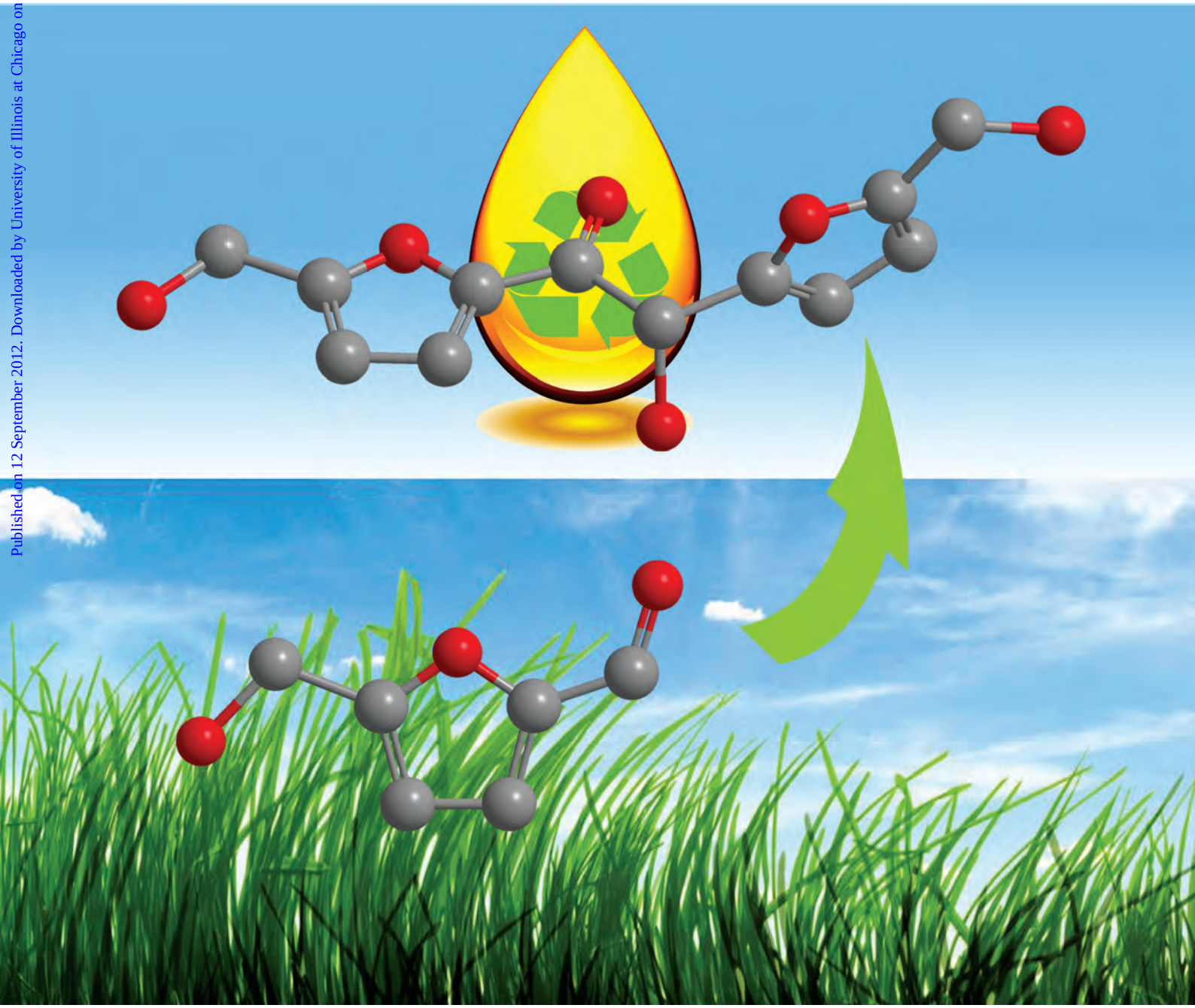
Green Chemistry

Cutting-edge research for a greener sustainable future

www.rsc.org/greenchem

Volume 14 | Number 10 | October 2012 | Pages 2649–2952



ISSN 1463-9262

RSC Publishing

COVER ARTICLE

Chen *et al.*

Organocatalytic upgrading of the key biorefining building block by a catalytic ionic liquid and N-heterocyclic carbenes

Green Chemistry

Cite this: *Green Chem.*, 2012, **14**, 2738

www.rsc.org/greenchem

PAPER

Organocatalytic upgrading of the key biorefining building block by a catalytic ionic liquid and N-heterocyclic carbenes

Dajiang (D. J.) Liu,[a,b] Yuetao Zhang[a] and Eugene Y.-X. Chen*[a]

Received 10th August 2012, Accepted 4th September 2012
DOI: 10.1039/c2gc36265a

The present study of rapid degradation of the key biorefining building block 5-hydroxymethylfurfural (HMF) in an ionic liquid (IL), 1-ethyl-3-methylimidazolium acetate ([EMIM]OAc), has led to highly selective and efficient upgrading of HMF to 5,5′-di(hydroxymethyl)furoin (DHMF), a promising C_{12} kerosene/jet fuel intermediate. This HMF upgrading reaction is carried out under industrially favourable conditions (*i.e.*, ambient atmosphere and 60–80 °C), catalyzed by N-heterocyclic carbenes (NHCs), and complete within 1 h; this process selectively produces DHMF with yields up to 98% (by HPLC or NMR) or 87% (unoptimized, isolated yield). Mechanistic studies have yielded four lines of evidence that support the proposed carbene catalytic cycle for this upgrading transformation catalyzed by the acetate IL and NHCs.

Introduction

Owing to their unique ability to dissolve lignocellulosic biomass[1] and related carbohydrates[2] under relatively mild conditions, plus several other concurrent advantages (*e.g.*, as designable and recyclable solvents with low volatility and toxicity), ionic liquids (ILs) such as 1-alkyl(R)-3-methyl(M)imidazolium (IM) chloride salts, [RMIM]Cl, have attracted rapidly growing interest,[3] particularly in the pursuit of renewable energy and sustainable chemicals from plant biomass.[4] For instance, ILs enabled homogenous hydrolysis of cellulose to sugars in high to quantitative conversion, with[5] or without[6] additional catalysts, and catalyzed conversion of glucose or cellulose into the biomass platform chemical 5-hydroxymethylfurfural (HMF),[6,7] a key and versatile biorefining building block for value-added chemicals and liquid fuels.[8] Upgrading of HMF can be achieved by acid-catalyzed etherification,[9] metal-catalyzed transformations such as hydrogenation/hydrogenolysis into 2,5-dimethylfuran,[10] a liquid fuel with a 40% higher energy density than ethanol, and aldol condensation with enolizable organic compounds followed by dehydration/hydrogenation into C_9 to C_{15} liquid alkanes (fuels),[11] thus upgrading it into the kerosene/jet fuel range (C_{12} to C_{15}). Direct coupling of two HMF molecules would make a C_{12} biofuel intermediate, but HMF or furfural cannot undergo aldol self-condensation because they possess no α-H.[11]

The acetate-based room-temperature (RT) IL 1-ethyl-3-methyl imidazolium acetate, [EMIM]OAc, has been identified as a better solvent than chloride-based ILs for biomass solution *processing* (*i.e.*, dissolution, fractionation, and re-precipitation), due to its lower melting point, viscosity and corrosive character as well as higher loading and non-toxicity.[4a,12] However, for biomass *conversion* into sugars and HMF, the chloride-based ILs such as [RMIM]Cl (R = Et, ^{n}Bu) are preferred solvents,[6,7] and we have found that [EMIM]OAc is completely *ineffective* for the glucose (or cellulose)-to-HMF conversion.[7a] A recent report disclosed that [EMIM]OAc rapidly degrades HMF (>99% degradation at 100 °C after 8 h), but neither was the degradation mechanism given nor was the degradation product identified.[7f] We found this IL also rapidly degrades glucose (70% degradation at 100 °C after 1 h, *vide infra*). To this end, we hypothesized that the observed rapid HMF degradation in [EMIM]-OAc is likely rendered by N-heterocyclic carbene (NHC) catalysis,[13] because it is known that a low concentration of carbene exists in this IL with the basic acetate anion,[14] as demonstrated experimentally by its carbene-type reaction with elemental sulfur or selenium[15] and as a catalyst for benzoin condensation of benzaldehyde.[16] While addressing the mechanism of HMF degradation in [EMIM]OAc, we discovered that this "detrimental" degradation process can be utilized for highly efficient upgrading of HMF into a high-value biorefinery product, 5,5′-di(hydroxymethyl)furoin (DHMF)—a potential C_{12} kerosene/jet fuel intermediate, through NHC-catalyzed self-condensation enabled by this organocatalytic IL. Subsequent use of a discrete NHC (5 mol%), the Enders triazolylidene carbene TPT (1,3,4-triphenyl-4,5-dihydro-1*H*-1,2,4-triazol-5-ylidene),[17] leads to rapid (1 h), highly selective and high-yield synthesis of DHMF from HMF. The *in situ* generated NHC by treating the chloride-based IL [EMIM]Cl with an organic base also rapidly upgrades HMF to DHMF in high yield (96%).

Results and discussion

Degradation of HMF and glucose in [EMIM]OAc

HPLC monitoring of the HMF degradation in [EMIM]OAc (1 : 1 molar ratio) revealed rapid degradation of HMF even at

[a]*Department of Chemistry, Colorado State University, Fort Collins, CO 80523-1872, USA. E-mail: eugene.chen@colostate.edu; Fax: (+1) 970-491-1872*
[b]*Department of Mechanical Engineering, Colorado State University, Fort Collins, CO 80523-1301, USA*

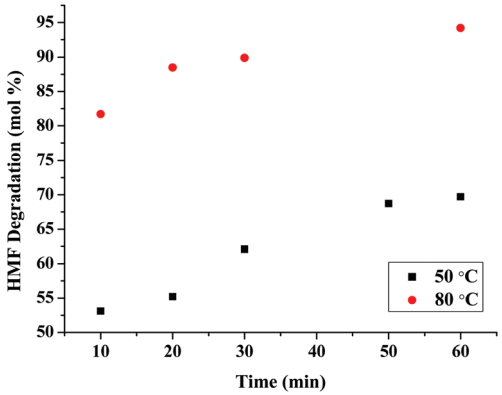


Fig. 1 Graphical profiles of HMF degradation in [EMIM]OAc (1 : 1 molar ratio) *vs.* time at two different temperatures (50 °C and 80 °C), monitored by HPLC.

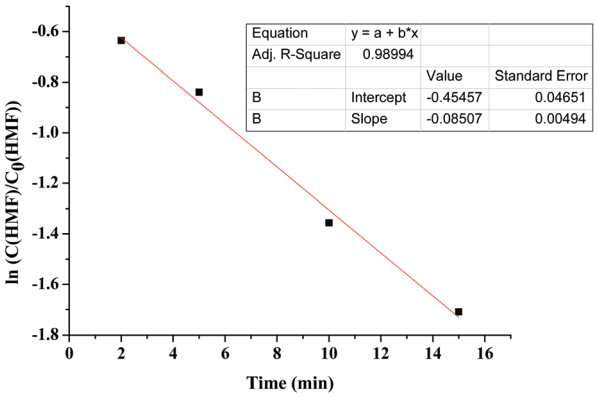


Fig. 2 The first-order plot of HMF degradation in [EMIM]OAc (1 : 1 molar ratio) at 80 °C monitored by NMR for the initial time period (2–15 min).

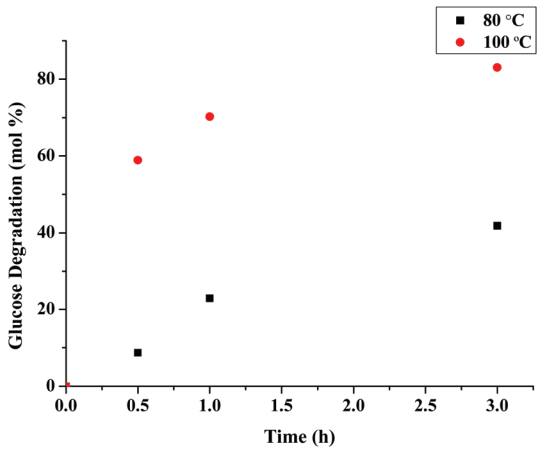


Fig. 3 Graphical profiles of glucose degradation in [EMIM]OAc at two different temperatures (80 °C and 100 °C), monitored by HPLC.

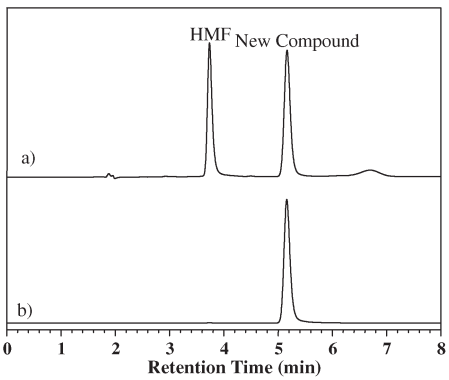


Fig. 4 Formation of a new compound as detected by HPLC from the HMF degradation reaction mixture in [EMIM]OAc at 80 °C: (a) crude sample; (b) after purification.

temperatures far below 120 °C, a typical temperature employed for biomass conversion; for example, 70% and 94% of HMF has been degraded after 1 h at 50 °C and 80 °C, respectively (Fig. 1). The degradation kinetics at 80 °C was examined with NMR by performing the degradation in DMSO-d_6 in a J. Young-type NMR tube with a 1/1 HMF/[EMIM]OAc molar ratio and using hexamethylbenzene as the internal standard. It is noted here that the results of kinetics performed in this NMR solvent containing the non-interreacting internal standard were very similar to those obtained by HPLC without this solvent and standard. A first-order kinetic plot (Fig. 2) of the initial degradation process (2–15 min) yielded a rate constant of $k = 0.085\ \text{min}^{-1}$ at 80 °C, corresponding to a degradation half-life of 8.2 min at this temperature.

Glucose also undergoes rapid degradation in [EMIM]OAc; for example, at 100 °C, glucose degraded by 70% and 83% after 1 and 3 h, respectively (Fig. 3). Interestingly, even the chloride-based IL, [BMIM]Cl, was reported to react with HMF at higher temperatures (≥200 °C), to form 1-butyl-2-(5′methyl-2′-furoyl)-imidazole, although the yield was rather low (9.3% at 250 °C).[18] This unusual product was determined by NMR and MS analysis, and the mechanism of its formation was proposed to proceed through an initial adduct formation between HMF and [BMIM]-Cl, followed by elimination of H_2O and CH_3Cl.[18]

Parallel scale-up runs of HMF degradation in [EMIM]OAc clearly showed formation of a new compound by HPLC as the predominant product (Fig. 4). Monitoring of the reaction by NMR showed a maximum yield of 72% at an HMF conversion of 86% at 80 °C (Fig. 5). Subsequent separation and purification afforded the pure compound (Fig. 4) in 50% isolated yield. This compound is stable in water and air, as it was isolated from the aqueous medium and no decomposition or oxidation was observed after exposing the solid sample to air for a week. NMR and MS data (see Experimental) clearly indicate it is a C_{12} furoin, DHMF.

The molecular structure of DHMF has been confirmed by X-ray diffraction analysis (Fig. 6). Structural data clearly show a C═O double bond for C(6) with a bond length of 1.224(7) Å and a CH–OH single bond for C(7) with a bond length of 1.420(10) Å, the latter of which is identical to the terminal CH_2–OH bond distance [*e.g.*, C(12)–O(6)H = 1.420(6) Å]. This assignment is further confirmed by the sum of the angles around C(6) (carbonyl) and C(7) (hydroxyl) carbons of 360.1° and 332.3°, for sp^2-hybridized trigonal-planar and sp^3-hybridized

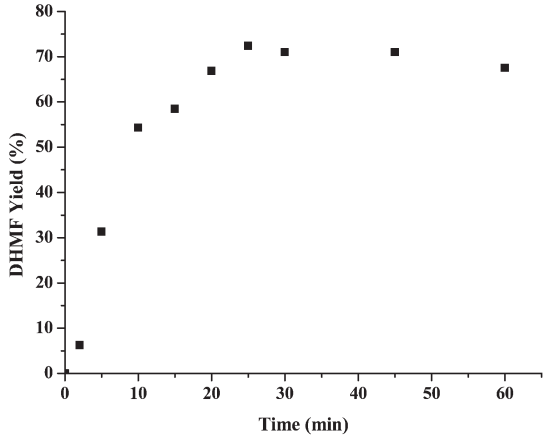


Fig. 5 DHMF yield (by NMR) as a function of HMF degradation time in [EMIM]OAc (1 : 1 molar ratio) at 80 °C.

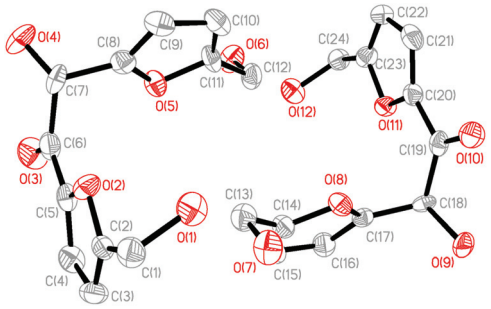
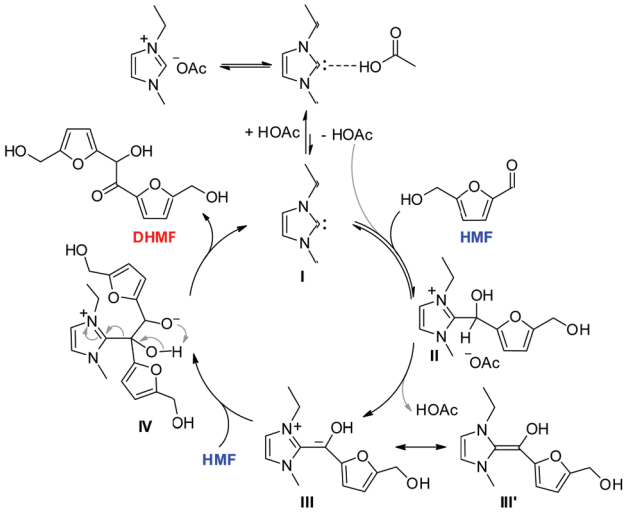


Fig. 6 X-ray crystal structure of 5,5′-di(hydroxymethyl)furoin (DHMF). Hydrogen atoms have been omitted for clarity and ellipsoids drawn at 50% probability.

tetrahedral carbon centers, respectively. There are two independent molecules with minor structural differences in the unit cell, which are associated with each other by moderate hydrogen bonds, as indicated by *d*(D–H)(O6–H6) = 0.820 Å, *d*(H···A)(H6···O12) = 1.896 Å, <D–H···A = 173.77°, and *d*(D···A) = 2.712 Å; *d*(D–H)(O7–H7) = 0.820 Å, *d*(H···A)(H7···O1) = 1.881 Å, <D–H···A = 179.19°, and *d*(D···A) = 2.701 Å.

Catalytic cycle for umpolung self-condensation of HMF to DHMF

The identification and characterization of the structure of the main product formed from the HMF degradation in [EMIM]OAc prompted us to realize that DHMF is the umpolung condensation product of HMF catalyzed by [EMIM]OAc. The catalytic cycle for this unique process enabled by the organocatalytic [EMIM]-OAc is proposed in Scheme 1. The catalyst in this carbene catalysis is 1-ethyl-3-methylimidazolin-2-ylidene carbene **I**, present in the [EMIM]OAc equilibrium that favors the ion pair form.[14–16] The early steps of the proposed elementary reactions involved in the catalysis deviate somewhat from those put forth for the NHC-catalyzed umpolung of aldehydes[13,19] and α,β-unsaturated esters,[20] due to the important role of HOAc, which co-exists with carbene **I** in the [EMIM]OAc equilibrium. Specifically, nucleophilic addition of the carbene **I** to the carbonyl



Scheme 1 Proposed catalytic cycle for umpolung self-condensation of HMF to DHMF by a catalytic IL, [EMIM]OAc.

group of HMF generates a zwitterionic tetrahedral intermediate, which is protonated by HOAc to afford a 2-(5-hydroxymethyl-2-α-hydroxyfuranyl)imidazolium acetate salt, the resting intermediate **II**.[21] Under elevated temperatures, intermediate **II** is deprotonated by the acetate anion to form a nucleophilic enaminol (**III′**). Like the Breslow intermediate involved in the benzoin reaction,[22] this enaminol is the acyl anion equivalent (**III**), thus attacking the carbonyl group of a second HMF molecule to form another tetrahedral intermediate (**IV**). Collapse of this tetrahedral intermediate, *via* proton transfer and elimination of **I**, produces DHMF and regenerates the NHC catalyst, thus closing the catalytic cycle (Scheme 1). Based on the data to-date (*vide infra*), the steps from **I** to **II** are fast (and reversible), relative to the slow step of going from **II** to **III**. This proposed overall mechanism explains well the observed catalysis for upgrading of HMF into DHMF by [EMIM]OAc and is consistent with the four lines of evidence presented as follows.

Four lines of evidence that support the proposed carbene catalysis

First, previous studies have shown that a low concentration of carbene exists in [EMIM]OAc,[14,15] which is capable of executing carbene catalysis.[16] To further confirm this point, we replaced [EMIM]OAc with 1-ethyl-2,3-dimethylimidazolium acetate, [EDMIM]OAc, in which the acidic proton at C(2) of the imidazolium ring is substituted with the methyl group. As predicted, the carbene catalysis is completely shut down and there is no condensation of HMF into DHMF, thereby supporting the proposed catalyst being the NHC released from [EMIM]OAc.

Second, on the basis of the proposed mechanism, ILs paired with non-basic anions, which are incapable of self-releasing NHCs like [EMIM]OAc, should be ineffective for this carbene catalysis but could be activated, with a strong organic base, to deliver the NHC catalyst and thus effect the same type of carbene catalysis. Indeed, [EMIM]Cl, while itself being ineffective for this catalysis, becomes a highly effective HMF

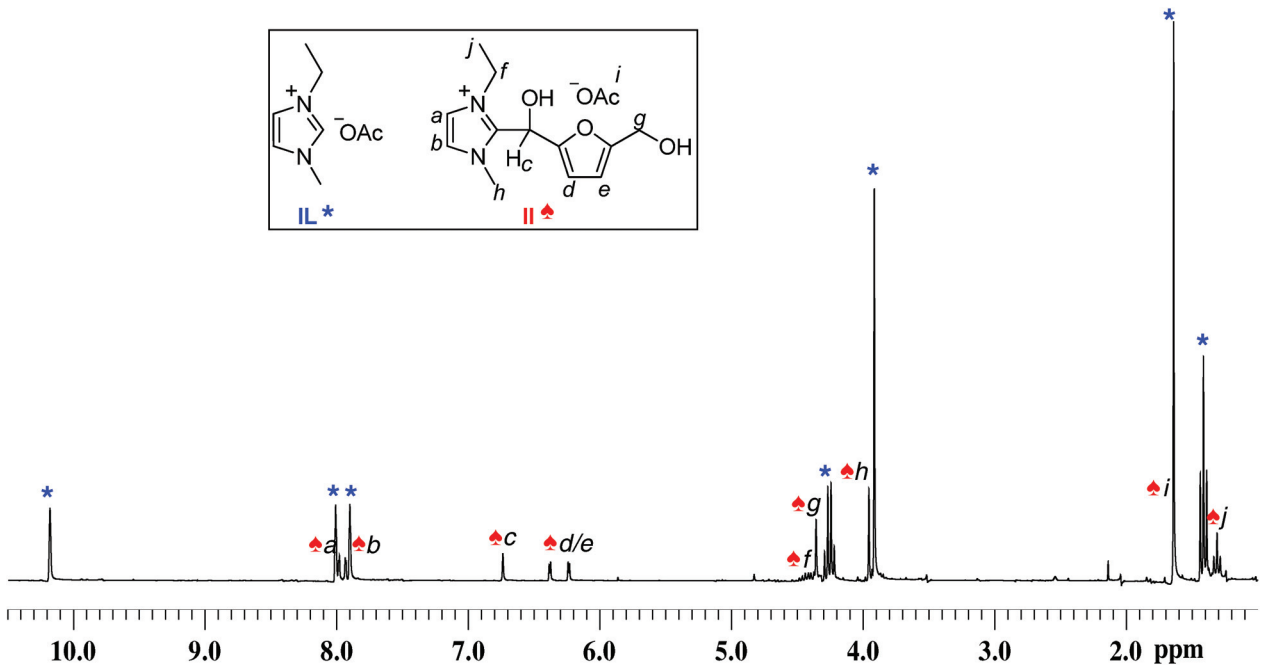


Fig. 7 ^{1}H NMR (DMSO-d_6) spectrum of the reaction between HMF and [EMIM]OAc (1 : 5 molar ratio) at RT for 1.5 h, showing clean formation of intermediate **II** in the presence of excess [EMIM]OAc (small unlabeled peaks are for a trace amount of the residual solvents brought from the IL).

upgrading catalyst system, when treated with DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) which generates the NHC catalyst *in situ*; thus, with a 5 mol% catalyst loading, which was controlled by the amount of DBU added, DHMF was obtained in 96% yield (by HPLC) at 80° for 1 h. Potential co-solvent effects were also examined, showing a minimal effect on the DHMF yield; thus, addition of the THF co-solvent gave a DHMF yield of 96.7%, while the yield was 93.8% when employing DMF as a co-solvent.

Third, we obtained direct evidence for the formation of the resting intermediate **II** through NMR monitoring of the HMF reaction with [EMIM]OAc (1 : 1 molar ratio) in DMSO-d_6 at RT and 80 °C with hexamethylbenzene as the internal standard. At RT, 17% HMF was consumed immediately upon mixing HMF with [EMIM]OAc, which approximately corresponds to the amount of the NHC catalyst accessible in [EMIM]OAc at this temperature for its reaction with HMF to form intermediate **II**; this intermediate is not converted into DHMF at RT, even after 24 h. With this valuable information, next we carried out the same reaction at RT but with a 1 : 5 molar ratio of HMF : [EMIM]OAc to form the intermediate exclusively (*i.e.*, devoid of HMF and DHMF), plus excess [EMIM]OAc; the reaction in this ratio at RT enabled conclusive spectroscopic characterization of intermediate **II** (Fig. 7 and 8). Noteworthy is that the most characteristic peak for the α-hydroxymethyl group *CH*(OH) at 6.74 ppm (DMSO-d_6) or 6.47 ppm (D_2O) in the ^{1}H NMR and 60.4 ppm (DMSO-d_6) in the ^{13}C NMR of intermediate **II** is comparable to the chemical shifts observed for the analogous 2-(α-hydroxybenzyl)thiazolium ions derived from the reaction of thiazolium salts and benzaldehydes, employing either *t*-BuOK as a base or $Et_3N/Et_3NH^+Cl^-$ as a buffer.[21]

At 80 °C, on the other hand, as the reaction proceeded from 2 min to 25 min, Fig. 9 shows a gradual consumption of HMF and intermediate **II**, formed instantaneously upon mixing HMF with [EMIM]OAc (1 : 1 ratio), which was accompanied by concurrent formation of DHMF. Another experiment that heating of the intermediate in the absence of HMF led to formation of DHMF suggests that the reaction of NHC **I** with HMF to form intermediate **II** is reversible (*i.e.*, release of HMF is needed to further convert **II** to DHMF at elevated temperatures). Overall, the above results indicate that the formation of intermediate **II** is fast (and reversible), relative to the **II**-to-**III** step.

Fourth, if the low concentration of NHC **I** present in [EMIM]-OAc is the catalyst for self-condensation of HMF to DHMF, then the use of the preformed, discrete NHCs should lead to even more rapid and efficient upgrading of HMF to DHMF. Indeed, with the Enders TPT being the catalyst (5 mol%), near quantitative (98% by NMR) conversion of HMF to DHMF was observed in THF at RT after 24 h, resulting in a high isolated yield (86%, unoptimized, Table 1) of DHMF. The rate of the TPT (5 mol%)-catalyzed condensation of HMF can be greatly enhanced at elevated temperatures; at 60 °C for 1 h, 94% DHMF (NMR yield) was achieved within 1 h, accomplishing an 87% isolated (unoptimized) yield. The performance of the two Arduengo carbenes, 1,3-di-*tert*-butylimidazolin-2-ylidene (I^{t}Bu) and 1,3-di-mesityl-butyl-imidazolin-2-ylidene (IMes),[23] is drastically different. While IMes is also a highly effective catalyst for umpolung condensation of HMF to DHMF (5 mol% NHC, 93% DHMF by NMR), the more nucleophilic (I^{t}Bu) is completely ineffective. When HMF is mixed with a stoichiometric amount of an NHC (TPT, IMes, or I^{t}Bu) at RT, HMF and the NHC were completely consumed without producing DHMF. The remarkable activity and efficiency of TPT in this carbene catalysis is presumably related to the fact that TPT is *both a good nucleophile and a leaving group*, the latter of which is essential for closing the catalytic cycle (*cf.*, Scheme 1). By the same analogy, the

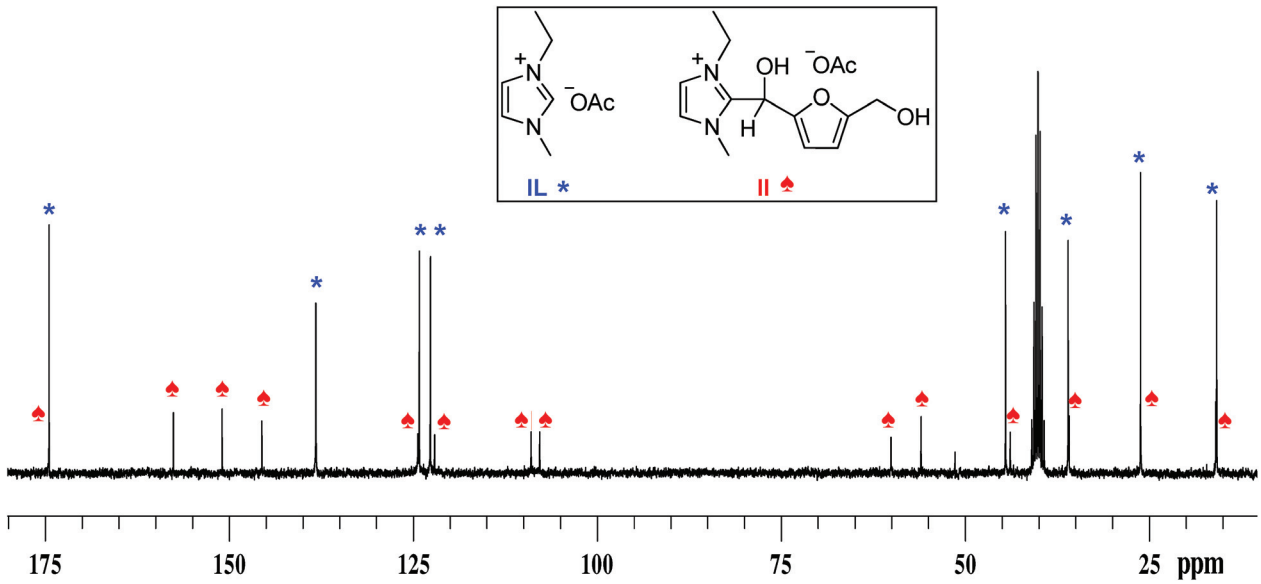


Fig. 8 ^{13}C NMR (DMSO-d_6) spectrum of the reaction between HMF and [EMIM]OAc (in a 1 : 5 molar ratio) at RT for 1.5 h, showing clean formation of intermediate **II** in the presence of excess [EMIM]OAc (a peak unlabeled is for a trace amount of the residual solvent (CH_2Cl_2) brought from the IL).

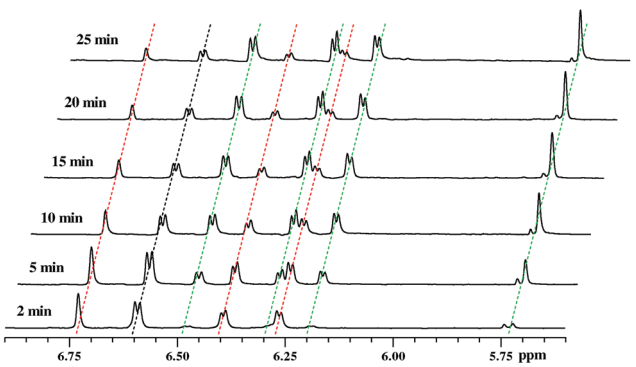


Fig. 9 Comparison of ^1H NMR spectra of the reaction between HMF and [EMIM]OAc (1 : 1 molar ratio) in DMSO-d_6 at 80 °C over the initial 25 min period. This spectral overlay in the most characteristic region shows the gradual decrease in the intensities (normalized by the C_6Me_6 internal standard) of the peaks for HMF (6.59 ppm, *black* line) and intermediate **II** (6.73, 6.39, 6.26 ppm, *red* lines), with the concomitant increasing of DHMF (6.48, 6.29, 6.19, 5.72 ppm, *green* lines). A small shoulder peak at 5.74 with a constant intensity is the residual solvent (CH_2Cl_2) brought into the system.

ineffectiveness of I^{t}Bu could be attributed to its strong binding to HMF and being too poor a leaving group to close the cycle. The trend with TPT being the best catalyst and I^{t}Bu being the worst catalyst (non-activity) in this series for umpolung condensation of HMF is completely opposite to the trend observed for conjugate-addition chain-growth polymerization of α-methylene-γ-butyrolactones.[24] Overall, the above results obtained from using the authentic, discrete NHC catalysts as well as the already established reactivity and fundamental steps of such NHCs towards aldehydes (*i.e.*, benzoin reaction)[13,19] further support the overall umpolung self-condensation of HMF to DHMF mechanism depicted in Scheme 1.

Table 1 Results on HMF self-condensation to DHMF catalyzed by NHCs

NHC	NHC loading (mol%)	Temperature (°C)	Time (h)	DHMF yield (NMR) (%)	DHMF yield (isolated) (%)
I^{t}Bu	5	25	24	0	0
	100	25	24	0	0
IMes	5	25	24	92.9	n.d.
	100	25	24	0	0
TPT	5	25	24	98.0	86.2
	100	25	24	Trace	n.d.
	5	60	1	93.6	87.1

Solvent: THF. n.d. = not determined.

Conclusions

In summary, through organocatalysis by the catalytic acetate-based IL [EMIM]OAc, the chloride-based IL [EMIM]Cl in combination with the organic base DBU, or the discrete NHC catalysts TPT and IMes, we have developed a rapid, highly selective and high-yield upgrading of the key biorefining building block HMF into DHMF, a potential high-value biorefinery product as an intermediate to kerosene/jet fuel. The reaction time for this HMF upgrading process is within 1 h under industrially preferred conditions (*i.e.*, ambient atmosphere, 60–80 °C), and the DHMF selectivity is typically near quantitative and yields are up to 98% (HPLC or NMR) or 87% (unoptimized, isolated yield). This work has also yielded the carbene catalysis mechanism for this upgrading transformation by the catalytic IL, which has been supported by four lines of evidence presented in this report, including the direct identification of the resting intermediate. The technological significance of this work is that, while direct aldol

self-condensation of HMF for its upgrading is not possible,[11] the direct umpolung self-condensation of HMF for its upgrading into DHMF is highly facile, which is made possible by *organocatalysis*. Additionally, as many efficient catalyst systems have been developed for conversion of plant biomass resources (glucose or cellulose) into HMF,[6,7] it should be possible to convert such nonfood biomass directly into DHMF *via* a two-step process. Indeed, our preliminary results in this regard showed the feasibility of transforming glucose directly into DHMF in a stepwise fashion, with the first step converting glucose into HMF by metal catalysis,[6,7a] followed by extraction of HMF and subsequent carbene catalysis. Our future studies will address integration of these two catalytic processes, transformation of DHMF into liquid fuels, and cross-condensation of HMF with other aldehydes into jet or diesel fuel intermediates.

Experimental

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, on a high-vacuum line, or in an inert gas (Ar or N_2)-filled glovebox. HPLC-grade organic solvents were first sparged extensively with nitrogen during filling 20 L solvent reservoirs 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. HPLC-grade DMF was degassed and dried over CaH_2 overnight, followed by vacuum distillation (CaH_2 was removed before distillation). DMSO-d_6 was first degassed and dried over CaH_2, followed by vacuum distillation. NMR-scale reactions were conducted in Teflon-valve-sealed J. Young-type NMR tubes with hexamethylbenzene as the internal standard. NMR spectra were recorded on a Varian Inova 300 (FT 300 MHz, ^{1}H; 75 MHz, ^{13}C) or a Varian Inova 400 MHz spectrometer. Chemical shifts for ^{1}H and ^{13}C spectra were referenced to internal NMR solvent residual resonances and are reported as parts per million relative to $SiMe_4$.

The water-soluble products were analyzed by an Agilent 1260 Infinity HPLC system equipped with either an Agilent Eclipse Plus C18 Column (100 × 4.6 mm; 80 : 20 water–methanol, 0.6 mL min^{-1}, 30 °C) with a UV detector (284 nm) for HMF and DHMF detection and quantification, or a Biorad Aminex HPX-87H Column (300 × 7.8 mm; water, 0.6 mL min^{-1}, 45 °C) with an Agilent 1260 Infinity ELSD detector (65 °C, 3.5 bar, gain 6) for glucose and other sugars detection. High-resolution mass spectrometry (HRMS) data were collected on an Agilent 6220 Accurate time-of-flight LC/MS spectrometer.

D-Glucose (Granular powder, Fisher Chemical), $CrCl_2$ (Alfa Aesar), HMF (Acros Organics), hexamethylbenzene (Alfa Aesar), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, Acros Organics), acetic acid (Mallinckrodt Chemicals, ACS grade), silver acetate (Strem Chemical) were used as received. N-Heterocyclic carbenes (NHCs), 1,3-bis(2,4,6-trimethyl-phenyl)imidazol-2-ylidene (IMes) and 1,3-di-*tert*-butylimidazol-2-ylidene (I^{t}Bu) were purchased from Strem Chemical Co. Literature procedures were used to prepare 1,3,4-triphenyl-4,5-dihydro-1*H*-1,2,4-triazol-5-ylidene (TPT),[25] while 1-ethyl-2,3-dimethylimidazolium acetate ([EDMIM]OAc)[26] was prepared using an anion exchange route (*vide infra*). 1-Ethyl-3-methylimidazolium acetate ([EMIM]OAc, Aldrich) and 1-ethyl-2,3-dimethylimidazolium chloride ([EDMIM]Cl, Aldrich) were dried under vacuum at 100 °C for 24 h. 1-Ethyl-3-methylimidazolium chloride ([EMIM]Cl, Fluka) was dried under vacuum at 100 °C for 24 h, followed by repeated recrystallization from CH_2Cl_2 and hexanes at room temperature. The purified ionic liquids were stored in an argon-filled glovebox.

Modified synthesis of [EDMIM]OAc

[EDMIM]OAc[26] was synthesized from the commercially available [EDMIM]Cl through anion exchange with AgOAc. [EDMIM]Cl (2.0 g, 0.012 mol) was mixed with AgOAc (2.09 g, 0.012 mol) in a conical flask, followed by addition of 25 mL deionized water. The suspension was covered with aluminum foil (avoiding the photo-degradation of AgOAc) and stirred overnight at room temperature. The resulting mixture was filtered to remove AgCl, and aliquots were taken from time to time for surplus anions test using the $AgNO_3$ or HCl solution. $AgNO_3$-resulted precipitation (AgCl) showed that there was a surplus of [EDMIM]Cl (*vice versa*). Accordingly, the [EDMIM]Cl or AgOAc solution was added to the mother solution dropwise until the anion test turned negative by both $AgNO_3$ and HCl solutions. The final reaction mixture was filtered and the filtrate was dried azeotropically with toluene. The resulting white solid was collected by filtration and washed with hexanes. After being dried at 50 °C under vacuum, [EDMIM]OAc was obtained as a white solid (1.68 g, 80.0%). Note that [EDMIM]OAc is highly hygroscopic and should be stored in a glovebox or a similar water-free environment. ^{1}H NMR ($CDCl_3$) for [EDMIM]OAc: δ 7.85 (d, J_{H-H} = 2.1 Hz, 1H, imidazolium ring H), 7.63 (d, J_{H-H} = 1.8 Hz, 1H, imidazolium ring H), 4.24 (q, J_{H-H} = 7.2 Hz, 2H, N–CH_2CH$_3$), 3.95 (s, 3H, N–CH_3), 2.73 (s, 3H, NCCH_3N), 1.84 (s, 3H, OAc), 1.44 (t, J_{H-H} = 7.2 Hz, 3H, N–CH$_2$CH_3). ^{13}C NMR ($CDCl_3$) for [EDMIM]OAc: δ 176 (*C*═O), 124 (N*C*N), 122, 121 (N–*C*H*C*H–N), 44.0 (N–*C*H$_2$CH$_3$), 35.8 (N–*C*H$_3$), 26.0 (NC*C*H$_3$N), 15.4 (O═C–*C*H$_3$), 10.0 (N–CH$_2$*C*H$_3$).

Typical procedure for studying HMF degradation in [EMIM]OAc

HMF (0.10 g, 0.79 mmol) was mixed with [EMIM]OAc (0.14 g, equimolar to HMF) in a 5 mL vial. The vial was sealed and heated at 80 °C for a predetermined time in a temperature-controlled orbit shaker (300 RPM). The reaction was quenched with ice-water and diluted with a known amount of deionized water. HMF was quantified with calibration curves generated from the commercially available standard in water.[7a] A typical HPLC chromatogram of the reaction product is shown in Fig. 4. The results of HMF degradation in [EMIM]OAc monitored by HPLC are summarized in Fig. 1, which shows that [EMIM]OAc rapidly degrades HMF at 80 °C; for instance, HMF degraded by 81.7 and 94.2 mol% after only 10 and 60 min, respectively.

For investigation of the HMF degradation kinetics in [EMIM]-OAc, HMF (40.0 mg, 0.32 mmol) and hexamethylbenzene

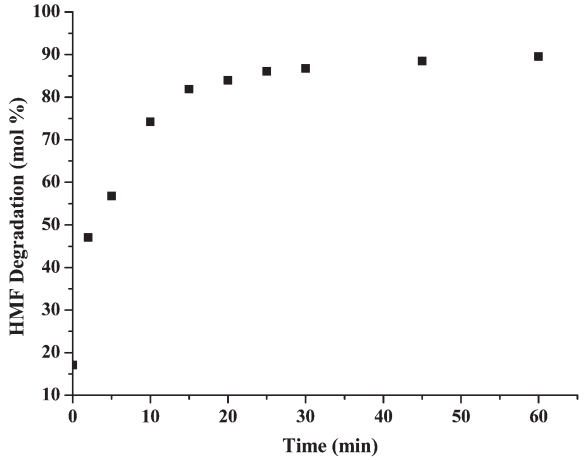


Fig. 10 Profile (by NMR) of HMF degradation in [EMIM]OAc (1 : 1 molar ratio) at 80 °C.

(2.0 mg, 0.012 mmol) were fully dissolved in 0.5 mL DMSO-d_6, followed by addition of [EMIM]OAc (1 equiv. relative to HMF) in 0.5 mL DMSO-d_6. The mixture was transferred into a J. Young-type NMR tube and sealed with the Teflon valve. The mixture was heated to 80 °C on an NMR spectrometer and the reaction was followed by taking ^{1}H NMR spectra of the reaction mixture at predetermined time intervals. The results of HMF degradation in [EMIM]OAc monitored by NMR are summarized in Fig. 10 (profile of HMF degradation as a function of time) and Fig. 2 (the first-order plot of HMF degradation for the initial time period).

Isolation and characterization of DHMF produced from HMF degradation in [EMIM]OAc

As shown in Fig. 4, the HPLC chromatogram of the reaction mixture from the incomplete HMF degradation in [EMIM]OAc exhibited a peak at 3.72 min for the unreacted HMF, plus a large peak at 5.15 min for a new compound formed during HMF degradation in [EMIM]OAc. To separate the new compound from the reaction mixture after the reaction at 80 °C for 30 min, 1 mL water was added to fully dissolve the mixture, after which 2 mL ethyl acetate (EtOAc) was added for extraction. The upper layer (EtOAc phase) was collected and the extraction was repeated four times. The new compound was obtained as a light yellow powder (50% isolated yield based on HMF) after purification by the silica gel column chromatography (eluent: EtOAc/hexane/methanol = 8/2/1) and vacuum drying.

The degradation product (new compound) was identified as 5,5′-di(hydroxymethyl)furoin (DHMF), as clearly shown by its ^{1}H and ^{13}C NMR spectra. ^{1}H NMR (CD_3OD): δ 7.39 (d, J_{H-H} = 3.6 Hz, 1H, furan ring proton), 6.52 (d, J_{H-H} = 3.6 Hz, 1H, furan ring proton), 6.40 (d, J_{H-H} = 3.3 Hz, 1H, furan ring proton), 6.30 (d, J_{H-H} = 3.3 Hz, 1H, furan ring proton), 5.87 (s, 1H, C*H*OH), 4.60 (s, 2H, CH_2OH), 4.49 (s, 2H, CH_2OH). ^{13}C NMR (CD_3OD): δ 187 (C═O), 163, 158, 154, 152, 123, 112, 111, 110 (a total of 8 resonances for the furan ring carbons), 71.7 (*C*HOH), 58.4 (*C*H_2OH), 58.2 (*C*H_2OH). Note that the ^{1}H NMR spectrum taken in DMSO-d_6 showed three broad peaks centered at ~5.3 ppm, 5.5 ppm, and 6.1 ppm for three types of the OH groups present in DHMF. M.p. = 124–125 °C; HRMS calculated for $C_{12}H_{11}O_6$ [M − H]$^-$: 251.0556; found: 251.0561.

The DHMF purified by the silica gel column chromatography was recrystallized by slow diffusion of hexanes into a methanol solution of DHMF at room temperature over 7 d, affording colorless single crystals suitable for X-ray diffraction analysis. Single crystals were quickly covered with a layer of Paratone-N oil (Exxon, dried and degassed at 120 °C/10^{-6} Torr for 24 h) after decanting the mother liquor. A crystal was then mounted onto a thin glass fiber and transferred into the cold nitrogen stream of a Bruker SMART CCD diffractometer. The structure was solved by direct methods and refined using the Bruker SHELXTL program library.[27] The structure was refined by full-matrix least-squares on F^2 for all reflections. All non-hydrogen atoms were refined with anisotropic displacement parameters, whereas hydrogen atoms were included in the structure factor calculations at idealized positions. There are two independent molecules with minor structural differences in the unit cell (Fig. 6). Selected crystallographic data for DHMF: $C_{24}H_{24}O_{12}$, orthorhombic, space group $Pna2_1$, a = 23.5497(17) Å, b = 5.9975(4) Å, c = 15.8768(10) Å, α = 90°, β = 90°, γ = 90°, V = 2242.4(3) Å^3, Z = 4, D_{calcd} = 1.494 mg m^{-3}, GOF = 1.040, R_1 = 0.0524 [$I > 2\sigma(I)$], wR_2 = 0.1309. CCDC 887451 contains the supplementary crystallographic data for this paper.

The identification as well as spectroscopic and structural characterizations of the HMF degradation product (DHMF) allowed for monitoring of DHMF formation and HMF degradation simultaneously by NMR (DMSO-d_6, 80 °C, hexamethylbenzene as the internal standard). The results are summarized in Fig. 5, showing that a maximum yield of 72.4% was achieved at 86.1% HMF conversion (degradation) after 25 min.

Identification of intermediate II from the reaction of HMF with [EMIM]OAc

The 1 : 1 reaction of HMF with [EMIM]OAc at RT was monitored by NMR (DMSO-d_6) in a J. Young-type NMR tube using hexamethylbenzene as the internal standard. This study showed that 17% HMF was consumed immediately upon mixing HMF with [EMIM]OAc at RT, which approximately corresponds to the amount of the NHC catalyst accessible in [EMIM]OAc at this temperature for its reaction with HMF to form intermediate **II**. This intermediate is not converted into DHMF at RT, even after 24 h, and the ^{1}H NMR remained the same from the beginning of the reaction up to 24 h at RT. To aid analysis of the spectra of the *in situ* reactions, the chemical shifts of the four species involved in the reaction of HMF with [EMIM]OAc were summarized as follows. All the chemical shifts were reported in DMSO-d_6, and the NMR solvent residual signal was referenced at 2.54 ppm, based on the chemical shift of the hexamethylbenzene internal standard set at 2.15 ppm.

^{1}H NMR for HMF (known compound): δ 9.56 (s, 1H, C*H*O), 7.51, 6.59 (d, 2H, furan ring H), 4.54 (s, 2H, CH_2OH). ^{1}H NMR for [EMIM]OAc (known compound): δ 9.60 (s, 1H, NC*H*N), 7.84, 7.76 (d, 2H, imidazolium ring H), 4.24 (q, 2H, NCH_2CH$_3$), 3.89 (s, 3H, NCH_3), 1.65 (s, 3H, OAc), 1.44 (t, 3H, NCH$_2$CH_3). ^{1}H NMR for DHMF: δ 7.54, 6.54, 6.38, 6.25

(d, 4H, furan ring H), 5.78 (s, 1H, C*H*OH), 4.50 (s, 2H, CH_2OH), 4.35 (s, 2H, CH_2OH). ^{1}H NMR for intermediate **II**: δ 7.98 (d, J_{H-H} = 2.1 Hz, imidazol ring H), 7.93 (d, J_{H-H} = 1.8 Hz, 1H, imidazol ring proton), 6.74 (s, 1H, C*H*–OH), 6.38 (d, J_{H-H} = 3.3, 1H, furan ring H), 6.24 (d, J_{H-H} = 3.0 Hz, 1H, furan ring H), 4.41 (m, 2H, NCH_2CH$_3$), 4.36 (s, 2H, CH_2OH), 3.96 (s, 3H, NCH_3), 1.64 (s, 3H, OAc), 1.31 (t, J_{H-H} = 7.2 Hz, 3H, NCH$_2$CH_3). ^{13}C NMR: δ 175 (*C*═O), 158 (N*C*N), 151, 146, 109, 108 (4 resonances for the furan ring), 125, 122 (2 resonances for the imidazol ring), 60.4 (*C*H–OH), 56.3 (*C*H$_2$OH), 44.2 (N*C*H$_2$CH$_3$), 36.2 (N*C*H$_3$), 26.5 (O═C–*C*H$_3$), 16.3 (NCH$_2$*C*H$_3$).

The reaction with a 1 : 5 molar ratio of HMF : [EMIM]OAc was carried out in the same fashion, producing the intermediate exclusively (*i.e.*, devoid of HMF and DHMF), plus excess [EMIM]OAc. The ^{1}H NMR spectrum (Fig. 7) of this reaction showed clean formation of intermediate **II** in the presence of excess [EMIM]OAc, which is further confirmed by its ^{13}C NMR spectrum (Fig. 8), thus enabling more conclusive spectroscopic characterization of intermediate **II**.

Typical procedure for studying umpolung condensation of HMF into DHMF by NHCs

In a typical procedure, HMF (115 mg, 0.91 mmol) was fully dissolved in 5 mL THF, followed by addition of TPT (5 mol%) in 0.5 mL THF. The resulting solution was stirred at room temperature, and aliquots were taken from time to time and dried under vacuum for analysis by ^{1}H NMR in DMSO-d$_6$. To isolate DHMF from the HMF self-condensation catalyzed by TPT, the reaction mixture was stirred at room temperature for 24 h and then concentrated, followed by addition of toluene to precipitate the product DHMF. DHMF (99 mg, 86% yield) was obtained as a white solid after filtration and vacuum drying. ^{1}H NMR in DMSO-d$_6$ (Fig. 11) of the product confirmed the clean formation of DHMF. The same reaction was repeated at 60 °C for 1 h, affording DHMF in 87% isolated yield.

Table 1 summarizes selected results on the DHMF yield under various conditions achieved by three NHC catalysts, TPT, I^{t}Bu, and IMes. The most efficient catalyst in this series is TPT, which converted HMF to DHMF in 98% yield (by NMR, or 86% isolated yield) with a low catalyst loading of 5 mol% at RT after 24 h. The rate of HMF condensation can be greatly enhanced when carrying out the reaction at 60 °C, which achieved 93.6% DHMF yield after 1 h, compared to 37.5% DHMF yield at RT after 3 h. In comparison, IMes is somewhat less effective than TPT, but I^{t}Bu is completely ineffective. The same reactions were repeated with a stoichiometric amount of an NHC (relative to HMF) at RT, but in all cases HMF was completely consumed without forming DHMF.

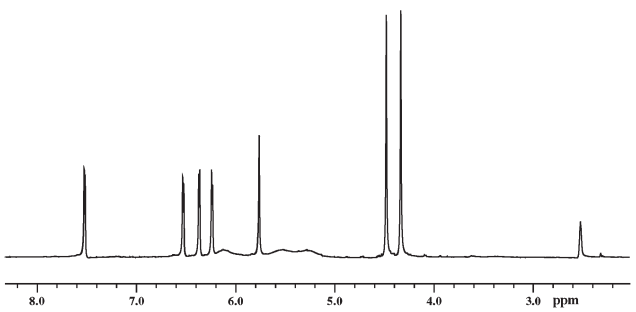


Fig. 11 ^{1}H NMR (DMSO-d$_6$) of DHMF derived from umpolung condensation of HMF by TPT. Note that the three broad peaks centered at ~5.3 ppm, 5.5 ppm, and 6.1 ppm, not appeared in the ^{1}H NMR taken in methanol-d$_4$, are for three types of the OH groups present in DHMF, and the peak at 2.54 ppm is from the NMR solvent residual signal.

Typical procedure for studying glucose degradation in [EMIM]OAc

This study followed the procedure similar to that used for the HMF degradation in [EMIM]OAc as described above. Glucose (0.04 g, 0.22 mmol) was mixed with [EMIM]OAc (0.2 g, 1 : 5 w/w) in a 5 mL vial. The vial was sealed and heated at 100 °C for 30 min in a temperature-controlled orbit shaker (300 RPM). The reaction was quenched with ice-water and transferred to a 5 mL volumetric flask. A fraction of the solution (0.5 mL) was removed of [EMIM]OAc by cation–anion exchange columns washed with distilled water. An initial 5 mL eluent was collected for sugar analysis by HPLC. Glucose was quantified with calibration curves generated from the commercially available standard in water. The recovery of glucose (if any left after the degradation reaction) by this method was shown to be ≥96% based on control experiments. The HPLC results showed no fructose and cellobiose formation from the degradation of glucose in [EMIM]OAc. Fig. 3 summarizes the results of glucose degradation in [EMIM]OAc, which shows that [EMIM]-OAc also rapidly degrades glucose at 100 °C; thus, glucose degraded by 58.9, 70.3, and 83.0 mol% after only 0.5, 1, and 3 h, respectively.

Typical procedure for two-step glucose conversion into DHMF

For the first step, glucose (100 mg, 0.56 mmol) was premixed with [EMIM]Cl (500 mg, 1 : 5 w/w) in a 5 mL vial in an argon-filled glove box, followed by further loading of the $CrCl_2$ catalyst (10 mol% relative to glucose). The sealed vial was placed in a temperature-controlled orbit shaker (100 °C, 300 RPM) and heated at this temperature for 3 h. The reaction was quenched with 1 mL deionized water, and HMF was extracted with ethyl acetate (2 mL × 4). HMF was quantitatively recovered by ethyl acetate extraction, and the HMF yield from glucose was 57% as determined by HPLC. The resulting solution was purified by the silica gel column chromatography (eluent: EtOAc/hexane = 7/3), and the eluent fraction for HMF was collected and dried under vacuum. For the second step, the obtained HMF was subsequently converted into DHMF by the TPT catalyst in THF, employing the same procedure already described.

Acknowledgements

This work was supported by the US Department of Energy-Office of Basic Energy Sciences, grant DE-FG02-10ER16193. DJL acknowledges Prof. Susan James as a co-advisor.

References

1 (*a*) R. C. Remsing, R. P. Swatloski, R. D. Rogers and G. Moyna, *Chem. Commun.*, 2006, 1271–1273; (*b*) R. P. Swatloski, S. K. Spear, J. D. Holbrey and R. D. Rogers, *J. Am. Chem. Soc.*, 2002, **124**, 4974–4975.

2 (*a*) M. E. Zakrzewska, E. Bogel-Łukasik and R. Bogel-Łukasik, *Energy Fuels*, 2010, **24**, 737–745; (*b*) O. A. El Seoud, A. Koschella, L. C. Fidale, S. Dorn and T. Heinze, *Biomacromolecules*, 2007, **8**, 2629–2647.

3 (*a*) *Ionic Liquids in Synthesis*, ed. P. Wasserscheid and T. Welton, Wiley-VCH, Weinheim, 2nd edn, 2008; (*b*) V. I. Pârvulescu and C. Hardacre, *Chem. Rev.*, 2007, **107**, 2615–2665; (*c*) A. Stark and K. Seddon, *Ionic Liquids in Kirk-Othmer Encyclopedia of Chemical Technology*, John Wiley and Sons, New York, 2007, vol. 26, pp. 836–8920.

4 (*a*) N. Sun, H. Rodriguez, M. Rahman and R. D. Rogers, *Chem. Commun.*, 2011, **47**, 1405–1421; (*b*) A. Pinkert, K. N. Marsh, S. Pang and M. P. Staiger, *Chem. Rev.*, 2009, **109**, 6712–6728.

5 Selected recent examples: (*a*) S. J. Dee and A. T. Bell, *ChemSusChem*, 2011, **4**, 1166–1173; (*b*) J. B. Binder and R. T. Raines, *Proc. Natl. Acad. Sci. U. S. A.*, 2010, **107**, 4516–4521; (*c*) L. Vanoye, M. Fanselow, J. Holbrey, M. P. Atkins and K. R. Seddon, *Green Chem.*, 2009, **11**, 390–396; (*d*) C. Li, Q. Wang and Z. K. Zhao, *Green Chem.*, 2008, **10**, 177–182; (*e*) C. Li and Z. K. Zhao, *Adv. Synth. Catal.*, 2007, **349**, 1847–1850.

6 Y. Zhang, H. Du, X. Qian and E. Y.-X. Chen, *Energy Fuels*, 2010, **24**, 2410–2417.

7 Selected recent reviews and examples: (*a*) D. Liu and E. Y.-X. Chen, *Appl. Catal., A.*, 2012, **435–436**, 78–85; (*b*) A. A. Rosatella, S. P. Simeonov, R. F. M. Frade and C. A. M. Afonso, *Green Chem.*, 2011, **13**, 754–793; (*c*) Z. Zhang, Q. Wang, H. Xie, W. Liu and Z. K. Zhao, *ChemSusChem*, 2011, **4**, 131–138; (*d*) B. Kim, J. Jeong, D. Lee, S. Kim, H.-J. Yoon, Y.-S. Lee and J. K. Cho, *Green Chem.*, 2011, **13**, 1503–1506; (*e*) E. Pidko, V. Degirmenci, R. A. van Santen and E. J. M. Hensen, *Angew. Chem., Int. Ed.*, 2010, **49**, 2530–2534; (*f*) T. Ståhlberg, M. G. Sørensen and A. Riisager, *Green Chem.*, 2010, **12**, 321–325; (*g*) F. Tao, H. Song and L. Chou, *ChemSusChem*, 2010, **3**, 1298–1303; (*h*) X. Qi, M. Watanabe, T. M. Aida and R. L. Smith Jr., *ChemSusChem*, 2010, **3**, 1071–1077; (*i*) J. B. Binder and R. T. Raines, *J. Am. Chem. Soc.*, 2009, **131**, 1979–1985; (*j*) S. Hu, Z. Zhang, J. Song, Y. Zhou and B. Han, *Green Chem.*, 2009, **11**, 1746–1749; (*k*) G. Yong, Y. Zhang and J. Y. Ying, *Angew. Chem., Int. Ed.*, 2008, **47**, 9345–9348; (*l*) H. Zhao, J. E. Holladay, H. Brown and Z. C. Zhang, *Science*, 2007, **316**, 1597–1600.

8 Selected recent reviews: (*a*) D. M. Alonso, J. Q. Bond and J. A. Dumesic, *Green Chem.*, 2010, **12**, 1493–1513; (*b*) M. Stöcker, *Angew. Chem., Int. Ed.*, 2008, **47**, 9200–9211; (*c*) A. Corma, S. Iborra and A. Velty, *Chem. Rev.*, 2007, **107**, 2411–2502; (*d*) J. N. Chheda, G. W. Huber and J. A. Dumesic, *Angew. Chem., Int. Ed.*, 2007, **46**, 7164–7183; (*e*) G. W. Huber, S. Iborra and A. Corma, *Chem. Rev.*, 2006, **106**, 4044–4098; (*f*) *Top Value Added Chemicals from Biomass*, ed. T. Werpy and G. Petersen, U.S. Department of Energy (DOE) report: DOE/GO-102004-1992, 2004.

9 M. Balakrishnan, E. R. Sacia and A. T. Bell, *Green Chem.*, 2012, **14**, 1626–1634.

10 (*a*) T. Thananatthanachon and T. B. Rauchfuss, *Angew. Chem., Int. Ed.*, 2010, **49**, 6616–6618; (*b*) M. Chidambaram and A. T. Bell, *Green Chem.*, 2010, **12**, 1253–1262; (*c*) Y. Román-Leshkov, C. J. Barrett, Z. Y. Liu and J. A. Dumesic, *Nature*, 2007, **447**, 982–986.

11 G. W. Huber, J. N. Chheda, C. J. Barrett and J. A. Dumesic, *Science*, 2005, **308**, 1446–1450.

12 (*a*) Y. Qin, X. Lu, N. Sun and R. D. Rogers, *Green Chem.*, 2010, **12**, 968–971; (*b*) N. Sun, M. Rahman, Y. Qin, M. L. Maxim, H. Rodríguez and R. D. Rogers, *Green Chem.*, 2009, **11**, 646–655.

13 Selected recent reviews: (*a*) T. Dröge and F. Glorius, *Angew. Chem., Int. Ed.*, 2010, **50**, 6940–6952; (*b*) P.-C. Chiang and J. W. Bode, *RSC Catalysis Series*, Royal Society of Chemistry, Cambridge, 2010, pp. 399–435; (*c*) J. L. Moore and T. Rovis, *Top. Curr. Chem.*, 2009, **291**, 77–144; (*d*) F. E. Hahn and M. C. Jahnke, *Angew. Chem., Int. Ed.*, 2008, **47**, 3122–3172; (*e*) V. Nair, S. Vellalath and B. P. Babu, *Chem. Soc. Rev.*, 2008, **37**, 2691–2698; (*f*) N. Marion, S. Díez-González and S. P. Nolan, *Angew. Chem., Int. Ed.*, 2007, **46**, 2988–3000; (*g*) D. Enders, O. Niemeier and A. Henseler, *Chem. Rev.*, 2007, **107**, 5606–5655; (*h*) D. Bourissou, O. Guerret, F. P. Gabbaï and G. Bertrand, *Chem. Rev.*, 2000, **100**, 39–91.

14 O. Hollóczki, D. Gerhard, K. Massone, L. Szarvas, B. Németh, T. Veszprémi and L. Nyulászi, *New J. Chem.*, 2010, **34**, 3004–3009.

15 H. Rodríguez, G. Gurau, J. D. Holbrey and R. D. Rogers, *Chem. Commun.*, 2011, **47**, 3222–3224.

16 Z. Kelemen, O. Hollóczki, J. Nagy and L. Nyulászi, *Org. Biomol. Chem.*, 2011, **9**, 5362–5364.

17 (*a*) D. Enders, K. Breuer, U. Kallfass and T. Balensiefer, *Synthesis*, 2003, 1292–1295; (*b*) D. Enders, K. Breuer, G. Raabe, J. Runsink, J. H. Teles, J.-P. Melder, K. Ebel and S. Brode, *Angew. Chem., Int. Ed.*, 1995, **34**, 1021–1023.

18 Z. Zhang, W. Liu, H. Xie and Z. K. Zhao, *Molecules*, 2011, **16**, 8463–8474.

19 Selected reviews and examples: (*a*) A. Berkessel, S. Elfert, K. Etzenbach-Efferts and J. H. Teles, *Angew. Chem., Int. Ed.*, 2010, **49**, 7120–7124; (*b*) K. Hirano, A. T. Biju, I. Piel and F. Glorius, *J. Am. Chem. Soc.*, 2009, **131**, 14190–14191; (*c*) Y. Kawanaka, E. M. Phillips and K. A. Scheidt, *J. Am. Chem. Soc.*, 2009, **131**, 14190–14191; (*d*) P.-C. Chiang, M. Rommel and J. W. Bode, *J. Am. Chem. Soc.*, 2009, **131**, 8714–8718; (*e*) D. A. DiRocco, K. M. Oberg, D. M. Dalton and T. Rovis, *J. Am. Chem. Soc.*, 2009, **131**, 10872–10874; (*f*) A. S. K. Hashmi, M. Wölfle, J. H. Teles and W. Frey, *Synlett*, 2007, 1747–1752; (*g*) D. Enders, O. Niemeier and T. Balensiefer, *Angew. Chem., Int. Ed.*, 2006, **45**, 1463–1467; (*h*) D. Enders and U. Kallfass, *Angew. Chem., Int. Ed.*, 2002, **41**, 1743–1745; (*i*) C. K. Lee, M. S. Kim, J. S. Gong and I.-S. H. Lee, *J. Heterocycl. Chem.*, 1992, **29**, 149–153.

20 (*a*) A. T. Biju, M. Padmanaban, N. E. Wurz and F. Glorius, *Angew. Chem., Int. Ed.*, 2011, **50**, 8412–8415; (*b*) S.-I. Matsuoka, Y. Ota, A. Washio, A. Katada, K. Ichioka, K. Takagi and M. Suzuki, *Org. Lett.*, 2011, **13**, 3722–3725; (*c*) C. Fisher, S. W. Smith, D. A. Powell and G. C. Fu, *J. Am. Chem. Soc.*, 2006, **128**, 1472–1473.

21 Analogous 2-(α-hydroxybenzyl)thiazolium ions derived from the reaction of thiazolium salts and benzaldehydes, employing either the *t*-BuOK base or the $Et_3N/Et_3NH^+Cl^-$ buffer, have been reported: (*a*) M. J. White and F. J. Leeper, *J. Org. Chem.*, 2001, **66**, 5124–5131; (*b*) Y.-T. Chen, G. L. Barletta, K. Haghjoo, J. T. Cheng and F. Jordan, *J. Org. Chem.*, 1994, **59**, 7714–7722; (*c*) R. Breslow and R. Kim, *Tetrahedron Lett.*, 1994, **35**, 699–702.

22 R. Breslow, *J. Am. Chem. Soc.*, 1958, **80**, 3719–3726.

23 (*a*) A. J. Arduengo III, H. Bock, H. Chen, M. Denk, D. A. Dixon, J. C. Green, W. A. Herrmann, N. L. Jones, M. Wagner and R. West, *J. Am. Chem. Soc.*, 1994, **116**, 6641–6649; (*b*) A. J. Arduengo III, H. V. R. Dias, R. L. Harlow and M. Kline, *J. Am. Chem. Soc.*, 1992, **114**, 5530–5534.

24 Y. Zhang and E. Y.-X. Chen, *Angew. Chem., Int. Ed.*, 2012, **51**, 2465–2469.

25 (*a*) D. Enders, K. Breuer, G. Raabe, J. Runsink, J. H. Teles, J. P. Melder, K. Ebel and S. Brode, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1021–1023; (*b*) D. Enders, K. Breuer, U. Kallfass and T. Balensiefer, *Synthesis*, 2003, 1292–1295.

26 A. Brandt, J. P. Hallett, D. J. Leak, R. J. Murphy and T. Welton, *Green Chem.*, 2010, **12**, 672–679.

27 *SHELXTL, Version 6.12*, Bruker Analytical X-ray Solutions, Madison, WI, 2001.

