Ayşe Ezgi Ünlü*, Azime Arıkaya and Serpil Takaç

Use of deep eutectic solvents as catalyst: A mini-review

https://doi.org/10.1515/gps-2019-0003
Received July 21, 2018; accepted September 13, 2018.

Abstract: Deep eutectic solvents (DESs) exhibit numerous advantages over conventional ones used in several chemical and biochemical processes. Besides addressing most of the principles of green chemistry, DESs can also act as catalyst depending on their nature. The use of DESs as acid catalyst has several advantages such as utilization at stoichiometric amount, non-toxicity, possibility of the recovery, similar or higher catalytic effect than the acid itself alone, the recyclability and reusability without a significant loss of activity. In this mini-review, the state- of-the-art in the use of DESs as catalyst is presented. The DESs, which show Lewis type acidity, Brønsted type acidity and other types of catalytic influence in various types of reactions including esterification, organic synthesis, glycolysis and depolymerisation are presented and their roles in the reactions are discussed.

Keywords: deep eutectic solvents; Brønsted acid; Lewis acid; catalysis

1 Introduction

Solvents are indispensable compounds of chemical and pharmaceutical industries. They find a wide variety of application areas such as the production of bulk chemicals, medicines, health care products, cleaning agents, and dyes. Although the solvents used in the industry are mainly organic substances, the use of inorganic solvents such as water, aqueous solutions and liquid ammonia is also encountered. The toxicity of organic solvents are demonstrated to a large extent. Therefore, the search and use of alternative solvents, which possess less or no health issues and are also eco-friendly, have attracted a growing interest. Water, supercritical carbon dioxide and ionic liquids (ILs) are specified as green solvents and the interest on employing them in processes is increasing with a great acceleration.

Deep eutectic solvents (DESs) are a class of ionic liquids and recently popular particularly in metal processing applications such as metal electrodeposition, metal electropolishing and metal extraction as well as in synthetic applications such as biotransformation, purifying and manufacturing biodiesel [1]. Extraction of bioactive compounds [2], extraction and separation of target analytes [3], liquid-liquid extraction [4], synthesis of noble metal nanomaterials [5] and CO_2 absorption [6] are the mostly known other applications of DESs. On the other hand, the use of DESs as catalyst in various organic reactions have also been reported [7–13] and this field of application of DESs appears to attain more importance in manufacturing industry in future.

In this mini-review, we highlight the application of DESs as *acid catalysts* in different types of reactions. Accordingly, it is obvious that DESs, especially acidic characterized types, have been successfully used in a broad range of reactions. Although there are numerous reports that show the catalytic effect of DESs, there are only a few reports that focus on the mechanism of the catalytic effect. Mostly hydrogen bonding between the reactants and DES components is proposed to be effective for the catalytic effect. On the other hand, the acidic character is also reported to facilitate the breakage of the required bonds. Additionally, the recyclability of DES was possible for most of the studies offering up to four to five times reuse of the catalyst. For most of the reactions DES is used both as a solvent and a catalyst providing homogeneous media. The review is organized according to the *acid character* of DESs. Lewis type acidity, Brønsted type acidity and other types of catalytic influence of DESs are considered and the role of DESs as catalyst in reactions is discussed.

*** Corresponding author: Ayşe Ezgi Ünlü,** Ankara University Faculty of Engineering Department of Chemical Engineering 06100 Tandoğan Ankara Turkey, e-mail: aeunlu@eng.ankara.edu.tr, 00903123456
Azime Arıkaya and Serpil Takaç, Ankara University Faculty of Engineering Department of Chemical Engineering 06100 Tandoğan Ankara Turkey

Open Access. © 2019 Ünlü et al., published by De Gruyter. This work is licensed under the Creative Commons Attribution alone 4.0 License.

1.1 Deep eutectic solvents

DESs are a category of ionic liquids and possess many of the characteristics and physical properties of ILs. Ionic liquids can be defined as salts that have lower melting point below the ambient temperature. They are composed of at least one ion possessing a delocalized charge and one organic substance. Design of the composition of an IL provides it to have a target-specific character [14]. Although ILs have several advantages over conventional solvents, the limitations in their industrial use arising mainly from their high cost and uncertainty in their toxicity have caused DESs to gain more interest in the last decades [15].

Deep eutectic solvents differ from ILs due to their impressive properties such as low cost, easy preparation techniques, low volatility, biodegradability and non-toxicity. Their uses as alternative to bulk organic solvents in several applications such as extraction and electrochemistry have been studied with increasing attention by scientific community.

DESs are comprised from two or more components, which at least two of them have a hydrogen bonding capability; one hydrogen bond donor (HBD) and one hydrogen bond acceptor (HBA). Self-association of HBD and HBA provides a eutectic mixture whose melting point is lower than that of any of its constituents. Quaternary ammonium salts (QAS) are the first and the mostly used HBAs whereas several metal halides and organic compounds with hydrogen bonding functional groups can be used as HBDs in the synthesis of DESs (Table 1) [1]. They may also be defined as a eutectic mixture of Lewis or Brønsted acids and bases that contain various cationic and/or anionic molecules [1].

Hydrogen bonding functional groups or species in DES composition provide the mixture a Lewis acidic or Brønsted acidic character. In Types I, II and IV DESs, the presence of metal salt such as $ZnCl_2$ gives DES a Lewis acidic character. On the other hand, in Type III DES, using a Brønsted acid acts as a proton donor such as di- and tri-carboxylic acids, provides the mixture Brønsted acidic character [16].

Table 1: Types of DESs [1].

Type	Composition	Example
I	Organic salt + Metal salt	QAS (ChCl) + Metal halide ($SnCl_2$, $ZnCl_2$, $FeCl_3$)
II	Organic salt + Metal salt hydrate	QAS (ChCl) + metal salt hydrate ($CrCl_3{\cdot}6H_2O$)
III	Organic salt + HBD	QAS (ChCl) + organic compound (polycarboxylic acids (malonic acid), polyamides (urea), polyalcohols (glycerol))
IV	Metal salt + HBD	Metal halide ($ZnCl_2$) + organic compound (urea, glycerol, ethylene glycol)

1.2 Reactions catalysed by Lewis acid type DESs

Group 3-15 metal chlorides are called Lewis acids. Lewis acids are capable of activating the substrates that are electron-rich due to their electron deficiency. They are often preferred as catalysts in different organic reactions [17]. The presence of a metal as electron-pair acceptor in the composition of DES provides it Lewis acidic property.

Although different metal salts are used in DES preparation, the DES containing choline chloride (ChCl) and $ZnCl_2$ is widespreadly used as Lewis acid catalyst as well as a reaction medium for several reactions such as Diels–Alder reactions [18], Fischer indole annulation [19], esterification of long chain carboxylic acid [20], *O*-acetylation of cellulose and monosaccharides [21] and protection of carbonyls [22]. The following part summarizes the-state-of-the-art on the application of DESs as Lewis type catalyst in several reactions:

Azizi and Batebi [23] investigated ChCl-$SnCl_2$ (1:2 molar ratio) as Lewis acid type DES as catalyst for chemoselective ring opening of epoxides with aromatic amines, thiols, alcohols, azide and cyanide (Figure 1). ChCl-$SnCl_2$ catalyzed almost all of the investigated reactions using a variety of commercially available epoxides with both aliphatic and aromatic thiols. Additionally, the use of DESs provided a visual monitoring of the reactions by becoming yellow and viscous as the reaction proceeded. The authors reported successful results also for direct ring opening reactions of various epoxides with aromatic amines (84-95% yield). Regeneration/recycling of DESs from the media provided extra advantage besides the mild conditions. ChCl-$SnCl_2$ could be used for four times providing 90% of yield at the last recycle.

The mostly used Lewis-acid type DES ChCl-$ZnCl_2$ was investigated for its performance as catalyst and solvent in the synthesis of primary amides from aldehydes and nitriles by Patil et al. [24] (Figure 2). Various aromatic, aliphatic and conjugated substrates were used and high product yields were obtained (89-94%). DES catalyzed

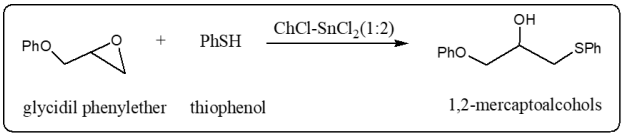

Figure 1: Ring opening of epoxides by using ChCl-$SnCl_2$ (1:2).

reactions showed that nitriles having electron donating groups at *ortho-para* positions resulted in splendid yields while *ortho-* substituted groups' reactions required more time caused by steric hindrance. The stronger the electron withdrawing group, the highest the reaction time was. On the other hand, reusability of DES was examined on the synthesis of benzamide from benzaldehyde and three recycling was reported to be the maximum for DES performance. The authors reported that the use of DES in the reactions provided green and atom efficient synthesis by reducing waste and toxic material.

Friedel-Crafts alkylation of electron-rich arenes was reported as another reaction type that DES acted as catalyst and solvent. Triarylmethanes (TRAMS) and diarylaalkanes (DIAAS) are extensively used as dye precursors and also intermediates in medicinal and material chemistry. Besides cross coupling, under catalyzation with metals or miscellaneous approaches, Friedel-Crafts alkylation and hydroxylation reaction of aldehydes are mainly used for the synthesis. Additionally, this procedure has many advantages such as high atom efficiency and non-toxic by-product, water. The catalysts that are generally used in these reactions are, Lewis acids, proton acids, ionic liquids, molecular iodine, or polystyrene-supported sulfonic acid. On the other hand, these procedures were reported to have many disadvantages such as unrecyclability of the catalyst, utilization of precious metals, high toxicity and air sensitivity of catalyst, long reaction times and the volatility of organic solvents [25–28]. To overcome these problems, Wang et al. [29] investigated different DES types such as urea U-$ZnCl_2$ (3.5:1), Acetamide-$ZnCl_2$ (4:1), ethylene glycol (EG)-$ZnCl_2$ (4:4), tetramethylammonium chloride (MeNCl)-$ZnCl_2$ (1:2), ChCl-$ZnCl_2$(1:2). According to the results, MeNCl-$ZnCl_2$ and ChCl-$ZnCl_2$ provided 72% and 94% yields while $ZnCl_2$ alone provided only 40% yield. Quaternary ammonium salt-$ZnCl_2$ DES showed good catalytic activity by generating C^+ and promoting the reaction. In the model reaction of 1,2,4-trimethoxybenzene and benzaldehyde, the highest TRAM (bis(2,4,5-trimethoxyphenyl)phenylmethane) yield was obtained as 94% by using ChCl-$ZnCl_2$ (Figure 3). Additionally, a series of reactions were performed using 1,2,4-trimethoxybenzene with different aldehydes under the catalysis of ChCl-$ZnCl_2$. The yields were between 65-94%. DES was reported to be used for 5 cycles in the range of 89-94% yield.

Tran et al. [30] used ChCl-$ZnCl_2$ as catalyst and green solvent in Friedel-Crafts acylation reactions. They reported high regio- and chemoselectivity in the reactions using acid anhydrides and ChCl-$ZnCl_2$ (1:3 molar ratio) as catalyst under microwave irradiation. Using anisole as model substrate, all acid anhydrides were found to provide ketone products having a majority of *p*-isomer (Figure 4). On the other hand, benzoic and propionic anhydride were reported to give highest yields. Additionally, when anisole and indole were utilized as substrates, indole derivatives were reported to be acylated in the 3-position without NH protection. According to the results, the disadvantages of moisture sensitive Lewis acids and also volatile organic solvents were overcome with the use of DESs and moreover high yields were reported with short reaction times. On the other hand, three new ketone products were reported to be synthesized under the catalyzation of DES. ChCl-$ZnCl_2$ (1:3) had many advantages such as low toxicity, low cost, easy handling and moreover could be reused up to 5 times conserving its catalytic activity.

Aromatic ketones are valuable precursors for the synthesis of agrochemicals, pharmaceuticals, fragrances and also dyes. These molecules are generally synthesized by Friedel–Crafts acylation using Lewis

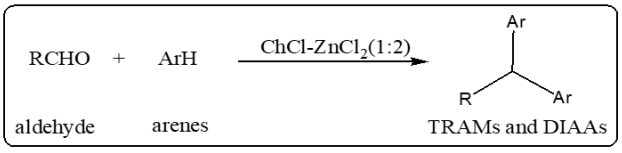

Figure 3: Synthesis of triarylmethanes and diarylaalkanes by using ChCl-$ZnCl_2$ (1:2).[a]

[a] See Wang et al. [29] for detailed reaction components and conditions.

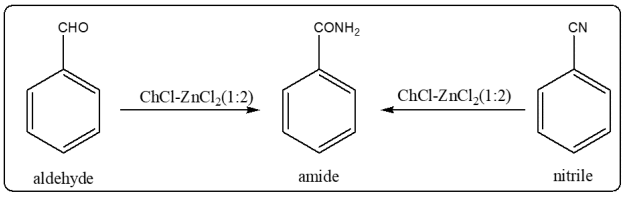

Figure 2: Synthesis of amides from aldehydes and nitriles catalyzed by ChCl-$ZnCl_2$ (1:2).

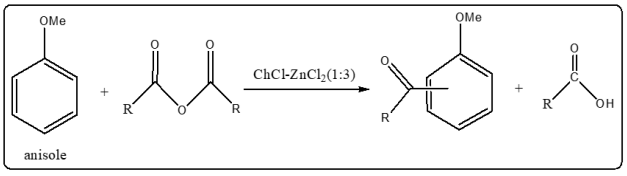

Figure 4: Friedel-Crafts acylation of anisole with respect to acid anhydride catalyzed by ChCl-$ZnCl_2$ (1:3).[b]

[b] See Tran et al. [30] for detailed reaction components and conditions.

acids as catalysts [31–36]. However, the need for the excess use of the catalyst, the unfeasible recovery process and the environmental problems have directed researchers to alternative methods. Among these methods, ILs have attracted interest and have been used successfully in a few studies [37,38]. Nevertheless, some limitations of this method such as the toxicity of ILs, their high cost and the need for the high purity resulted in the search for another method. Nguyen and Tran [39] investigated the use of ChCl-$ZnCl_2$ as a Lewis acid character DES for the acylation of secondary alcohols, phenols and naphthols with acid anhydrides. They utilized DES both as a catalyst and green solvent in the reaction. They reported that Lewis acidity of ChCl-$ZnCl_2$ (1:3 molar ratio) was clearly robust for the promotion of acylation of sterically hindered secondary alcohols to yield acylated products. On the other hand, it was also stable to air and moisture. As a result, 96% of yield was achieved in the solvent-free propionylation of 1-phenylethanol with propionic anhydride at room temperature in 30 min of reaction time (Figure 5). ChCl-$ZnCl_2$ (1:3) could be recycled many times and no significant sign of activity loss was detected.

Polyethylene terephthalate (PET) is extensively used in many fields such as disposable soft drink bottles, textile fibers, packaging and also films and tapes. Its consumption in the world has been reported to exceed 13 million tonnes [40]. Therefore, the recycling of PET polymer gains critical importance in terms of environmental safety [41].

Wang et al. [29] reported the first example on the glycolysis of PET using DESs as catalyst. PET degradation was performed under the catalysis of urea-metal salt mixtures' DESs. The Lewis acid type DESs used were listed as; U-$MnAc_2 \cdot 4H_2O$ (manganese acetate), U-$ZnCl_2$, U-$ZnAc_2 \cdot 2H_2O$ (zinc acetate) from 12:1 to 6:1 molar ratios. It was reported that reaction time was shortened significantly under mild reaction conditions and high selectivity of the monomer was achieved. The conversion of PET and selectivity of bis(hydroxyalkyl) teraphthalate (BHET) were reported as 100% and 83% under the optimized conditions at atmospheric pressure and at 170°C, respectively. The comparable result with the supercritical method was presented as an advantage of this method. The authors proposed that the anion of the metal salt had a great influence on the degradation rate. When Ac^- was used as the anion, various cations of the metal salts greatly influenced the rate of degradation. However, when the cation of the metal salt was Zn^{+2}, the change of the anions had no effect on the PET degradation. The authors proposed a mechanism for the effect of DES as catalyst. The interaction between the substrates and the catalyst was formed by H-bonding and coordination bonding. In detail, H-bonds were between the following molecules: i) hydrogen atom of hydroxyl group that is present in ethylene glycol and oxygen atom of carbonyl group in urea, ii) hydrogen atom of amidogen group in urea, and oxygen atom of ester group of PET, iii) hydrogen atom of hydroxyl group in ethylene glycol and oxygen atom of ester group of PET, iv) hydrogen atom of amidogen group in urea and oxygen atom of hydroxyl group that is present in ethylene glycol. To summarize, the authors claimed that DESs could form more H-bonds between different molecules than ionic liquids and metal salts, thus, they mimic to have more catalytic active sites. In terms of the mechanism of the reaction, the H-bonds let the O-H bond of hydroxyl group in ethylene glycol get longer and therefore the electronegativity of the oxygen atoms increased causing the easier loss of the hydrogen atoms and increased nucleophilicity of the oxygen. This facilitated the attack of oxygen on the carbon of the ester group of PET. Additionally, the coordination bonds between Zn^{+2} and oxygen atom of PET increased the interaction of DES and substrate. All of these effects together resulted in the increased degradation rate of PET by DESs.

Lewis acid type DESs were also reported to be capable of initiating cationic mechanism polymerization. Maka et al. [17] described the curing process of epoxy resin using ChCl-$ZnCl_2$ (1:2) and ChCl-$SnCl_2$ (1:2) as DESs. They reported that homogeneous reaction media could be formed and catalytic activity increased when DESs were used as catalyst. It was proposed that there was a competition between activated chain end mechanism and activated monomer mechanism. Hydroxyl moieties of epoxy resin and ChCl molecules were reported to be engaged and also metal halides of DES were active at lower temperature ranges. On the other hand, $SnCl_2$ based DES was reported to be more efficient catalyst when compared to $ZnCl_2$ based DES. The authors concluded that mentioned DESs could also be used simultaneously as catalyst for polymerization of epoxy resin efficiently.

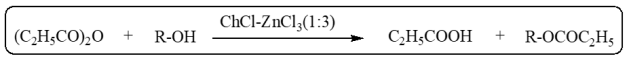

Figure 5: Propionylation of secondary alcohols, phenols and naphthols catalyzed by ChCl-$ZnCl_2$.[c]

[c] See Nguyen and Tran [39] for detailed reaction components and conditions.

Biomass derived materials are under research in many different fields to replace synthetic materials. For example, noble metal based electrocatalyst in electrochemical devices for critical oxygen reduction reaction (ORR) are searched for the replacement with low-cost, long-term stable and high activity materials [42]. Related to this, Mondal et al. [42] investigated the synthesis of Fe_3O_4/Fe doped graphene nanosheets from fresh seaweed biomass resource, *Sargassum tenerrimum*. They used Lewis acid type DES, ChCl-$FeCl_3$ as a template and also a catalyst in this reaction. Seaweed granules and DES were pyrolised at 700-900°C under 95% N_2 and 5% H_2 atmosphere. Synthesized graphene nanosheets had high surface area (220 m^2g^{-1}) and high conductivity (2384.6 mS m^{-1}). Additionally synthesized nanosheets were reported to have greater ORR activity when compared to conventional catalysts.

Another type of organic reaction that DESs were successfully used as catalysts is the esterification reaction. Esterification is one of the most crucial reactions whose products are mainly used in cosmetic and pharmaceutical industries. Nevertheless, the need for the use of liquid inorganic acids is a disadvantage in terms of corrosivity, reusability and harsh reaction conditions. Cao et al. [37] investigated many Lewis type DESs on the esterification reaction of formic acid and acetic acid with alcohols, such as: ChCl-$CrCl_3 \cdot 6H_2O$ (1:2 molar ratio), ChCl-$FeCl_3$ (1:2), ChCl-$AlCl_3 \cdot 6H_2O$ (1:2), ChCl-$MgCl_2 \cdot 6H_2O$ (1:2), ChCl-$MnCl_2 \cdot 4H_2O$ (1:2), ChCl-$CoCl_2 \cdot 6H_2O$ (1:2), ChCl-$NiCl_2 \cdot 6H_2O$ (1:2), ChCl-$CuCl_2 \cdot 2H_2O$ (1:2), ChCl-$ZnCl_2$ (1:2), ChCl-$SnCl_2$ (1:2). All tested DESs were reported to show 100% selectivity to *n*-butyl acetate while the yield values were variable at a broad range. However, ChCl-$CrCl_3 \cdot 6H_2O$ (1:2) and ChCl-$FeCl_3$ (1:2) provided high yield values as 93% and 64.5%, respectively. Especially, ChCl-$CrCl_3 \cdot 6H_2O$ (1:2) was reported to be an efficient catalyst for the esterification formic acid and acetic acid with alcohols. Besides high activity, efficiency and selectivity of ChCl-$CrCl_3 \cdot 6H_2O$ (1:2), easy preparation, low cost, low temperature and reusability were informed as advantages of the procedure.

Besides the use of DESs in reaction media in its free form, immobilized utilization strategies were also studied and performed efficiently in some reports. SBA-15, as a nanostructured mesoporous silica matrice, having large surface area, narrow pore size distribution is a good candidate for different organic reactions [43–48]. Therefore, the adsorption or covalently bonding of organic functional groups at the surface of this material is presented in many studies [47,49–51]. Azizi and Edrisi [52] reported a research on the immobilization of DES on this solid support using the advantages of the ease of preparation and low cost of DESs. They prepared a recyclable nanocomposite by impregnation of *N*-methyl pyrrolidonium-zinc chloride (HNMPCl-$ZnCl_2$) (1:1 molar ratio) based deep eutectic solvent on mesoporous silica, SBA-15. The authors investigated three-component Mannich type reactions of aldehydes, ketones and amines as model reactions to synthesize β-amino ketones (Figure 6). The aim was to overcome the disadvantages of the classic method; such as long reaction time, substrate limitations and side-reactions. As a result, the immobilization of DES onto a solid support was reported as an advantage for the down-stream processes. 45-95% of yields were achieved when immobilized DESs were used as catalyst. On the other hand, efficient and green catalyst utilization, easy work up, simple preparation and also the reusability of the catalyst (at least four times) were the additional advantages reported.

In their other study, Azizi et al. [53] prepared the same catalyst and utilized for the *N*-formylation of a variety of amines that are valuable intermediates (Figure 7). They reported that the catalyst was efficient for both primary, secondary and heterocyclic amines and could be recycled for many times without a significant loss of activity. On the other hand, overcoming many disadvantages such as harsh reaction conditions, high amount of expensive catalyst, tedious work-up, inert atmosphere were reported. The catalyst HNMPCl/$ZnCl_2$/SBA-15 showed higher activity than DES itself or mesoporous silica SBA-165 alone. The yield reached

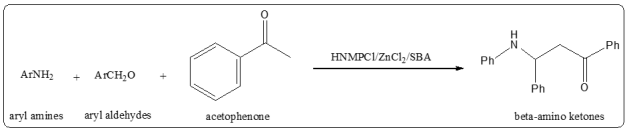

Figure 6: Three-component Mannich reaction of various aryl aldehydes, aryl amines, and acetophenone by using HNMPCl/$ZnCl_2$/SBA-15.[d]

[d] See Azizi and Edrisi [52] for detailed reaction components and conditions.

Figure 7: N-formylation of variety of amines.[e]

[e] See Azizi et al. [53] for detailed reaction components and conditions.

97% for reaction between aniline and formic acid at the optimized conditions.

1.3 Reactions catalyzed by Brønsted acid type DESs

The Brønsted acidic site of DES can protonate a compound to give further reactions. The Brønsted acidity character of DES is mainly provided by sulfonic acids and organic acids presented in the composition of DES. *p*-Toluene sulfonic acid (*p*TSA) is a significant Brønsted acid catalyst and is successfully used in the reactions because of its strong acidity. On the other hand, the disadvantage of this catalyst is the deliquescent behaviour and the difficulty of the recovery. However, these disadvantages could be overcome by the formation of deep eutectic structure of *p*TSA with ChCl. Consequently, it shows good catalytic activity and moreover gains the advantages of recovery and reusability [54].

De Santi et al. [55] reported that lately many of the esterification reactions are being related with green chemistry principles as the shift of organic solvents with new green media. Accordingly, they prepared a novel class of DESs without a halogen or metal atom that showed strong Brønsted acid characteristics. These DESs were prepared by quaternary ammonium salt possessing methanesulfonate as counterion, *p*TSA. The quaternary ammonium salts tested were trimethylcyclohexyl ammonium methanesulfonate (TCy-AMsO), trimethylbenzyl ammonium methanesulfonate (TBn-AMsO), trimethyloctyl ammonium methanesulfonate (TOAMsO), and trimethylcyclohexyl ammonium p-toluenesulfonate (TCyATos). The molar ratio was kept as 1:1 for all DESs prepared. The model reaction was performed between lauric acid and methanol. 97% yield was obtained under the catalysis of DES where 16% yield was obtained when only *p*TSA was used. When different alcohols and acids were used, the reaction also proceeded (Figure 8). The advantages of the use of the DESs in the reaction medium were reported as the mild conditions, the facility of the recovery of the products, and the reusability of the reaction medium.

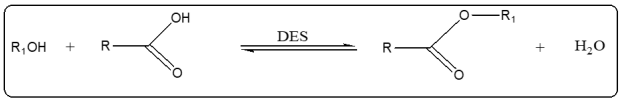

Figure 8: Esterification reaction catalyzed by DES.[f]
[f]See De Santi et al. [55] for detailed reaction components and conditions.

On the other hand, Taysun et al. [56] studied the use of Brønsted type DESs in the esterification of acetic acid with 2-ethyl hexanol. The authors investigated the catalytic activity of benzyl triethylammonium chloride (BTEAC) based DESs in this model reaction. They used BTEAC as hydrogen bond acceptor and *p*TSA, citric acid (CA) and oxalic acid (OA) as hydrogen bond donor and prepared the following DESs; BTEAC- *p*TSA (DESA) (1:4, 3:7, 2:3, 1:1, 3:2, 7:3 molar ratio), BTEAC-citric acid (DESB) (3:7, 2:3, 1:1, 3:2, 7:3 molar ratio), BTEAC-oxalic acid (DESC) (3:7, 2:3, 1:1, 3:2, 7:3 molar ratio). For 10 wt% of DES, alcohol:acid ratio (1:1) and 180 min of reaction time DESA provided highest conversions at different temperatures tested (353, 363 and 373 K). The authors claimed that this was due to the acidity of DESA, which was the highest. Additionally, the reaction time could be shortened with the use of DESA with high conversion values that was a great advantage on solid catalysts.

Hayyan et al. [57] investigated the use of DES on the biodiesel production. As known, biodiesel fuel can be prepared from oils and fats and can directly be used in diesel engine [58,59]. Additionally, it is biodegradable and non-toxic, however, total cost needs to be decreased [60]. Hayyan et al. [57] presented a strategy to produce low grade crude palm oil based biodiesel by phosphonium based Brønsted DES. In the two stage process that they offered, palm oil was pretreated with allyltriphenylphosphonium bromide-*p*TSA (1:3 molar ratio) in the presence of methanol to diminish free acid level. The step was performed in order to obtain an acceptable level of free acids for the alcaline transesterification reaction. DES was reported to be used 1-3.5 wt%. High yield and fatty acid methyl ester (FAME) conversion were acquired with a proportional increase of catalyst dosage and catalyst loading. The authors also offered a process plant layout for the pretreatment procedure for low grade crude palm oil (LGPCO) consisting of reactors for esterification and transesterification, and also evaporation unit to remove excess methanol, centrifugation for the recovery of catalyst and washing vessel. The optimum conditions were reported as, 1 wt% phosphonium based DES, 10:1 methanol:LGPCO, 60°C and 30 min.

5-hydroxymethylfurfural (5HMF) is regarded as a versatile bio-based molecule that it may lead to diverse high value chemicals and biofuel molecules. Assanosi et al. [61] studied the conversion of fructose to 5-hydroxymethylfurfural (5HMF) using Brønsted acidic DES formed with ChCl and *p*TSA in different molar ratio values (1:0.5, 1:1, 1:1.5, 1:2) (Figure 9). The aim was to overcome the main drawback of the reaction that is

high temperature, causing low yield of 5HMF due to the rehydration of the product. They claimed that DES played a HBD role and also catalyst role for the dehydration reaction. The highest 5HMF yield was obtained as 90.7% at 80°C in 1 h when 2.5 wt% feed ratio, and 1:1 molar DES mixing ratio were used. They reported that the use of DES in this reaction was a green, non-toxic and cheap process.

Similar to 5HMF, 5-ethoxymethylfurfural (5EMF) is regarded as a potential and viable biofuel. Having relatively high energy density, it has a good potential to be used as an additive to diesel and also gasoline [62–65]. On the other hand, it is also used as flavouring agent in beer and wine [66]. Gawade and Yadaw [67] presented the use of DESs as catalyst in the synthesis of 5EMF, aiming to develop a new, cheap and green method (Figure 10). With this aim, they tested various Brønsted acid type DESs as; ChCl-oxalic acid, ChCl-malonic acid, ChCl-succinic acid, ChCl-malic acid, ChCl-tartaric acid and ChCl-itaconic acid of 1:1 molar ratio.

Having the strongest acidity; ChCl-oxalic acid provided the highest yield (73%) among DESs. On the other hand the reaction did not proceed in the absence of DES, proving the catalyst effect in the reaction. The increase of the ChCl-oxalic acid concentration was reported to increase the conversion; however, decreased the yield by causing the formation of a side product, ethyl levulinate (EL). On the other hand, the initial rate of the reaction was found to be proportional to the concentration of D-fructose. The optimum reaction temperature and time were reported as 343 K and 3 h, respectively. The reusability studies showed that DES catalysed the reaction for four times, each time having highly preserved initial activity.

The synthesis of chalcones that show significant pharmaceutical properties are under research in terms of green chemistry framework. With this aim, Tiecco et al. [68] prepared a DES using 3-(cyclohexyldimethylammonio) propane-1-sulfonate and (1*S*)-(+)-10-camphorsulfonic acid (SB3-Cy:CSA). They used this Brønsted acid type DES as a catalyst for carbon–carbon bond formation reaction through Claisen–Schmidt condensation and also as a reaction medium. Fourteen substituted chalcone molecules from benzaldehydes and substituted benzaldehydes and acetophenone and substituted acetophenones were successively synthesized (Figure 11). The CSA that is present in the DES as an acidic component provided catalyst effect on the reaction. The advantages of the DES utilization were reported as the excellent conversion and yield values and also the mild conditions of the reaction and reusability of DES. With the use of DES, harmful and toxic catalysts usage could be eliminated from the synthesis pathway.

Diarylmethanes and their derivatives synthesized by the Friedel-Crafts benzylation reaction of aromatic compounds have great importance due to the utilisation in pharmaceutical industry, dyes and perfumes [69,70]. Generally aryl methanes and the derivatives are manufactured by using benzyl halide. However, due to the strong corrosivity of the by-product hydrogen halide; benzyl alcohol (BA) is preferred and investigated as an environmentally friendly alternative molecule. Nevertheless, there are also some disadvantages of BA such as the formation of by-product, low activity and difficulty in the separation of the products. To overcome these disadvantages, Yuan et al. [71] prepared a new Brønsted acid type DES, using ChCl and trifluoromethanesulfonic acid to be used as a catalyst. The new DES was reported to be more stable than trifluoromethanesulfonic acid and moreover had higher catalytic performance in the reaction of with benzyl alcohol. Another interesting property of the catalyst DES was to dissolve in the reaction medium providing homogeneous system and moreover, self-separation from the organic phase after the consumption of BA.

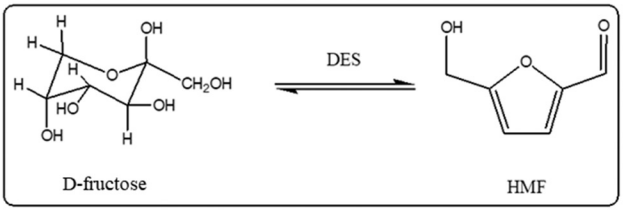

Figure 9: Conversion of fructose to 5-hydroxymethylfurfural (5HMF) catalyzed by DES.

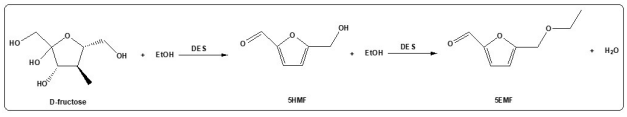

Figure 10: DES catalysed synthesis of 5-EMF.

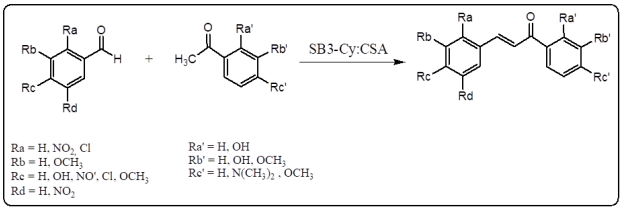

Figure 11: Claisen-Schmidt reaction of acetophenones and mono- and bi- substituted benzaldehydes catalyzed by DES.[g]

[g]See Tiecco et al. [68] for detailed reaction components and conditions.

This also facilitated the reusability of DES about six times without noticeable diminish in the activity.

Beyond the literature described above, some authors preferred comparing different types of DESs in several reactions. Some examples of these studies are summarized below that used Lewis-type, Brønsted type and organocatalyst type DESs.

Azizi et al. [72] used different types of DESs in Biginelli reaction that leaded the synthesis of polyfunctionalized dihydropyrimidinones (DHMPs) that have attractive antibacterial, antitumoral and anti-inflammatory properties [73,74]. The disadvantage of the conventional methods were reported as harsh reaction conditions, low yield and long reaction times. Different DESs were tested (ChCl-$SnCl_2$ (1:2), ChCl-U (1:2), ChCl-$ZnCl_2$ (1:2), ChCl-$ZnCl_2$-$SnCl_2$ (1:1:1), ChCl-Gly (1:3)) in the model reaction of benzaldehyde, urea and ethyl acetoacetate. ChCl-$SnCl_2$ was found to provide the highest yield as 95% in 30 min. When it was used as a catalyst for the broad range of 1,3-dicarbonyl compounds such as ethylacetoacetate, methylacetoacetate, pentane-2,4-dione, ethyl 3-oxo-3-phenylpropanoate, 5,5-dimethyl-1,3-cyclohexanedione, 3-oxo-N-(2-chlorophenyl) butanamide, aromatic and aliphatic aldehydes and urea, high yield values (74-95%) and high reaction rates were reported (Figure 12). Besides, the authors reported that no side products were identified, additionally the desired products were at such a high purity that no further purification was needed after crystallization.

Bis(indolyl)alkane derivatives that are mainly present in different natural products have significant biological activities. The synthesis of these derivatives is performed at acidic conditions either using a protic acid or a Lewis acid with the reaction of indole and an aldehyde or a ketone. To present a greener route, Azizi and Manocheri [75] used ChCl-$SnCl_2$ (1:2), ChCl-U (1:2), ChCl-$ZnCl_2$ (1:2), ChCl-$ZnCl_2$-$SnCl_2$ (1:1:1), ChCl-Gly (1:3), ChCl-$SnCl_2$-H_2O (1:2:3) and ChCl-$SnCl_2$-polyethylene glycol (1:2:3) in the reaction as catalyst. The best results were obtained using ChCl-$SnCl_2$. The amount of DESs were reported to affect the yield of the reaction and high temperature values were found to provide higher yield values by increasing the viscosity of the reaction mixture. Additionally 78-97% of yield could be achieved using both aromatic and heterocyclic aldehydes (Figure 13). On the other hand, aliphatic aldehydes and simple ketones were reported to give high yield bis(indolyl) methanes. The reusability of DES, simplicity of the synthesis route and the lack of a by-product were presented as the advantages of the study.

Azizi et al. [76] investigated the use of DESs as a catalyst and also solvent in the chemoselective synthesis of tetraketone and xanthene derivatives using Knoevenagel condensation and Michael addition reactions. The aim was to overcome the long reaction time, high cost and the sensitivity of the catalyst to moisture. Green solvents were selected among Lewis acid type, Brønsted acid type and other types of DESs as: ChCl-U (2:1), ChCl-malonic acid (1:1), ChCl-$SnCl_2$ (1:2), ChCl-$ZnCl_2$ (1:2), ChCl-$SnCl_2$-$ZnCl_2$ (1:1:1), ChCl-$LaCl_3$ (1:2), ChCl-*p*TSA (1:1) and ChCl-Gly (1:2).

ChCl-U and ChCl-$SnCl_2$ were reported to provide higher yields of tetraketones when compared to other DESs (Figure 14). On the other hand, ChCl-$ZnCl_2$ and ChCl-malonic acid were reported to generate xanthene derivatives, selectively (Figure 15). The authors claimed that independent of the type of the aldehyde used, (electron-rich, electron-poor, aromatic, heterocyclic and sterically encumbered aldehydes) the efficiency of the condensations were quite good. The authors reported that DESs could be efficiently used in the reactions as a catalyst presenting a green method.

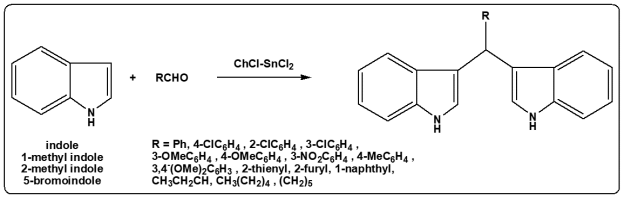

Figure 13: Condensation reaction of aldehydes and indoles catalysed by ChCl-$SnCl_2$.[i]
[i] See Azizi and Manocheri [75] for detailed reaction components and conditions.

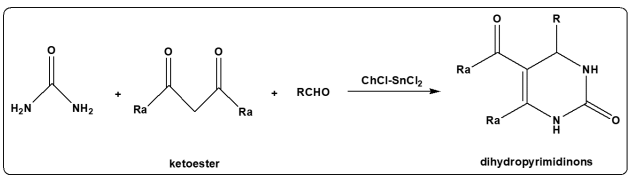

Figure 12: ChCl-$SnCl_2$ catalysed synthesis of dihydropyrimidinons.[h]
[h] See Azizi et al. [72] for detailed reaction components and conditions.

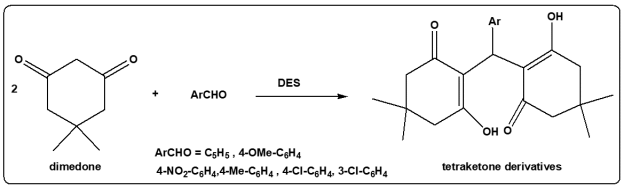

Figure 14: DES catalysed synthesis of tetraketone derivatives.[j]
[j] See Azizi et al. [76] for detailed reaction components and conditions.

Jin et al. [77] studied the synthesis of aromatic ketones using Friedel-Crafts acylation reaction that is simple and has high selectivity and responsiveness (Figure 16). They investigated both Brønsted and Lewis acid type DESs as an alternative to conventional methods to overcome the disadvantages such as high dosage, complexity of controlling and in terms of environmental problems. With this aim, they prepared benzyltrimethylammonium chloride (TMBAC)-$ZnCl_2$ (1.5:2 molar ratio), (TMBAC)-*p*TSA (1:1 molar ratio), triethylamine borane (TEAB)-*p*TSA (1:2), TMBAC-trifluoromethanesulfonic acid (CF_3SO_3H) (1:1), ChCl-*p*TSA (1:1), ChCl-$ZnCl_2$ (1:2). They selected the reaction between 1,2,4-trimethoxybenzene and benzoyl chloride to yield 2,4,5-trimethoxybenzophenone to test traditional Lewis acid $ZnCl_2$ and mentioned DESs as catalysts. They reported that only (TMBAC)-$ZnCl_2$ (1.5:2) (34%) and ChCl-$ZnCl_2$ (1:2) (74%) were able to synthesize target molecules. As a general conclusion of DESs tested proton acid-type DESs ChCl- *p*TSA (1:1), (TMBAC)-*p*TSA (1:1), (TEAB)-*p*TSA (1:2) and TMBAC-CF_3SO_3H (1:1) had no catalytic activity while Lewis $ZnCl_2$ containing DESs could promote the reaction effectively.

In series of reactions they tested using different acylation reagents with 1,2,4-trimethoxybenzene, they reported the excellent reaction between the electron donating aromatics with acyl halides, under catalyzation of ChCl-$ZnCl_2$ (1:2). They proposed that ChCl-$ZnCl_2$ (1:2) as a catalyst formed an electrostatic mask ring-like body and $Zn_2Cl_5^-$ attacked carbonyl oxygen triggering electron transfer to break carbon-chloride bond resulting in free Cl^- and cationic carbon intermediates. Then, for the formation of the target compound, the carbocation attacks aromatic arenes and generates carbon-carbon bonds. Meanwhile hydrogen and chloride combine and generate HCl. As a result, ChCl-$ZnCl_2$ was exhibited to be an effective catalyst under optimized conditions. Moreover, recovered catalyst could be used several times without significant loss of activity.

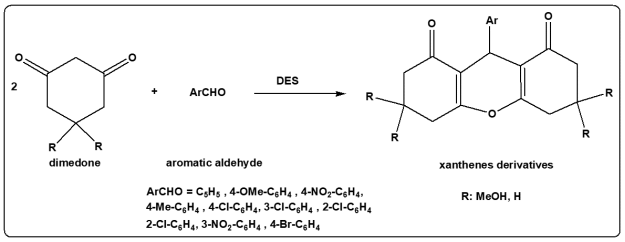

Figure 15: DES catalysed synthesis of xanthenes derivatives.[k]
[k] See Azizi et al [76] for detailed reaction components and conditions.

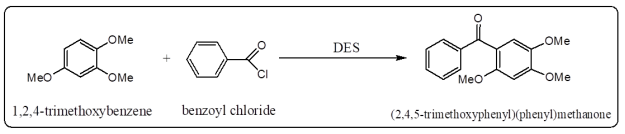

Figure 16: DES catalyzed Friedel-Crafts acylation of 1,2,4-trimethoxybenzene and benzoyl chloride.

Multicomponent reactions (MCRs) have been extensively searched as a substantial strategy for the synthesis of multiple bond formation reactions. However, synthesis media contain toxic solvents that are not favored. Lately, Lewis or Brønsted acid catalysts have been investigated as catalyst for MCRs [78].

Wang et al. [54] studied the synthesis of phthalazine moiety containing nitrogen heterocycles, since they have taken increased attention because of their biological and pharmacological activities including anticonvulsant, vasorelexant and cardiotonic properties. They preferred MCR of phthalhydrazide, an aldehyde, and dimedone to give 2H-indazolo[2,1-b]phthalazinetriones (Figure 17). They used ChCl-*p*TSA (1:1 molar ratio) as Brønsted acid type DES in the one-pot synthesis of 2*H*-indazolo[2,1-b] phthalazine-trione derivatives. For this MCR system, the authors tested different reaction media such as, water, methanol, ethanol, acetonitrile, and toluene. DES was added as 5-20% (molar amount) as catalyst. According to the results, ethanol and methanol were reported to give good yields while water was found to be poor in this aspect. This phenomenon was related with the solubility of DES in polar solvents providing homogeneous reaction medium. The optimum catalyst amount was reported as 15 mol% of ChCl-*p*TSA (1:1) in methanol. A number of substituted aromatic aldehydes tested also provided good yields.

Another case of the use of various kinds of DESs as catalyst is the MCR is the synthesis of imidazo[1,2-a] pyridines by Groebke reaction [79] (Figure 18). The three-component reaction of 2-aminopyridine, aromatic aldehydes and cyclohexyl isocynaide was investigated in the presence of ChCl based DESs; without using

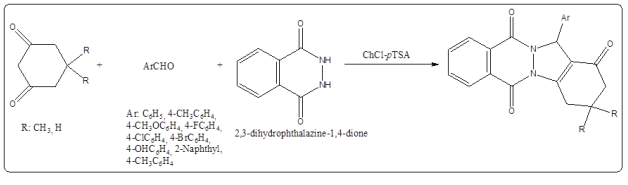

Figure 17: One-pot synthesis of 2H-indizolo[2,1-b]phthalazine-triones catalyzed by ChCl-*p*TSA.[l]
[l] See Wang et al. [54] for detailed reaction components and conditions.

a catalyst. The role of ChCl-U (1:2), ChCl-$SnCl_2$ (1:2), ChCl-$ZnCl_2$ (1:2), ChCl-$LaCl_3$-$6H_2O$ (1:2), ChCl-*p*TSA (1:1) and ChCl-Gly (1:2) as solvent and also catalyst in the model reaction of benzaldehyde, 2-aminopyridine and cyclohexylisocyanide was investigated. ChCl-U was selected as the most effective media for the synthesis of the target product. When the media was used for the synthesis of imidazo[1,2-a] pyridine derivatives, high yields were obtained with many kind of different functional groups at the aromatic group, including Cl, OMe, Me and OH. On the other hand, some aldehyde derivatives such as 4-methoxy benzaldehyde, was resulted in moderate yield values likely because of the negative charge induced on the carbon atom that is bonded to aldehyde group. The authors proposed a mechanism for the catalyst effect of the DES. Urea is known to be responsible for the activation of C=O bond through hydrogen bonding. Therefore DES is proposed to facilitate the formation of imine intermediate by the nucluophilic addition of amine and also for isocyanide nucleophilic attack. The resulting imine intermediate and the cyclohexyl isocyanide are combined by cycloaddition reaction and bicyclic adduct is formed. Then a rearrangement on 1,3-*H* shift gives the final product, imidazo[1,2-a] pyridine.

The reusability tests of ChCl-U provided satisfactory results, with at least four runs conserving the activity. The advantages of the developed green method were reported as the easy purification, biodegradable solvent and also easy methodology.

The discovery of cromakalim, which is a typical ATP_sensitive potassium channel opener, has gained much attention for the synthesis of benzo[b]pyran and their derivatives. The conventional synthesis for 4H-benzo[b]pyrans includes the use of organic solvents such as DMF, DMSO, acetonitrile, and etc. Azizi et al.'s [80] aim was to report an eco-friendly MCR to synthesize benzopyran and benzopyrane derivatives using one-pot three component reactions of 1,3-dicarbonyl compounds, aldehydes and malononitrile in DESs (Figure 19). They prepared different Brønsted acid type DESs such as ChCl-malonic acid (1:2), ChCl-citric acid (1:1), ChCl-tartaric acid (1:0.5), and also ChCl-U (1:2), ChCl-glycine (1:2), ChCl-$LaCl_3$ (lanthanum chloride) (1:2). The model reaction included benzaldehyde (1 mmol), malononitrile (1 mmol), dimedone (1 mmol) and DESs. Equimolar reactants in DES at 80°C and 60 min, provided 95% yield. The highest yield was obtained in ChCl-U (1:2). Additionally, various substituted aromatic and hetero aromatic aldehydes were tested and good to excellent yield values were reported. The authors stated that the role of DES was unclear as a catalyst. On the other hand, they claimed that hydrogen bonding and also basic character of urea were the primary factors for the selectivity and also reactivity in the process. They suggested that substrate-solvent complex formed between urea and carbonyl groups. Then, arylidene malononitrile formed and nucleophilic addition of enolizable ethylacetoacetate to arylidene malononitrile occurred. The resulting species were cyclized to produce 4*H*-pyran derivatives.

Azizi et al. [81] reported another multicomponent reaction system using similar DESs to their previous work. They studied the synthesis of spirooxindole derivatives by one-pot MCR system using DESs (Figure 20). Having a quaternary carbon center, spirooxindoles are significant molecules and are found in many phytochemicals. The authors aimed to present a green and also economical route for the synthesis. They used isatin or acenaphthoquinone, and malononitrile (2) having active methylene compounds (3a–e) in ChCl-U without catalyst. Using 80°C as the optimum temperature, they obtained 95% yield for the reaction using ChCl-U (1:2). Other DESs tested such as ChCl-*p*TSA

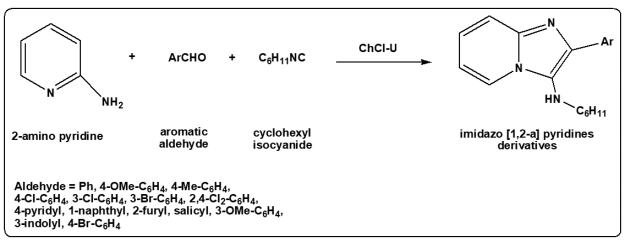

Figure 18: The synthesis of imidazo [1,2-a] pyridines derivatives from 2-amino pyridine catalysed by DES.[m]

[m] See Azizi and Deezfoli [79] for detailed reaction components and conditions.

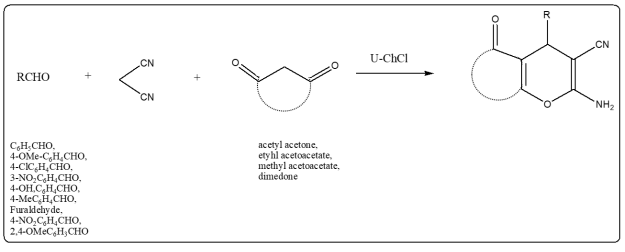

Figure 19: Three component reactions of 1,3-dicarbonyl compounds, aldehydes and malononitrile in DESs.[n]

[n] See Azizi et al. [80] for detailed reaction components and conditions.

(1:2), and ChCl-malonic acid (1:1 molar ratio) provided lower yields (38-76%). They reported that DES played both solvent and catalysis role in the reaction.

Sulfoxides are critical midproducts for the synthesis of biologically active biomolecules. The common way to synthesize sulfoxides are the oxidation of sulfides [82]. The key point on this oxidation process is to prevent overoxidation of sulfoxides to sulfones. Therefore, selective oxidation has a great importance on this reaction. The drawbacks of the methods currently used are the complex catalytic systems [83,84], high demand for the oxidant or catalyst [85,86] and poor yield and also poor selectivity values. On the other hand, hydrogen peroxide has also been studied as an environmentally friendly and cheap oxidant for the oxidation of sulfides however; the activation of hydrogen peroxide is reported as bottleneck that results in the slow rate of reaction. Dai et al. [87] claimed that DES could activate hydrogen peroxide through hydrogen bonding. Among the different DESs (ChCl-U (1:2), ChCl-malonic acid (1:2), ChCl-glycerol (1:2), ChCl-hexafluoroisopropanol (1:1.5 molar ratio), ChCl-*p*TSA(1:1), ChCl-*p*TSA as a Brønsted acid type DES was chosen as the superlative catalyst to provide the highest yield (89%) for the model reaction conducted with benzyl phenyl sulfide, containing ethanol as organic solvent (Figure 21). They claimed that DES formed a strong hydrogen bond with hydrogen peroxide and increased the electrophilicity of one of the peroxy oxygen atoms of hydrogen peroxide. Moreover, prevention of the further oxidation of sulfoxide was claimed to occur by the hydrogen bond between catalyst and oxygen of sulfoxides that decreased the nucleophilic character of the sulfur atom of sulfoxides. As a result of the study, they reported broad substrate compatibility, high yield and selectivity values, and the advantage of the gram-scale synthesis. On the other hand recyclability of DES was also reported as one of the major advantages of the process.

Musale and Shukla [41] studied the ChCl-$ZnCl_2$ (1:1 to 1:3 molar ratio) and ChCl-U (1:2 molar ratio) on the aminolytic depolymerization of PET bottle waste (Figure 22). The reaction was started by using diethanolamine and ethanolamine. The products were *N1,N1,N4,N4*-tetrakis (2-hydroxyethyl)-terephthalamide (THETA), terephthalic acid (TPA), and bis (2-hydroxy ethylene) terephthalamide (BHETA). ChCl-$ZnCl_2$ provided higher yield for the products when compared to ChCl-U (1:2) as catalyst. When reaction time was prolonged, the yield of products were found to increase. On the other hand, the yield was found to increase instantly when the catalyst was increased to 5%. Additionally, in the presence of DES, PET was reported to pass into solution more quickly from solid

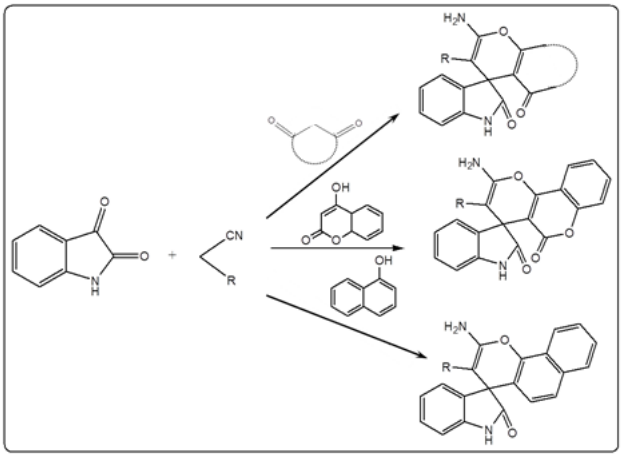

Figure 20: ChCl-U catalyzed synthesis of spiro-2-oxindole.[o]
[o] See Azizi et al. [81] for detailed reaction components and conditions.

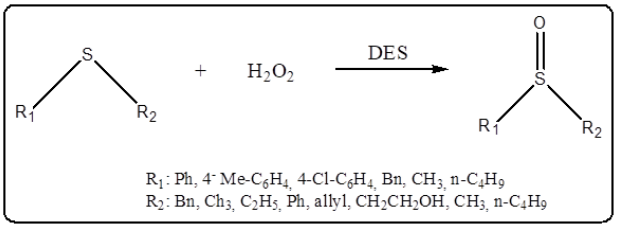

Figure 21: Selective oxidation of sulfides to sulfoxides bu using DES.[p]
[p] See Dai et al. [87] for detailed reaction components and conditions.

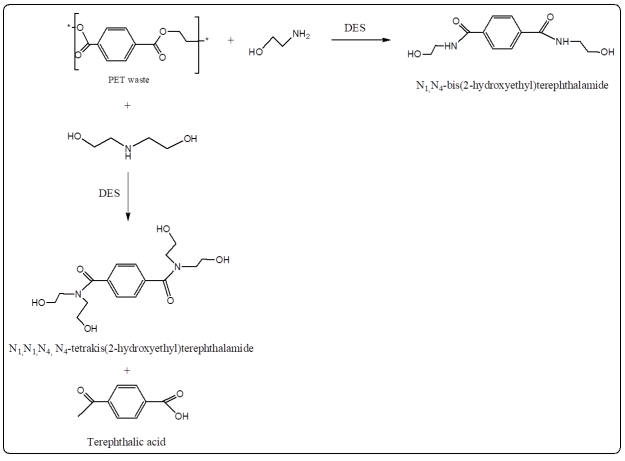

Figure 22: Aminolytic depolymerisation of PET catalyzed by DES.

phase. THETA - TPA and BHETA yields were reported as 82.83 and 95% respectively. DESs; especially, ChCl-$ZnCl_2$ (2:1 molar ratio) provided higher yield of all the three products. The authors reported that DESs showed efficient catalyst performance. The reason was reported as the high rate of dissolution of PET in DESs.

As also mentioned above, liquid inorganic acids are needed as catalyst for the esterification reactions. However, they have disadvantages such as corrosivity, reusability and also harsh reaction conditions. Lee et al. [88] studied the esterification reaction of palmitic acid and methanol using DESs both as solvent and catalyst to overcome the disadvantages (Figure 23). They tested various DESs such as; ChCl-U (1:2), ChCl-EG (1:2), ChCl-G (1:2), and also Brønsted acid type DESs such as ChCl-malonic acid (1:1), tetramethyl ammonium chloride-oxalic acid (1:2), tetramethyl ammonium chloride-acetic acid (1:2), lactic acid–D-glucose (5:1). The authors proposed a mechanism for the process. The ammonium ion in the DES structure is proposed to loose proton, and it is moved to the oxygen that belongs to the carbonyl moiety palmitic acid. Palmitic acid acts as a nucleophilic reagent and therefore supports the strike of methanol. Accordingly, methyl palmitate and methanol are formed via the new bond between the carbonyl carbon and oxygen of the hydroxyl moiety connected to methanol. On the other hand, in the second mechanism acetic acid of the DES looses proton and it is moved to the oxygen on the carbonyl moiety of palmitic acid. Lee et al. [88] reported the most convenient DES as tetrabutyl ammonium chloride and acetic acid (1:2), and the optimum ratio of starting materials to DES ratio was reported as 1:0.5 (v/v). Additionally, the optimum reaction conditions were reported as methanol / palmitic acid 10:1 (mol/mol), and the reaction time was 1 h at 60°C. High yield value was achieved as 94.3% under the optimized conditions.

N-phenylphthalimide and its derivatives are significant molecules that are anticonvulsant [89] and anti-inflammatory [90,91]. Some derivatives also have growth stimulation effect for plants [92,93] and also some for tuberculosis therapy. Additionally, some are utilized in polymer and synthetic chemistry [94,95]. The disadvantage of the current processes were reported as the utilization of acids, organic solvents and hazardous catalysts and long reaction times. Lobo et al. [96] aimed to develop low-cost and environmentally friendly synthesis route for the preparation of N-aryl phtalimide derivatives (Figure 24). They tested glycerol, and ChCl-U (2:1), and also Brønsted acidic ChCl-malonic acid on the synthesis of *N*-phenylphthalimide from phthalic anhydride and aniline. ChCl-malonic acid (1:1) was reported to be an efficient catalyst; on the other hand, glycerol and also ChCl-U DES functioned as both solvent and catalyst. They reported moderate to high yield values and high recyclability of DESs. The highest yield obtained for the reaction of phtalic anhydride with aniline was 84% using methanol as solvent, and ChCl-malonic acid as catalyst at 65°C. They also stated that DES preserved its original form when 30% diluted as a result of 1H NMR spectra.

Apart from organic synthesis, DESs are also investigated as catalyst concurrently co-solvent in the liquefaction of biomass. Although ionic liquids were researched and used in this process previously, many disadvantages were reported on the cost, prolonged time and the employment of evaporable solvents. Alhassan et al. [97] studied on the use of DESs as catalyst on the hydrothermal liquefaction of de-oiled *Jatropha curcas* cake biomass and also co-solvents for selective extraction. For this aim, ChCl-KOH (1:4), ChCl-glycerol (1:3), Brønsted acid type DES ChCl-*p*TSA (1:4), and Lewis acid type DES ChCl-$FeCl_3$(1:3) were prepared. They reported that highest bio-crude yields (43.53 %wt) were obtained using ChCl-KOH.

As a general result, higher yields were obtained using ChCl–HBD (KOH, *p*TSA and glycerol) than (ChCl–$FeCl_3$). The favorization of ChCl–HBD DES on the reported process was proposed.

The pyrrole nucleus is a significant heterocycle that is present in numerous agrochemical and pharmaceutical products [98]. Numerous pyrolle-comprising compounds have a potential biological

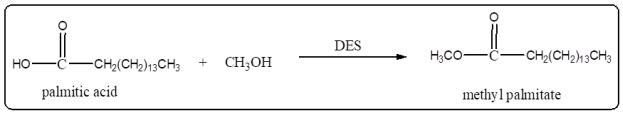

Figure 23: DES catalyzed esterification of palmitic acid with methanol.

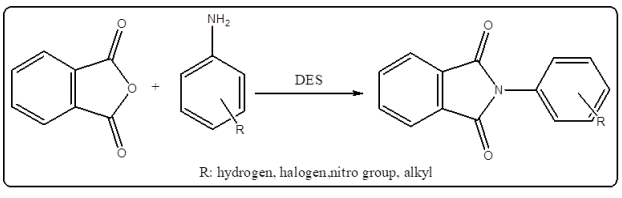

Figure 24: DES catalyzed synthesis of N-phenylphthalimide derivatives.[r]

[r] See Lobo et al. [96] for detailed reaction components and conditions.

activity [99,100]. On the other hand, the compounds derived from pyrolle have significant role in materials science [101]. Therefore, the synthesis has been studied using many strategies; such as, Hantzsch, Paal–Knorr and Clauson-Kaas reactions.

MCRs are successfully used for the synthesis of substituted and functionalized pyrrole derivatives from simple molecules [102]. However, due to prolonged reactions, insufficient yield of products and laborious procedures, new efforts have been made for a simple and efficient method to enhance the conversion. The motivation of Hu et al. [38] was the construction of *N*-protected functionalized pyrroles using MCR in shorter times by presenting an alternative way to conventional MCR media (Figure 25). For this aim, they investigated the reaction of amines, aldeyhdes, 1,3-dicarbonyl compounds and nitromethane using different DESs such as ChCl with the combination of urea, *L*-(+)-tartaric acid (2:1 molar ratio), citric acid (2:1), oxalic acid (1:1), $FeCl_3$ (1:2), $ZnBr_2$ (1:2), itaconic acid (1:1), fumaric acid (1:1), malic acid (1:1), succinic acid (1:1), malonic acid (1:1). It was reported that MCR could proceed in nearly all of the media tested. The highest yield (88%) was obtained using ChCl-malonic acid (1:1 molar ratio) in the MCR of 4-chloro benzaldehyde, aniline, acetlyacetone, nitromethane. The variety in the yields obtained with different DESs were attributed to the different acidic characteristics of the DESs used. The large scale synthesis was also found to be applicable with high yield value of 89%. The investigation on the use of DES to a broader range of substrates showed that a wide range of anilines, aldehydes, and 1,3-dicarbonyl compounds could undergo the reaction.

Shaabani and Hooshman [78] utilised urea- metal- and organic based ChCl DES/organocatalysts on the synthesis of 3-aminoimidazo-fused heterocycles using one pot domino reaction of an aldehyde, an isocyanide and 2-aminoheterocycles. ChCl-U (1:2) and DESs such as ChCl-malonic acid (1:1), ChCl-citric acid (2:1), ChCl-*p*TSA (1:1), ChCl-$ZnCl_2$ (1:2) and ChCl-$SnCl_2$ (1:2) on GBB three component domino reactions. ChCl-U (1:2) was found to provide the highest yield in the model reaction, therefore used for further investigations. The authors reported that 2-aminoazine derivatives could be successfully used in the reactions with high yields (80-90%), and short reaction times under the catalysis of ChCl-U. Synthesized DESs could also be used several times without any significant loss in the activity.

Apart from the studies presenting the Lewis acid type or Brønsted acid type catalyst effect of DESs, Shaibuna et al. [103] introduced three new DES types, showing both Lewis acidity and Brønsted type acidity. The authors prepared Type IV DESs that are composed of a metal chloride hydrate that is $ZrOCl_2 \cdot 8H_2O$ (Zr) and used urea, ethylene glycol or glycerol as HBDs. They tested different molar combinations of the components and selected Zr-U (1:5), Zr-EG (1:2) and Zr-EG (1:2) as stable DESs to be furtherly used in the reactions. The acidity of DESs were determined by the combined use of both FTIR and pH. According to the results, Zr-U was found to have both Lewis acid site and Brønsted acid site, while the other two had only slight Brønsted acid site. These new DESs were reported to miscible with protic solvents such as MeOH, EtOH and water; while immiscible with aprotic solvents such as toluene, hexane and ethyl acetate. The Paal-Knorr reaction was performed using aniline (1 mmol) and 2,5-hexanedione (1 mmol) as the model reaction and 93% yield was achieved at the optimum conditions (1 mmol Zr-U, 5 min, room temperature) (Figure 26). The authors also tested the Zr-U as catalyst for a variety of amines including both aliphatic and aromatic amines and obtained 93-98% pyrrole yields. The yield value of 88% in the reaction between 2-aminopyridine, a heteroaromatic amine, and 2,5-hexanedione additionally showed the effectiveness of Zr-U as a catalyst.

The authors proposed a mechanism for the catalytic activity of Zr-U. Accordingly, DES interacted with the oxygen atom of the carbonyl group in 2,5-hexanedione and produced a hydrogen bonded activated complex. The amino group of the aniline was proposed to attack the complex forming an adduct. The NH group of the adduct

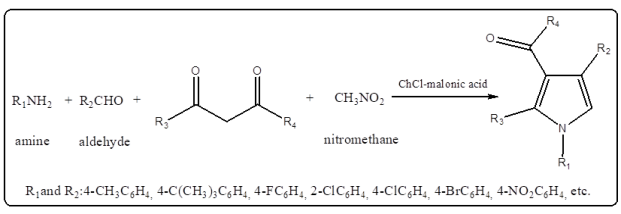

Figure 25: DES catalyzed synthesis of functionalized pyrroles.[s]
[s] See Hu et al. [38] for detailed reaction components and conditions.

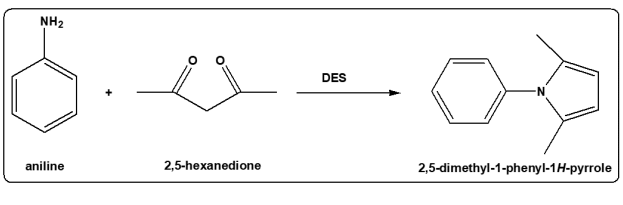

Figure 26: DES catalyzed Paal-Knorr reaction.[t]
[t] See Shaibuna et al. [103] for detailed reaction components and conditions.

attacked second carbonyl carbon causing the loss of two water molecules and finally pyrrole was formed and DES was regenerated as catalyst. The result of the recyclability of the DES showed that it could be used four times without a crucial loss in the activity.

2 Conclusions and outlook

With the increasing consciousness of the environmental issues, researchers exhibited great effort to replace toxic constituents with less or non-toxic ones. Ionic liquids being the pioneer in this field had taken great attention and found many successful applications in many different areas. Later on, by the presentation of deep eutectic solvents, the comparative studies showed that DESs had a major superiority in many aspects such as non-toxicity, easy and low-cost preparation opportunity. DESs were used successfully in various areas such as metal processing, extraction, organic synthesis and biotransformations. The role of DES in most of these applications was a solvent or co-solvent, incorporating the advantages of high solubility of the substituents, non-vaporisation and easy handling. Recently, an additional role of DESs showed up, as a catalyst in diverse type of reactions. Acid type catalysis including Lewis and Brønsted type acids were the irrevocable catalysts for most of the organic reactions. Based on the tuning of the characteristics of DESs, such as unlimited combinations of HBAs and HBDs, researchers synthesized DESs including Lewis acids or Brønsted acids possessing different catalytic activity. The use of DESs as acid catalyst has several advantages such as the utilisation at stoichiometric amount, non-toxicity, possibility of the recovery, similar or higher catalytic effect than the acid itself alone, the recyclability and reusability without a significant loss of activity. Therefore, DESs can readily be regarded as alternative catalysts to conventional ones.

This mini-review provides a site of some of the most recent applications of Lewis and Brønsted type DESs as catalysts in various types of reactions including esterification, organic synthesis, glycolysis, depolymerisation, etc. In spite of a limited number of studies reviewed here, we consider that both Lewis and Brønsted acid type DESs can efficiently be used in a plenty of synthesis reactions. Although their role as catalyst has not been fully defined yet, some mechanisms were proposed, mostly being related with the H-bonding character of DESs. Therefore, more endeavour is required to enhance the utilization of DESs in catalysis. Dual functionality of DESs as solvent and also as catalyst will provide them an excellent range of usage in future.

References

[1] Smith E.L., Abbott A.P., Ryder K.S., Deep Eutectic Solvents (DESs) and Their Applications. Chem. Rev., 2014, 114, 11060-11082.

[2] Zainal-Abidin M.H., Hayyan M., Hayyan A., Jayakumar N.S., New horizons in the extraction of bioactive compounds using deep eutectic solvents: A review. Anal. Chim. Acta, 2017, 979, 1-23.

[3] Shishov A., Bulatov A., Locatelli M., Carradori S., Andruch V., Application of deep eutectic solvents in analytical chemistry. A review. Microchem. J., 2017, 135, 33-38.

[4] Hadj-Kali M.K., Separation of ethylbenzene and n-octane using deep eutectic solvents. Green Process. Synth., 2015, 4, 117-123.

[5] Lee J.S., Deep eutectic solvents as versatile media for the synthesis of noble metal nanomaterials. Nanotechnol. Rev., 2017, 6, 271-278.

[6] Isaifan R.J., Amhamed A., Review on Carbon Dioxide Absorption by Choline Chloride/Urea Deep Eutectic Solvents. Adv. Chem., 2018, 2018, 1-6.

[7] Azizi N., Yadollahy Z., Rahimzadeh-Oskooee A., An atom-economic and odorless thia-Michael addition in a deep eutectic solvent. Tetrahedron Lett., 2014, 55, 1722-1725.

[8] Azizi N., Alipour M., Eco-efficiency and scalable synthesis of bisamides in deep eutectic solvent. J. Mol. Liq., 2015, 206, 268-271.

[9] Azizi N., Ahooie T.S., Hashemi M.M., Multicomponent domino reactions in deep eutectic solvent: An efficient strategy to synthesize multisubstituted cyclohexa-1,3-dienamines. J. Mol. Liq., 2017, 246, 221-224.

[10] Dutta A.K., Gogoi P., Borah R., Diethyldisulfoammonium chlorometallates as heterogeneous Brønsted-Lewis acidic catalysts for one-pot synthesis of 14-aryl-7-(N-phenyl)-14H-dibenzo[a,j]acridines. Appl. Organomet. Chem., 2018, 32, e3900.

[11] Merza F., Fawzy A., AlNashef I., Al-Zuhair S., Taher H., Effectiveness of using deep eutectic solvents as an alternative to conventional solvents in enzymatic biodiesel production from waste oils. Energy Reports, 2018, 4, 77-83.

[12] Wu M., Ma H., Ma Z., Jin Y., Chen C., Guo X., et al., Deep Eutectic Solvents: Green Solvents and Catalysts for the Preparation of Pyrazine Derivatives by Self-Condensation of d -Glucosamine. ACS Sustain. Chem. Eng., 2018, 6, 9434-9441.

[13] Xu H., Zhang D., Wu F., Wei X., Zhang J., Deep desulfurization of fuels with cobalt chloride-choline chloride/polyethylene

glycol metal deep eutectic solvents. Fuel, 2018, 225, 104-110.

[14] Park S., Kazlauskas R.J., Biocatalysis in ionic liquids - Advantages beyond green technology. Curr. Opin. Biotechnol., 2003, 14, 432-437.

[15] Shamsuri A.A., Abdullah D.K., Protonation and Complexation Approaches for Production of Protic Eutectic Ionic Liquids. J. Phys. Sci., 2010, 21, 15-28.

[16] Handy S., Deep Eutectic Solvents in Organic Synthesis. In: Handy, S. (Ed.), In Ionic Liquids-Current State of the Art. Intech Open, London, 2015.

[17] Mąka H., Spychaj T., Adamus J., Lewis acid type deep eutectic solvents as catalysts for epoxy resin crosslinking. RSC Adv., 2015, 5, 82813-82821.

[18] Abbott A.P., Capper G., Davies D.L., Rasheed R.K., Tambyrajah V., Quaternary ammonium zinc-or tin-containing ionic liquids: water insensitive, recyclable catalysts for Diels–Alder reactions. Green Chem., 2002, 4, 24-26.

[19] Morales R.C., Tambyrajah V., Jenkins P.R., Davies D.L., Abbott A.P., The regiospecific Fischer indole reaction in choline chloride·2$ZnCl_2$ with product isolation by direct sublimation from the ionic liquid. Chem. Commun., 2004, 2, 158-159.

[20] Sunitha S., Kanjilal S., Reddy P.S., Prasad R.B.N., Liquid-liquid biphasic synthesis of long chain wax esters using the Lewis acidic ionic liquid choline chloride·2$ZnCl_2$. Tetrahedron Lett., 2007, 48, 6962-6965.

[21] Abbott A.P., Bell T.J., Handa S., Stoddart B., O-Acetylation of cellulose and monosaccharides using a zinc based ionic liquid. Green Chem., 2005, 7, 705-707.

[22] Duan Z., Gu Y., Deng Y., Green and moisture-stable Lewis acidic ionic liquids (choline chloride·x$ZnCl_2$) catalyzed protection of carbonyls at room temperature under solvent-free conditions. Catal. Commun., 2006, 7, 651-656.

[23] Azizi N., Batebi E., Highly efficient deep eutectic solvent catalyzed ring opening of epoxides. Catal. Sci. Technol., 2012, 2, 2445-2448.

[24] Patil U.B., Singh A.S., Nagarkar J.M., Choline chloride based eutectic solvent: an efficient and reusable solvent system for the synthesis of primary amides from aldehydes and from nitriles. RSC Adv., 2014, 4, 1102-1106.

[25] Pratt E.F., Green L.Q., Reaction Rates by Distillation. IV. The Effect of Changes in Structure on the Rate of the Baeyer Condensation. J. Am. Chem. Soci, 1953, 75, 275-278.

[26] Riad A., Mouloungui Z., Delmas M., Gaset A., New synthesis of substituted difuryl or dithienyl methrnes. Synth. Commun., 1989, 19, 3169-3173.

[27] Muthyala R., Katritzky A.R., Lan X., A Synthetic Study on the Preparation of Triarylmethanes. Dye. Pigment., 1994, 25, 303-324.

[28] Shirakawa S., Kobayashi S., Surfactant-type Brønsted acid catalyzed dehydrative nucleophilic substitutions of alcohols in water. Org. Lett., 2007, 9, 311-314.

[29] Wang A., Xing P., Zheng X., Cao H., Yang G., Zheng X., Deep eutectic solvent catalyzed Friedel–Crafts alkylation of electron-rich arenes with aldehydes. RSC Adv., 2015, 5, 59022-59026.

[30] Tran P.H., Nguyen H.T., Hansen P.E., Le T.N., An efficient and green method for regio-and chemo-selective Friedel–Crafts acylations using a deep eutectic solvent ([CholineCl][ZnCl 2] 3). RSC Adv., 2016, 6, 37031-37038.

[31] Chakraborti A.K., Gulhane R., Perchloric acid adsorbed on silica gel as a new, highly efficient, and versatile catalyst for acetylation of phenols, thiols, alcohols, and amines. Chem. Commun., 2003, 15, 1896-1897.

[32] Nahmany M., Melman A., Chemoselectivity in reactions of esterification. Orgabic Biomol. Chem., 2004, 2, 1563-1572.

[33] Liu Z., Ma Q., Liu Y., Wang Q., 4-(N, N-Dimethylamino) pyridine hydrochloride as a recyclable catalyst for acylation of inert alcohols: substrate scope and reaction mechanism. Org. Lett., 2014, 16, 236-239.

[34] Jäger M., Minnaard A.J., Regioselective modification of unprotected glycosides. Chem. Commun., 2016, 52, 656-664.

[35] Moon H.K., Sung G.H., Kim B.R., Park J.K., Yoon Y.J., Yoon H.J., One for Many: A Universal Reagent for Acylation Processes. Adv. Synth. Catal., 2016, 358, 1725-1730.

[36] Pollastro F., Golin S., Chianese G., Putra M.Y., Schiano Moriello A., De Petrocellis L., García V., et al., Neuroactive and Anti-inflammatory Frankincense Cembranes: A Structure-Activity Study. J. Nat. Prod., 2016, 79, 1762-1768.

[37] Cao J., Qi B., Liu J., Shang Y., Liu H., Wang W., et al., Deep eutectic solvent choline chloride·2$CrCl_3$·6H_2O: an efficient catalyst for esterification of formic and acetic acid at room temperature. RSC Adv., 2016, 6, 21612-21616.

[38] Hu H.-C., Liu Y.-H., Li B.-L., Cui Z.-S., Zhang Z.-H., Deep eutectic solvent based on choline chloride and malonic acid as an efficient and reusable catalytic system for one-pot synthesis of functionalized pyrroles. RSC Adv., 2015, 5, 7720-7728.

[39] Nguyen H.T., Tran P.H., An extremely efficient and green method for the acylation of secondary alcohols, phenols and naphthols with a deep eutectic solvent as the catalyst. RSC Adv., 2016, 6, 98365-98368.

[40] George N., Kurian T., Recent developments in the chemical recycling of postconsumer poly (ethylene terephthalate) waste. Ind. Eng. Chem. Res., 2014, 53, 14185-14198.

[41] Musale R.M., Shukla S.R., Deep eutectic solvent as effective catalyst for aminolysis of polyethylene terephthalate (PET) waste. Int. J. Plast. Technol., 2016, 20, 106-120.

[42] Mondal D., Sharma M., Wang C.-H., Lin Y.-C., Huang H.-C., Saha A., et al., Deep eutectic solvent promoted one step sustainable

conversion of fresh seaweed biomass to functionalized graphene as a potential electrocatalyst. Green Chem., 2016, 18, 2819-2826.

[43] Manabe K., Kobayashi S., Mannich-Type Reactions of Aldehydes, Amines, and Ketones in a Colloidal Dispersion System Created by a Brønsted Acid-Surfactant-Combined Catalyst in Water. Org. Lett., 1999, 1, 1965-1967.

[44] Manabe K., Mori Y., Kobayashi S.Å., Three-component carbon–carbon bond-forming reactions catalyzed by a Brønsted acid–surfactant-combined catalyst in water. Tetrahedron, 2001, 57, 2537-2544.

[45] Zhao G., Jiang T., Gao H., Han B., Huang J., Sun D., Mannich reaction using acidic ionic liquids as catalysts and solvents. Green Chem., 2004, 6, 75-77.

[46] Azizi N., Torkiyan L., Saidi M.R., Highly efficient one-pot three-component Mannich reaction in water catalyzed by heteropoly acids. Org. Lett., 2006, 8, 2079-2082.

[47] Azizi N., Mirmashhori B., Saidi M.R., Lithium perchlorate promoted highly regioselective ring opening of epoxides under solvent-free conditions. Catal. Commun., 2007, 8, 2198-2203.

[48] Chang T., He L., Bian L., Han H., Yuan M., Gao X., Brønsted acid-surfactant-combined catalyst for the Mannich reaction in water. RSC Adv., 2014, 4, 727-731.

[49] Abbott A.P., Capper G., Davies D.L., Rasheed R.K., Tambyrajah V., Novel solvent properties of choline chloride/urea mixtures. Chem. Commun., 2003, 1, 70-71.

[50] Lu J., Li X.-T., Ma E.-Q., Mo L.-P., Zhang Z.-H., Superparamagnetic $CuFeO_2$ Nanoparticles in Deep Eutectic Solvent: an Efficient and Recyclable Catalytic System for the Synthesis of Imidazo [1, 2-a] pyridines. ChemCatChem, 2014, 6, 2854-2859.

[51] Wu P., Petersen M.Å., Petersen R., Flagstad T., Guilleux R., Ohsten M., et al., Tandem Mannich/Diels–Alder reactions for the synthesis of indole compound libraries. RSC Adv., 2016, 6, 46654-46657.

[52] Azizi N., Edrisi M., Deep eutectic solvent immobilized on SBA-15 as a novel separable catalyst for one-pot three-component Mannich reaction. Microporous Mesoporous Mater., 2017, 240, 130-136.

[53] Azizi N., Edrisi M., Abbasi F., Mesoporous silica SBA-15 functionalized with acidic deep eutectic solvent: A highly active heterogeneous N-formylation catalyst under solvent-free conditions. Appl. Organomet. Chem., 2017, 32,

[54] Wang L., Zhou M., Chen Q., He M.-Y., Brønsted acidic deep eutectic solvent catalysed the one-pot synthesis of 2H-indazolo[2,1-b]phthalazine-triones. J. Chem. Res., 2013, 37, 598-600.

[55] De Santi V., Cardellini F., Brinchi L., Germani R., Novel Brønsted acidic deep eutectic solvent as reaction media for esterification of carboxylic acid with alcohols. Tetrahedron Lett., 2012, 53, 5151-5155.

[56] Taysun M.B., Sert E., Atalay F.S., Effect of Hydrogen Bond Donor on the Physical Properties of Benzyltriethylammonium Chloride Based Deep Eutectic Solvents and Their Usage in 2-Ethyl-Hexyl Acetate Synthesis as a Catalyst. J. Chem. Eng. Data, 2017, 62, 1173-1181.

[57] Hayyan A., Ali Hashim M., Mjalli F.S., Hayyan M., AlNashef I.M., A novel phosphonium-based deep eutectic catalyst for biodiesel production from industrial low grade crude palm oil. Chem. Eng. Sci., 2013, 92, 81-88.

[58] Ma F., Hanna M.A., Biodiesel production: A review. Bioresour. Technol., 1999, 70.

[59] Canakci M., The potential of restaurant waste lipids as biodiesel feedstocks. Bioresour. Technol., 2007, 98, 183-190.

[60] M. Canakci, J. Van Gerpen, Biodiesel production from oils and fats with high free fatty acids. Trans. ASAE, 2001, 44, 1429.

[61] Assanosi A.A., Farah M.M., Wood J., Al-Duri B., A facile acidic choline chloride–p-TSA DES-catalysed dehydration of fructose to 5-hydroxymethylfurfural. RSC Adv., 2014, 4, 39359-39364.

[62] Dutta S., Pal S., Promises in direct conversion of cellulose and lignocellulosic biomass to chemicals and fuels: Combined solvent-nanocatalysis approach for biorefinary. Biomass and Bioenergy, 2014, 62, 182-197.

[63] Imteyaz Alam M., De S., Dutta S., Saha B., Solid-acid and ionic-liquid catalyzed one-pot transformation of biorenewable substrates into a platform chemical and a promising biofuel. RSC Adv., 2012, 2, 6890-6896.

[64] Li H., Saravanamurugan S., Yang S., Riisager A., Direct transformation of carbohydrates to the biofuel 5-ethoxymethylfurfural by solid acid catalysts. Green Chem., 2016, 18, 726-734.

[65] Lew C.M., Rajabbeigi N., Tsapatsis M., One-pot synthesis of 5-(Ethoxymethyl)furfural from glucose using Sn-BEA and Amberlyst catalysts. Ind. Eng. Chem. Res., 2012, 51, 5364-5366.

[66] Wang H., Deng T., Wang Y., Qi Y., Hou X., Zhu Y., Efficient catalytic system for the conversion of fructose into 5-ethoxymethylfurfural. Bioresour. Technol., 2013, 136, 394-400.

[67] Gawade A.B., Yadav G.D., Microwave assisted synthesis of 5-ethoxymethylfurfural in one pot from D-fructose by using deep eutectic solvent as catalyst under mild condition. Biomass and Bioenergy, 2018, 117, 38-43.

[68] Tiecco M., Germani R., Cardellini F., Carbon–carbon bond formation in acid deep eutectic solvent: chalcones synthesis via Claisen–Schmidt reaction. RSC Adv., 2016, 6, 43740-43747.

[69] Olah G., Friedel-Crafts Chemistry. Wiley, New York, 1973,

[70] Yang G., Jiang X., Liu Y., Li N., Yin G., Yu C., Palladium-Catalyzed Direct Benzylation of Polyfluoroarenes with Benzyl Carbonates

through Selective C–H Functionalization. Asian J. Org. Chem., 2016, 5, 882-885.

[71] Yuan B., Li Y., Yu F., Li X., Xie C., Yu S., Benzylation with Benzyl Alcohol Catalyzed By [ChCl][TfOH]2, a Brønsted Acidic DES with Reaction Control Self-Separation Performance. Catal. Letters, 2018, 148, 2133-2138.

[72] Azizi N., Dezfuli S., Hahsemi M.M., Eutectic salt catalyzed environmentally benign and highly efficient biginelli reaction. Sci. World J., 2012, 2012,

[73] Atwal K.S., Swanson B.N., Unger S.E., Floyd D.M., Moreland S., Hedberg A., Oreilly B.C., Dihydropyrimidine Calvium-Channel Blockers .3. 3-carbamoyl-4-aryl-1,2,3,4-tetrahydro-6-methyl-5-pyrimidinecarboxylic Acid-Esters as Orally Effective Antihypertensive Agents. J. Med. Chem., 1991.

[74] Rovnyak G.C., Kimball S.D., Beyer B., Cucinotta G., DiMarco J.D., Gougoutas J., Hedberg A., et al., Calcium Entry Blockers and Activators: Conformational and Structural Determinants of Dihydropyrimidine Calcium Channel Modulators. J. Med. Chem., 1995.

[75] Azizi N., Manocheri Z., Eutectic salts promote green synthesis of bis(indolyl) methanes. Res. Chem. Intermed., 2012, 38, 1495-1500.

[76] Azizi N., Dezfooli S., Hashemi M.M., Chemoselective synthesis of xanthenes and tetraketones in a choline chloride-based deep eutectic solvent. Comptes Rendus Chim., 2013, 16, 997-1001.

[77] Jin X., Wang A., Cao H., Zhang S., Wang L., Zheng X., Zheng X., A new efficient method for the preparation of intermediate aromatic ketones by Friedel–Crafts acylation. Res. Chem. Intermed., 2018.

[78] Shaabani A., Hooshmand S.E., Choline chloride/urea as a deep eutectic solvent/organocatalyst promoted three-component synthesis of 3-aminoimidazo-fused heterocycles via Groebke-Blackburn-Bienayme process. Tetrahedron Lett., 2016, 57, 310-313.

[79] Azizi N., Dezfooli S., Catalyst-free synthesis of imidazo [1,2-a] pyridines via Groebke multicomponent reaction. Environ. Chem. Lett., 2016, 14, 201-206.

[80] Azizi N., Dezfooli S., Khajeh M., Hashemi M.M., Efficient deep eutectic solvents catalyzed synthesis of pyran and benzopyran derivatives. J. Mol. Liq., 2013, 186, 76-80.

[81] Azizi N., Dezfooli S., Mahmoudi Hashemi M., Greener synthesis of spirooxindole in deep eutectic solvent. J. Mol. Liq., 2014, 194, 62-67.

[82] Fernández I., Khiar N., Recent developments in the synthesis and utilization of chiral sulfoxides. Chem. Rev., 2003, 103, 3651-3706.

[83] Prasanth K.L., Maheswaran H., Selective oxidation of sulfides to sulfoxides in water using 30% hydrogen peroxide catalyzed with a recoverable VO (acac) 2 exchanged sulfonic acid resin catalyst. J. Mol. Catal. A Chem., 2007, 268, 45-49.

[84] Rajabi F., Naserian S., Primo A., Luque R., Efficient and highly selective aqueous oxidation of sulfides to sulfoxides at room temperature catalysed by supported iron oxide nanoparticles on SBA-15. Adv. Synth. Catal., 2011, 353, 2060-2066.

[85] Sato K., Hyodo M., Aoki M., Zheng X.Q., Noyori R., Oxidation of sulfides to sulfoxides and sulfones with 30% hydrogen peroxide under organic solvent- and halogen-free conditions. Tetrahedron, 2001, 57, 2469-2476.

[86] Pordea A., Mathis D., Ward T.R., Incorporation of biotinylated manganese-salen complexes into streptavidin: New artificial metalloenzymes for enantioselective sulfoxidation. J. Organomet. Chem., 2009, 694, 930-936.

[87] Dai D.-Y., Wang L., Chen Q., He M.-Y., Selective oxidation of sulfides to sulfoxides catalysed by deep eutectic solvent with H_2O_2. J. Chem. Res., 2014, 38, 183-185.

[88] Lee Y.R., Lee Y.J., Ma W., Row K.H., Determination of deep eutectic solvents as eco-friendly catalysts for biodiesel esterification from an alcohol-palmitic acid mixture. Korean J. Chem. Eng., 2016, 33, 2337-2341.

[89] Abdel-Monem Abdel-Hafez A., Synthesis and Anticonvulsant Evaluation of N-Substituted- Isoindolinedione Derivatives. Arch Pharm Res, 2004, 27, 495-501.

[90] Bailleux V., Vallee L., Nuyts J.-P., Vamecq J., Synthesis and Anticonvulsant Activity of Some N-Phenylphthalimides. Chem. Pharm. Bull., 1994, 42, 1817-1821.

[91] Sano H., Noguchi T., Tanatani A., Miyachi H., Hashimoto Y., N-phenylphthalimide-type cyclooxygenase (COX) inhibitors derived from thalidomide: substituent effects on subtype selectivity. Chem. Pharm. Bull., 2004, 52, 1021-1022.

[92] Hargreaves M.K., Pritchard J.G., Dave H.R., Cyclic carboxylic monoimides. Chem. Rev., 1970, 70, 439-469.

[93] Shibata Y., Sasaki K., Hashimoto Y., Iwasaki S., Phenylphthalimides with tumor necrosis factor alpha production-enhancing activity. Chem. Pharm. Bull., 1996, 44, 156-162.

[94] Jayakumar R., Balaji R., Nanjundan S., Studies on copolymers of 2-(N-phthalimido)ethyl methacrylate with methyl methacrylate. Eur. Polym. J., 2000, 36, 1659-1666.

[95] Lima L.M., Castro P., Machado A.L., Fraga C.A.M., Lugnier C., De Moraes V.L.G., et al., Synthesis and anti-inflammatory activity of phthalimide derivatives, designed as new thalidomide analogues. Bioorganic Med. Chem., 2002, 10, 3067-3073.

[96] Lobo H.R., Singh B.S., Shankarling G.S., Deep eutectic solvents and glycerol: A simple, environmentally benign and efficient catalyst/reaction media for synthesis of N-aryl phthalimide derivatives. Green Chem. Lett. Rev., 2012, 5, 487-533.

[97] Alhassan Y., Kumar N., Bugaje I.M., Hydrothermal liquefaction of de-oiled Jatropha curcas cake using Deep Eutectic Solvents (DESs) as catalysts and co-solvents. Bioresour. Technol., 2016, 199, 375-381.

[98] Heugebaert T.S.A., Roman B.I., Stevens C. V., Synthesis of isoindoles and related iso-condensed heteroaromatic pyrroles. Chem. Soc. Rev., 2012, 41, 5626-5640.

[99] Al-Mourabit A., Zancanella M.A., Tilvi S., Romo D., Biosynthesis, asymmetric synthesis, and pharmacology, including cellular targets, of the pyrrole-2-aminoimidazole marine alkaloids. Nat. Prod. Rep., 2011, 28, 1229-1260.

[100] Durgamma S., Muralikrishna A., Padmavathi V., Padmaja A., Synthesis and antioxidant activity of amido-linked benzoxazolyl/ benzothiazolyl/benzimidazolyl-pyrroles and pyrazoles. Med. Chem. Res., 2014, 23, 2916-2929.

[101] Takase M., Yoshida N., Narita T., Fujio T., Nishinaga T., Iyoda M., Sterically congested pyrrole-fused tetrathiafulvalene decamers as highly conductive amorphous molecular materials. RSC Adv., 2012, 2, 3221-3224.

[102] Francisco M., van den Bruinhorst A., Kroon M.C., New natural and renewable low transition temperature mixtures (LTTMs): screening as solvents for lignocellulosic biomass processing. Green Chem., 2012, 14, 2153-2157.

[103] Shaibuna M., Theresa L. V., Sreekumar K., A New Green and Efficient Brønsted: Lewis Acidic DES for Pyrrole Synthesis. Catal. Letters, 2018, 148, 2359-2372.