NOTE

Conversion of Glucose in CPL-LiCl to 5-Hydroxymethylfurfural[†]

Chen, Tianming(陈天明)　　Lin, Lu*(林鹿)

State Key Laboratory of Pulp and Paper Engineering, South China University of Technology, Guangzhou, Guangdong 510640, China

5-Hydroxymethylfurfural (HMF), an important versatile sugar derivative, is also considered a key intermediate between petroleum-based industrial organic chemistry and bio-based carbohydrate chemistry. Here, we report that caprolactam (CPL) containing lithium chloride (LiCl) is a privileged solvent that enables the synthesis of the renewable platform chemical 5-hydroxymethylfurfural (HMF) from purified glucose. Metal halides in CPL-LiCl are catalysts, among which $CrCl_3$, $CrCl_2$, $SnCl_4$ and $SnCl_2$ are found to be uniquely effective, leading to the conversion of glucose to HMF with yields of 55%—67%. The simplicity of this chemical transformation of glucose contrasts markedly with the complexity of extant processes and provides a new paradigm for the use of biomass as a raw material for a renewable energy and chemical industries.

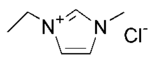
Keywords biomass, glucose, CPL-LiCl, halides, 5-hydroxymethylfurfural (HMF)

Introduction

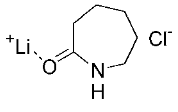
The present consumption of fossil fuels has led to significant levels of environmental pollution and rapidly diminishing petrochemical reserves. The diminishing fossil fuel reserves and the globe warming effects have become major concerns. The search for sustainable, alternative energy is of critical importance.[1,2]

Biofuels are highly attractive as the only sustainable source of liquid fuels currently.[3] However, the replacement of petroleum feedstock by biomass is limited by the lack of highly efficient methods to selectively convert carbohydrates to chemical compounds for the biofuel production.[4] A practical catalytic process that can transform the abundant biomass into versatile chemicals would also provide the chemical industry with renewable feedstocks.[5] Biomass-derived carbohydrates represent a promising carbon-based alternative as an energy source and a sustainable chemical feedstock. However, more efficient processes need to be developed for the selective conversion of carbohydrates into useful organic intermediates.

The five-membered ring compound, 5-hydroxymethylfurfural (HMF), is one of the top bio-based platform compounds. HMF can be converted to a novel biofuel molecule 2,5-dimethylfuran[3] via selective hydrogenation. Thus, making HMF with renewable feedstock is highly demanding. Because glucose is liable to form a stable six-membered pyranoside structure,[6] it failed to form HMF with satisfactory yields under those known conditions.[7] In the case of HMF, its formation by the dehydration of fructofuranose is straightforward and has been demonstrated in water, traditional organic solvents,[8] multiphase systems,[9,10] and ionic liquids.[11-13] Zhao *et al.*[12] reported that chromium catalysts in alkylimidazolium chloride ionic liquids, such as 1-ethyl-3-methylimidazolium chloride ([EMIM]Cl), enable synthesis of HMF from glucose, a less expensive feedstock, in good yield. While promising, this method depends on expensive ionic liquid solvents. In our research, we sought to address these concerns by minimizing the use of ionic liquids for HMF production.



[EMIM]Cl



CPL-LiCl

Noting that the chloride counterions in [EMIM]Cl form only weak ion pairs,[14] we reasoned that other nonaqueous solvents containing a high concentration of chloride ions could be as effective as [EMIM]Cl for HMF synthesis. We were aware that CPL containing LiCl is one of solvents that can dissolve purified simple sugars. These useful properties likely stem from the association of lithium ions with CPL to form CPL•Li^+ macrocations, resulting in a high concentration of weakly ion-paired chloride ions. Here, we report that using CPL-LiCl as a solvent enables the efficient syn-

---

* E-mail: lclulin@scut.edu.cn; Tel.: 0086-020-22236719; Fax: 0086-020-22236719

Received July 12, 2010; revised and accepted August 17, 2010.

Project supported by the National Key Basic Research Program (No. 2010CB732201) from the Ministry of Science and Technology of China.

[†] Dedicated to the 60th Anniversary of Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences.

thesis of HMF in a single step from glucose. The CPL-LiCl solvent is cheaper and more easily prepared than traditional ionic liquids. Preparation of 5-hydroxymethylfurfural from glucose in CPL-LiCl has the prospect of industrialization.

Experimental

General

Commercial chemicals were of reagent grade or better and were used without further purification. Reactions were performed in glass vessels heated in a temperature-controlled oil bath with magnetic stirring. 5-Hydroxymethylfurfural was from Energy Chemical Company.

Analytical methods

All reaction products were analyzed by ion chromatography (IC) and quantified with calibration curves generated from commercially available standards. After handling samples simply, HMF and glucose were analyzed using Dionex ICS-3000 ion-exchange chromatography with electrochemical detector (Figure 1). The glucose and HMF were separated on a CarboPacTM PA1 column (i.d. 2 mm×250 mm) by using isocratic elution consisting of 70 mmol/L sodium hydroxide at a flow rate of 0.35 mL/min. The experimental results showed that linear correlations of glucose and HMF were observed, and the correlation coefficient r^2 was over 0.999.

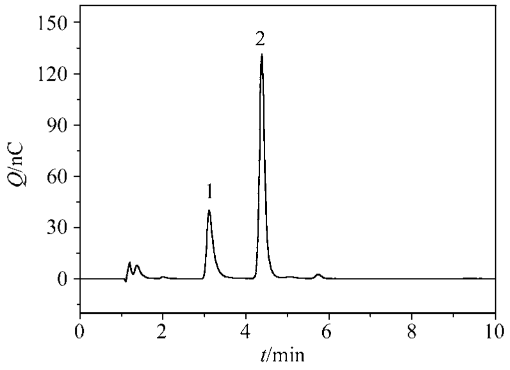


Figure 1 Chromatogram of the standard mixture. 1—HMF (0.6424 mg/L); 2—glucose (1.001 mg/L).

Typical workup procedure

LiCl (0.424 g, 0.01 mol) was dissolved in CPL (3.395 g, 0.03 mol) at 100 ℃. The reaction mixture was stirred at 120 ℃ for 1.5 h, cooled to 80 ℃. Thereafter, $CrCl_3 \cdot 6H_2O$ (0.035 g, 0.131 mmol) and glucose (0.4 g, 2.222 mmol) were added. The reaction mixture was stirred at 100 ℃ for 3 h. At 1 h intervals, aliquots of the reaction mixture were removed for IC analysis. HMF yields for optimized reactions of sugars were reproduced to within 2%—3%.

Ion-exclusion chromatographic separation of HMF

Deionized water (2.0 g) was mixed with above reaction mixture (4.254 g) containing HMF (182 mg). This solution was loaded onto a column of ion-exclusion resin (Dowex 50X8-200, Li+ form, 70 cm×1.5 cm) and eluted with deionized water at a rate of 3 cm/min. Fractions (25 mL) were collected and analyzed by IC. IC analysis indicated that ＞75% of the HMF was recovered in the HMF-containing fractions.

Results and discussion

Influence of the reaction medium's composition on the 5-HMF yield

N,*N*-Dimethylacetamide (DMA)-LiCl has been shown to be an effective solvent for the dehydration of glucose to 5-HMF.[15] We found that CPL-LiCl also is an effective solvent for the dehydration of glucose to 5-HMF. Therefore, mixtures of CPL and LiCl were used as the solvent for the process, and the effect of the solvent composition was studied. The experimental results are shown in Table 1. We found HMF yield was 27.3% from glucose in the absence of LiCl. With the addition of LiCl or LiBr to CPL, we obtained substantial yield of HMF (40%—67%). But we found a bit of HMF yields (10%—14%) with the addition of $ZnCl_2$ to CPL. It can be seen that the mole ratio in CPL-LiCl or CPL-LiBr had some influence on the molar yield of HMF. A high HMF yield was obtained in 3∶1 (mole ratio) CPL-LiCl or CPL-LiBr. The results demonstrate that CPL-LiCl or CPL-LiBr mixture are effective solvent for the dehydration of glucose to 5-HMF

Table 1 Influence of solvent composition on the 5-HMF yield[a]

Solvent (mole ratio)	Catalyst, mol%	T/℃	Time/h	Molar yield/%
CPL	$CrCl_3$, 6	100	3	27.3
CPL-LiCl (5∶1)	$CrCl_3$, 6	100	3	56.1
CPL-LiCl (4∶1)	$CrCl_3$, 6	100	3	39.2
CPL-LiCl (3∶1)	$CrCl_3$, 6	100	3	66.7
CPL-LiCl (2∶1)	$CrCl_3$, 6	100	3	56.2
CPL-LiBr (5∶1)	$CrCl_3$, 6	100	3	51.3
CPL-LiBr (4∶1)	$CrCl_3$, 6	100	3	42.8
CPL-LiBr (3∶1)	$CrCl_3$, 6	100	3	61.5
CPL-$ZnCl_2$ (5∶1)	$CrCl_3$, 6	100	3	13.4
CPL-$ZnCl_2$ (4∶1)	$CrCl_3$, 6	100	3	14.1
CPL-$ZnCl_2$ (3∶1)	$CrCl_3$, 6	100	3	9.7

[a] Glucose was reacted at a concentration of 10% relative to the total mass of the reaction mixture. Catalyst loading is relative to glucose. Yields are based on IC analysis.

Conversion of glucose into HMF in CPL-LiCl treated with various metal halide and acid catalysts

Figure 2 is a histogram showing conversion results for glucose in CPL-LiCl, pretreated with various metal halide catalysts. As shown in the figure, Glucose conversion was high for the metal halide catalysts tested. These metal halide showed a conversion of glucose of 85% or greater. However, HMF yields were low using $AlCl_3$ or $CuCl_2$. HMF yields from conversion of glucose were also low using acids (*e.g.*, H_2SO_4) as catalysts. Four catalysts, $CrCl_3$, $CrCl_2$, $SnCl_4$ and $SnCl_2$, gave HMF yields of 55%—67%, good efficiency for conversion of glucose. The experimental results are shown in Table 2. HMF yield for CPL-LiCl solvent systems not containing $CrCl_3$, $CrCl_2$, $SnCl_4$ or $SnCl_2$ were consistently 15% or less. Although Zhao *et al.*[12] reported that $CrCl_2$ was markedly less effective than $CrCl_3$, we found that chromium in either oxidation state gave a similar yield. Stannum in either oxidation state also gave a similar yield.

Chromium and stannum likely enables conversion of glucose to HMF by catalyzing the isomerization of glucose into fructose (Figure 3).[12,16] The fructose is then converted to HMF. Our observations suggest that the yields of HMF from glucose in reactions utilizing chromium or stannum correlate with metal coordination. Highly coordinating ligands such as amines decrease the yields of HMF. On the other hand, halide ligands enhance HMF yields. Our data suggest that the halide additives must balance two roles in the conversion of glucose into HMF: serving as ligands for chromium or stannum and facilitating the selective conversion of fructose. In contrast, chloride potentially offers the optimal balance of nucleophilicity and coordinating ability, enabling unparalleled transformation of glucose into HMF.

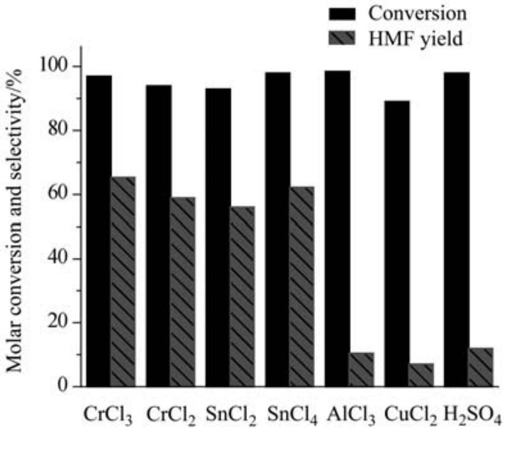


Figure 2 Glucose conversion in CPL-LiCl (3∶1) treated with numerous catalysts. Glucose was reacted at a concentration of 10% relative to the total mass of the reaction mixture. Catalyst loading is reacted at a concentration of 6% relative to the mol of glucose. The reaction systems were heated to 100 ℃ for 3 h. Yields are based on IC analysis.

Table 2 Influence of various metal halide and acid catalysts on the 5-HMF yield[a]

Solvent (mole ratio)	Catalyst, mol%	*T*/℃	Time/h	Molar yield/%
CPL-LiCl (5∶1)	$CrCl_2$, 6	100	3	46.2
CPL-LiCl (4∶1)	$CrCl_2$, 6	100	3	31.4
CPL-LiCl (3∶1)	$CrCl_2$, 6	100	3	58.7
CPL-LiCl (2∶1)	$CrCl_2$, 6	100	3	45.2
CPL-LiCl (5∶1)	$SnCl_4$, 6	100	3	54.8
CPL-LiCl (4∶1)	$SnCl_4$, 6	100	3	41.4
CPL-LiCl (3∶1)	$SnCl_4$, 6	100	3	64.7
CPL-LiCl (2∶1)	$SnCl_4$, 6	100	3	54.3
CPL-LiCl (5∶1)	$SnCl_2$, 6	100	3	41.9
CPL-LiCl (4∶1)	$SnCl_2$, 6	100	3	28.6
CPL-LiCl (3∶1)	$SnCl_2$, 6	100	3	55.4
CPL-LiCl (2∶1)	$SnCl_2$, 6	100	3	41.7
CPL-LiCl (3∶1)	$AlCl_3$, 6	100	3	9.7
CPL-LiCl (3∶1)	$CuCl_2$, 6	100	3	7.3
CPL-LiCl (3∶1)	H_2SO_4, 6	100	3	12.6

[a] Glucose was reacted at a concentration of 10% relative to the total mass of the reaction mixture. Catalyst loading is relative to glucose. Yields are based on IC analysis.

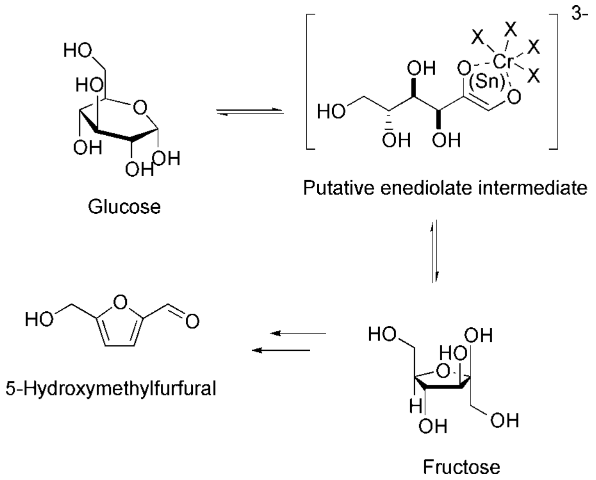


Figure 3 Putative mechanisms for the chromium-catalyzed or stannum-catalyzed transformation of glucose into HMF.

Conclusion

Catalytic dehydration of glucose to 5-HMF using $CrCl_3$ as the catalyst in CPL-LiCl mixtures by heating was investigated. CPL-LiCl mixtures were shown to be effective for the dehydration of glucose to 5-HMF. A high 5-HMF yield of 66.7% was obtained for a 3 h reaction time in (3∶1 mole ratio) CPL-LiCl mixtures at 100 ℃.

We demonstrated that $CrCl_2$, $SnCl_4$ and $SnCl_2$ also are excellent catalysts for the conversion of glucose into

HMF in the CPL-LiCl mixtures. Formation of the five-membered-ring chelate complex of Cr (or Sn) and glucose may play a key role in the formation of HMF. The efficient, cheaper, low toxicity and reusable catalytic system has great potential for application.

References

1 Phil, S.; Barbara, J.; Daniel, C.; James, A.; Brooks, H. *Science* **2007**, *315*, 781.

2 Arthur, J. R.; Charlotte, K. W.; Brian, H. D.; George, B.; John, C.; Charles, A. E.; William, J. F. Jr.; Jason, P. H.; David, J. L.; Charles, L. L.; Jonathan, R. M.; Richard, M.; Richard, T.; Timothy, T. *Science* **2006**, *311*, 484.

3 Yuriy, R.; Christopher, J. B.; Zhen, Y. L.; James, A. D. *Nature* **2007**, *447*, 982.

4 Chheda, J. N.; Huber, G. W.; Dumesic, J. A. *Angew. Chem.* **2007**, *119*, 7298.

5 Bicker, M.; Hirth, J.; Vogel, H. *Green Chem.* **2003**, *5*, 280.

6 Kuster, B. F. M. *Starch* **1990**, *42*, 314.

7 Qi, X.; Masaru, W.; Aida, T. M.; Richard, L.; Smith, J. *Green Chem.* **2008**, *10*, 799.

8 Gary, A. H.; Robert, J. Y. Jr.; Vladimir, V. G. *Org. Lett.* **2003**, *5*, 2003.

9 Roman-Leshkov, Y.; Chheda, J. N.; Dumesic, J. A. *Science* **2006**, *312*, 1933.

10 Chheda, J. N.; Roman-Leshkov, Y.; Dumesic, J. A. *Green Chem.* **2007**, *9*, 342.

11 Moreau, C.; Finiels, A.; Vanoye, L. *J. Mol. Catal. A: Chem.* **2006**, *253*, 165.

12 Zhao, H.; Holladay, J. E.; Brown, H.; Zhang, Z. C. *Science* **2007**, *316*, 1597.

13 Zhao, H.; Holladay, J. E.; Brown, H.; Zhang, Z. C. *US 20080033187*, **2008** [*Chem. Abstr.* **2008**, *148*, 241411].

14 Chowdhury, S.; Mohan, R. S.; Scott, J. *Tetrahedron* **2007**, *63*, 2363.

15 Joseph, B. B.; Ronald, T. R. *J. Am. Chem. Soc.* **2009**, *131*, 1979.

16 Hu, S.; Zhang, Z.; Song, J.; Zhou, Y.; Han, B. *Green Chem.* **2009**, *11*, 1746.

(E1007125 Cheng, B.)