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Integrated Catalytic Process for Biomass Conversion and Upgrading to C_{12} Furoin and Alkane Fuel

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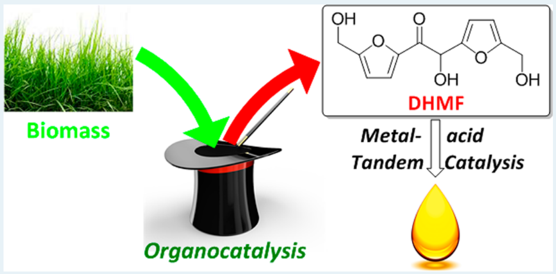
Supporting Information



ABSTRACT: Report herein is an integrated catalytic process for conversion and upgrading of biomass feedstocks into 5,5′-dihydroxymethyl furoin (DHMF), through self-coupling of 5-hydroxymethyl furfural (HMF) via organocatalysis, and subsequently into n-$C_{12}H_{26}$ alkane fuel via metal–acid tandem catalysis. The first step of the process involves semicontinuous organocatalytic conversion of biomass (fructose, in particular) to the high-purity HMF. *N*-Heterocyclic carbenes (NHCs) are found to catalyze glucose-to-fructose isomerization, and the relatively inexpensive thiazolium chloride [TM]Cl, a Vitamin B1 analog, catalyzes fructose dehydration to HMF of good purity (>99% by HPLC), achieving a constant HMF yield of 72% over 10 semicontinuous extraction batch runs. Crystallization of the crude HMF from toluene yields the spectroscopically and analytically pure HMF as needle crystals. The second step of the process is the NHC-catalyzed coupling of C_6 HMF produced by the semicontinuous process to C_{12} DHMF; the most effective organic NHC catalyst produces DHMF in 93% or 91% isolated yield with an NHC loading of 0.70 mol % or 0.10 mol % at 60 °C for 3 h under solvent-free conditions. The third step of the process converts C_{12} DHMF to linear alkanes via hydrodeoxygenation. With a bifunctional catalyst system consisting of Pd/C + acetic acid + $La(OTf)_3$ at 250 °C and 300 psi H_2 for 16 h, DHMF has been transformed to liquid hydrocarbon fuel (78% alkanes), with a 64% selectivity to n-$C_{12}H_{26}$ and an overall C/H/O % ratio of 84/11/5.0.

KEYWORDS: *biomass, fructose, glucose, cellulose, biomass upgrading, organocatalysis, biofuel*

INTRODUCTION

The depletion of fossil fuels has directed society's increasing interest toward the use of plant biomass as a sustainable source of building blocks for chemicals, materials, and biofuels.[1] The furan-based compounds, mostly derived from dehydration of C_5 or C_6 (poly)sugars, have emerged as the promising platform chemicals in selective transformations for the following: (1) benzene derivatives by the Diels–Alder reaction with dienophiles;[2] (2) levulinic acid, γ-valerolactone, and their derivatives;[3] (3) higher-energy-density fuel intermediates bearing higher carbon numbers (chain extension) derived from coupling with other chemicals.[4] In particular, 5-hydroxymethylfurfural (HMF), a selective hydrolysis product from C_6 sugars, has been identified as a versatile intermediate for top-value-added chemicals, thanks to various functional groups possibly derived from the 2,5-positioned hydroxyl and aldehyde groups in HMF.[5] Glucose, the most abundant C_6 sugar, has been extensively studied for its direct conversion to HMF in ILs[6] and biphase systems[7] catalyzed by Lewis and Brønsted acids, with typically moderate to high yields of 40–80%. Most recently, bifunctional catalysts consisting of superhydrophobic acid and superhydrophilic base were applied for the glucose-to-HMF conversion, achieving the HMF yield up to 95% in a THF–DMSO mixed solvent at 100 °C for 10 h.[8] Fructose has been proposed as the key intermediate involved in the glucose-to-HMF conversion process,[9] whereas the direct dehydration of fructose to HMF is facile and highly efficient. High to quantitative yields and selectivity of HMF from fructose were achieved in organic solvents (e.g., DMSO),[10] ionic liquids (ILs),[9,11] and even in water,[12] with or without catalysts.

In view of the facile fructose-to-HMF route, the development of an effective glucose-to-fructose isomerization process has been of great interest. In this context, heterogeneous acidic zeolite catalysts have been extensively studied for isomerization of glucose to fructose.[13,14] Specifically, Davis et al. showed that Sn or Ti modified large-pore zeolite (beta zeolite) was an effective Lewis acid catalyst for glucose-to-fructose isomerization in water: a product containing 46% glucose, 29% fructose, and 8% mannose was obtained after reacting a 45 wt % glucose solution catalyzed by Sn-Beta for 60 min at 110 °C.[13] Enhanced fructose yield from glucose was achieved by Riisager et al. using large-pore zeolite Y, especially H-USY (Si/Al = 6), through the glucose–methyl fructoside–fructose strategy: a product containing 28% glucose, 55% fructose, and 4% methyl fructoside was obtained at 120 °C by a stepwise reaction.[14] This novel reaction pathway involves glucose isomerization to

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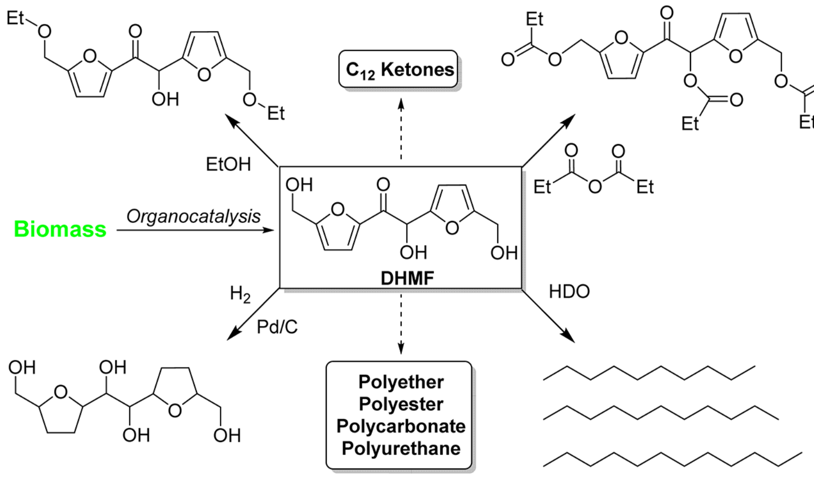


Figure 1. DHMF as a proposed new C_{12} "platform chemical" for renewable chemicals, materials, and biofuels.

fructose and subsequent etherification to methyl fructoside in methanol, followed by hydrolysis to reform fructose after water addition.

In addition to the widely studied metal-based catalyst systems, the application of *organocatalysis* in biomass conversion and upgrading has also come to light recently, showing the potential of using relatively non- or less toxic, more environmentally benign, atom-economical, and more sustainable catalysis for biorefining.[15] For instance, we recently demonstrated that furaldehydes (e.g., furfural, 5-methylfurfural, and HMF) undergo benzoin-condensation-type self-coupling in the presence of an *N*-heterocyclic carbene (NHC) catalyst under mild conditions.[15b] Using a room-temperature (RT) ionic liquid, 1-ethyl-3-methylimidazolium acetate ([EMIM]-OAc), where 1-ethyl-3-methylimidazol-2- ylidene ([EMIM] NHC) exists in an equilibrium with [EMIM]OAc and is stabilized by HOAc, HMF was readily dimerized to C_{12} 5,5′-dihydroxymethyl furoin (DHMF) in high conversion and good isolated yield.[15c] An understanding of the mechanism and catalytically active species for the [EMIM]OAc-promoted HMF self-coupling led to a more effective HMF upgrading process that uses a discrete, stable NHC, 1,3,4-triphenyl-4,5-dihydro-1H-1,2,4-triazol-5-ylidene (TPT), the process of which afforded DHMF in an isolated yield up to 95% with 1 mol % of TPT in a solvent-free process at 60 °C for 1 h.[15b]

Compared with HMF, DHMF is a higher-energy-density and perhaps more versatile, C_{12} "platform chemical", featuring 12 carbons, 3 hydroxyl groups, 2 substituted furan rings, and 1 carbonyl group (Figure 1). As a C_{12} fuel intermediate, DHMF has been converted to oxygenated diesels by hydrogenation, etherification, and esterification or high-quality alkane fuels by hydrodeoxygenation (HDO) in water.[15b] As a furan derivative, DHMF could be potentially hydrolyzed under acidic conditions, rending C_{12} ketones after furan ring opening. In terms of producing polymeric materials, as a triol, DHMF could be (co)polymerized into various types of polymers, such as polyethers, polyesters, polycarbonates, and polyurethanes.

Despite its great potential as a promising C_{12} platform chemical, the current process to DHMF relies on the expensive HMF, which is commercially available (currently sold at ~\$37 per g) but requires further crystallization to give the sufficiently pure HMF (with a typical 70−80% recovery yield) suitable for the subsequent organocatalytic upgrading (self-coupling) process. Although a large number of catalytic processes were reported for biomass conversion to HMF, the dehydration of fructose and the isomerization of glucose have remained to be the two bottlenecks in the production of HMF, and the separation and purification methods of HMF to produce the high-purity HMF suitable for subsequent chemical transformations were barely studied.[16] Furthermore, although the HDO process catalyzed by Pt/C and $TaOPO_4$ converted DHMF to a mixture of C_{10} (27.0%), C_{11} (22.9%), and C_{12} (45.6%) linear alkanes,[15b] it is preferable to convert the C_{12} DHMF selectively to C_{12} alkanes from a viewpoint of atom efficiency. Accordingly, this work was directed at accomplishing the following three goals: (a) to investigate possible glucose isomerization to fructose by organocatalysis; (b) to establish an efficient, economical, integrated catalytic process for converting inexpensive biomass feedstocks such as fructose (currently at ~\$32 per 100 g) to DHMF through generation of the high-purity HMF intermediate; and (c) to identify a bifunctional HDO catalyst system that can convert C_{12} DHMF to n-$C_{12}H_{26}$ alkane more selectively for achieving higher atom efficiency.

■ EXPERIMENTAL SECTION

Materials, Reagents, and Methods. All syntheses and manipulations of air- and moisture-sensitive materials were carried out in flamed Schlenk-type glassware on a dual-manifold Schlenk line or in an inert gas (Ar or N_2) filled glovebox. HPLC-grade organic solvents were sparged extensively with nitrogen during filling of the solvent reservoir and then dried by passage through activated alumina (for Et_2O, THF, and CH_2Cl_2) followed by passage through Q-5-supported copper catalyst (for toluene and hexanes) stainless steel columns. Deuterated dimethyl sulfoxide (DMSO-d_6) was degassed, dried over CaH_2, filtered, and vacuum-distilled; the dried DMSO-d_6 was stored over activated molecular sieves.

NMR spectra were recorded on a Varian Inova 300 (FT 300 MHz) or a Varian Inova 400 MHz spectrometer. Chemical shifts for ^1H and ^{13}C NMR spectra were referenced to internal solvent resonances and were reported as parts per million relative to tetramethylsilane. HMF (5-hydroxymethylfurfural) and DHMF (5,5′-dihydroxymethylfuroin) were analyzed by an Agilent 1260 Infinity HPLC system equipped with an Agilent Eclipse Plus C18 Column (100 × 4.6 mm; 80/20 water/methanol, 0.6 mL/min, 30 °C) and a UV detector (284 nm). Sugar contents of the products were measured by an Agilent 1260 Infinity HPLC system equipped with a Biorad Aminex HPX-87H Column (300 × 7.8 mm; water, 0.6 mL/min, 45 °C) and a RI detector; under such conditions, possible sugars (e.g., glucose and fructose) in the reaction mixture can be well separated and quantified. Hydrodeoxygenation (HDO) reactions were carried out in a Parr 4842

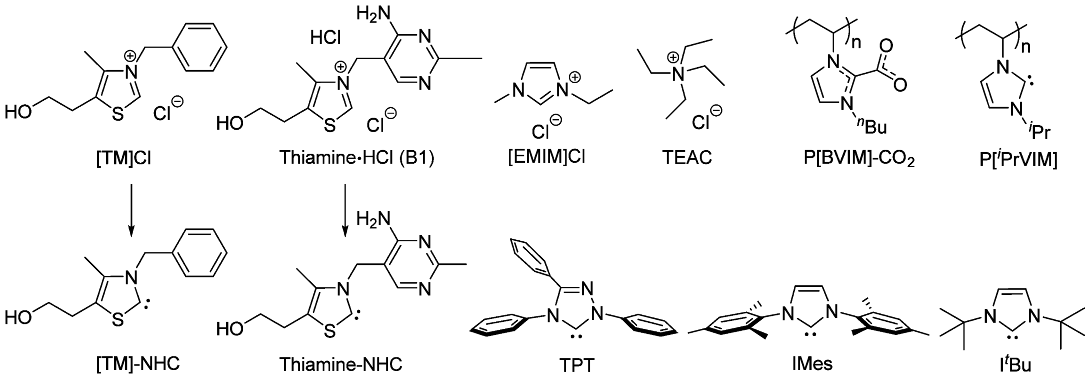


Figure 2. Structures of chloride salts and NHCs employed in this study.

Table 1. Glucose-to-Fructose Isomerization Catalyzed by NHCs[a]

entry	solvent	catalysts	temp (°C)	glucose conversion (%)	fructose yield (%)	fructose selectivity (%)	HMF yield (%)
1	[EMIM]Cl	$CrCl_2$	100	>99			58
2	[EMIM]Cl	$CrCl_2$ + 1IMes	100	97			40
3	[EMIM]Cl	$CrCl_2$ + 2IMes	100	46	15	33	5
4	[EMIM]Cl	$CrCl_2$ + 3IMes	100	63	20	32	3
5	[EMIM]Cl	IMes	100	83	16	19	
6	[EMIM]Cl	none	100	20			
7	[EMIM]Cl	IMes	80	83	13	16	
8	DMF	IMes	80	59	24	40	
9	DMSO	IMes	80	57	26	45	
10	DMSO	IMes	25	26	16	62	
11	DMSO	TPT	60	12	1	10	
12	DMSO	I-*t*-Bu	25	25	20	83	

[a]Catalyst loading: 10 mol %. Reaction time: 3 h.

pressure reactor (Parr Instrument Co.). The products were analyzed either by an Agilent 6890N GC-FID system with a Durabond DB-5 column (60 m, 0.25 mm i.d., 0.25 μm film) or by an Agilent 6890 GC-MS system equipped with a Phenomenex Zebron ZB-5 ms column (30 m, 0.25 mm i.d., 0.25 μm film). Any DHMF remained in the acetic acid after HDO was analyzed by HPLC. Elemental analyses were carried out by Robertson Microlit Laboratories (Ledgewood, NJ).

Sugars (fructose, glucose, and cellulose, Sigma Aldrich), furfural (Alfa Aesar), HMF (Acros Organics), 5-methyl-2-furaldehyde (Alfa Aesar), 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride ([TM]Cl, Alfa Aesar), thiamine·HCl (Alfa Aesar), potassium bis(trimethylsilyl)amine (KHMDS, Alfa Aesar), tetraethylammonium chloride (TEAC, Alfa Aesar), KO^{t}Bu (Acros Organics), Amberlyst-15 cation exchange resin (Acros Organics), and Dowex M43 Anion Exchange Resin (Supelco) were used as received. The ionic liquid 1-ethyl-3-methylimidazolium chloride ([EMIM]Cl, Sigma Aldrich) was dried under vacuum at 100 °C for 24 h, followed by repeated recrystallization from CH_2Cl_2 and hexanes at room temperature. Catalysts for HDO reactions, including Pd/C (10 wt % Pd on activated carbon, wet support, Sigma Aldrich), La$(OTf)_3$ (Alfa Aesar), were used as received. NHCs (*N*-heterocyclic carbenes), 1,3-ditert-butylimidazol-2-ylidene (I^{t}Bu, TCI America), and 1,3-bis(2,4,6-trimethylphenyl)-1,3-dihydro-2*H*-imidazole-2-ylidene (IMes, Sigma Aldrich) were used as received. Literature procedures were used to prepare 1,3,4-triphenyl-4,5-dihydro-1*H*-1,2,4-triazol-5-ylidene (TPT).[17] [TM]-NHC and thiamine-NHC were preformed through deprotonation of [TM]Cl and thiamine·HCl by KHMDS in THF, followed by extensively washing with hexanes to remove an excess amount of KHMDS. Polymeric NHC precursor P[BVIM]-CO_2 and polymeric NHC P[^{i}PrVIM] (Figure 2) were synthesized from their respective bromide salts following literature procedures.[18]

Glucose Isomerization to Fructose Catalyzed by NHCs. In a typical reaction, 20 mg of glucose was loaded into a 5 mL vial, to which 3.3 mg of IMes (10 mol % relative to glucose) in 0.5 mL dry DMSO was added. After it was stirred at room temperature for 3 h, the solution was quenched and diluted by 25 mL of water for an HPLC test. For reactions carried in ILs, glucose and fructose contents were measured by HPLC analysis (RI detector) after the diluted ILs phase passing through the cation and anion exchange columns to discharge ILs.

Integrated Three-Step Process of Fructose Conversion to C_{12} Alkane Fuel. Experimental procedures were briefly described herein, and detailed descriptions for each step were included in the Supporting Information. In the first step, the commercial fructose was converted to the high-purity HMF by a semicontinuous process followed by crystallization. For the semicontinuous extraction of HMF by the THF/[TM]Cl biphasic system, 2.0 g of fructose was mixed with 10 g of [TM]Cl in a 75 mL pressure glass reactor, to which 20 mL of THF was added. The reactor was capped and heated at 120 °C for 1.5 h under stirring. When the glass reactor was cooled to room temperature after the reaction, the THF phase was collected. For each of the further 9 batches, 2.0 g of fructose and 20 mL of THF were loaded to the reactor, which was capped and heated at 120 °C for 1 h. The THF phases obtained were combined and decolored by activate carbon. Analysis of the THF phases by HPLC showed HMF was formed in good purity (>99% by HPLC), perhaps sutiable for some applications without further purification, but in this work, HMF was subsequently isolated as crystals according to the following procedures. THF was removed by evaporation under vacuum, and the remaining liquid product was redissolved in toluene and crystallized to afford HMF needle crystals. A typical yield for the isolated high-purity, crystalline HMF was about 30–36%, depending on the reaction scale.

In the second step, the purified HMF was upgraded into DHMF catalyzed by TPT or in situ-generated [TM] NHC. The HMF umpolung catalyzed by TPT was performed similarly as previously reported.[15] HMF (3.0 g, 24 mmol) was premixed with [TM]Cl (0.60 g, 10 mol % to HMF) and KO^{t}Bu (0.40 g, 15 mol % to HMF) in a 20 mL vial. The sealed vial was placed in a temperature-controlled orbit shaker (80 °C, 300 rpm) and heated for 3 h. The crude product was purified by silica-gel chromatography. After removing the solvent under vacuum, DHMF (1.6 g) was isolated in 53% yield. However, the same reaction catalyzed by TPT (0.7% mol) achieved a high yield of 93%.

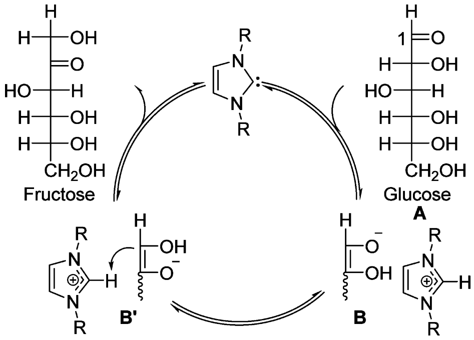
In the third step, DHMF was converted to n-$C_{12}H_{26}$ alkane fuel by HDO. DHMF (0.25 g, 0.99 mmol) was dissolved in 40 mL of glacial acetic acid and transferred to a Parr pressure reactor. To this reactor was added water-wetted Pd/C (0.12 g, ~12 mol % Pd relative to DHMF) and $La(OTf)_3$ (0.25 g, 43 mol % relative to DHMF). The reactor was purged with H_2 for 15 min and heated at 250 °C for 16 h under 300 psi H_2. After completion of the reaction, an aliquot was analyzed by GC-MS, GC-FID, and HPLC. To separate the HDO products, the acetic acid solution was concentrated and extracted by hexanes; the extracts were dried by anhydrous $MgSO_4$, and the solvent was removed under vacuum. The resulting oil product was subjected to elemental analysis.

■ RESULTS AND DISCUSSIONS

Step 1: Semi-Continuous Organocatalytic Process for High-Purity HMF Production. *Organocatalyzed Glucose-to-Fructose Isomerization.* In view of facile conversion of fructose to HMF, at the outset of this project we sought to develop organocatalyzed isomerization of glucose to fructose, thus possibly enabling conversion of glucose to HMF via organocatalysis. This possible route was prompted by our recent study, which revealed that NHCs (e.g., IMes) actually poisoned the $CrCl_2$ catalyst for the glucose-to-HMF conversion in [EMIM]Cl.[19] When a stoichiometic amount IMes (1 equiv to $CrCl_2$) was added, HMF yield decreased from 58% to 40% (Table 1, entries 1 and 2); further addition of IMes led to complete catalyst poisoning toward HMF production. Alternatively, we observed up to 20% of fructose yield and 32% fructose selectivity from glucose when a superstoichiometic amount (2 or 3 equiv to $CrCl_2$) of NHCs was added (entries 3 and 4). Control experiments (entries 1, 5, and 6) clearly showed the following results: (1) the glucose-to-fructose isomerization was not achieved in the IL alone (entry 6); (2) in the presence of $CrCl_2$, the isomerization was achieved in high efficiency, but with a faster rate for further fructose dehydration to HMF, the overall reaction afforded HMF in 58% yield but no fructose (entry 1); and (3) IMes catalyzed the isomerization in [EMIM]Cl while impeding fructose dehydration to HMF, thus forming fructose in 16% yield but no HMF (entry 5). Although there was no further dehydration of fructose to HMF, the fructose selectivity was only 19%.

In the search for ways to possibly increase the fructose yield and selectivity, we varied the temperature, solvents, and NHC catalysts. It was revealed that under the same conditions (10 mol % IMes, 80 °C, 3 h), fructose yield increased from 13% to 24% and 26% by changing the IL [EMIM]Cl to organic solvents DMF and DMSO, with an increase in fructose selectivity from 16% (entry 7) to 40% and 45%, respectively (entries 8 and 9). Interestingly, this isomerization can even be carried out at RT (entry 10), achieving a similar fructose yield (16%) but relatively high fructose selectivity (62%). For other types of NHCs, the weaker base TPT was unable to catalyze the glucose-to-fructose isomerization in high efficiency (entry 11), although the stronger base I-*t*-Bu rendered a higher fructose yield (20%) and selectivity (83%) (entry 12). Accordingly, this glucose-to-fructose isomerization catalyzed by NHCs is proposed to follow the base-catalyzed isomerization mechanism (Scheme 1).[13b] A fast mutarotation from α-D-glucose to β-D-glucose with a molar ratio of 1:1.8 was observed upon the initial mixing of I-*t*-Bu with glucose, through the open-chain form (**A**) of glucose. Deprotonation of the C-2 proton of **A** by an NHC base affords the enolate intermediate (**B**). Through further proton transfer steps involving enolate intermediates, fructose is formed and the NHC catalyst is regenerated (Scheme 1). Hence, in this NHC-catalyzed glucose-to-fructose isomerization, the yield and selectivity of fructose are strongly related to the basicity of NHCs. As expected, besides TPT, other weaker bases (e.g., NaOH and DBU) achieved only less than 5% of fructose yield under similar conditions. Noteworthy is that this reaction cycle is also *reversible* under the NHC-catalyzed conditions: when starting from fructose, a 30% glucose yield and a 61% glucose selectivity were observed at 60 °C for 1 h catalyzed by IMes.

Scheme 1. Proposed Proton Transfer Mechanism for Isomerization of Glucose to Fructose Catalyzed by NHCs



Recently, Chi et al. reported an interesting finding that NHCs can catalyze the retro-benzoin condensation of glucose to form acyl anion intermediates through C−C bond cleavage of glucose.[20] In their case, glucose was used as the acyl anion resource for subsequent Stetter reaction with chalcone. A high yield of Stetter product (80%) from the glucose and chalcone reaction was formed, which was catalyzed by in situ-generated thiazolium-based NHCs in 30 min at 130 °C under microwave irradiation. Interestingly, they revealed that the imidazolium-based NHCs were not effective for the retro-benzoin condensation of glucose under their reaction conditions, and the current results showed that the imidaozlium-based NHCs such as I-*t*-Bu and IMes are effective for catalyzing the glucose-to-fructose isomerization even at room temperature.

HMF from Biomass (Fructose, Glucose, and Cellulose). To explore inexpensive alternatives to commonly used imidazolium-based ILs for biomass conversion to HMF, we found that [TM]Cl, an analog of thiamine (Vitamin B1), which is about 3.5 times less expensive than the typically employed IL [EMIM]Cl, can catalyze fructose conversion to HMF in high efficiency. Although the melting point of [TM]Cl (142−144 °C) is well above 100 °C, a homogeneous solution is readily formed from the mixture of fructose and [TM]Cl upon heating to 100 °C, affording HMF in 56% yield after heating the mixture at this temperature for 1 h (Table 2, entry 2). At higher temperatures of 120 and 130 °C, the HMF yield increased to 72% (entry 3) and 68% (entry 4), respectively, which was comparable with that achieved by [EMIM]Cl (entry 1). As for the thiamine·HCl (B1) catalyzed fructose-to-HMF conversion, no homogeneous solution was formed by heating the mixture of thiamine·HCl and fructose, and no HMF was produced. However, by adding water (50 wt % relative to thiamine·HCl) to increase fructose solubility in thiamine·HCl, a moderate HMF yield of 56% was obtained at 120 °C after 1 h (entry 5).

Table 2. Biomass Conversion to HMF by an Organic or Metal Catalyst[a]

entry	biomass	ILs	catalyst	temp (°C)	time (h)	HMF yield (%)
1	fructose	[EMIM]Cl		100	1	74
2	fructose	[TM]Cl		100	1	56
3	fructose	[TM]Cl		120	1	72
4	fructose	[TM]Cl		130	0.5	68
5[b]	fructose	thiamine·HCl		120	1	56
6	glucose	[EMIM]Cl	$CrCl_2$	100	3	58
7	glucose	[TM]Cl	$CrCl_2$	120	1	51
8	glucose	[TM]Cl	$CrCl_3 \cdot 6H_2O$	120	1	45
9	glucose	[TM]Cl	$CrCl_3 \cdot 6H_2O$	130	0.5	47
10	cellulose	[TM]Cl	$CrCl_3 \cdot 6H_2O$	140	1	1
11[c]	cellulose	TEAC	$CrCl_3 \cdot 6H_2O$	130	0.5	27
12[d]	cellulose	TEAC	$CrCl_3 \cdot 6H_2O$	130	0.5	42

[a] Biomass/ILs 1/5 wt %, 10 mol % catalyst loading. [b] 50 wt % water relative to thiamine·HCl was added. [c] Cellulose/ILs 1/10 wt %. [d] Cellulose/ILs 1/10 wt %, 50 wt % water relative to cellulose was added.

For glucose conversion to HMF, an isomerization catalyst (e.g., $CrCl_2$, $CrCl_3 \cdot 6H_2O$) is required. In the presence of 10 mol % of $CrCl_2$, HMF was obtained in 51% yield from glucose in [TM]Cl at 120 °C after 1 h (entry 7), which was comparable with the glucose conversion in [EMIM]Cl at 100 °C after 1 h (entry 6). A lower HMF yield (45%) was achieved by $CrCl_3 \cdot 6H_2O$ (entry 8), whereas a slightly higher HMF yield (47%) was obtained within 0.5 h by increasing the reaction temperature to 130 °C (entry 9). Direct conversion of cellulose to HMF in [TM]Cl and TEAC was also investigated. Although a low HMF yield was observed with [TM]Cl and $CrCl_3 \cdot 6H_2O$ even at 140 °C (entry 10), 27% of HMF was achieved with $CrCl_3 \cdot 6H_2O$ in TEAC at 130 °C after 0.5 h (entry 11). Addition of water (50 wt % relative to cellulose) enhanced HMF yield to 42% (entry 12), presumably because water facilitated the initial hydrolysis of cellulose to reducing sugars.

High-Purity HMF from Fructose by Semicontinuous Extraction. On the basis of the above established one-pot conversion of fructose to HMF in [TM]Cl, semicontinuous extraction between the organic and [TM]Cl phases was adopted to separate HMF from [TM]Cl. THF was selected as the organic solvent, considering the high solubility of HMF and low solubility of [TM]Cl in this solvent. Moreover, THF can continuously remove water generated from fructose dehydration to HMF, thus suppressing HMF rehydration to organic acids and humins. During the initial five batches, HMF yield extracted by THF gradually increased to 70%, after which it remained nearly constant (Figure 3). It is noteworthy that this semicontinuous process for HMF production from fructose is efficient and robust: (1) 72% HMF yield and 74% of HMF selectivity were achieved over the 10 batch runs, and 90% of HMF formed was extracted by THF; (2) no apparent loss of the HMF yield was observed even after 10 batches, with a consistent HMF yield after the fifth batch; and (3) for each of subsequent batches, fructose and THF were loaded to the reactor, and no more [TM]Cl was needed. After completion of the reaction, the product HMF was isolated, and the collected THF can be recycled. Overall, this semicontinuous process is efficient and economical, representing a net transformation of the inexpensive feedstock fructose to the high-value platform chemical HMF, which is currently about 100 times more expensive than the starting fructose.

The above semicontinuous process in [TM]Cl and extraction with THF was also applied to the glucose-to-HMF conversion in the presence of $CrCl_3 \cdot 6H_2O$ (10 mol % relative to glucose).

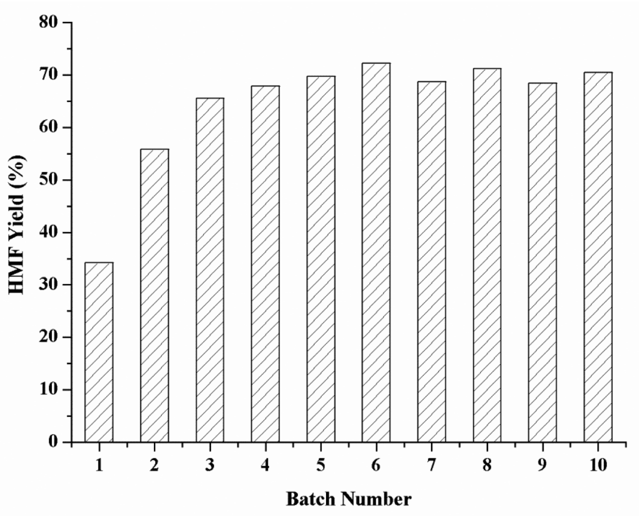


Figure 3. HMF yields obtained from fructose conversion in [TM]Cl at 120 °C for 1 h (1.5 h for the first batch) by semicontinuous extraction with THF. Data were shown as the average value of at least two runs with typical errors within ±3%. Lower yields of the initial two batches were presumably due to absorption of HMF by [TM]Cl until it reaches a saturation point.

During the initial four batches, HMF yield gradually reached the maximum at 50%, after which it decreased to 44% at the sixth batch (Figure 4), presumably due to the Cr catalyst loss upon repeated extractions with THF. After six batches, HMF was obtained from glucose in 49% yield and 52% selectivity, and 92% of HMF formed was extracted by THF. When EtOAc was used as the organic solvent, HMF yield (31%) was consistently lower than that extracted by THF, although no loss of catalyst activity was observed after the fifth batch. For the cellulose-to-HMF conversion, semicontinuous extraction of HMF by THF/TEAC gave a low HMF yield. Nevertheless, extraction with water/EtOAc (1/4 v/v) after the reaction achieved 39% of HMF yield and 94% of HMF recovery.

The HMF product obtained from fructose dehydration by the above-described semicontinuous extraction was sufficiently pure (>99% by HPLC, Figure S2), presumably sutiable for most applications without further purification. However, there were still a small amount of impurities (e.g., [TM]Cl, H_2O, and organic acids) present in the product according to ^{1}H NMR analysis (Figure 6a). To produce the spectroscopically and

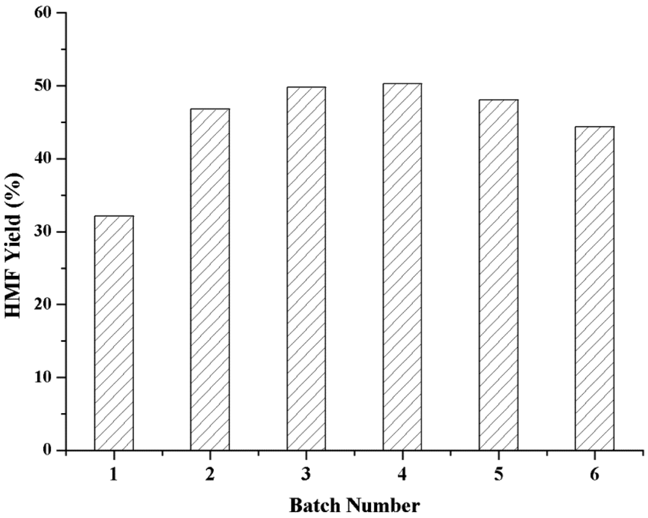


Figure 4. HMF yields obtained from glucose conversion in [TM]Cl/$CrCl_3·6H_2O$ (10 mol %) at 130 °C for 0.5 h (1 h for the first batch) by semicontinuous extraction with THF. Data were shown as the average of at least two runs with errors within ±3%.

analytically pure HMF, we investigated two purification routes. This first route was extraction with diethyl ether and subsequent solvent removal under vacuum, affording the purer HMF (54% yield) as dark yellow liquid (Figure 5, route 1), but ^1H NMR analysis showed the presence of only a tiny amount of an impurity appeared as a broad signal at ~2.8 ppm (Figure 6b). The second route was recrystallization of the crude HMF product (Figure 5, route 2). Screening of solvents suitable for recrystallization led to toluene, which yielded the analytically and spectroscopically pure HMF as needle crystals (Figure 6c). In this purification route, the crude HMF obtained from the above semicontinuous process was dissolved in hot toluene (50−60 °C) and crystallized in a freezer overnight, affording the pure HMF as needle crystals (yield 30−36%). A step of decoloration with activated carbon can be added to treat the crude HMF before crystallization. The crystallized HMF was used for further umpolung to DHMF catalyzed by either TPT or other NHC catalysts.

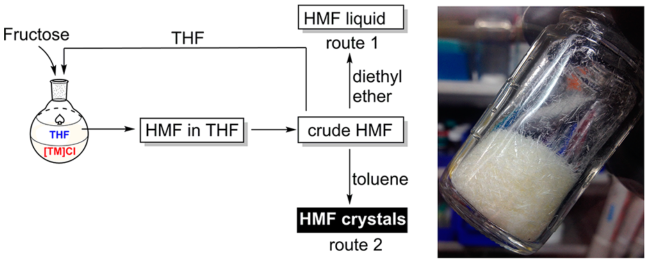


Figure 5. Integrated process for the production of the spectroscopically and analytically pure HMF from fructose catalyzed by [TM]Cl.

Step 2: HMF Coupling to C_{12} DHMF by Organocatalysis. We have previously shown that furaldehydes such as furfural, 5-methylfurfural, and HMF can be efficiently self-coupled in a 100% atom-economical manner into furoin, 5,5′-dimethylfuroin (5,5′-DMF), and C_{12} furoin (DHMF), respectively, through an organocatalytic umpolung process (i.e., self-condensation) involving an enol intermediate (Scheme 2).[15] In this study, we explored the NHC catalysts derived from readily available, inexpensive precursors, including [TM] NHC, thiamine NHC, and poly(NHC)s. The more expensive, proven efficient TPT catalyst was also used for comparison and for examining the purity and suitability of the HMF produced from fructose by the current semicontinuous process. The results of this investigation were summarized in Table 3.

The results showed that TPT is still the most efficient catalyst. With a low catalyst loading of 0.70 mol % at 60 °C for 1 h, the HMF self-condensation in neat gave DHMF in 93% isolated yield (Table 3, entry 1). The catalyst loading can be further lowered to only 0.10 mol %, whereas DHMF can still be isolated in high yield (91%, entry 2). These results clearly demonstrated that the HMF produced from fructose by our semicontinuous process was in high purity and readily suitable for this critical chain-extension coupling step by organocatalysis.

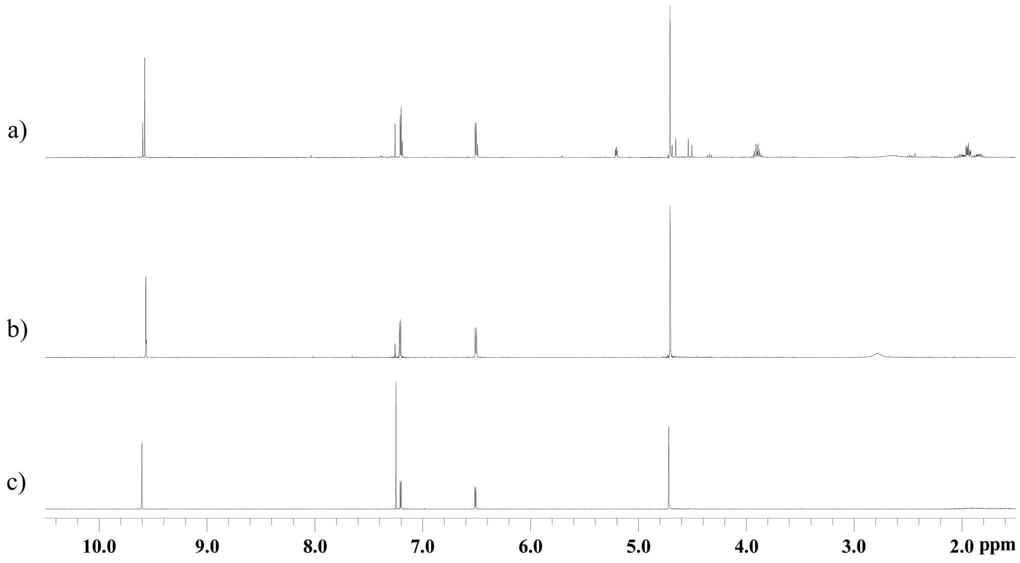
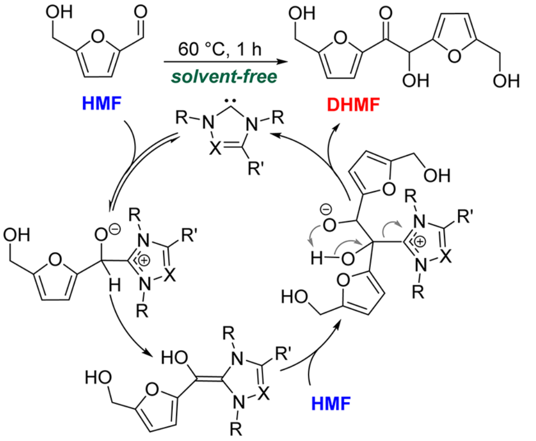


Figure 6. ^1H NMR ($CDCl_3$) of HMF (*δ* 9.61, 7.21, 6.52, 4.72 ppm) by two different purification routes: (a) crude HMF; (b) HMF after extraction with diethyl ether (cf., Figure 5, route 1); and (c) HMF needle crystals after recrystallization from toluene (cf., Figure 5, route 2).

Scheme 2. Solvent-Free NHC-Catalyzed Self-Condensation of HMF to DHMF and Depicted Umpolung Catalytic Cycle

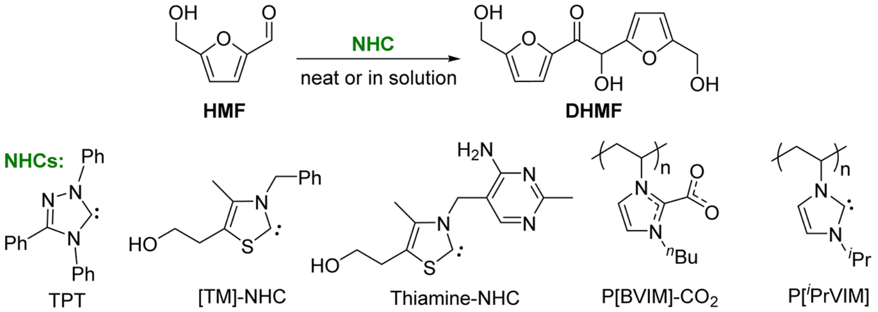


In comparison, [TM]-NHC produced DHMF in only moderate isolated yield of 60%, even with a 10 mol % catalyst loading (entry 3). Using the in situ-generated [TM]-NHC through deprotonation of [TM]Cl by KO-*t*-Bu, a comparable DHMF yield (53%, entry 4) was obtained after purification by silica-gel chromatography. However, thiamine-NHC exhibited no catalytic activity toward DHMF formation under similar conditions (entry 5). We also employed poly(NHC)s as catalysts for HMF coupling. Specifically, the masked poly(NHC), P[BVIM]-CO_2, and the preformed poly(NHC), P[*i*-PrVIM], produced DHMF in only 32% and 18% yields (by ^1H NMR), respectively. These results were sharply different from those obtained by adopting poly(NHC)s to catalyze the umpolung of benzaldehyde, in which up to 92% yield of benzoin was achieved at room temperature for 24 h.[18b] This difference can be attributed to the acidic proton in the hydroxyl group of HMF which impedes the catalytic activity of poly(NHC)s. Supporting this reasoning, furfural behaved much like benzaldehyde in the umpolung reaction catalyzed by NHCs. For example, with a low loading of [TM]-NHC (1 mol %), furfural was readily coupled to furoin in 86% isolated yield, as compared to a much lower yield of 60% in the case of the HMF umpolung reaction, under otherwise identical conditions.

Step 3: HDO of DHMF to n-$C_{12}H_{26}$ Alkane Fuel by Metal–Acid Tandem Catalysis. Previously, we reported a method of converting DHMF to a mixture of linear alkanes consisting of C_{10} (27.0%), C_{11} (22.9%), and C_{12} (45.6%) using a bifunctional catalyst system containing Pt/C and $TaOPO_4$ in water under 500 psi H_2 at 300 °C.[15b] Recently, a highly selective HDO process utilizing acetic acid, Pd/C and $La(OTf)_3$ was developed, which converted cross-aldol condensation products (e.g., furan aldehydes and enolizable ketones) into their corresponding alkanes under relatively mild conditions (200 °C and 300 psi H_2).[21] In light of this important development, we employed this metal/acid (Brønsted + Lewis acid) catalyst system, Pd/C + acetic acid + $La(OTf)_3$, for the HDO of DHMF, the results of which study were shown in Table 4.

The initial HDO process carried out at 200 °C and 300 psi H_2 gave a selectivity of 26% for n-$C_{12}H_{26}$ and 1.5% for n-$C_{11}H_{24}$, and the HDO products contained 31% alkanes (including branched and cyclic C_{11} and C_{12} alkanes) and 69% oxygenated compounds (entry 1). Although a low selectivity of n-$C_{12}H_{26}$ was obtained from this trial run, the majority of the oxygenated compounds were found to be C_{12} esters and ketones, which could be further converted to C_{12} alkanes under modified conditions. Hence, two reaction parameters, H_2 pressure and reaction temperature, were varied. By increasing the H_2 pressure from 300 to 500 psi, even lower n-$C_{12}H_{26}$ selectivity (22%) was obtained (entry 2). On the other hand, increasing the reaction temperature from 200 to 250 °C while keeping the H_2 pressure the same (300 psi) resulted in a significant increase of the n-$C_{12}H_{26}$ selectivity from 26% to 64% (entry 3), under otherwise identical conditions. The fuel produced at this temperature contained 78% alkanes and 22% oxygenated compounds (Figure 7), and the elemental analysis showed 84% C, 11% H, and 5.0% O. Using 5,5′-DMF as a comparable substrate to DHMF, the HDO process at 200 °C and 300 psi H_2 for 16 h afforded alkane fuel with a selectivity of 66% for n-$C_{12}H_{26}$ (43% yield) and 1.5% for n-$C_{11}H_{24}$ without the formation of C_{12} esters (entry 4, Figure S5). Meanwhile, the

Table 3. DHMF Yields from the HMF Umpolung Reaction Catalyzed by NHCs



entry	solvent	NHCs	NHC loading (mol %)	temp (°C)	time (h)	DHMF (%)
1	none	TPT	0.7	60	1	93
2	none	TPT	0.1	60	3	91
3	toluene	[TM]-NHC	10	80	3	60
4	none	in situ [TM]-NHC	10	80	3	53
5	toluene	thiamine-NHC	10	60	3	0
6	THF	P[BVIM]-CO_2	10	80	3	32
7	THF	P[*i*-PrVIM]	10	80	3	18

Table 4. Analytical Results of Liquid Fuels after HDO in Acetic Acid[a]

entry	furoins	temp (°C)	pressure (psi)	n-$C_{11}H_{24}$ (%)	n-$C_{12}H_{26}$ (%)	alkanes (%)	oxygenated (%)	isolated fuels C (%)	isolated fuels H (%)	isolated fuels O (%)
1	DHMF	200	300	1.5	26	31	69	76	11	13
2	DHMF	200	500		22	25	75	73	10	17
3	DHMF	250	300	5.7	64	78	22	84	11	5.0
4	5,5′-DMF	200	300	1.5	66	75	25	83	13	4.0

[a] Reaction conditions: reaction time, 16 h; solvent, acetic acid, 40 mL; catalysts, Pd/C + $La(OTf)_3$. In all cases, furoins were completely converted. Branched and cyclic C_{11} and C_{12} were included in the calculation of alkane selectivity. 5,5′-DMF = 5,5′-dimethylfuroin.

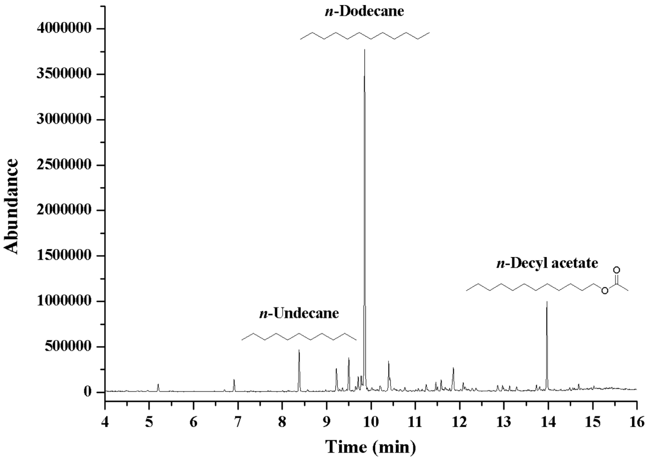


Figure 7. GC-MS chromatogram of the crude products produced by the HDO of DHMF in acetic acid catalyzed by Pd/C+ $La(OTf)_3$ at 250 °C under 300 psi H_2 for 16 h (Table 4, run 3).

isolated fuel exhibited similarly high C and H molar ratios (83% and 13%) and a correspondingly low O ratio of 4.0%.

■ CONCLUSION

In summary, we have developed an integrated catalytic process for biomass conversion and upgrading to C_{12} DHMF and subsequently to n-$C_{12}H_{26}$ alkane by organocatalysis and subsequent metal−acid tandem catalysis. The first step of the process involves semicontinuous organocatalytic conversion of biomass (fructose, in particular) to the high-purity HMF. In this step, NHCs were found to be effective in catalyzing glucose-to-fructose isomerization, even at room temperature. Particularly, treatment of glucose with 10 mol % of I-*t*-Bu in DMSO for 3 h afforded fructose in 20% yield with a 83% selectivity. For biomass conversion to HMF, the inexpensive [TM]Cl, a Vitamin B1 analog, was utilized for fructose and glucose dehydration to HMF, achieving a 72% HMF yield from fructose (no metal catalysts) and up to 51% yield from glucose (in the presence of additional chromium(II) or (III) catalyst) at 120 °C for 1 h. The semicontinuous extraction process developed for the HMF production from fructose is efficient and robust: a constant HMF yield of 72% was achieved over 10 batch runs. The HMF product obtained from the semicontinuous process is sufficiently pure (>99% by HPLC), presumably sutiable for most applications without further purification. On the other hand, further purification by extraction with diethyl ether gave the purer HMF (54% yield) as a liquid or by crystallization from toluene afforded the spectroscopically and analytically pure HMF as needle crystals. Overall, this semicontinuous process represents a net transformation of the inexpensive feedstock fructose to the higher-value platform chemical HMF (~100-fold price increase) as the [TM]Cl and the extraction solvent THF can be readily recycled for subsequent batch runs.

The second step of the process is the organocatalytic coupling of the C_6 HMF produced by the above semicontinuous process to C_{12} DHMF in the presence of an NHC catalyst. Among several types of NHCs investigated for this coupling reaction, TPT was proven to be most effective, achieving 93% or 91% isolated yield of DHMF in the presence of 0.70 mol % or 0.10 mol % TPT at 60 °C for 3 h (in a solvent-free process). The [TM]Cl-derived NHC is less effective, affording DHMF in 60% isolated yield with a 10 mol % catalyst loading. The two poly(NHC)s investigated are least effective, producing DHMF in much lower yields of only 18−32%. Overall, the TPT-catalyzed HMF self-condensation (chain-extension) process to DHMF can be regarded as a greener process, with 100% atom-economy, solvent-free operation, and near quantitative yield from an organocatalytic reaction.

The third step of the process is the hydrodeoxygenation of C_{12} DHMF to linear alkanes as a potential high-quality hydrocarbon fuel. With the metal (Pd/C)/acid ($La(OTf)_3$) catalyst system, the HDO of DHMF in acetic acid at 250 °C and 300 psi H_2 for 16 h afforded liquid hydrocarbon fuel (78% alkanes) with a 64% selectivity to n-$C_{12}H_{26}$ and an overall C/H/O % ratio of 84/11/5.0.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed experimental procedures and additional figures. This information is available free of charge via the Internet at http://pubs.acs.org/.

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Notes

The authors declare no competing financial interest.

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