

Metal-free mild oxidation of 5-hydroxymethylfurfural to 2,5-diformylfuran

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(Received 27 September 2013 • accepted 28 January 2014)

Abstract—The potential of 4-hydroxy-2,2,6,6-tetramethyl-piperidine-1-oxyl (4-hydroxy-TEMPO radical) as an oxidant with [bis(acetoxy)-iodo]benzene (BAIB) and acetic acid (CH₃COOH) as co-oxidants to convert 5-hydroxymethylfurfural (5-HMF) into 2,5-diformylfuran (2,5-DFF) was investigated. The effects of oxidant/acid dosages, choice of appropriate solvent, reaction temperature and time were determined to maximize the 2,5-DFF yield. Optimally, 66% 2,5-DFF yield was achieved in TEMPO/BAIB/CH₃COOH system at 30 °C after 45 min in ethyl acetate. The reaction system is environmentally benign (metal-free) and energy efficient (mild at short reaction period). With scarce reports on 2,5-DFF production, the developed system provides an alternative route for a better access and wider application of this important platform chemical.

Keywords: 2,5-Diformylfuran, 5-Hydroxymethylfurfural, Homogeneous, Oxidation, Radical, TEMPO

INTRODUCTION

5-Hydroxymethylfurfural (5-HMF) is a versatile bridge molecule for the production of important platform chemicals from biomass feedstocks [1,2]. 5-HMF can be produced from biomass-derived hexoses and can be further converted into a wide array of valuable furanic chemicals through various catalytic transformations [3-9]. An attractive 5-HMF derivative is 2,5-diformylfuran (2,5-DFF), an important dialdehyde precursor for various pharmaceutical products, fungicides, macrocyclic ligands and polymers [10-16]. 2,5-DFF is typically produced from the oxidation of the primary hydroxyl group of 5-HMF. However, improper control in reaction conditions and unsuitable choices of oxidants or catalysts could lead to non-selective oxidation of the hydroxyl and α,β -unsaturated aldehyde groups of 5-HMF. Formation of other 5-HMF oxidation products such as 5-hydroxymethylfuran-2-carboxylic acid (HMFA), 5-formyl-2-carboxylic acid (FFCA) and 2,5-furandicarboxylic acid (2,5-FDCA) could reduce the reaction selectivity towards 2,5-DFF production [4-6,17]. Furthermore, severe reaction conditions could result in the formation of side products from over-oxidation, decarbonylation and cross-polymerization of 5-HMF [18].

Selective oxidation reactions of 5-HMF to 2,5-DFF are continuously being developed with various approaches to minimize side product formation [19]. Recently, vanadium and noble metals like Au, Pt, Ru and complexes like metal/bromide (Co/Mn/Br) have been effectively applied as catalysts for the synthesis of 2,5-DFF and 2,5-FDCA [18,20-26]. Homogeneous oxidants such as Pb(OAc)₄-pyridine, pyridinium chlorochromate (PCC), K₂Cr₂O₇-DMSO, 2,2,6,6-tetramethylpiperidine-1-oxide (TEMPO) free radicals and NaOCl-Mn (III)-salen complex have also been used for competent synthe-

sis of 2,5-DFF [27-32]. But despite the acceptable 2,5-DFF yields, most of the reported systems are metal-based. These reactions often use nocuous solvents as well as require severe reaction conditions (i.e., high temperature and long reaction period); both features do not satisfy the current demands for green and energy-efficient technologies. In this regard, the use of metal-free organic catalysts or oxidants appears very interesting.

Among various homogeneous catalytic systems, TEMPO free radical derivatives are renowned oxidants with several applications in organic chemistry for the oxidation of primary and secondary alcohols, sulfides and organometallic compounds [33-36]. TEMPO-mediated oxidation of 5-HMF to furanaldehydes has been reported previously in the presence of hypochlorite as co-oxidants [29]. But hypochlorites result in the formation of toxic chlorinated side products [37]. Alternatively, hypervalent iodine compounds, with their affordability and non-toxicity, are popular secondary oxidants [38,39]. Their role in regenerating TEMPO in order to complete the catalytic cycle for alcohol oxidation has been demonstrated in several studies [40,41].

This work presents the production of 2,5 DFF from 5-HMF oxidation using 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (4-hydroxy-TEMPO) radical as a homogeneous oxidant with hypervalent iodine-based secondary oxidant [bis(acetoxy)-iodo]benzene (BAIB) [PhI(OAc)₂]. Reactions were intentionally performed in low boiling point solvents (with b.p. \leq 100 °C) for convenient and energy-efficient recovery of 2,5 DFF. Effects of reaction temperature, time, oxidant dosages and acid addition were examined to achieve acceptable 2,5-DFF yields.

MATERIALS AND METHODS

1. Reagents

4-Hydroxy-TEMPO (97%) and BAIB (98%) were obtained from Sigma-Aldrich (South Korea). Substrate 5-HMF (98%), product standard 2,5-DFF (>98%) were purchased from Acros Organics

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and Tokyo Chemicals (Japan), respectively. Solvents toluene, dichloromethane (DCM) and diethyl ether (Et₂O) were obtained from Dae Jung Chemicals (South Korea). Acetonitrile (ACN), ethyl acetate (EtOAc) and hexane were purchased from Fisher Scientific while CH₃COOH was from Acros Organics (Belgium). All chemicals were at least of reagent grade or better and were directly used without further purification. The reactions were performed in round bottom flasks heated in a temperature-controlled oil bath with magnetic stirring. Thin-layer chromatography (TLC) was performed on silica gel 60 F₂₅₄ plates (Merck). Acros silica gel (0.075-0.250 mm, 150 Å) was used for column chromatography.

2. General Procedure of Oxidation of 5-HMF

All reactions were carried out in closed reaction vessels. Reactants 5-HMF (1.0 mmol), 4-hydroxy-TEMPO (0-0.2 mmol), BAIB (0-2.0 mmol) and/or CH₃COOH (0-0.5 mmol) were stirred in an appropriate solvent (6 mL) at a controlled reaction temperature (25-120 °C) for a certain amount of time (0-48 h) to produce 2,5-DFF. Samples were collected periodically and the solvent was evaporated under reduced pressure. The dried reaction sample was analyzed by high performance liquid chromatography (HPLC) as detailed in the analytical methods section.

3. Analytical Methods

Production of 2,5-DFF was monitored using (Waters) HPLC, equipped with two 1525 pumps, a 2707 auto sampler, a 1500 column temperature controller and 2414 refractive index detector maintained at 40 °C using Biorad Aminex HPX-87H ion-exclusion column (300 × 7.8 mm). The column oven temperature was maintained at 60 °C, and the degassed and filtered 5 mM H₂SO₄ mobile phase was pumped at a flow rate of 0.6 mL/min. Substrate and product quantifications were calculated against standard curves. In a typical reaction, each dried sample (Section 2 of Materials and Methods) was diluted with a known volume of ultra pure deionized water and filtered through 0.2 μm Nylon syringe filter before HPLC analysis. All data were reported as average values of three trials.

4. 2,5-DFF Quantification

An aliquot from reaction mixture was diluted and shaken in 5 mL of deionized water. After the precipitates were allowed to settle, the supernatant was collected for HPLC analysis. 2,5-DFF concentrations (i.e., [DFF]) were used for yield calculations as shown in Eqs. (1) and (2). Here, M_{DFF} is the total mass of DFF formed in the reaction mixture, V is the mixture volume (5 mL), W_{RM} is the total mass of reaction mixture, W_{AL} is aliquot mass, M_{HMF} mass of 5-HMF in the reaction mixture and MW pertains to the molecular weights of 5-HMF (126.11 g/mole) and 2,5-DFF (124.09 g/mole).

$$M_{DFF}(\text{mg}) = \frac{[\text{DFF}] \times V \times W_{RM}}{W_{AL}} \quad (1)$$

$$\text{DFF yield (\%)} = \left(\frac{M_{DFF}}{M_{HMF}} \right) \left(\frac{MW_{HMF}}{MW_{DFF}} \right) \times 100 \quad (2)$$

5. Isolation and Purification of 2,5-DFF

To retrieve a purified 2,5-DFF product, the dried reaction sample (under reduced pressure) was passed through a chromatography column over silica gel using a gradient mixture of (4%-10%) EtOAc and hexane as eluent. Elution of 2,5-DFF was verified via TLC; a pale yellow crystalline product was isolated after the eluent was removed under reduced pressure. The dried crystalline solids

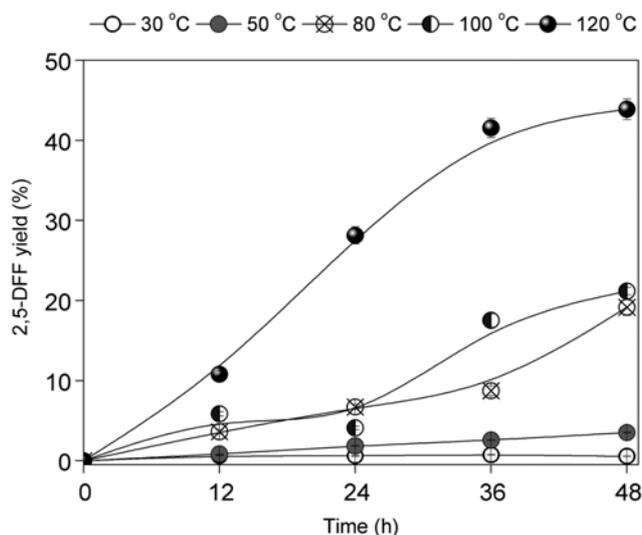


Fig. 1. Time profile of 2,5-DFF production from 5-HMF (1.0 mmol) oxidation by 4-hydroxy TEMPO (1.0 mmol) at different temperatures in toluene.

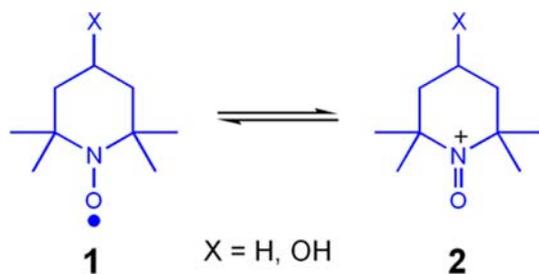
were washed with hexane and re-crystallized in EtOAc to obtain the white crystalline 2,5-DFF product of >99% purity (0.9884 g, isolated yield=50.2%, yield from HPLC=55.7%; melting point (mp) 108 °C, lit. mp 108-110 °C) [20]. Identification of the product 2,5-DFF was confirmed by elemental analysis and ¹H NMR on a Varian 400 MHz NMR spectrometer in deuterated chloroform (CDCl₃); results are provided as supplementary Fig. S1 and Table S1.

RESULTS AND DISCUSSION

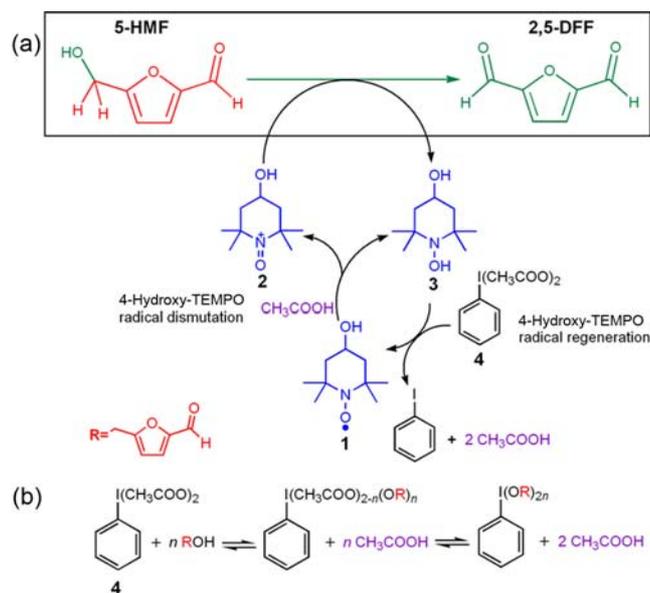
1. 5-HMF Oxidation by 4-Hydroxy-TEMPO

The potential of 4-hydroxy-TEMPO to oxidize 5-HMF into 2,5-DFF was initially determined by combining equimolar amounts of the reactants in toluene at different temperatures between 30 °C and 120 °C for 48 h (Fig. 1). At ≤50 °C, negligible (<5%) 2,5-DFF yields were obtained even after 48 h reaction. On the other hand, 2,5-DFF production eventually increased especially for reactions ≥80 °C. The highest 2,5-DFF yield of 44% was achieved after 48 h at 120 °C. Considering that solvents with low to moderate boiling points are preferred for an energy-efficient product recovery step (i.e., solvent evaporation), low temperature reactions involving volatile solvents would be more suitable. Thus, 5-HMF oxidation experiments were not performed at temperatures beyond 120 °C.

The observed yields at ≥80 °C after 48 h demonstrate the capability of 4-hydroxy-TEMPO to oxidize 5-HMF into 2,5-DFF (Supplementary Fig. S2A). However, the high temperature and long reaction time requirements indicate that 4-hydroxy-TEMPO is insufficient as a sole 5-HMF oxidant even when added at stoichiometric amount. Early reports identified that the oxoammonium salt (2) form of TEMPO radical is in fact the main oxidant in TEMPO-mediated oxidation of primary alcohols (Scheme 1) [33,40,42]. Oxoammonium salts (2) can be formed via dismutation of 4-hydroxy-TEMPO radical (1) upon addition of a (1) secondary oxidant and/or (2) an acid in the reaction [33,40]. Hence to improve the 2,5-DFF yields, effects of (1) BAIB and/or (2) CH₃COOH as co-oxidants were next investigated.



Scheme 1. Oxidation of TEMPO radical to oxoammonium salt.



Scheme 2. Possible reaction pathway for 4-hydroxy-TEMPO and BAIB catalyzed oxidation of 5-HMF to 2,5-DFF [40,41].

2. 5-HMF Oxidation by 4-Hydroxy-TEMPO/BAIB

Previous studies presented TEMPO/BAIB-mediated oxidation mechanism of primary alcohols into ketones or aldehydes [40,41]. As the basis of this study, oxidation mechanism of 5-HMF into 2,5-DFF by TEMPO/BAIB is shown in Scheme 2. Earlier reports noted the indirect involvement of BAIB [$\text{PhI}(\text{OAc})_2$] in primary alcohol oxidation [40,43]. The interactions of BAIB with TEMPO and 5-HMF have two distinctive functions in the presented mechanism. The first role of BAIB involves the ligand exchange between its

acetate groups and the primary alcohol group of 5-HMF (Scheme 2b). This would result in the release of CH_3COOH from BAIB, which would catalyze the initial dismutation (Scheme 2a) of TEMPO radical (1) into oxoammonium salt (2) and hydroxylamine (3). The produced oxoammonium salt (2) then oxidizes 5-HMF into 2,5-DFF while it is being reduced to hydroxylamine (3). The second function of BAIB is to complete the oxidation cycle by regenerating the TEMPO radical (1) through hydroxylamine (3) oxidation. Concomitantly, the released CH_3COOH from BAIB as a by-product of hydroxylamine oxidation could further participate in the subsequent cycles of dismutation of the regenerated TEMPO radical (1) into (2) and (3) [40,41].

2-1. Effect of BAIB as a Co-oxidant

The mild reaction conditions performed in previous studies involving BAIB as TEMPO radical co-oxidant was adapted in the current study [40]. As BAIB regenerates TEMPO radical, the TEMPO amount can be significantly reduced from stoichiometric to catalytic level. Initial 5-HMF oxidation at room temperature with low TEMPO amount and stoichiometric BAIB dosage yielded 34% 2,5-DFF (Table 1, Entry 2). The result demonstrates that BAIB addition facilitated 5-HMF oxidation under mild condition, even at low TEMPO dosage. This further suggests that TEMPO radical was regenerated by BAIB. Additionally, the presence of CH_3COOH in TEMPO/BAIB system along with 2,5-DFF production (Supplementary Fig. S2B) is consistent with the mechanism presented in Scheme 2a. The detected CH_3COOH could either be the released by-product from TEMPO radical regeneration (Scheme 2a) or those from the ligand exchange of BAIB with 5-HMF in Scheme 2b. While results imply that TEMPO dosage can be significantly minimized in the presence of BAIB, the appropriate amount of TEMPO must still be determined to improve product yields.

2-2. Effect of TEMPO Dosage at Fixed BAIB Amount

At fixed BAIB amount, reactions with different 4-hydroxy-TEMPO dosages were performed in DCM at room temperature ($\text{RT}=25\text{--}27^\circ\text{C}$). Fig. 2 was constructed to observe the 2,5-DFF production rates at varied TEMPO amounts. At the lowest 4-hydroxy-TEMPO dosage (0.05 mmol), the yield continuously increased within the tested reaction period. However, the rate of 2,5-DFF formation was relatively slow; a maximum yield of 42% was achieved after 5 h. At ≥ 0.1 mmol of 4-hydroxy-TEMPO, yields eventually declined after the maximum values were reached (Fig. 2). This indicates consumption or further degradation of 2,5-DFF. However, no side- or degradation products were observed from the reaction samples. Thus,

Table 1. 2,5-DFF yields at various reaction systems and conditions

Entry	5-HMF (mmol)	TEMPO (mmol)	BAIB (mmol)	CH_3COOH (mmol)	Solvent	Temp ($^\circ\text{C}$)	Time	2,5-DFF yield (%)
1	1.0	1.0	-	-	Toluene	120	48 hr	44
2	1.0	0.1	1.0	-	DCM	*RT	4 hr	34
3	1.0	0.2	1.0	-	DCM	RT	45 min	45
4	1.0	0.2	1.5	-	DCM	RT	45 min	54
5	1.0	0.2	1.5	-	EtOAc	RT	45 min	56
6	1.0	1.0	-	1.0	EtOAc	RT	45 min	40
7	1.0	0.2	-	1.0	EtOAc	RT	45 min	2
8	1.0	0.2	1.5	0.1	EtOAc	RT	45 min	66

*Room temperature (25-27 $^\circ\text{C}$)

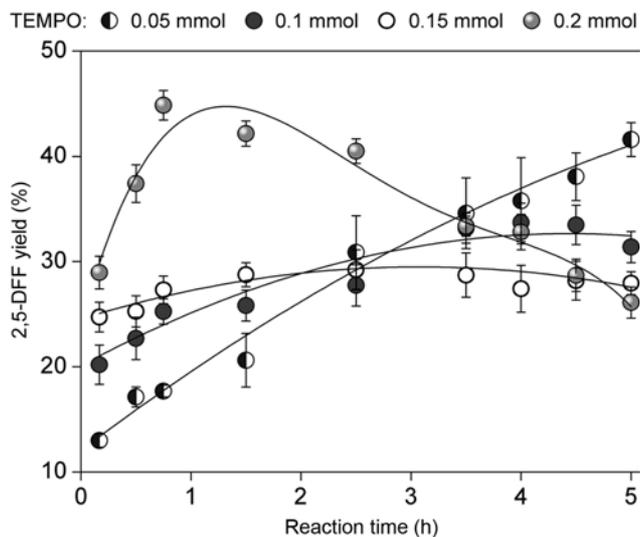


Fig. 2. Time profiles of 5-HMF oxidation into 2,5-DFF at various 4-hydroxy-TEMPO dosages using 1 : 1 molar ratio of 5-HMF and BAIB in DCM at RT (25-27 °C).

the produced 2,5-DFF might have been converted into other related compounds which were analytically undetected [32]. But with increase in TEMPO dosage, shorter reaction periods were needed to achieve the maximum 2,5-DFF yields. This suggests the direct effect of 4-hydroxy-TEMPO amount on the kinetics of 2,5-DFF-related reactions. Thus, to maximize 2,5-DFF recovery, reactions must be terminated immediately after the maximum yield is attained. Among the tested dosages, highest 2,5-DFF yield of 45% (Table 1, Entry 3) was achieved in the presence of 0.2 mmol 4-hydroxy-TEMPO after 45 min, hence was selected for further reactions.

The presence of BAIB as a secondary oxidant of 4-hydroxy-TEMPO resulted in mild reaction conditions for 2,5-DFF production; it required (1) shorter period (from 48 h to 45 min), (2) lower temperature (from 120 °C to RT) and (3) lower 4-hydroxy-TEMPO dosage (from equimolar level to 0.2 mmol) to afford a comparable yield with that of the highest value attained by pure 4-hydroxy-TEMPO reactions (Table 1, Entry 1). As the temperature requirement was significantly lowered, the convenience of using solvents with low to moderate boiling points like DCM becomes an extra advantage as the solvent can be conveniently removed after the reaction.

2-3. Effect of BAIB Dosage

To further improve the yield of 2,5-DFF, varied amounts of BAIB were reacted with 0.2 : 1 mole ratio of 4-hydroxy-TEMPO and 5-HMF, respectively, for 45 min at RT (Fig. 3). Increased BAIB dosage gradually enhanced the 2,5-DFF production; highest 2,5-DFF yield of 54% was achieved at 1.5 mmol BAIB (for every 1 mmol of 5-HMF; Table 1, Entry 4). Results suggest that BAIB must be present in excess to achieve higher 2,5-DFF yield. Higher dosage of BAIB indicates more CH_3COOH production from the ligand exchange of BAIB with 5-HMF and from TEMPO free radical regeneration [40,41]. However, further increase in BAIB at 0.2 mmol of 4-hydroxy TEMPO did not afford higher 2,5-DFF yield hence the experiment was halted at this dosage. Furthermore, high BAIB amount could result in excessive CH_3COOH production, which could react with 5-HMF and generate esterification product, which could result

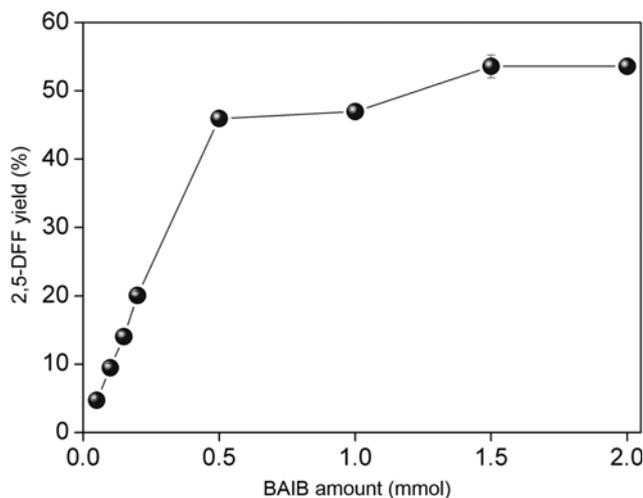


Fig. 3. Effect BAIB dosage on the oxidation of 5-HMF into 2,5-DFF using 1 : 0.2 molar ratio of 5-HMF and 4-hydroxy TEMPO in DCM for 45 min at RT (25-27 °C).

in the loss of the starting material [32]. Thus from the results, a BAIB dosage of 1.5 mmol was determined as the most appropriate stoichiometric dosage for 2,5-DFF production.

2-4. Effect of Reaction Solvent on 2,5-DFF Yield

The most suitable solvent was selected among several candidates based on practicality, convenience and energy requirement of the reactions. In previous works, 2,5-DFF was prepared mainly in high boiling point solvents like dimethyl sulfoxide, *N,N*-dimethyl acetamide and dimethylformamide [5,20,21,44]. But the most significant challenge in these reactions is the difficulty of product isolation and solvent separation. Furthermore, the high temperature requirements for reactions and solvent removal rendered the systems more energy intensive. As room temperature reactions were desired, the use of solvents with low to moderate boiling points could be beneficial. First, the concern on the hazard of solvent volatilization would be minimal for low temperature reactions. Second, product purification would be simpler as less energy is required for solvent removal.

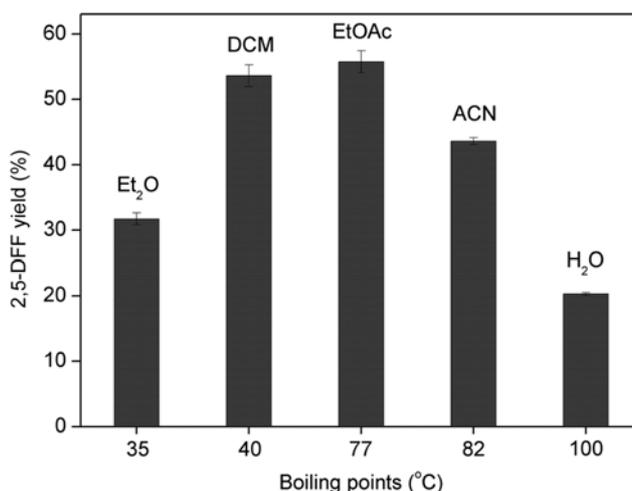


Fig. 4. 2,5-DFF yields in different solvents using 1 : 0.2 : 1.5 molar ratio of 5-HMF, 4-hydroxy TEMPO and BAIB, respectively, for 45 min at RT (25-27 °C).

Fig. 4 illustrates 2,5-DFF yields from the reactions (1.0 mmol 5-HMF: 0.2 mmol 4-hydroxy-TEMPO: 1.5 mmol BAIB) performed at RT for 45 min using various solvents with low to moderate boiling points (mostly ≤ 100 °C). Reactions in EtOAc and DCM afforded comparable yields, but the highest was achieved in EtOAc with 56% 2,5-DFF. On the other hand, moderate yields of 44% and 32% were measured in ACN and Et₂O, respectively. These results indicate that non-polar and polar aprotic solvents with excellent reactant solubility are appropriate for the reaction. However, a protic solvent like water (H₂O) afforded the lowest yield of 18%. In aqueous system, BAIB was probably hydrolyzed into iodobenzene (PhI=O), which depleted its availability to regenerate TEMPO radical [45]. As it achieved the highest 2,5-DFF production (Table 1, Entry 5), EtOAc with its moderate boiling point was determined as the suitable solvent among the tested candidates for 4-hydroxy-TEMPO/BAIB-mediated 5-HMF oxidation.

2-5. Effect of Reaction Temperature

In EtOAc medium, reaction temperature was further raised up to the sub-boiling point of the solvent to observe its effect on 2,5-DFF yield. Results in Fig. 5 show that instantaneous formation of 2,5-DFF became more remarkable with temperature increase. At lower temperatures (≤ 45 °C), maximum yields were achieved after 30-60 min before 2,5-DFF yields declined. But at ≥ 60 °C, maximum yields were lower, which were achieved at the beginning of the reaction followed by steady decline in 2,5-DFF production. The trend at ≥ 60 °C may be due to 5-HMF esterification at high temperature in the presence of acetic acid [46]. Therefore, among the tested temperature conditions, highest yield of 56% can be obtained at 30 °C by terminating the reaction after 45-60 min.

3. 5-HMF Oxidation by 4-Hydroxy-TEMPO/BAIB/CH₃COOH

To examine the role of CH₃COOH in 5-HMF oxidation, BAIB-free reaction with equimolar stoichiometric amounts of 4-hydroxy-TEMPO and CH₃COOH yielded 40% 2,5-DFF (Table 1, Entry 6). The result confirms the importance of CH₃COOH in TEMPO radical dismutation, which generated the oxoammonium salt (2) that is

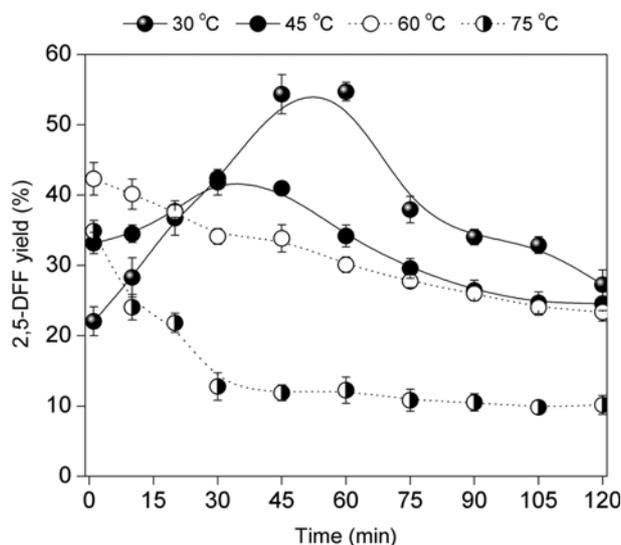


Fig. 5. 2,5-DFF yields at various reaction temperatures and time using 1 : 0.2 : 1.5 molar ratio of 5-HMF, 4-hydroxy TEMPO and BAIB in EtOAc.

responsible for 5-HMF oxidation (Scheme 2a). However, low 4-hydroxy-TEMPO amount would still result in low oxoammonium salt (2) production in spite of sufficient CH₃COOH addition in a BAIB-free reaction. Hence, low 2,5-DFF yield was achieved when 4-hydroxy-TEMPO dosage was limited (Table 1, Entry 7). This implies that BAIB-free reaction with sole addition of CH₃COOH is not efficient as it would require excess addition of 4-hydroxy-TEMPO to achieve similar product yields. Recall that CH₃COOH-facilitated 4-hydroxy-TEMPO dismutation partially generates hydroxylamine (3), but this is not an oxidant of 5-HMF.

Earlier discussion (Section 2.1 of Results) pointed out the importance of BAIB in TEMPO radical regeneration. But the other role of BAIB as CH₃COOH source from ligand exchange (Scheme 2b) is also critical in prompting the initial TEMPO radical dismutation, hence was also examined. A TEMPO-free reaction between BAIB and 5-HMF was performed. The reaction did not yield any 2,5-DFF, mainly due to the absence of the main oxidant. Furthermore, the reaction did not exhibit significant CH₃COOH production (data not shown), suggesting that Scheme 2b did not proceed efficiently. This implies that despite being an effective TEMPO radical regenerant, BAIB apparently was not a reliable source (via ligand exchange) of CH₃COOH that is needed for initial TEMPO radical dismutation. Hence, the effect of CH₃COOH dosage in TEMPO/BAIB systems was further determined.

Under optimal TEMPO/BAIB reaction conditions, Fig. 6 reveals that only small additions of CH₃COOH further improved the 2,5-DFF productions. The highest yield of 66% was achieved with 0.1 mmol of CH₃COOH (Table 1, Entry 8). These results show that CH₃COOH addition in TEMPO/BAIB system was necessary to prompt TEMPO radical dismutation and improve 2,5-DFF yields.

CONCLUSIONS

2,5-DFF from 5-HMF was successfully produced by TEMPO in the presence of BAIB and CH₃COOH as secondary oxidants. The reaction system is energy-efficient and works rapidly (<1 h)

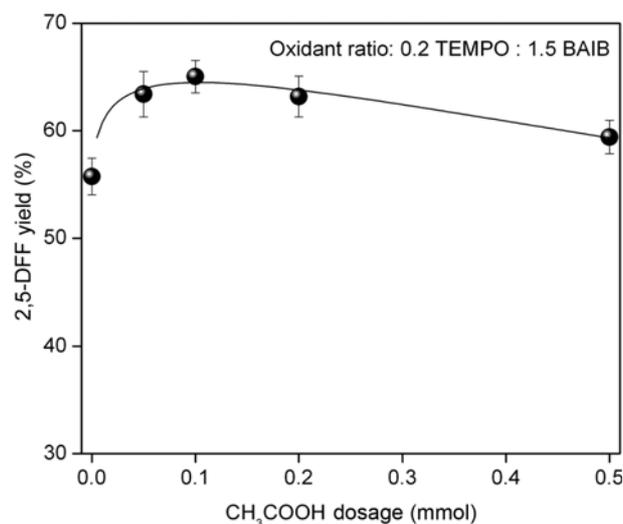


Fig. 6. 2,5-DFF yields at various CH₃COOH dosages using 1 : 0.2 : 1.5 molar ratio of 5-HMF, 4-hydroxy TEMPO and BAIB in EtOAc.

under metal-free conditions at room temperature. As a TEMPO radical regenerant, BAIB addition resulted in acceptable 2,5-DFF yields even at low TEMPO dosage. On the other hand, its role as CH_3COOH source via ligand exchange was found minimal. Small addition of CH_3COOH further improved 2,5-DFF production, probably as it assisted the initial TEMPO radical dismutation. Oxidant dosages, choice of appropriate solvent and reaction period were all found critical in improving the 2,5-DFF yields. The presented metal-free mild reaction system provides an opportunity to render a scarcely produced 2,5-DFF more accessible for wider application. Future investigations on the development and application of a heterogeneous TEMPO/BAIB/ CH_3COOH system could render a more economically viable process for 2,5-DFF production.

ACKNOWLEDGEMENTS

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Ministry of Education (No. 2009-0093816) and 2013 Myongji University Research Fund.

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Supporting Information

Metal-free mild oxidation of 5-hydroxymethylfurfural to 2,5-diformylfuran

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(Received 27 September 2013 • accepted 28 January 2014)

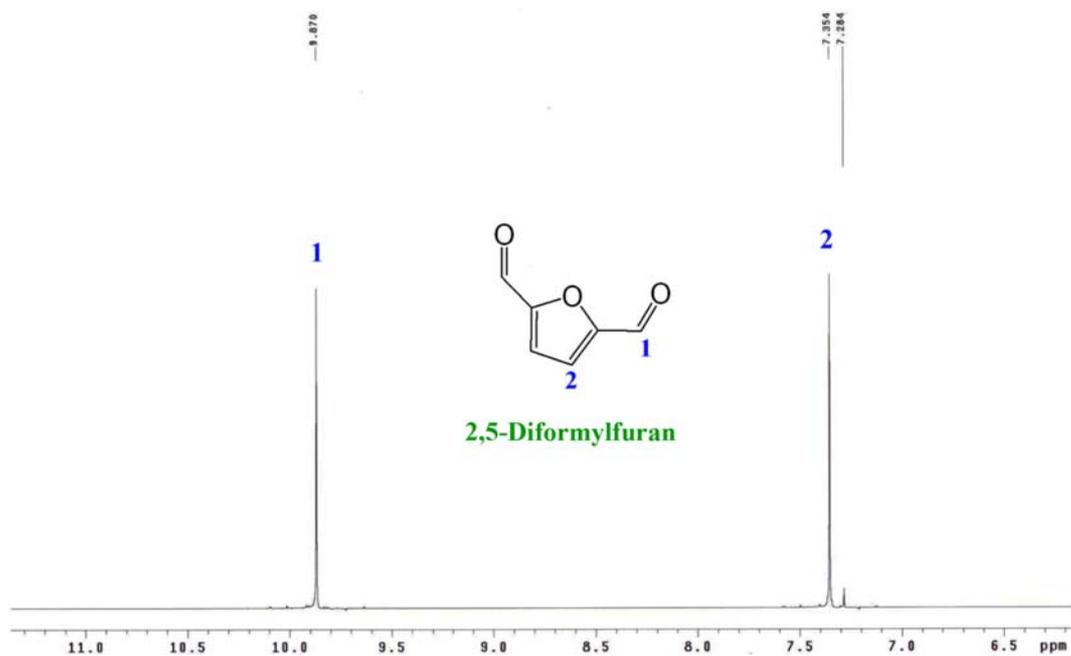


Fig. S1. ¹H NMR (CDCl₃) of 2,5-diformylfuran (2,5-DFF). ¹H-NMR (CDCl₃, 400 MHz) δ : 9.87 (s, 2H, CHO), 7.35 (s, 2H, furan H), ppm^{1,32}.

Table S1. Elemental analysis (2,5-DFF)

Element	Theoretical (%)	Found (%)
C	58.1	58.4
H	3.2	3.2
O	38.7	38.4

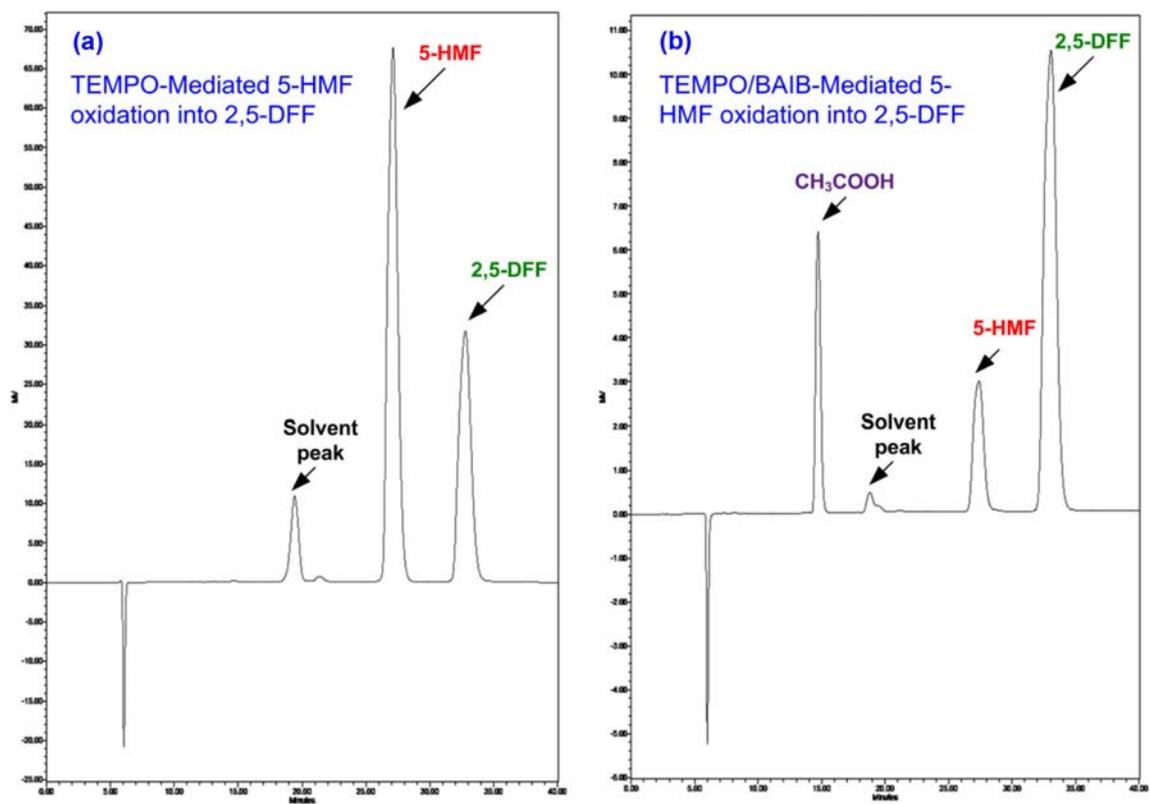


Fig. S2. Sample product HPLC chromatograms from system with different oxidants. (a) 1.0 mmol TEMPO: 1.0 mmol 5-HMF in toluene (120 °C) after 36 hr reaction (b) 0.2 mmol TEMPO: 1.0 mmol 5-HMF: 1.5 mmol BAIB in EtOAc (30 °C) after 45 min reaction.