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Biofuels

Efficient Catalytic System for the Selective Production of 5-Hydroxymethylfurfural from Glucose and Fructose**

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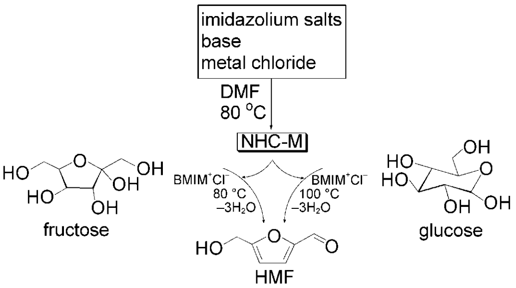
The diminishing fossil fuel reserves and global warming effects have become major concerns, and the search for sustainable, alternative energy is of critical importance.[1,2] Biofuels are highly attractive as they are the only sustainable source of liquid fuels currently available[3] however, the replacement of a petroleum feedstock by biomass is limited by the lack of highly efficient methods to selectively convert carbohydrates into chemical compounds for 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] Recently, efforts have been devoted to the conversion of biomass into 5-hydroxymethylfurfural (HMF), a versatile and key intermediate in biofuel chemistry and the petroleum industry.[6] HMF and its 2,5-disubstituted furan derivatives can replace key petroleum-based building blocks.[7] There are currently a number of catalysts that are active in the dehydration of sugars to form HMF. However, most of them also promote side reactions that form undesired byproducts, and rehydrate HMF to form levulinic acid and formic acid. Thus, these catalysts are often limited to simple sugar feedstocks, such as fructose.[4,6,8] Recent reports illustrate the use of 1-H-3-methyl imidazolium chloride ($HMIM^+Cl^-$) as a solvent and an acid catalyst to efficiently convert fructose into HMF with approximately a 90 % yield.[9] However, such a system has not been shown to convert glucose, which is a more stable and abundant sugar source, into HMF. Dumesic and co-workers have developed a two-phase (aqueous/organic) system for the separation and stabilization of the HMF product.[6a,b] Zhang and co-workers have reported a metal chloride/ionic liquid system that gives moderate to good HMF yields for both fructose (83 % with Pt or Rh chloride, 65 % with $CrCl_2$) and glucose (a record high of 68 % with $CrCl_2$).[10] Herein, we report a new catalyst system that efficiently converts both fructose and glucose into HMF in good to excellent yields (81–96 %).

Zhang and co-workers showed that transition metals were good catalysts for the transformation of sugars into HMF.[10] We selected NHC/metal (NHC = N-heterocyclic carbene) complexes as catalysts for the sugar dehydration reaction.[11] These ligands offer a great deal of flexibility as the catalytic activity can be modified by varying the stereo and electronic properties of the NHCs. The conversions of fructose and glucose into HMF were tested using 1-butyl-3-methyl imidazolium chloride ($BMIM^+Cl^-$) with different catalysts (Scheme 1). The NHC–metal complexes were pre-generated by heating a mixture of imidazolium salts, potassium *tert*-butoxide (KO*t*Bu), and metal chlorides in *N*,*N*-dimethylformamide (DMF) for several hours before adding to the reaction system. In a typical reaction protocol, 100 mg of sugar was mixed with 1 g of $BMIM^+Cl^-$ and 2–9 mol % of pre-prepared NHC/Cr catalyst. The reaction mixture was kept at 100 °C for 6 hours. HMF was extracted using diethyl ether (three times). All experiments were repeated, and the HMF yields were confirmed through analysis of the extracted product by both gas chromatography (GC) and nuclear magnetic resonance (NMR) spectroscopy using an external standard (see the Supporting Information for experimental details of the catalyst preparation, catalytic reaction, and product characterization).



Scheme 1. Conversion of sugars into HMF over NHC/metal catalysts.

Several metals were selected for the screening studies, but only Cr^{II} and Cr^{III} gave promising results. Unlike the previously reported metal chloride/ionic liquid system,[10] herein Cr^{II} and Cr^{III} showed similar activities toward converting fructose or glucose into HMF (Table 1). Remarkably, catalytic activity was found to be closely related to the stereochemical properties of the NHC ligands. **1**/$CrCl_2$ catalyzed the dehydration of fructose and glucose to give HMF yields of 65 % and 66 %, respectively (Figure 1, Table 1). This finding was similar to that of the $CrCl_2$/1-ethyl-3-methyl-imidazolium (EMIM) system.[10] The catalyst with the isopropyl-substituted NHC ligand, **2**/$CrCl_2$, showed similar efficiency to that of **1**/$CrCl_2$. In contrast, the HMF yields from the sugars were significantly increased using

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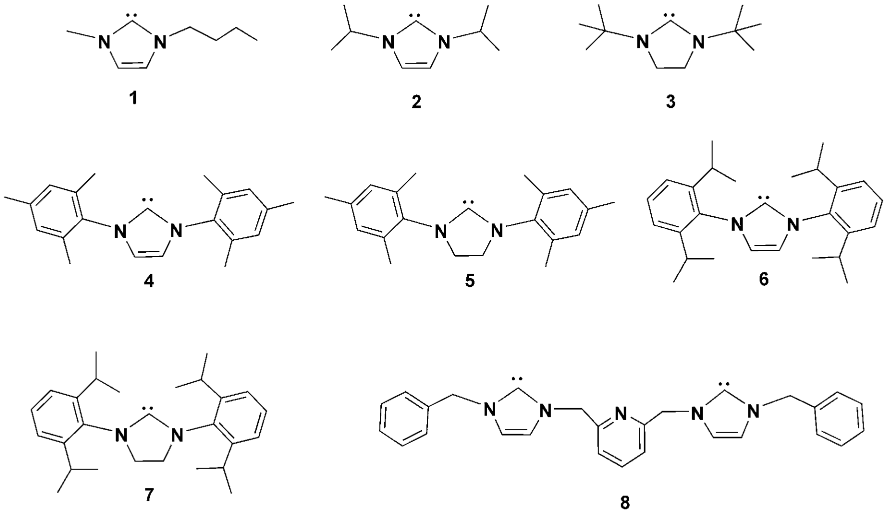

Figure 1. Structures of NHC ligands used.

Table 1: Conversion of sugars into HMF by NHC/Cr catalysts in $BMIM^+Cl^-$.[a]

Entry	Catalyst	Yield [%][b] (from fructose)	Yield [%][b] (from glucose)
1	**1**/$CrCl_2$	65	66
2	**2**/$CrCl_2$	68	65
3	**3**/$CrCl_2$	76	62
4	**4**/$CrCl_2$	89	80
5	**5**/$CrCl_2$	76	50
6	**6**/$CrCl_2$	96	81
7	**7**/$CrCl_2$	93	70
8	[**8**/$(CrCl_2)_2$]	–	81
9	**8**/$CrCl_2$	74	14
10	**4**/$CrCl_3$	90	78
11	**5**/$CrCl_3$	77	72
12	**6**/$CrCl_3$	96	78
13	**7**/$CrCl_3$	83	81
14[c]	**6**/$CrCl_2$	82	65
15[d]	**6**/$CrCl_2$	–	76
16[e]	**6**/$CrCl_2$	95	77
17[f]	**6**/$CrCl_2$	98	68
18[g]	**6**/$CrCl_2$	99	60
19[h]	**6**/$CrCl_2$	96	80

[a] Reaction conditions: solvent (500 mg), sugar (50 mg), catalyst (9 mol%), 100°C, 6 h in air, unless otherwise noted. All reactions were repeated on 100 mg scale of sugar. The average yields were reported. [b] Yield was determined by GC methods using an internal standard and the isolated pure product. [c] Reaction was conducted under argon. [d] 9 mol% of bipyridine was added to the reaction. [e] Recycled catalyst/ionic liquid from entry 6. [f] Recycled catalyst/ionic liquid from entry 16. [g] Recycled catalyst/ionic liquid from entry 17. [h] Reaction conditions: solvent (1250 mg), sugar (250 mg), catalyst (9 mol%), 100°C, 6 h in air.

chromium catalysts with the more bulky NHC ligands, such as **3**–**7**. The **6**/$CrCl_2$ system provided an HMF yield as high as 96% from fructose and a yield of 81% from glucose, which is the highest recorded efficiency for this feedstock. There was no significant difference in the HMF yield obtained using the metal catalysts with saturated versus unsaturated NHC ligands (e.g.,**6** versus **7**). The catalysts with the most bulky NHC ligand, 1,3-bis(2,6-diisopropylphenyl)imidazolylidene (**6**) and 1,3-bis(2,6-diisopropyl)phenylimidazolinylidene (**7**), provided the highest yields. To better understand the details of this reaction, bidentate ligand **8** was examined.[12] Interestingly, [**8**/$(CrCl_2)_2$] gave a good HMF yield (81%) from glucose, whereas **8**/$CrCl_2$ gave a poor HMF yield (14%). These results suggested that a sterically crowded complex would have a lower activity in binding with substrates and initiating the reaction. Bulky NHC ligands, such as **6** and **7**, protected the Cr center from reacting with $BMIM^+Cl^-$ to form a sterically crowded metal center, therefore providing the highest catalytic efficiency. A control reaction in which the catalyst was absent, resulted in very low HMF yields (less than 40% and 1% from fructose and glucose, respectively). The reaction temperature was over a range from 80°C to 140°C for both fructose and glucose. Lower temperatures led to a lower HMF yield and higher temperatures gave rise to byproducts (primarily diformylfuran (DFF); see Figure 2a).

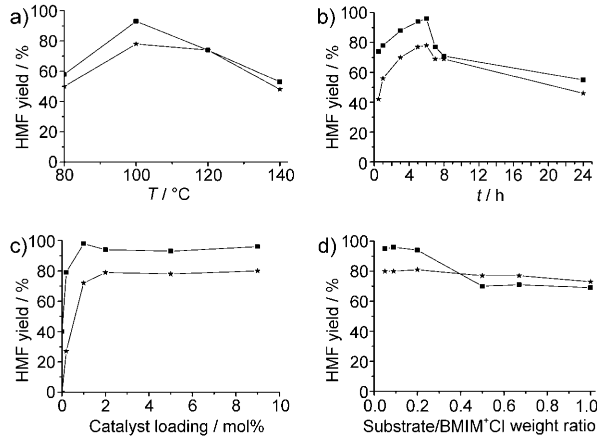

Figure 2. a) Effect of reaction temperature, b) reaction time, c) **6**/$CrCl_2$ loading, and d) substrate loading on HMF yield from fructose (■) and glucose (★). Default conditions unless otherwise noted: 9 mol% of **6**/$CrCl_2$, substrate/$BMIM^+Cl^-$ weight ratio = 0.2:1, 100°C, 6 h.

Kinetic studies of this reaction using **6**/$CrCl_2$ showed that the HMF yield peaked at our standard reaction conditions after 6 hours for both fructose and glucose (see Figure 2b), and then gradually decreased with reaction periods beyond 6 hours. This decrease may arise because of the decomposition of HMF under the reaction conditions. HMF yields for fructose and glucose after 6 hours began to decrease as the NHC/Cr catalyst loading was reduced to less than 1 mol% (see Figure 2c). Generally, the lower catalyst loading would require a longer reaction time to achieve a high conversion. However, in this system, the product may decompose under the reaction conditions, so a longer reaction time would lead to lower yield of the desired product. Thus, if a low catalyst loading of 1 mol% was to be employed, the reaction conditions would have to be optimized to maximize the HMF yield.

The substrate/solvent weight ratio was also found to be important for the overall efficiency of the reaction system (see Figure 2d). When the fructose/$BMIM^+Cl^-$ weight ratio was increased from 0.05:1 to 0.2:1, the HMF yield changed slightly from 95% to 94%. As the fructose/$BMIM^+Cl^-$ weight ratio increased from 0.2:1 to 0.5:1, the HMF yield decreased substantially to 70%. Additional increases in the fructose/ionic $BMIM^+Cl^-$ weight ratio did not lead to significant variation in the HMF yield. Remarkably, the HMF yield remained rather unaffected (81–77%) as the glucose/$BMIM^+Cl^-$ weight ratio was varied from 0.05 to 0.67. The HMF yield decreased slightly (73%) when the glucose/$BMIM^+Cl^-$ weight ratio was increased to 1.0:1. In this case, $BMIM^+Cl^-$ assisted in the reaction rather than serve as a solvent.

The different behavior of fructose and glucose in Figure 1d suggested different reaction mechanisms for the two feedstocks. In the latter, glucose might be converted into fructose first and subsequently into HMF[10] over the NHC/Cr catalyst. In this case, the fructose concentration would be relatively low even when the glucose substrate loading was high since fructose would merely be an intermediate in the conversion of glucose into HMF. Interestingly, HMF yields were approximately 14% lower for the reaction conducted in argon versus that conducted in air (Table 1, entry 14 versus entry 6). The NHC/Cr catalysts were also tested in dimethylsulfoxide (DMSO) as the solvent and lower HMF yields were obtained both from fructose (28–52%) and glucose (25–32%; see Table S1 in the Supporting Information). Again, catalysts with bulky NHC ligands showed higher efficiency in the DMSO system.

This reaction process allows recycling of NHC/Cr catalyst and the ionic liquid. HMF was the sole product from the diethyl ether extraction when the conversions of glucose or fructose were conducted at temperatures below 100 °C (see the Supporting Information). After the diethyl ether extraction, the reaction medium was preheated to 100 °C for 2 hours to remove the low boiling point components, such as diethyl ether and water, and then directly used in the next run by adding the sugar substrate. The recycled reaction system retained high activity in the conversion of fructose into HMF (Table 1, entries 16–18). The HMF yield from fructose in the recycled system was even higher than that in the system with the fresh catalyst. This might be because of the retention of some small amount of unreacted fructose after 6 hours of reaction in the previous cycle. For the glucose feedstock, HMF yields decreased gradually over multiple runs with the recycled catalyst.

In the $CrCl_2$/EMIM system,[10] it was proposed that the $CrCl_3^-$ anion rather than NHC/$CrCl_2$ complex acted as the catalyst, and the reaction was suppressed with additional ligands, such as bipyridine or glyceraldehyde. However, our results clearly suggest that NHC/$CrCl_x$ complexes play the key role in glucose dehydration in $BMIM^+Cl^-$. Bulky NHC ligands prevent chromium from forming multiple coordinations to the NHC ligand in $BMIM^+Cl^-$, thereby reducing the catalytic activity as in the case of **8**/$CrCl_2$. In contrast, inhibition effects were not observed with the addition of the bipyridine ligand as in the case of **6**/$CrCl_2$ (HMF yield of 76% from glucose) (Table 1, entry 15). Additionally, in the $CrCl_2$/EMIM system, a NHC/Cr complex could be formed under the reaction conditions and therefore serves as a catalyst.[13]

In summary, a new NHC–Cr/ionic liquid system has been developed for the selective conversion of sugars into HMF. Excellent efficiencies were achieved and we attained the highest HMF yields reported thus far for both fructose and glucose feedstocks. The HMF yields were as high as 96% and 81% for fructose and glucose, respectively. The new system is tolerant towards high substrate loading, and the catalyst and ionic liquid can be recycled. HMF is provided as the sole product isolated after simple extraction.

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