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Metal Catalyst and Hydrogen Gas-Free Selective Reduction of Biomass-Derived Substituted Furfuraldehyde to Alkyl Furan as a Key Biofuel Additive

Arvind Singh Chauhan, Ajay Kumar, and Pralay Das*

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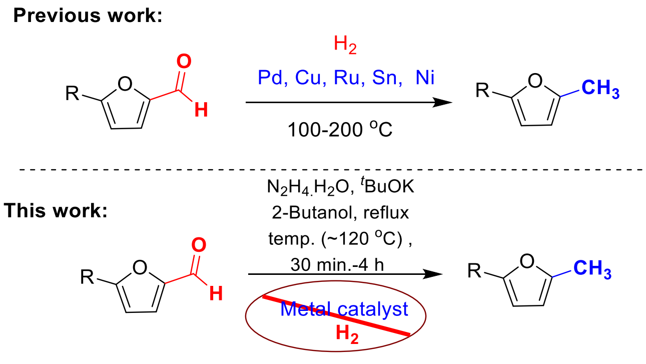
ABSTRACT: A metal catalyst and a hydrogen gas-free approach has been developed for selective reduction of aldehyde to an alkyl group of different substituted furan compounds. In this process, hydrazine hydrate under basic conditions at reflux temperature selectively participated in the reduction of the aldehyde moiety to the corresponding alkyl group of highly reactive furan compounds in a selective manner. The developed protocol was applied for selective and scalable reduction of 5-hydroxymethylfurfural (5-HMF) up to 250 g to 5-methylfurfuryl alcohol (MFA) in a 70% yield. Under the same process, furfuraldehyde was also tested in a 250 g reaction for 2-methylfuran (MF) synthesis in a highly selective manner and the product was distilled out from a single-pot reaction with gas chromatography (GC) purity ≥90%. The scope of the process was further extended for different substituted furfuraldehydes successfully. In addition, the protocol is found to be efficient for scalable production and easy separation of the product.

KEYWORDS: *metal and hydrogen gas-free, 5-hydroxymethylfurfural, 5-methylfurfuryl alcohol, 2-methylfuran, biomass, furfuraldehydes, alkyl furans, Wolff Kishner reduction, biofuel*

■ INTRODUCTION

The ongoing depletion of fossil resources due to an increase in energy demand globally has been causing an alarming situation worldwide.[1,2] In this context, biomass is the other naturally abundant renewable energy source available, which can be viewed as an alternate of fossil resources. Globally, a total of 170 billion metric tons of biomass are produced annually.[3] Hence, pioneering valorization of this cellulosic biomass is of utmost importance for the sustainable energy and biobased economy. 5-Hydroxymethylfurfural (5-HMF) and furfural are the two major biomass-derived furan-based molecules having a huge market value and applications. Further, their synthesis and separation are well explored in the literature by the scientific community.[4−7] In this context, the conversion of lignocellulosic biomass into valuable alkyl furans is a challenging task to achieve in the current scenario. Most of the alkyl furans, such as 2,5-dimethylfuran (DMF) and 2-methylfuran (MF), are known for their fuel and fuel additive properties.[8−11] These alkyl furans exhibit superior fuel properties over more established biofuels, such as ethanol.[12] Also, the compatibility of such alkyl furan-based biofuels with SI engines excludes major modification in the engine and causes less emission of harmful carbonyl compounds, when compared with existing fuels and bioalcohols.[12] The rational production of these alkyl furans mainly involved various catalytic approaches, which majorly include numerous metal catalysts, highly flammable H_2 gas, and very harsh reaction conditions.[13] However, these approaches encountered many unwanted reactions such as over-reduction of the furan ring, C−C bond dissociation, and polymerization, which directly affect the selectivity of the desired compounds.[14−17] Generally, most of the literature references on the reduction of biomass-derived 5-HMF to 2,5-dimethylfuran (2,5-DMF) mainly include the methods that have been performed over noble metals such as Pd, Cu, Ru, Sn, Ni, hybrid metal catalysts, and few metal complexes like Zr-benzylphosphonate and zirconium *N*-alkyltriphosphate nanohybrid (ZrPN) (Scheme 1).[18−28] In 2007, Dumesic et al. reported a catalytic approach for the synthesis of 2,5-DMF by hydrogenolysis of the C−O bond over a hybrid Cu/Ru metal catalyst with a yield of about 76−

Scheme 1. Comparative Studies with the Reported Process for Alkyl Furan Synthesis



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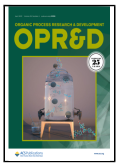

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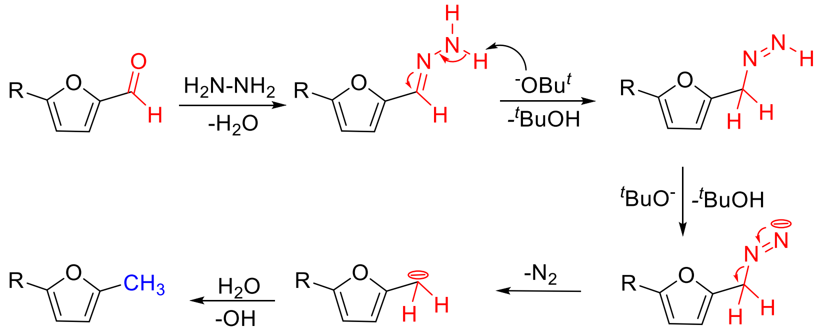
Scheme 2. Probable Mechanism for Alkyl Furan Synthesis from Furfuraldehyde



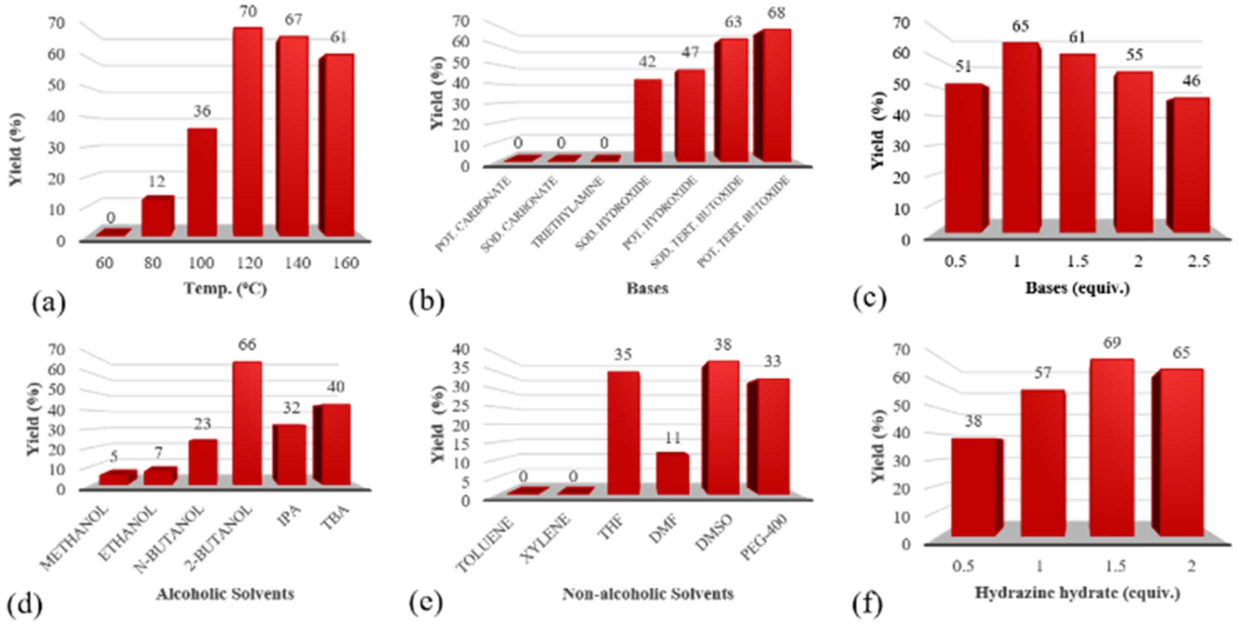


Figure 1. Synthesis of 5-MFA from 5-HMF. Effect of (a) the temperature, (b) bases, (c) ^{t}BuOK base equivalency, (d) alcoholic solvents, (e) nonalcoholic solvents, and (f) hydrazine hydrate equivalency on selective reduction of furan aldehydes to alkyl furans and all of the studies (a–f) were performed with other best-optimized parameters. Reaction conditions: 5-HMF (1.0 equiv), hydrazine hydrate (1.5 equiv), base (1.0 equiv), and 2-butanol at reflux temperature (~120 °C) for 4 h. All yields are isolated yields.

79%.[8] Interestingly, 5-MFA has been identified as the major intermediate for the synthesis of biofuel DMF from 5-HMF and its synthesis has only been performed on the laboratory scale. 5-MFA is one among the class of furans that could be considered as a prime precursor for biofuel production because of its salient features, such as low oxygen content, high energy density, chemical stability, low volatility, and good solubility in hydrocarbons. It is also widely used as a flavoring agent and food additive.[29] The presence of various active functional group moieties such as furan rings, double bonds, and primary alcohols makes it a potential candidate for further synthesis of various important molecules and fine chemicals.[30,31] Unfortunately, the scalable production of 5-MFA is a challenging task to perform because the production of this molecule is accompanied by the use of metal catalysts and flammable hydrogen gas, which makes the process costly and difficult to handle in a scale-up synthesis. Therefore, an alternative process is in high demand for low-cost and scalable production for 5-MFA from 5-HMF. An interesting alkyl furan candidate, 2-methylfuran (2-MF), has also been synthesized from biomass-derived furfuraldehyde. 2-MF is envisioned as a biofuel due to its finer combustion performance, as well as high octane number (RON = 103).[32] Various metal-catalyzed methodologies have been reported in the literature for the reduction of furfuraldehyde to 2-MF under external hydrogen gas conditions. Vlachos et al. recently reported the conversion of furfuryl alcohol to 2-MF through a DFT study by C−O bond activation under Pt/TiO_2.[33] Researchers also tried to reduce furan hydrazone to the respective methylfuran under Pt/Clay-catalyzed conditions and obtained a 65% yield.[34] All of the existing methodologies referenced above used high-cost metals, external hydrogen gas, high temperatures and pressures, and also faced scalable-issues and hurdles such as polymerization of the furan compound at high temperatures and over-reduction of the furan ring under experimental conditions.

In the last few years, we have carried out scalable process development for 5-HMF production from lignocellulosic biomass and carbohydrates.[35,36] In this context, we developed a metal and a hydrogen gas-free, highly selective and scalable approach for selective reduction of aldehyde to the alkyl group of different substituted furans, and the process was also tested up to a 250 g scale reaction. Moreover, our work not only demonstrates the metal catalyst and hydrogen gas-free patented approach for the production of alkyl furan analogues but also provides an atom-economic, easy-to-handle, and scalable process for maximizing the liquid-fuel product from carbohydrates and bioresources.

Further, we know that hydrazine hydrate is a costly reducing agent in comparison to hydrogen, but compared to the overall complexity of the earlier processes, such as over-reduction, costly catalyst, difficult to handle under high pressure in general laboratory practices, the proposed process is highly selective to the carbonyl group and much easier to handle under general laboratory conditions. Moreover, hydrazine hydrate after decomposition gives N_2 gas, which is also easy to handle, separable, and also has commercial value. The proposed approach is a very common Wolff Kishner (WK) reaction but rarely investigated by researchers due to its unspecific reactivity with furfurals. In this study, these challenges have been overcome through modification of its processing technique.

■ RESULTS AND DISCUSSION

In the reported literature, the WK approach for the reduction reaction of 5-HMF has not been investigated yet. Herein, we critically explored the WK reduction approach specifically for 5-HMF reduction to MFA. Moreover, this approach of 5-HMF reduction is quite tough to perform, as when we used 5-HMF directly in the reaction system, we obtained a very poor yield of the desired product. This might be why the WK reduction approach in the case of 5-HMF is underexplored. After continuous efforts and a critical study, we observed that the main reason for this was the acidic nature of 5-HMF (pH ∼ 3), as most of the furan products are synthesized in acidic media and stable in acidic environments. Keeping this observation in mind, we neutralized 5-HMF (pH ∼ 7) prior to the reaction. Then, when we carried out the reaction with neutral 5-HMF, the yield of the desired product enhanced dramatically.

In this process, we have used a hydrazine hydrate ($N_2H_4 \cdot H_2O$) and ^{t}BuOK combination in a 2-butanol solvent system as the reducing agent instead of H_2 gas and a metal catalyst. Initially, the aldehyde group of furfural in the presence of $N_2H_4 \cdot H_2O$ was immediately converted to hydrazone, which further under basic conditions reduced to an alkane, followed by oxidation of hydrazine to gaseous N_2 (Scheme 2).[37] As the reaction proceeded through the hydrazone intermediate, only the carbonyl group selectively participated in the reduction reaction to its corresponding alkane similar to that in the WK reduction approach.

Initially, we have investigated the effect of different conditions, such as temperature, base, the equivalence of base, alcoholic and nonalcoholic solvents, and simultaneous optimization of hydrazine hydrate, to obtain the best-optimized process for the synthesis of 5-MFA from 5-HMF (Figure 1).

Further, to estimate the time-based progress of the reaction, we performed a reaction under our established protocol using 5-HMF as the model substrate. Under this investigation, we observed an increase in the yield of the desired product 5-MFA with an increase in the reaction time up to 4 h, which then decreased gradually, as shown in Figure 2 (Supporting Information, SI).

Five-Gram Scale Synthesis of Alkyl-Substituted Furans. After optimization of the process, the conditions were further tested with a five-gram scale reaction. Under this study, the standard protocol was first applied on a tested substrate, i.e., 5-HMF **1a** (5.0 g, 1.0 equiv), hydrazine hydrate (2.92 mL, 1.5 equiv), and ^{t}BuOK (4.45 g, 1.0 equiv) in a 2-butanol (25 mL) solvent system at reflux temperature (∼120 °C) for 4 h. The reaction was monitored using a thin-layer chromatograph (TLC), and after completion of the reaction, distilled water was added to the reaction mixture, and the final product was extracted with diethyl ether two to three times. The solvent was further removed by fractional distillation in a controlled manner, which finally gave 5-MFA **2a** in a 70% yield (Table 1, entry 1) with >99% purity by gas chromatography−mass spectrometry (GC−MS) (SI, spectrum S4).

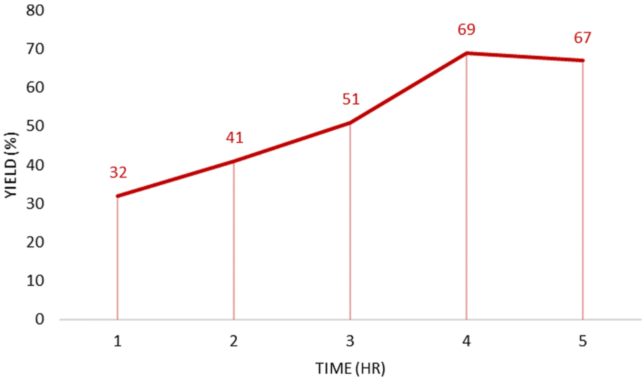
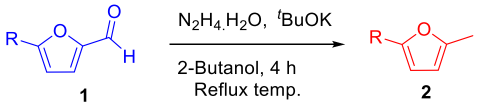


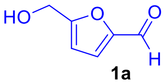
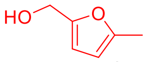
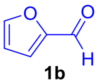
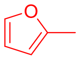
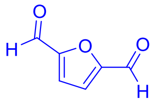
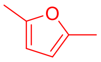
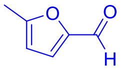
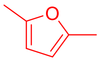
Figure 2. Time-based progress of the reaction of 5-HMF to 5-MFA under standard reaction conditions.

Similarly, furfural (**1b**) was also subjected under established reaction conditions to yield 2-MF (**2b**). In this study, as soon as 2-MF (**2b**) was formed in the reaction mixture, it simultaneously distilled out through the condenser and was collected in a collection flask. After completion of the reaction, the liquid in the collection flask was redistilled carefully to remove 2-butanol, giving the final compound 2-MF (**2b**) in a 72% yield and >95% NMR purity (Table 1, entry 2). Interestingly, when we extended the same process for 2,5-diformylfuran (DFF), which is a tricky and highly reactive substrate as it constitutes two aldehyde groups, we obtained 2,5-dimethylfuran **2c** (DMF) with high selectivity and a considerably good yield of 56% after distillation with GC purity >95% (Table 1, entry 3). Any alteration in the reagent equivalency led to a decrease in the product yield of **2c**. Complex unidentified mass formation was noticed during the reaction, which may be responsible for lowering the yield of the desired product **2c**. To avoid the difficulties in handling DFF, a less stringent substrate, 5-methyl-2-furfuraldehyde (**1d**), was selected for the synthesis of the same product, **2c**, using a similar approach, and the reaction displayed an improvement of the yield by 5−10% compared to the earlier reaction (Table 1, entry 4).

Scale-Up Synthesis of 5-MFA and 2-MF. There are a number of successful processes available in small-scale reactions, but it is not possible to apply all of these processes in a scale-up reaction, which limits their technological applications. Therefore, we tested our developed process further only on two industrially challenging targets of 5-MFA and 2-MF production from 5-HMF and 2-furfuraldehyde, respectively. We begin our scale-up trial with 5-HMF up to 250 g scale for the synthesis of 5-MFA (**2a**) under optimized reaction conditions described in Table 2 and the Experimental Section. The stepwise addition of the reagents is crucial for the fruitful conversion of the product. Initially, 5-HMF was dissolved in the 2-butanol solvent, and then $N_2H_4 \cdot H_2O$ was

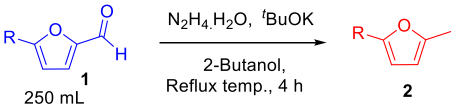
Table 1. 5.0 g Scale Synthesis of Alkyl-Substituted Furans[a]

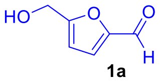
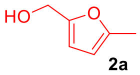
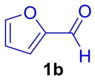
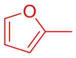


S. No.	Reactant (**1**)	Product (**2**)	Conversion/Selectivity	Yield (%)[b]
1.	 **1a**	 **2a**	100/70	70
[c]2.	 **1b**	 **2b**	100/72	72
3.	 **1c**	 **2c**	100/56	56
4.	 **1d**	 **2c**	100/62	62

[a]Reaction conditions: substituted furfural 1 (1.0 equiv), $N_2H_4 \cdot H_2O$ (1.5 equiv), ^tBuOK (1.0 equiv), and 2-butanol at reflux temperature (~120 °C) for 1−4 h under reflux conditions. [b]Isolated yields. [c]The reaction time, 1.5 h.

Table 2. 250 g Scale Synthesis of Alkyl-Substituted Furan[a] and Large-Scale Synthesis of 5-MFA from 5-HMF



S. No.	Reactant	Product	Conversion	Selectivity	Yield (%)[c]
1.	 **1a**	 **2a**	100	69	69
[b]2.	 **1b**	 **2b**	100	70	70

[a]Reaction conditions: HMF (250 g, 1.0 equiv), $N_2H_4 \cdot H_2O$ (146 mL, 1.5 equiv), ^tBuOK (222.6 g, 1.0 equiv), and solvent 2-butanol at reflux temperature (~120 °C) for 4 h. [b]Large-scale synthesis of 2-MF from furfuraldehyde. Reaction conditions: furfuraldehyde (250 g, 1.0 equiv), hydrazine hydrate (1.2 equiv), ^tBuOK (0.5 equiv), and solvent 2-butanol at reflux temperature for 90 min. [c]Isolated yields.

added dropwise to this mixture. In another reaction vessel, ^tBuOK was added to the 2-butanol solvent and heated at reflux temperature till it was completely homogenized. Then, the mixture of 5-HMF was added to the ^tBuOK basic solution dropwise. Initially, as the reaction started, the vigorous effervescence of N_2 gas was observed in the reaction medium. Further progress of the reaction was monitored on a TLC, and a dark pinkish spot appeared on the TLC after spraying with concn H_2SO_4. After completion of the reaction, the reaction mass was subjected to fractional distillation under vacuum to remove the solvent and finally gave the desired product 5-MFA, **2a** (153 mL), in a yield of 69% (Table 2, entry 1). The reaction was highly selective, and additional purification to achieve product purity >90% was not required. Inspired by these results, we subjected the established protocol to furfuraldehyde as the feedstock up to a 250 g scale for 2-MF synthesis (Table 2). Furfuraldehyde has been selected by the U.S. Department of Energy in the top 30 biomass-based key compounds due to its characteristics such as being a raw material, its market value, evaluated processing price, etc.[38]

The product 2-MF (**2b**) is volatile in nature; therefore,to avoid product loss, the reaction is carried out with distillation for easy collection of the corresponding product 2-MF in a single-pot reaction with a yield of up to 70% (150 mL) and purity ≥ 90% (Table 2, entry 2).

Moreover, the shorter reaction time and simultaneous collection of desired products through distillation in a one-pot system made this approach more feasible and inexpensive for scale-up production of 2-MF. Both 5-MFA and 2-MF are of high importance due to their biofuel precursor or direct biofuel nature. The results are highly encouraging and this is the first scalable metal catalyst and hydrogen gas-free approach for the selective reduction of aldehyde-substituted furans to alkyl furans, which are key biofuel precursors or biofuel additives.

The metal catalyst and hydrogen gas-free easy approach, which is faster and atom-economic and has minimum waste production, easy separation, and scalability, clearly showed the potentiality of the process for future technology development. Moreover, when we compared our process with the existing approaches present in the literature,[39,40] we found our protocol to be far better because of its operational simplicity. Additionally, refinement of the process is ongoing in our laboratory for further scale-up production to make the process more economic, less time-consuming, and easy to handle.

■ TECHNOLOGICAL ADVANTAGES

In this process, the major technological advantages are that (i) all substrates used in this reaction are in a single solution phase, (ii) the temperature and time of the reaction are highly favorable, (iii) the product is easy to separate through distillation at the same reaction temperature and, therefore, energy-efficient, (iv) selectivity and purity of the product are ≥90%, (v) there is minimum byproduct formation, (vi) the solvent is recyclable, (vii) as a major byproduct, clean N_2 gas is generated, and (viii) no or negligible hazard waste is generated.

■ FATE OF THE REAGENT USED

The developed process has constituted with the specific reagentsused, which made the process more cost-effective (Table 3). However, the overall cost of the developed process fully depends upon the future price of hydrazine hydrate as the current cost of hydrazine hydrate is high.

Table 3. Fate of the Reagents after the Reaction

entry	reagent used	reagent after reaction
1.	2-butanol	100% recoverable
2.	hydrazine hydrate	nitrogen gas and water
3.	^{t}BuOK base	tertiary butyl alcohol and KOH
4.	furfural compounds	major alkyl furan product, furan hydrazone, and some unidentified small molecules

Overall, an effective and scalable strategy has been developed to produce alkyl furans comparable to those of other reports in the literature where the use of metal catalysts and a high-pressure hydrogen gas reactor is crucial for the desired transformation (Figures 3and 4).

■ CONCLUSIONS

A metal catalyst and hydrogen gas-free hydrazine hydrate-mediated first approach for selective reduction of the aldehyde functional group of highly reactive furans was used for alkyl furan synthesis. The scope of the reaction was also investigated for different aldehyde-substituted furan moieties successfully. In most of the earlier reduction approaches, over-reduction of the highly reactive furan ring was noticed, whereas the present process is highly selective only for reduction of the aldehyde group and the reactive furan ring remains unchanged. The reaction is so selective that tedious purification to achieve purity of the product up to ≥99% is not required. The reaction was also tested up to a 250 g scale reaction and was further extendable for scale-up production. Most of the reagents are recoverable, and byproducts are also reusable and commercially important.

■ EXPERIMENTAL SECTION

All chemicals and solvents used in the present process were of analytical grade and used without further purification. 5-Hydroxymethylfurfural was prepared using our own patented method (Application number: 201811023331) and utilized without purification. The compounds furfuraldehyde, 2,5-diformylfuran (DFF), triethylamine (Sigma Aldrich), 5-methylfurfuraldehyde, 4,5-dimethylfurfuraldehyde (TCI), hydrazine hydrate 99% (Thomas Baker and Sigma Aldrich), potassium tertiary butoxide (Avra), 2-butanol, KOH, K_2CO_3, NaOH (CDH Fine Chemicals), and Na_2CO_3 (SD Fine Chemicals) were purchased from commercial sources and used without further purification. NMR spectra were acquired using Bruker Advance 300 and 600 MHz (^{1}H) and 150 MHz (^{13}C) spectrometers. Spectra were recorded at 25 °C in $CDCl_3$ [residual $CHCl_3$ (δH 7.28 ppm) or $CDCl_3$ (δC 77.00 ppm)]. Chemical shifts were recorded in δ (ppm) relative to the tetramethylsilane (TMS) and NMR solvent signals. Coupling constants (J) are given in Hz and multiplicities of signals are reported as follows: s, singlet; d, doublet; and m, multiplet. GC−MS analysis was carried out on a Shimadzu (QP 2010) series gas chromatograph-mass spectrometer (Tokyo, Japan) equipped with a FID, an AOC 5000 autosampler, and a DB-5MS capillary column (30 m × 0.25 mm, i.e., with film thickness 0.25 μm). The scale-up reaction was performed in a Radley's reactor equipped with a Julabo temperature control unit.

Typical Procedure for the Synthesis of 5-MFA from 5-HMF. A reaction vessel was charged with ^{t}BuOK (222.6 g, 1.0 equiv) and 2-butanol (500 mL). The reaction mixture was heated and stirred at reflux temperature (~120 °C), till the base was completely dissolved. In another reaction vessel, 5-HMF (250 g, 1.0 equiv) was charged along with 2-butanol

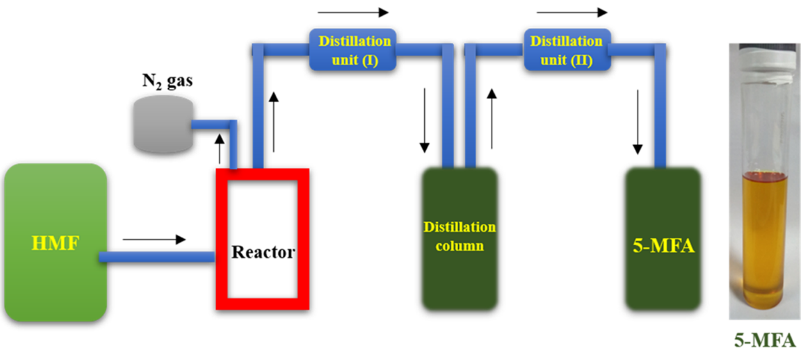


Figure 3. Proposed design for the production of 5-MFA in a scale-up synthesis.

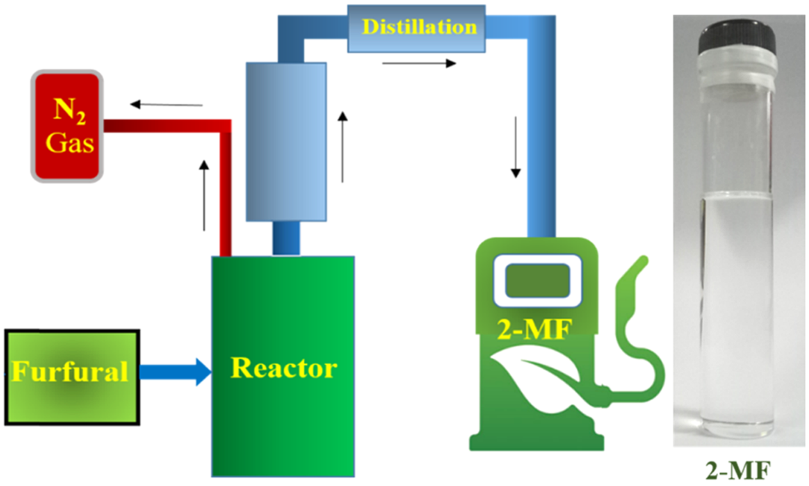


Figure 4. Proposed design for the production of 2-MF in a scale-up synthesis.

(150 mL), followed by the dropwise addition of hydrazine hydrate (146 mL, 1.5 equiv) with gentle agitation. The 5-HMF mixture was added to the predissolved basic solution gradually and refluxed at ~120 °C for 4 h. The progress of the reaction was monitored using a thin-layer chromatograph, and after completion of the reaction, the reaction mixture was subjected to fractional distillation under vacuum, which finally gave 5-MFA (**2a**), 153.0 mL, in a 69% yield. The crude product was further analyzed by GC−MS and NMR. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.29 (s, 3H), 4.52 (s, 2H), 5.92 (d, J = 2.76 MHz, 1H), 6.16 (d, J = 2.97 MHz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.40, 57.27, 106.11, 108.59, 152.22, 152.23.; GC−MS $[M]^+$ = 112.

Typical Procedure for the Synthesis of 2-MF from Furfural. A reaction vessel was charged with ^{t}BuOK (146.0 g, 0.5 equiv) and 2-butanol (450 mL). The reaction mixture was heated and stirred at reflux temperature ~120 °C till the base was completely dissolved. In another reaction vessel, furfural (215.5 mL, 1.0 equiv) was charged along with 2-butanol (150 mL), followed by the dropwise addition of hydrazine hydrate (153 mL, 1.2 equiv) with gentle agitation. The furfural mixture was added to the predissolved basic solution gradually and refluxed at ~120 °C for 90 min. The product was formed after 10−15 min and collected simultaneously through a distillation setup designed along with the reaction assembly till completion of the reaction in the specified time. The distilled product sometimes contains a mixture of 2-butanol, which may require another careful distillation for complete separation to obtain product 2-MF (150.0 mL) in a 70% yield (**2b**). The crude product was further analyzed by NMR. ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (s, 3H), 6.06 (s, 1H), 6.36 (d, J = 1.92 MHz, 1H), 7.38 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 12.96, 105.22, 110.09, 140.55, 151.84; GC−MS $[M]^+$ = 82.

Typical Procedure for the Synthesis of 2,5-Dimethylfuran from 2,5-Diformylfuran. In a 100 mL round-bottom flask, ^{t}BuOK (4.52 g, 1.0 equiv) was dissolved in 2-butanol (15 mL) under a heating condition. In another round-bottom flask charged with DFF (5.0 g, 1.0 equiv), 2-butanol (4 mL) followed by hydrazine hydrate (2.96 mL, 1.5 equiv) was added dropwise at room temperature. Then, the DFF reaction mixture was added to the predissolved ^{t}BuOK basic solution dropwise at reflux temperature ~120 °C for 4 h. After completion of the reaction, the reaction mass was diluted with distilled water and then extracted with diethyl ether two to three times. The extracted reaction mass was further distilled carefully to remove the 2-butanol solvent, which finally led to a pale-yellow liquid of the desired product DMF (**2c**) with a 56% yield. DMF was further analyzed by NMR and GC−MS. ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.38 (s, 6H), 5.96 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 13.17, 105.88, 149.97. GC−MS $[M]^+$ = 96.

Typical Procedure for the Synthesis of 2,5-Dimethylfuran from 5-Methylfurfuraldehyde. In a 100 mL round-bottom flask, ^{t}BuOK (5.09 g, 1.0 equiv) was dissolved in 2-butanol (15 mL) under a heating condition. In another round-bottom flask charged with 5-methylfurfural (5.0 g, 1.0 equiv), 2-butanol (10 mL) followed by hydrazine hydrate (3.33 mL, 1.5 equiv) was added dropwise at room temperature. Then, the 5-methylfurfural reaction mixture was added into the predissolved basic solution dropwise at reflux temperature ~120 °C for 4 h. After completion of the reaction, the reaction mass was diluted with distilled water and then extracted with ethyl acetate/diethyl ether two to three times and dried over Na_2SO_4. The extracted reaction mass was then further distilled carefully to remove the solvent, which finally led to a pale-yellow liquid of the desired product DMF with a 62% yield. The product was further analyzed by NMR and GC−MS. The spectral data was the same as that mentioned in the experimental description (**2c**).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.oprd.0c00541.

List of abbreviations; general procedure for the synthesis of alkyl furans; five-gram scale-up synthesis of alkyl furans; 250 g scale-up synthesis of 5-MFA and 2-MF; and NMR and GC−MS spectra of products (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Pralay Das − *Chemical Technology Division, CSIR-Institute of Himalayan Bioresource Technology, Palampur 176061, Himachal Pradesh, India; Academy of Scientific & Innovative Research (AcSIR), Ghaziabad 201002, India;* orcid.org/0000-0003-2732-5270; Email: pdas@ihbt.res.in, pralaydas1976@gmail.com; Fax: +91-1894-230433

Authors

Arvind Singh Chauhan − *Chemical Technology Division, CSIR-Institute of Himalayan Bioresource Technology, Palampur 176061, Himachal Pradesh, India; Academy of Scientific & Innovative Research (AcSIR), Ghaziabad 201002, India*

Ajay Kumar − *Chemical Technology Division, CSIR-Institute of Himalayan Bioresource Technology, Palampur 176061, Himachal Pradesh, India; Academy of Scientific & Innovative Research (AcSIR), Ghaziabad 201002, India*

Complete contact information is available at:
https://pubs.acs.org/10.1021/acs.oprd.0c00541

Notes

The authors declare no competing financial interest.

In the process development, hydrazine hydrate has been used for a long time in a safe and successful manner for different reactions.[41,42] The use of specific personnel protective equipment is rational and safe regarding the toxicity of hydrazine hydrate.

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