

Efficient formation of 2,5-diformylfuran (DFF) in ionic liquids at high substrate loadings and low oxygen pressure with separation through sublimation

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ABSTRACT: The oxidation of 5-hydroxymethylfurfural (HMF) to 2,5-diformylfuran (DFF) using oxygen (1 atm) with a TEMPO and CuCl catalyst system is investigated using a range of imidazolium-based ionic liquids (ILs) and various bases at different HMF substrate loadings (10-50%). This represents the first example of HMF to DFF conversion in ionic liquid media under homogeneous catalysis conditions, revealing dramatic differences in performance between the ILs. In the non-coordinating, hydrophobic ionic liquid, [bmim][NTf₂], 90% DFF yield is obtained at 5 mol% catalyst loading after 6 hours at 80 °C at a very high 40% HMF loading. Increasing the temperature to 100 °C leads to a lower yield, attributed to loss of volatile TEMPO from the reaction medium. A system using TEMPO and pyridine immobilized within the ionic liquid [bmim][NTf₂] results in selective conversion of HMF to high purity DFF. It also allows the DFF formed to be isolated by sublimation in 81% yield before a further cycle is performed. Subsequent catalyst deactivation is probed by X-ray photoelectron spectroscopy (XPS). Synthesis from fructose in a two-step process achieves a 55% isolated DFF yield. This approach overcomes significant drawbacks previously reported for this transformation, such as solvent toxicity, separation and purification problems as well as the need for high oxygen pressures. Further oxidation of HMF with this system leads to a 62% yield of 5-formyl-2-furancarboxylic acid (FFCA). The separation of this compound can be achieved by sublimation of DFF followed by solvent extraction.

INTRODUCTION

The increasingly strict policies on CO₂ emissions and the depletion of oil reserves have initiated research efforts towards finding alternative routes to biorenewable materials that can reduce dependence on fossil reserves. The compound 5-hydroxymethyl furfural (HMF), derived from the dehydration of sugars, is considered one of the leading platform chemicals with the potential to replace many oil-derived compounds. The high yield production of HMF from sugar feedstocks (such as glucose and fructose) has proven to be very efficient in ionic liquid media.¹⁻³ Quantitative yields can be obtained from fructose in halide-based ionic liquids in short reaction times under relatively mild conditions.^{1,4,5} Good results were also achieved in ionic liquids without halide counteranions with high yields being achieved in a biphasic system of 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide, [bmim][NTf₂], and water with a vanadium-based heterogeneous catalyst.⁶ However, the generation of HMF in ionic liquids suffers from a significant drawback concerning the separation of this compound from the reaction mixture. The high affinity of this compound with the ionic liquid medium and the high boiling points of both components, makes liquid-liquid extraction and distillation unfeasible for any scaled up process.⁷⁻⁹ One strategy to overcome this problem is the *in situ* conversion of the HMF generated into a higher value, more easily separated product that can avoid this issue. Other authors have exploited this approach by producing the potential biofuel, 2,5-dimethylfuran, from sugars in [bmim]Cl,^{10,11} or levulinic acid combined with formic acid in acidic ionic liquids.^{12,13} These processes proceed in good yields and show good catalyst recyclability, however, the market value of the compounds produced are limited compared to DFF and FDCA,¹⁴ with DFF also being easily oxidized to FDCA in high yield.¹⁵ Many literature reports summarized in recent reviews^{16,17} address the conversion of HMF to the dicarboxylic acid monomer, 2,5-furandicarboxylic acid (FDCA), which represents a very attractive route for the valorization of HMF since FDCA is a valuable building block for the bioplastic, polyethylene furanoate (PEF), which already has an important market demand.¹⁸ The reaction requires the oxidation of the alcohol and aldehyde groups of HMF to the carboxylic acid, according to the route depicted in Figure 1. Two different intermediates can form, 5-hydroxymethyl-2-furancarboxylic acid (HMFCA), through aldehyde oxidation, or 2,5-diformylfuran (DFF) through alcohol oxidation. Both intermediates are oxidized to 5-formyl-2-furancarboxylic acid (FFCA) before conversion to FDCA.

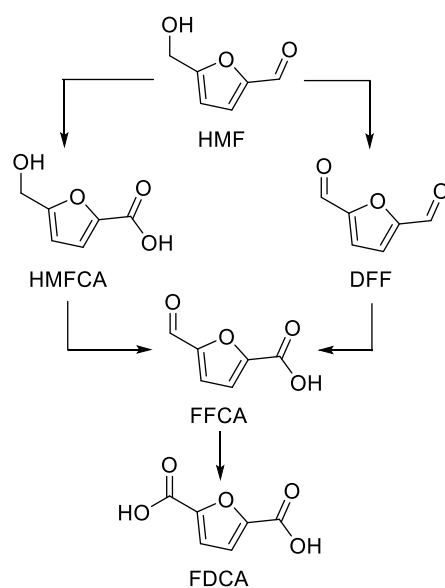


Figure 1. Scheme for oxidation of HMF to FDCA, showing that the reaction can pass through two intermediates, depending on which functional group is oxidized first.

The oxidation of HMF to FDCA is widely discussed in the literature and catalysts with high activity and selectivity have been successfully developed in systems that use water as solvent.^{17,19} However, important challenges remain since FDCA is insoluble in water, requiring the addition of a base to increase the solubility of FDCA and avoid precipitation onto the surface of the heterogeneous catalyst. Moreover, the need to add a base makes this route unsuitable for use with sugars as the feedstock, since an acid catalyst is needed for the dehydration, complicating reaction workup and recycling. In contrast, only a few reports have addressed the oxidation of HMF to FDCA in ionic liquids (ILs). In 2012, Stahlberg and co-workers tested different supports for heterogeneous ruthenium catalysts, achieving 40% FDCA yield in the ionic liquid [bmim][OAc],²⁰ while other work reported a 60% yield of FDCA in [bmim]Cl with a highly recyclable Zr/Fe-based catalyst (2% substrate loading, 20 bar O₂, 24 h).⁵ Despite the low substrate loading, the latter system also has the potential for FDCA production directly from sugars since [bmim]Cl has been shown to be a good solvent for sugar dehydration.²¹ Very recently, Zhang and co-workers²² used a heteropolyacid catalyst in combination with [bmim]Cl to achieve 89% FDCA yield in 6 h. However the loading used was very low (1.2%) and the catalyst showed poorly recyclability since it is dissolved in the ionic liquid. However, the oxidation step still remains the limiting factor with much room for improvement in terms of oxygen pressure, operating temperature, substrate loading and reaction time. The oxidation of HMF in ionic liquids suffers from substantial drawbacks compared to water, since only low concentrations of HMF can be used and high temperatures and pressures (over 140 °C and 20 bar oxygen pressure) are required, compromising the possible scale up of such technology. One of the reasons for these difficulties lies in the thermodynamics of the aldehyde oxidation in a non-aqueous system. It has been shown that the oxidation of the aldehyde to the carboxylic acid passes through the formation of the geminal diol²³ formed by nucleophilic attack of water at the carbonyl group. This unit is subsequently oxidized to a carboxylic acid through a β-hydride elimination when coordinated to the metal center of the catalyst used. The rate of oxidation is strictly dependent on the

equilibrium constant for the formation of the geminal diol, which is favored when water is the solvent.^{23,24} Moreover, in all the examples reported so far in ionic liquid media, the separation of FDCA from the reaction mixture still represents a major challenge as high loadings of HMF are necessary to achieve an efficient recovery.²⁵

While FDCA has garnered much attention due to its use as a monomer for the production of polyethylene furanoate (PEF),¹⁸ the true potential of biorenewable feedstocks will only be realized when there are effective routes to platform chemicals with a range of other functional groups. For example, aldehydes have a rich and versatile chemistry but the potential of the bioderived dialdehyde, 2,5-diformylfuran (DFF), has remained underexplored. The very successful conversion of sugars to HMF in ionic liquids has revealed the associated difficulties in isolating the HMF formed. One solution is to integrate the *in situ* conversion of HMF to DFF into the same medium. For this to be achieved, a different route was needed that can bypass the limitations surrounding the oxidation of the HMF aldehyde group in non-aqueous solvent systems. DFF displays different properties to HMF since it has low solubility in water, is stable to air and also sublimates at relatively low temperatures (≈ 40 °C). While DFF does not sublime from solution in water and organic solvents, we have observed that the sublimation properties of this compound are maintained in the ionic liquids used here, representing a potential path to obtain a high purity product in high yield. Recently, heterogeneous catalysts for the direct conversion of fructose into DFF have been developed successfully. The key step in these studies is to choose a solvent that can guarantee both high yield dehydration of sugars and partial oxidation of HMF.²⁶ In this regard, it has already been proven that dimethylformamide (DMF) and dimethylsulfoxide (DMSO) are good solvents that can guarantee high yield of dehydration.²⁷⁻³² Based on these factors most of the work in the literature has focused on the development of heterogeneous catalysts for the selective oxidation of HMF or fructose in these solvents. Recently, good yields were achieved in a two-step reaction using Amberlyst-15 (to provide acidic sites) for the dehydration step with Mn-Fe oxide or Cs/MnO as catalysts for the oxidation, operating at 110 °C and 10-15 bar O₂ partial pressures.^{33,34} Other catalysts have been developed for a one step conversion of fructose directly to HMF. For example, a combination of Amberlyst-15 with polyaniline-grafted VO(acac)₂ achieved a 42% DFF yield from fructose at 110 °C in 12 h.³⁵ Improvements in yield have been achieved by various groups using polyoxometallate and Mo-doped catalysts reaching over 70% yield in DMSO.^{36,37} Notwithstanding the high yield achieved from sugars, all the systems reported so far suffer from similar drawbacks which limit the techno-economic feasibility of any potential process. High temperatures (> 110 °C) and pressures (> 10 bar O₂) are required over long reaction times (typically > 10 hours) in toxic, flammable, high boiling-point (> 150 °C) solvents, such as DMF. Typically, low substrate loadings ($< 5\%$) are also used. These factors drastically limit the application of these processes in terms of energy use, safety, reactor design and separation. With the emphasis on the discussion of catalyst development, surprisingly little consideration is often given to these aspects, particularly isolation of the product. The low substrate loading used leads to a low DFF concentration after the reaction, which makes solvent extraction or precipitation unfeasible, and solvent evaporation is too energy intensive for the high boiling point of the solvents employed. A new approach is thus needed to overcome these issues, which would help pave the way towards potential scale up of production of DFF.

Ionic liquids represent a valuable class of solvent that can overcome the safety issues related to flammability and low vapor pressure, making them very attractive for oxidation

reactions.³⁸⁻⁴⁰ Moreover, our observation that the sublimation properties of DFF are retained in the ionic liquid and that the molecule can be easily separated under vacuum at relatively low temperature (80 °C) to provide a high purity product.²⁵ The selective oxidation of alcohols in ionic liquids has been studied widely and various systems based mostly on homogeneous catalysts have been proposed.^{41,42} It is usually considered that aerobic oxidation is the most environmentally-friendly oxidation technique for these transformations since oxygen (at low pressures) is relatively cheap and safe. Stoichiometric oxidants can produce toxic waste or introduce a large amount of water into the system, which can compromise the selectivity and yield of the reaction. While the products of oxidation by hydrogen peroxide, for example, are innocuous, its production requires many steps that compromise its reputation as a 'green oxidant' and its use in high concentration has serious safety implications. Moreover, it has been demonstrated that hydrogen peroxide can degrade imidazolium ionic liquids through Fenton oxidation, undermining the use of this oxidant with ionic liquids.⁴³ A catalyst system based on CuCl and the oxidant TEMPO (TEMPO = (2,2,6,6-tetramethylpiperidin-1-yl)oxyl) has proved to be one of the most efficient for the selective oxidation of alcohols to aldehydes due to its wide substrate scope.⁴⁴ However, this system suffers from recyclability problems and product separation due to the homogeneous nature of the system. It proved possible to recycle TEMPO up to 5 times by extracting the aldehydes formed with diethyl ether, though this method proved to be inefficient due to the high solubility of TEMPO in diethyl ether, resulting in the need for long reaction times due to catalyst leaching.⁴⁵ Hansen and co-workers successfully achieved high yields for the conversion of HMF to DFF using a CuCl/bipyridine/TEMPO system (without recycling) but long reaction times were again required and toxic acetonitrile was used as the solvent.⁴⁶ Another report⁴⁷ demonstrated that a wide variety of alcohols can be oxidized in [bmim][PF₆] with high efficiency in less than 3 hours, however, the attractiveness of this system is compromised by the toxicity of this ionic liquid and the alcohols investigated did not include HMF.

In this contribution, a new system is presented based on TEMPO and a pyridine immobilized ionic liquid for use with CuCl in the ionic liquids, [bmim][OTf] and [bmim][NTf₂]. This allows high isolated yields of DFF to be obtained at high HMF loading (40%). In contrast to HMF, the separation of DFF from the ionic liquid is straightforward since DFF sublimes readily from the medium. This significant difference is traced to the absence of the hydroxyl group, which leads to the high affinity of HMF for ionic liquids.⁷ Following our previous study on the dehydration of fructose to HMF in [bmim][OTf] with HCl in high yield,⁴⁸ the oxidation was also performed in two steps from fructose achieving 55% isolated yield. This system represents a very attractive method for the transformation of HMF to high purity DFF.

EXPERIMENTAL

Materials. Methylimidazole (99%), chlorobutane (99%), anhydrous benzene (99.8%), calcium hydride (95%), phosphorous pentoxide (99.9%), copper(I) chloride (99.995%) and dibromobutane (99%) were purchased from Sigma-Aldrich, while HMF (98%), 4-hydroxy-TEMPO (98%) and TEMPO (99%) were obtained from Fluorochem. Acetonitrile (>99.8%) and ethyl acetate (>99.5%) were procured from VWR. Methylimidazole was distilled under reduced pressure over CaH₂. Chlorobutane was distilled at atmospheric pressure over P₂O₅. All other reagents were used as received. Procedures for the synthesis of [bmim][X] (X = Cl, Br, OTf,

NTf₂, HSO₄), [TEMPO-bmim][NTf₂], and [bbpy][NTf₂] (bbpy = *N*-butyl-4,4'-bipyridinium) are provided in the Supporting Information.

Procedures. Screening experiments were performed in triplicate. A stock solution was prepared by mixing the ionic liquid (1 g) with the catalyst (copper chloride and TEMPO) to obtain the desired catalyst/substrate ratio. The solution was left stirring overnight at room temperature. HMF was added and stirred until the substrate dissolved completely. The reaction was conducted in a 3 mL vial with 200 mg of sample. The vial was purged with oxygen for 5 minutes and a balloon of oxygen attached. The reaction vial was then heated in a heating block at the desired temperature. Sublimation of DFF was observed in all cases. The HPLC yield was determined by measuring both the sublimed and dissolved DFF. The combined product was diluted with 3 mL of phosphate buffer (pH 6.8) and then further diluted with buffer in a 1:5 ratio. Experiments performed with the hydrophobic ionic liquid, [bmim][NTf₂], were analyzed by washing the ionic liquid 8 times with 3 mL of phosphate buffer.

The synthesis of FFCA at 4 bar pressure was performed in a microbatch reactor. Separation of DFF for recycling was achieved by sublimation at 80 °C under vacuum.

Isolation of DFF. DFF was isolated from the reaction mixture by attaching the reaction vial to a vacuum pump with a regulator set at 2 mbar. After vacuum was applied, the vial was heated slowly at 80 °C using a heating block on a hotplate. After 6 h, most of the DFF was observed to have collected on the upper walls of the vials as a white solid block (Figure S26 in Supporting Information).

Characterization of the catalyst. Catalyst characterization was performed by X-ray photoelectron spectroscopy (XPS) on a Thermo NEXSA XPS instrument fitted with a monochromated Al K α X-ray source (1486.7 eV), a spherical sector analyser, 3 multichannel resistive plate and 128 channel delay line detectors. All data were recorded at 19.2 W and an X-ray beam size of 200 x 100 μ m. Survey scans were recorded at a pass energy of 160 eV and high-resolution scans recorded at a pass energy of 20 eV. Electronic charge neutralization was achieved using a dual-beam, low-energy electron/ion source (Thermo Scientific FG-03). The ion gun current was 150 μ A at a voltage of 45 V. All sample data were recorded at a pressure below 10⁻⁸ Torr and at room temperature (294 K). XPS spectra were fitted with OriginPro 2017 using the Savitzky-Golay method over a 10 point window.

In order to perform the characterization of the catalyst, the complex Cu-ligand complex was prepared and isolated (rather than *in situ* as in the catalytic runs) using the following method. Stoichiometric amounts of ligand and CuCl (100 mg) were mixed in dry acetonitrile (10 mL) at room temperature overnight. After solvent removal under vacuum, the catalyst was washed with diethyl ether (3 x 2 mL) and dried in a vacuum oven overnight at 60 °C.

The recovery of the catalyst after the reaction was achieved by addition of water to the reaction mixture (in a 10:1 ratio) causing the copper-ligand complex to precipitate from the reaction mixture before recovery by decantation. Catalyst recovery was performed for the experiments where recycling was employed. It proved possible only when using hydrophobic [bbpy][NTf₂], since this prevents the ligand being lost in the water phase and maintains the interaction with the copper center.

RESULTS AND DISCUSSION

Selection of the solvent system. The performance of the CuCl/TEMPO system was analyzed in four different ionic liquids: [bmim][OTf], [bmim]Cl, [bmim]Br and [bmim][HSO₄] (Figure 2) at 80 °C for 12 h under O₂ (balloon).

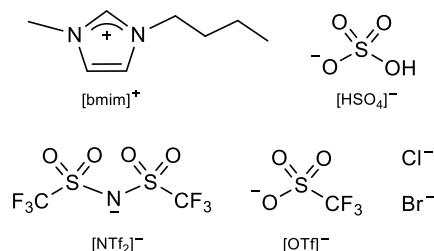


Figure 2. The cations and anions in the ionic liquids used in this contribution.

It was observed (Table 1) that in halogenated ionic liquids the reaction fails to proceed with only [bmim][OTf] successfully achieving the oxidation, in 88% yield. Only 3% DFF yield was recorded in [bmim][HSO₄]. These results already indicated a strong dependency on the nature of the ionic liquid medium.

Table 1. Solvent system selection for the oxidation of HMF to DFF at 80 °C, O₂ balloon, 12 h, 5 mol% TEMPO/CuCl, HMF loading 10%. Data are the average of 3 repeats.

ionic liquid	conversion (%)	DFF yield (%)	FFCA yield (%)
[bmim][OTf]	100	88 ± 1	9 ± 1
[bmim]Cl	8 ± 1	0	0
[bmim]Br	0	0	0
[bmim][HSO ₄]	26 ± 1	3 ± 1	0

This suggests that the coordinating ability of the halide anions could be responsible for catalyst inhibition in [bmim]Cl and [bmim]Br media. To confirm this hypothesis, it was attempted to perform the oxidation with a stoichiometric amount of catalyst, however, this led only to HMF degradation and no production of DFF. Surprisingly, this result appears to diverge from the results obtained previously, where [CuCl₂]⁻ was employed with an ionic liquid attached to TEMPO via a PEG linker (PEG = polyethylene glycol) in the oxidation of a wide range of alcohols.⁴⁹ In that study, only catalytic amounts of chloride were added and no excess of anions was present. Another possible reason for the reactivity described in Table 1 is the low solubility of O₂ in [bmim]Cl and [bmim]Br⁵⁰ compared to the TEMPO-PEG-IL system mentioned above.

Selection of the ligand. To improve the kinetics of the reaction, the effect of a basic promoter was investigated. This approach has been shown to increase dramatically the efficiency of the oxidation of alcohols under homogeneous catalysis conditions.^{51,52} The base can promote the reaction by deprotonation of the alcohol or act as a ligand for the copper center, increasing its catalytic activity. The amines, pyridine, DABCO (1,4-diazabicyclo[2.2.2]octane), DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) and triethylamine, were selected to cover a pKa range from

5 to 13. As can be observed in Figure 3, no direct correlation between the pKa and the final DFF yield is observed since triethylamine (with the highest pKa of 13) slows down the reaction more than the other amines. This can be explained by the low coordinating ability of this amine, suggesting that such metal-ligand interactions play a major role in enhancing the reaction rate compared to alcohol deprotonation by the amine. The oxidation performance in [bmim][OTf] proved to be very efficient, proceeding with full conversion to produce yields over 90% of DFF with DABCO, DBU and pyridine in 6 hours.

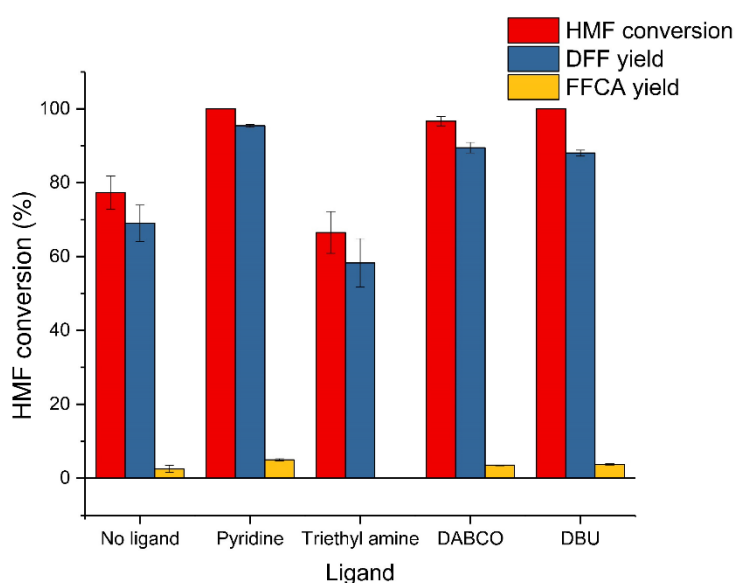


Figure 3. Effect of different ligands/promoters on the yields and conversion of HMF. Experiments performed for 6 h with O₂ balloon at 80 °C, 200 mg [bmim][OTf], 20 mg HMF, TEMPO/CuCl/promoter loading 5 mol%.

The high conversion after 6 hours led to the investigation of shorter reaction times to assess the relative performance of the bases. After 3 hours, it was found that pyridine was slightly more efficient with respect to DBU (Figure 4, left). Comparing the data for 3 and 6 hours, there is a slight increase in selectivity at 100% conversion after 6 hours. This agrees well with observations by Hansen and co-workers for the same reaction performed in acetonitrile solution, attributed by those authors to the formation of an intermediate.⁴⁶ A modest amount of over-oxidation to FFCA was observed in all cases possibly due to the water generated in the system, which forms geminal diols with the electrophilic DFF.

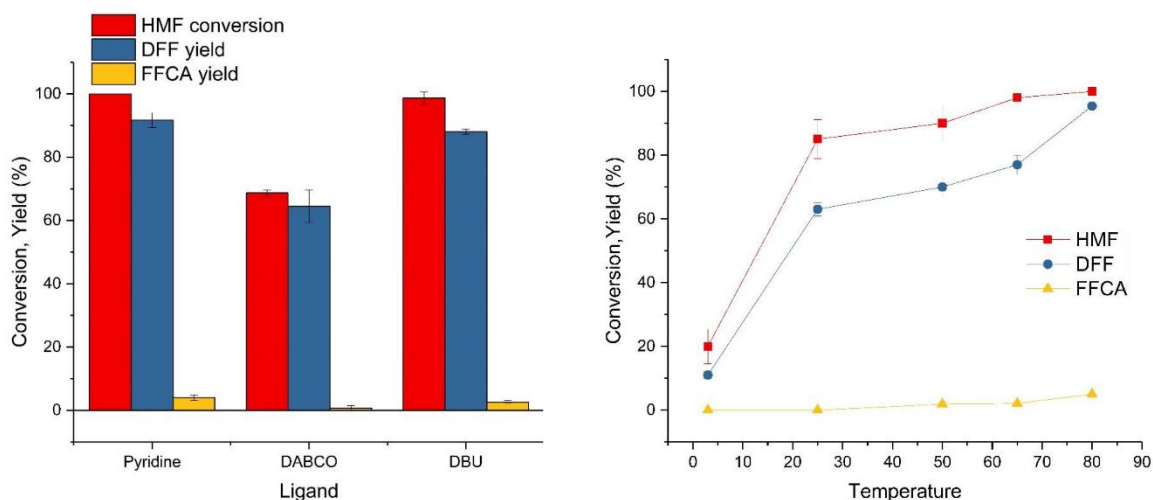


Figure 4. On the left, effect of different ligands/promoters on the yields of DFF/FFCA and conversion of HMF after 3 hours. Experiments performed with O₂ balloon at 80 °C, 200 mg [bmim][OTf], 20 mg HMF, TEMPO/CuCl/promoter loading 5 mol%. On the right, temperature effect on yields of DFF/FFCA and conversion of HMF at 6 h reaction time with CuCl/pyridine/TEMPO at 10 % HMF loading.

Further studies were performed to analyze the effect of temperature on the reaction. (Figure 4, right), showing that it had a favorable effect, with over 95% DFF yield observed at 80 °C. At lower temperatures, the reaction rate decreases, limiting the HMF conversion. In this case, the mass balance is incomplete, further enforcing the theory that an intermediate is involved in the mechanism of reaction. At temperatures below 50 °C (e.g., at 3 °C in the fridge), it was noticed that the reaction mixture solidified due to the insolubility of DFF in the reaction media, further slowing down the reaction due to mass transfer limitations.

Initial HMF concentration and catalyst loading. To maximize the DFF throughput, the initial amount of HMF used was increased. As shown in Figure 5, a gradual decrease of yield and conversion were observed with a high selectivity of over 95% being maintained at 50% HMF loading. It is believed that the observed decrease in rate constant is due to the water generated in the system. In order to analyze the effect of the water content on the reaction rate, experiments were conducted to minimize the water content in the reaction mixture. This was achieved by various means, such as thermal evaporation (heating to 100 °C), physical removal through the use of a hydrophobic solvent (using [bmim][NTf₂]) or adding a drying agent (molecular sieves at 80 °C).

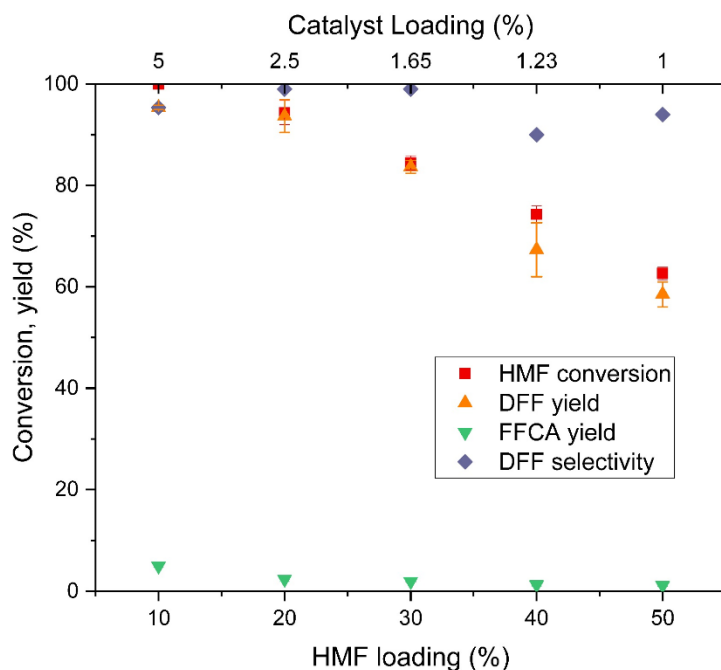


Figure 5. Influence of HMF loading on conversion and yield in [bmim][OTf] showing that higher HMF loadings slow down the reaction while maintaining high selectivity. Experiments performed for 6 h with O₂ balloon at 80 °C, TEMPO/CuCl/pyridine loading of 5 mol%.

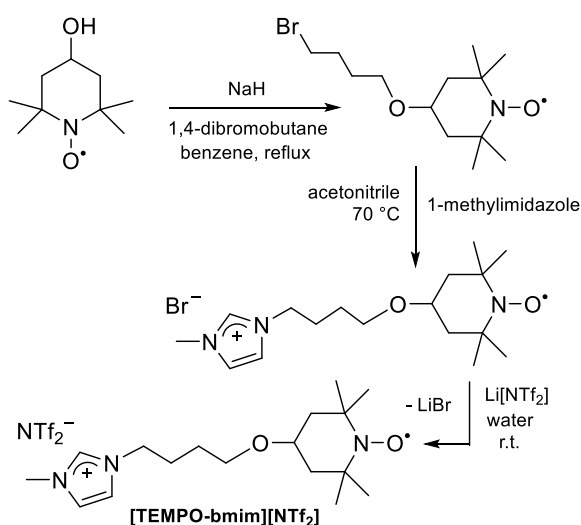
Table 2 suggests that, while molecular sieves have a detrimental effect on the reaction, the substitution of the hydrophilic [bmim][OTf] with the hydrophobic [bmim][NTf₂] has a beneficial effect. Higher temperatures result in a decrease in the rate of the reaction, probably due to partial sublimation of TEMPO from the reaction mixture or catalyst deactivation through the formation of side products or undefined copper complexes. However, increasing the reaction time to 12 h using [bmim][NTf₂] (Entry 6) did not improve on the performance after 6 h, suggesting the deactivation of the catalyst. This has been observed in the oxidation of *trans*-hex-2-ene-1-ol under similar conditions, for which the authors observed no reaction at low catalyst loading (1 mol%) and deactivation of the catalyst when the reaction reached 100% conversion with higher loadings.⁵³ It has also been proposed by Hoover and co-workers that the deactivation is due to the formation of a copper hydroxide dimer complex at high water content, which is insoluble in the reaction mixture.⁵² However, in our reactions, insoluble solid was not observed, leading us to suspect a different form of deactivation. One possibility is that the TEMPO sublimates during the course of the reaction, resulting in a negligible increase in yield between 6 and 12 hours (Entries 4 and 6 in Table 2) under the same conditions. Moreover, it has been demonstrated that alcohol oxidation by TEMPO can follow second order reaction kinetics, making the conversion and yield dependent on the initial concentration of substrate.⁵³ This led us to suspect that higher substrate loadings would lead to the need for longer reaction times and hence a greater negative impact from TEMPO sublimation. To address this, the catalyst loading was increased from 1.23% to 5%, leading to a yield of 90% at full conversion in 6 hours (Entry 7). While this was effective, other approaches to address the loss of TEMPO through sublimation were explored. It was decided to exploit the well-known potential of ionic liquids for chemical modification to immobilize TEMPO. This would prevent the loss of activity through TEMPO sublimation and allow further improvements for catalyst recycling at high HMF loadings.

Table 2. Oxidation of HMF at 40% loading of HMF and TEMPO/CuCl/pyridine as the catalyst

entry	ionic liquid	T (°C)	cat. loading (mol%)	time (h)	conversion (%)	DFF yield (%)	FFCA yield (%)
1	[bmim][OTf]	80	1.23	6	74 ± 2	69 ± 5	1 ± 0.2
2	[bmim][OTf]	100	1.23	6	64 ± 1	61 ± 3	2 ± 0.2
3	[bmim][OTf] + mol. sieves	80	1.23	6	64 ± 2	61 ± 1	0
4	[bmim][NTf ₂]	80	1.23	6	82 ± 1	76 ± 2	0
5	[bmim][NTf ₂]	100	1.23	6	72 ± 2	57 ± 2	0
6	[bmim][NTf ₂]	80	1.23	12	83 ± 1	75 ± 2	0
7	[bmim][NTf ₂]	80	5.0	6	100	90 ± 1	0

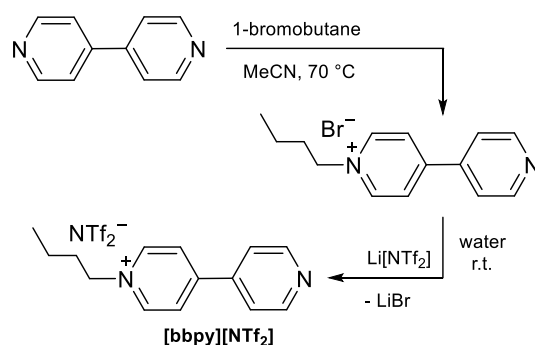
system. Data shown are the average of 3 repeat experiments.

TEMPO and pyridine immobilization. Since the reaction depends on the continued presence of TEMPO in the reaction mixture even at high temperatures, its retention is key to the recyclability of the system. It was anticipated that this could be achieved by immobilizing TEMPO by attaching it to the ionic liquid, thus also allowing the selective sublimation of DFF from the mixture. The immobilization of TEMPO within ionic liquid media has been explored for various applications. Wang and co-workers immobilized TEMPO on a PEG-1000 imidazolium ionic liquid and then used the PEG as a combined solvent and catalyst system.⁵⁴ A triazolium salt has also been employed to immobilize TEMPO in order to perform oxidation reactions with the stoichiometric oxidant BAIB (bis(acetoxy)iodobenzene) in [Hmim][BF₄].⁴⁹ In the present work it was decided to immobilize TEMPO using dibromobutane to form a linker between TEMPO and the imidazolium ring. The synthetic pathway used to form this system is shown in Scheme 1 and is based on a modified literature procedure (Supporting Information).⁵⁵

**Scheme 1.** Synthesis of the ionic liquid immobilized TEMPO, [TEMPO-bmim][NTf₂].

The analogue, 4-hydroxy-TEMPO was treated with 1,4-dibromobutane in benzene under reflux using sodium hydride to yield the bromide-terminated TEMPO unit before addition of methylimidazole and heating at reflux in acetonitrile. The imidazolium salt formed was then metathesized with LiNTf₂ to form the triflimide salt, [TEMPO-bmim][NTf₂]. This compound was characterized using multinuclear NMR spectroscopy and mass spectrometry. The [TEMPO-bmim][NTf₂] was used as a catalyst in [bmim][NTf₂] solvent under the same conditions as entries 5-7 in Table 2. While the same result was obtained under the conditions used for entries 6 and 7, higher conversion (81 ± 1%) and yield (73 ± 3%) was obtained at 100 °C (Table 2, Entry 5 conditions). This suggested that the DFF yield was indeed being compromised by the loss of TEMPO through sublimation when using the non-immobilized system at 100 °C (Entry 5). However, the fact that the reaction does not proceed further even with longer reaction times (Entry 6 conditions) suggests deactivation of the copper catalyst.

As can be seen in Figures 2 and 3, the use of pyridine as a promoter is effective and so we explored its use under the same conditions employed for [TEMPO-bmim][NTf₂]. As with TEMPO, pyridine will also evaporate at elevated temperatures under low pressure conditions. To address this, an immobilized version of pyridine was prepared based on 4,4'-bipyridine (Scheme 2). Alkylation of this compound and metathesis with Li[NTf₂] provided the ionic liquid, [bbpy][NTf₂], following a modified literature procedure (Supporting Information).⁵⁶

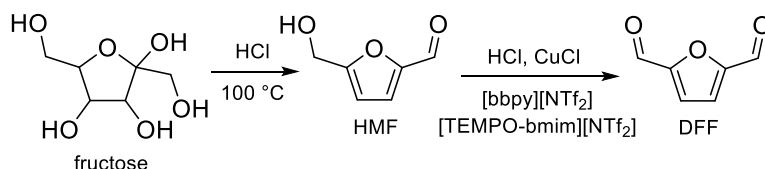


Scheme 2. Synthesis of the pyridine-immobilized ionic liquid, [bbpy][NTf₂].

Investigation of recycling with immobilized TEMPO. In terms of scale up, the recycling of the catalytic system represents an essential feature to achieve economic feasibility. Despite the often-cited potential for recycling ionic liquid media, this process is very rarely reported in the vast number of studies employing ionic liquids. In order to probe this aspect, the reaction was carried out in triplicate using [bmim][NTf₂] as solvent with immobilized versions of TEMPO and pyridine, [TEMPO-bmim][NTf₂] (5 mol%) and [bbpy][NTf₂] (5 mol%), and CuCl (5 mol%) as catalyst at 40% HMF loading. The DFF formed was separated by sublimation from the reaction mixture and the reaction then repeated by adding another portion of HMF. Although sublimation occurs during the 6 h reaction, most of the DFF precipitate from the mixture forms a very viscous slurry at room temperature (Figure S26 in Supporting Information). To complete the separation of the product, the system was left at 80 °C under vacuum for 8 h. This caused the DFF to sublime on the upper walls of the vials as a white solid block, allowing the product to be collected with ease. Using a very high 40% HMF substrate loading at 80 °C with an O₂ balloon, 100% conversion was observed after 6 h and 81% (± 8%) DFF was isolated by

sublimation. NMR analysis of the reaction mixture at the end of each run did not show any degradation of the ionic liquid (Figure S29, Supporting Information). A second run was performed with fresh substrate resulting in 75% conversion and an isolated DFF yield of 68% ($\pm 8\%$). This indicates that the system is still active on the second cycle but performs less well. One reason for this could be the generation of copper complexes with a reduced catalytic activity. To counter this, the reaction time of the second cycle was increased to 12 h, achieving a slight increase in conversion to 89% and led to an isolated DFF yield of 77% ($\pm 4\%$), comparable to that obtained for the first run. Addition of TEMPO or pyridine to the reaction mixture did not lead to an enhancement in activity, suggesting that it is the copper component of the system that contributes to the deactivation observed. This phenomenon was observed in acetonitrile solution by other researchers,^{28,29} who showed that the acid generated by further oxidation and water are the main causes of deactivation as they lead to formation of a copper hydroxide dimer that is insoluble in the reaction mixture. The authors demonstrated that, by switching to $[\text{Cu}(\text{OTf})_2]$, improved yields were achieved since the dimer complex with a triflate counterion has a higher solubility in the solvent.⁵³ However, despite this, the catalyst still suffered a degree of deactivation.

Synthesis of DFF from fructose in a two-step reaction. In a contrast to metal-catalyzed approaches,^{57,58} we recently described⁴⁸ the efficient dehydration of fructose to HMF in $[\text{bmim}][\text{OTf}]$ at 10 and 14% loadings with 3.5% water content and 10 mol% HCl at 100 °C. This led us to investigate the one-pot formation of DFF from fructose (Scheme 3) using the same conditions for the dehydration step, achieving 83% yield. Subsequent addition of CuCl and immobilized pyridine and TEMPO (10% loading with respect to HMF) led to an overall HPLC yield of $62 \pm 3\%$ (isolated yield $55 \pm 7\%$).



Scheme 3. Reaction path from fructose to DFF.

The oxidation step was found to proceed more slowly compared to the experiments performed over 6 h and required 10 h to achieve full conversion. This could be due to an equilibrium between TEMPO and its protonated form,⁵⁹ leading to lower effective catalyst concentration.

Study of the oxidation of HMF beyond DFF. As an extension of the oxidation of HMF to DFF, it was decided to explore the further oxidation to 5-formyl-2-furancarboxylic acid (FFCA) and 2,5-furandicarboxylic acid (FDCA).^{60,61} This was carried out in a one-pot process by varying reaction time, temperature and oxygen pressure. For this part of the study, the ionic liquid $[\text{bmim}][\text{OTf}]$ was used as solvent since hydrophilicity is an important property that can favor the formation of carboxylic acids. Compared to the results obtained previously, there is a significant change in the product distribution, increasing the production of FFCA over longer reaction times. At 80 °C and 1 bar O₂ pressure with the $\text{CuCl}/[\text{bbpy}][\text{NTf}_2]/[\text{TEMPO}-$

bmim][NTf₂] system (10 mol%), the conversion of HMF to DFF reached 95% (by HPLC) with only 5% FFCA observed after 6 h. Increasing the reaction time to 12 h led to a decrease in DFF observed (64%) and an increase in FFCA yield (26%). Since the use of higher temperatures leads to the sublimation of DFF, favoring the formation of this product, the reaction temperature and oxygen pressure were increased to 100 °C and 4 bar, respectively. At this pressure, no DFF sublimation was observed, favoring its further oxidation towards the carboxylic acids. At 100 °C, traces of FDCA appeared (3 ± 0.1%) but no further change in selectivity was observed from FFCA to FDCA at higher temperature (Figure 6). This could indicate that catalyst deactivation was occurring due to the acidity of the product formed, in particular FDCA (pKa = 2.5), which can protonate TEMPO and so inhibit its catalyst activity. A maximum of 63% yield of FFCA was obtained.

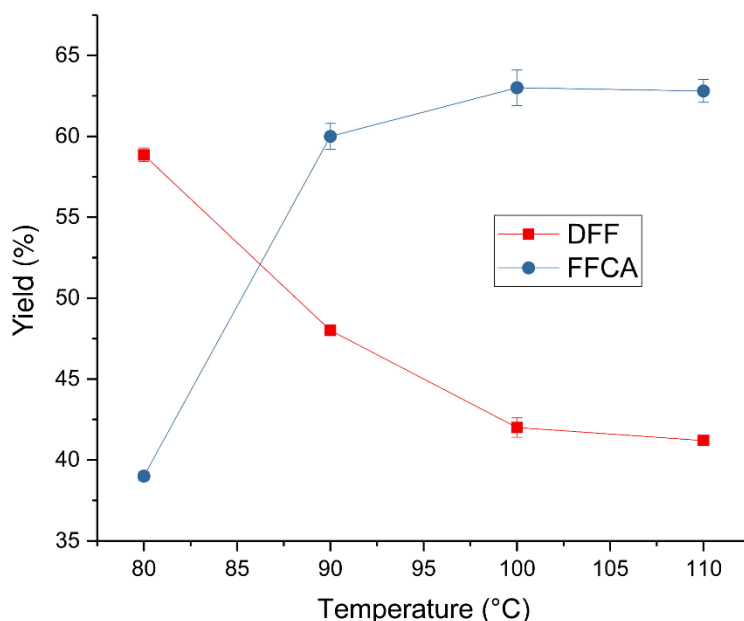


Figure 6. Yield of DFF and FFCA from HMF at different temperatures in [bmim][OTf]. Reaction conditions: 4 bar O₂ partial pressure, 10% HMF loading using the CuCl/[bbpy][NTf₂]/TEMPO-[bmim][NTf₂] system at 10 mol% catalyst loading.

The fractionation of DFF and FFCA was easily achieved by sublimation of DFF at low temperature and solvent extraction from the ionic liquid phase. The collection of FFCA was performed by solvent extraction with diethyl ether (5 x 5 mL) and the FFCA was collected as a yellowish powder.

Catalyst characterization. Various combinations of catalyst with different ligands/promoters were characterized by XPS (Figure S30, Supporting Information). In the catalytic cycle, copper is known to exist in oxidation states +1 and +2 and these can be identified by XPS from the presence (Cu^{II}) or absence (Cu^I) of broad satellite features centered around 943 and 962 eV.⁶² Two main characteristic features typically observed in XPS spectra of copper species are the 2p_{1/2} and 2p_{3/2} peaks. The main 2p_{3/2} peak is broader for Cu(II) and exhibits a higher binding energy compared to Cu(I), while the latter is a much sharper peak at a lower binding energy.

The presence of satellites in all the copper complexes investigated in this study indicate that the Cu(I) has been oxidized to Cu(II) prior to the organic transformation taking place, suggesting that, while CuCl is stable, the addition of the ligand makes the catalyst more sensitive to oxygen, leading to oxidation. Hence, TEMPO is needed to reduce the copper and commence the catalytic cycle. A mechanistic study by Stahl and co-workers suggested that dioxygen forms a bridge between two Cu(II) complexes which then undergo a TEMPO-mediated transformation to a Cu(II) hydroxide complex, which catalyzes the oxidation of the alcohol in conjunction with the radical TEMPO.⁶³ The binding energies for the main $2p_{3/2}$ peak (Table S1, Supporting Information) for CuCl with pyridine, DBU, DABCO and [bbpy][NTf₂] are all lower than that of CuCl₂,⁶⁴ indicating that the copper center is in an environment with lower electron density, suggesting that the Cu-Cl bond could have been broken to form different Cu(II) structures.

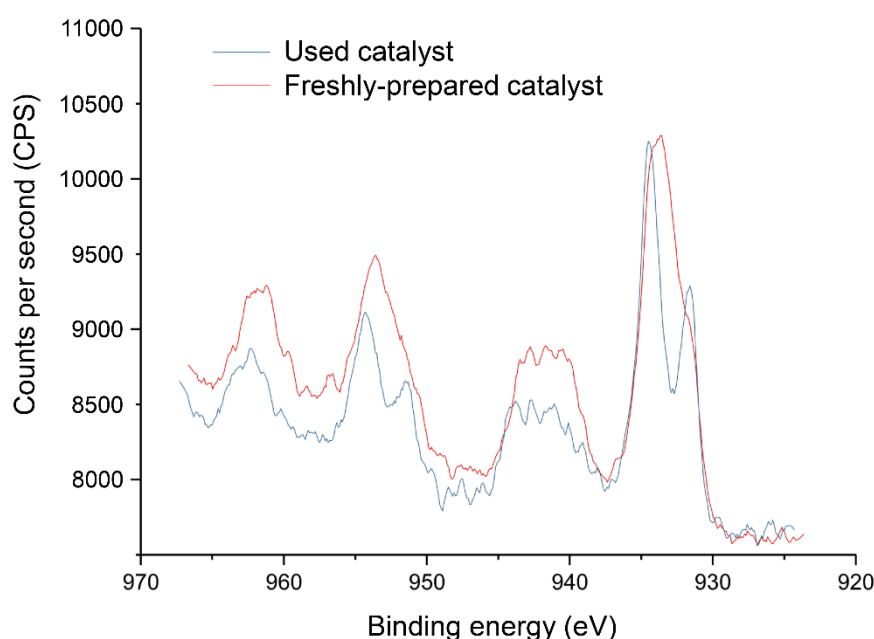


Figure 7. XPS analysis of freshly-prepared and used CuCl + [bbpy][NTf₂] catalyst.

The characterization by XPS of the used catalyst (Figure 7) shows a different copper structure with the broad $2p_{3/2}$ peak at 933.54 eV becoming two sharp peaks at 931.6 and 934.5 eV. The further splitting of the $2p_{1/2}$ peak suggests that a combination of copper(I) and copper(II) is present. The indicative peak for copper(I) at 931.6 eV is shifted at lower binding energy compared to the original peak for CuCl at 932.4 eV, while the Cu(II) peaks are shifted to higher binding energy compared to those of the freshly prepared catalyst. These data, combined with the formation of a sharp peak for Cu(II), suggest that a bimetallic Cu(II)-Cu(I) complex could be formed, which is catalytically inactive. The higher electron density associated with the Cu(I) center could cause the shift of the Cu(II) peaks and *vice versa*. The hypothesis of a bimetallic complex is supported by the findings of Yang and co-workers,⁶⁵ who reported that the formation of bimetallic copper complexes was associated with a split in the XPS spectral features, though the origins were not discussed.

CONCLUSIONS

While the conversion of 5-hydroxymethylfurfural (HMF) to 2,5-diformylfuran (DFF) using TEMPO and a copper catalyst has been investigated previously, these systems possessed significant drawbacks, such as the toxicity of the solvents used (acetonitrile), separation and purification problems (due to difficulties in removing TEMPO), low substrate loadings or high oxygen pressures. This transformation has never been attempted previously in ionic liquid media under homogeneous conditions, despite this medium offering many potential benefits to the generation and isolation of DFF from HMF. Among these advantages are the lack of volatility and potential for recyclability of ionic liquids (ILs), which has led to their widespread use with biomass processing. This is exemplified by the developments in the transformation of fructose, glucose and cellulose to HMF in these media. Despite this success, the difficulty in isolating HMF from the ionic liquid medium has led to the potential for further (*in situ*) reactivity of HMF to be explored. Thus, the conversion of HMF to DFF in ionic liquids is particularly attractive due to the negligible volatility of the IL solvent and the ability of DFF to sublime from the IL.²⁵ This study has shown that the four different ILs chosen (chloride, bromide, protic/non-coordinating and non-coordinating) display a dramatic difference in conversion of HMF to DFF (Table 1). The CuCl/TEMPO system only showed good activity in the non-protic, non-coordinating ionic liquid, [bmim][OTf], yielding 88% DFF (5 mol% catalyst loading, 12 hours). The addition of a range of nitrogen bases (pyridine, trimethylamine, DABCO and DBU) revealed that pyridine and DBU are the most effective. In all cases, a good selectivity for DFF was observed over the product of further oxidation (FFCA), even at high (50%) substrate loadings. All reactions proceeded at high substrate loadings and without the need for high oxygen pressures, in contrast to the typical conditions for processes based on *heterogeneous* catalysis.

For the same catalyst loading (1.2 mol%), it was found that the hydrophobic, non-coordinating ionic liquid, [bmim][NTf₂] led to a better HMF conversion (83%) and DFF yield (75%) at 80 °C than observed for [bmim][OTf] (64% and 61%, respectively) after 6 hours. Increasing the catalyst loading to 5 mol% gave the best results obtained with complete conversion and 90% DFF yield (with no FFCA formed).

Increasing the temperature from 80 °C to 100 °C had a detrimental effect on the conversion and yield and this was attributed to the loss of volatile TEMPO from the reaction medium. The versatility of design inherent to ionic liquids allowed this issue to be addressed by immobilizing TEMPO and pyridine within the ionic liquid. The use of this supported TEMPO system in [bmim][NTf₂] led to an HPLC-determined DFF yield of 91%. Since the TEMPO could no longer sublime along with the DFF, this allowed high **isolated** yields (81%) of DFF to be obtained in high purity by sublimation, overcoming issues encountered by other researchers using copper catalysts and TEMPO for this transformation. The introduction of immobilized TEMPO and pyridine components allowed recycling of the catalytic system to be achieved following sublimation of the DFF product (complete conversion, 81% DFF yield). After addition of fresh substrate, a lower conversion of 75% and a yield of 68% were obtained due to partial catalyst deactivation. Analysis of XPS data for freshly prepared and used catalysts suggest that a bimetallic, mixed valence, Cu(II)-Cu(I) species is formed, which could be catalytically inactive.

In studies aimed at extending the scope both in terms of possible precursors and products, DFF was synthesized from fructose in a two-step reaction in 55% isolated yield. The oxidation of HMF to FFCA yielded 63% of the carboxylic acid product alongside 41% DFF with separation easily achieved by sublimation and solvent extraction.

If the great promise for biomass transformation in ionic liquid media is to be realized, oxidation routes to specific platform chemicals such as DFF need to be developed. To be scaled up, these processes must operate at high substrate loadings, low oxygen pressures and involve scalable isolation and purification steps. The recycling of the solvent medium is also a key challenge. All of these points are addressed in the approach described here, which is the first to report the synthesis of DFF from HMF in ionic liquids under homogeneous conditions.

ASSOCIATED CONTENT

Supporting Information is available free of charge at X. Contents include the synthetic procedures and characterization with selected spectra and analytical data (PDF).

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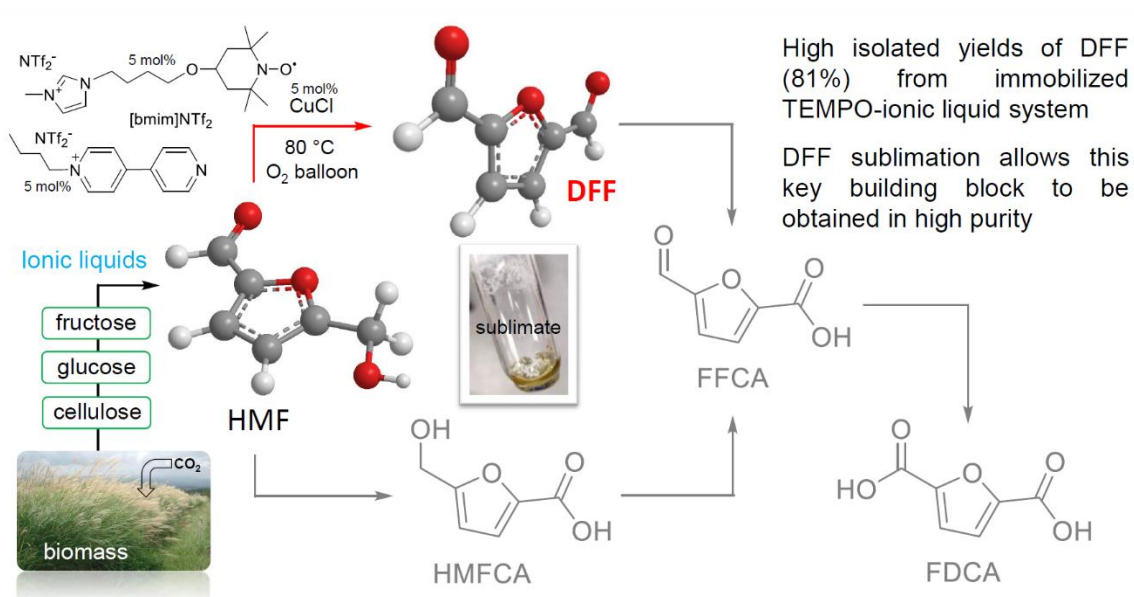
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The oxidation of HMF to DFF using oxygen (1 atm) with TEMPO/CuCl/base at different substrate loadings (10-50%) in different ionic liquids leads to dramatic differences in conversion. Immobilizing TEMPO and pyridine within [bmim][NTf₂] results in selective conversion of HMF to high-purity DFF (81%), separated by sublimation before recycling.

Supporting information

Efficient formation of 2,5-diformylfuran (DFF) in ionic liquids at high substrate loadings and low oxygen pressure with separation through sublimation

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S1 General considerations

Methylimidazole, chlorobutane, dry benzene, calcium hydride, phosphorous pentoxide, copper(I) chloride and dibromobutane were purchased from Sigma-Aldrich, while HMF, 4-hydroxy-TEMPO and TEMPO were obtained from Fluorochem. Acetonitrile and ethyl acetate were procured from VWR. Methylimidazole was distilled under reduced pressure over CaH₂. Chlorobutane was distilled at atmospheric pressure under P₂O₅. All reagents were used as received unless stated otherwise. Petroleum ether refers to the fraction boiling in the range 40-60 °C. Electrospray mass spectra were obtained using a Synapt G2 instrument (in positive mode). Nuclear magnetic resonance (NMR) spectroscopy was performed using a Bruker 400 MHz spectrometer using CDCl₃ or deuterated DMSO as solvent. All couplings are reported in Hertz. Substrate loadings were calculated by weight (w/w). Quantification of HMF yield was performed using a Shimadzu Prominence preparative HPLC (Shimadzu, Kyoto, Japan) with refractive index (RI) and ultraviolet (UV) detectors and equipped with an Aminex HPX-87H column using 0.005 M H₂SO₄ as the mobile phase at 55 °C and flow rate of 0.6 mL/min.

S2 Synthesis of ionic liquids

S2.1 Synthesis of [bmim]Cl and [bmim]Br

[bmim]Cl was synthesized on a large scale (350 g). Handling of all chemicals was performed by cannulation under inert conditions. 1-methylimidazole (160 mL, 2.00 mol) was transferred to a three-necked flask equipped with an air cooler followed by the addition of acetonitrile (100 mL). The mixture was heated at 60 °C under stirring. Chlorobutane (230 mL, 2.10 mol, 1.1 eq) was added dropwise using a dropping funnel. The reaction mixture was heated for 3 days at 60 °C and 3 days at 70 °C. Complete consumption of methyl imidazole was confirmed by ¹H NMR spectroscopy. [bmim]Cl was precipitated by gradual addition of ethyl acetate at 70 °C until a cloudy solution is formed and then crystallized at 3 °C. The colorless crystals obtained were washed under inert conditions with ethyl acetate (in portions, up to 2 L), dried under vacuum and stored in a glovebox. Yield: 340 g (97 % yield).

[bmim]Cl: ¹H NMR (DMSO-d₆): δ 9.62 (s, 1H, N₂CH), 7.92, 7.84 (m x 2, 2 x 1H, 2 x N-CH), 4.20 (t, 2H, N-CH₂-CH₂, J_{HH} = 7.2 Hz), 3.88 (s, 3H, N-CH₃), 1.77, 1.24 (m x 2, 2 x 2H, N-CH₂-CH₂-CH₂-CH₃), 0.87 (t, 3H, -CH₂-CH₃, J_{HH} = 7.3 Hz) ppm. ¹³C{¹H} NMR (DMSO-d₆): δ 137.2 (N₂-CH), 124.1, 122.7 (2 x N-CH), 48.8 (N-CH₂-CH₂-CH₂-CH₃), 36.14 (NCH₃), 31.8 (NCH₂-CH₂-CH₂-CH₃), 19.2 (NCH₂-CH₂-CH₂-CH₃), 13.7 (N-(CH₂)₂-CH₂-CH₃) ppm. MS (ES, +ve mode): *m/z* (abundance) = 139 (100) [bmim]⁺.

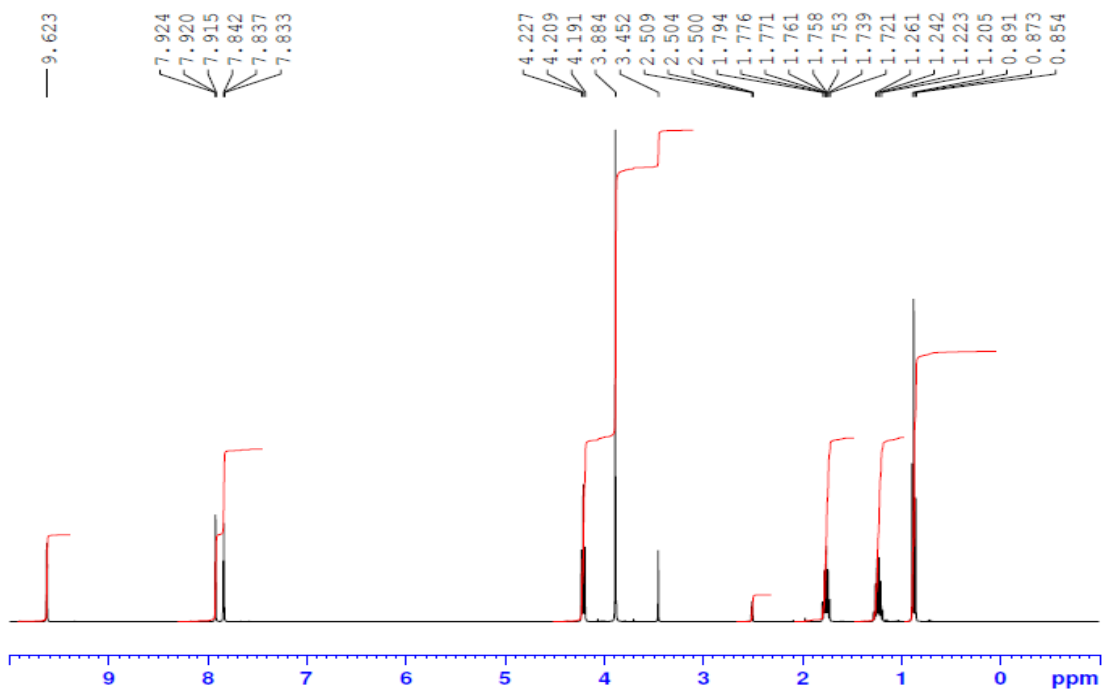


Figure S1. ^1H NMR spectrum of [bmim]Cl in deuterated DMSO.

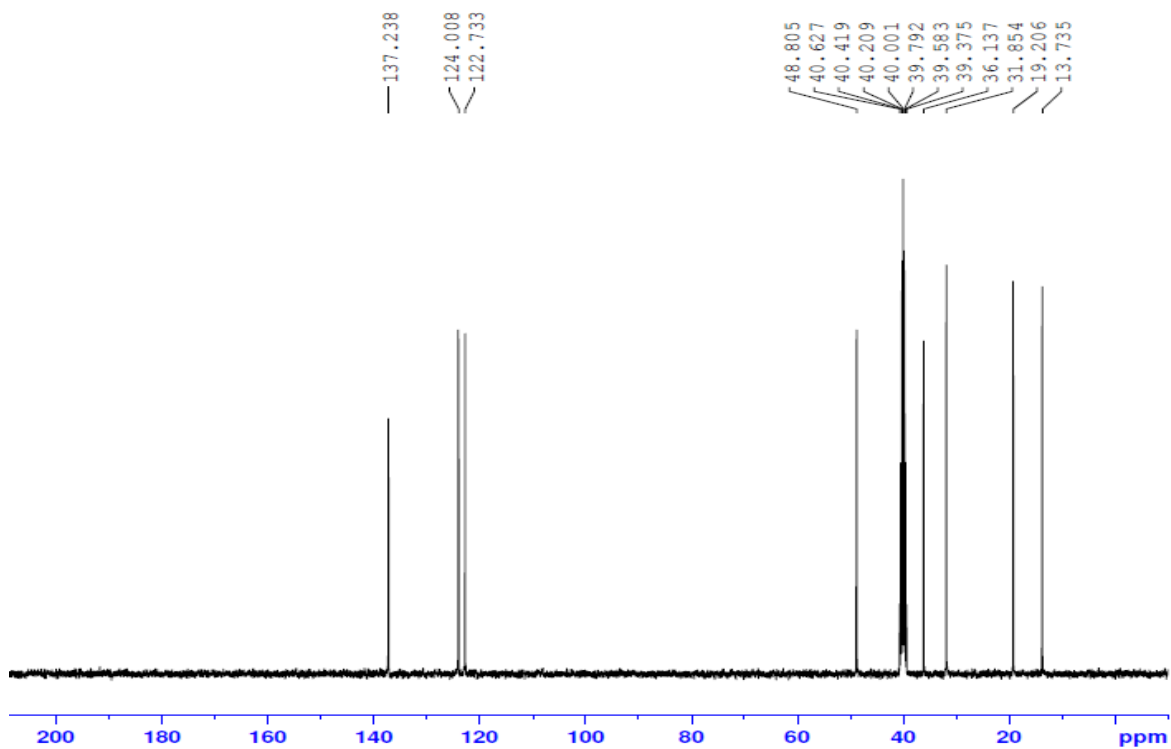


Figure S2. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [bmim]Cl in deuterated DMSO.



Figure S3. Mass spectrum of [bmim]Cl.

[bmim]Br was synthesized using the same procedure from bromobutane:

[bmim]Br: ^1H NMR (DMSO- d_6): δ 9.33 (s, 1H, N_2CH), 7.86, 7.78 (m x 2, 2 x 1H, 2 x N-CH), 4.20 (t, 2H, N- CH_2 - CH_2 , $J_{\text{HH}} = 7.2$ Hz), 3.87 (s, 3H, N- CH_3), 1.76, 1.25 (m x 2, 2 x 2H, N- CH_2 - CH_2 - CH_2 - CH_3), 0.88 (t, 3H, - CH_2 - CH_3 , $J_{\text{HH}} = 7.3$ Hz) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (DMSO- d_6): δ 137.2 (N $_2$ -CH), 124.1, 122.7 (2 x N-CH), 48.8 (N- CH_2 - CH_2 - CH_2 - CH_3), 36.14 (NCH $_3$), 31.8 (NCH $_2$ - CH_2 - CH_2 - CH_3), 19.2 (NCH $_2$ - CH_2 - CH_2 - CH_3), 13.7 (N-(CH_2) $_2$ - CH_2 - CH_3) ppm. MS (ES, +ve mode): m/z (abundance) = 357 (31) [(bmim) $_2$ Br] $^+$, 139 (100) [bmim] $^+$.

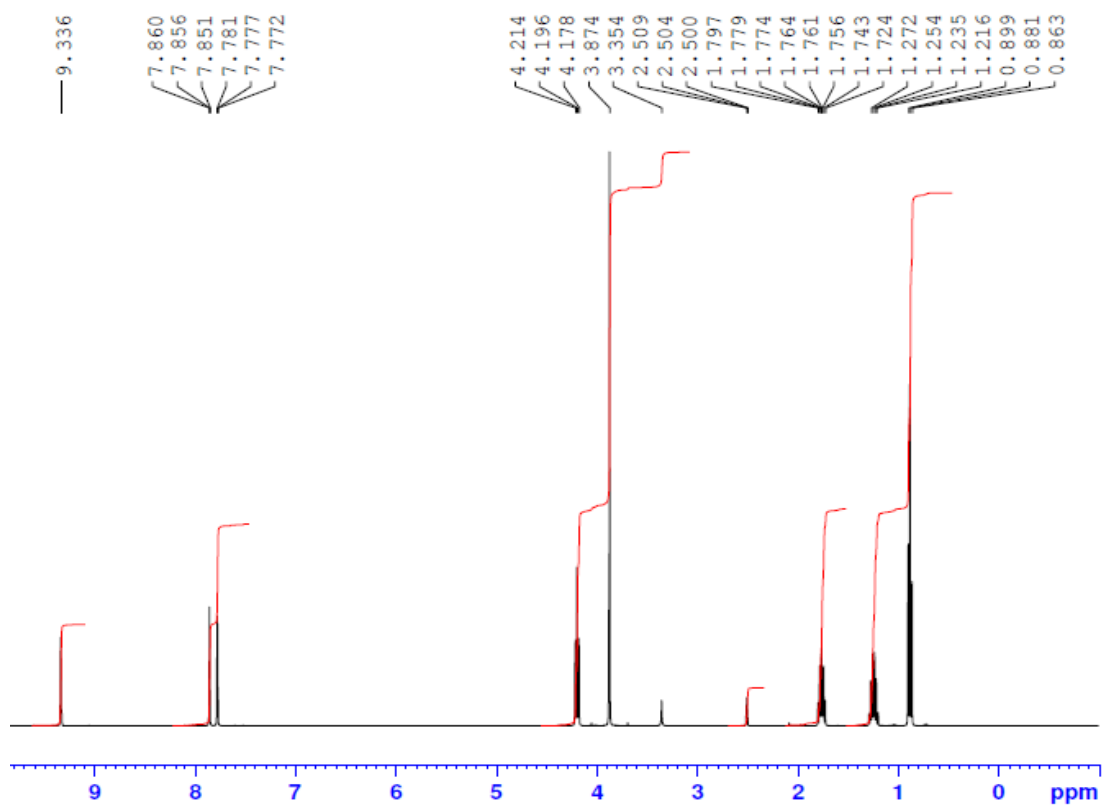


Figure S4. ^1H NMR spectrum of [bmim]Br in deuterated DMSO.

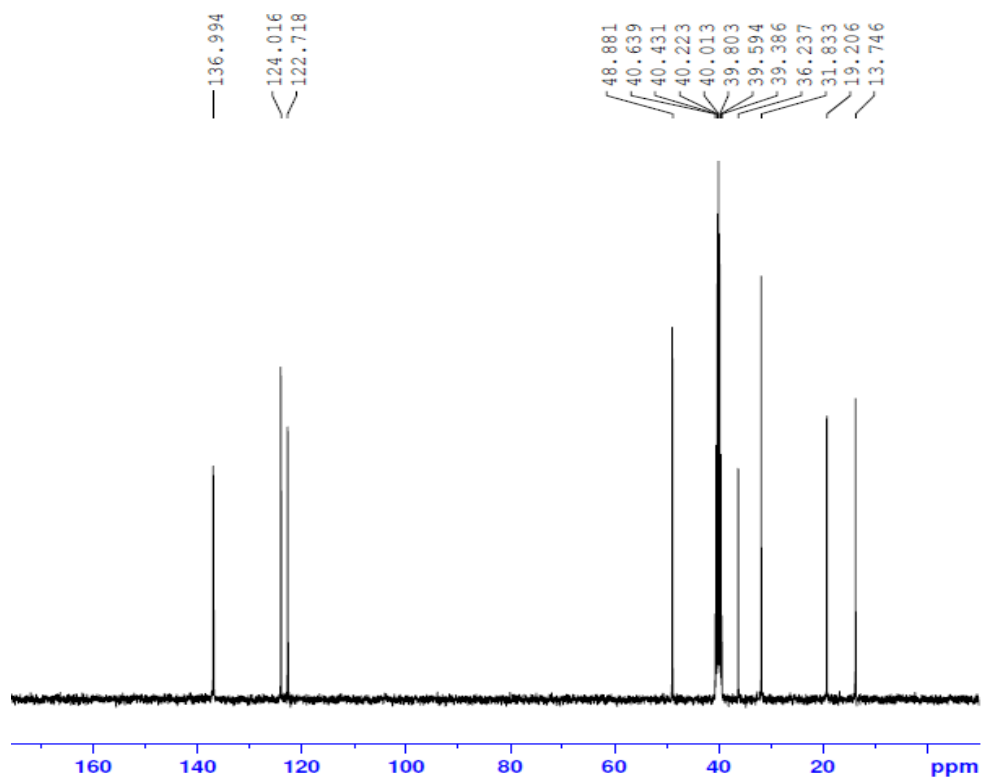


Figure S5. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [bmim]Br in deuterated DMSO.

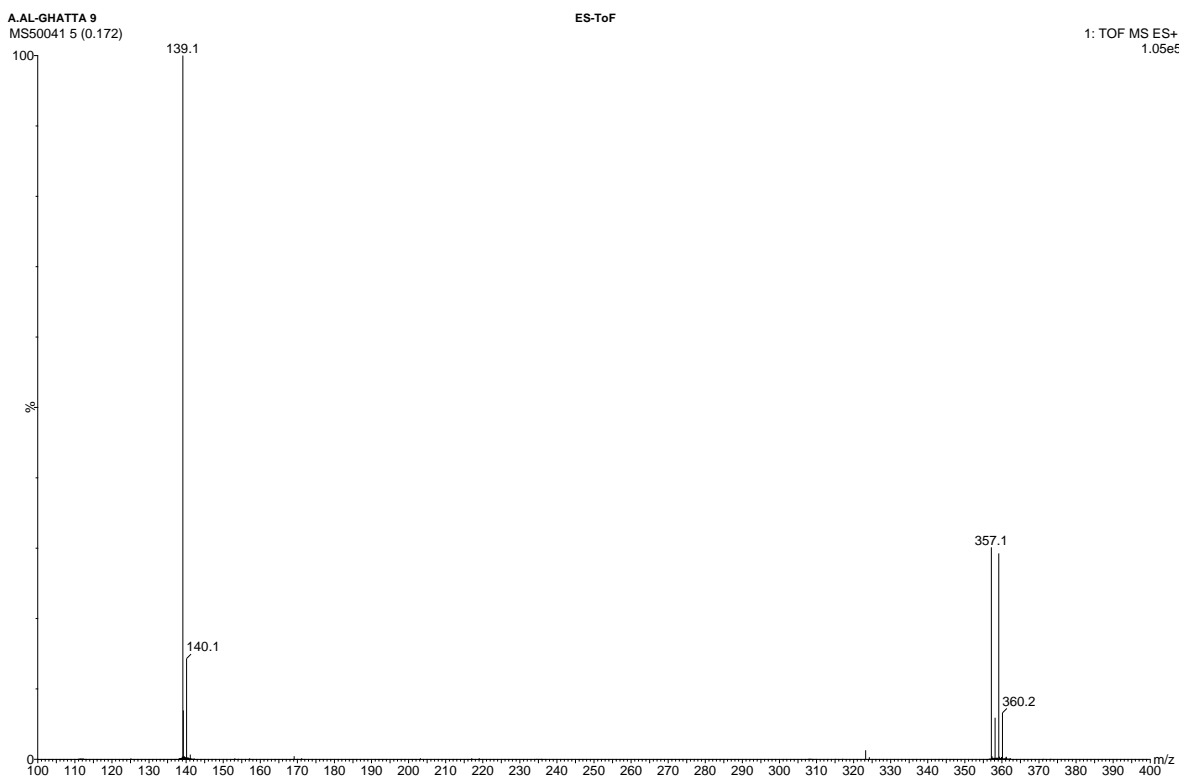


Figure S6. Mass spectrum of [bmim]Br.

The characterization data for both [bmim]Cl and [bmim]Br were in good agreement with those reported in the literature. ^{S1,S2}

S2.2 Synthesis of [bmim][OTf] and [bmim][NTf₂]

[bmim]Cl (30 g, 0.17 mol) was dissolved in water (100 mL) and Li[OTf] (30 g, 0.179 mol) was dissolved in water (50 mL). The lithium triflate solution was added dropwise to the chloride solution under vigorous stirring and the reaction left overnight. The product was extracted from aqueous solution using a total of 800 mL dichloromethane. The organic extracts were washed repeatedly with water (5 mL) until the silver nitrate test revealed no halide ions (5-6 washes). The organic phase was dried with magnesium sulfate and then evaporated to dryness under reduced pressure. The ionic liquid, [bmim][OTf] was further dried under reduced pressure overnight at 60 °C (final yield: 47 g, 96%) and handled thereafter under an inert atmosphere.

[bmim][OTf]: ¹H NMR (DMSO-d₆): δ 9.08 (s, 1H, N₂CH), 7.76-7.69- (m x 2, 2 x 1H, 2 x N-CH), 4.17 (t, 2H, N-CH₂-CH₂, J_{HH} = 7.2 Hz), 3.85 (s, 3H, N-CH₃), 1.77- 1.26 (m x 2, 2 x 2H, N-CH₂-CH₂-CH₂-CH₃), 0.9 (t, 3H, -CH₂-CH₃, J_{HH} = 7.4 Hz) ppm. ¹³C{¹H} NMR (DMSO-d₆): δ 137.7 (N₂-CH), 123.6-122.4 (2 x N-CH), 119.2 (CF₃), 49.1 (N-CH₂-CH₂-CH₂-CH₃), 35.8 (NCH₃), 32.0 (NCH₂-CH₂-CH₂-CH₃), 19.0 (NCH₂-CH₂-CH₂-CH₃), 13.8 (N-(CH₂)₂-CH₂-CH₃) ppm. MS (ES, +ve mode): m/z (abundance) = 139 (100) [bmim]⁺.

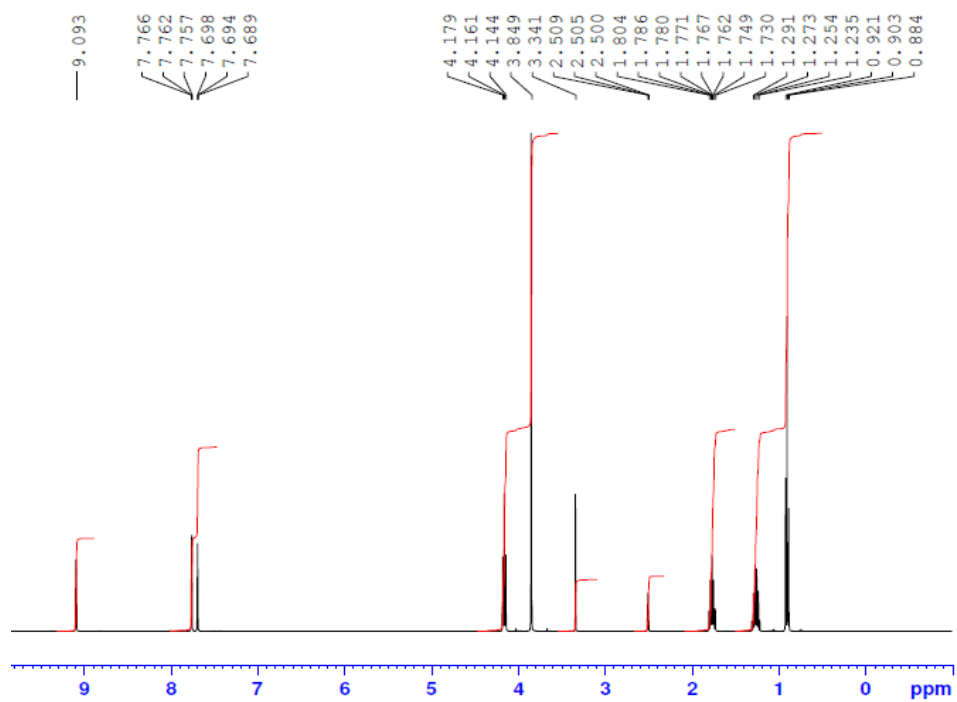


Figure S7. ^1H NMR spectrum of [bmim][OTf] in deuterated DMSO.

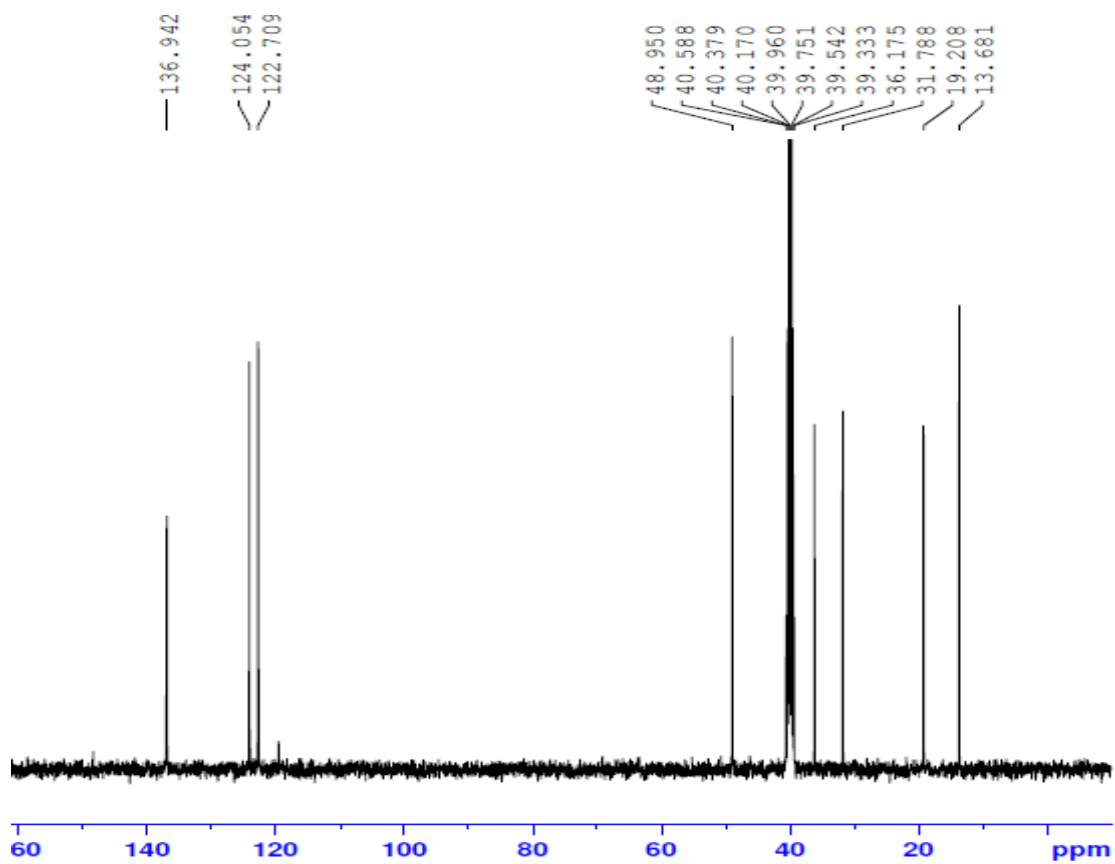


Figure S8. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [bmim][OTf] in deuterated DMSO.

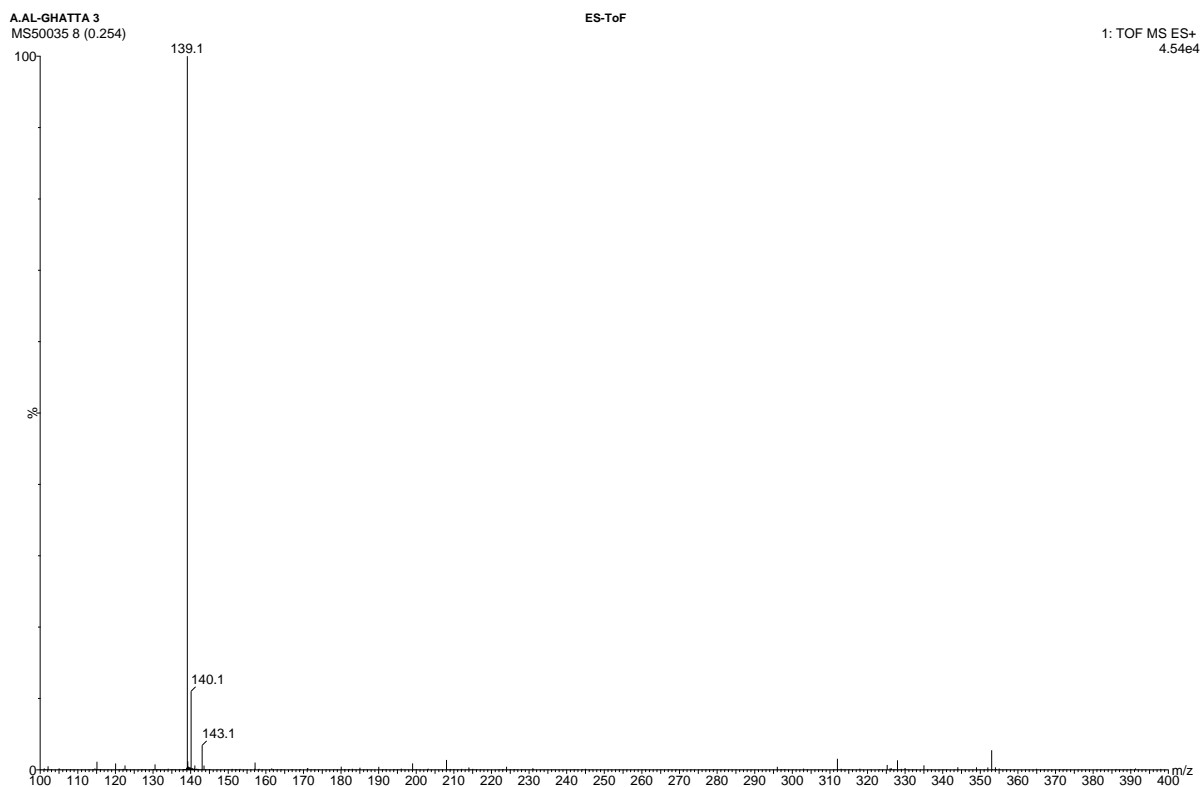


Figure S9. Mass spectrum of [bmim][OTf].

[bmim]NTf₂ was synthesized by the same procedure using Li[NTf₂].

[bmim][NTf₂]: ¹H NMR (DMSO-d₆): δ 9.08 (s, 1H, N₂CH), 7.86, 7.78 (m x 2, 2 x 1H, 2 x N-CH), 4.20 (t, 2H, N-CH₂-CH₂, J_{HH} = 7.3 Hz), 3.87 (s, 3H, N-CH₃), 1.76, 1.25 (m x 2, 2 x 2H, N-CH₂-CH₂-CH₂-CH₃), 0.88 (t, 3H, CH₂-CH₃, J_{HH} = 7.4 Hz) ppm. ¹³C{¹H} NMR (DMSO-d₆): δ 136.7 (N₂-CH), 124.06, 122.6 (2 x N-CH), 121.7 (CF₃) 48.9 (N-CH₂-CH₂-CH₂-CH₃), 36.1 (NCH₃), 31.7 (NCH₂-CH₂-CH₂-CH₃), 19.1 (NCH₂-CH₂-CH₂-CH₃), 13.5 (N-(CH₂)₂-CH₂-CH₃) ppm. MS (ES, +ve mode): m/z (abundance) = 558 (100) [(bmim)₂NTf₂]⁺, 139 (25) [bmim]⁺.

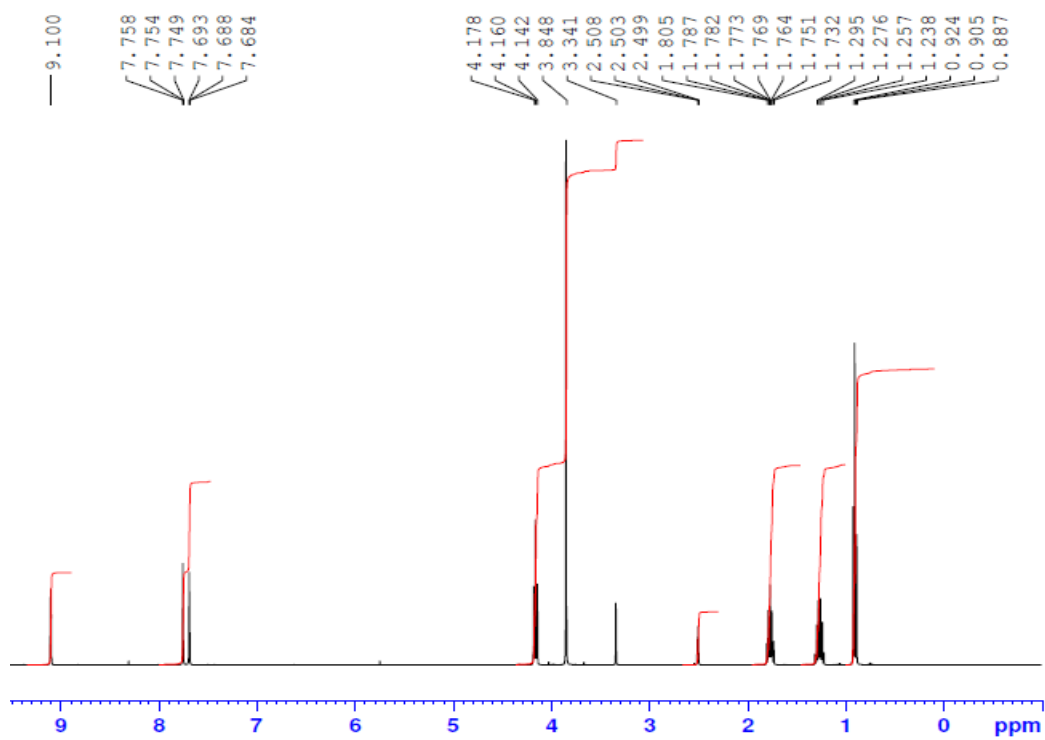


Figure S10. ^1H NMR spectrum of [bmim][NTf₂] in deuterated DMSO.

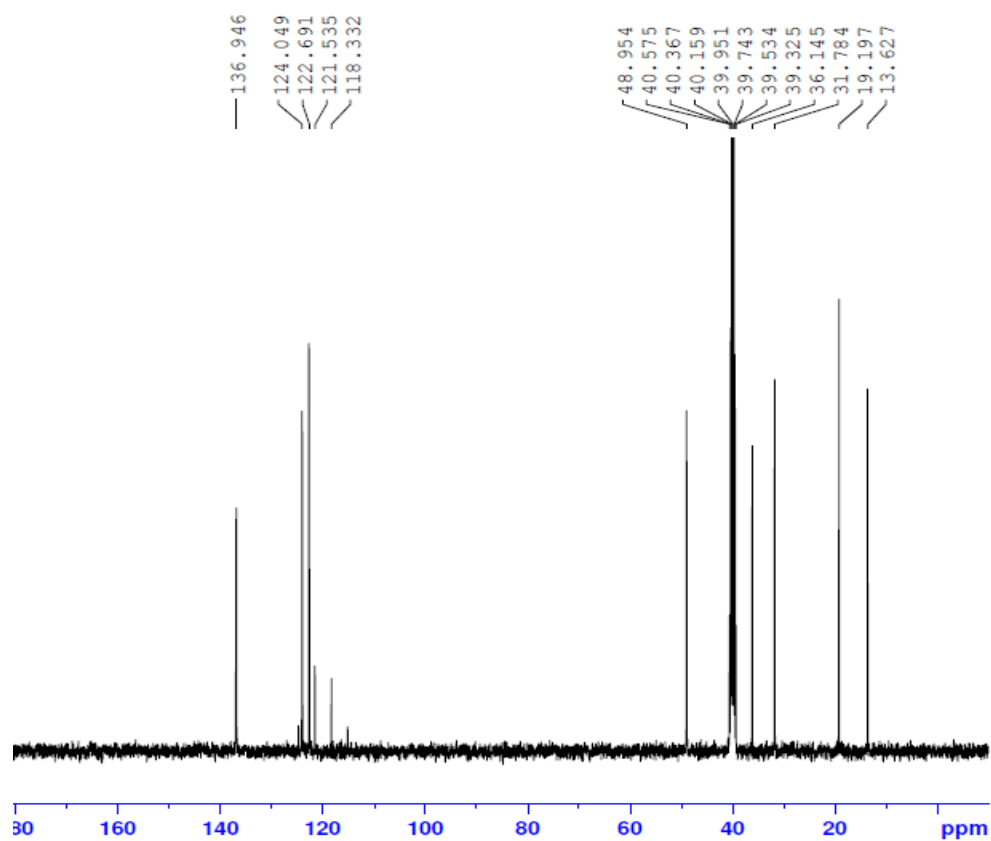


Figure S11. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [bmim][NTf₂] in deuterated DMSO.

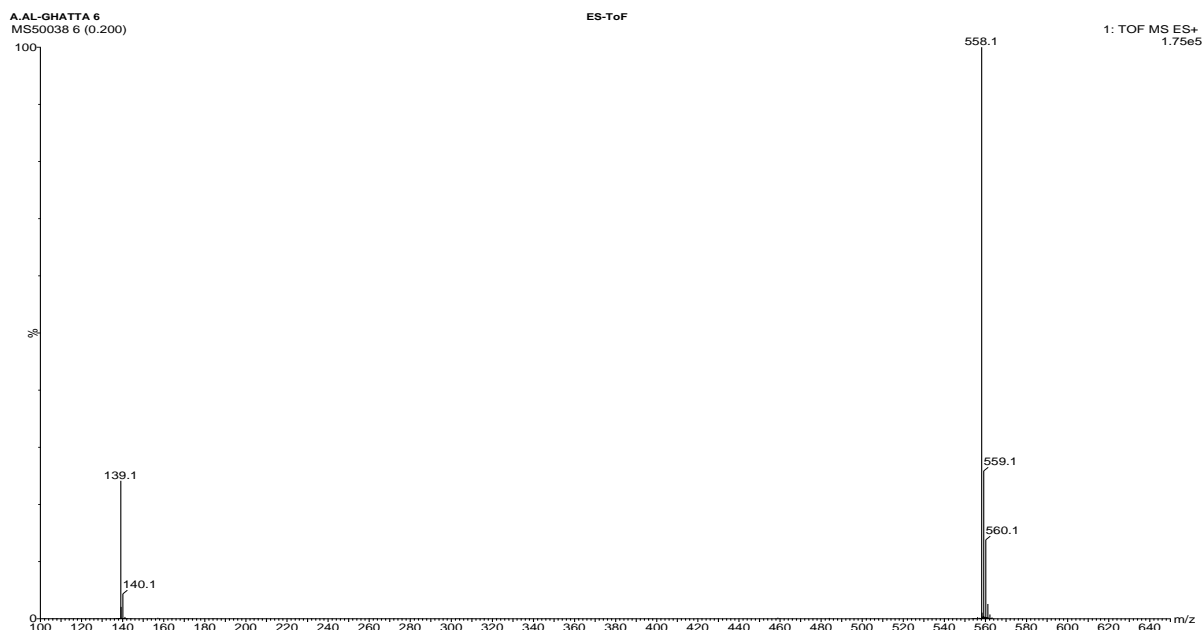


Figure S12. Mass spectrum of [bmim][NTf₂].

The characterization data for both [bmim][OTf] and [bmim][NTf₂] were in good agreement with those reported in the literature.^{S3}

S2.3 Synthesis of [bmim][HSO₄]

A mixture of distilled *N*-butylimidazole (78.8 mL, 600.0 mmol) and toluene (50.0 mL) was cooled in an ice bath under N₂. Dimethyl sulfate was added dropwise (56.8 mL, 600.0 mmol). Then the mixture was stirred at room temperature overnight. The upper layer was decanted while the lower layer was washed with toluene (3 x 50 mL). The solvent was removed under vacuum at 70 °C and the intermediate [bmim][MeSO₄] obtained was employed in the synthesis of [bmim][HSO₄] without further purification. [bmim][MeSO₄] (139.1g, 555.7 mmol) was diluted in distilled water (20.0 mL). The mixture was heated at 215 °C in the open air. After 4 hours, the reaction mixture was dried overnight at 65 °C under reduced pressure to obtain a yellow viscous liquid, [Bmim][HSO₄] in 98% yield.

[bmim][HSO₄]: ¹H NMR (400 MHz, DMSO) δ 9.08 (s, 1H, N₂CH), 7.76 - 7.69 (m x 2, 2 x 1H, 2 x N-CH), 4.17 (t, 2H, N-CH₂-CH₂, J_{HH} = 7.2 Hz), 3.85 (s, 3H, N-CH₃), 1.77 - 1.26 (m x 2, 2 x 2H, N-CH₂-CH₂-CH₂-CH₃), 0.9 (t, 3H, -CH₂-CH₃, J_{HH} = 7.4 Hz) ppm. ¹³C{¹H} NMR (100 MHz, DMSO) δ 137.7 (N₂-CH), 123.6 - 122.4 (2 x N-CH), 119.2 (CF₃), 49.1 (N-CH₂-CH₂-CH₂-CH₃), 35.8 (NCH₃), 32.0 (NCH₂-CH₂-CH₂-CH₃), 19.0 (NCH₂-CH₂-CH₂-CH₃), 13.8 (N-(CH₂)₂-CH₂-CH₃) ppm. MS (ES, +ve mode): *m/z* (abundance) = 139 (100) [bmim]⁺.

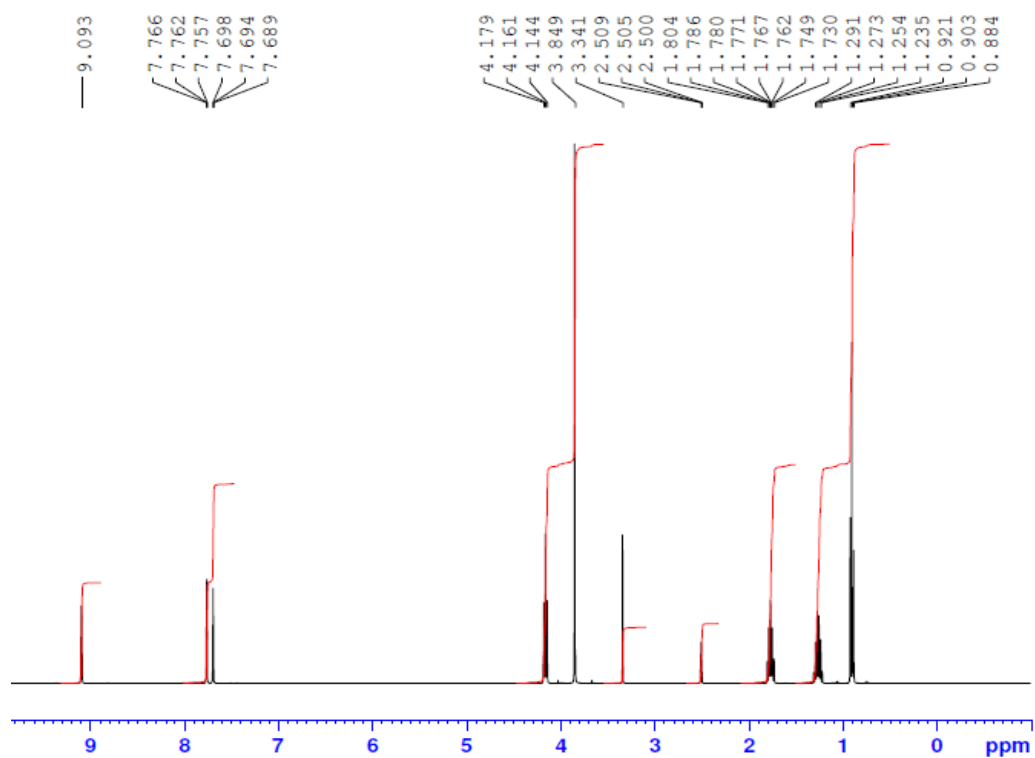


Figure S13. ^1H NMR spectrum of [bmim][HSO_4] in deuterated DMSO.

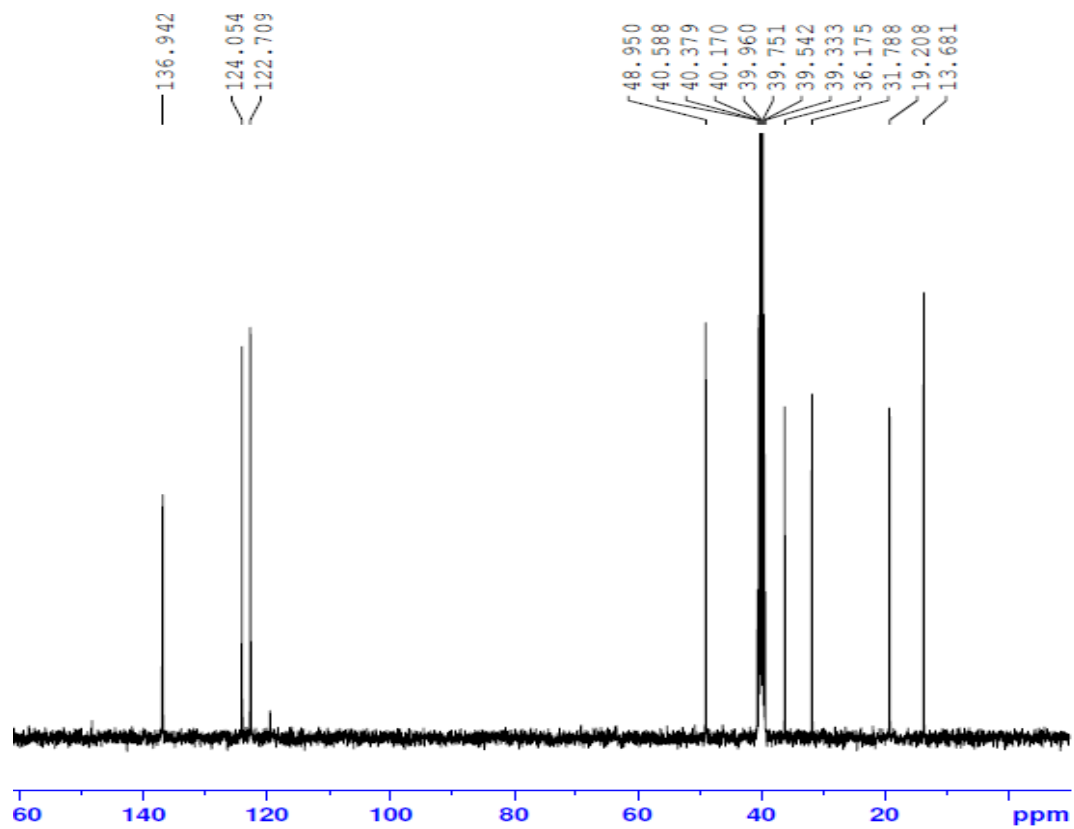


Figure S14. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [bmim][HSO_4] in deuterated DMSO.

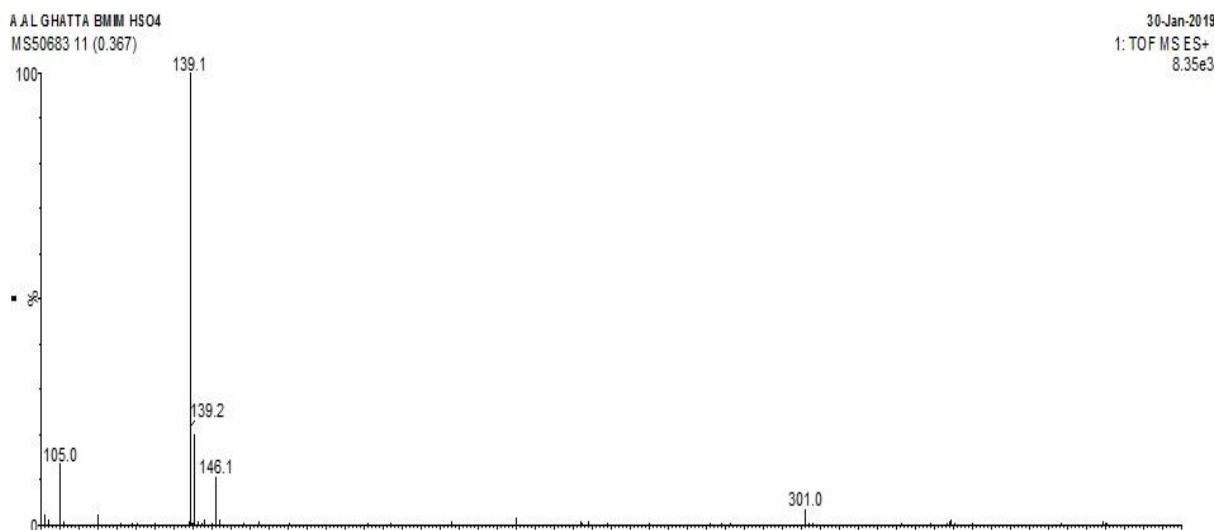


Figure S15. Mass spectrum of [bmim][HSO₄].

The characterization data for [bmim][HSO₄] were in good agreement with those reported in the literature.^{S4}

S2.4 Synthesis of [TEMPO-bmim][NTf₂]

The product was synthesized in two steps according to a modified literature procedure.⁵

4-hydroxy-2,2,6,6-tetramethylpiperidinyloxy (5.0 g, 29 mmol) and dry benzene (100 mL) were added to a 250-mL 3-neck flask equipped with a reflux condenser and nitrogen inlet line. Sodium hydride (0.72 g, 30.0 mmol) was slowly added. Once the addition was complete, the reaction was brought to reflux for 24 hours. The resulting suspension was cooled in an ice bath and 1,4-dibromobutane (8.6 g, 40.0 mmol) was added and the solution was again brought to reflux for 24 hours. After the reaction was complete, the reaction solution was cooled and water (50 mL) was added. The contents of the reaction vessel were transferred to a separating funnel and extracted with diethyl ether (100 mL). The organic layer was decanted and dried over MgSO₄ then concentrated under reduced pressure to afford the crude Intermediate product containing unreacted 1,4-dibromobutane. The Intermediate was purified by chromatography on silica gel [gradient elution: 100% hexane to 1:1 hexane/diethyl ether]. The solvent was removed under vacuum to afford the desired product as a red oil (2.0 g, 6.5 mmol, 23 %). This compound (**Intermediate A**, 2.0 g, 1 eq) was slowly added to a solution of 1-methylimidazole (0.5 ml, 6.5 mol, 1 eq) in acetonitrile (1 mL). The mixture was stirred for 3 days at 70 °C. After cooling to room temperature, ethyl acetate was (2 mL) added to the mixture causing precipitation of 1-methyl-3-(4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl)butyl)imidazolium bromide as a red solid (1.2 g, 3.0 mmol). The solid was dissolved in water with Li[NTf₂] (0.98 g, 3.4 mmol, 1.1 eq) and stirred overnight at room temperature. The ionic liquid 1-methyl-3-(4-(2,2,6,6-tetramethyl-1-oxyl-4-piperidoxyl)butyl)imidazolium

bistriflimide precipitated from the solution as a red viscous liquid. This ionic liquid was dissolved in dichloromethane (1 mL) and washed with water until the AgNO_3 test gave a negative result. Yield 1.9 g (50%).

Intermediate A (reduced form, phenylhydrazine resonances omitted): ^1H NMR (400 MHz, CDCl_3): δ 1.18 (s, 6H, piperidine-Me), 1.24 (s, 6H, piperidine-Me), 1.46 (t, 2H, piperidine-CH, $J_{\text{HH}} = 11.8$ Hz), 1.69 - 1.77 (m, 2H, O-CH₂-CH₂-CH₂-CH₂-Br), 1.91 - 2.08 (m, 4H, O-CH₂-CH₂-CH₂-CH₂-Br, piperidine-CH), 3.44 - 3.63 (m, 5H, O-CH₂, BrCH₂, piperidine-CH) ppm.

[TEMPO-bmim][NTf₂] (reduced form, phenylhydrazine resonances omitted): ^1H NMR (400 MHz, CDCl_3): δ 1.26 (s, 6H, piperidine-Me), 1.35 (s, 6H, piperidine-Me), 1.53 - 2.12 (m, piperidine-CH; O-CH₂-CH₂-CH₂-CH₂-imidazolium; O-CH₂-CH₂-CH₂-CH₂-Br; piperidine-CH), 3.51 (t, 2H, imidazolium-CH₂, $J_{\text{HH}} = 11.9$ Hz), 3.59 - 3.72 (m, 3H, O-CH₂, piperidine-CH), 3.84 (s, 3H, CH₃-imidazolium), 7.18 (m, 1H, CH-imidazolium), 7.22 (m, 1H, CH-imidazolium), 7.41 (s, 1H, C-CH-C) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 137.1 (N_2CH), 123.0 - 121.0 (2 x NCH), 69.1 (N-CH₂-CH₂-CH₂-CH₂), 67.1 (-CH₂-CH₂-O), 61.0 (piperidine O-C-C), 49.6 (piperidine, C-C-N), 43.8 (piperidine, C-C-C), 36.1 (NCH₃), 26.1 - 27.2 (N-CH₂-CH₂-CH₂-CH₂), 20.9 (piperidine, 2 x C-CH₃) ppm. MS (ES, +ve mode): 309 (100) [TEMPO-bmim]⁺. MS (ES, -ve mode): 279 (100) [NTf₂]⁻.

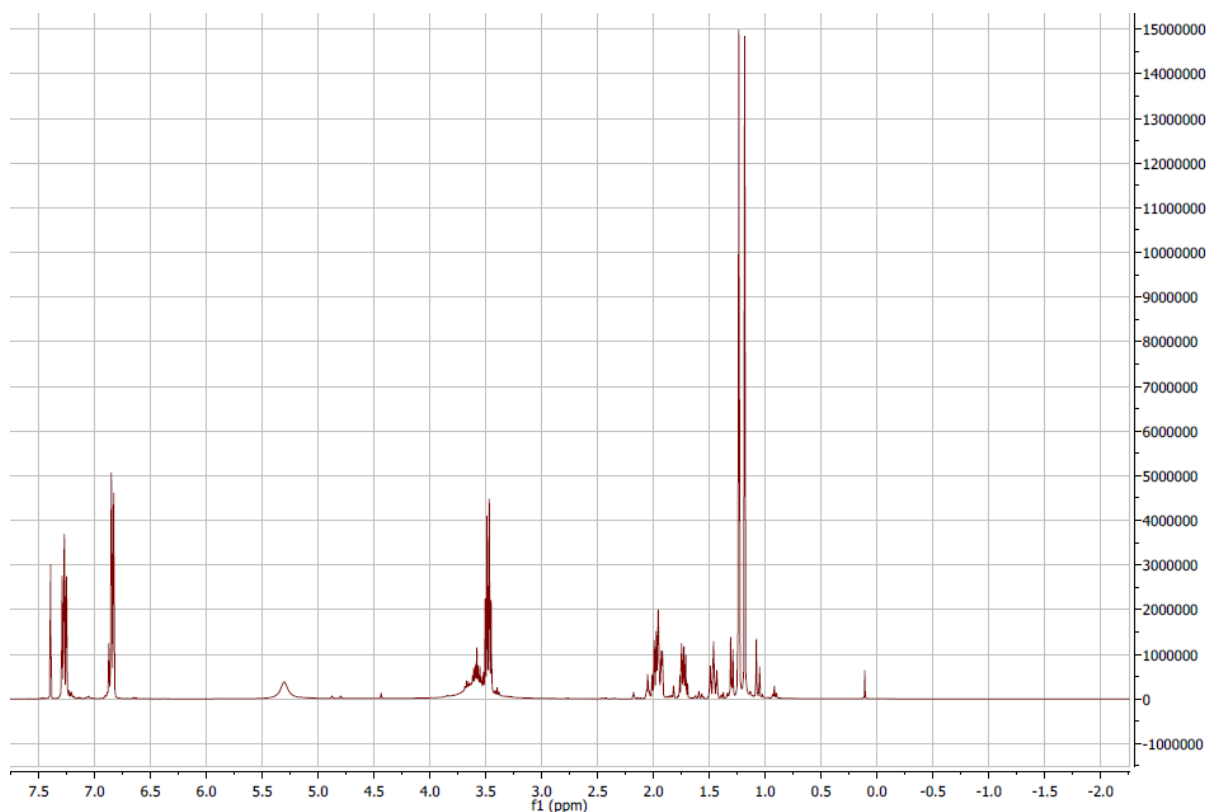


Figure S16. ^1H NMR spectrum of Intermediate A reduced with excess phenylhydrazine in deuterated CDCl_3 .

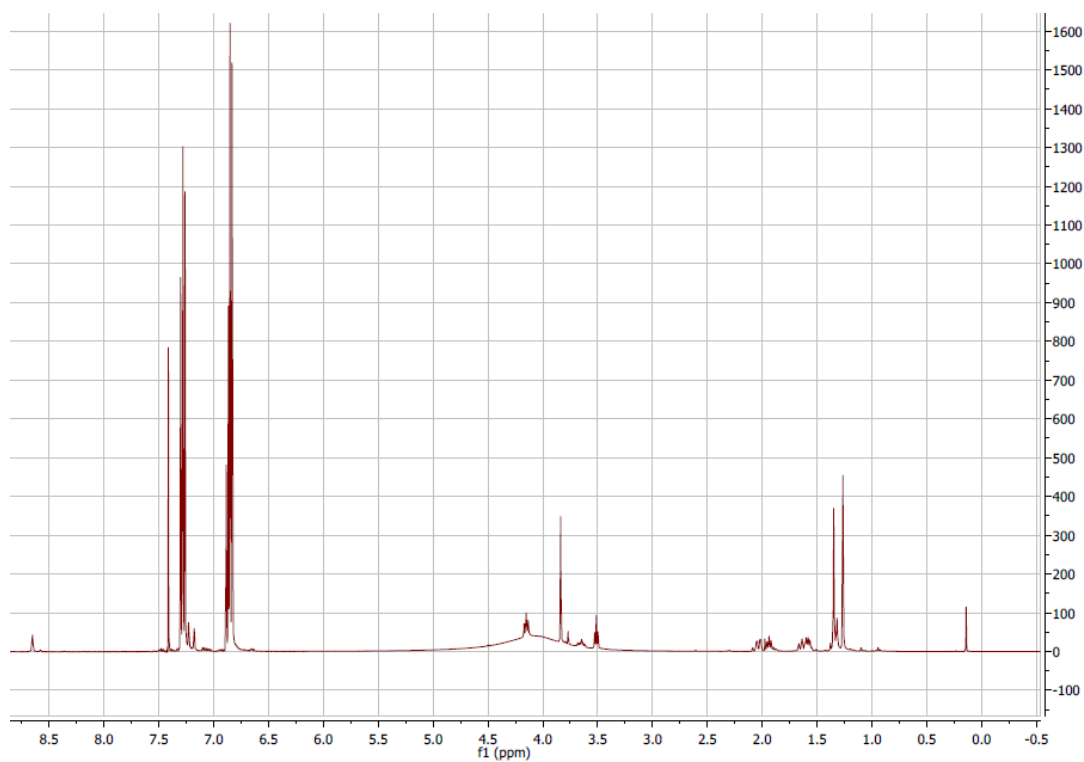


Figure S17. ^1H NMR spectrum of [TEMPO-bmim][NTf₂] reduced with excess phenylhydrazine in deuterated CDCl₃.

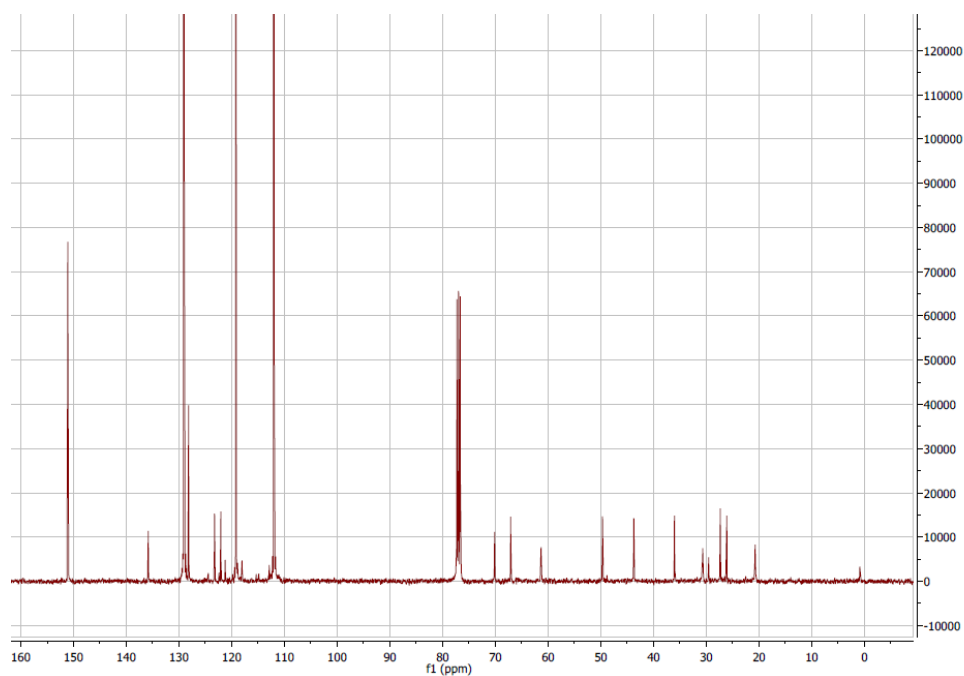


Figure S18. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [TEMPO-bmim][NTf₂] reduced with excess phenylhydrazine in deuterated CDCl₃.

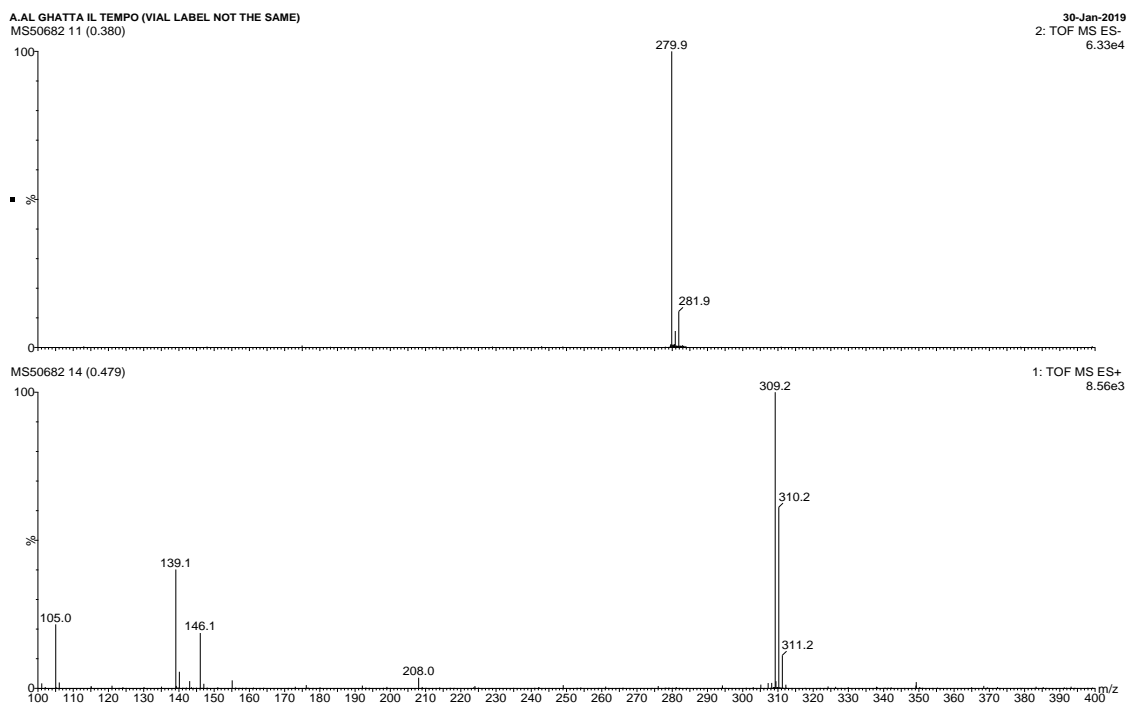


Figure S19. Mass spectrum of [TEMPO-bmim][NTf₂].

The characterization data for [TEMPO-bmim][NTf₂] were in good agreement with those reported in the literature.^{S5}

S2.5 Synthesis of [bbpy][NTf₂]

4,4'-Bipyridine (8.00 g, 51.0 mmol) was dissolved in acetonitrile (90 mL) and 1-bromobutane (8.87 g, 7.00 mL, 61.0 mmol) was added dropwise under an inert atmosphere. The mixture was heated with stirring at 70 °C for 3 days. After cooling, the solution was concentrated and the resulting precipitate was isolated by filtration. The solid product was stirred and heated at reflux in chloroform overnight. The insoluble material was separated and was identified to be the dialkyl product by ¹H NMR spectroscopy. The chloroform solution was evaporated and recrystallized to give a light green solid (10.3 g, 69%). The solid was dissolved in water with LiNTf₂ and stirred overnight. The ionic liquid separated from the water as a viscous liquid. Purification from residual bromide was achieved by dissolution in dichloromethane and washing until AgNO₃ gave a negative test for halide. Yield: 18.1 g (72%).

[bbpy][NTf₂]: ¹H NMR (400 MHz, DMSO) δ 9.25 (m, 2H, pyridine, C-CH-N-C), 8.87 (m, 2H, pyridine C-CH-C), 8.64 (m, 2H, pyridine N-CH-C), 8.04 (d, 2H, pyridine C-CH-C), 4.20 (t, 2H, N-CH₂-CH₂, $J_{HH} = 7.4$ Hz), 1.76, 1.25 (m x 2, 2 x 2H, N-CH₂-CH₂-CH₂-CH₃), 0.88 (t, 3H, -CH₂-CH₃, $J_{HH} = 7.4$ Hz) ppm. ¹³C{¹H} NMR (100 MHz, DMSO) δ 153.0 (C-C), 151.0 (C-C-N), 146.0 (pyridine C-C-C), 141.3 (C-C), 126.3 (pyridine C-C-N), 121.3 (pyridine C-C-C), 121.0 – 117.0 (CF₃), 60.1 (N-CH₂-CH₂-CH₂-CH₃), 32.9 (NCH₂CH₂CH₂CH₃), 19.4 (NCH₂-CH₂-CH₂-CH₃), 13.8 (N-(CH₂)₂-CH₂-CH₃) ppm. MS (ES, +ve mode): m/z 279 (100) [bbpy]⁺.

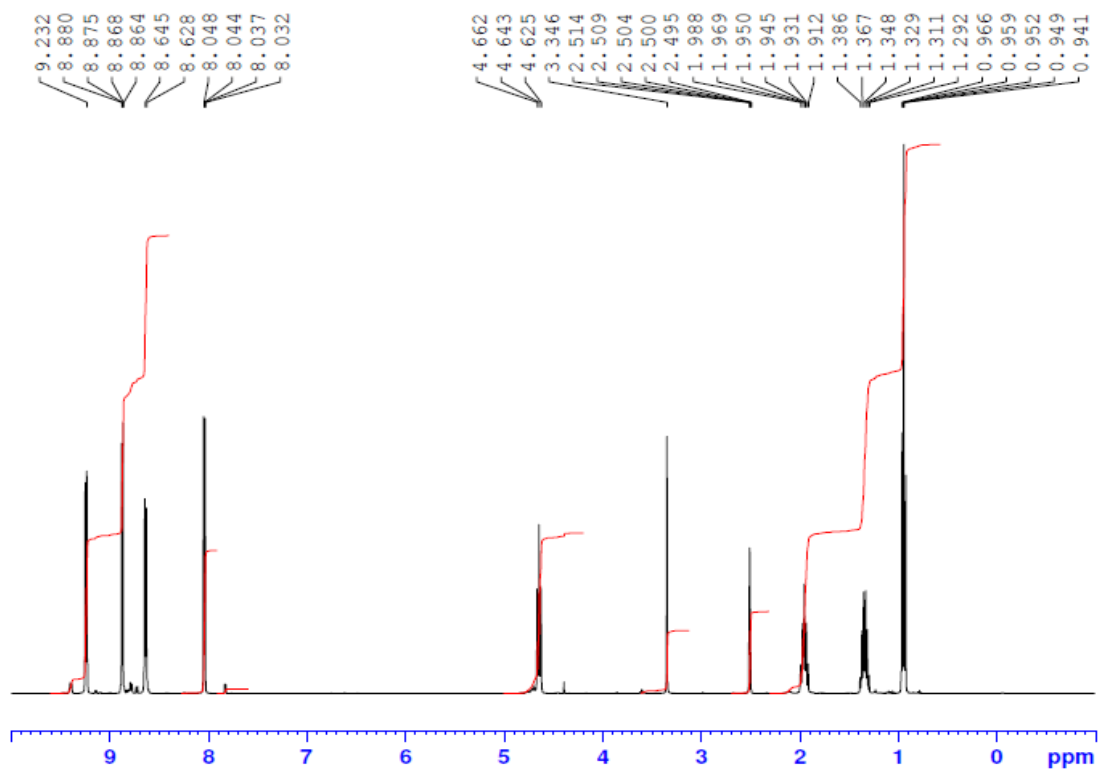


Figure S20. ^1H NMR spectrum of [bbpy]NTf₂ in deuterated DMSO.

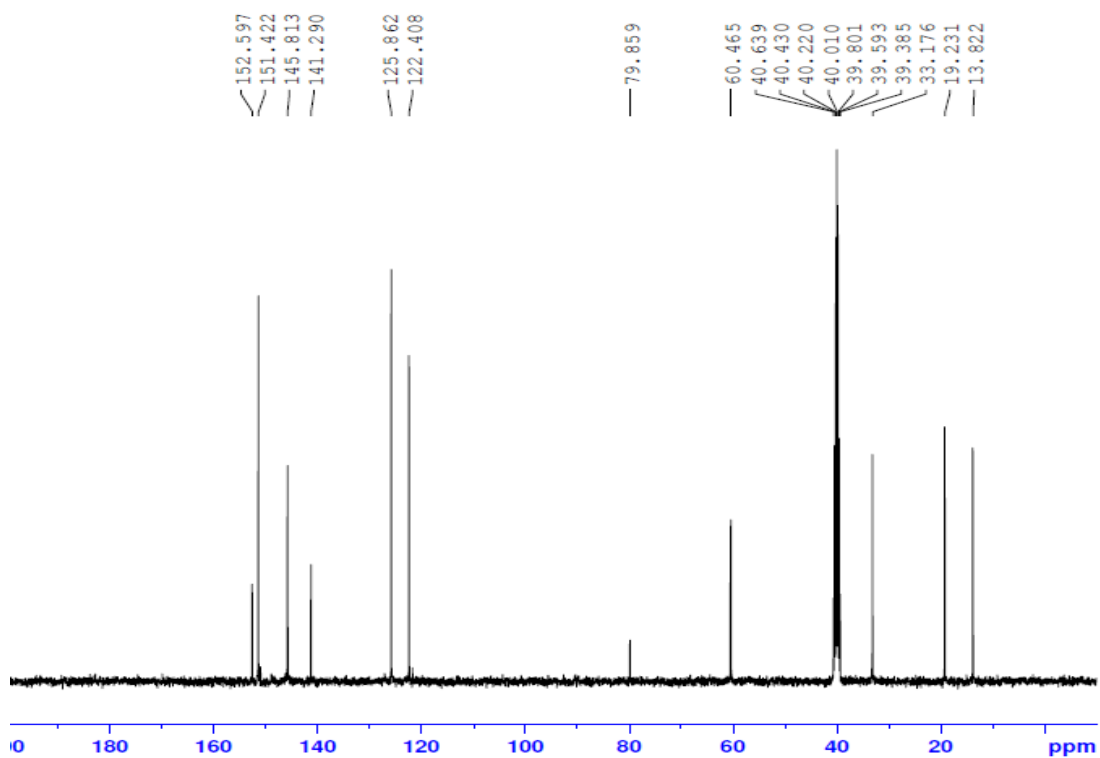


Figure S21. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of [bbpy]NTf₂ in deuterated DMSO.

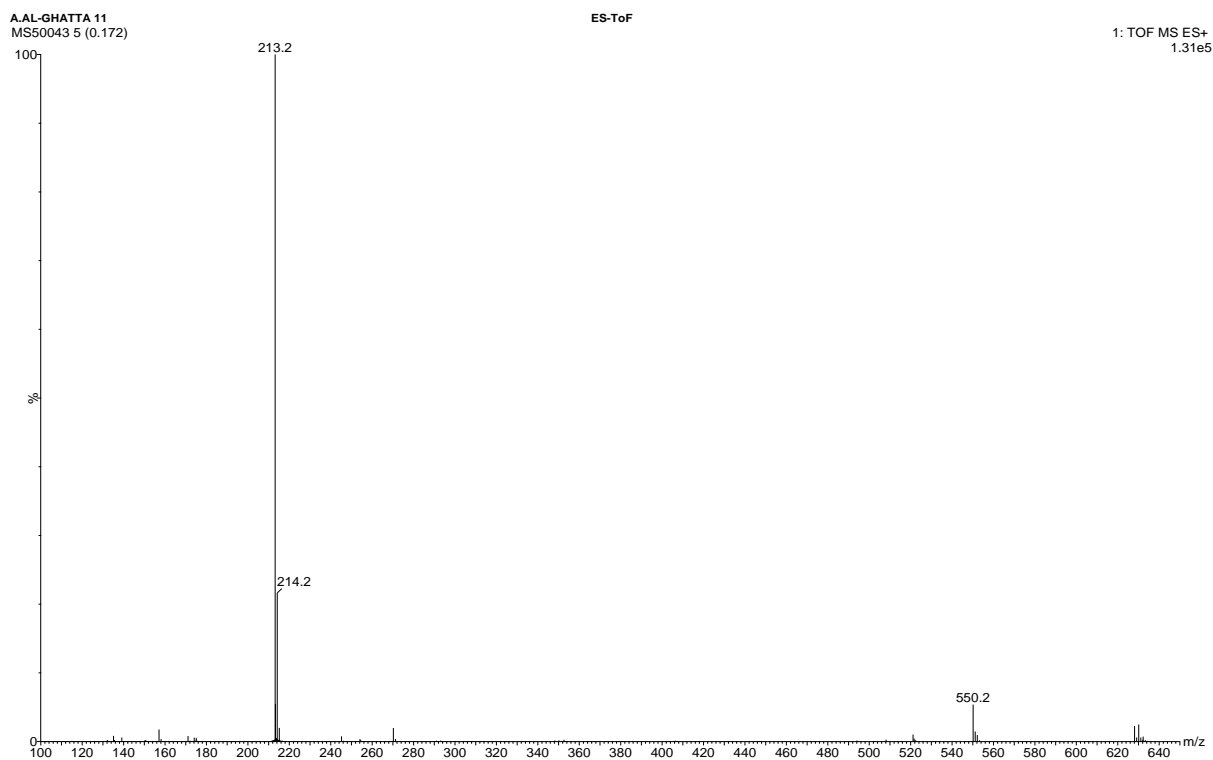


Figure S22. Mass spectrum of [bbpy][NTf₂].

The characterization data for [bbpy][NTf₂] were in good agreement with those reported in the literature.^{S6}

S2.6 Characterization of sublimed DFF

DFF: ¹H NMR (400 MHz, DMSO) δ 9.78 (s, 2H, CHO), 7.64 (s, 2H, furan-CH) ppm. ¹³C{¹H} NMR (100 MHz, DMSO) δ 121.9 (furan C=C), 154.0 (O=C), 180.7 (O=C) ppm. MS (ES, +ve mode): *m/z* 125 (100) [M+H]⁺.

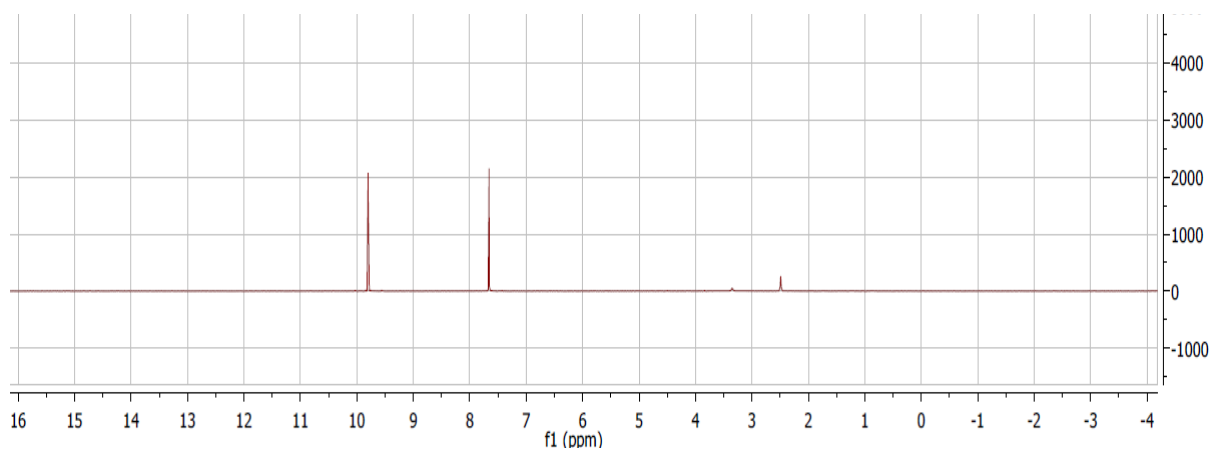


Figure S23. ¹H NMR spectrum of DFF in deuterated DMSO.

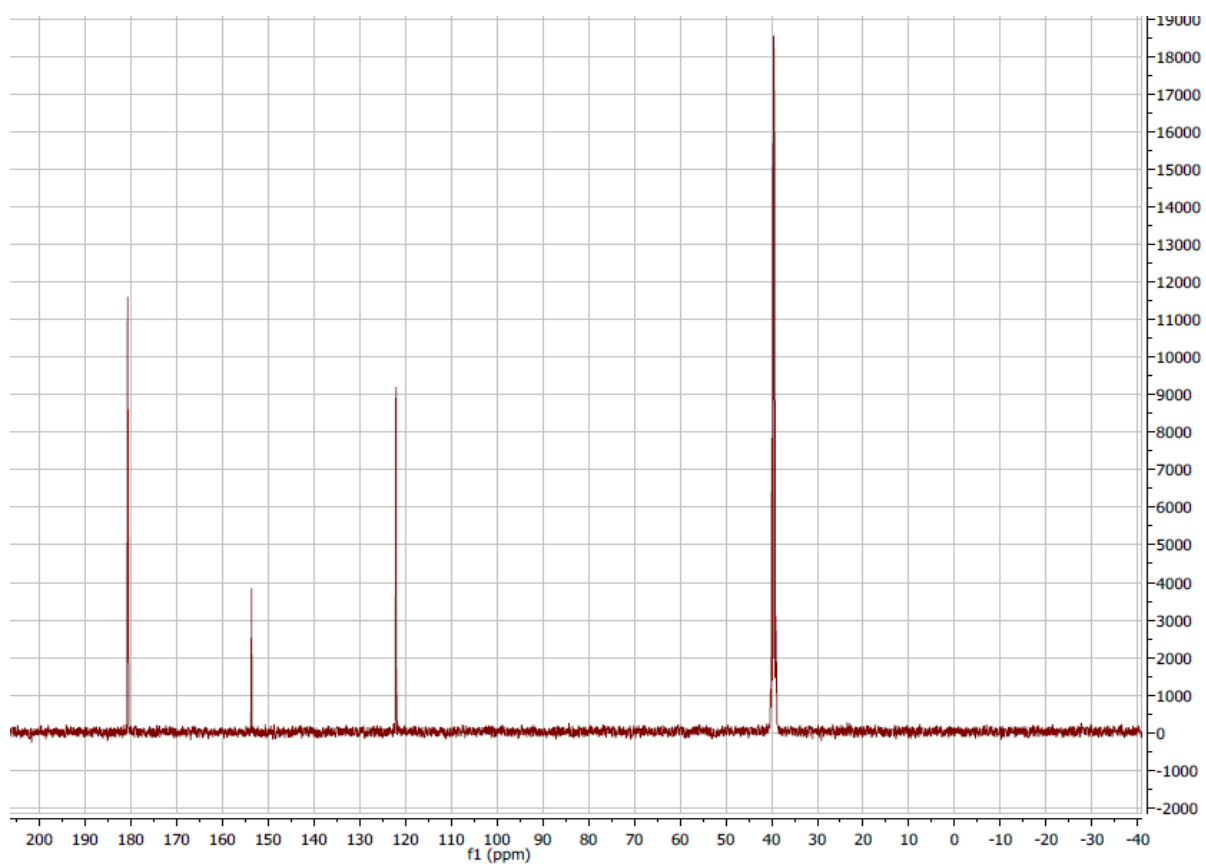


Figure S24. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of DFF in deuterated DMSO.

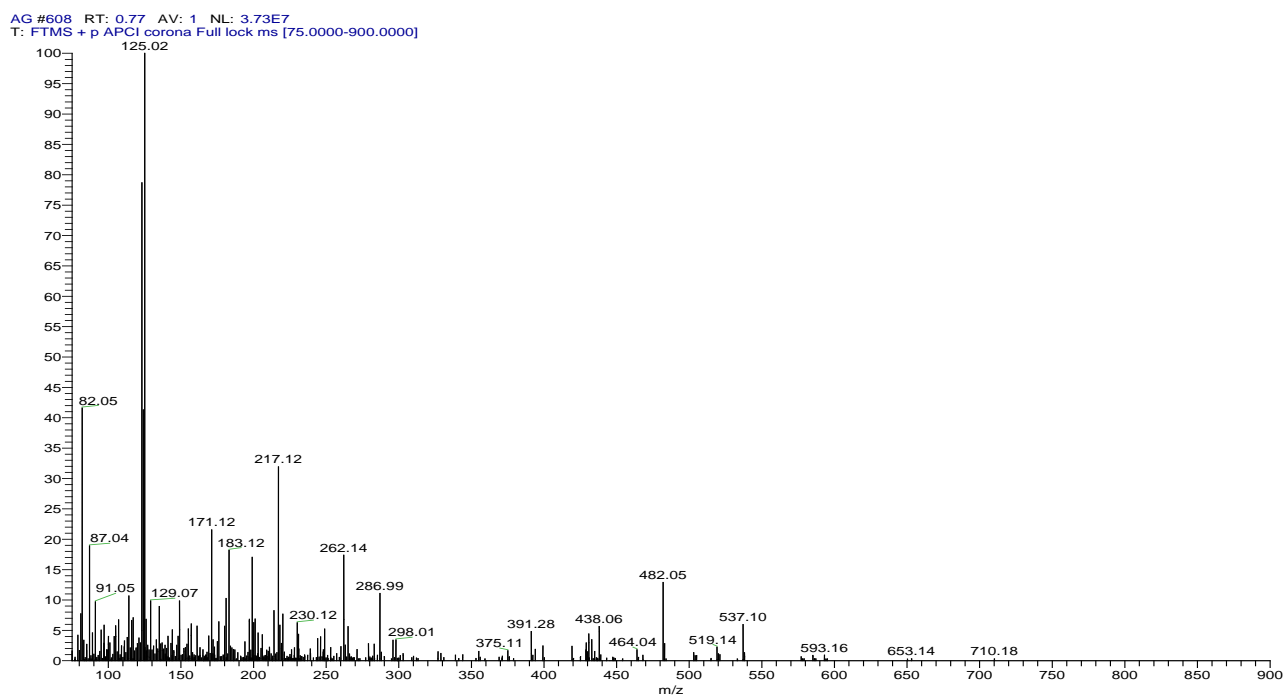


Figure S25. Mass spectrum of DFF.



Figure S26. On the left, photograph of the reaction mixture after 6 h showing sublimed DFF (white) while further material precipitates from the reaction mixture. On the right, DFF after vacuum was applied for 6 h at 80 °C.

S2.7 Characterization of FFCA

FFCA: ^1H NMR (400 MHz, DMSO) δ 9.73 (s, 1H, $\text{CH}=\text{O}$), 7.60 - 7.40 (d, 2 x 1H, 2 x $\text{C}-\text{CH}-\text{CH}-\text{C}$, $J_{\text{HH}}=7.4$ Hz) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO) δ 193.3 ($\text{O}=\text{CH}-\text{C}$), 159.5 - 153. (2 x $\text{C}-\text{CH}-\text{CH}-\text{C}$), 149.0 ($-\text{C}-\text{OOH}$), 122.7-118.9 (2 x $\text{C}-\text{C}-\text{O}$) ppm. MS (ES, +ve mode): m/z 141 (100) $[\text{M}+\text{H}]^+$.

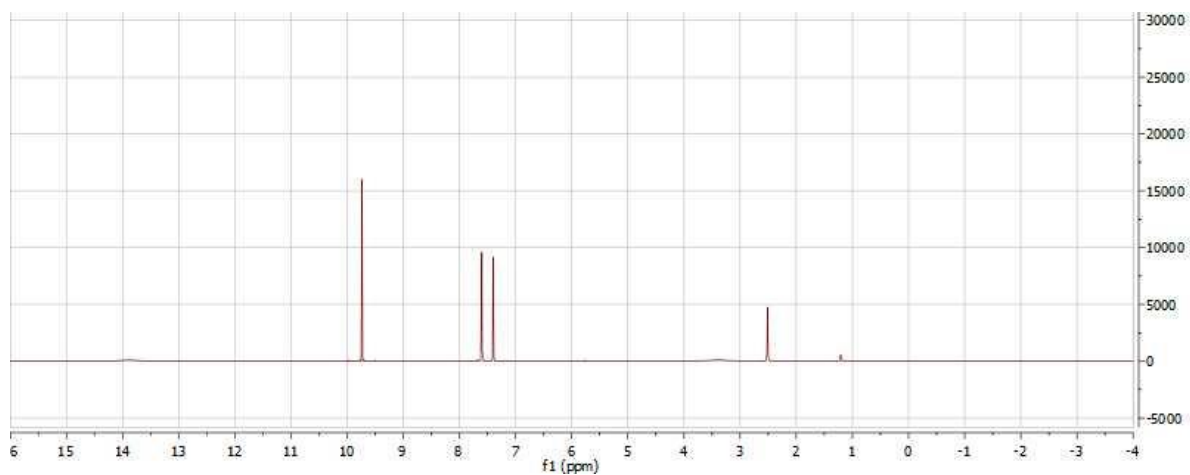


Figure S27. ^1H NMR spectrum of FFCA in deuterated DMSO.

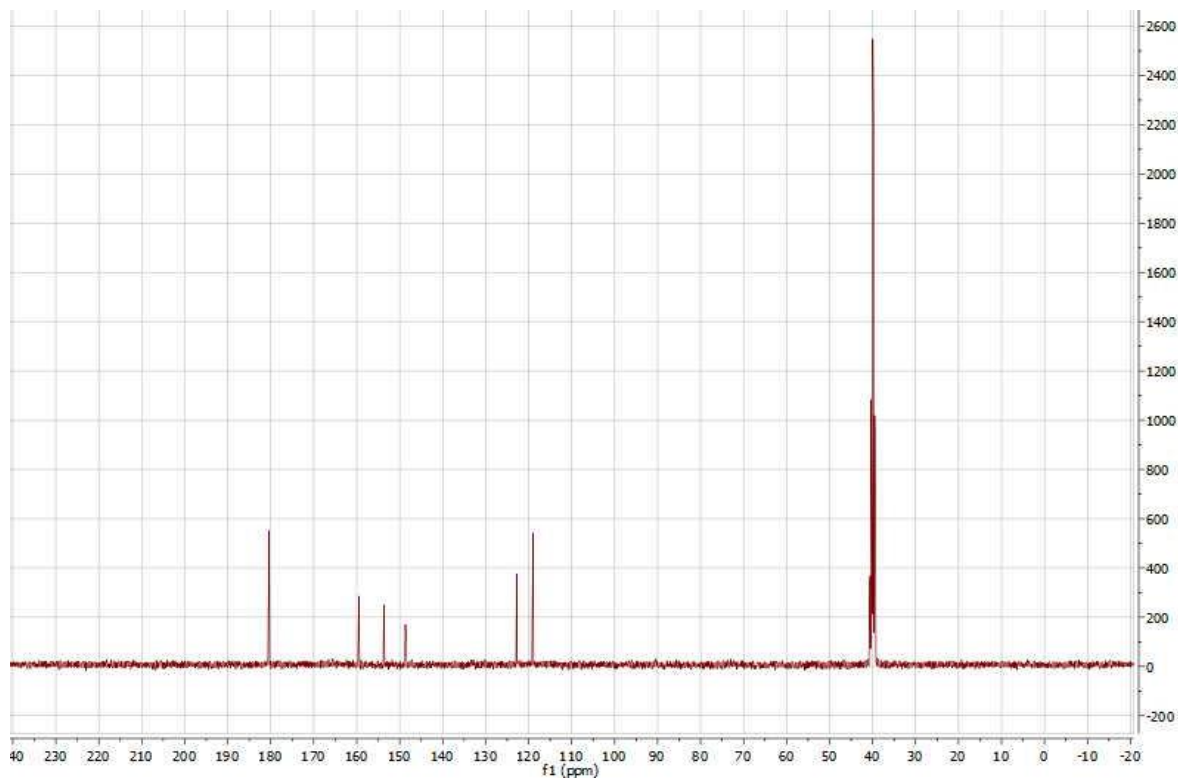


Figure S28. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of FFCA in deuterated DMSO.

S2.8 NMR analysis of the reaction mixture after the reaction

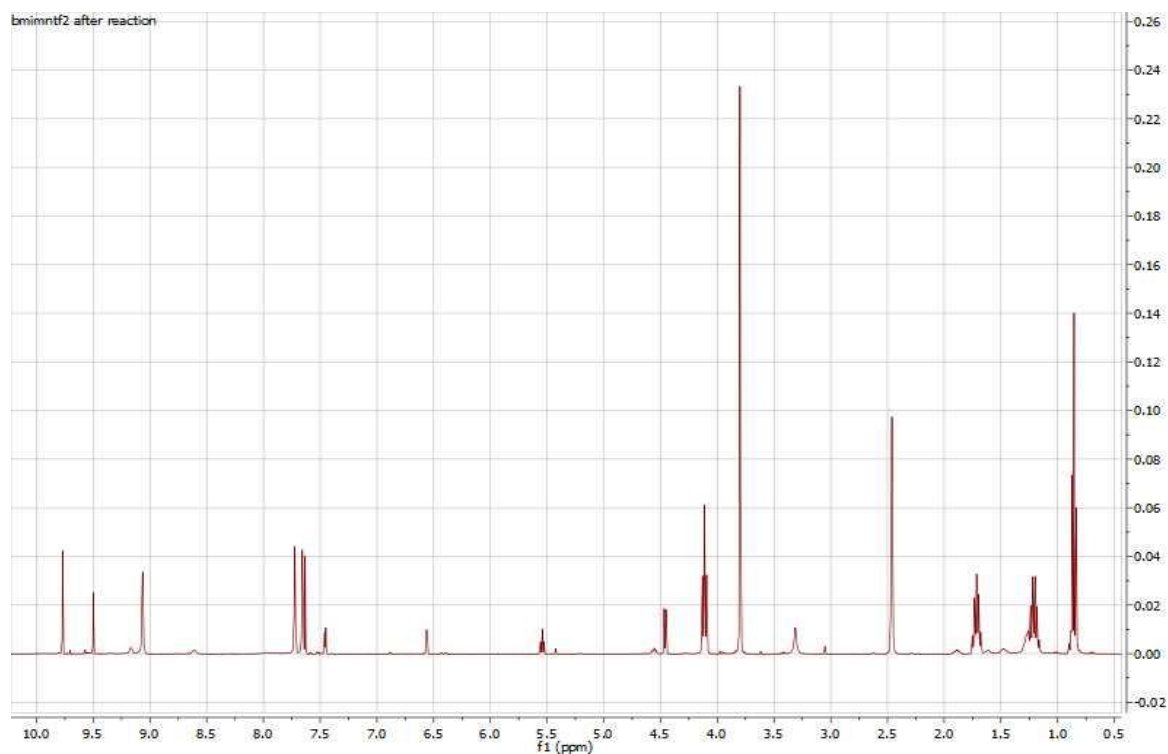


Figure S29. Typical ^1H NMR spectrum (in $\text{d}^6\text{-DMSO}$) of the reaction mixture at the end of the reaction, after 6 h at 50% HMF loading, 80 °C.

[bmim][NTf₂] resonances: δ 9.05 (s, 1H, N₂CH), 7.86, 7.78 (m x 2, 2 x 1H, 2 x N-CH), 4.20 (t, 2H, N-CH₂-CH₂, $J_{\text{HH}} = 7.3$ Hz), 3.87 (s, 3H, N-CH₃), 1.76, 1.25 (m x 2, 2 x 2H, N-CH₂-CH₂-CH₂-CH₃), 0.88 (t, 3H, CH₂-CH₃, $J_{\text{HH}} = 7.4$ Hz) ppm

Residual HMF resonances: δ 9.51 (s, 1H, CHO), 7.46 - 6.58 (d, 2 x 1H, furan-CH, $J_{\text{HH}} = 3.5$ Hz), 5.54 (t, 1H, OH, $J_{\text{HH}} = 6.0$ Hz), 4.46 (d, 2H, -CH₂OH, $J_{\text{HH}} = 6.0$ Hz) ppm.

Residual DFF resonances: δ 9.77 (s, 2H, CHO), 7.63 (s, 2H, furan-CH) ppm.

S2.9 Catalyst characterization by X-ray photoelectron spectroscopy

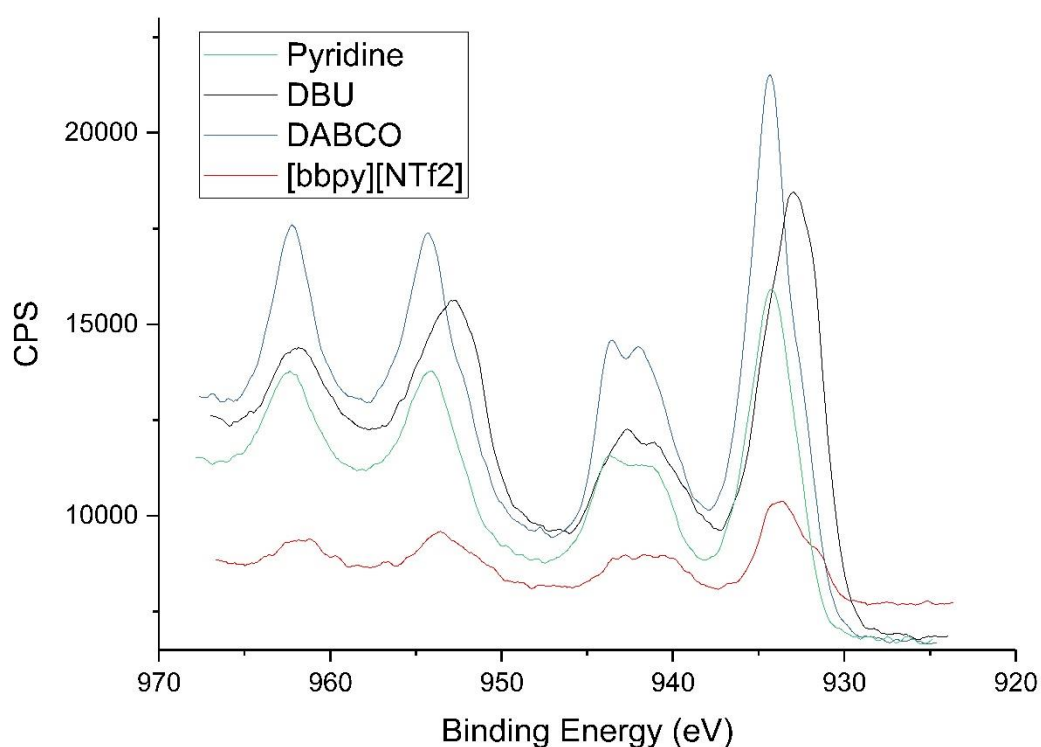


Figure S30. XPS analysis of the catalyst system showing CuCl with different ligands.

Table S1. Binding energies for different copper-ligand combinations.

Ligand	Cu 2p _{3/2} (eV)
CuCl only ^{S7}	932.4
CuCl ₂ only ^{S7}	934.8
CuCl + [bbpy][NTf ₂]	933.5
CuCl + DABCO	934.3
CuCl + DBU	933.1
CuCl + Pyridine	934.2

The XPS spectrum for C1s exhibits two peaks at 284 eV attributed to C-C bonds, while the peaks at 292 eV can be assigned to the C-N bond of the ligand. Since no further peaks were apparent in the C1s spectra (Figure S31), this suggests that no insoluble humins (typical side-products in reactions involving HMF) had formed that can deactivate the catalyst.

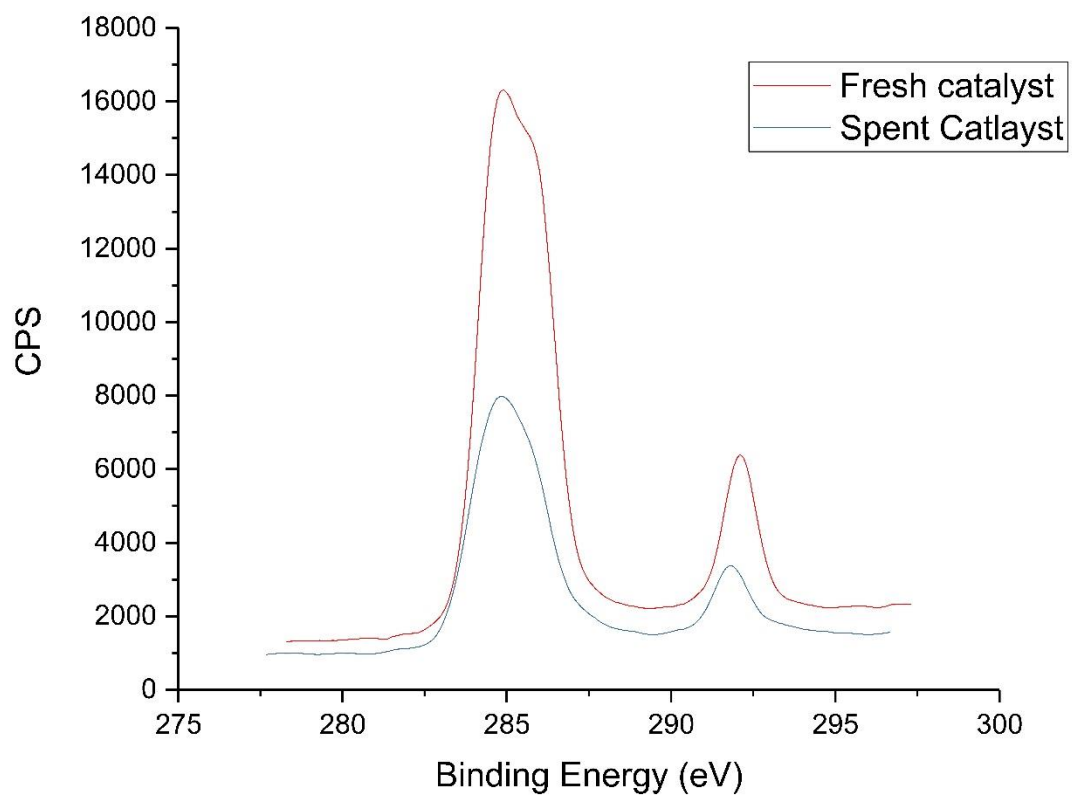


Figure S31. XPS data for C1s for freshly-prepared and used CuCl + [bbpy][NTf₂] catalyst system.

S3 Numerical data

Table S2. Effect of different promoters on the yields and conversion of HMF. Experiments performed for 6 h with O₂ balloon at 80 °C, 200 mg [bmim]OTf, 20 mg HMF, TEMPO/CuCl/promoter loading 5 mol%.

Promoter	Conversion of HMF (%)	Yield DFF (%)	Yield FFCA (%)
none	77.3 ± 4.5	69.0 ± 4.9	2.5 ± 1.0
pyridine	100	95.4 ± 0.4	5.0 ± 0.3
triethylamine	66.5 ± 5.6	58.3 ± 6.6	0.0
DABCO	96.7 ± 1.3	89.5 ± 1.4	3.5 ± 0.1
DBU	100	88.0 ± 0.8	3.7 ± 0.2

Table S3. Effect of different promoters on the yields and conversion of HMF after 3 hours. Experiments performed with O₂ balloon at 80 °C, 200 mg [bmim]OTf, 20 mg HMF, TEMPO/CuCl/promoter loading 5 mol%.

Promoter	Conversion of HMF (%)	Yield DFF (%)	Yield FFCA (%)
pyridine	100	91.7 ± 2.4	4.0 ± 0.9
DABCO	68.7	64.5 ± 5.1	0.7 ± 0.7
DBU	98.7	88.0 ± 0.8	2.6 ± 0.4

Table S4 Influence of HMF loading on conversion and yield. Higher HMF loading slows down the reaction but retains high selectivity. Experiments performed for 6 h with O₂ balloon at 80 °C, TEMPO/CuCl/promoter loading 5 mol%.

HMF loading (%)	Catalyst loading (mol%)	HMF conversion (%)	DFF yield (%)	FFCA Yield (%)
10	5	100	95.4 ± 0.3	4.98 ± 0.3
20	2.5	94.4 ± 2.4	93.7 ± 3.2	2.38 ± 0.4
30	1.65	84.5 ± 1.4	83.7 ± 1.3	1.96 ± 0.1
40	1.23	74.4 ± 1.6	67.3 ± 5.3	1.3 ± 0.2
50	1	62.7 ± 1.3	52.8 ± 2.5	1.2 ± 0.184

Note: At 50% HMF loading, it was observed that the solution remained brown. In contrast, when using 10% or 20% HMF loadings to produce near quantitative yields, the solution became green after being brown initially.

S4 References

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