ACS Catalysis

Letter

pubs.acs.org/acscatalysis

Production of 5-Hydroxymethylfurfural from Glucose Using a Combination of Lewis and Brønsted Acid Catalysts in Water in a Biphasic Reactor with an Alkylphenol Solvent

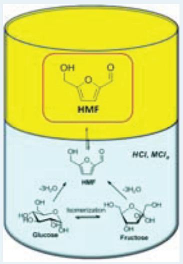
Yomaira J. Pagán-Torres,[†] Tianfu Wang,[‡] Jean Marcel R. Gallo,[†] Brent H. Shanks,[‡] and James A. Dumesic*[,†]

[†]Department of Chemical and Biological Engineering, University of Wisconsin-Madison, Madison, 1415 Engineering Drive, Madison, Wisconsin, 53706, United States

[‡]Department of Chemical and Biological Engineering, Iowa State University, 1140 L BRL, Ames, Iowa, 50011, United States

Ⓢ *Supporting Information*

ABSTRACT: We report the catalytic conversion of glucose in high yields (62%) to 5-hydroxymethylfurfural (HMF), a versatile platform chemical. The reaction system consists of a Lewis acid metal chloride (e.g., $AlCl_3$) and a Brønsted acid (HCl) in a biphasic reactor consisting of water and an alkylphenol compound (2-*sec*-butylphenol) as the organic phase. The conversion of glucose in the presence of Lewis and Brønsted acidity proceeds through a tandem pathway involving isomerization of glucose to fructose, followed by dehydration of fructose to HMF. The organic phase extracts 97% of the HMF produced, while both acid catalysts remain in the aqueous phase.



KEYWORDS: *biomass, Lewis acid, HMF, glucose, biphasic*

Biomass has been intensely investigated as a renewable feedstock for the production of chemicals and transportation fuels in view of economic, environmental, and political concerns associated with diminishing fossil fuel resources. The development of economically viable processes for the production of chemical intermediates from biomass-derived carbohydrates has become an important challenge for research in this area, such as the development of efficient processes for the production of the platform chemical 5-hydroxymethylfurfural (HMF).[1−5] In this respect, HMF has been identified as a primary building block for the production of furanic polyesters, polyamides, and polyurethanes analogous to those derived from the petroleum polymer industry.[6−9]

HMF is produced from the acid-catalyzed dehydration of C_6-sugars (i.e., hexoses). The formation of HMF is proposed to take place through the dehydration of a 5 member monosaccharide ring. Hence, fructose which contains 21.5% of furanose tautomers in aqueous solution can be converted to HMF more efficiently than glucose which contains 1% of furanose tautomers in aqueous solutions.[10] Accordingly, while considerable efforts have focused on the production of HMF from fructose in high yields,[1,3,4] a catalytic system that efficiently converts glucose to HMF in water has yet to be developed. Although glucose can be converted with low yields to HMF using Brønsted acids, the yield to HMF can be increased significantly if glucose is first isomerized to fructose, and fructose is then dehydrated to HMF.

While the dehydration of fructose is catalyzed by strong acids, the challenge for the conversion of glucose to HMF is to find a catalytic system that can selectively isomerize glucose to fructose in tandem with the dehydration reaction. Glucose isomerization proceeds by hydrogen transfer from the C-2 to the C-1 position and from the O-2 to the O-1 position of the α-hydroxy aldehyde to form the α-hydroxy ketone.[11] The mechanism of hydrogen transfer from the O-2 to the O-1 position of the aldose is by a proton transfer between the electronegative carbonyl and the hydroxyl groups, whereas the transfer of hydrogen from the C-2 to the C-1 position may occur through a hydride ion, or in alkaline conditions as a proton.[12] Lewis acids and Brønsted bases are catalysts commonly used for this reaction. However, basic catalysts typically lead to side reactions.[13]

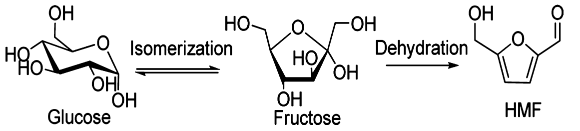
Recent studies have been published on the development of new processing strategies focused on the isomerization of glucose to fructose with subsequent acid-catalyzed dehydration of fructose to HMF. Lewis acid catalysts in ionic liquids have been shown to be the most promising systems for the conversion of glucose to HMF.[5] Zhao et al. first reported HMF yields of 68−70% in a system consisting of 1-ethyl-3-methyl-imidazolium chloride and a $CrCl_2$ catalyst.[2] It is believed that the high activity and selectivity observed for the production of HMF in ionic liquids with chromium catalysts are caused by the stabilization of the transition state for ring-opening of glucose by the Lewis acidic Cr center during glucose isomerization.[14] Other studies have been carried out on this same reaction using different ionic liquids or Lewis acid catalysts.[15−17] The main disadvantages of using ionic liquids are

Received: March 22, 2012
Published: April 18, 2012

that they are expensive and subject to deactivation by small amounts of water formed during dehydration reactions.[18] Binder et al. reported that a mixture consisting of dimethylacetamide (DMA), NaBr, and a Lewis acid, $CrCl_2$, could reach HMF yields of 81%, being as effective as ionic liquid systems.[3] Huang et al. reported an HMF yield of 63% from glucose by a two step process consisting of the isomerization of glucose to fructose in the presence of glucose isomerase and borate ions, followed by the acid catalyzed dehydration of fructose to HMF using HCl as a catalyst in a biphasic system.[19] Takagaki et al. reported HMF yields of 42% at a 73% conversion by a similar two step process by combining a solid acid catalyst, Amberlyst-15, and a solid base catalyst, Mg–Al hydrotalcite, in *N*,*N*-dimethylformamide.[20] Nikolla et al. reported HMF yields of 57% at 79% conversion of glucose using a Lewis acidic Sn-Beta zeolite and HCl in a water/NaCl/THF biphasic reaction system.[21] Recently, Abu-Omar et al. reported an HMF yield of 61% from glucose using $AlCl_3 \cdot 6H_2O$ as the catalyst in a biphasic system where THF was used as the extracting solvent.[22,23]

In general, the conversion of glucose to HMF can follow two reaction pathways. One pathway is through a Lewis acid catalyzed isomerization of glucose to fructose combined with the dehydration of fructose to HMF (see Supporting Information, Scheme S1). The other pathway is through the direct dehydration of glucose to HMF (Supporting Information, Scheme S2). From these two reaction pathways the one passing through fructose should be more selective toward HMF formation. On the basis of studies of the Lewis acid-catalyzed isomerization of hexoses, one can hypothesize that the combination of Lewis and Brønsted acidity could produce HMF by a combined isomerization/dehydration reaction of glucose to HMF, as illustrated in Scheme 1.

Scheme 1. Conversion of Glucose to HMF by a Combined Isomerization/Dehydration Reaction Pathway



RESULTS AND DISCUSSION

In this letter, we report the conversion of glucose to HMF in a biphasic reactor system in the presence of Lewis acid salts ($AlCl_3$, $SnCl_4$, VCl_3, $InCl_3$, $GaCl_3$, $LaCl_3$, $DyCl_3$, and $YbCl_3$). The biphasic reactor consists of an aqueous layer saturated with sodium chloride and an extracting organic layer consisting of 2-*sec*-butylphenol (SBP). Metal chlorides were dissolved in the aqueous layer, and the pH was adjusted to 2.5 by the addition of HCl, with the exception of $SnCl_4$ for which dissolution of the salt produced a solution with a pH of 1.8. The rationale for using a biphasic reactor is that the reactive HMF product can be continuously extracted from the acidic aqueous phase, thereby minimizing condensation reactions of HMF with glucose that lead to solid humins and rehydration reactions of HMF to form levulinic and formic acid.[1,24] In this respect, we have recently identified that alkylphenol compounds are effective for the extraction of levulinic acid and furan compounds from acidic aqueous solutions.[25] Thus, we employed this extracting solvent for the removal of HMF from the reactive aqueous layer. Preliminary reaction kinetics of glucose dehydration with different metal chlorides as Lewis acid catalysts were also studied, which could provide more insight into the reaction mechanism and aid the rational design of bifunctional Lewis/Brønsted acid catalytic system for dehydration reactions in the future. Experiments for the conversion of glucose to HMF were performed at 443 K under autonomous pressure. The main products observed were fructose, HMF, and solid humins.

It can be seen in Table 1, entries 1–2, that glucose can be converted in the presence of the mineral acid, HCl, without any metal chloride catalyst; however, the selectivity for production of HMF is only 30% at 91% conversion. In the absence of an isomerization catalyst, the formation of HMF may follow a mechanism in which the open-chain form of glucose is dehydrated at the C-2 position, forming a carbocation which reacts with the hydroxyl group at C-5 position, forming tetrahydro-3,4-dihydroxy-5-(hydroxymethyl)-2-furaldehyde followed by further dehydration to form HMF (see Supporting Information, Scheme S2).[10] The addition of a Lewis acid salt clearly leads to a significant increase in HMF selectivity, as shown in Table 1, entries 3–10. The presence of $AlCl_3$ leads to 68% HMF selectivity at 91% conversion, with a short reaction time. Moderate HMF selectivities of 53, 52, and 50% were obtained at conversions of 92, 86, and 90% for the addition of VCl_3, $InCl_3$, and $GaCl_3$, respectively, to the aqueous layer. $YbCl_3$, $DyCl_3$, and $LaCl_3$ were also studied, displaying HMF selectivities of 46, 41, and 44%, respectively. The addition of $SnCl_4$ to the aqueous layer led to a glucose conversion of 90% with 58% selectivity to HMF; however, the pH of this solution was 1.8. At this same pH of 1.8, $AlCl_3$ generated a conversion of 90% with 68% selectivity to HMF.

Table 1. Conversion of Glucose to HMF in a Biphasic System with SBP as Extracting Organic Layer[a]

entry	catalyst	conversion [%]	selectivity [%]	time [min]
1		15	52	30
2		91	30	420
3	$AlCl_3$	91	68	40
4	$SnCl_4$	90	58	45
5	VCl_3	92	53	90
6	$GaCl_3$	90	50	120
7	$InCl_3$	86	52	150
8	$YbCl_3$	93	46	120
9	$DyCl_3$	93	41	160
10	$LaCl_3$	87	44	240

[a] Reaction conditions: 5 wt % glucose in water saturated with NaCl, reaction temperature of 443 K, organic to aqueous mass ratio of 2, pH = 2.5 with the exception of entry 4 which has a pH = 1.8. Entries 3–5, glucose to Lewis acid molar ratio of 67. Entries 6–10, glucose to Lewis acid molar ratio of 13.

The reaction effluent obtained using $AlCl_3$ as the Lewis acid catalyst (Table 1 entry 3) was analyzed by HPLC and Fourier Transform Ion Cyclotron Resonance (FT-ICR) mass spectrometry for the identification of byproducts. A 4% yield of levulinic acid was determined by HPLC, and disaccharides and levoglucosan were identified by FT-ICR. The formation of these products is in agreement with previous literature.[26] In addition, insoluble humins were observed, these species being produced by the cross-polymerization of glucose and HMF.[26]

Although typical Lewis acids, such as metal halides, are generally considered to be inactive in water, Fringuelli et al.[27,28] recently demonstrated that $AlCl_3$, $TiCl_4$, and $SnCl_4$ are active in Lewis acid-catalyzed reactions in water at pH < 4. Metals salts can form different species depending on the pH of the aqueous solution. Aluminum, for example, can form the Keggin heteropolycation in alkaline aqueous solution, while it is present as solvated Al^{3+} at pH < 3.[29] For $SnCl_4$, the mononuclear species $Sn(OH)_y^{(4-y)+}$ has been proposed primarily in cationic form in pH < 2.[29,30] At the pH employed in this study, vanadium is present as VO_2^+, whereas all other metal ions are present as solvated cations.[29] Fringuelli et al.[27,28] have shown the pH of the solution plays a key role in controlling the Lewis acidity of metal halides in an aqueous solution. Therefore, in the system used in this work for glucose conversion to HMF, the acidic pH is responsible for the formation of the catalytically active metal species, thus facilitating glucose ring-opening and the subsequent dehydration reactions.

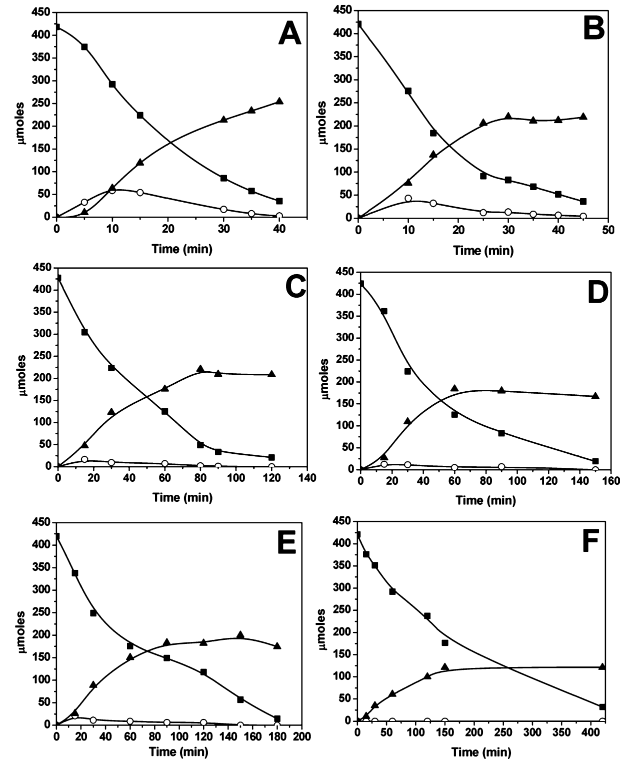


Figure 1. Glucose conversion in a biphasic system with HCl and (A) $AlCl_3$, (B) $SnCl_4$, (C) VCl_3, (D) $GaCl_3$, (E) $InCl_3$, and (F) no Lewis acid as a function of time. (■) Glucose, (○) Fructose, and (▲) HMF.

Figure 1 shows the conversion of glucose to HMF as a function of time in the presence of $AlCl_3$, $SnCl_4$, VCl_3, $GaCl_3$, $InCl_3$ and without the metal chloride. (See the Supporting Information, Figure S1 for reaction kinetics data upon addition of lanthanide salts.) In Figure 1A–B, fructose is observed to be a dominant intermediate which reaches a maximum concentration during the first 10 min of reaction in the presence of $AlCl_3$ and $SnCl_4$. At longer reaction times fructose is consumed with a concomitant formation of HMF. For reactions catalyzed by VCl_3, $GaCl_3$, and $InCl_3$, fructose is also produced as an intermediate (Figure 1C–E), but in lower quantities compared to $AlCl_3$ and $SnCl_4$. For the experiment performed in the absence of a Lewis acid salt (Figure 1F), fructose is not observed, suggesting that HMF is produced from the acid catalyzed dehydration of glucose. It is clear from Figure 1 that reaction systems with higher fructose quantities show higher HMF yields, as observed for $AlCl_3$ and $SnCl_4$ (Table 1 entries 3–4). For systems with lower rates of fructose formation, such as for the cases of VCl_3, $GaCl_3$, and $InCl_3$, the direct dehydration of glucose to HMF could have a significant contribution, leading to lower selectivities to HMF.

The effectiveness of the Lewis acids studied in this work for the conversion of glucose to fructose can be understood in terms of their intrinsic properties, such as the Lewis acid softness and ionic radius. For example, aluminum is the hardest of the Lewis acids studied, and it should interact strongly with the oxygen atoms of the hydroxyl groups in glucose, which are hard Lewis bases. Similarly, the ionic radius of the Lewis acid metal cations can be related to the reactivity of glucose. For example, the activity for glucose conversion and HMF formation increase with decreasing ionic radii from In^{3+} > Ga^{3+} > Al^{3+} and for the lanthanide series from La^{3+} > Dy^{3+} > Yb^{3+}. The increased catalytic activity with decreasing ionic radius can be attributed to stronger electrostatic interaction between glucose and the smaller cations, caused by an increase in the effective surface charge density of the ion.[31,32] Ionic radii for the cations studied can be found in the Supporting Information, Table S1.

The dehydration of fructose to HMF with high yields has been reported in previous studies using mineral acids and salts in a biphasic reactor with organic solvents such as tetrahydrofuran (THF), methyl isobutyl ketone (MIBK), and 2-butanol.[24] In this study, THF showed the highest partitioning of HMF into the organic phase. Therefore, we have investigated the use of THF as the extracting organic layer in our reaction system. Results are shown in Table 2 for the production of HMF from glucose in a biphasic reactor using THF or SBP as the organic phase.

Table 2. Comparison between Extracting Organic Layers for the Conversion of Glucose to HMF in a Biphasic Reaction System Using $AlCl_3$ and HCl as Catalysts[a]

extracting organic layer	conversion [%]	selectivity [%]	% HMF in org	% HCl in org
THF	80	71	93	30
SBP	88	70	97	0

[a] Reaction conditions: 5 wt % glucose in water saturated with NaCl, glucose to Lewis acid molar ratio of 67, pH = 2.5, reaction temperature of 443 K, organic to aqueous mass ratio of 2.

Using SBP as the extracting solvent led to an HMF yield of 62%, and 97% of the HMF produced was extracted to the organic layer. In contrast, when using THF as the extracting solvent, an HMF yield of 57% was obtained, and 93% of the HMF was extracted into the organic phase. In addition to the higher HMF yields obtained using SBP, an important advantage of the SBP solvent with this biphasic system is that no HCl was detected in the organic layer, in contrast to the system with THF in which 30% of the HCl was extracted into the organic layer. The extraction of mineral acid into the organic solvent containing HMF can cause problems in further separation/purification steps, because of the high reactivity of HMF in the presence of acids.

To further demonstrate the effectiveness of the water-SBP biphasic system with $AlCl_3$ and HCl as catalysts in the conversion of glucose to HMF, experiments were conducted to assess the extent to which the acidic aqueous layer could be recycled for glucose conversion. For these experiments, four consecutive runs were carried out, each with a reaction time of 40 min. Between each run, the organic layer containing HMF was extracted, and fresh SBP and glucose were added to the acidic aqueous solution in the reactor. For the first run, the conversion and selectivity were those observed in Table 1 Entry 3. For consecutive experiments, no significant decreases in conversion and selectivity were observed, as shown in Figure 2.

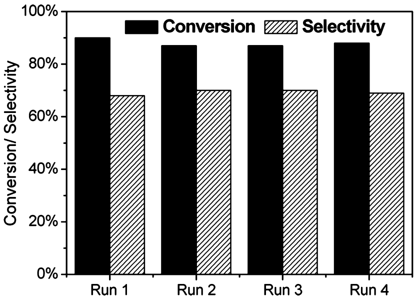


Figure 2. Conversion and selectivity for production of HMF from glucose in consecutive runs using the same acidic aqueous solution containing $AlCl_3$ and HCl as catalysts. Reaction conditions: 5 wt % glucose in water saturated with NaCl, reaction temperature of 443 K, organic to aqueous mass ratio of 2, pH = 2.5, glucose to aluminum molar ratio of 67.

The boiling points of HMF and SBP are similar, making it difficult to separate HMF from the solvent by distillation. Thus, an alternative approach is to extract HMF into a lower boiling point solvent, such as water. In this respect, contacting an organic solution of 1 wt % HMF in SBP with water extracts 12% and 26% of HMF into water using an organic/water mass ratio of 1:1 and 1:2, respectively (Supporting Information, Table S3). The extraction of HMF into water is more extensive when the SBP phase is contacted with hexane, and 94% of the HMF can be extracted into water in this manner (Supporting Information, Table S3).

■ CONCLUSIONS

We have shown in this letter that HMF can be produced efficiently from glucose in a biphasic reactor system using SBP as the organic extracting layer in contact with an aqueous phase saturated with NaCl, at pH equal to 2.5, and containing Lewis acidic metal halides, such as $AlCl_3$. The overall yield of HMF is 62% in this biphasic system using $AlCl_3$ and HCl as catalysts. The presence of the Lewis and Brønsted acids allows the conversion of glucose to proceed through a tandem reaction pathway involving isomerization of glucose to fructose followed by dehydration of the latter to HMF.

In the biphasic system employed here, the organic phase extracts 97% of the HMF from the aqueous phase, while the Lewis and Brønsted acid catalysts ($AlCl_3$ and HCl, respectively) remain in the aqueous phase. This reaction system has significant advantages over existing systems, such as the recovery of the HMF produced by removal of the organic layer and recycle of the reactive aqueous layer. Considering that all of the HMF in the organic phase can be recovered, a purified HMF yield of 60% can be obtained. Although this yield is lower than that achieved using ionic liquids[2] and dimethylacetamide[3] as solvents and $CrCl_2$ as catalyst, our system avoids the use of expensive solvents and toxic salts. Furthermore, in these previous reaction systems, the yield of HMF is based on the reaction mixture, and further separation and purification of HMF from the reactive solution are required, leading to additional costs and product loss.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental section. Reaction schemes S1−S3 for the conversion of glucose to HMF. Figure S1 showing the conversion of glucose in the presence of $YbCl_3$, $DyCl_3$ and $LaCl_3$ as a function of time. Table S1 containing the ionic radii of cations. Table S2 showing HMIS rating for common organic solvent. Table S3 showing extraction of HMF from SBP into water. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: dumesic@engr.wisc.edu.

Funding

This material is based on work supported by the National Science Foundation under Award No. EEC-0813570 (i.e., the Center for Biorenewable Chemicals, CBiRC, at Iowa State University). Chartanay D. J. Bonner was funded by the Center for Enabling New Technologies Through Catalysis, CENTC, at the University of Washington, Seattle.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Chartanay D. J. Bonner and Cristina Díaz-Lozada for assistance with biphasic reaction experiments. We thank Adam Okerlund for studies involving the separation of HMF from SBP.

■ REFERENCES

(1) Román-Leshkov, Y.; Chheda, J. N.; Dumesic, J. A. *Science* **2006**, *312*, 1933−1937.

(2) Zhao, H.; Holladay, J. E.; Brown, H.; Zhang, Z. C. *Science* **2007**, *316*, 1597−1600.

(3) Binder, J. B.; Raines, R. T. *J. Am. Chem. Soc.* **2009**, *131*, 1979−1985.

(4) Corma, A.; Iborra, S.; Velty, A. *Chem. Rev.* **2007**, *107*, 2411−2502.

(5) Zakrzewska, M. E.; Bogel-Łukasik, E.; Bogel-Łukasik, R. *Chem. Rev.* **2010**, *111*, 397−417.

(6) Gandini, A.; Belgacem, M. N. *Prog. Polym. Sci.* **1997**, *22*, 1203−1379.

(7) Moreau, C.; Belgacem, M. N.; Gandini, A. *Top. Catal.* **2004**, *27*, 11−29.

(8) Buntara, T.; Noel, S.; Phua, P. H.; Melián-Cabrera, I.; de Vries, J. G.; Heeres, H. J. *Angew. Chem., Int. Ed.* **2011**, *50*, 7083−7087.

(9) Lewkowski, J. *Arkivoc* **2001**, 17−54.

(10) Robyt, J. F. In *Essentials of Carbohydrate Chemistry*; Springer: New York, 1998; pp 48−74.

(11) Román-Leshkov, Y.; Moliner, M.; Labinger, J. A.; Davis, M. E. *Angew. Chem., Int. Ed.* **2010**, *49*, 8954−8957.

(12) Nagorski, R. W.; Richard, J. P. *J. Am. Chem. Soc.* **2001**, *123*, 794−802.

(13) Yang, B. Y.; Montgomery, R. *Carbohydr. Res.* **1996**, *280*, 27−45.

(14) Pidko, E. A.; Degirmenci, V.; van Santen, R. A.; Hensen, E. J. M. *Angew. Chem., Int. Ed.* **2010**, *49*, 2530−2534.
(15) Hu, S. Q.; Zhang, Z. F.; Song, J. L.; Zhou, Y. X.; Han, B. X. *Green Chem.* **2009**, *11*, 1746−1749.
(16) Fristrup, P.; Stahlberg, T.; Rodriguez-Rodriguez, S.; Riisager, A. *Chem.—Eur. J.* **2011**, *17*, 1456−1464.
(17) Chidambaram, M.; Bell, A. T. *Green Chem.* **2010**, *12*, 1253−1262.
(18) Moreau, C.; Finiels, A.; Vanoye, L. *J. Mol. Catal. A: Chem.* **2006**, *253*, 165.
(19) Huang, R.; Qi, W.; Su, R.; He, Z. *Chem. Commun.* **2010**, *46*, 1115−1117.
(20) Takagaki, A.; Ohara, M.; Nishimura, S.; Ebitani, K. *Chem. Commun.* **2009**, 6276−6278.
(21) Nikolla, E.; Román-Leshkov, Y.; Moliner, M.; Davis, M. E. *ACS Catal.* **2011**, *1*, 408−410.
(22) Yang, Y.; Hu, C.; Abu-Omar, M. M. *Green Chem.* **2012**, *14*, 509−513.
(23) Dutta, S.; De, S.; Alam, M. I.; Abu-Omar, M. M.; Saha, B. *J. Catal.* **2012**, *288*, 8−15.
(24) Román-Leshkov, Y.; Dumesic, J. A. *Top. Catal.* **2009**, *52*, 297−303.
(25) Alonso, D. M.; Wettstein, S. G.; Bond, J. Q.; Root, T. W.; Dumesic, J. A. *ChemSusChem* **2011**, *4*, 1078−1081.
(26) Pilath, H. M.; Nimlos, M. R.; Mittal, A.; Himmel, M. E.; Johnson, D. K. *J. Agric. Food. Chem.* **2010**, *58*, 6131−6140.
(27) Fringuelli, F.; Pizzo, F.; Vaccaro, L. *Tetrahedron Lett.* **2001**, *42*, 1131−1133.
(28) Fringuelli, F.; Pizzo, F.; Vaccaro, L. *J. Org. Chem.* **2001**, *66*, 4719−4722.
(29) Baes, C. F.; Mesmer, R. E. In *The Hydrolysis of Cations*; Wiley: New York, 1976.
(30) Jackson, K. J.; Helgeson, H. C. *Geochim. Cosmochim. Acta* **1985**, *49*, 1−22.
(31) Ishida, H.; Seri, K. *J. Mol. Catal. A: Chem.* **1996**, *112*, 163−165.
(32) Seri, K.; Inoue, Y.; Ishida, H. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 1145−1150.