

# Chiral Solvent Discovery: Exploring Chiral Eutectic Mixtures and Deep Eutectic Solvents

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**ABSTRACT.**

Deep eutectic solvents (DES) are mixtures that have a melting point much lower than either component. Because the properties of a DES, such as chiral discrimination, can be controlled through choice of components, DES have potential as solvents in many chemical and industrial applications. However, the large number of potential components makes high throughput methods of DES discovery critical for their development. In this study, mixtures of small quantities of hydrogen bond acceptors (HBAs) and chiral hydrogen bond donors (HBDs) were mixed at 55 °C and cooled to 20 °C to screen for potential liquid formation. Variable molar ratios of 10 HBAs were mixed with 93 chiral HBDs to measure a total of 1250 mixtures, and 356 mixtures were liquid

at 20 °C. All of the results are provided in a publicly available database. Several of the mixtures were prepared in larger quantities to characterize their physical properties, including melting points, densities, and viscosities. The results of this study can be used to guide the discovery and development of new chiral DES.

## **Introduction**

A eutectic mixture is a mixture of components that has a melting point below that of the pure components, and a deep eutectic solvent (DES) is a type of eutectic mixture that has a particularly deep depression of the melting point from that of the pure components.<sup>1-5</sup> In a DES, the deep melting point depression is the result of strong interactions, such as hydrogen bonding and ionic interactions, between the components of the mixture. As liquids, DES have properties similar to ionic liquids, including low volatility, high thermal stability, and tunable physicochemical properties.<sup>1-3,6-83</sup> Many DES are considered “green” solvents, because they are biodegradable, non-toxic, and inexpensive to synthesize.<sup>9-14</sup> When the melting point is low enough, DES can be utilized as solvents for use in many chemical and industrial applications, including battery technologies, catalysis, separations, and waste processing.<sup>1,15-22</sup>

Deep eutectic solvents are composed of a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD), and are classified by what is used as the HBA and HBD. For example, type III DES have a quaternary ammonium salt as HBA, and the HBD is an organic molecule, whereas type V DES have organic molecules as the HBA and HBD.<sup>1,2</sup> Many of the studies in the current literature involve type III DES with choline chloride ((2-hydroxyethyl)-trimethylammonium chloride) or tetrabutylammonium chloride as the HBA,<sup>6,18,19,23-30</sup> but there has also been an increase in the study of type V DES.<sup>14,31,32</sup> Given the number of HBA and HBDs available, the possible binary (and ternary) DES combinations is extremely large, but there are no models capable of

predicting what combinations will result in DES.<sup>1</sup> In principle, the properties of a DES depend upon the choice of HBA and HBD, which should make it possible to “tune” the properties of a DES. For example, incorporating a chiral HBA or HBD results in a chiral DES solvent which can be utilized in asymmetric synthesis,<sup>33–37</sup> chiral separations,<sup>24,38</sup> and circularly polarized light emitting materials.<sup>39–41</sup>

The role of chirality in chemistry and biochemistry highlights the importance of developing new chiral DES solvents. However, the large number of possible chiral HBAs and HBDs and lack of predictive capability make finding new chiral DES a time-consuming process of trial and error. In this study, a process was utilized to screen a small number of achiral HBAs, both type III and type V DES components, with a large number of chiral HBDs for potential DES formation. The HBA-HBDs were mixed and heated in various molar ratios, and combinations that remain a liquid at room temperature are recorded as potential chiral DES candidates. The results of the screening are maintained in a publicly available database showing mixtures that form liquids, and more importantly showing mixtures that do not form liquids.<sup>42</sup> The mixtures in the database are compared for the impact of HBA and HBD on liquid formation. Several of the chiral DES candidates have been prepared in larger quantities to measure physical properties, such as density and viscosity. This includes thermal measurements that are used to determine if the mixtures are DES or simple eutectic mixtures.<sup>1,31</sup>

## Experimental

**Mixture preparation.** All chemicals used in this study are shown in Table S1 in supporting information. They were purchased commercially from VWR, Sigma-Aldrich, Combi-Blocks, Chem-Impex and Tokyo Chemicals Inc. (TCI), and used without further purification. Chemicals

were used within 1-2 days of receiving them or stored in a vacuum desiccator before use in mixture testing. Mixtures of HBA's and HBD's were added to wells in a 64-well plate in molar ratios (HBA:HBD) ranging from 1:6-12:1, although most mixtures were only evaluated a ratios from 1:2-3, with a total mass of 0.1 g. The well plate was placed in a Benchmark Incu-Shaker Mini incubator-shaker, shaken at 175 rpm and 55 °C for two hours. The samples in the well plate were observed to identify which mixtures were liquid, solid, or a combination. The well plate was allowed to cool to room temperature (20 °C), and once again observed within 30 minutes to identify which mixtures were liquid, solid or a combination. These observations were recorded into an accessible database.<sup>42</sup> Many of the eutectic mixtures that were liquids in the well plates were also prepared in larger quantities, ~ 1-2 g, for further study. These mixtures were prepared by adding the correct molar ratios of hydrogen bond acceptor and hydrogen bond donor to a sample vial, and stirring under heat at temperatures < 60 °C until a homogeneous liquid was formed (typically less than 1 hour). Water content of the mixtures was measured by volumetric Karl-Fischer titration (Metroohm 870 KF Titrino Plus).

**Physical measurements.** The melting points of mixtures were measured with a differential scanning calorimeter (DSC) (Instrument Specialists Incorporated DSC 550). Samples were prepared by adding 3-10 mg of the mixture to an aluminum pan and lid. The DSC was operated with a heating rate of 2 °C/min. under a constant flow of nitrogen gas. The water content of the larger mass samples was measured immediately before measuring the density, or viscosity. Densities were obtained by determining the mass of DES in a 2.02 mL or a 0.500 mL glass pycnometer. The viscosity was measured with a Brookfield DV2T viscometer using a circulating water bath to control temperature. Viscosities were measured for mixtures between 283-323 K.

## **Results and Discussion**

**Table 1.** An excerpt from the mixture screening database.

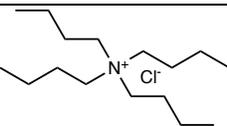
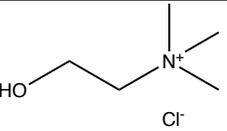
HBA mole ratio	HBD mole ratio	HBA	HBA (SMILES)	HBD	HBD (SMILES)	liquid at 55C	liquid at 20C
1	2	L-Menthol	<chem>C[C@@H]1CC[C@H]([C@@H](C1)O)C(C)C</chem>	L-glutamic acid	<chem>N[C@@H](CCC(O)=O)C(O)=O</chem>	n	n
1	1	L-Menthol	<chem>C[C@@H]1CC[C@H]([C@@H](C1)O)C(C)C</chem>	L-glutamic acid	<chem>N[C@@H](CCC(O)=O)C(O)=O</chem>	n	n
2	1	L-Menthol	<chem>C[C@@H]1CC[C@H]([C@@H](C1)O)C(C)C</chem>	L-glutamic acid	<chem>N[C@@H](CCC(O)=O)C(O)=O</chem>	n	n
3	1	L-Menthol	<chem>C[C@@H]1CC[C@H]([C@@H](C1)O)C(C)C</chem>	L-glutamic acid	<chem>N[C@@H](CCC(O)=O)C(O)=O</chem>	n	n
4	1	L-Menthol	<chem>C[C@@H]1CC[C@H]([C@@H](C1)O)C(C)C</chem>	L-glutamic acid	<chem>N[C@@H](CCC(O)=O)C(O)=O</chem>	n	n
5	1	L-Menthol	<chem>C[C@@H]1CC[C@H]([C@@H](C1)O)C(C)C</chem>	L-glutamic acid	<chem>N[C@@H](CCC(O)=O)C(O)=O</chem>	y	n
6	1	L-Menthol	<chem>C[C@@H]1CC[C@H]([C@@H](C1)O)C(C)C</chem>	L-glutamic acid	<chem>N[C@@H](CCC(O)=O)C(O)=O</chem>	y	n

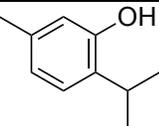
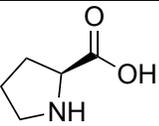
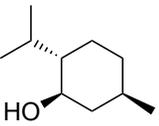
**Chiral mixture screening.** Ten compounds were screened as HBAs, including L-menthol, thymol, choline chloride, tetrabutylammonium chloride, tetrabutylammonium bromide, tetraethylammonium chloride, tetrabutylphosphonium chloride, L-proline, citric acid, and (S)-2-acetoxypropionic acid, with 93 individual chiral HBDs to determine which mixtures form chiral solvents below 55 and 20 °C. HBA-HBD mixtures were screened in molar ratios between 1:6-12:1 HBA:HBD, but most mixtures were only screened at 1:2, 1:1, 2:1, and 3:1 HBA:HBD. Including all of the molar ratios, 1250 mixtures, at the time of submission of this manuscript, have been prepared and measured for liquid formation. Of these combinations, 539 mixtures were liquid at 55 °C and 356 of those were also liquid at 20 °C. All of the mixture screening data is contained in an accessible database.<sup>42</sup> A small excerpt of the database showing the screening of L-menthol as HBA and L glutamic acid as HBD is presented in Table 1. Columns include mole ratios of HBA and HBD, names of the HBA and HBD, SMILES structure representation of the HBA and HBD, and columns indicating if the mixture was observed as a complete liquid (y), complete solid (n),

or partial liquid (p) at 55 and 20 °C. The database is organized by the identity of the HBA. For example, all of the ChCl mixtures with the 93 chiral HBDs are grouped together in the database.

There are factors that need to be considered in the analysis of the chiral mixture screening database. First, since the mixtures were screened in ambient conditions, every sample has some amount of environmental water, but sample size (~0.1 g) precludes quantitative water determination.<sup>43-46</sup> This means that many of the mixtures in the database should be considered a ternary mixture of HBA:HBD:water, and it is unclear what role water content plays in the formation of the liquid at 55 or 20 °C. Second, only a limited number of mole ratios have been explored for each of the mixtures, where different molar ratios may form liquids at 55 or 20 °C. Since the melting point information is gathered as two binary conditions, less than or greater than 55 and 20 °C, there is no way to use the results to determine the eutectic point of a mixture. However, the chiral mixture database does give qualitative information about what HBA and HBD mixtures could lead to new chiral solvents/eutectic mixtures/DES, and maybe more importantly, what mixtures would not. The results in the database are compared and discussed with respect to the impact of the HBA and HBD.

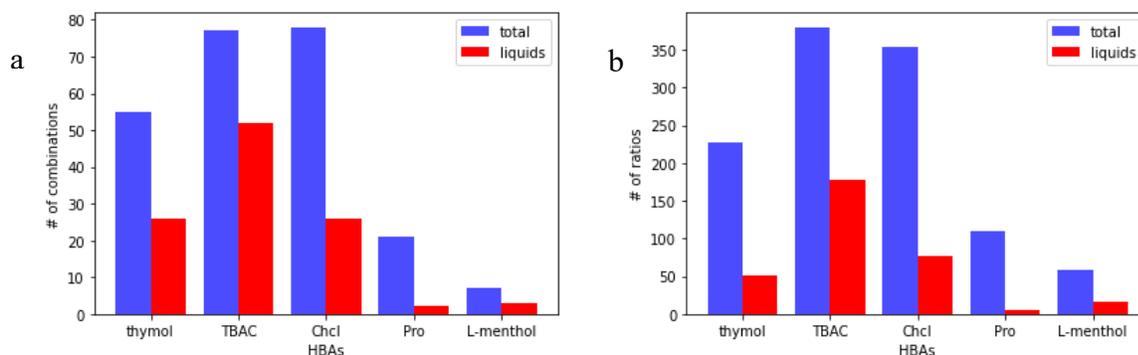
**Table 2.** Compounds used as HBAs.

Name	Structure	T <sub>fus</sub> (°C) <sup>a</sup>
Tetrabutylammonium Chloride (TBACl)		37
Choline chloride (ChCl)		324 <sup>b</sup>

Thymol		50
L-Proline (Pro)		205
L-menthol		37

<sup>a</sup> from ref 47 and 48, <sup>b</sup> estimated from ref 49.

**Impact of HBA component.** The structures and melting points of five of the eleven compounds used as HBAs are shown in Table 2.<sup>47-49</sup> The other six HBAs not included in table 2 were screened with far fewer HBDs. Therefore, the discussion will focus on the five HBAs shown in Table 2. Among the five HBAs, there are two ionic compounds (TBACl and ChCl), one Brønsted-Lowry weak acid (Pro), and two non-ionic organic compounds, thymol and L-menthol. All but TBACl have the capability to donate and accept hydrogen bonds with the HBDs. Only three of the seven HBAs in the database are chiral, L-proline, L-menthol and (S)-acetoxypropionic acid. The majority of the eutectic mixtures have been developed by mixing an achiral HBA with a chiral HBD. Three of the five HBAs have melting points below 55 °C, and therefore, will melt at the high temperature in the shaker/incubator. This is likely to improve the effectiveness of the mixing in the well plate, and may increase the likelihood of forming a liquid at the higher temperature (55 °C).



**Figure 1.** a) Comparison of total HBA-HBD combinations (blue) vs. HBA-HBD combinations that resulted in a liquid at 20 °C (red). The comparison is independent of the molar ratio, and is simply based on HBA-HBD combinations. b) Comparison of total binary HBA:HBD molar ratios (blue) vs. HBA-HBD molar ratios that resulted in a liquid at 20 °C (red).

Figure 1 shows a comparison of the total HBA:HBD combinations attempted vs. combinations that resulted in liquid formation at room temperature (20 °C) based on the identity of the HBA:HBD combination (Figure 1a), and the molar ratios (Figure 1b). Because of the focus on mixtures with chiral HBDs, rather than chiral HBAs, L-proline and L-menthol were studied with the least number of HBDs (Figure 1a). The most effective HBA for forming liquids at room temperature was TBACl with over 50% of its molar ratios successful at forming liquids. In fact, TBACl was the HBA in approximately 50% of all liquid mixtures discovered in the entire database.<sup>42</sup> As a comparison, both TBACl and ChCl were screened with the same number of HBDs, but only ~25% of the ChCl:HBD ratios were liquid at room temperature. Both TBACl and ChCl are hygroscopic salts, but the difference in successful ratios indicates that the absorption of environmental water is not the only factor determining which combinations form liquids at 20 °C. In fact, the data in Figure 1 shows that the HBAs with melting points below 55 °C, TBACl, thymol, and menthol, result in the highest proportion of liquid combinations at room temperature.

**HBD components.** As of this writing, the database has 93 unique HBDs that were combined with one or more of the 10 HBAs. All but two of the HBDs in the database are chiral, and there is considerable structural diversity, including acids, alcohols, amines, and amides. There are 32 combinations of HBA-HBDs with 24 unique HBDs that were liquid at room temperature for every ratio attempted. Table 3 lists the HBDs that successfully formed liquids at all ratios along with the HBA. The structural diversity of the HBDs in Table 3 makes it difficult to rationalize liquid formation of the mixtures based on the structure of the HBDs. However, the one common feature of the HBDs in Table 3 is the lower melting point. Ten of the 24 HBDs in Table 3 start as liquids at room temperature (shown in red in Table 3) before mixing, whereas the remaining 14 HBDs are solids, but only three have a melting point > 100 °C.<sup>50</sup> The majority (21 out of 32) of the combinations in Table 3 include TBACl as the HBA, which is consistent with the data in Figure 1 that shows TBACl as the most effective HBA for liquid formation.

**Table 3.** Hydrogen bond donors that formed liquids at all molar ratios

HBD <sup>a</sup>	HBA (liquid in all ratios)	HBD <sup>a</sup>	HBA (liquid in all ratios)
(S)/(R)-2-acetoxypropionic acid	TBACl	L-tert-leucinol (30 °C)	TBACl
(R)-2-bromo-3-methylbutyric acid (39 °C)	TBACl, ChCl, thymol	L- $\alpha$ -hydroxyisovaleric acid	TBACl, ChCl
(R)-2-hydroxy-4-phenylbutyric acid (114 °C)	TBACl	L-proline methyl ester hydrochloride (73 °C)	TBACl, ChCl
Methyl-(S)-3-hydroxybutyrate	TBACl	Ethyl-(S)-3-hydroxybutyrate	TBACl
(S)-1-phenylethanol	TBACl	$\alpha$ -terpineol	TBACl
(R)-lactamide (73 °C)	ChCl	(-)-Terpinen-4-ol	TBACl
Methyl-(S)-lactate	TBACl, thymol	(2S,3S)-2-Amino-3-Methylpentan-1-ol (36 °C)	TBACl
(R)-2-octanol	TBACl	Dimethyl-D-malate (104 °C)	TBACl, ChCl

Methyl-(2R)-2-hydroxy-3-phenylpropanoate (43 °C)	TBACl, thymol	(R)-methyl mandelate (54 °C)	TBACl
(R)-ethyl mandelate (35 °C)	TBACl, thymol	(R)-citronellol	TBACl
L-lactic acid (53 °C)	ChCl	D-fructose (103 °C)	ChCl
(+)-diethyl L-tartrate	TBACl	(R)-(-)-1-Phenyl-1,2-ethanediol (64 °C)	TBACl

<sup>a</sup> melting points of pure substance in parentheses

**Mixture Physical Characterization.** While the chiral mixture screening does provide insight into what mixtures result in liquids, it does very little to help explain why. For example, this screening cannot be used to distinguish between DES and simple eutectic mixtures, or even understand how environmental water may play a role in liquid formation.<sup>43,44</sup> Over the course of this study to identify chiral solvents, >100 mixtures have been prepared in larger quantities to measure water content, thermal and physical properties. Since it is beyond the scope of this manuscript to document the properties of all of the mixtures, a subset (< 20) will be characterized in the remaining sections of this manuscript. A table of the measured water content along with the component mole fraction for these mixtures is included in the supporting information. Water content of most of the samples varied from 0.2-6.0 % (w/w), which is water mole fractions between 0.02-0.42. The samples with the highest water content show that water is the largest component by moles of the mixture, but the mole fractions are within a range that has been characterized as “water in DES”.<sup>43,44</sup> It is probably best to characterize most of the chiral mixtures developed as a ternary eutectic mixture that includes HBA, HBD, and water.

**Table 4.** Melting points for several mixtures.

Mixture	T <sub>fus</sub> (K) <sup>a</sup>	Mixture	T <sub>fus</sub> (K) <sup>a</sup>
2:1 TBACl:D-glucose	269 <sup>b</sup>	2:1 TBACl:D-fructose	288 <sup>b</sup>
1:1 TBACl:dimethyl-D-malate	[T <sub>g</sub> = 233]	1:1 [Ch]Cl:L-ascorbic acid	260 <sup>c</sup>

2:1 TBACl: Methyl-(2R)-2-hydroxy-3-phenylpropanoate	225	1:1 [TBA]Cl:L-leucic acid	[T <sub>g</sub> = 280] <sup>c</sup>
1:1 TBACl: (R)-(-)-1-Phenyl-1,2-ethanediol	241	2:1 [TBA]Cl:(S)-acetoxypionic acid	298 <sup>c</sup>
1:2 TBACl: (-)-terpinen-4-ol	236		

<sup>a</sup> uncertainty is  $\pm 2$  K, glass transitions in brackets

<sup>b</sup> from reference Liam's paper

<sup>c</sup> from reference 39

In the absence of complete solid-liquid equilibrium curves, a measure of the melting point depression provides a method to classify the mixtures (eutectic mixtures, or DES).<sup>27,31</sup> When the freezing point depression is below that of an ideal mixture, it can be considered a DES, although in many cases the term “deep” loses much of its original meaning. The thermodynamics of the solid liquid equilibrium for the mixtures can be described using the freezing point depression expression shown in equation 1

$$\ln(\gamma_A x_A) = \frac{\Delta H_{fus}}{R} \left( \frac{1}{T_{fus}} - \frac{1}{T} \right) \quad (1)$$

where  $x_A$  and  $\gamma_A$  are the mole fraction and activity coefficients of component A of the mixture, R is the gas constant,  $T_{fus}$  and  $\Delta H_{fus}$  are the melting point and enthalpy of fusion of the component A, and T is the melting point of the mixture. This equation is written assuming that the contribution from the change in heat capacity upon melting ( $\Delta_{fus}C_p$ ) is negligible.<sup>4</sup>

Table 4 shows the freezing points and glass transition measured for the successful mixtures that exhibited a transition in the DSC measurement. The main complication in applying equation 1 to the mixtures in Table 4 is the absence of literature values of the  $\Delta H_{fus}$  for many of the individual components. However, there are literature values for the enthalpy of fusion and melting point of TBACl and lactic acid, which allows the use of equation 1 to calculate activity coefficients for at least one component of most mixtures in Table 4.<sup>47,48</sup> Using the mole fractions from Table S2

(supporting information), the melting point data from Table 4, and equation 1 shows that only 1:3 ChCl:L-lactic acid ( $\gamma_{L\text{-lacticacid}} = 0.94$ ) and 2:1 TBACl:(S)-acetoxypionic acid ( $\gamma_{\text{TBACl}} = 1.1$ ) have  $\gamma \geq 1$ .<sup>39</sup> The 1:1 TBACl:L-leucic acid and 1:1 TBACl: dimethyl-D-malate only show glass transitions, and the remaining mixtures in table 4 have  $\gamma_A < 1$  at the measured molar ratios indicating that the interactions are consistent with the presence of a DES.

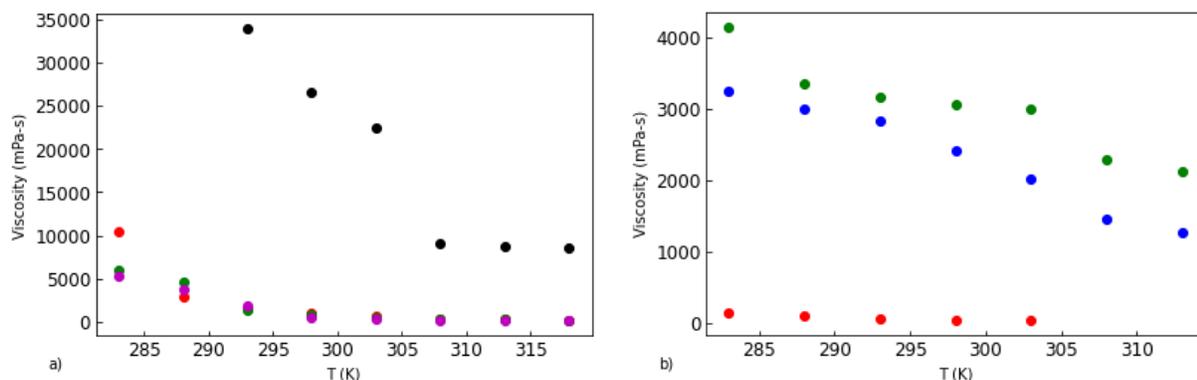
**Table 5.** Densities and viscosities of several mixtures at 293 K.

Mixture	$\rho$ (g/mL) <sup>a</sup>	$\eta$ (mPa-s) <sup>a</sup>	mol % water
1:2 TBACl: (S)-acetoxypionic acid	1.030	1586	3.0
1:2 TBACl: (+)-terpinen-4-ol	0.942	1890	10
1:1 TBACl: L-leucic acid	0.992	1700	15
1:1 TBACl: (+)-diethyl-L-tartrate	1.03	1900	15
2:1 TBACl: N-Boc-D-Phenylalaninol	0.976	33980	9.0
1:2 TBACl : $\alpha$ -terpineol	0.936	1290	13
2:1 Thymol: $\alpha$ -terpineol	0.946	3155	2.0
1:2 Thymol: (2S,3S)-2-Amino-3-Methylpentan-1-ol	0.958	2836	8.0
2:1 Thymol: (S)-(+)-1-Cyclohexylethylamine	0.918	57	3.0

<sup>a</sup> uncertainty in density is  $\pm 0.001$  g/mL, and the uncertainty in viscosity is  $\pm 3$ -5 mPa-s

**Density and Viscosity.** Table 5 shows the densities and viscosities measured at 293 K for eight mixtures with TBACl or thymol as HBA. The density and viscosity was measured for > 20 mixtures, but Table 5 only shows the ten mixtures with water content < 1.5% w/w (Table S2 in supporting information). Only two of the ten mixtures have densities greater than that of water (at 293 K) with a range of 0.918-1.03 g/mL The viscosities (at 293 K) of most of the mixtures in Table 6 were in the range of 1000- 3000 mPa-s. The exceptions are the two higher viscosity mixtures with >28000 mPa-s, and the mixture, 2:1 thymol: (S)-(+)-1-cyclohexylethylamine, with the lowest

viscosity in the table, 57 mPa-s. To the authors knowledge, only three of the mixtures in Table 5 have been utilized in DES or eutectic mixtures prior to this study.<sup>39,51,52</sup> Therefore, it is impossible to make direct comparisons with similar mixtures, but the viscosities in Table 5 are all much higher than those reported for ChCl based DES.<sup>1,6,53</sup> The temperature dependent viscosities (283-313 K range) for seven of the mixtures from Table 6 are shown in Figure 2.



**Figure 2.** a) Viscosity vs. temperature (left panel) for 1:2 TBACl: (S)-acetoxypionic acid (green circles), 1:2 TBACl :  $\alpha$ -terpineol (red circles), 1:2 TBACl: (+)-terpinen-4-ol (purple circles), and 2:1 TBACl: N-Boc-D-Phenylalaninol (black circles). b) Viscosity vs temperature (right panel) for 2:1 Thymol: (S)-(+)-1-cyclohexylethylamine (red circles), 2:1 Thymol:  $\alpha$ -terpineol (green circles), and 1:2 Thymol: (2S,3S)-2-Amino-3-Methylpentan-1-ol (blue circles).

Figure 2a shows the viscosities of four ionic mixtures with TBACl as the HBA, and figure 2b shows the viscosities of three non-ionic mixtures with thymol as the HBA. Three of the TBACl-based mixtures demonstrate Arrhenius-like temperature dependence to their viscosities.<sup>54</sup> The temperature range for the viscosity of the 2:1 TBACl:N-Boc-D-Phenylalaninol was 293-313 K, because the mixture was freezing below 293 K. The 2:1 TBACl:N-Boc-D-Phenylalaninol demonstrated distinct lower and higher temperature viscosity regions with very high viscosities at the lowest temperatures (Figure 2a), which could be an increase that occurs as the mixture

approaches a phase transition (freezing or glass transition). Even at the higher temperatures, the viscosities of 2:1 TBACl:N-Boc-D-Phenylalaninol are much higher than the other TBACl mixtures (Figure 2a and Table 5). Of the data in Figure 2b, 2:1 Thymol: (S)-(+)-1-cyclohexylethylamine mixture has the lowest viscosities, and is the only mixture that shows Arrhenius-like temperature dependence. The viscosities of the other two of the thymol-based mixtures are > 1000 mPa-s, higher than typically reported for thymol DES in the literature, and the temperature-dependence is inconsistent with simple models of liquid viscosity (Arrhenius or VFT).<sup>14</sup> Since all of the thymol mixtures have relatively low water content (Table S2), the large difference between the lowest viscosity mixture (2:1 Thymol: (S)-(+)-1-cyclohexylethylamine), and the higher viscosity mixtures (2:1 Thymol:  $\alpha$ -terpineol and 1:2 Thymol: (2S,3S)-2-Amino-3-Methylpentan-1-ol) is dependent upon the interactions between the different HBAs and the thymol HBA.

## Conclusion

A number of HBAs were combined with >80 chiral HBAs to screen for formation of low melting point mixtures that could be chiral DES. The screening included over 1000 mixtures of variable molar ratios, which resulted in > 300 mixtures as liquids at room temperature. Thirty-two HBA-HBA mixtures formed liquids at all molar ratios examined, which was most common for chiral HBAs with the lowest melting points. All of the screening data is recorded in a publicly available database. The melting point measurements of a small number of mixtures showed that most had melting point depression indicative of DES and not simple eutectic mixtures. The densities and viscosities of the mixtures are comparable to other DES.

**Supporting Information.** Supporting information includes a list of HBDS and purity information, water content of measured mixtures, and DSC data. The chiral DES database can be found at [10.6084/m9.figshare.19526092](https://doi.org/10.6084/m9.figshare.19526092).

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