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Article

Synthesis of 5-Hydroxymethylfurfural from Dehydration of Fructose And Glucose Using Ionic Liquids

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A produção do 5-hidroximetilfurfural (HMF) a partir da desidratação de açúcares é uma alternativa para a obtenção de materiais de partida na produção de poliésteres, poliamidas e poliuretano a partir de fontes renováveis. Além disso, a oxidação do HMF leva ao ácido 2,5-furanodicarboxílico (FDCA) potencial substituto para o ácido tereftálico (TA), proveniente do petróleo, intensamente utilizado na produção de polímeros, tais como, o poli(tereftalato de etileno) (PET). A substituição do TA por materiais obtidos a partir de fontes renováveis é de grande interesse do ponto de vista de obtenção de produtos com elevado grau de sustentabilidade.

The production of 5-hydroxymethylfurfural (HMF) from sugars dehydration is an alternative for obtaining starting materials for the production of polyesters, polyamides and polyurethanes, due to the development of the new materials not derived from petroleum. Moreover, by oxidizing the HMF, the 2,5-furandicarboxylic acid (FDCA) can be obtained, which can replace the terephthalic acid (TA) (from petroleum) in the polymers production as poly(ethylene terephthalate) (PET). The replacement of TA with materials derived from renewable sources is of great interest from an environmental and sustainable point of view.

Keywords: 5-hydroxymethylfurfural, dehydration, fructose, glucose, HMF

Introduction

Since the end of the 20th century the interest in the use of raw materials from renewable resources for the production of a variety of petrochemical intermediates has been growing in order to develop the replacement of petroleum as a source of raw materials and energy. Such techniques enabling the achievement of alternative sources will gradually be available for industrial application, depending on economic interests, social and availability of appropriate technologies.[1-3] Several product classes are promising natural substitutes of petroleum derivatives, the biomass being the first one obtained from renewable sources. Among all biomass, carbohydrates represent more than 75%, therefore the interest to convert them into fine chemicals is increasing and could represent a real alternative to non renewable sources.[4-7]

Currently the sustainable industrial conversion of biomass still depends on the development of specific technologies involving processes for biomass conversion related to equipment for producing fuels, chemical products and energy.[1,4,8,9] An example of this is the obtainment of 5-hydroxymethylfurfural (HMF), see structure in Figure 1, and furfural from cellulose or other carbohydrates as glucose, fructose and starch. A lot of renewable intermediates obtainable from biomass enable the production of green polymers or are precursors for the production of fuel, diesel or jet fuel.[10-13]

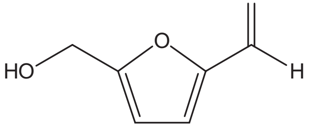

Figure 1. Structure of 5-hydroxymethylfurfural (HMF).

The catalytic oxidation of HMF produces 2,5-furandicarboxylic acid (FDCA), a material that can

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substitute the terephthalic acid (TA) in PET production or isophthalic acids in the manufacture of polyamides, polyesters and polyurethanes. The replacement of TA by FDCA constitutes an important step for sustainable processes development, thus FDCA production could represent a huge market. Nowadays polyurethanes using FDCA are already manufactured industrially for several applications.[1,14-16]

The synthesis of HMF, shown in Scheme 1, comprises many problems, especially those associated with the formation of byproducts through parallel reactions. The formation of secondary products as levulinic acid (LA) and formic acid (FA) influence the overall efficiency of the process, as well as formation of humins polymers which is the main cause of low HMF yields reported in most of studies available in this area.[11,17,18]

HMF produced with low yield and the high cost of industrial production are the factors that limit its availability. Some processes described in the literature produce HMF using acid catalysts for the conversion of fructose as substrate. However, the disadvantage in the use of these catalysts is that secondary reactions usually occur, burdening the process by the loss of material and the necessity of purifying the product. Moreover, HMF decomposes under acidic conditions in water.[19]

When using glucose as substrate, the situation is more critical due to the low HMF yield and the production of larger amounts of byproducts. Using glucose implies the isomerization into fructose by selective methods, leading to an increase in yield of the desired final product.[18]

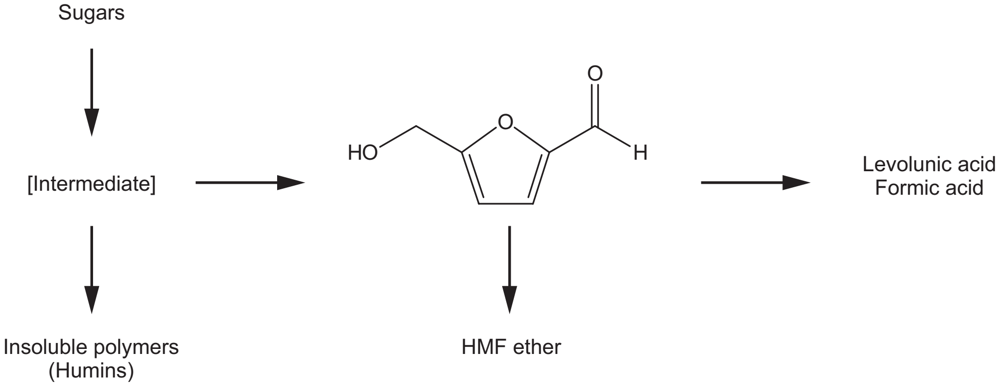
Different catalysts are employed for the synthesis of HMF, such as, ion exchange resins,[20-22] minerals and organic acids,[23-25] zeolites[6,26] and oxides.[27] These catalytic systems, besides producing HMF with low yields and forming byproducts, high temperatures and longer reaction times are usually required.[28]

Solid acid catalysts such as $SO_4^{2-}/ZrO_2\text{-}Al_2O_3$ present strong acidity and were used in the conversion of glucose and fructose to HMF yielding 47.6% and 68.2%, respectively in 4 h at 130 ºC. Nb_2O_5 catalyst (calcined at 400 ºC) was effective for the production of HMF due to its Lewis acid sites. This catalyst showed a total fructose conversion with 86.2% HMF yield (2 h reaction at 120 ºC).[27,29]

Qi *et al.*[20] studied the catalytic dehydration of fructose into HMF using microwave heating and a solvent media composed by acetone-water, the catalyst being a strong acid cation exchange resin (Dowex 50wx8-100) that is insoluble in water. Yields of 73.4% for 5-HMF and a conversion of 94% at 150 ºC were obtained. The resin showed a good stability at high temperatures enabling its reuse 5 times without observing catalytic activity decrease.

An efficient strategy for the direct production of HMF from glucose and cellulose (from ligninocellulose) was proposed using ionic liquids (ILs) based in imidazolium in the presence of $CrCl_3$ by microwave radiations, yields behind 60-90% were obtained. This reaction was considered a significant advance in the use of ligninocellulose for the production of carbohydrates via a green process.[30] The use ILs, besides leading to satisfactory results, provides an environmental alternative process where volatile organic solvents are substituted representing an attracted interest in different areas.[31]

Hu *et al.* proposed a mechanism employing $SnCl_4$ as catalyst for the glucose to HMF conversion in IL, 1-ethyl-3-methylimidazolium tetrafluoroborate ($EMI.BF_4$), where the Sn^{+4} center interacts with a acyclic and five or six member ring intermediates.[32] Zhao *et al.*[19] studied an alternative system, for which dehydration takes place more easily as the metallic halides catalyst ($CrCl_2$, $CrCl_3$, $FeCl_2$, $FeCl_3$, CuCl, $CuCl_2$, VCl_3, $MoCl_3$, $PdCl_2$, $PtCl_2$, $PtCl_4$ or $RuCl_3$) is dissolved in the IL. With this method HMF is obtained in high yields (63 to 83%) and secondary reactions are minimized (for example, levulinic acid formation is 0.08%). Among the catalysts tested the highest HMF yield was achieved using $CrCl_2$ which reaches values around 70%.[18]



Scheme 1. Synthesis of HMF (adapted from reference 17).

Sidhpuria *et al.* used nanoparticles immobilized in ILs in the dehydration of fructose obtaining 63% HMF yield.[32,33]

Another alternative is employing an IL as catalyst and solvent. For example, the use of 1-H-3-methylimidazolium chloride (HMI.Cl) in the dehydration of fructose produced HMF with a yield of 92% after 45 minutes of reaction time. When this catalytic system was used with sucrose, a rapid cleavage of sucrose into fructose and glucose was observed. The fructose was then transformed quickly into HMF with high yield and without the formation of byproducts and on the other hand at the same time, only 3% of the glucose was converted in HMF. The low transformation of glucose is due the necessity of its previous isomerization into fructose before the dehydration reaction to produce HMF.[34,35]

Furans produced from carbohydrates have high potential for the synthesis of monomers and then polymeric materials based on renewable sources. They can be obtained by synthesis which provides high yields and low production costs, but still should be investigated in order to optimize the process. A prime example is the use of ILs based on imidazolium in dehydration processes sugar (fructose or glucose) with satisfactory results related to the selectivity that can be improved in the case of the glucose and showed in this paper.[36,37]

This study reports results of HMF synthesis from dehydration of fructose or glucose using imidazolium based ILs as solvent and acid catalyst.

Experimental

Synthesis imidazolium based ionic liquids

1-buthyl-3-methylimidazolium chloride (C_4MI.Cl), 1-methyl-3-octhylimidazolium chloride (C_8MI.Cl), 1-decyl-3-methylimidazolium chloride (C_{10}MI.Cl), 1-dodecyl-3-methylimidazolium chloride (C_{12}MI.Cl) and 1-hexadecyl-3-methylimidazolium chloride (C_{16}MI.Cl) were prepared to methods previously described (Figure 2 (n = 4-16)).[38,39]

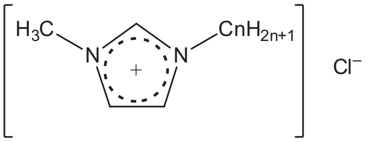


Figure 2. General structure of the salts studied, C_nMI.Cl (n = 4-16), based on the 1-alkyl-3-methylimidazolium cation.

Synthesis of HMF

All the dehydration reaction experiments were performed in a 50 mL flask equipped with magnetic stirrer. Were charged into the flask ionic liquid (4 g), fructose or glucose (0.4 g) and HCl acid (9%) (wt.%). The reaction system was placed in an oil bath adjusted to a range of 80 to 120 °C (according IL melting point), during 8 or 12 minutes.[40] After reaction time, the reaction mixture was analyzed by high performance liquid chromatography (HPLC) equipped with UV and refractive index detectors.

The HPLC measurements are conducted using a Shimadzu LC-20AD with UV and refractive index detector. The column Aminex HPX-87H (300 mm × 7.8 mm) is employed to separate the reaction mixture. General HPLC conditions for analysis of sugars conversion and HMF yield: refractive index detector; column temperature: 65 ºC; eluent: 0.6 mL min^{-1} H_2SO_4 pH 2; injection amount: 40 µL.[41] The amount of fructose, glucose and HMF was determined by using calibration curves. Analysis chromatogram of a standard solution containing glucose, fructose and HMF by HPLC are shown in Figure 3.

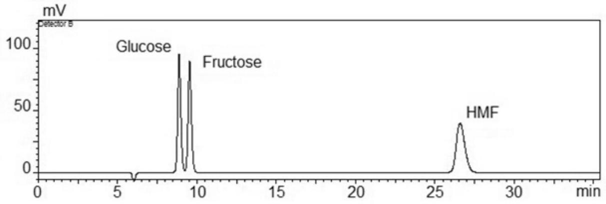


Figure 3. Example of a chromatogram showing separation of glucose, fructose and HMF.

The sugar conversion, HMF yield and HMF selectivity were defined as follows:

Sugar conversion (mol%)

$$C = \frac{[sugar]_i - [sugar]_f}{[sugar]_i} \times 100 \tag{1}$$

HMF Selectivity (mol%)

$$S = \frac{[HMF]_f}{[sugar]_i - [sugar]_f} \times 100 \tag{2}$$

HMF yield (mol%)

$$R = C \times S \tag{3}$$

Results and Discussion

Results of sugar conversion, HMF yield and selectivity using HCl acid and ILs (C_4MI.Cl, C_8MI.Cl, C_{10}MI.Cl, C_{12}MI.Cl or C_{16}MI.Cl) are reported Table 1. These data show that it is easier to convert fructose into HMF (yields above 85%) than glucose (yields about 30%). The acid dissolved in the ILs is very selective in HMF formation (> 85%). The same performances are not observed when tests are performed with glucose as substrate. The poor conversion of glucose is linked to the need to isomerize glucose to fructose for subsequent dehydration, as described in literature.[40,42]

Figure 4 and 5 repeat data of Table 1 evidencing the effect of the alkyl chain lengh of the ILs in dehydration of frutose and glucose respectively. The modification of ILs nature leads to considerable difference in selectivity and yield data for fructose reaction when the reaction time is 12 minutes, but not for 8 minutes reaction time (Figure 4). This results can indicate that with a higher reaction time decomposition of HMF occurs and ILs with a longer alkyl chain avoid the formation of byproducts (compare in Table 1, HMF selectivity in reaction 2 with reactions 6, 10 and 14). About the glucose reaction (Figure 5), conversion is observed only when C_{12}MI.Cl and C_{16}MI.Cl are employed and attains high value (ca. 80%), but the corresponding HMF selectivities and yields remain low (< 50%).

Relating to fructose as substrate, when using C_4MI.Cl at 80 °C, after 8 minutes, the yield is 91% (Table 1, reaction 1) and is reduced to 70% (Table 1, reaction 2) after 12 minutes of reaction time. This result indicates that the reaction is completed rapidly and that HMF decomposition occurs subsequently generating byproducts and decreasing the yield. In this IL (C_4MI.Cl), HMF is not formed by dehydration of glucose (Table 1, reactions 3 and 4). The same occurs when C_8MI.Cl (Table 1, reactions 7 and 8) and C_{10}MI.Cl (Table 1, reactions 11 and 12) are employed.

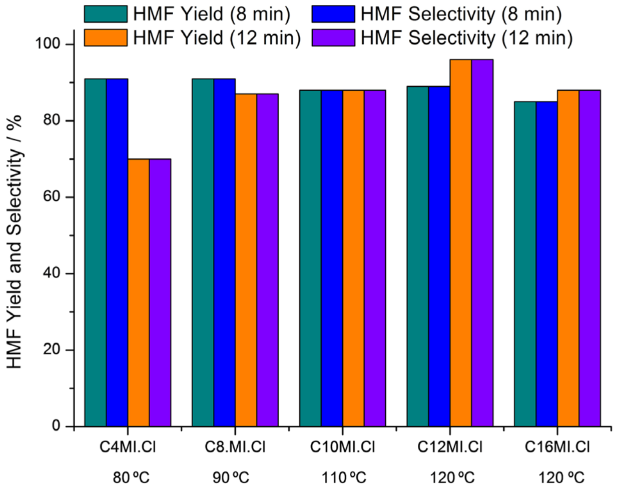


Figure 4. Effect of ILs in the dehydration of fructose.

Table 1. Dehydration of fructose and glucose in different ILs

Reaction[a]	Sugar	Ionic liquid	T / °C	t / min	Conv. / %	Yield HMF / %	Sel. HMF / %
1	Fructose	C_4MI.Cl	80	8	100	91	91
2	Fructose	C_4MI.Cl	80	12	100	70	70
3	Glucose	C_4MI.Cl	80	8	27	0	0
4	Glucose	C_4MI.Cl	80	12	35	0	0
5	Fructose	C_8MI.Cl	90	8	100	91	91
6	Fructose	C_8MI.Cl	90	12	100	87	87
7	Glucose	C_8MI.Cl	90	8	0	0	0
8	Glucose	C_8MI.Cl	90	12	0	0	0
9	Fructose	C_{10}MI.Cl	110	8	100	88	88
10	Fructose	C_{10}MI.Cl	110	12	100	88	88
11	Glucose	C_{10}MI.Cl	110	8	0	0	0
12	Glucose	C_{10}MI.Cl	110	12	0	0	0
13	Fructose	C_{12}MI.Cl	120	8	100	89	89
14	Fructose	C_{12}MI.Cl	120	12	100	96	96
15	Glucose	C_{12}MI.Cl	120	8	79	30	38
16	Glucose	C_{12}MI.Cl	120	12	75	34	45
17	Fructose	C_{16}MI.Cl	120	8	100	85	85
18	Fructose	C_{16}MI.Cl	120	12	100	88	88
19	Glucose	C_{16}MI.Cl	120	8	79	31	39
20	Glucose	C_{16}MI.Cl	120	12	81	31	38

[a] Reactions conditions: 4 g ionic liquid, 0.4 g sugar, 9% HCl (m/m).

When C_{12}MI.Cl is used in the fructose dehydration, (Table 1, reactions 13 and 14) the yield increases from 89% to 96% corresponding to 8 and 12 minutes respectively, indicating that after 8 minutes the reaction was not finished. For glucose (Table 1, reactions 15 and 16), the increase of the time reaction also leads to increasing the yield, but this one remains low (34%). This low yield obtained for glucose is not improved by the use of C_{16}MI.Cl (Table 1, reactions 19 and 20). These low yields related to glucose indicate that its isomerization in this environment does not occur, probably due to the stability of its ring structure.[33]

Results of reactions 17 and 18 in Table 1, where fructose and C_{16}MI.Cl are used, show that the change of the reaction time from 8 to 12 minutes does not affect the catalytic properties evidencing that no decomposition of HMF occurs as no byproducts are observed.

The set of these results show that, independently of IL used in this study, high HMF yields are obtained from dehydration of fructose in a relatively short reaction time (8 minutes). These results corroborate those described in the literature.[40,42]

Scheme 2 shows a proposal for mechanism dehydration of fructose catalyzed by acid such as the systems developed in this work. Antal[43] and Newth[44] suggest that the formation of HMF easily occurs from fructose by cyclic intermediate enol, 2,5-anhydro-D-mannose, formed in tautomerization step.[42] In this mechanism dehydration of fructose is initiated by protonation of the most basic hydroxyl group of the molecule that directly attached to the ring in a position alpha to the oxygen. The protonated form leading to spontaneous dehydration generates the intermediate enol that rearranges and then loses another water molecule, followed by deprotonation regenerating the catalyst and eliminating HMF.

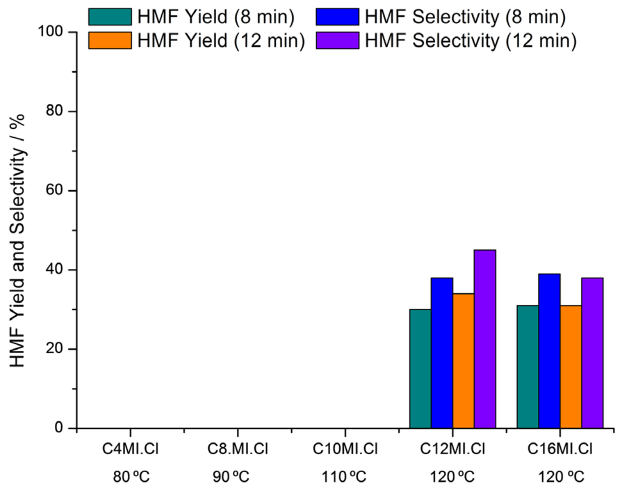
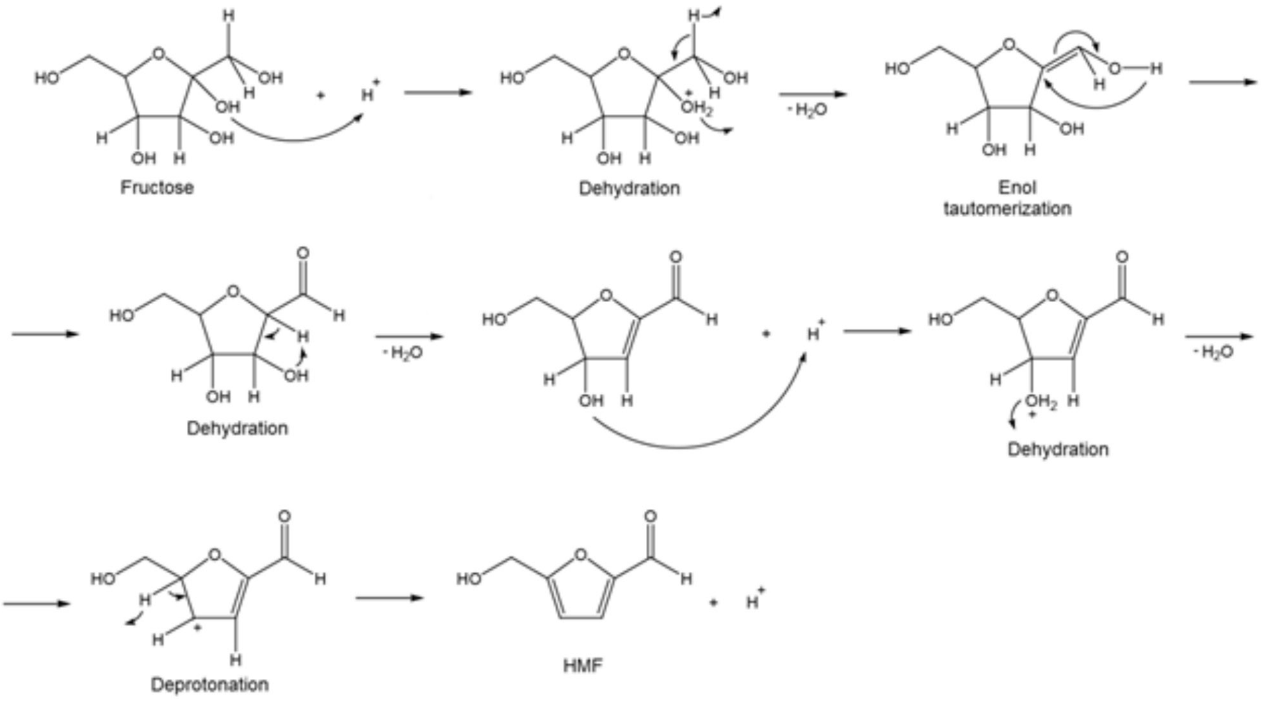


Figure 5. Effect of ILs in the dehydration of glucose.

It isn't surprising that the IL/HCl system catalyzed the dehydration of frutose due to the high acidity of the medium, as mechanism proposed, but also ensures the phase separation, in particular in the case of BMI.Cl IL, due to the lipophilic character coming from the chain length of the imidazolium ring. Balance of these different properties provides the best systems for avoiding decomposition of HMF from frutose and the conversion of glucose. In this



Scheme 2. Mechanism of fructose dehydration.

case ILs C_{12}MI.Cl and C_{16}MI.Cl correspond to the best systems.

Conclusions

This work shows that the catalyst system used, C_nMI.Cl (n = 4, 8, 10, 12 and 16) and HCl is efficient to produce HMF from fructose with yields higher than 90%. This did not occur when glucose is used as starting material, showing that this catalyst system has a low capacity to isomerize glucose to fructose, substance which would subsequently be dehydrated to obtain HMF. ILs C_{12}MI.Cl and C_{16}MI.Cl were the most effective for formation of HMF from glucose. Further studies of other catalytic systems are being conducted with the aim of improving the HMF yields when glucose is used as substrate.

Supplementary Information

Supplementary data are available free of charge at http://jbcs.sbq.org.br as PDF file.

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The authors dedicate this work to Roberto Fernando de Souza. Paulo L. A. Coutinho from Braskem expresses our feelings.

“Roberto distinguished himself as very enthusiastic researcher who excelled in formulating innovative ideas in academic environment and in partnership with the chemical industry. Throughout his career, as teacher, researcher and administrator he achieved outstanding results. He trained hundreds of professionals since the 1980s, introduced the topic of ionic liquids into Brazilian research and forwarded importantly the domain of catalysis and the area of green chemistry. He was an outstanding professional not only in academic administration but also in the interaction with the industry. His capability of understanding different points of view was one of his major strengths. Not only did we loose an unprecedented professional but more importantly an irreplaceable friend.”

References

1. Moreau, C.; Belgacem, M. N.; Gandini, A.; *Top. Catal.* **2004**, *27*, 11.
2. Pervaiz, M.; Correa, C. A.; *Polim.: Cienc. e Tecnol.* **2009**, *19*, E9.
3. Climent, M. J.; Corma, A.; Iborra, S.; *Green Chem.* **2014**, *16*, 516.
4. Verevkin, S. P.; Emel’yanenko, V. N.; Stepurko, E. N.; Ralys, R. V.; Zaitsau, D. H.; *Ind. Eng. Chem. Res.* **2009**, *48*, 10087.
5. Ilgen, F.; Ott, D.; Kralisch, D.; Reil, C.; Palmberger, A.; König, B.; *Green Chem.* **2009**, *11*, 1948.
6. Jadhav, H.; Taarning, E.; Pedersen, C. M.; Bols, M.; *Tetrahedron Lett.* **2012**, *53*, 983.
7. Jin, H.; Li, H.; Liu, X.; Ban, Y.; Peng, Y.; Jiao, W.; Yang, W.; *Chem. Eng. Sci.* DOI: 10.1016/j.ces.2014.07.017, in press.
8. Zhang, Z.; Wang, Q.; Xie, H.; Liu, W.; Zhao, Z.; *ChemSusChem* **2011**, *4*, 131.
9. Carniti, P.; Ferreira,V. F.; Rocha, D. R.; Silva, F. C.; *Quim. Nova* **2009**, *32*, 623.
10. Alonso, D. M.; Bond, J. Q.; Dumesic, J. A.; *Green Chem.* **2010**, *12*, 1493.
11. Carniti, P.; Gervasini, A.; Marzo, M.; *Catal. Commun.* **2011**, *12*, 1122.
12. Eerhart, A. J. J. E.; Huijgen, W. J. J.; Grisel, R. J. H.; van der Waal, J. C.; Jong, E.; Dias, A. S.; Faaij, A. P. C.; Patel, M. K.; *RSC Adv.* **2014**, *4*, 3536.
13. Shi, C.; Zhao,Y.; Xin, J.; Wang, J.; Lu, X.; Zhang, X.; Zhang, S.; *Chem. Commun.* **2012**, *48*, 4103.
14. Partenheimer, W.; Grushin,V. V.; *Adv. Synth. Catal.* **2001**, *343*, 102.
15. Gallezot, P.; *Chem. Soc. Rev.* **2012**, *41*, 1538.
16. Siankevich, S.; Savoglidis, G.; Fei, Z.; Laurenczy, G.; Alexander, D. T. L.; Yan, N.; Dyson, P. J.; *J. Catal.* **2014**, *315*, 67.
17. Lewkowski, J.; *Arkivoc* **2001**, *(i)*, 17.
18. Song, J.; Fan, H.; Ma, J.; Han, B.; *Green Chem.* **2013**, *15*, 2619.
19. Zhao, H.; Holladay, J. E.; Brown, H.; Zhang, Z. C.; *Science* **2007**, *316*, 1597.
20. Qi, X.; Watanabe, M.; Aida, T. M.; Smith, R. L.; *Green Chem.* **2008**, *10*, 799.
21. Li, Y.; Liu, H.; Song, C.; Gu, X.; H.; Li, W.; Zhu, S. Y.; Han, C.; *Bioresour. Technol.* **2013**, *133*, 347.
22. Qi, X.; Watanabe, M.; Aida, T. M.; Smith, R. L.; *Ind. Eng. Chem. Res.* **2008**, *47*, 9234.
23. Qi, X.; Watanabe, M.; Aida, T. M.; Smith, R. L.; *Green Chem.* **2009**, *11*, 1327.
24. Chheda, J. N.; Leshkov, Y. R.; Dumesic, J. A.; *Green Chem.* **2007**, *9*, 342.
25. Stahlberg, T.; Rodriguez, S. R.; Fristrup, P.; Riisager, A.; *Chem. Eur. J.* **2011**, *17*, 1456.
26. Lourvanij, K.; Rorrer, G. L.; *Ind. Eng. Chem. Res.* **1993**, *32*, 11.
27. Wang, F.; Wu, H. Z.; Liu, C. L.; Yang, R. Z.; Dong, W. S.; *Carbohydr. Res.* **2013**, *368*, 78.
28. Ray, D.; Mittal, N.; Chung, W. J.; *Carbohydr. Res.* **2011**, *346,* 2145.
29. Yan, H.; Yang, Y.; Tong, D.; Xiang, X.; Hu, C.; *Catal. Commun.* **2009**, *10*, 1558.

30. Li, C.; Zhang, Z.; Zhao, Z. K.; *Tetrahedron Lett.* **2009**, *50*, 5403.
31. Zhang, Y.; Du, H.; Qian, X.; Chen, E. Y. X.; *Energy Fuels* **2010**, *24*, 2410.
32. Dutta, S.; De, S.; Saha, B.; *Biomass Bioenergy* **2013**, *55*, 355.
33. Sidhpuria, K. B.; Silva, A. L. D.; Trindade, T.; Coutinho, J. A. P.; *Green Chem.* **2011**, *13*, 340.
34. Moreau, C.; Finiels, A.; Vanoye, L.; *J. Mol. Catal. A: Chem.* **2006**, *253*, 165.
35. Liu, W.; Holladay, J.; *Catal. Today* **2013**, *200*, 106.
36. Chheda, J. N.; Yuriy, R. L.; Dumesic, J. A.; *Green Chem.* **2007**, *9*, 342.
37. Tong, X.; Li, M.; Yan, N.; Ma,Y.; Dyson, P. J.; Li, Y.; *Catal. Today* **2011**, *175*, 524.
38. de Souza, R. F.; Dupont, J.; Consorti, C. S.; Suarez, P. A. Z.; *Org. Synth.* **2002**, *79*, 236.
39. Bradley, A. E.; Hardacre, C.; Holbrey, J. D.; Johnston, S.; McMath, S. E. J.; Nieuwenhuyzen, M.; *Chem. Mater.* **2002**, *14*, 629.
40. Li, C.; Zhao, Z. K.; Wang, A.; Zheng, M.; Zhang, T.; *Carbohydr. Res.* **2010**, *345*, 1846.
41. Lemos, G. S.; Santos, J. S.; Santos, M. L. P.; *Quim. Nova* **2010**, *33*, 1682.
42. Tong, X.; Ma, Y.; Li, Y.; *Appl. Catal.* **2010**, *385*, 01.
43. Antal Jr., M. J.; Mok, W. S. L.; Richards, G. N.; *Carbohydr. Res.* **1990**, *199*, 111.
44. Newth, F. H.; *Adv. Carbohydr. Chem.* **1951**, *6*, 83; Li, C.; Zhao, Z. K.; Wang, A.; Zheng, M.; Zhang, T.; *Carbohydr. Res.* **2010**, *345*, 1846.

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