

# Insights into the Synthesis and Properties of Deep Eutectic Solvents Based on Cholinium Chloride and Carboxylic Acids

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## Supporting Information

**ABSTRACT:** Recently, many studies concerning the environmental impact of ionic liquids (ILs) have shown that despite their unique properties and clear advantages in an ever wide range of applications and processes, ILs are not intrinsically green. In a search for biodegradable and low toxicity, a new type of ILs has been developed, the deep eutectic solvents (DESs). In this context, the aim of this work is to provide accurate densities, viscosities, and refractive indices for DESs prepared using cholinium chloride as the hydrogen bond acceptor and several carboxylic acids (levulinic, glutaric, malonic, oxalic, and glycolic) as the hydrogen bond donors. The impact of two different synthetic methodologies, heating and grinding, in the thermophysical properties of the prepared DESs was assessed. The obtained DESs were analyzed using NMR spectroscopy, FTIR, and electrospray ionization mass spectrometry in order to check their structures and purities. Thermophysical properties, densities, viscosities, and refractive indices were rationalized in terms of the chemical structure of the prepared DESs. The effect of the presence of water in the thermophysical properties of the compounds was also evaluated. Finally, comparisons between the DESs and the corresponding ILs are presented.

**KEYWORDS:** Deep eutectic solvents, Cholinium chloride, Carboxylic acids, Thermophysical properties



## INTRODUCTION

During the past decade, a new generation of designer solvents, deep eutectic solvents, with a great potential for many industrial applications, emerged. The term “deep eutectic solvents” was first coined by Abbott and co-workers in 2003, who reported a very large depression of melting temperature, more than 100 °C, of cholinium chloride and urea mixtures.<sup>1</sup> In fact, eutectic mixtures of nonionic compounds have been known for a long time. They are commonly used in soldering, where eutectic mixtures of tin and lead solders have been widely used for electrical joints due to their low melting points, good wettability, good plasticity, and reasonable electrical conductivity.<sup>2</sup> Other example is the eutectic mixture of sodium chloride and water that is widely used in the removal of ice or in the production of low temperature ice because it has an eutectic point of -21.2 °C.<sup>3</sup> In addition, eutectic mixtures have also been extensively used in pharmaceuticals, with the lidocaine/prilocaine eutectic mixture being the most well-known example. This mixture is an oil with anesthetic properties, allowing higher concentrations of anesthetic to be formulated into the preparation and maintained during application.<sup>4</sup> In this work, we will use the designation of deep eutectic solvents when one of the components is an ionic liquid or a salt.

Deep eutectic solvents can be regarded as a new generation of ionic solvents composed of a mixture of two or more

compounds where one of them is a salt, which presents a lower melting point than that of any of its individual components. In certain cases, the melting point is even eliminated, and a glass transition temperature is obtained.<sup>5–7</sup> As a consequence, several authors adopted the terminology *low melting transition temperature* mixtures. The formation of liquid molten salts at room temperature is due to the establishment of hydrogen bonds between a hydrogen bond donor (HBD) and a hydrogen bond acceptor (HBA), usually a halide anion present in the salt.<sup>8–10</sup> The freezing point depression of the mixture results from the formation of halide ion–hydrogen bond donor supramolecular complexes that alter the free energy of the solid phase compared to that of the liquid.<sup>11</sup> DESs are currently attracting widespread scientific and technological interest as low cost alternatives to conventional and unconventional solvents, such as ionic liquids (ILs).

The first reported DES<sup>1</sup> is based on cholinium chloride and urea and is by far the most widely investigated, followed by cholinium chloride and glycerol and cholinium chloride and ethylene glycol. Since then, other combinations of HBD and HBA have been explored, in particular other salts, such as imidazoliums,<sup>12</sup> ammoniums,<sup>13,14</sup> and phosphoniums.<sup>15,16</sup>

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However, the most popular DESs synthesized so far are those based on cholinium chloride (used as HBA) because of its low cost, low toxicity, biodegradability, and biocompatibility. It is considered an essential nutrient, which can be extracted from biomass and is often regarded as a part of the B complex vitamins.<sup>17</sup> Cholinium chloride has been combined with several classes of HBD such as renewable polyols, carbohydrates, amides, amines, alcohols, and carboxylic acids.<sup>18</sup> Cholinium and other ammonium cations, for example, betaine, combined with convenient anions, such as saccharinate, lactate, and hexanoate, have been largely explored in the search for natural, biocompatible, biorenewable, and “drinkable” solvents.<sup>19</sup>

The preparation of DESs can be regarded as a strategy to overcome some of the disadvantages of ILs, such as high melting temperature, high price, and toxicity, because they share many of the ILs appealing solvent properties, like low volatility, high thermal stability and conductivity, wide liquid range, and high solvation capacity.<sup>19–21</sup> Besides these properties, DESs possess other interesting advantages over ILs. They are easier to synthesize because the components are easily mixed without any further purification. They have low production cost due to the low price of starting materials. They are chemically inert in water, and most of the synthesized DESs are biodegradable, biocompatible, and nontoxic.<sup>6,21</sup>

Recently, various applications of DESs have been reported. Due to their high solvation capacity and biocompatibility, Morrison et al.<sup>22</sup> concluded that DESs can be promising vehicles for increasing exposure of poorly soluble compounds in preclinical studies. Abbott et al.<sup>23</sup> and Hayyan et al.<sup>24</sup> have shown that low cost quaternary ammonium salt glycerol-based DESs are efficient extraction media for glycerol from biodiesel based on rapeseed and soy beans and palm oil. In addition, DESs have been used in many industrial applications such as electroplating, electrowinning, and electropolishing.<sup>25</sup> Recent research reported the applicability of DESs as solvents in the bulk processing of metals,<sup>26,27</sup> biodiesel purification,<sup>23</sup> polymer synthesis,<sup>28,29</sup> drug solubilization,<sup>22</sup> biological transformations,<sup>30</sup> CO<sub>2</sub> absorption,<sup>31–33</sup> and even in the separation of azeotropic mixtures.<sup>34</sup>

The fact that DESs are cheap and very easy to synthesize led to their wide application in a large number of different fields in a trial and error type of approach. However, taking into account the large number of DESs with very different properties that can be easily synthesized, studies concerning the thermophysical characterization and phase behavior of these compounds, which are very important for their application, are still scarce.

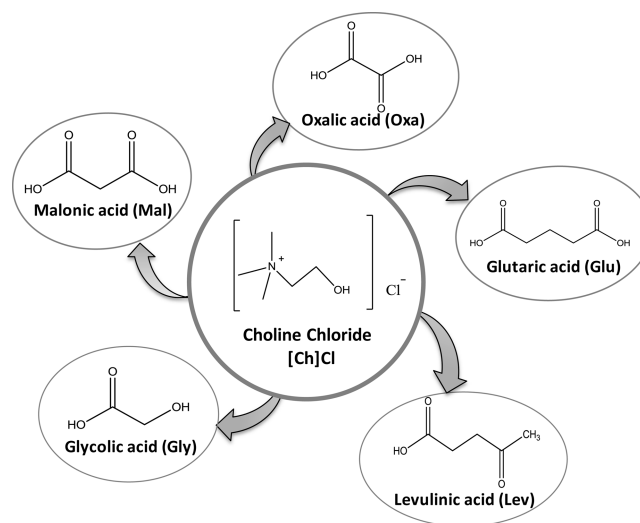
Abbott et al.<sup>1</sup> measured thermophysical properties of DESs based on [Ch]Cl, namely, viscosity and conductivity of [Ch]Cl:urea; viscosity, refractive index, surface tension, and conductivity of [Ch]Cl:mono (phenylpropionic, phenylacetic); di (oxalic, succinic, adipic and malonic) and tri (citric) acids;<sup>35</sup> and density, viscosity, conductivity, and surface tensions of [Ch]Cl:ethylene glycol, glycerol, and 1,4 butanediol.<sup>36</sup> Later these authors explored in more detail [Ch]Cl:glycerol DESs,<sup>37,38</sup> measuring density, viscosity, conductivity, diffusion coefficients, and polarity parameters, showing that there is a marked reduction in viscosity for this specific DES. Leron et al.<sup>32</sup> also measured densities and refractive indexes of the DES [Ch]Cl:ethylene glycol and [Ch]Cl:glycerol and their aqueous solutions in a temperature range between 298.15 and 333.15 K. Shahbaz et al.<sup>33</sup> measured densities of nine different salts combining cholinium chloride, N,N-diethylethanol ammonium chloride, and methyltriphenyl phosphonium as HBA with

several HBD such as glycerol, ethylene glycol, and 2,2,2-trifluoroacetamide. Francisco et al.<sup>39</sup> detailed densities and viscosities of the [Ch]Cl:lactic acid DES. Maugeri et al.<sup>40</sup> prepared and measured viscosities of DESs based on [Ch]Cl and several acids and sugars, such as glucose, xylitol, and sorbitol. Also to be mentioned is the work of Karem et al.,<sup>16</sup> who reported density, viscosity, pH, conductivity, and dissolved oxygen content of phosphonium-based DESs based on methyltriphenyl phosphonium bromide and benzyltriphenyl phosphonium chloride as salts and glycerin, ethylene glycol, and 2,2,2-trifluoroacetamide as HBD, at several mole ratios of salt/HBD.

In this work, we aimed at studying [Ch]Cl:organic acids DESs. For that purpose, mixtures of [Ch]Cl and several organic acids such as oxalic, malonic, adipic, levulinic, glutaric, glycolic, succinic, malic, tartaric, fumaric, azelaic, and citric acids were screened for the formation of DESs. Two approaches for the synthesis of DESs were tested: the heating method and the grinding method. The thermophysical properties, viscosity, density, and refractive index, as well as the thermal stability of the dried and water-saturated DESs, were studied. Additionally, a comparison of the thermophysical properties between the DESs and their IL counterparts (cholinium-based ionic liquids combined with acid anions) was also included.

## EXPERIMENTAL SECTION

**Materials.** Cholinium chloride ([Ch]Cl) ( $\geq 98\%$  mass fraction purity) was purchased from Sigma-Aldrich and was dried under vacuum prior to use. Oxalic, malonic, adipic, levulinic, glutaric, glycolic, succinic, malic, tartaric, fumaric, azelaic, and citric acids (all  $\geq 99\%$  mass fraction purity) were purchased from Sigma-Aldrich and used as supplied. In Figure 1, the chemical structures and respective acronyms of the five DESs used in this work are presented.



**Figure 1.** Chemical structures and respective acronyms of the DESs studied in this work.

## APPARATUSES AND PROCEDURES

**Preparation Methodology.** Deep eutectic solvents were prepared by two different methods: the heating method and the grinding method. The heating method (the most commonly used in literature) is based on mixing the two components, which are then heated at 100 °C under constant stirring until a homogeneous liquid is formed. The grinding method, which has been largely explored in the preparation of DESs for pharmaceutical purposes, consists in mixing the two

components and then grinding them in a mortar with a pestle at room temperature until a homogeneous liquid is formed.

The eutectic mixtures were prepared using an analytical high-precision balance with an uncertainty of  $\pm 10^{-5}$  g by weighing known masses of each component into bottles with caps and in a glovebox within a nitrogen atmosphere. Cholinium chloride was first dried in a high vacuum pump at 40 °C for at least 2 days, while the hydrogen bond donors were used without any further purification.

For the preparation of the dried samples, the DESs were maintained for at least 4 days in a Schlenk under high vacuum (about  $10^{-1}$  Pa) at room temperature, while for the water-saturated samples, the DESs were maintained for one month in contact with air. Then, the amount of water present in each sample was measured in order to infer the relative hygroscopicity and thus hydrophobicity. The water content was determined by Karl Fisher titration (model Metrohm 831 Karl Fisher coulometer), and the percentages of water present in the DESs (dried and water-saturated) are listed in Table 1. The pH

**Table 1. Molar Masses (MW) and Water Content in Percentage (wt %) of Dried and Water-Saturated DESs and Ionic Liquids Samples**

DESs	MW (g mol <sup>-1</sup> )	water content (wt %)	
		dried	saturated
[Ch]Cl:Gly	215.67	0.52	14.50
[Ch]Cl:Oxa	229.65	0.32	19.40
[Ch]Cl:Mal	243.68	0.47	16.16
[Ch]Cl:Lev	371.84	0.23	9.88
[Ch]Cl:Glu <sup>a</sup>	271.74	0.57	17.38
[Ch]Cl:Glu <sup>b</sup>	271.74	0.65	—
[Ch][Gly]	—	0.11 <sup>c</sup>	19.38
[Ch][Mal]	—	0.10 <sup>c</sup>	19.05
[Ch][Lev]	—	0.23 <sup>c</sup>	18.85

<sup>a</sup>DESs obtained by grinding. <sup>b</sup>DESs obtained by heating. <sup>c</sup>Data taken from ref 45.

measurement was carried out with a Mettler-Toledo pH/conductivity meter, and the pH values were assessed directly by inserting the electrode into the DES. pH buffer solutions (at pH 4 and 7) were used to check and calibrate the measurements of the electrode.

The five DESs studied in this work were completely characterized by <sup>1</sup>H and <sup>13</sup>C NMR in order to check their expected structures and final purities. The [Ch]Cl:Gly, [Ch]Cl:Glu, and [Ch]Cl:Lev DESs prepared by the heating method were also characterized by electrospray ionization mass spectrometry (ESI-MS) and tandem mass spectrometry (ESI-MS-MS) using a Micromass Q-ToF 2 (Micromass, Manchester, U.K.) mass spectrometer equipped with a Z-spray source. In addition, FTIR was also used to confirm the formation of hydrogen bonds, as shown in Figure S11 of the Supporting Information) between the chloride anion and the acidic proton in glutaric acid for the [Ch]Cl:Gly DES. All the other characterization details of DESs synthesized are reported in Figures S1–S10 of the Supporting Information.

**NMR Measurements.** All the experiments were carried out on a Bruker AVANCE 400 spectrometer operated at room temperature with 16 and 500 scans for the <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra, respectively. The DES samples were prepared on 5 mm NMR tubes using approximately 30 mg of DES and then adding 0.5 mL of deuterium oxide (D<sub>2</sub>O). The homogeneity of the sample was assured by vortex mixing. For the samples where the DESs were mixed with other compounds, a stoppered flask was used to prepare the mixture first, and only after homogeneity was obtained, the NMR tube was prepared.

**Thermophysical Characterization.** A DSC (differential scanning calorimeter TA Instrument Model DSC Q200) and a TGA (TA Instruments Model TGA Q50) were used to measure the thermal properties of the prepared DESs. In the DSC, the samples were continuously purged with 50 mL min<sup>-1</sup> of nitrogen. About 10 mg of

the compound was crimped in an aluminum standard sample pan and analyzed under a nitrogen atmosphere by heating (10 K min<sup>-1</sup>)–cooling (5 K min<sup>-1</sup>) cycles between 193.15 and 373.15 K. Indium ( $T_{\text{melting}} = 429.76$  K) was used as the standard compound for the calibration of the DSC. The TGA was used for measuring the decomposition temperature of the DESs, using also nitrogen at a flow rate of 60 mL min<sup>-1</sup>. Samples were placed inside aluminum pans and heated to 600 °C at a rate of 10 °C min<sup>-1</sup> until complete thermal degradation was achieved.

Measurements of densities and viscosities for the DESs were performed in the temperature range between 293.15 and 353.15 K, using an automated SVM 3000 Anton Paar rotational Stabinger viscometer densimeter. The temperature uncertainty is  $\pm 0.02$  K. The precision of the viscosity measurements is  $\pm 0.5\%$ , and the absolute uncertainty of the density is  $\pm 0.0005$  g cm<sup>-3</sup> (taking into account the purity and handling of the samples). Triplicates of the physical properties were measured for each of the DESs to ensure accuracy, and the reported result is the average value with a maximum relative standard deviation (RSD) of 0.47%.

The refractive indices of the DESs were determined using the automatic refractometer ABBEMAT 500 Anton Paar with a resolution of  $\pm 10^{-6}$  and an uncertainty in the experimental measurements of  $\pm 4 \times 10^{-5}$ . The apparatus was calibrated by measuring the refractive index of Millipore water before each series of measurements.

## RESULTS AND DISCUSSION

**Evaluation of DESs Synthetic Procedure.** Since the first reported DESs, the most common method to synthesize these compounds has been by heating and stirring until a liquid mixture is obtained. Due to this very simplistic preparation method, the assessment of purity is often dropped. One of the purposes of this work is to analyze and discuss the two distinct synthetic methodologies of preparation of DES.

Table 2 depicts the results of the mixtures of [Ch]Cl with all acids used. It can be seen that not all the acids tested yielded a

**Table 2. Summary of Different DESs Studied in This Work Using Cholinium Chloride as the Hydrogen Bond Acceptor and Carboxylic Acids as Hydrogen Bond Acceptors**

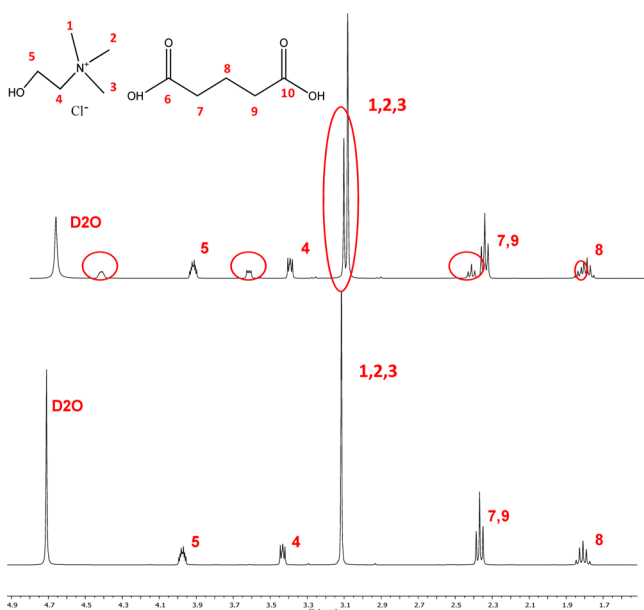
hydrogen bond donor	mole ratio	aspect
glutaric acid	1:1	transparent liquid
glycolic acid	1:1	transparent liquid
malonic acid	1:1	transparent viscous liquid
oxalic acid	1:1	transparent viscous liquid
levulinic acid	1:2	yellow liquid
citric acid	1:1	highly viscous liquid
succinic acid	1.5:1, 1:1, 1:1.5	white liquid with particles in suspension
malic acid	1:1	transparent viscous liquid
tartaric acid	1:1	highly viscous liquid
adipic acid	1.5:1, 1:1, 1:1.5	white solid (no interaction between the solids)
fumaric acid	1.5:1, 1:1, 1:1.5	white solid (no interaction between the solids)
azelaic acid	1.5:1, 1:1, 1:1.5	white solid (no interaction between the solids)

DES: succinic, adipic, fumaric and azelaic acids did not form a DES even when different molar ratios of the compounds were tested. For the remaining acids a DES was obtained at a equimolar concentration, with the exception of levulinic acid, which required a molar ratio of 1 mol of HBA for 2 of HBD. Nevertheless, in the case of citric, malic and tartaric acids, the DESs obtained were highly viscous, which did not allow an easy



handle of the compound, and therefore these three DES were discarded.

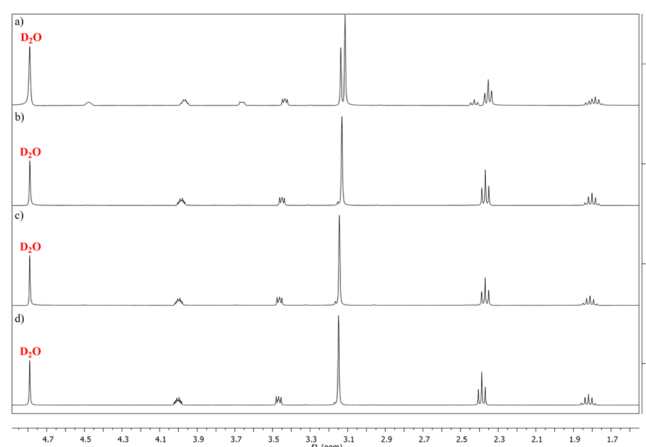
For the five DESs studied in this work, the  $^1\text{H}$  NMR spectra indicated that when using the grinding method the DESs obtained were pure, while when the heating method was used, impurities were present in variable amounts ranging from 5% to 30%. Figure 2 shows the comparison between the  $^1\text{H}$  NMR



**Figure 2.** Comparison between the  $^1\text{H}$  NMR spectra obtained for DES [Ch]Cl:Glu synthesized by two different methods: heating the compounds at 100 °C (upper spectrum) and grinding (lower spectrum).

spectra of DES [Ch]Cl:Glu obtained with the two methods. This DES was used as an example for the comparison between the two synthetic methodologies because it presented the highest amount of impurities.

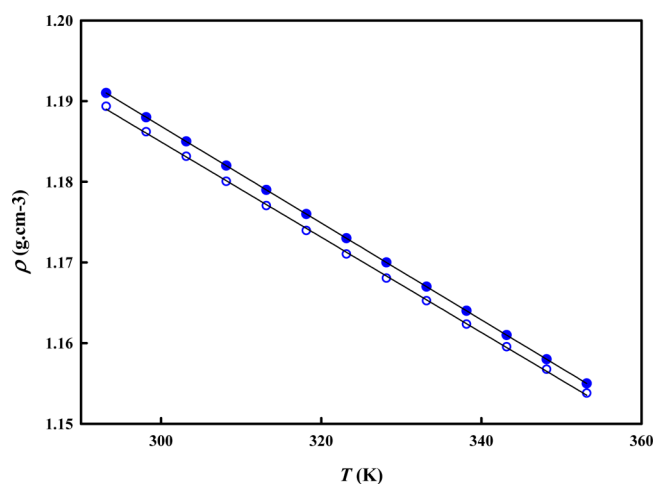
In order to further investigate this phenomenon, a literature search was performed, and it was verified that several authors presented similar  $^1\text{H}$  NMR spectra to those observed in this work when using the heating method. Francisco et al.<sup>17</sup> presented similar  $^1\text{H}$  NMR spectra for DESs, although the authors did not examine the possible cause of these peaks. In addition, the reaction of cholinium chloride with the studied acid and thus the formation of HCl, which might have been possible due to the high temperature, is ruled out by the authors. A quick way to evaluate the formation of HCl during the heating process is by measuring the pH of the resulting DES. The results obtained in this work showed that pH ranged from 0 to 1 for all the DESs synthesized using the heating method, while for the DESs obtained from grinding the values ranged from 2 to 4. In order to identify the impurities that were formed, [Ch]Cl:Glu DES was mixed with small amounts (10 wt %) of cholinium chloride, glutaric acid, IL choline glutarate, and HCl, and the  $^1\text{H}$  NMR spectrum of each mixture was acquired. Figure 3 presents the  $^1\text{H}$  NMR spectra for these mixtures with the exception of that with an excess of cholinium chloride because this IL was not soluble in the DESs. The spectra show that both intensities of peaks of the impurities increase and also the chemical shifts change only when HCl is added, meaning that the formation of these impurities is promoted by acidic media.



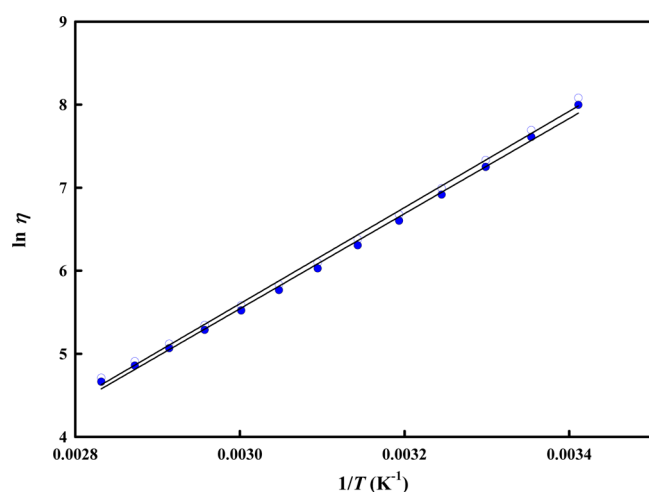
**Figure 3.**  $^1\text{H}$  NMR spectra of mixtures of DES [Ch]Cl:Glu and (a) HCl, (b) glutaric acid, and (c) choline glutarate. (d) Spectrum of pure [Ch]Cl:Glu obtained by the grinding method.

The shape and the chemical shifts of the peaks of the impurities suggest that an ester is being formed between the cholinium cation and the glutaric acid. To confirm this possibility, a 2D HMBC spectrum was also acquired from the mixture of DES + HCl, which is presented in Figure S12 of the Supporting Information. It is possible to observe that there is an interaction between the protons of the choline part of the ester to the carboxylic carbon of the acid part of the ester, thus confirming ester formation. Moreover, in the ESI mass spectra (positive mode) of the [Ch]Cl:Gly, [Ch]Cl:Glu, and [Ch]Cl:Lev DESs prepared by the heating method, the base peaks correspond in terms of  $m/z$  values of 162, 218, and 202, respectively, to an ion with the chemical composition  $[(\text{Ch} + \text{Acid}) - \text{H}_2\text{O}]^+$ . Figure S13 of the Supporting Information presents the mass spectrum of [Ch]Cl:Glu as an illustrative example. Structural analysis of this ion was performed by ESI-MS-MS, selecting the precursor ion  $m/z$  218 with the quadrupole analyzer, performing collisions with argon in the hexapole and analyzing the fragment ions thus produced with the TOF analyzer (Figure S14, Supporting Information for [Ch]Cl:Glu). The fragment ion observed corresponds to the loss of the neutral molecule  $\text{N}(\text{CH}_3)_3$  from ion  $m/z$  218. This observation, together with the collision energy necessary for the fragmentation, points to the formation of an ester between the cholinium cation and the glutaric acid (Scheme S1, Supporting Information). Similar results were obtained for the other DESs analyzed by mass spectrometry. Noteworthy, are the DESs mass spectra in the negative mode, where a peak corresponding to  $[\text{Acid}.\text{Cl}]^-$  is observed, with relative abundances ranging from 17% to 89%, demonstrating the interaction between the carboxylic acid and the chloride anion (Table S15, Supporting Information). Indeed, Gull et al.<sup>41</sup> recently published a paper on the synthesis of a prebiotic phosphate ester using [Ch]Cl 1:2 urea as the solvent and demonstrated that by using heat the DES system was capable of promoting a dehydration reaction, leading to the formation of an ester between the phosphorus source and the cholinium.

In order to study the effect of the formation of the ester in the DESs properties, the density and viscosity of [Ch]Cl:Glu synthesized by both methods were measured, and the results are depicted in Figures 4 and 5, respectively. The data obtained shows a marked difference in the viscosity values of both samples, with average absolute deviation of 6.52%, whereas in



**Figure 4.** Crossing data relative to experimental densities ( $\rho$ ) as a function of temperature for the DESs composed of glutaric acid, [Ch]Cl:Glu, obtained using the two different methods: (○) heating and (●) grinding.



**Figure 5.** Crossing data relative to experimental viscosities ( $\eta$ ) as a function of temperature for the DESs composed of glutaric acid, [Ch]Cl:Glu, obtained using the two different methods: (○) heating and (●) grinding.

the case of density, the difference is smaller, presenting an average absolute deviation of 0.15%.

From the results shown here, it can be concluded that there is a difference between the two synthetic methodologies. The grinding method proved to be the more suitable method for the preparation of these DESs because the formation of ester is not favored. Therefore, this method was adopted in this work for the synthesis of the DESs used for the determination of thermophysical properties.

**Thermophysical Characterization of DESs.** It is well known from the IL literature that the presence of water in ILs can be regarded as an impurity, essentially because it can interfere with the thermophysical properties of ILs. Because DESs are regarded as ILs, it is also of great importance to study the water effect on their physical properties, such as density, viscosity, and refractive index. For that purpose, water-saturated DES samples were also studied in this work.

From Table 1, it is possible to see that the amount of water for the dried samples is always below 1 wt %, whereas for the

water-saturated samples, it ranges from 14–20 wt %. The only exception in the water-saturated samples is [Ch]Cl:Lev, where the water content was found to be lower than the other DESs (9.88 wt %). Unlike the other acids, levulinic acid is the only one that has a terminal methyl group, while the others present terminal hydroxyl groups. The presence of this methyl group has a dramatic effect on the hydrophilicity of the DESs, reducing the quantity of water it can absorb, leading to a more hydrophobic DESs.

**Thermal Properties.** Melting and decomposition temperatures are one of the most remarkable properties in deep eutectic solvents, especially for their application as alternative solvents. These properties determine the range of temperature at which a deep eutectic solvent can maintain its liquid form and consequently its range of application. The thermal properties (decomposition temperatures and glass transition temperatures) of DESs studied in this work are summarized in Table 3.

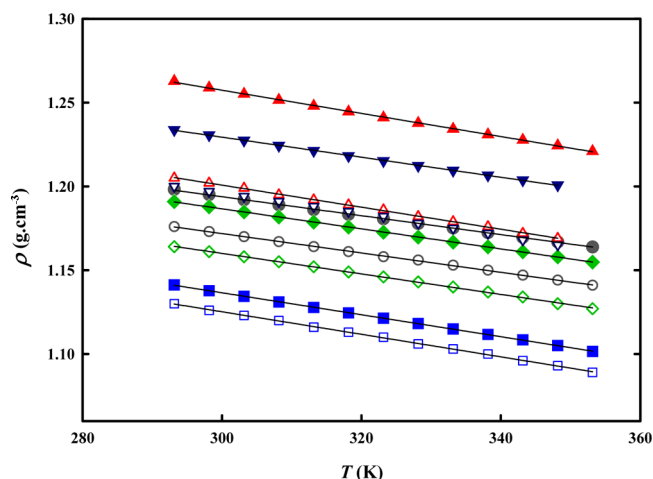
**Table 3.** Thermal Properties of Studied Deep Eutectic Solvents: Decomposition Temperature ( $T_{\text{dec}}$ ) and Glass Transition Temperature ( $T_{\text{g}}$ )

DESs	$T_{\text{dec}}$ (K)	$T_{\text{g}}$ (K)
[Ch]Cl:Gly	500.30	257.08
[Ch]Cl:Oxa	433.01	251.42
[Ch]Cl:Mal	397.83	259.08
[Ch]Cl:Lev	449.72	261.28
[Ch]Cl:Glu	512.20	256.37

It is clearly shown in all cases that the melting temperatures of the mixtures are lower than those of the pure starting components, so low that it cannot be detected by DSC. Instead, all DESs presented a glass transition temperature around 260 K, which confirms that these DESs are supramolecular complexes with the liquid state over a wide temperature range. Regarding the decomposition temperature, the studied DESs presented decomposition temperatures between 400 and 500 K, very close to each other, where the lowest value was found for [Ch]Cl:Mal and the highest for [Ch]Cl:Glu.

**Density.** The experimental density results for the dried and water-saturated samples of DESs as a function of temperature are plotted in Figure 6, and the data is presented in Tables S2–S6 in the Supporting Information. The obtained data shows that the DESs composed of glutaric acid and levulinic acid have lower density values than the remaining DESs, most likely due to the large length of their alkyl chains (both acids have the same chain length,  $C_5$ ) when compared with that of other acids ( $C_2$  and  $C_3$ ). However, the density of [Ch]Cl:Lev is much lower than that of [Ch]Cl:Glu, probably due to the presence of more moles of acid in [Ch]Cl:Lev because its molar ratio is 1:2. These results show that the increase in the hydrocarbon chain from oxalic/glycolic acids ( $C_2$ ) to malonic acid ( $C_3$ ) ending in glutaric/levulinic acids ( $C_5$ ) leads to a decrease in the density of the DES, which corresponds to an increase in the molar volume of the acids used, as their alkyl chains increase in length.<sup>42</sup>

Another parameter that can be analyzed is the effect of the addition of one carboxylic group. When comparing [Ch]Cl:Gly to [Ch]Cl:Oxa, it can be concluded that the introduction of the carboxylic group leads to an increase in density. The density trend can be then organized in the following order: [Ch]Cl:Lev < [Ch]Cl:Glu < [Ch]Cl:Gly < [Ch]Cl:Mal < [Ch]Cl:Oxa, where the latter is the DES with the highest density.



**Figure 6.** Experimental densities ( $\rho$ ) of the dried and water-saturated DESs as a function of temperature: [Ch]Cl:Oxa ( $\blacktriangle$ ), [Ch]Cl:Mal ( $\blacktriangledown$ ), [Ch]Cl:Gly ( $\bullet$ ), [Ch]Cl:Glu ( $\blacklozenge$ ), and [Ch]Cl:Lev ( $\blacksquare$ ). The filled symbols correspond to the dried DESs, and the empty symbols correspond to the water-saturated DESs. The lines represent the fitted data calculated using eq 1.

Regarding the water-saturated DESs and when comparing the values obtained for the densities of the dried and the water-saturated DESs, it can be observed that the latter are lower, as expected. However, despite the very different amount of water present in [Ch]Cl:Lev, the same density trend was observed from the dried and the water-saturated samples. The difference in density between a dried and water-saturated DES at the same temperature is around 5%, indicating that this property is not very sensitive to the amount of water present in the sample. In the cases of [Ch]Cl:Oxa and [Ch]Cl:Mal, it was not possible to measure the density at 353.15 K due to instability of the measurement.

As observed, the density decreases linearly with temperature for all DESs (dried and water saturated) in the whole temperature range studied, and a linear equation was used to express the correlation with the temperature

$$\rho = a + bT \quad (1)$$

where  $\rho$  corresponds to density in  $\text{g cm}^{-3}$ ,  $T$  is the temperature in K, and  $a$  and  $b$  are the fitting parameters. The  $a$  and  $b$  values derived from eq 1 as well as the standard deviation for all the studied DESs are presented in Table S7 of the Supporting Information.

Despite the controversy around the application of a linear or a second-order polynomial equation to describe the experimental density data, we found the use of a linear function of temperature to be adequate within the studied temperature range. This choice implies that the isobaric thermal expansion coefficient,  $\alpha_p$ , is constant at a given pressure. The isobaric thermal expansion coefficient,  $\alpha_p$ , which accounts for the volumetric changes with temperature, was calculated using eq 2

$$\alpha_p = -\frac{1}{\rho} \left( \frac{\delta \rho}{\delta T} \right)_p = - \left( \frac{\delta \ln \rho}{\delta T} \right)_p \quad (2)$$

where  $\rho$  is the density in  $\text{g cm}^{-3}$ ,  $T$  is the temperature in K, and  $p$  is the pressure in MPa. In Table S8 of the Supporting Information, the  $\alpha_p$  values are presented for the dried and saturated DESs at 298.15 K.

The values obtained for DESs vary between  $4.73$  to  $5.76 \times 10^{-4} \text{ K}^{-1}$  in the case of the dried samples and are up to 4–8% higher for the water-saturated samples. The highest thermal expansion coefficients were observed for [Ch]Cl:Lev, whereas [Ch]Cl:Gly displayed the lowest ones. This can be explained by the size of the chain in the HBD, where the glycolic acid has the smallest alkyl chain and levulinic acid has the longest alkyl chain, suggesting a reduction of electrostatic interactions and thus facilitating expansion.

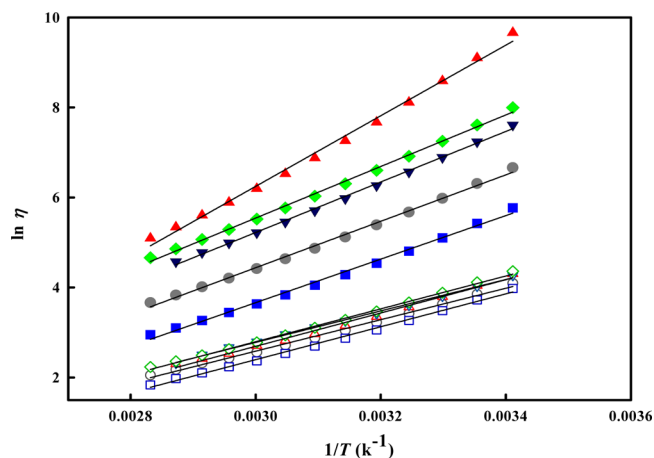
The molar volumes ( $V_m$ ) of dried and water-saturated DESs studied in this work were calculated from the density results and are presented in Table S10–S14 of the Supporting Information. Molar volumes were determined for a range of temperatures from 293.15 and 343.15 K and were obtained from the following equation

$$V_m = \frac{M}{\rho} \quad (3)$$

where  $M$  corresponds to the molar mass in  $\text{g mol}^{-1}$ , and  $\rho$  is the density in  $\text{g cm}^{-3}$ . The molar volumes increase in the following order: [Ch]Cl:Gly < [Ch]Cl:Oxa < [Ch]Cl:Mal < [Ch]Cl:Glu < [Ch]Cl:Lev, which is in agreement with the molar mass of each compound (Table 1), because the DES with the highest molar mass (DES composed by the acid with the highest molar mass) exhibits the highest molar volume.

**Viscosity.** Viscosity is an important property of any fluid because it influences the mass transport phenomena and the conductivity for ionic fluids, thereby affecting their suitability for particular applications. DESs are usually quite viscous fluids when compared to organic solvents, and for that reason, they are usually used in solutions with water or other solvents.

The experimental viscosity data for the dried and water-saturated samples of the five studied DESs, as a function of temperature, are depicted in Figure 7 and are reported in Tables S2–S6 of the Supporting Information. Again, for [Ch]Cl:Mal and [Ch]Cl:Oxa, it was not possible to obtain viscosity results at the highest temperature (353.15 K) due to instability of the viscosity measurement.



**Figure 7.** Experimental viscosities ( $\eta$ ) of the dried and water-saturated DESs as a function of temperature: [Ch]Cl:Oxa ( $\blacktriangle$ ), [Ch]Cl:Mal ( $\blacktriangledown$ ), [Ch]Cl:Gly ( $\bullet$ ), [Ch]Cl:Glu ( $\blacklozenge$ ), and [Ch]Cl:Lev ( $\blacksquare$ ). The filled symbols correspond to the dried DESs, and the empty symbols correspond to the water-saturated DESs. The lines represent the fitted data calculated using eq 4.

For the dried DESs, the viscosity increases in the following order: [Ch]Cl:Lev < [Ch]Cl:Gly < [Ch]Cl:Mal < [Ch]Cl:Glu << [Ch]Cl:Oxa. In fact, the viscosities of the measured DESs can be rationalized according to the chemical structure of the HBD and thus divided in two groups: DESs containing diacids as HBDs and DESs containing monoacids as HBDs. It is shown that the DESs containing a diacid are much more viscous than those containing a monoacid. Furthermore, the presence of one extra carboxylic group ([Ch]Cl:Oxa and [Ch]Cl:Gly) or extra hydroxyl group ([Ch]Cl:Glu and [Ch]Cl:Lev) leads to an increase in viscosity, most probably due to the establishment of extra hydrogen bonds. Regarding the size of the alkyl chain, usually an increase in the size of the hydrocarbon chain leads to an increase in the viscosity, yet it seems that the presence of carbonyl or hydroxyl groups overcomes this effect. Indeed, [Ch]Cl:Oxa is the DES with the smaller alkyl chain (only two carbons) and simultaneously is the most viscous. Another possible explanation was proposed by Hunt et al.<sup>31</sup>, who attributed this type of behavior to a loss in entropy due to a more restricted conformational freedom of this acid when compared to that of the other acids.

As expected, the presence of water strongly decreases the viscosity of these fluids when compared to the viscosity of the dried DESs. This phenomenon is particularly dramatic in the case of the most viscous DES, [Ch]Cl:Oxa, for which the viscosity of the water-saturated sample at 293 K is 200 times lower than the dried sample. For the other DESs studied, the presence of water reduces the viscosity by 10–30 times, depending on the HBD.

For all the studied DESs, the viscosity decreases with temperature. This behavior was correlated using a logarithmic equation based on the Arrhenius model described by the following equation

$$\eta = \eta_{\infty} \exp\left(-\frac{E_a}{RT}\right) \quad (4)$$

where  $\eta$  is the viscosity in mPa s,  $\eta_{\infty}$  is a pre-exponential constant in mPa s,  $E_a$  is the activation energy in KJ mol<sup>-1</sup>,  $R$  is the ideal gas constant, and  $T$  is the temperature in K. The values corresponding to  $\eta_{\infty}$ ,  $E_a$ , and standard deviation for each DES obtained from eq 4 are given in Table S9 of the Supporting Information.

The use of eq 4 to describe the temperature behavior of viscosity allows the discussion of the energy barrier of a fluid to shear stress,  $E_a$ , values. The higher the  $E_a$  the more difficult it is for the ions to move past each other. This can be a direct consequence of the size or entanglement of the ions and/or the presence of stronger interactions within the fluid. Regarding the size of the anions and using the calculated molar volume in Table S13 of the Supporting Information, it can be observed that this parameter has a negligible influence in viscosity because [Ch]Cl:Lev has a large  $V_m$  and is the less viscous DES. Consequently, the interactions between the different species in the eutectic mixtures seem to play a very important role in the viscosity of these compounds. However, for the water-saturated samples, the  $E_a$  values obtained are similar to each other, indicating that the presence of water, even in different amounts, promotes an easier and similar flux of the different ions. It is thus understandable that the use of DESs as solvents is usually approached through the use of aqueous solutions.

In the case of the DESs used in this work, the decrease in viscosity with temperature observed for all the studied samples

can be linked to the substantial decrease in the magnitude of H-bonding interactions with temperature. It is interesting to observe that [Ch]Cl:Oxa viscosity shows a more pronounced temperature dependence than the other DESs, which can be evaluated through its larger  $E_a$  value. The viscosity of DESs containing diacids seems to be different when there is a spacer between the two terminal carboxylic acids, as in [Ch]Cl:Mal and [Ch]Cl:Glu, whereas in [Ch]Cl:Oxa the two carboxylic groups are connected to each other, resulting in closer viscosity values between [Ch]Cl:Mal ( $C_3$ ) and [Ch]Cl:Glu ( $C_5$ ) than for [Ch]Cl:Oxa ( $C_2$ ) and [Ch]Cl:Mal ( $C_3$ ). The DESs where the ions have higher mobility are [Ch]Cl:Lev and [Ch]Cl:Gly, which are the most hydrophobic in accordance to the water uptake content.

**Refractive Index.** The refractive index can be used as a measure of the electronic polarizability of a molecule and can provide useful information when studying the forces between molecules or their behavior in solution. The Lorentz–Lorentz equation relates the refractive index ( $n_D$ ) with the electronic polarizability ( $\alpha_e$ ) and can be used to calculate the molar refraction or molar polarizability ( $R_m$ ) using eq 5<sup>43</sup>

$$R_m = \frac{N_A \alpha_e}{3\epsilon_0} = \left(\frac{n_D^2 - 1}{n_D^2 + 2}\right) V_m \quad (5)$$

where  $N_A$  is Avogadro's constant,  $\alpha_e$  is the electronic polarizability,  $\epsilon$  is the dielectric constant,  $n_D$  is the refractive index, and  $V_m$  is the molar volume. Molar refractions can be considered as a measure of the hard-core molecular volumes because the electronic polarizability can be related to a spherical molecular radius,  $a$ , by

$$\alpha_e = 4\pi\epsilon_0 a^3 \quad (6)$$

and the Lorentz–Lorentz equation can be expressed in the following form<sup>44</sup>

$$n_D^2 - 1 = 3 \left(\frac{V_m}{R_m - 1}\right)^{-1} = 3 \left(\frac{R_m}{f_m}\right) \quad (7)$$

where  $f_m$  is the free volume defined as

$$f_m = V_m - R_m \quad (8)$$

which means that the refractive index is directly proportional to the occupied part of the molar volume,  $R_m$ , being then considered as the hard-core molecular volume.

The refractive indices as a function of temperature for the studied DESs are shown in Table S10–S14 of the Supporting Information, along with the molar volume, molar refraction, and free molar volume values. The refractive indices were measured within the range of temperatures from 293.15 to 353.15 K. In general and for all the DESs, the refractive index decreased with an increase in temperature.

For the studied DESs, the refractive index decreases in the order [Ch]Cl:Mal > [Ch]Cl:Oxa > [Ch]Cl:Gly > [Ch]Cl:Glu >> [Ch]Cl:Lev at all temperatures.

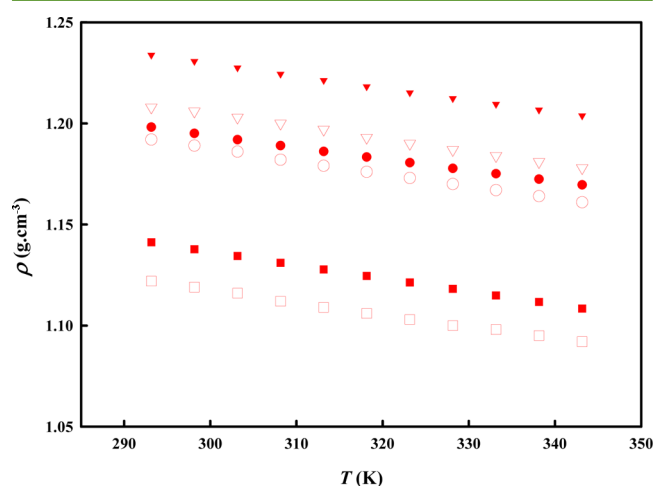
The range of the obtained refractive indexes is 1.48–1.49 for all DESs, except for [Ch]Cl:Lev that has a refractive index value of 1.46, clearly indicating that the anion has a large influence on this property. However, it should be kept in mind that this DES is the only one where the 1:2 molar ratio was used.

Figure S15 of the Supporting Information illustrates the molar free volumes for all studied DESs as a function of temperature. As expected, the molar free volumes increase with



temperature. The molar free volume follows the trend of the alkyl chain length:  $[\text{Ch}]\text{Cl}:\text{Lev}$  ( $C_3$ )  $\approx$   $[\text{Ch}]\text{Cl}:\text{Glu}$  ( $C_5$ )  $>$   $[\text{Ch}]\text{Cl}:\text{Mal}$  ( $C_3$ )  $>$   $[\text{Ch}]\text{Cl}:\text{Gly}$  ( $C_3$ )  $\approx$   $[\text{Ch}]\text{Cl}:\text{Oxa}$  ( $C_2$ ). The analysis of the molar free volumes can lead to important conclusions associated with the solubility of different species present in a solvent.

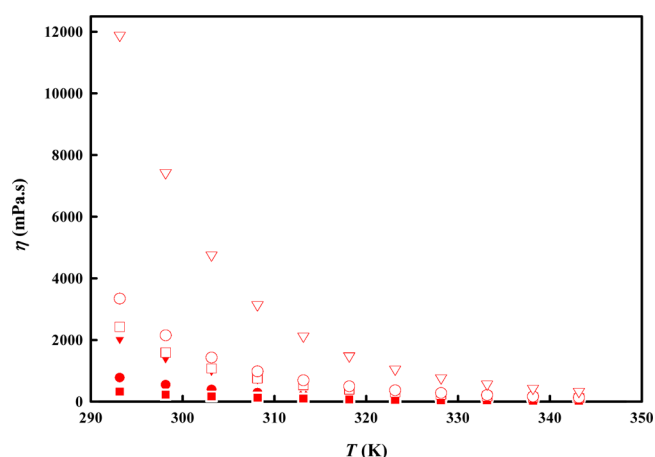
**Comparison of Thermophysical Properties between DESs and Cholinium-Based ILs.** We have recently published the thermophysical properties of several cholinium-based ionic liquids, where the anions are derived from the same carboxylic acids used in this work to prepare DESs.<sup>45</sup> Due to the chemical similarities between these two families of compounds, it is interesting to establish a direct comparison of the thermophysical properties of ionic liquids ( $[\text{Ch}][\text{Gly}]$ ,  $[\text{Ch}][\text{Mal}]$ , and  $[\text{Ch}][\text{Lev}]$ ) and the respective DESs ( $[\text{Ch}]\text{Cl}:\text{Gly}$ ,  $[\text{Ch}]\text{Cl}:\text{Mal}$ , and  $[\text{Ch}]\text{Cl}:\text{Lev}$ ). Figure 8 shows that no significant



**Figure 8.** Crossing data relative to experimental densities ( $\rho$ ) as a function of temperature for two sets of different compounds: deep eutectic solvents of  $[\text{Ch}]\text{Cl}:\text{Mal}$  ( $\blacktriangle$ ),  $[\text{Ch}]\text{Cl}:\text{Gly}$  ( $\bullet$ ), and  $[\text{Ch}]\text{Cl}:\text{Lev}$  ( $\blacksquare$ ) and ionic liquids of  $[\text{Ch}][\text{Mal}]$  ( $\triangle$ ),  $[\text{Ch}][\text{Gly}]$  ( $\circ$ ), and  $[\text{Ch}][\text{Lev}]$  ( $\square$ ). The ILs data is taken from the literature.<sup>30</sup>

differences in the densities of these two families of compounds can be observed. Although the density values obtained for the DESs are consistently higher than those of the corresponding cholinium-based ILs, the increment in density is only 1.021 and 1.016 times for the compounds with malonic and levulinic acids, respectively, and 1.006 times in the case of glycolic acid. Both the DESs and the ILs follow the same trend of densities, with the compounds based on levulinic acid presenting the lowest densities, while those based on malonic acid display the highest. In addition, the thermal expansion coefficients of the ILs presented in Table S8 of the Supporting Information show that both DESs and ILs have values of expansion thermal coefficients on the same order of magnitude.

In Figure 9, a comparison between the viscosities of the DESs and ILs is pictured. It is shown that the DESs have much lower viscosities than their cholinium-based ILs counterparts. Indeed, at 293.15 K, the ionic liquid  $[\text{Ch}][\text{Mal}]$  has a viscosity of 11883.7 mPa s, while its DES counterpart has a viscosity of 2015.9 mPa s, almost six times lower. For the DES  $[\text{Ch}]\text{Cl}:\text{Gly}$ , the viscosity at 293.15 K is four times lower than the corresponding IL. The largest difference in viscosities was registered for the levulinic-based compounds, where the IL showed a viscosity around eight times higher than the DES.



**Figure 9.** Crossing data relative to experimental viscosities ( $\eta$ ) as a function of temperature for two sets of different compounds: deep eutectic solvents of  $[\text{Ch}]\text{Cl}:\text{Mal}$  ( $\blacktriangle$ ),  $[\text{Ch}]\text{Cl}:\text{Gly}$  ( $\bullet$ ), and  $[\text{Ch}]\text{Cl}:\text{Lev}$  ( $\blacksquare$ ) and ionic liquids of  $[\text{Ch}][\text{Mal}]$  ( $\triangle$ ),  $[\text{Ch}][\text{Gly}]$  ( $\circ$ ), and  $[\text{Ch}][\text{Lev}]$  ( $\square$ ). The ILs data is taken from the literature.<sup>30</sup>

Nevertheless, this disparity could be enhanced by the different molar ratios, i.e., for the formation of the DES, a molar ratio of 1:2 is required, with levulinic acid presenting the higher concentration, while in the IL the ions are in equimolar concentrations. Nevertheless, the viscosity trend is not changed from the DESs to the ILs, with the DES viscosities following the same trend as the ILs:  $[\text{Ch}]\text{Cl}:\text{Lev} < [\text{Ch}]\text{Cl}:\text{Gly} < [\text{Ch}]\text{Cl}:\text{Mal}$  and  $[\text{Ch}][\text{Lev}] < [\text{Ch}][\text{Gly}] \ll [\text{Ch}][\text{Mal}]$ , where the latter is the most viscous liquid.

In conclusion, DESs prepared with cholinium chloride and carboxylic acids have similar densities but much lower viscosities than the corresponding cholinium-based ILs, meaning that mass transfer operations can be carried out in DES with a smaller amount of energy than in the corresponding cholinium-based ILs used for the same purpose. DESs also have the advantage of a simpler and cheaper synthetic methodology. Due to the similarities between DESs and ILs, it is possible to affirm that these solvents present tunable properties in a similar manner to that portrayed by ILs. Also to be mentioned is that the knowledge of the properties of the cholinium-based ILs does not provide a correct extrapolation for the corresponding DES, as shown by the huge differences registered in the compounds based on malonic acid, thus confirming the need of accurate measurements of the thermophysical properties of these solvents.

## CONCLUSIONS

In this work, a variety of eutectic mixtures were synthesized by a relatively simple, economical, and environmentally benign process. Deep eutectic solvents were synthesized by mixing cholinium chloride with different carboxylic acids used as hydrogen bond donors. Two different synthetic methods were used, and the formation of an ester during the heating method leads to the conclusion that when carboxylic acids are used as HBD in combination with cholinium chloride, the grinding method should be preferred to prepare DESs due to differences in the experimental thermophysical properties, especially in viscosity.

Thermal properties and physical properties (densities, viscosities, and refractive indices) were studied in the range of temperatures from 293.15 to 353.15 K. As expected, water



presents a strong influence in the properties of the DESs, mainly in the viscosity values of the DESs. The comparison of the values of the thermophysical properties of the prepared DESs and the corresponding ILs leads to the conclusion that DESs present similar densities but much lower viscosities, rendering easier mass transference operations. Moreover, DESs can be prepared with different molar ratios HBA:HBD, affording an extra degree of tunability.

## ■ ASSOCIATED CONTENT

### ● Supporting Information

Characterization of DESs; experimental data of thermal properties, density, viscosity, and refractive index of deep eutectic solvents studied in this work; fitted values of the density, viscosity, and refractive index for the studied DESs; and molar volume, molar refraction, and free volume calculated from experimental results. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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### Notes

The authors declare no competing financial interest.

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## ■ REFERENCES

- (1) Abbott, A. P.; Capper, G.; Davies, D. L.; Rasheed, R. K.; Tambyrajah, V. Novel solvent properties of choline chloride/urea mixtures. *Chem. Commun.* **2003**, 70–71.
- (2) Kanchanomai, C.; Miyashita, Y.; Mutoh, Y. Strain-rate effects on low cycle fatigue mechanism of eutectic Sn–Pb solder. *Int. J. Fatigue* **2002**, *24*, 987–993.
- (3) Chen, N.; Morikawa, J.; Hashimoto, T. Effect of cryoprotectants on eutectics of NaCl·2H<sub>2</sub>O/ice and KCl/ice studied by temperature wave analysis and differential scanning calorimetry. *Thermochim. Acta* **2005**, *431*, 106–112.
- (4) Buckley, M. M.; Paul, B. Eutectic lidocaine/prilocaine cream. A review of the topical anaesthetic/analgesic efficacy of a eutectic mixture of local anaesthetics (EMLA). *Drugs* **1993**, *46*, 126–151.
- (5) Dai, Y.; van Spronsen, J.; Witkamp, G.-J.; Verpoorte, R.; Choi, Y. H. Natural deep eutectic solvents as new potential media for green technology. *Anal. Chim. Acta* **2013**, *766*, 61–68.
- (6) Singh, B. S.; Lobo, H. R.; Shankarling, G. S. Choline chloride based eutectic solvents: Magical catalytic system for carbon–carbon bond formation in the rapid synthesis of  $\beta$ -hydroxy functionalized derivatives. *Catal. Commun.* **2012**, *24*, 70–74.
- (7) Siongco, K. R.; Leron, R. B.; Caparanga, A. R.; Li, M.-H. Molar heat capacities and electrical conductivities of two ammonium-based deep eutectic solvents and their aqueous solutions. *Thermochim. Acta* **2013**, *566*, 50–56.
- (8) Welton, T. Room-temperature ionic liquids. solvents for synthesis and catalysis. *Chem. Rev.* **1999**, *99*, 2071–2084.
- (9) Wasserscheid, P.; Keim, W. Ionic liquids—New “solutions” for transition metal catalysis. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772–3789.
- (10) Abbott, A. P.; Capper, G.; Davies, D. L.; Munro, H. L.; Rasheed, R. K.; Tambyrajah, V. Preparation of novel, moisture-stable, Lewis-acidic ionic liquids containing quaternary ammonium salts with functional side chains. *Chem. Commun.* **2001**, 2010–2011.
- (11) Hayyan, A.; Mjalli, F. S.; AlNashef, I. M.; Al-Wahaibi, T.; Al-Wahaibi, Y. M.; Hashim, M. A. Fruit sugar-based deep eutectic solvents and their physical properties. *Thermochim. Acta* **2012**, *541*, 70–75.
- (12) Hou, Y.; Gu, Y.; Zhang, S.; Yang, F.; Ding, H.; Shan, Y. Novel binary eutectic mixtures based on imidazole. *J. Mol. Liq.* **2008**, *143*, 154–159.
- (13) Shahbaz, K.; Baroutian, S.; Mjalli, F. S.; Hashim, M. A.; AlNashef, I. M. Densities of ammonium and phosphonium based deep eutectic solvents: Prediction using artificial intelligence and group contribution techniques. *Thermochim. Acta* **2012**, *527*, 59–66.
- (14) Ghareh Bagh, F. S.; Mjalli, F. S.; Hashim, M. A.; Hadj-Kali, M. K. O.; AlNashef, I. M. Solubility of sodium salts in ammonium-based deep eutectic solvents. *J. Chem. Eng. Data* **2013**, *58*, 2154–2162.
- (15) 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.
- (16) Kareem, M. A.; Mjalli, F. S.; Hashim, M. A.; AlNashef, I. M. Phosphonium-based ionic liquids analogues and their physical properties. *J. Chem. Eng. Data* **2010**, *55*, 4632–4637.
- (17) Francisco, M.; van den Bruinhorst, A.; Kroon, M. C. Low-transition-temperature mixtures (LTTMs): A new generation of designer solvents. *Angew. Chem., Int. Ed.* **2013**, *52*, 3074–3085.
- (18) 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.
- (19) Zhang, Q.; De Oliveira Vigier, K.; Royer, S.; Jerome, F. Deep eutectic solvents: Syntheses, properties and applications. *Chem. Soc. Rev.* **2012**, *41*, 7108–7146.
- (20) Yu, Y.; Lu, X.; Zhou, Q.; Dong, K.; Yao, H.; Zhang, S. Biodegradable naphthenic acid ionic liquids: Synthesis, characterization, and quantitative structure–biodegradation relationship. *Chem.–Eur. J.* **2008**, *14*, 11174–11182.
- (21) Jhong, H.-R.; Wong, D. S.-H.; Wan, C.-C.; Wang, Y.-Y.; Wei, T.-C. A novel deep eutectic solvent-based ionic liquid used as electrolyte for dye-sensitized solar cells. *Electrochem. Commun.* **2009**, *11*, 209–211.
- (22) Morrison, H. G.; Sun, C. C.; Neervannan, S. Characterization of thermal behavior of deep eutectic solvents and their potential as drug solubilization vehicles. *Int. J. Pharm.* **2009**, *378*, 136–139.
- (23) Abbott, A. P.; Cullis, P. M.; Gibson, M. J.; Harris, R. C.; Raven, E. Extraction of glycerol from biodiesel into a eutectic based ionic liquid. *Green Chem.* **2007**, *9*, 868–872.
- (24) Hayyan, M.; Mjalli, F. S.; Hashim, M. A.; AlNashef, I. M. A novel technique for separating glycerine from palm oil-based biodiesel using ionic liquids. *Fuel Process. Technol.* **2010**, *91*, 116–120.
- (25) Abbott, A. P.; Capper, G.; Gray, S. Design of improved deep eutectic solvents using hole theory. *ChemPhysChem* **2006**, *7*, 803–806.
- (26) Abbott, A. P.; Capper, G.; McKenzie, K. J.; Glidle, A.; Ryder, K. S. Electropolishing of stainless steels in a choline chloride based ionic liquid: An electrochemical study with surface characterisation using SEM and atomic force microscopy. *Phys. Chem. Chem. Phys.* **2006**, *8*, 4214–4221.
- (27) Abbott, A. P.; Capper, G.; Davies, D. L.; Rasheed, R. K.; Shikotra, P. Selective extraction of metals from mixed oxide matrixes using choline-based ionic liquids. *Inorg. Chem.* **2005**, *44*, 6497–6499.

(28) Liao, J.-H.; Wu, P.-C.; Bai, Y.-H. Eutectic mixture of choline chloride/urea as a green solvent in synthesis of a coordination polymer:  $[\text{Zn}(\text{O}_3\text{PCH}_2\text{CO}_2)]\cdot\text{NH}_4$ . *Inorg. Chem. Commun.* **2005**, *8*, 390–392.

(29) Carriazo, D.; Serrano, M. C.; Gutierrez, M. C.; Ferrer, M. L.; del Monte, F. Deep-eutectic solvents playing multiple roles in the synthesis of polymers and related materials. *Chem. Soc. Rev.* **2012**, *41*, 4996–5014.

(30) Gutiérrez, M. a. C.; Ferrer, M. a. L.; Mateo, C. R.; del Monte, F. Freeze-drying of aqueous solutions of deep eutectic solvents: A suitable approach to deep eutectic suspensions of self-assembled structures. *Langmuir* **2009**, *25*, 5509–5515.

(31) Li, X.; Hou, M.; Han, B.; Wang, X.; Zou, L. Solubility of  $\text{CO}_2$  in a choline chloride + urea eutectic mixture. *J. Chem. Eng. Data* **2008**, *53*, 548–550.

(32) Leron, R. B.; Soriano, A. N.; Li, M.-H. Densities and refractive indices of the deep eutectic solvents (choline chloride + ethylene glycol or glycerol) and their aqueous mixtures at the temperature ranging from 298.15 to 333.15 K. *J. Taiwan Inst. Chem. Eng.* **2012**, *43*, 551–557.

(33) Shahbaz, K.; Mjalli, F. S.; Hashim, M. A.; AlNashef, I. M. Prediction of deep eutectic solvents densities at different temperatures. *Thermochim. Acta* **2011**, *515*, 67–72.

(34) Oliveira, F. S.; Pereiro, A. B.; Rebelo, L. P. N.; Marrucho, I. M. Deep eutectic solvents as extraction media for azeotropic mixtures. *Green Chem.* **2013**, *15*, 1326–1330.

(35) Abbott, A. P.; Boothby, D.; Capper, G.; Davies, D. L.; Rasheed, R. K. Deep eutectic solvents formed between choline chloride and carboxylic acids: Versatile alternatives to ionic liquids. *J. Am. Chem. Soc.* **2004**, *126*, 9142–9147.

(36) Abbott, A. P.; Harris, R. C.; Ryder, K. S. Application of hole theory to define ionic liquids by their transport properties. *J. Phys. Chem. B* **2007**, *111*, 4910–4913.

(37) Abbott, A. P.; Harris, R. C.; Ryder, K. S.; D'Agostino, C.; Gladden, L. F.; Mantle, M. D. Glycerol eutectics as sustainable solvent systems. *Green Chem.* **2011**, *13*, 82–90.

(38) D'Agostino, C.; Harris, R. C.; Abbott, A. P.; Gladden, L. F.; Mantle, M. D. Molecular motion and ion diffusion in choline chloride based deep eutectic solvents studied by  $^1\text{H}$  pulsed field gradient NMR spectroscopy. *Phys. Chem. Chem. Phys.* **2011**, *13*, 21383–21391.

(39) Francisco, M.; Gonzalez, A. S. B.; Garcia de Dios, S. L.; Weggemans, W.; Kroon, M. C. Comparison of a low transition temperature mixture (LTTM) formed by lactic acid and choline chloride with choline lactate ionic liquid and the choline chloride salt: Physical properties and vapour–liquid equilibria of mixtures containing water and ethanol. *RSC Adv.* **2013**, *3*, 23553–23561.

(40) Maugeri, Z.; Dominguez de Maria, P. Novel choline-chloride-based deep-eutectic-solvents with renewable hydrogen bond donors: Levulinic acid and sugar-based polyols. *RSC Adv.* **2012**, *2*, 421–425.

(41) Gull, M.; Zhou, M.; Fernández, F.; Pasek, M. Prebiotic phosphate ester syntheses in a deep eutectic solvent. *J. Mol. Evol.* **2014**, *78*, 109–117.

(42) Smith, R.; Tanford, C. Hydrophobicity of long chain n-alkyl carboxylic acids, as measured by their distribution between heptane and aqueous solutions. *Proc. Natl. Acad. Sci. U.S.A.* **1973**, *70*, 289–293.

(43) Iglesias-Otero, M. A.; Troncoso, J.; Carballo, E.; Romani, L. Density and refractive index in mixtures of ionic liquids and organic solvents: Correlations and predictions. *J. Chem. Thermodyn.* **2008**, *40*, 949–956.

(44) Deetlefs, M.; Seddon, K. R.; Shara, M. Predicting physical properties of ionic liquids. *Phys. Chem. Chem. Phys.* **2006**, *8*, 642–649.

(45) Tomé, L. C.; Patinha, D. J. S.; Ferreira, R.; Garcia, H.; Silva Pereira, C.; Freire, C. S. R.; Rebelo, L. P. N.; Marrucho, I. M. Cholinium-based supported ionic liquid membranes: A sustainable route for carbon dioxide separation. *ChemSusChem* **2014**, *7*, 110–113.