Selective Oxidation of 5-Hydroxymethylfurfural to 2,5-Diformylfuran by Polymer-Supported IBX Amide

Hyo-Jin Yoon,[a] Jung-Woo Choi,[a] Hyung-Seok Jang,[a] Jin Ku Cho,[b] Jang-Woong Byun,[c] Woo-Jae Chung,[a]
Sang-Myung Lee,[a] Yoon-Sik Lee*[a]

[a] School of Chemical and Biological Engineering, Seoul National University, Seoul 151-744, Korea
Fax +82(2)8769625; E-mail: yslee@snu.ac.kr

[b] Green Process R&D Department, Korea Institute of Industrial Technology, Cheonan, 331-825, Korea

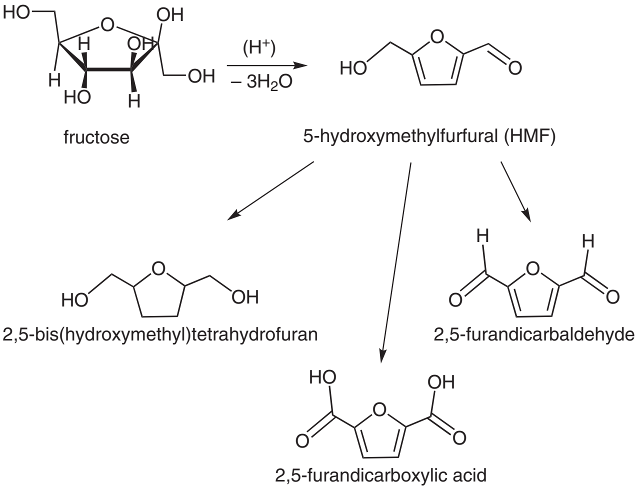
[c] BeadTech Inc, Institute for Chemical Processes, Seoul National University, Seoul 151-744, Korea

Received 12 October 2010

Abstract: 5-Hydroxymethyl-2-furfural (HMF) was selectively converted to 2,5-diformylfuran (DFF) under mild conditions by polymer-supported IBX amide reagent, thus providing a new platform for the production of highly valuable chemicals from biomass.

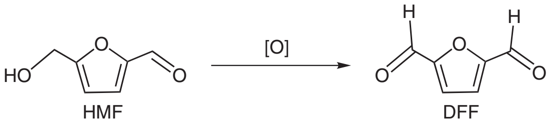
Key words: 2,5-diformylfuran (DFF), heterogeneous reagents, oxidation, polymer-supported IBX

Carbohydrates are currently focused as promising alternative feedstock for various commodity chemicals[1] due to their abundance and ability to remediate carbon dioxide.[2] They can be transformed into valuable products such as plastics, fine chemicals, and fuels.[3] Among them, 5-hydroxymethyl-2-furfural (HMF) is known as a platform intermediate that affords a variety of fine chemicals and fuels (Scheme 1).[4]



Scheme 1 Dehydration of fructose to HMF and variable products

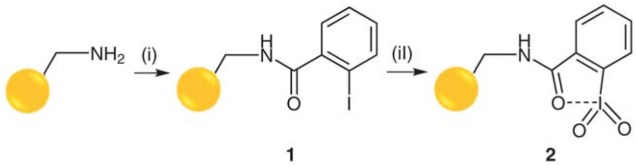
In terms of application, 2,5-diformylfuran (DFF), obtained by the selective oxidation of HMF, is a versatile chemical that acts as a monomer in the synthesis of furan-containing polymers,[5] macrocyclic ligand,[6] precursor for organic metals,[7] starting material for the synthesis of pharmaceuticals and antifungal agents,[8] and cross-linking agent of poly(vinyl alcohol) for battery separations.[9] Additionally, there have been a number of reports describing various oxidants and catalysts for the selective oxidation of HMF to DFF (Scheme 2).[10]



Scheme 2 Oxidation from HMF to DFF

However, most of these reports are accompanied by an elaborate purification step and/or use of toxic metal catalyst(s), which can be obstacles to mass production. Here, we report a facile and practical synthetic method for the selective oxidation of HMF using a heterogeneous oxidant. Furthermore, direct conversion from carbohydrate (fructose) to DFF is also described.

Hypervalent iodine reagent, IBX (*o*-iodobenzoic acid), is a useful oxidizing agent due to its high efficiency, availability, mild reaction conditions, and stability in moisture and air.[11] We recently developed a polymer-supported IBX ester and amide reagent and applied it to a wide range of oxidative chemical transformations. The polymer-supported IBX amide reagent exhibited fast and efficient oxidative activities toward a series of alcohols under mild conditions. The oxidation of the primary alcohol like benzyl alcohol derivatives resulted in nearly complete conversion after only 1 hour.[12] Also, polymer-supported IBX amide reagent can be readily separated from the reaction mixture by simple filtration to yield the corresponding oxidative product in high purity and overcome solubility problems of traditional IBX reagent. In addition, polymer-supported IBX amide reagent can be practically reused after recovery and regeneration, which is an attractive point for industrial applications.



Scheme 3 Preparation of polymer-supported IBX amide reagent[14]

SYNLETT 2011, No. 2, pp 0165–0168
Advanced online publication: 23.12.2010
DOI: 10.1055/s-0030-1259284; Art ID: U09010ST

In order to find the optimum conditions for the selective oxidation of HMF to DFF, we initially screened various solvents including dimethylformamide (DMF), dimethylacetamide (DMA), dimethylsufoxide (DMSO), *N*-methyl-2-pyrrolidone (NMP), acetone, acetonitile, chloroform, dichloromethane, and 1,2-dichloroethane (1,2-DCE). In a typical procedure, the reaction was carried out by adding polymer-supported IBX amide (2 equiv) and HMF (0.1 mmol) to 1 mL of each solvent with shaking at room temperature for 2 hours. The selectivity for DFF over HMF was high for all solvents (over 98%), but interestingly solvent polarity had a crucial effect on the conversion rate of HMF. Nonpolar solvent such as chloroform showed the highest oxidation performance (87% of conversion in 2 h), even though the solubility of HMF was very poor. Meanwhile, HMF was slowly converted to DFF by polar solvent at room temperature (Table 1).

Table 1 Investigation of Solvent Conditions for Selective Oxidation of HMF to DFF by Polymer-Supported IBX Amide[a]

Entry	Solvent	Conversion (%)	Selectivity (%)
1	DMA	8	100
2	DMF	9	99
3	NMP	3	98
4	acetone	14	99
5	DMSO	67	96
6	MeCN	25	100
7	$CHCl_3$	87	100
8	CH_2Cl_2	36	100
9	1,2-DCE	44	99

[a] Conversion and selectivity were determined by GC-MS analysis.

To minimize the amount of polymer-supported IBX amide used in the oxidation, DFF yield was measured after the designated time (3 h) using the ratio of oxidant (polymer-supported IBX amide)/substrate (HMF). The results show that 2 equivalents of oxidant were sufficient for the oxidation (Figure 1).

Next, the time course of the selective oxidation of HMF to DFF by polymer-supported IBX amide was evaluated. A mixture of HMF and polymer-supported IBX amide (2 equiv of HMF) in chloroform was stirred at room temperature, after which an aliquot of sample was analyzed by GC-MS at intervals. At the beginning of the reaction, oxidation occurred at a rapid rate but then lagged after 30 minutes as the concentration of HMF was decreased. Nevertheless, HMF was completely oxidized to DFF within 3 hours (Figure 2).

A reuse test of polymer-supported IBX amide was also performed. Regenerated polymer-supported IBX[15] can be reused at least five times without any loss in efficiency to produce DFF without side products (Figure 3).

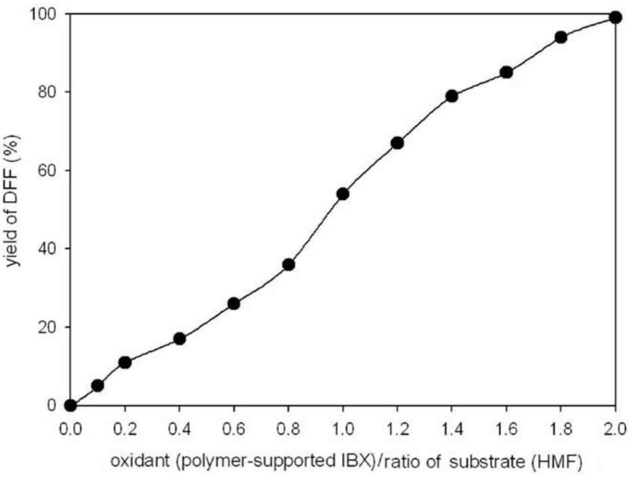


Figure 1 Evaluation of minimal amounts of polymer-supported IBX amide reagent for complete oxidation of HMF to DFF

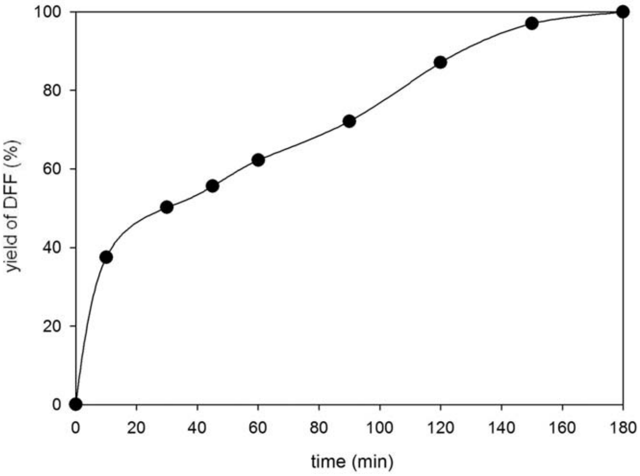


Figure 2 Time course for selective oxidation of HMF to DFF by polymer-supported IBX amide

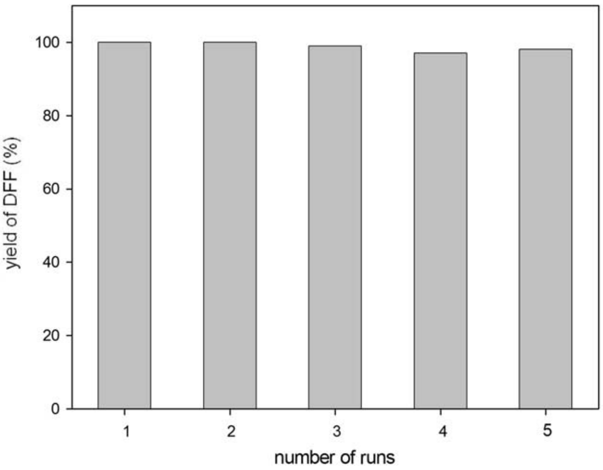
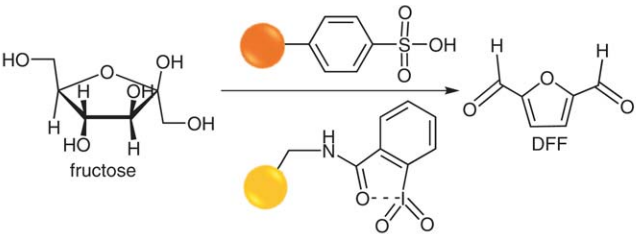


Figure 3 Yields of DFF produced by regenerated polymer-supported IBX amide reagent

Furthermore, direct conversion of fructose to DFF was performed.[16]



Scheme 4 Direct conversion of fructose to DFF under heterogeneous conditions in an one-pot reaction

Acid-catalyzed dehydration of fructose followed by subsequent oxidation of HMF was performed in a one-pot reaction. It is well known that HMF can be produced with high yield in the presence of DMSO and Brønsted acid. However, due to the high solubility of HMF and high boiling point of DMSO, isolation of HMF still remains to be addressed. Therefore, direct production of DFF from fructose without isolation of HMF would be helpful in developing an industrial process (Scheme 4).

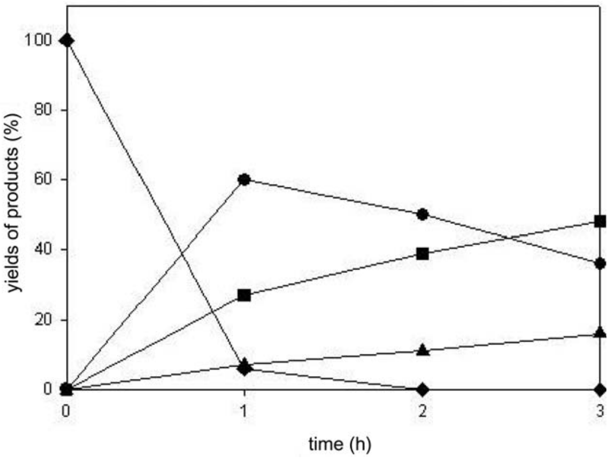


Figure 4 Conversion of fructose (substrate, diamond) along with the production of HMF (circle), DFF (square) and unknown chemicals (triangle) in a one-pot reaction in the presence of Amberlist 15® resin and polymer-supported IBX amide reagent (DMSO, 100 °C)

Fructose was converted with approximately 95% yield to HMF (60%) and DFF (27%) within 1 hour (Figure 4). As the reaction proceeded, HMF was gradually consumed while DFF was produced. After 3 hours, 36% of HMF remained with the yield of DFF reaching 48%. However, unknown chemicals including two main byproducts, AMF (5-acetoxymethyl-2-furaldehyde) and OBMF {5,5′-[oxybis(methylene)-bis-2-furaldehyde]}, were also increased in amount as reaction time was prolonged.[17]

In conclusion, we have described the first application of a recyclable polymer-supported IBX amide reagent for the highly-selective oxidation of HMF to DFF under mild conditions. Moreover, we showed that readily-prepared, polymer-supported IBX amide reagent with solid-acid catalyst was suitable for the direct conversion of fructose to DFF. We expect that our efforts would be helpful for the development of other processes related to biomass-derived chemical production.

Acknowledgment

This work has been supported by the Seoul Fellowship and the WCU (World Class University) program through the Korea Science and Engineering Foundation funded by the Ministry of Education, Science and Technology (grant number R32-2008-000-10213-0).

References and Notes

(1) (a) Bridgwater, A. V. *Chem. Eng. J.* **2003**, *91*, 87.
(b) Corma, A.; Iborra, S.; Velty, A. *Chem. Rev.* **2007**, *107*, 2411.

(2) (a) Werpy, T.; Petersen, G.; Aden, A.; Bozell, J.; Holladay, J.; White, J.; Manheim, A.; Elliot, D.; Lasure, L.; Jones, S.; Gerber, M.; Ibsen, K.; Lumberg, L.; Kelley, S. *Top Value Added Chemicals from Biomass,* In *Results of Screening for Potential Candidates from Sugars and Synthesis Gas*, Vol. 1; U.S. Department of Energy (DOE): Oak Ridge, TN, **2004**. (b) Chheda, J. N.; Huber, G. W.; Dumesic, J. A. *Angew. Chem. Int. Ed.* **2007**, *46*, 7164.

(3) Kunkes, E. L.; Simonetti, D. A.; West, R. M.; Serrano-Ruiz, J. C.; Gärtner, C.; Dumesic, J. A. *Science* **2008**, *322*, 417.

(4) (a) Lewkowski, J. *ARKIVOC* **2001**, *(i)*, 17.
(b) Lichtenthaler, F. W. *Acc. Chem. Res.* **2002**, *35*, 728.
(c) Ribeiro, M. L.; Schuchardt, U. *Catal. Commun.* **2003**, *4*, 83.

(5) (a) Gandini, A.; Belgacem, N. M. *Polym. Int.* **1998**, *47*, 267.
(b) Gandini, A.; Belgacem, N. M. *Prog. Polym. Sci.* **1997**, *22*, 1203.

(6) Richter, D. T.; Lash, T. D. *Tetrahedron Lett.* **1999**, *40*, 6735.

(7) (a) Takimiya, K.; Otsubo, T.; Ogura, F.; Ashitaka, H.; Morita, K.; Suehiro, T. *Chem. Lett.* **1994**, *23*, 255.
(b) Adams, H.; Bastida, R.; de Blas, A.; Carnota, M.; Fenton, D. E.; Macías, A.; Rodriguez, A.; Rodriguez-Blas, T. *Polyhedron* **1997**, *16*, 567.

(8) (a) Del Poeta, M.; Schell, W. A.; Dykstra, C. C.; Jones, S.; Tidwell, R. R.; Czarny, A.; Bajic, M.; Kumar, A.; Boykin, D.; Perfect, J. R. *Antimicrob. Agents Chemother.* **1998**, *42*, 2495. (b) Hopkins, K. T.; Wilson, W. D.; Bendan, B. C.; McCurdy, D. R.; Hall, J. E.; Tidwell, R. R.; Kumar, A.; Bajic, M.; Boykin, D. W. *J. Med. Chem.* **1998**, *41*, 3872.

(9) (a) Sheibley, D. W.; Manzo, M. A.; Gonzalez-Sanabria, O. D. *J. Electrochem. Soc.* **1983**, *130*, 255. (b) Daub, J.; Salbeck, J.; Knöchel, T.; Fischer, C.; Kunkely, H.; Rapp, K. M. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1494.

(10) (a) Cottier, L.; Descotes, G.; Lewkowski, J. *Synth. Commun.* **1994**, *24*, 939. (b) Partenheimer, W.; Grushin, V. V. *Adv. Synth. Catal.* **2001**, *343*, 102. (c) Grushin, V.; Partenheimer, W.; Manzer, L. E. US 2003/0055271, **2003**. (d) Halliday, G. A.; Young, R. J. Jr.; Grushin, V. V. *Org. Lett.* **2003**, *5*, 2003. (e) Carlini, C.; Patrono, P.; Galletti, A. M. R.; Sbrana, G.; Zima, V. *Appl. Catal., A* **2005**, *289*, 197.
(f) Amarasekara, A. S.; Green, D.; McMillan, E. *Catal. Commun.* **2008**, *9*, 286. (g) Navarro, O. C.; Canos, A. C.; Chornet, S. I. *Top. Catal.* **2009**, *52*, 304.

(11) (a) Wirth, T. *Angew. Chem. Int. Ed.* **2005**, *44*, 3656. (b) Ladziata, U.; Zhdankin, V. V. *ARKIVOC* **2006**, *(ix)*, 26. (c) Stang, P. J. *J. Org. Chem.* **2003**, *68*, 2997. (d) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523. (e) Varvoglis, A.; Meth-Cohn, O.; Kirschning, A.; Rees, C. *Hypervalent Iodine in Organic Synthesis*; Academic Press: London, **1996**.

(12) (a) Chung, W.; Kim, D.; Lee, Y. *Tetrahedron Lett.* **2003**, *44*, 9251. (b) Kim, D.; Chung, W.; Lee, Y. *Synlett* **2005**, 279. (c) Chung, W.; Kim, D.; Lee, Y. *Synlett* **2005**, 2175. (d) Jang, H.; Chung, W.; Lee, Y. *Tetrahedron Lett.* **2007**, *48*, 3731. (e) Lei, Z.; Denecker, C.; Jegasothy, S.; Sherrington, D. C.; Slater, N. K. H.; Sutherland, A. J. *Tetrahedron Lett.* **2003**, *44*, 1635. (f) Mülbaier, M.; Giannis, A. *Angew. Chem. Int. Ed.* **2001**, *40*, 4393. (g) Sorg, G.; Mengel, A.; Jung, G.; Rademann, J. *Angew. Chem. Int. Ed.* **2001**, *40*, 4395.

(13) Trost, B. M.; Braslau, R. *J. Org. Chem.* **1988**, *53*, 532.

(14) **Synthesis of Polymer-Supported IBX Amide Reagent**
Polymer-supported IBX amide reagent was prepared from aminomethyl polystyrene resin (AM PS, 2.1 mmol of NH_2/g, Beadtech Inc.). After AM PS resin was pre-swollen with DMF at r.t. for 1 h, 2-iodobenzoic acid was coupled to the resin using DIPCDI/HOBt (3 equiv, each) at r.t. for 4 h to produce 2-iodobenzamide resin (**1**, Scheme 3). The resin was then oxidized by tetrabutylammonium oxone (5 equiv) with methylsulfonic acid in CH_2Cl_2 for 12 h.[13] The loading level of polymer-supported oxidants was determined to be 1.02 mmol/g by methoxybenzyl alcohol oxidation method.[12]

(15) **Reusability Test of Polymer-Supported IBX Amide Reagent**
Upon completion of oxidation, DFF was extracted with CH_2Cl_2 and the remaining polymer-supported IBA (iodosobenzoic acid, reduced form of IBX) amide was separated by simple filtration. The filtered polymer-supported IBA was easily regenerated after treatment with tetrabutylammonium oxone (5 equiv) and methanesulfonic acid for 12 h as previously reported.[12]

(16) **Direct Production of DFF from Fructose**
In the one-pot reaction, Amberlist 15® resin (100 mg, purchased from Aldrich) as a solid-acid catalyst along with polymer-supported IBX amide reagent (100 mg) as an oxidant reagent were reacted together with fructose (1 mmol) under DMSO at 100 °C.

(17) **Analysis of Products from Direct Conversion from Fructose**
Direct conversion of fructose to DFF was analyzed using HPLC equipped with a refractive index detector. The column oven temperature was 30 °C, and mobile phase was a 25% MeCN aq solution applied at a flow rate of 1 mL/min. The amounts of HMF and DFF in the reaction mixture were also analyzed by HPLC with a UV detector, and the yields were calculated by GC-MS analysis. From this experiment, we identified two main byproducts as AMF (5-acetoxymethyl-2-furaldehyde, MS: $m/z = 168.15$) and OBMF {5,5′-[oxybis(methylene)-bis-2-furaldehyde], MS: $m/z = 234.05$}.