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Highly Efficient Aqueous Oxidation of Furfural to Succinic Acid Using Reusable Heterogeneous Acid Catalyst with Hydrogen Peroxide

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Green oxidation of inedible biomass-based 2-furaldehyde (furfural) to succinic acid (SA), one of the most important building blocks, was successfully achieved using Amberlyst-15 as a reusable solid acid catalyst in water at 353 K in the presence of hydrogen peroxide (H_2O_2).

Recently, the use of biomass to produce transportation fuels and other value-added chemicals has been focused on strongly both politically and technically. Biomass, an inexpensive, renewable, and abundant source of carbon, has the potential to serve as a sustainable source of energy for our industrialized society.[1] The utilization of renewable sources is a key factor for reducing energy use and synthesis of chemicals in an environmentally benign manner. The heterogeneous catalysts have several intrinsic advantages over their homogeneous counterparts: e.g. ease of product separation and catalyst reuse, bifunctional phenomena involving reactant activation and spillover between support and active phases, and process advantages through reactor operation in continuous flow versus batch configuration.[2]

Furan derivatives such as 5-hydroxymethylfurfural (HMF) and furfural, obtained by the acid-catalyzed dehydration of carbohydrates, have been described as key substances that bridge carbohydrate chemistry and petroleum-based industrial chemistry because of the wide range of chemical intermediates and end products that can be produced from these compounds.[3] One such compound of immense importance is SA which is used as a building block[4] for fuel additives,[5] food, cosmetic, pharma,[6] biopolymers, polyesters,[7] solvents,[8] polyurethane,[9] plasticizers,[10] and fine chemicals.[11]

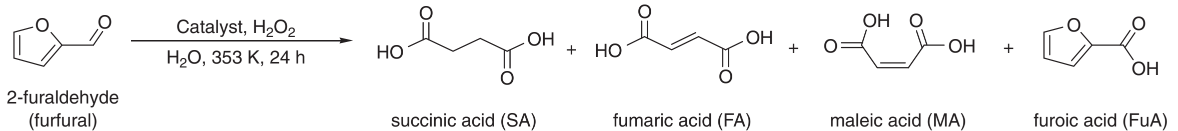
In plants and animals, SA is formed in the citric acid cycle.[12] Production of SA through the fermentation of glucose, fructose, lactose, maltose, mannitol, mannose, sucrose, xylose, and cellobiose by *A. succinogenes* has been known.[13] Studies on the production of SA from maleic acid by hydrogenation using Pd/C,[14] Zn/Hg,[15] and H_3PO_2[16] have been reported earlier. Other studies demonstrated that electrolytic reduction of aqueous or aqueous–alcoholic sulfuric acid, benzenesulfonic acid, or hydrochloric acid media,[17] spongy nickel,[18] lead,[19] and TiO_2 cathodes[20] produces SA in moderate yield. Ishikawa and Kurusu have patented a vapor-phase catalytic process in which 2-butene is oxidized, followed by a hydrogenation step to SA in good yield.[21] The oxidation of furfural to SA using sodium molybdate,[22] palladium(II),[23] H_2SO_4,[24] and $Hg(NO_3)_2$,[25] was also examined. Interestingly, Tachibana et al. have studied a two-step generation of SA from furfural using sodium chlorate and vanadium pentoxide in water at 368 K followed by the reduction of the product by Pd/C in an autoclave (433 K, 13 MPa) to afford SA in 46.6% overall yield.[8,26] Although industrialized methods[27] have been proposed in good yield, their practicability is limited by several factors: the requirement of a supporting electrolyte in the electrochemical cell, need for costly and hazardous reagents, and separation of electrolyte and catalyst from the reaction mixture or product.

Herein, we report a simple and an environmentally friendly strategy for the production of SA from furfural using reusable heterogeneous acid catalysts with hydrogen peroxide. Amberlyst-15, an efficient acid catalyst,[28] was found to exhibit a remarkable catalytic activity for SA synthesis via the oxidation of furfural in aqueous solution at 353 K.

Table 1 shows the results of the furfural oxidation in water using various well-established heterogeneous and homogeneous acid catalysts to compare their efficiencies for the oxidation reaction of furfural. Amberlyst-15, a macroreticular polystyrene-based ion-exchange resin with strongly acidic sulfonic groups,[29] was found to display the highest activity for oxidation of furfural into SA (Entry 1) among all the solid acid catalysts. Fumaric acid (FA), maleic acid (MA), furoic acid (FuA), and formic acid were detected as by-products. Nafion catalysts exhibited moderate selectivities (Entries 2 and 3) whereas other solid acid catalysts had low selectivities (Entries 4–7). Among the homogeneous acid catalysts (Entries 8–11), *p*-toluenesulfonic acid (*p*-TsOH) exhibited good catalytic activity. Besides, the maximum yield of FuA (18.2%) from furfural was obtained when H_2O_2 was used without Amberlyst-15 (blank, Entry 12) whereas no identified products by HPLC was observed using Amberlyst-15 alone (Entry 13) or blank (Entry 14). It seems that some furfural decomposes and/or polymerizes under the reaction conditions, leading to decrease the carbon balance in all cases. The combination of acid catalyst and H_2O_2 plays an important role for the selective oxidation of furfural to SA.

As the results show in Table 1, it was also confirmed that sulfonic acid group bearing catalyst had pronounced effect in conversion of furfural to SA, and not only the presence of $-SO_3H$ functionality but also the structure become a key factor. Amberlyst-15 and *p*-TsOH share a structural similarity that is both have tolyl groups which somehow enhance the catalytic activity. The moderate activity of Nafion NR50, Nafion SAC13, and H_2SO_4 could be attributed to the absence of tolyl moiety in the catalyst. At present, we wondered that the π–π interaction between a tolyl ring and a furan ring allowed a suitable conformation in the catalysis for the SA formation. Moreover, it can be observed that Nb_2O_5, sulfated zirconia (SO_4/ZrO_2), HCl, and acetic acid favored the formation of FA (Entries 4 and 7–9). The moderate acidic strength of Amberlyst-15 ($H_o = -2.2$) as compared to the high acidic strength of Nafion catalysts ($H_o < -12$) can account for the high selectivity for SA, since in presence of strong acid dehydration of carboxylic acid is favored as in the case of HCl (Entry 8).[28]

Table 1. Furfural oxidation in water using various acid catalysts in the presence of hydrogen peroxide[a]



Entry	Catalyst	Furfural conv./%[b]	SA selec./%	Yield/%[b]				Carbon mass balance/%[c]
				SA	FA	MA	FuA	
1	Amberlyst-15	>99	74.2	74.2	0.1	11.0	1.9	70.1
2	Nafion NR50	>99	41.2	40.8	0.8	11.3	2.1	44.4
3	Nafion SAC13	>99	28.5	28.2	0.5	9.5	1.6	32.2
4	Nb_2O_5	>99	24.6	24.4	4.5	4.6	0.0	26.8
5	ZSM-5[d]	>99	16.7	16.5	1.5	2.4	0.0	16.3
6	ZrO_2	>99	16.6	16.5	2.1	5.4	0.0	19.2
7	SO_4/ZrO_2	96.5	10.4	10.1	4.3	5.9	0.0	16.2
8	HCl[e]	>99	49.4	49.0	2.9	10.5	0.0	49.9
9	Acetic acid[e]	>99	26.0	25.7	27.6	2.2	0.0	44.4
10	H_2SO_4[e]	>99	44.9	44.9	0.3	5.9	0.0	40.9
11	*p*-TsOH[e]	>99	72.4	72.3	0.4	11.4	1.2	68.5
12	Blank	68.8	1.3	0.6	1.4	4.8	18.2	23.6
13[f]	Amberlyst-15	34.4	0.0	0.0	0.0	0.0	0.0	0
14[f]	Blank	22.5	0.0	0.0	0.0	0.0	0.0	0

[a]Reaction conditions: Furfural (1 mmol), H_2O_2 (4 mmol, determined by iodometry titration), H_2O (3 mL), catalyst (50 mg), 353 K, 24 h, 500 rpm. [b]Furfural conv. was calculated by $\{(\text{furfural}_{\text{input}} - \text{furfural}_{\text{remain}})/\text{furfural}_{\text{input}}\} \times 100$ where the product yield was $(\text{product}_{\text{detected}}/\text{furfural}_{\text{input}}) \times 100$ with the HPLC analysis. [c]Determined on the basis of obserbed SA, FA, MA, and FuA products. [d]$SiO_2/Al_2O_3 = 90$, JRC-Z-5-90H(1). [e]1 mmol. [f]Without H_2O_2.

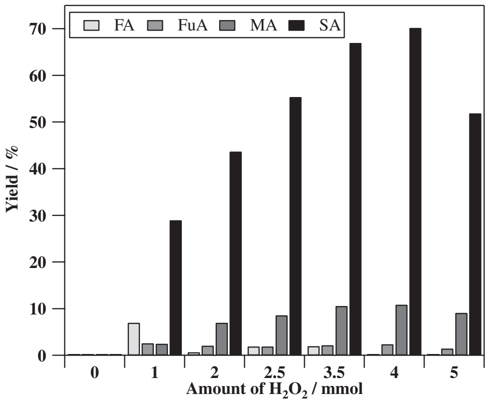


Figure 1. Effect of changing amount of H_2O_2 for oxidation of furfural using Amberlyst-15. Reaction conditions: Furfural (1 mmol), H_2O (3 mL), Amberlyst-15 (50 mg), 353 K, 24 h, 500 rpm.

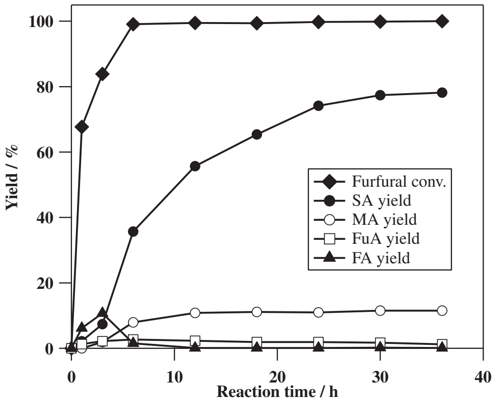


Figure 2. Time course of furfural oxidation into SA over Amberlyst-15. Reaction conditions: Furfural (1 mmol), Amberlyst-15 (50 mg), H_2O_2 (4 mmol, determined by iodometric titration), H_2O (3 mL), 353 K, 500 rpm.

To investigate the role of H_2O_2 in the presence of acid catalyst, the catalytic activities as a function of amount of H_2O_2 were plotted in Figure 1. Detailed information is provided in Table S1.[30] The amount of H_2O_2 strongly attributed to an increase of yield of SA in the presence of Amberlyst-15, maximum yield up to 4 mmol of oxidant after which the yield decreased sharply. The acid catalyst seems to enhance the efficiency of H_2O_2 dramatically, although the reaction using only acid catalyst exhibited no activity. The amount of H_2O_2 in the reaction mixture after the 24 h reaction was found to be 0.61 mmol in the case of 4 mmol H_2O_2 use, indicating approximately 85% H_2O_2 efficiency.[31]

The monitoring of the reaction profile confirmed the increase in furfural conversion and SA yield with increasing reaction time (Figure 2). The conversion of furfural was >99% after 6 h of the reaction progress. FA was formed in higher yields than SA in the initial stages of reaction; thereafter, the decrease of FA with increase of MA was observed. This tendency proposed that a low solubility of FA in water converts to a highly soluble MA in water via isomerization during the reaction. Interestingly, this isomerization seemed to be enhanced by the formed formic acid in the presence of Amberlyst-15 (Table S2).[30] The yield of SA showed a dramatic increase as the reaction progressed; however, it was almost constant after 30 h of the reaction. FuA, an oxidized form of furfural, was found to form in low yields under the reaction conditions. In addition, though furan-2(5*H*)-one was found to form in traces in the reaction mixture, no other intermediates were identified by HPLC.

Besides, an increase in reaction temperature to 353 K favors the formation of SA, whereas with further increase in temperature the yield decreases (Table S3).[30] In the case of higher temperatures, an unidentified peak at a retention time of 36.2 min appeared for the particular reaction, though which was not detected during the reaction under 353 K. It is known that Amberlyst-15 favors the cyclization of 1,4-dicarbonyl compounds to furan derivatives at higher temperature such as 393–396 K.[32] Therefore, the cyclization of SA and MA was not related to the reaction pathway. Furthermore, a control experiment with radical scavenger supported that the reaction does not proceed via radical pathway (Table S4).[30]

To unveil the reaction progress, two reaction pathways were proposed as shown in Schemes S1 and S2.[30] In Scheme S1[30] the furan ring is proposed to open up to undergo oxidation by H_2O_2 as demonstrated by Bunton.[33] Following the proposal by Kul'nevich et al.,[34] in Scheme S2,[30] the reaction was proposed to undergo Baeyer–Villiger oxidation to form SA via furan-2(3*H*)-one. Although reactions from intermediates such as 2-furanol formate and furan-2(3*H*)-one were hardly investigated owing to their undersupplies and difficult synthesis, the reaction of furan-2(5*H*)-one to MA was progressive in the same conditions (Table S5).[30] Moreover, it was also indicated that the formed FA and MA could not transfer to the SA under the reaction conditions (Tables S2 and S6).[30] The time course of NMR (Figures S1 and S2)[30] was helpful in establishing the fact that neither furan-2(5*H*)-one nor MA or FA was the intermediate in the synthesis of SA from furfural under the present condition.[30]

Subsequently, the reusability of Amberlyst-15 was investigated. Amberlyst-15 was simply reused by decantation, thorough washing with water at room temperature followed by drying in vacuum. Therefore, the SO_3H leaching from Amberlyst-15 scarcely occurred. It was found that the Amberlyst-15 was reproducible with a good yield of 68–74% for three runs (Figure S3).[30] Furthermore, the productivity of the reaction was confirmed by the large-scale reaction using 20 mmol furfural under the same reaction conditions (Table S7).[30] SA was obtained in 66.4% as an isolated yield (TON = 2.82) with almost complete conversion of furfural. ^{1}H NMR (400 MHz, D_2O, TMS) and ^{13}C NMR (400 MHz, D_2O, TMS) for the synthesized product clearly demonstrate the purity of the crystalline product (Figures S1 and S2).[30]

In conclusion, we have found that Amberlyst-15 is a highly effective heterogeneous catalyst for direct oxidation of inedible biomass-based 2-furaldehyde to succinic acid in good yields in aqueous media under mild reaction conditions, with the advantage of reusability of catalyst without significant loss of catalytic activity and selectivity. Although the detailed catalytic mechanism needs to be further studied precisely, the above-mentioned process promises to be a viable alternative to current synthesis of SA using microorganism since it has the advantages of easy purification and high yields of succinic acid.

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References and Notes

1 a) G. W. Huber, A. Corma, *Angew. Chem., Int. Ed.* **2007**, *46*, 7184. b) J. P. Holdren, *Science* **2007**, *315*, 737. c) N. S. Lewis, *Science* **2007**, *315*, 798. d) J. N. Chheda, G. W. Huber, J. A. Dumesic, *Angew. Chem., Int. Ed.* **2007**, *46*, 7164.

2 K. Wilson, J. H. Clark, *Pure Appl. Chem.* **2000**, *72*, 1313.

3 J. Jurczak, E. Kobrzycka, J. Raczko, *Pol. J. Chem.* **1999**, *73*, 29.

4 C. Delhomme, D. Weuster-Botz, F. E. Kühn, *Green Chem.* **2009**, *11*, 13.

5 a) L. Volkel, A. Lange, C. Lockemann, D. Posselt, U.S. Patent, US 2009/0235576 A1, **2009**. b) N. Nghiem, B. H. Davison, M. I. Donnelly, S.-P. Tsai, J. G. Frye, *Chemicals and Materials from Renewable Resources* in *ACS Symposium Series*, ed. by J. J. Bozell, American Chemical Society, Washington DC, **2001**, Vol. 784, pp. 160–173. doi:10.1021/bk-2001-0784.ch013. c) K.-L. Ring, T. Kaelin, M. Yoneyama, CEH Report: Tetrahydrofuran, SRI, Menlo Park, CA, **2001**.

6 a) M. K. Kumar, Y. P. Reddy, V. K. Kumar, C. Sowmya, A. M. Deshmukh, *Int. J. Pharm. Sci. Rev. Res.* **2010**, *3*, 142. b) L. Lachman, J. B. Schwartz, *Pharmaceutical Dosage Forms: Tablets*, Marcel Dekker, **1990**, p. 288.

7 a) N. R. Luman, T. Kim, M. W. Grinstaff, *Pure Appl. Chem.* **2004**, *76*, 1375. b) L. Sacan, A. Cirpan, P. Camurlu, L. Toppare, *Synth. Met.* **2006**, *156*, 190.

8 Y. Tachibana, T. Masuda, M. Funabashi, M. Kunioka, *Biomacromolecules* **2010**, *11*, 2760.

9 W. A. Carey, W. C. Ehrhardt, L. A. Perez, A. Solov, D. T. Freese, Eur. Patent, EP 0628539 B1, **1994**.

10 J. Mittal, R. B. Mathur, O. P. Bahl, M. Inagaki, *Carbon* **1998**, *36*, 893.

11 *Kirk-Othmer Encyclopedia of Chemical Technology*, 4th ed., ed. by H.-G. Mary, John Wiley & Sons, New York, **1997**, Vol. 22, p. 1074.

12 J. M. Berg, J. L. Tymoczko, L. Stryer, *Biochemistry*, 6th ed., Freeman, New York, **2006**.

13 M. J. Van der Werf, M. V. Guettler, M. K. Jain, J. G. Zeikus, *Arch. Microbiol.* **1997**, *167*, 332.

14 S. Yamada, H. Haramaki, S. Matsumoto, Y. Akazawa, Jpn Patent, JP 0931,011, **1997**.

15 T. V. Lysyak, I. S. Kolomnikov, Yu. Ya. Kharitinov, *Koord. Khim.* **1983**, *9*, 1000.

16 X. Wang, G. Yedi, *Chin. Chem. Lett.* **1993**, *4*, 407.

17 L. P. Kyrides, J. A. Bertsch, U.S. Patent, US 1 927 289, **1933**.

18 U. Pomilio, *Z Electrochem.* **1915**, *21*, 444.

19 J. F. Norris, E. O. Cummings, U.S. Patent, US 1 457 79 1, **1943**.

20 D. Vasudevan, *J. Appl. Electrochem.* **1995**, *25*, 176.

21 a) R. Ishikawa, A. Kurusu, Jpn Patent, JP 9 95,464, **1997**. b) J. H. Murib, C. E. Frank, U.S. Patent, US 3 923 881, **1975**.

22 E. P. Grunskaya, L. A. Badovskaya, V. V. Poskonin, Yu. F. Yakuba, *Chem. Heterocycl. Compd.* **1998**, *34*, 775.

23 V. I. Krupenskii, *Zh. Obshch. Khim.* **1996**, *66*, 1874.

24 M. Taniyama, *Toho Reiyon Kenkyu Hokoku* **1954**, *1*, 40.

25 V. I. Krupenskii, *Nauchn. Tr.-Leningr. Lesotekh. Akad. im. S. M. Kirova* **1973**, *158*, 68.

26 a) C. F. Cross, E. J. Bevan, J. F. Briggs, *Ber. Dtsch. Chem. Ges.* **1900**, *33*, 3132. b) H. F. McShane, Jr., W. W. Gilbert, U.S. Patent, US 2 772 291, **1956**.

27 B. Cornils, P. Lappe, *Dicarboxylic Acids, Aliphatic* in *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH Verlag GmbH & Co., KGaA, Weinheim, **2010**, p. 287. doi:10.1002/14356007.a08_523.pub2.

28 a) A. Takagaki, M. Ohara, S. Nishimura, K. Ebitani, *Chem. Commun.* **2009**, 6276. b) A. Takagaki, K. Ebitani, *Chem. Lett.* **2009**, *38*, 650. c) M. A. Harmer, Q. Sun, *Appl. Catal., A* **2001**, *221*, 45. d) S. A. Patwardhan, S. Dev, *Synthesis* **1974**, 348. e) V. I. Stenberg, G. F. Vesley, D. Kubik, *J. Org. Chem.* **1971**, *36*, 2550. f) G. M. Coppola, *Synthesis* **1984**, 1021.

29 R. Kunin, E. F. Meitzner, J. A. Oline, S. A. Fisher, N. Frisch, *Ind. Eng. Chem. Prod. Res. Dev.* **1962**, *1*, 140.

30 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

31 H_2O_2 labeled as 30% was used for the reaction; however the actual concentration was estimated as 25.7% by iodometric titration. The H_2O_2 efficiency was calculated with the formula described as $\{(H_2O_{2,\mathrm{input}} - H_2O_{2,\mathrm{remain}})/H_2O_{2,\mathrm{input}}\} \times 100$.

32 *Handbook of Reagents for Organic Synthesis: Reagents for High-Throughput Solid-Phase and Solution-Phase Organic Synthesis*, ed. by P. Wipf, John Wiley & Sons Ltd, England, **2005**, p. 242.

33 C. A. Bunton, *Nature* **1949**, *163*, 444, and references therein.

34 V. G. Kul'nevich, L. A. Bodovskaya, G. F. Muzychenko, *Khim. Geterotsikl. Soedin.* **1970**, 582.