg *et al.* 2011). Its HMF yield of 7.1% was much less than those from  $\text{NaH}_2\text{PO}_4$  and  $\text{KH}_2\text{PO}_4$  catalyst systems (Table 1, entry 11), which demonstrated  $\text{B}(\text{OH})_3$  was not an available catalyst in this water-based catalytic system. The use of mineral acids ( $\text{HCl}$  and  $\text{H}_2\text{SO}_4$ ) as catalysts in these reactions (Table 1, entries 12-16) yielded less

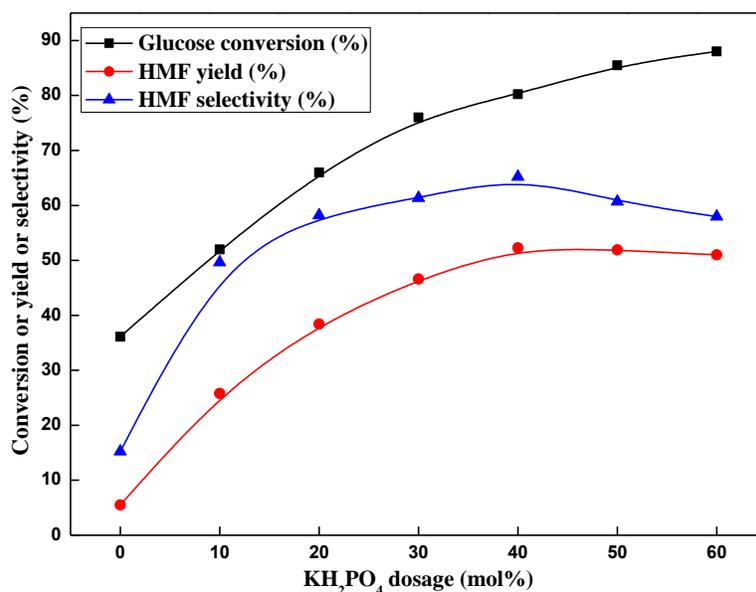
HMF than the catalyst-free system (5.5%). These results were ascribed to the miscibility of mineral with water and MIBK, which resulted in the distribution of the acid in organic phase, the subsequent decomposition/rehydration of the formed HMF into organic acids or other byproducts (van Putten *et al.* 2013), and lower yields of HMF. Based on the results above, the dihydrogen phosphate was the preferred catalyst in this reaction. Therefore,  $\text{KH}_2\text{PO}_4$  was chosen as the best catalyst for subsequent studies on process parameters.

### Effect of Process Parameters

With  $\text{KH}_2\text{PO}_4$  as the appropriate catalyst, several experiments were designed to study the catalytic dehydration of glucose into HMF under various experimental conditions, such as catalyst dosage, reaction temperature, and reaction time. The effect of several reaction parameters on HMF yield and the catalyst's effectiveness are described below.

#### *Effect of catalyst dosage*

As shown in Table 1, the nature of the catalyst played an important role in this system, and, similarly, the intake of catalyst is another crucial factor in producing HMF from glucose. Hence, the effect of catalyst dosage when converting glucose into HMF was investigated, and the results are pictured in Fig. 2.

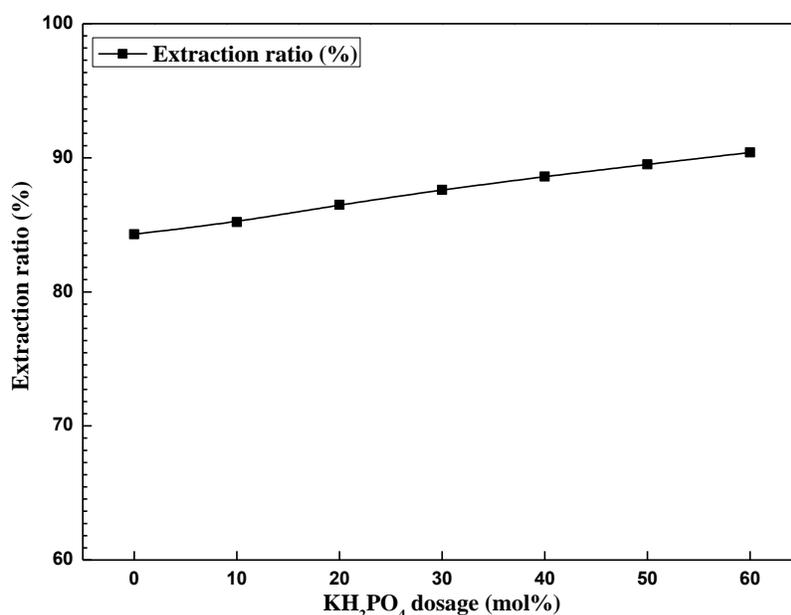


**Fig. 2.** The effect of catalyst dosage on conversion of glucose into HMF. Reaction conditions: 5 mmol glucose, 2 mL  $\text{H}_2\text{O}$ , 8 mL MIBK, 160 °C for 2 h

It can be seen that the glucose conversion increased from 36.1% to 88.0% when the  $\text{KH}_2\text{PO}_4$  dosage was increased from 0% to 60%. The experiments highly loaded with catalysts had increased glucose conversion, implying that the kinetic of glucose dehydration was faster with a higher catalyst dosage. Analysis of the HMF yields shows a different trend: up to 52.3% of HMF was yielded at a 40% catalyst dosage, but higher dosages revealed a decline in the HMF yield (51.0% at 60% catalyst dosage). The selectivity of HMF showed a similar trend; its peak value of 65.2% was also achieved at

the 40% catalyst dosage. The decrease in both the HMF yield and the selectivity at higher catalyst dosages can be ascribed to the fact that more catalyst can also accelerate side reactions of HMF, such as rehydration or condensation (Hu *et al.* 2012). With the aim to obtain the maximum HMF yield and selectivity, the 40% mole ratio of  $\text{KH}_2\text{PO}_4$  to glucose was chosen as the preferred catalyst dosage for subsequent experiments.

It should be noted that the addition of salt can improve the partition coefficient of HMF in a biphasic system (Román-Leshkov and Dumesic 2009). To check the salting-out effect in the present study, the extraction ratio of MIBK in this biphasic system was given as a function of catalyst loading (Fig. 3). It was found that the higher catalyst dosage did improve the extraction ratio of HMF during the reaction phase, and, at 60 mol% catalyst dosage, the extraction ratio of HMF reached up to 90.4%. Therefore, the salting-out effect may have a potential influence in increasing HMF yield in this biphasic solvent mediated dehydration reaction.



**Fig. 3.** The extraction ratio of this catalytic system at different catalyst dosages. Reaction conditions 5 mmol glucose, 2 mL  $\text{H}_2\text{O}$ , 8 mL MIBK, 160 °C for 2 h.

#### *Effect of reaction temperature and time*

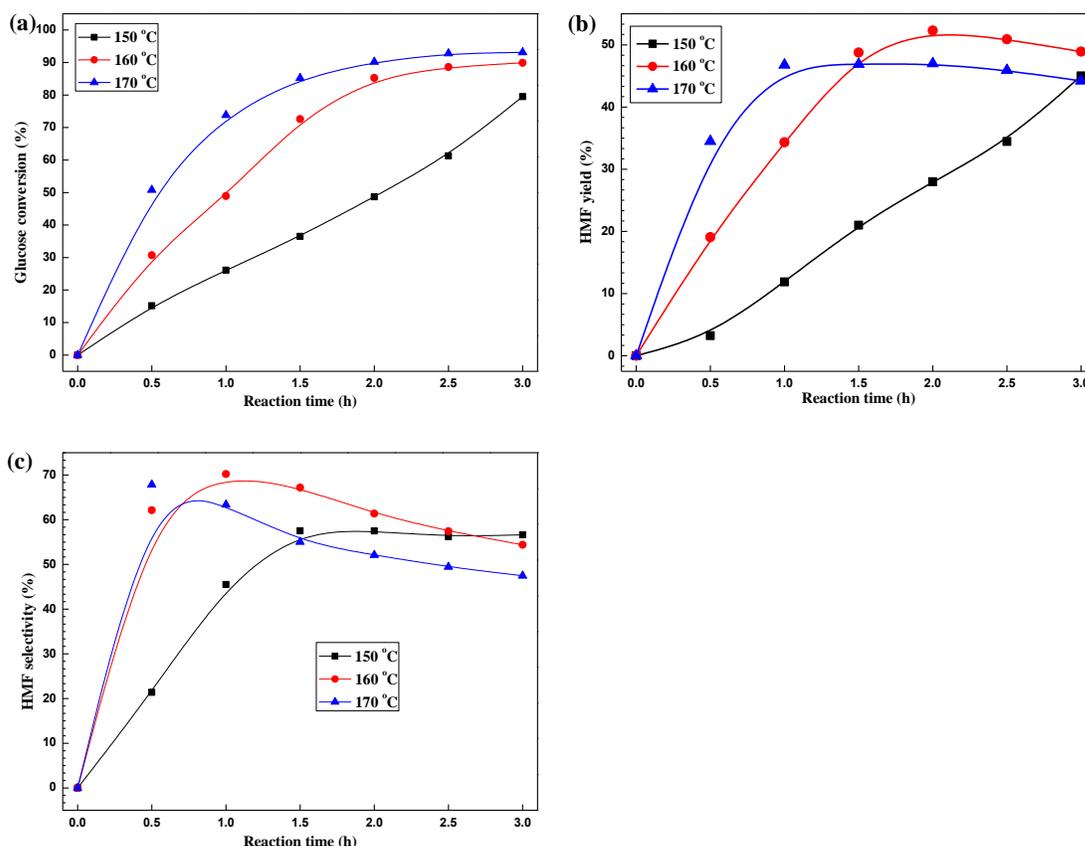
In this study, reaction was not tested at higher temperatures because such temperatures would cause high energy consumption and difficulties in control. Therefore, the reaction temperatures of 150, 160, and 170 °C were employed for different reaction times hereafter.

The results are shown in Fig. 4, which indicates that the reaction temperature and reaction time had a significant influence on this reaction. For example, as shown in Fig. 4a, at the reaction temperature of 150 °C, the glucose conversion was only 15.2% after 0.5 h; however, when the reaction temperature was elevated to 170 °C, the conversion of glucose reached up to 50.8% in the same reaction time. Furthermore, prolonging the reaction time improved the conversion of glucose, implying the positive influence of increased reaction time on glucose conversion.

The reaction temperature and reaction time also played important roles determining the HMF yield (Fig. 4b). Elevating the reaction temperature or extending the

reaction time consistently improved the HMF yield, until it reached its peak value. For example, at 160 °C, the peak value of HMF yield was 52.3%, which occurred at 2 h. However, further extending the reaction time decreased the HMF yield due to the side reactions in which the produced HMF participated (Chuntanapum *et al.* 2008).

At different initial reaction temperatures, initially the HMF selectivity increased when reaction time increased (Fig. 4c). When the HMF selectivity reached its peak value, any further increase in reaction time resulted in lower selectivity of HMF due to the competitive side reactions of HMF (Hu *et al.* 2012). Hence, based on the results above, to obtain the highest yield of HMF (52.3%), the preferred reaction temperature and reaction time was 160 °C for 2 h. The optimum conditions were concluded to be 40% of catalyst dosage at a temperature of 160 °C for 2 h.



**Fig. 4.** The effect of reaction time temperature and reaction time on: (a) the glucose conversion, (b) HMF yield, and (c) HMF selectivity. Default condition: 5 mmol glucose, 2 mmol  $\text{KH}_2\text{PO}_4$ , 2 mL  $\text{H}_2\text{O}$ , 8 mL MIBK.

#### Substrate concentration and scope

The efficient conversion of a high concentration of substrates is crucial for the practical production of HMF. In general, the substrate concentration has a significant influence on the HMF yield. Thus, in this work, the effect of the initial glucose concentration, *viz.*, 22.5 wt%, 45.0 wt%, 67.5 wt%, and 90.0 wt%, on the HMF yield was investigated in detail (Table 3). It can be seen that the glucose conversion and the HMF yield were partly affected by the initial concentration of glucose. The highest HMF yield was 56.4% at 22.5% of the initial glucose concentration. Although there was a slight

decrease when the initial glucose concentration was further increased to 90.0%, an HMF yield of 40.4% was still achieved. This yield indicated that the  $\text{KH}_2\text{PO}_4$  catalyst was more effective in converting high glucose concentrations into a high yield of HMF. In addition, the partial loss of HMF at high glucose concentrations might be attributed to higher rates of side reactions, which are associated with high glucose concentrations, and which produce some undesired by-products (Ma *et al.* 2015b).

**Table 3.** Effect of Glucose Concentration<sup>[a]</sup>

Entry	Concentration (wt%) <sup>[b]</sup>	Conversion (%)	HMF	
			Yield (%)	Selectivity (%)
1	22.5	88.7	56.4	63.6
2	45.0	85.2	52.3	61.4
3	67.5	78.4	46.1	58.8
4	90.0	70.6	40.4	57.2
5 <sup>[c]</sup>	45.0	80.7	48.8	60.5

<sup>[a]</sup> Conditions: 2 mmol catalyst, 2 mL H<sub>2</sub>O, 8 mL MIBK, 160 °C for 2 h; <sup>[b]</sup> glucose concentration in an aqueous solution; <sup>[c]</sup> 20 mmol catalyst, 20 mL H<sub>2</sub>O, 80 mL MIBK, 160 °C for 2 h

To further assess the practicality of this biphasic catalyst system, a large-scale production of HMF was carried out at a glucose concentration of 45.0% with 9.0 g glucose intake (Table 3, entry 5). The acceptable HMF yield of 48.8% was obtained, demonstrating that this catalyst system could be promising for scalable production of HMF.

**Table 4.** Substrate Range of this System in Sugar Dehydration <sup>[a]</sup>

Entry	Substrates	Conversion (%)	HMF	
			Yield (%)	Selectivity (%)
1	Glucose	85.2	52.3	61.4
2	Fructose	97.4	45.7	46.9
3 <sup>[b]</sup>	Fructose	87.8	57.9	65.9
4	Maltose	98.6	44.2	44.8
5	Sucrose	99.1	49.6	50.1
6	Starch	30.4	6.7	22.0
7	Cellulose	5.9	trace	/
8 <sup>[c]</sup>	Starch	63.7	27.1	42.5
9 <sup>[c]</sup>	Cellulose	20.6	5.9	28.6

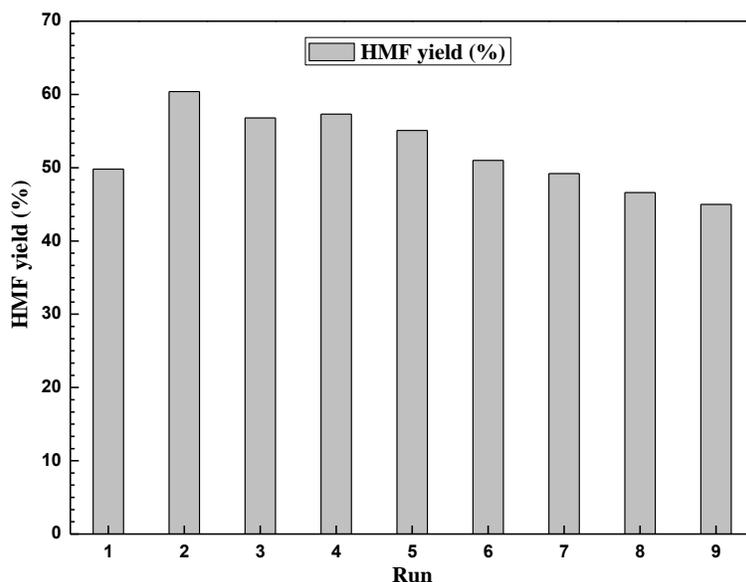
<sup>[a]</sup> Condition: 5 mmol sugar unit, 2 mmol catalyst, 2 mL H<sub>2</sub>O, 8 mL MIBK, 160 °C for 2 h; <sup>[b]</sup> 160 °C for 1 h; <sup>[c]</sup> 180 °C for 3 h; the conversion of starch and cellulose was calculated through weight comparison.

Subsequently, because of the robustness of the  $\text{KH}_2\text{PO}_4$  catalyst in synthesizing HMF from glucose, the capability of this catalyst system for converting more complex carbohydrates, such as disaccharides (maltose and sucrose) and polysaccharides (starch and cellulose), was carried out (Table 4). Synthesis of HMF from maltose, sucrose, starch, and cellulose involves the hydrolysis, isomerization, and dehydration steps with an acid or enzyme, and complicates the process. Here, maltose and sucrose were converted into HMF by the catalyst, and the yield of HMF was more than 40% without

introducing other acids or enzyme catalysts (Table 4, entries 1 to 5). This result implied that this biphasic system was effective in hydrolyzing the glycosidic linkage of disaccharides (Charmot and Katz 2010). Conversion of starch and cellulose to HMF was not as efficient and selective. Cellulose conversion was especially poor, affording trace HMF yield under the same conditions (Table 4, entries 6 and 7). The majority of the cellulose remained unconverted, as a solid suspension in the aqueous phase. This poor reactivity with cellulose was most likely due to ineffective depolymerization and decrystallization with  $\text{KH}_2\text{PO}_4$  at 160 °C. Indeed, a higher temperature was needed for starch and cellulose conversion. When the reactions were run at 180 °C for 3 h, HMF yields increased to 27.1% for starch and 5.9% for cellulose (Table 4, entries 8 and 9). These results were promising since they show that  $\text{KH}_2\text{PO}_4$  in MIBK/ $\text{H}_2\text{O}$  biphasic system were used directly for the conversion of complex carbohydrates to HMF without other acid catalysts.

### Recycling Performance of Catalyst

The recyclability of a catalyst in industrial processes is of great importance. To reinforce the advantage of this catalyst system, the recyclability of the  $\text{KH}_2\text{PO}_4$  catalyst was evaluated by recycling the reaction mixture containing the spent catalyst nine times. The lifetime study of the catalyst was carried out with 45.0% glucose and a 40%  $\text{KH}_2\text{PO}_4$  dosage at 160 °C for 2 h.



**Fig. 5.** Recycling experiments of  $\text{KH}_2\text{PO}_4$  for conversion of glucose into HMF. Reaction conditions: 5 mmol glucose, 2 mmol  $\text{KH}_2\text{PO}_4$ , 2 mL  $\text{H}_2\text{O}$ , 8 mL MIBK, 160 °C for 2 h.

As can be seen in Fig. 5, the  $\text{KH}_2\text{PO}_4$ -MIBK/ $\text{H}_2\text{O}$  system retained high catalytic activity for the conversion of glucose into HMF, and the yield of HMF remained above 50% even after being recycled nine times. The yield of HMF in some recycled material was even higher than the first yield, which can be attributed to the retention of HMF and unreacted glucose from the previous cycle (Lai and Zhang 2010). These recyclability studies indicate the potential application of  $\text{KH}_2\text{PO}_4$  as a catalyst for the production of HMF from glucose. Lastly, it should be noted that the recovered dihydric phosphates could be used as a phosphatic fertilizer in agriculture, implying its eco-friendly nature.

## CONCLUSIONS

1. A simple, facile, and environmentally friendly catalytic system was established for the highly efficient conversion of glucose into HMF in a biphasic system (MIBK/H<sub>2</sub>O) with the cheap and nontoxic KH<sub>2</sub>PO<sub>4</sub> as a catalyst.
2. An excellent HMF yield of 52.3% was achieved at a point of compromise between the reaction temperature and the reaction time (160 °C for 2 h) with 45.0% of glucose concentration.
3. This catalytic system was broadly substrate-tolerant; the satisfactory HMF yield was obtained from higher substrate concentration (67.5%) and complex substrates (maltose, sucrose, etc.).
4. This catalyst system was reused nine times without marked activity loss.

## ACKNOWLEDGMENTS

The authors gratefully acknowledge the financial support of the Natural Science Foundation of China (No. 21336002 and 21276094), the Doctoral Fund of the Ministry of Education of China (No. 20130172110043), and the Natural Science Foundation of Guangdong Province, China (No. 2015A030311048).

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Article submitted: November 2, 2015; Peer review completed: December 8, 2015;  
Revised version received and accepted: December 29, 2015; Published: January 19, 2016.  
DOI: 10.15376/biores.11.1.2152-2165