Investigating the variation in solvation interactions of choline chloride-based deep eutectic solvents formed using different hydrogen bond donors

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Abstract

Choline chloride-based DESs have gained widespread recognition as green solvents in catalysis and separation science as their designer properties permit solvation properties to be modulated by the choice of hydrogen bond donor (HBD) as well as its molar ratio. Despite being one of the most popular classes of DESs, very little is currently understood regarding how their solvation characteristics differ amongst themselves as well as from other classes of DESs. Previous studies have shown that the catalytic activity, extraction efficiency, and solubilities of natural compounds can be influenced by the type of choline salt and HBD, but no study has systematically related these parameters with its solvation properties. In this study, inverse gas chromatography was employed for the first time to study the individual solvation characteristics of a diverse range of choline chloride and acetate-based DESs comprised of amides, diols, organic acids, and carbohydrates. Hydrogen bond acidity was found to be a dominant interaction for all DESs, especially those comprised of organic acid HBDs. DESs composed of isomers of butane diol and hexane diol as HBDs exhibited higher hydrogen bond basicity and dispersive-type interactions compared to those comprised of urea, acetamide, and organic acids with the position of the hydroxyl functional group influencing their solvation interactions. Choline acetate-based DESs exhibited lower dipolarity and stronger hydrogen bond basicity and dispersive-type interactions compared to choline chloride DESs. The solvation models developed in this study were used to interpret and explain DES behavior in previously reported studies involving catalysis, organic synthesis, and extractions demonstrating that the measured solute-solvent interactions can serve to predict the performance of choline chloride-based DESs when used in various applications.

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1. Introduction

Deep eutectic solvents (DESs) have gained widespread recognition as alternative solvents in promoting sustainability in scientific research.[1,2] DESs typically consist of a hydrogen bond donor (HBD) and hydrogen bond acceptor (HBA) mixed together in a certain molar ratio.[2,3] The resulting eutectic mixture possesses a melting point that is lower than that of the individual HBA and HBD components.[4,5] Ammonium, phosphonium, and imidazolium salts are common HBAs while organic acids, alcohols, amides, amines, and carbohydrates form the majority of employed HBDs.[6,7] DESs often possess low melting points, tunable viscosities, low vapor pressures, and involve preparation methods that eliminate the use of organic solvents.[3,8] These desirable characteristics make DESs excellent substitutes for organic solvents in numerous scientific applications,[9] including the extraction of metals[10,11] and natural compounds,[12,13] carbon dioxide capture,[14] desulfurization of fuel,[15,16] and protein purification.[17]

Choline chloride-based DESs constitute the most popular class of DESs due to their biodegradability, relatively low toxicity and the ability of choline chloride ($[Ch^+][Cl^-]$) to easily form DESs with many different types of HBDs.[6,18,19] Some of these eutectic mixtures can be employed in the preparation of aqueous DES solutions.[20,21] To comprehensively study important physical and chemical properties of DESs, a wide range of techniques are often employed. For instance, fourier transform infrared (FTIR) spectroscopy and nuclear magnetic resonance (NMR) spectroscopy studies have shed light on important hydrogen bonding interactions that are largely responsible for the freezing point depression of a eutectic mixture.[20] Karl Fischer titration, NMR spectroscopy, and viscometry have been used to measure and monitor the water content within a DES as both viscosity and strength of hydrogen bonding between the donor and acceptor have been found to be influenced by the amount of water present in a eutectic mixture.[20,22,23,24] Similarly,

the purity of a DES is often measured using NMR spectroscopy[25] and differential scanning calorimetry (DSC), as a pure DES is expected to melt at a specific temperature.[26] Each of the aforementioned techniques offer a unique perspective into the property they are measuring.

In scientific studies involving extractions, catalysis, and organic synthesis, the physico-chemical properties of DESs have been found to influence key parameters such as extraction efficiency and purity of reaction products. For example, acidic DESs comprised of choline chloride HBAs and organic acid HBDs were shown to enhance the degree of crystallinity of chitin nanocrystals by solubilizing and removing the amorphous components of chitin.[27] The physico-chemical properties of choline chloride DESs can be modified by altering the molar ratio of HBA/HBD as well as by changing the anion of the HBA or the type of HBD.[28,29] To understand the effect of these modifications on solvation characteristics, polarity studies based on solvatochromic dyes have been extensively conducted.[30,31,32,33] The normalized polarity scale (E_TN) constructed using the solvatochromic response of these dyes has highlighted important differences in polarity among various DESs. For example, Florindo et al. reported E_TN values of 0.35 and 0.83 for the $[Ch^+][Cl^-]$: 2 levulinic acid and $[Ch^+][Cl^-]$: 2 ethylene glycol DESs, respectively, indicating a vast polarity difference between them.[29] The solvatochromic approach involving Kamlet-Taft parameters provides deeper insight by deconvoluting polarity into individual solvation interactions, namely, the hydrogen bond donating ability (α), hydrogen bond accepting ability (β), and dipolarity/polarizability (π*).[29] While this approach has proven to be useful in deciphering DES solvation characteristics, challenges arise in cases where ambiguity persists. In biocatalysis, the aldol reaction between *p*-nitrobenzaldehyde and acetone catalyzed by L-proline produced an 80% conversion and 54% enantiomeric excess in the $[Ch^+][Cl^-]$: 2 glycerol DES and 32% conversion and 38% enantiomeric excess in the $[Ch^+][Cl^-]$: 2 urea DES.[34] However,

E_TN values of 0.845 and 0.835 for the $[Ch^+][Cl^-]$: 2 glycerol and $[Ch^+][Cl^-]$: 2 urea DESs, respectively, do not reveal significant variation in their polarity.[35] The α, β, and π* values of 1.49, 0.52, and 1.11, respectively, for the $[Ch^+][Cl^-]$: 2 glycerol DES and 1.42, 0.50, and 1.14, respectively, for the $[Ch^+][Cl^-]$: 2 urea DES also do not indicate significant variation in their individual solvation interactions. For the same two DESs, Massolo et al. reported enantiomeric excesses of 80% ($[Ch^+][Cl^-]$: 2 urea DES) and 62% ($[Ch^+][Cl^-]$: 2 glycerol DES) in the enantioselective Michael addition reaction of isobutyraldehyde and nitrostyrene.[36] Similarly, nearly a 10% difference in chitin yield extracted from Hermetia illucens was observed.[37] Thus, the unique solvation characteristics offered by these DESs are not adequately explained by either their E_TN values or Kamlet-Taft parameters.

Clearly, an alternative technique able to sensitively measure solute-solvent interactions as a function of HBA/HBD composition is needed. Inverse gas chromatography (IGC) measures solute-solvent interactions through the chromatographic retention of a diverse range of probe molecules, each capable of offering unique and simultaneous interactions. These interactions can be measured as a function of temperature and the strength of individual solvation interactions can be determined using a linear free energy relationship.[38] IGC has previously been used to investigate the solvation characteristics of phosphonium and ammonium DESs and the results have shown significant variation in solvation properties between different eutectic mixtures within the same class of DESs.[39] To date, the solvatochromic approach has provided a limited understanding as to the role of HBA and HBD on overall solvation characteristics for choline chloride-based DESs.

In this study, IGC is employed to investigate the solvation characteristics of 25 DESs comprised of choline chloride, choline acetate, and tetrabutylammonium chloride HBAs and glycols, carboxylic acids, amides, and carbohydrates as HBDs. DES combinations were carefully

chosen to systematically investigate the effect of the following variables on DES solvation characteristics: (a) chemical structure and functional group class of HBD, (b) HBA anion, (c) molar ratio of HBA/HBD, and (d) alkyl chain length of HBD. Results from this study are used to explain the behavior of choline chloride-based DESs when used as solvents in catalysis, extractions, and organic synthesis. This study demonstrates that certain HBA/HBD combinations are more capable of promoting specific types of solvation interactions than others, making them more suited towards particular applications.

2. Experimental

2.1 Chemicals, reagents, DES preparation and characterization

A comprehensive list of all chemicals and reagents used in this work are provided in the supporting information. Deuterated chloroform and dimethyl sulfoxide were obtained from Cambridge Isotope Laboratories (Andover, MA, USA). Deactivated capillary (5 m x 250 μm) was obtained from MEGA (Legnano, Milano, Italy) and used as received. Prior to DES preparation, all HBAs and HBDs were dried in a vacuum oven at room temperature for two days and subsequently stored in a desiccator. The stirring method with mild heating and the grinding method at room temperature were used to prepare DESs.[25] Exact masses corresponding to precise molar ratios of HBA and HBD in each DES (see Figure 1) were carefully weighed out on a Denver Instruments (SI-64) analytical balance in a climate-controlled environment using a transfer pipette for liquid HBDs and a clean spatula for solid compounds. It has been previously reported that DESs comprised of the $[Ch^+][Cl^-]$ HBA and organic acid HBDs have a tendency to form esters when prepared using the heat and stir method.[25] Therefore, DESs composed of the $[Ch^+][Cl^-]$ HBA and malonic acid and levulinic acid HBDs were ground together using a mortar and pestle. All other HBAs and HBDs were mixed in 20 mL glass vials and their DESs prepared using the stir method

with gentle heating, if necessary. The water content for all DESs was measured using a Metrohm 831 Karl Fischer coulometric titrator and all eutectic mixtures were found to contain less than 0.9 wt.% water, as shown in Table S1. The purity of all DESs was verified using ^{13}C and ^{1}H NMR; all spectra are provided in the supporting information.

DSC measurements were taken using a DSC Q2000 calorimeter (TA Instruments) for those DESs in which melting point and/or glass transition temperatures were not previously reported in the literature. DESs that appeared to be liquids at room temperature were cooled from 40 °C to -120 °C at a rate of 20 K min^{-1} before being heated to 80 °C at a rate of 20 K min^{-1}. However, DESs that appeared as solids at room temperature were cooled to -65 °C at a rate of 20 K min^{-1} and subsequently heated to 200 °C at a rate of 20 K min^{-1}. All DSC data was analyzed using TA universal analysis software (TA Instruments). Melting point and/or glass transition temperatures for all DESs are provided in Table S2.

2.2 Preparation of chromatographic columns and employed separation characteristics

Chromatographic columns containing DES stationary phases were prepared using the static method of column coating. In order to coat a uniform film of DES on the inner capillary wall, a volatile organic solvent is employed. DESs comprised of $[N_{4444}^{+}][Cl^{-}]$ HBAs and triethylene glycol HBDs were dissolved in neat methylene chloride. In cases where the DES was not completely soluble in methylene chloride, a mixed solvent system comprised of methylene chloride and 5-10% methanol (by volume) was employed. All DESs were dissolved in either of these two solvent systems at a concentration of 0.32% w/v. Five meter segments of deactivated fused silica capillary were filled with the DES coating solution and sealed at one end. The open end of the capillary was connected to a vacuum and the capillary column placed in a water bath maintained at 40 °C. The approximate DES film thickness for all columns was 0.20 μm.[40] All DES columns were

conditioned at 50 ℃ for 30 minutes under a constant flow of helium (1 mL/min) in a gas chromatograph equipped with a flame ionization detector. Column efficiencies were determined by injection of a naphthalene solution (1 mg/mL) at 50 ℃ and were found to range from 1150 to 4300 plates/meter.

All DESs were studied using two Agilent 7890 B and two 6890 N gas chromatographs. The inlet and detector were maintained at 150 ℃ with oven temperatures ranging between 30 and 50 ℃. Helium was employed as the carrier gas at 1 mL/min. An inlet split ratio of 20:1 was employed throughout the study. To evaluate solute retention, probes were dissolved in methylene chloride at a concentration of 1 mg/mL and 1 μL of each solution was subjected to separation. Table S3 lists the fifty-one probes that were employed in this study. Multiple linear regression analysis (MLRA) and statistical evaluation of all regression plots was performed using Analyze-it (Microsoft, USA).

3. Results and discussion

Choline chloride-based DESs have distinct structural features that differentiate them from other classes of DESs. Compared to the [N_{4444}^+][Cl^-] salt, [Ch^+][Cl^-] possesses an extra acidic proton that has been shown to interact with waste ammonia[41] and contribute to the desulfurization oxidation/extraction mechanism.[16] The diverse range of HBDs investigated in this study includes diols, amides, carboxylic acids, and carbohydrates, as shown in Figure 1. Two choline salts ([Ch^+][Cl^-] and [Ch^+][Ace^-]) were employed as HBAs to investigate the effect of anion. Three structural isomers of butane diol (1,4-butane diol, 1,3-butane diol, and 2,3-butane diol) were employed as HBDs, as the position of the hydroxyl functional groups is known to affect the physico-chemical properties of the resulting DESs.[7,42]

To relate the chromatographic retention of probe molecules to individual solute-solvent interactions, the Abraham solvation parameter model (equation 1) was employed.[38]

$$Log\ k = c + eE + sS + aA + bB + lL \quad (1)$$

According to equation 1, *k* represents the retention factor of each probe molecule calculated using the retention time and dead time of each chromatographic column. The solute descriptors *E, S, A, B,* and *L* are specific to the probe molecules and represent the excess molar refraction, dipolarity/polarizability, hydrogen bond acidity, hydrogen bond basicity, and gas-hexadecane partition coefficient at 298 K, respectively.[38] The system constants *e*, *s*, *a*, *b*, and *l* represent the specific solvation interactions of the DES stationary phase, where *e* measures n-π and π-π interactions, *s* the dipolarity/polarizability, *a* the hydrogen bond basicity, *b* the hydrogen bond acidity, and *l* provides a measure of dispersive-type interactions.[43]

To obtain highly efficient chromatographic columns, the DES stationary phase must be coated as a thin, continuous film on the inner wall of the capillary. In order to preserve the integrity of the DES stationary phase throughout the study, GC inlet/detector temperatures less than 150 °C and oven temperatures below 70 °C were maintained.[39] However, some HBDs examined in this study had slightly higher vapor pressures necessitating the use of lower oven temperatures. Therefore, all system constants were measured at 30, 40, and 50 °C.

3.1 Comparison of $[N_{4444}^+][Cl^-]$ and $[Ch^+][Cl^-]$ DESs

DESs comprised of $[N_{4444}^+][Cl^-]$ and $[Ch^+][Cl^-]$ HBAs with the same HBDs (Figure 1) were studied to investigate their differences in solvation interactions. All models were statistically sound based on the magnitude of Fisher *F*-statistics and high correlation coefficients (0.99) of the multiple linear regression fit, as shown in Tables 1 and 2. The DESs within both classes exhibited

significant dipolarity (*s*-term), hydrogen bond basicity (*a*-term), and dispersive-type (*l*-term) interactions. Dispersive-type interactions generally exhibited greater variation for $[Ch^+][Cl^-]$ DESs than for $[N_{4444}^+][Cl^-]$ DESs. The *e*-term, representing n-π and π-π interactions, was generally higher for $[Ch^+][Cl^-]$ DESs. Within the $[N_{4444}^+][Cl^-]$ DESs, only those comprised of the glycerol HBD at very high molar ratios (1:3, 1:4, and 1:5) exhibited significant n-π and π-π interactions due to additional electron lone pairs on glycerol. A similar trend was observed for the hydrogen bond acidity (*b*-term) which was more dominant in $[Ch^+][Cl^-]$ DESs. The hydrogen bond basicity (*a*-term) ranged from (3.58±0.20) to (5.18±0.10) for $[Ch^+][Cl^-]$ DESs and from (4.45±0.08) to (7.57±0.16) at 40 °C for $[N_{4444}^+][Cl^-]$ DESs.

DESs were further investigated by classifying them into groups based on their solvation properties. Figure 2A shows values of hydrogen bond basicity plotted against dispersive-type interactions for all 25 DESs at 40 °C. Using k-means clustering (see supporting information for details), it can be observed that the $[Ch^+][Cl^-]$: 2 U, $[Ch^+][Cl^-]$: MA, $[Ch^+][Cl^-]$: 2 MA, and $[Ch^+][Cl^-]$: 2 Iso DESs exclusively formed clusters A, B, C, and D, respectively. Cluster E is generally composed of DESs with $[N_{4444}^+][Cl^-]$ (red triangles) and $[Ch^+][Cl^-]$ (blue squares) HBAs and diols as HBDs. Cluster F is entirely composed of DESs formed by $[N_{4444}^+][Cl^-]$ HBAs and the TEG HBD. $[Ch^+][Cl^-]$ DESs exhibit low to medium hydrogen bond accepting ability while most $[N_{4444}^+][Cl^-]$ DESs possess strong hydrogen bond basicity character. It can also be observed that DESs possessing higher hydrogen bond basicity are generally also capable of stronger dispersive type-interactions. The correlation of dispersive-type interactions with hydrogen bond acidity is shown in Figure 2B. The same 25 DESs fell into 5 groupings using k-means clustering and the hydrogen bond acidity was observed to generally decrease with an increase in dispersive-type interactions. Figures 2A and 2B demonstrate that the $[Ch^+][Cl^-]$ DESs generally possess higher

hydrogen bond acidity and lower dispersive-type interactions than [N_{4444}^+][Cl^-] DESs. Higher hydrogen bond basicity and dispersive-type interactions in [N_{4444}^+][Cl^-] DESs are attributed to longer alkyl chain substituents on the cation, as is consistent with previous studies.[28,29,39] The differences in solvation interactions between the two DES systems lead to some probe molecules exhibiting longer chromatographic retention factors, as shown in Tables S4 and S5. Alcohols interacted less on [Ch^+][Cl^-] DESs due to their lower hydrogen bond basicity but interacted much more strongly with basic probe molecules, such as *N,N*-DMF and *N,N*-DMAC, compared to [N_{4444}^+][Cl^-] DESs (Table S6).

3.2 Effect of HBD in [Ch^+][Cl^-] DESs

DESs comprised of the [Ch^+][Cl^-] HBA and diols, amides, carbohydrates, and organic acids as HBDs were studied to examine the effect of HBD on solvation interactions. The hydrogen bond acidity (*b*-term) was found to be the highest when organic acids were employed as HBDs, as shown for the [Ch^+][Cl^-] : 2 MA DES (1.06±0.15) at 40 °C (Table 1). Urea and malonic acid produced DESs with very high hydrogen bond acidity compared to TEG, isosorbide, and the diols. A similar trend was observed for n-π and π-π interactions (*e*-term) where the highest value of 0.51±0.12 was obtained for the [Ch^+][Cl^-] : 2 U DES at 40 °C, which can be attributed to the π-bonds in urea as well as lone pair of electrons in both [Ch^+][Cl^-] and urea. The hydrogen bond basicity (*a*-term) was generally higher for DESs comprised of diols and carbohydrates compared to amides and organic acids. For example, the *a*-term value at 40 °C for the [Ch^+][Cl^-] : (1,4-BD) DES was (4.96±0.11) compared to (4.23±0.16) for the [Ch^+][Cl^-] : MA DES. Diols possessing longer alkyl chains also resulted in DESs with higher dispersive-type interactions (*l*-term) compared to those comprised of amides and organic acid HBDs. These results are further illustrated in Figure 3 which shows the chromatographic separation of 12 probe molecules on the [Ch^+][Cl^-] : 2 MA, [Ch^+][Cl^-] : 2 (1,6-

HD), and [N_{4444}^+][Cl^-] : TEG DESs at 50 °C. Most probe molecules exhibited shorter retention times on the [Ch^+][Cl^-] : 2 MA DES compared to the [Ch^+][Cl^-] : 2 (1,6-HD) DES. For example, both cyclohexanol and acetophenone co-eluted in under 6 minutes on the [Ch^+][Cl^-] : 2 MA DES whereas they retained for over 12 minutes on the [Ch^+][Cl^-] : 2 (1,6-HD) DES. In addition, the separation selectivity and analyte elution order were drastically altered for these two DESs due to their different hydrogen bond basicity and dispersive-type interactions.

Solvation interactions were also observed to vary for DESs comprised of [Ch^+][Cl^-] HBA and various diols as HBDs. For example, the *a*-term was (4.73±0.12) for the [Ch^+][Cl^-] : 3 TEG DES and (4.59±0.11) for the [Ch^+][Cl^-] : 4 TEG DES compared to (5.13±0.12) for the [Ch^+][Cl^-] : 3 (1,4-BD) DES and (4.97±0.12) for the [Ch^+][Cl^-] : 4 (1,4-BD) DES. Dispersive-type interactions were higher for DESs comprised of diols possessing long alkyl chain substituents. In some [Ch^+][Cl^-] DESs comprised of diols, the system constants exhibited less smooth trends when either the length of alkyl chain was varied or additional functional groups were incorporated in the HBD. It is known that the location of the hydroxyl group substituent in the butane diol HBD impacts the solvation interactions of [Ch^+][Cl^-] DESs.[7] The *a*-term values for the [Ch^+][Cl^-] : 2 (1,4-BD), [Ch^+][Cl^-] : 2 (1,3-BD), and [Ch^+][Cl^-] : 2 (2,3-BD) DESs did not differ significantly. However, the retention factors of alcohols such as cyclohexanol increased from 44.10 to 58.61 for the [Ch^+][Cl^-] : 2 (1,3-BD) and [Ch^+][Cl^-] : 2 (2,3-BD) DESs, respectively, as shown in Table S4.

3.3 Comparison of [Ch^+][Cl^-] and [Ch^+][Ace^-]-based DESs

To investigate the influence of HBA anion on solvation interactions, DESs comprised of [Ch^+][Cl^-] and [Ch^+][Ace^-] HBAs and TEG and 1,4-BD HBDs were studied. [Ch^+][Cl^-] DESs exhibited slightly higher dipolarity and lower dispersive-type interactions compared to those comprised of the acetate anion. Higher hydrogen bond basicity was observed for the [Ch^+][Ace^-] :

4 TEG DES (4.84±0.11) at 40 °C compared to (4.59±0.11) for the [Ch^+][Cl^-] : 4 TEG DES. The hydrogen basicity for the [Ch^+][Ace^-] : 4 (1,4-BD) DES (5.18±0.10) was similar to that of the [Ch^+][Cl^-] : 4 (1,4-BD) DES (4.97±0.12) but stronger chromatographic retention of alcohols at 50 °C (see Figure S1) was observed on the [Ch^+][Ace^-] : 4 (1,4-BD) DES.

3.4 Effect of varying the HBA/HBD molar ratio in [Ch^+][Cl^-]-based DESs

DESs comprised of the [Ch^+][Cl^-] HBA and 1,4-BD, TEG, 1,6-HD, and MA as HBDs were prepared at various HBA/HBD ratios to investigate the change in solvation interactions. Dispersive-type interactions at 40 °C (Table 1) increased from (0.49±0.01) to (0.58±0.01) for the DES system comprised of the [Ch^+][Cl^-] HBA and 1,4-BD HBD and from (0.53±0.01) to (0.57±0.01) for the [Ch^+][Cl^-] : 3 TEG and [Ch^+][Cl^-] : 4 TEG DESs, respectively. A similar trend was observed with the hydrogen bond acidity where it was generally found to increase with an increase in molar ratio of HBD, especially for DESs comprised of organic acid HBDs. Figure 4A shows the retention factors of straight-chain alcohol probe molecules at 30 °C for the 1:1, 1:2, 1:3, and 1:4 molar ratios of the DES containing the [Ch^+][Cl^-] HBA and 1,4-BD HBD. Retention factors increased with larger molar ratios of HBD. Interestingly, retention was observed to decrease in DES systems comprised of [N_{4444}^+][Cl^-] HBAs, as shown in Figure 4B and 4C.

3.5 DES solvation model

Choline chloride-based DESs have gained increasing popularity as sustainable solvents in catalysis, organic synthesis, and chemical separations due to their tunable solvation properties.[1,36] This section focuses on relating data from the solvation models to their catalytic and separations performance that has been previously reported in the literature to demonstrate that the effectiveness of DESs can be predicted and explained using the system constants generated in this study.

3.5.1 DESs in catalysis and organic synthesis

Choline chloride-based DESs have been widely used as catalysts and reaction media in organic synthesis to provide enhanced reaction yields and enantioselectivities.[34,36] Hu et al. reported a product yield of 88% at 80 °C for the one pot synthesis of functionalized pyrroles using the $[Ch^+][Cl^-]$: MA DES as a catalyst compared to trace amounts of product formed using two 1-butyl-3-methyl imidazolium (BMIM) ionic liquids (ILs) ([BMIM][PF_6] and [BMIM][BF_4]).[44] The $[Ch^+][Cl^-]$: MA DES catalyzed the reaction by enhancing the carbonyl group's electrophilicity of acetylacetone and 4-chlorobenzaldehyde based on its acidic protons. Table 1 shows that the $[Ch^+][Cl^-]$: MA DES possesses a higher hydrogen bond acidity (0.72±0.15) at 40 °C compared to (0.000) and (-0.102) for the [BMIM][PF_6] and [BMIM][BF_4] ILs, respectively.[45] For the synthesis of *N*-phenylphthalimide, Lobo et al. reported superior product yields of 81% and 67% using the $[Ch^+][Cl^-]$: 2 U and $[Ch^+][Cl^-]$: MA DESs, respectively, compared to only 56% in the $[Ch^+][Cl^-]$: Gly DES.[46] While no explanation was provided for this particular behavior, a separate study revealed that the synthesis of *N*-phenylphthalimide can be catalyzed by heterogenous acidic catalysts such as acidic ILs.[47] Table 1 shows that both the $[Ch^+][Cl^-]$: 2 U and $[Ch^+][Cl^-]$: MA DESs possess relatively higher hydrogen bond acidity and fall into the same cluster in Figure 2B compared to $[Ch^+][Cl^-]$ DESs comprised of alcohol HBDs.

3.5.2 Extraction of metals/metal oxides using $[Ch^+][Cl^-]$ DESs

Choline chloride-based DESs have been extensively employed in the extraction of metals and their oxides from various matrices.[48,49] Abbott reported the solubility of 17 metal oxides in the $[Ch^+][Cl^-]$: MA, $[Ch^+][Cl^-]$: 2 U, and $[Ch^+][Cl^-]$: 2 ethylene glycol DESs and compared their solubilities in hydrochloric acid (HCl) and sodium chloride solution (NaCl).[48] For most metal oxides, the solubility at 50 °C ranged in the following order: HCl > $[Ch^+][Cl^-]$: MA DES >

$[Ch^+][Cl^-]$: 2 U DES > NaCl > $[Ch^+][Cl^-]$: 2 ethylene glycol DES. A separate study revealed that metal oxides generally dissolve well in acidic DESs.[49] As observed in Table 1, the hydrogen bond acidity values at 50 °C are among the highest for the $[Ch^+][Cl^-]$: MA (0.71±0.14) and $[Ch^+][Cl^-]$: 2 U (0.84±0.15) DESs compared to those containing alcohol HBDs. In the preconcentration of lead and cadmium in edible oils, Karimi et al. reported similar behavior for $[Ch^+][Cl^-]$ DESs where the $[Ch^+][Cl^-]$: 2 U DES provided extraction efficiencies of over 90% compared to less than 60% for the $[Ch^+][Cl^-]$: 2 ethylene glycol DES.[50]

3.5.3 Extraction of phenolic compounds using DESs

Extraction of phenolic compounds using DESs has gained widespread popularity.[3,51] Garcia et al. reported a higher total phenolic content of (120.2±5.8 mg/kg) from virgin olive oil using the $[Ch^+][Cl^-]$: 5 (1,4-BD) DES compared to only (85.40±7.6 mg/kg) for the $[Ch^+][Cl^-]$: MA DES.[12] Since phenolic compounds possess a large number of hydroxyl groups, DESs possessing higher hydrogen basicity are preferred due to analyte competition in the interaction with chloride anion.[12] Table 1 shows that the hydrogen bond basicity of the $[Ch^+][Cl^-]$ HBA and 1,4-BD HBD varies from (4.96±0.11) to (5.13±0.12) at 40 °C compared to (4.23±0.16) for the $[Ch^+][Cl^-]$: MA DES. Peng et al. obtained a higher extraction yield of (19.80±0.79 mg/g) for chlorogenic acid from Lonicerae japonicae Flos using the $[Ch^+][Cl^-]$: 2 (1,3-BD) DES compared to (7.84±0.51 mg/g) using the $[Ch^+][Cl^-]$: 2 U DES.[51] This can be explained by the significantly higher hydrogen bond basicity of (5.03±0.11) for the $[Ch^+][Cl^-]$: 2 (1,3-BD) DES at 40 °C compared to (3.58±0.20) for the $[Ch^+][Cl^-]$: 2 U DES. Xia et al. extracted (1.34±0.52 mg/g) of rosmarinic acid from Prunella vulgaris using the $[Ch^+][Cl^-]$: 2 (1,4-BD) DES compared to (1.45±0.18 mg/g) for the $[Ch^+][Cl^-]$: 3 (1,4-BD) DES and (1.82±0.31 mg/g) for the $[Ch^+][Cl^-]$: 4 (1,4-BD) DES.[52] As shown in Figure 4A, a consistent increase in the chromatographic retention

of alcohols was observed when the HBA/HBD ratio increased from 1:1 to 1:4, further validating that DES interactions with hydroxyl-containing compounds increase at higher molar ratios of HBD.

3.5.4 Extraction of carbohydrates using [Ch^+][Cl^-]-based DESs

DESs have been extensively used in biomass fractionation because of their ability to disrupt hydrogen bonds in carbohydrate complexes.[53,54] The delignification process is particularly effective when DESs possess higher hydrogen bond acidity.[53] Zhang et al. reported the extraction of 56.5% lignin using the [Ch^+][Cl^-] : MA DES in the pretreatment of corncob compared to 43.0% for the [Ch^+][Cl^-] : 2 LvA DES.[54] Table 1 shows a higher hydrogen bond acidity of (0.72±0.15) for the [Ch^+][Cl^-] : MA DES at 40 ℃ compared to (0.34±0.09) for the [Ch^+][Cl^-] : 2 LvA DES. Zhu et al. reported that the [Ch^+][Cl^-] : 2 MA DES was able to extract chitin from lobster shells at 50 ℃ with higher purity compared to the [Ch^+][Cl^-] : 2 U DES, which can be attributed to its high hydrogen bond acidity of (1.02±0.15) at that temperature (Table 1).[55] Chitin extracted from crustacean waste using the [Ch^+][Cl^-] : 2 MA DES was of commercial grade purity containing (0.74%±0.02) of ash and (1.53%±0.02) of proteins compared to lower amounts of ash and proteins using the [Ch^+][Cl^-] : 2 (1,4-BD) and [Ch^+][Cl^-] : 2 (1,6-HD) DESs, respectively.[56] As shown in Table 1, the hydrogen bond acidity was the highest for the [Ch^+][Cl^-] : 2 MA DES (1.06±0.15) at 40 ℃ compared to (0.44±0.09) for the [Ch^+][Cl^-] : 2 (1,4-BD) DES and (0.30±0.08) for the [Ch^+][Cl^-] : 2 (1,6-HD) DES.

4. Conclusions

Choline chloride-based DESs have become increasingly popular in catalysis, organic synthesis, and chemical separations due to their biodegradability and low cost of preparation.

Many different types of HBDs are known to form DESs with $[Ch^+][Cl^-]$ and $[Ch^+][Ace^-]$ salts resulting in solvents with varied solvation characteristics and physico-chemical properties. While previously reported methods have provided limited differentiation of solvation properties for DESs within the same class, the chromatographic approach employed in this study simultaneously measures various solute-solvent interactions for $[Ch^+][Cl^-]$ DESs.

Choline chloride-based DESs comprised of HBDs with shorter alkyl chain substituents and strong organic acids possessed lower hydrogen bond basicity and dispersive-type interactions as well as higher hydrogen bond acidity compared to those composed of various isomers of butane diol and hexane diol as HBDs. $[Ch^+][Ace^-]$ DESs possessed higher hydrogen bond basicity, dispersive-type, and dipolar interactions compared to those comprised of the $[Ch^+][Cl^-]$ HBA. These trends were further supported by the chromatographic retention of different types of probe molecules as both alcohols as well as probes with large aliphatic moieties retained longer on choline chloride and acetate-based DESs comprised of long alkyl chain substituents and alcohol HBDs. Interactions between alcohol probe molecules and $[Ch^+][Cl^-]$ DESs were also stronger when the molar ratio of HBD was increased. The chromatographic retention behavior of probe molecules revealed that the position of the hydroxyl substituent in various isomers of butane diol HBDs can influence hydrogen bonding interactions between DESs and alcohol probe molecules. System constants for the choline chloride class of DESs were used to understand their behavior in previously reported studies related to catalysis, organic synthesis, and chemical separations. This study demonstrates that the performance of $[Ch^+][Cl^-]$ DESs can be predicted on the basis of their multiple solvation interactions, which aids in providing a framework for the selection of DESs for particular applications.

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Supporting Information. List of chemicals and reagents, justification for k-means clustering, water content of DESs, melting point/glass transition temperatures of DESs, list of probe molecules and corresponding solute descriptors, retention factors of probe molecules on ammonium, choline chloride and acetate-based DES stationary phases, chromatographic separation of probe molecules on choline chloride and acetate-based DESs, and ^{1}H and ^{13}C NMR spectra for DESs evaluated in the study.

References

1 Á. Mourelle-Insua, I. Lavandera and V. Gotor-Fernández, *Green Chem.*, 2019, **21**, 2946–2951.

2 O. S. Hammond, D. T. Bowron and K. J. Edler, *Green Chem.*, 2016, **18**, 2736–2744.

3 W. M. A. Wan Mahmood, A. Lorwirachsutee, C. Theodoropoulos and M. Gonzalez-Miquel, *ACS Sustain. Chem. Eng.*, 2019, **7**, 5018–5026.

4 R. Craveiro, L. Meneses, L. Durazzo, Â. Rocha, J. M. Silva, R. L. Reis, S. Barreiros, A. R. C. Duarte and A. Paiva, *ACS Sustain. Chem. Eng.*, 2019, **7**, 19943–19950.

5 F. O. Farias, H. Passos, Á. S. Lima, M. R. Mafra and J. A. P. Coutinho, *ACS Sustain. Chem. Eng.*, 2017, **5**, 9402–9411.

6 D. Yang, M. Hou, H. Ning, J. Zhang, J. Ma, G. Yang and B. Han, *Green Chem.*, 2013, **15**, 2261–2265.

7 H. Wang, S. Liu, Y. Zhao, J. Wang and Z. Yu, *ACS Sustain. Chem. Eng.*, 2019, **7**, 7760–7767.

8 N. Yadav, K. Bhakuni, M. Bisht, I. Bahadur and P. Venkatesu, *ACS Sustain. Chem. Eng.*, 2020, **8**, 10151–10160.

9 L. Yi, J. Feng, W. Li and Z. Luo, *ACS Sustain. Chem. Eng.*, 2019, **7**, 7777–7783.

10 M. K. Tran, M. T. F. Rodrigues, K. Kato, G. Babu and P. M. Ajayan, *Nat. Energy*, 2019, **4**, 339–345.

11 S. Anggara, F. Bevan, R. C. Harris, J. M. Hartley, G. Frisch, G. R. T. Jenkin and A. P.

Abbott, *Green Chem.*, 2019, **21**, 6502–6512.

12 A. García, E. Rodríguez-Juan, G. Rodríguez-Gutiérrez, J. J. Rios and J. Fernández-Bolaños, *Food Chem.*, 2016, **197**, 554–561.

13 M. W. Nam, J. Zhao, M. S. Lee, J. H. Jeong and J. Lee, *Green Chem.*, 2015, **17**, 1718–1727.

14 S. K. Shukla and J. P. Mikkola, *Phys. Chem. Chem. Phys.*, 2018, **20**, 24591–24601.

15 C. Li, D. Li, S. Zou, Z. Li, J. Yin, A. Wang, Y. Cui, Z. Yao and Q. Zhao, *Green Chem.*, 2013, **15**, 2793–2799.

16 J. Yin, J. Wang, Z. Li, D. Li, G. Yang, Y. Cui, A. Wang and C. Li, *Green Chem.*, 2015, **17**, 4552–4559.

17 M. Marchel, A. S. Coroadinha and I. M. Marrucho, *ACS Sustain. Chem. Eng.*, 2020, **8**, 12400–12408.

18 H. Cruz, N. Jordão and L. C. Branco, *Green Chem.*, 2017, **19**, 1653–1658.

19 Y. Huang, Y. Wang, Q. Pan, Y. Wang, X. Ding, K. Xu, N. Li and Q. Wen, *Anal. Chim. Acta*, 2015, **877**, 90–99.

20 F. Gabriele, M. Chiarini, R. Germani, M. Tiecco and N. Spreti, *J. Mol. Liq.*, 2019, **291**, 111301.

21 R. Craveiro, I. Aroso, V. Flammia, T. Carvalho, M. T. Viciosa, M. Dionísio, S. Barreiros, R. L. Reis, A. R. C. Duarte and A. Paiva, *J. Mol. Liq.*, 2016, **215**, 534–540.

22 Z. Wei, X. Qi, T. Li, M. Luo, W. Wang, Y. Zu and Y. Fu, *Sep. Purif. Technol.*, 2015, **149**,

237–244.

23 Y. Huang, F. Feng, J. Jiang, Y. Qiao, T. Wu, J. Voglmeir and Z. G. Chen, *Food Chem.*, 2017, **221**, 1400–1405.

24 Y. Dai, G. J. Witkamp, R. Verpoorte and Y. H. Choi, *Food Chem.*, 2015, **187**, 14–19.

25 C. Florindo, F. S. Oliveira, L. P. N. Rebelo, A. M. Fernandes and I. M. Marrucho, *ACS Sustain. Chem. Eng.*, 2014, **2**, 2416–2425.

26 A. Alhadid, L. Mokrushina and M. Minceva, *Molecules*, 2020, **25**, 1–11.

27 Y. Yuan, S. Hong, H. Lian, K. Zhang and H. Liimatainen, *Carbohydr. Polym.*, 2020, **236**, 116095.

28 A. R. R. Teles, E. V. Capela, R. S. Carmo, J. A. P. Coutinho, A. J. D. Silvestre and M. G. Freire, *Fluid Phase Equilib.*, 2017, **448**, 15–21.

29 C. Florindo, A. J. S. McIntosh, T. Welton, L. C. Branco and I. M. Marrucho, *Phys. Chem. Chem. Phys.*, 2017, **20**, 206–213.

30 A. P. Abbott, R. C. Harris, K. S. Ryder, C. D'Agostino, L. F. Gladden and M. D. Mantle, *Green Chem.*, 2011, **13**, 82–90.

31 A. Pandey, R. Rai, M. Pal and S. Pandey, *Phys. Chem. Chem. Phys.*, 2014, **16**, 1559–1568.

32 A. Pandey and S. Pandey, *J. Phys. Chem. B*, 2014, **118**, 14652–14661.

33 A. K. Dwamena and D. E. Raynie, *J. Chem. Eng. Data*, 2020, **65**, 640–646.

34 R. Martínez, L. Berbegal, G. Guillena and D. J. Ramón, *Green Chem.*, 2016, **18**, 1724–

1730.

35 S. H. Kim, S. Park, H. Yu, J. H. Kim, H. J. Kim, Y. H. Yang, Y. H. Kim, K. J. Kim, E. Kan and S. H. Lee, *J. Mol. Catal. B Enzym.*, 2016, **128**, 65–72.

36 E. Massolo, S. Palmieri, M. Benaglia, V. Capriati and F. M. Perna, *Green Chem.*, 2016, **18**, 792–797.

37 P. Zhou, J. Li, T. Yan, X. Wang, J. Huang, Z. Kuang, M. Ye and M. Pan, *Carbohydr. Polym.*, 2019, **225**, 115255.

38 C. F. Poole and S. K. Poole, *J. Chromatogr. A*, 2002, **965**, 263–299.

39 M. Q. Farooq, G. A. Odugbesi, N. M. Abbasi and J. L. Anderson, *ACS Sustain. Chem. Eng.*, 2020, **8**, 18286–18296.

40 J. Bouche and M. Verzele, *J. Chromatogr. Sci.*, 1968, **6**, 501.

41 J. Palomar, M. Gonzalez-Miquel, J. Bedia, F. Rodriguez and J. J. Rodriguez, *Sep. Purif. Technol.*, 2011, **82**, 43–52.

42 W. Bi, M. Tian and K. H. Row, *J. Chromatogr. A*, 2013, **1285**, 22–30.

43 M. H. Abraham, W. E. Acree, A. F. Fucaloro and A. W. Zanella, *New J. Chem.*, 2017, **41**, 14259–14265.

44 H. C. Hu, Y. H. Liu, B. Le Li, Z. S. Cui and Z. H. Zhang, *RSC Adv.*, 2015, **5**, 7720–7728.

45 J. L. Anderson, J. Ding, T. Welton and D. W. Armstrong, *J. Am. Chem. Soc.*, 2002, **124**, 14247–14254.

46 H. R. Lobo, B. S. Singh and G. S. Shankarling, *Green Chem. Lett. Rev.*, 2012, **5**, 487–533.

47 M. Dabiri, P. Salehi, M. Baghbanzadeh, M. Shakouri, S. Otokesh, T. Ekrami and R. Doosti, *J. Iran. Chem. Soc.*, 2007, **4**, 393–401.

48 A. P. Abbott, G. Capper, D. L. Davies, K. J. McKenzie and S. U. Obi, *J. Chem. Eng. Data*, 2006, **51**, 1280–1282.

49 A. Söldner, J. Zach and B. König, *Green Chem.*, 2019, **21**, 321–328.

50 M. Karimi, S. Dadfarnia, A. M. H. Shabani, F. Tamaddon and D. Azadi, *Talanta*, 2015, **144**, 648–654.

51 X. Peng, M. H. Duan, X. H. Yao, Y. H. Zhang, C. J. Zhao, Y. G. Zu and Y. J. Fu, *Sep. Purif. Technol.*, 2016, **157**, 249–257.

52 B. Xia, D. Yan, Y. Bai, J. Xie, Y. Cao, D. Liao and L. Lin, *Anal. Methods*, 2015, **7**, 9354–9364.

53 Y. Liu, W. Chen, Q. Xia, B. Guo, Q. Wang, S. Liu, Y. Liu, J. Li and H. Yu, *ChemSusChem*, 2017, **10**, 1692–1700.

54 C. W. Zhang, S. Q. Xia and P. S. Ma, *Bioresour. Technol.*, 2016, **219**, 1–5.

55 P. Zhu, Z. Gu, S. Hong and H. Lian, *Carbohydr. Polym.*, 2017, **177**, 217–223.

56 P. S. Saravana, T. C. Ho, S. J. Chae, Y. J. Cho, J. S. Park, H. J. Lee and B. S. Chun, *Carbohydr. Polym.*, 2018, **195**, 622–630.

Table 1. System constants for DESs comprised of [Ch^+][Cl^-] and [Ch^+][Ace^-] salts as HBAs and various HBDs (TEG, 1,4-BD, 1,3-BD, 2,3-BD, 1,6-HD, MA, LvA, U, Ace, and Iso). See Figure 1 for names, explanation of abbreviations, and chemical structures of all HBAs and HBDs.

No.	DES	Temp. (°C)	System constants								
			c	*e*	*s*	*a*	*b*	*l*	*n* [a]	R^2 [b]	*F* [c]
1	[Ch^+][Cl^-] : 3 TEG	30	-3.36 (0.07)	0.19 (0.07)	2.55 (0.08)	5.00 (0.13)	0 (0)	0.57 (0.02)	36	0.99	1019
		40	-3.37 (0.06)	0.19 (0.06)	2.47 (0.07)	4.73 (0.12)	0 (0)	0.53 (0.01)	36	0.99	1123
		50	-3.38 (0.06)	0.20 (0.06)	2.37 (0.07)	4.50 (0.12)	0 (0)	0.50 (0.01)	36	0.99	1087
2	[Ch^+][Cl^-] : 4 TEG	30	-3.21 (0.06)	0.12 (0.06)	2.46 (0.08)	4.87 (0.12)	0 (0)	0.61 (0.02)	37	0.99	1071
		40	-3.21 (0.06)	0.13 (0.06)	2.36 (0.07)	4.59 (0.11)	0 (0)	0.57 (0.01)	37	0.99	1114
		50	-3.22 (0.06)	0.11 (0.06)	2.29 (0.08)	4.33 (0.12)	0 (0)	0.54 (0.02)	37	0.99	900
3	[Ch^+][Cl^-] : (1,4-BD)	30	-3.39 (0.06)	0.22 (0.06)	2.38 (0.07)	5.10 (0.12)	0.31 (0.10)	0.53 (0.02)	36	0.99	1168
		40	-3.49 (0.05)	0.24 (0.06)	2.36 (0.07)	4.96 (0.11)	0.30 (0.09)	0.49 (0.01)	36	0.99	1267
		50	-3.52 (0.06)	0.25 (0.07)	2.35 (0.07)	4.82 (0.12)	0.27 (0.10)	0.45 (0.02)	36	0.99	991
4	[Ch^+][Cl^-] : 2 (1,4-BD)	30	-3.41 (0.06)	0.22 (0.06)	2.45 (0.07)	5.26 (0.11)	0.47 (0.10)	0.53 (0.02)	35	0.99	1334
		40	-3.41 (0.05)	0.24 (0.06)	2.39 (0.07)	5.04 (0.11)	0.44 (0.09)	0.49 (0.01)	36	0.99	1389
		50	-3.38 (0.05)	0.25 (0.05)	2.32 (0.06)	4.77 (0.10)	0.41 (0.08)	0.45 (0.01)	35	0.99	1467
5	[Ch^+][Cl^-] : 3 (1,4-BD)	30	-3.47 (0.06)	0.10 (0.06)	2.41 (0.07)	5.31 (0.11)	0.49 (0.09)	0.60 (0.01)	37	0.99	1521
		40	-3.56 (0.06)	0.11 (0.06)	2.38 (0.07)	5.13 (0.12)	0.49 (0.10)	0.56 (0.01)	37	0.99	1224
		50	-3.58 (0.06)	0.13 (0.06)	2.34 (0.07)	4.91 (0.12)	0.47 (0.10)	0.53 (0.01)	36	0.99	1151
6	[Ch^+][Cl^-] : 4 (1,4-BD)	30	-3.44 (0.05)	0 (0)	2.29 (0.06)	5.18 (0.10)	0.44 (0.08)	0.64 (0.01)	36	0.99	1716
		40	-3.36 (0.06)	0 (0)	2.26 (0.07)	4.97 (0.12)	0.37 (0.10)	0.58 (0.01)	37	0.99	1120
		50	-3.48 (0.06)	0 (0)	2.20 (0.07)	4.76 (0.11)	0.40 (0.09)	0.56 (0.01)	37	0.99	1154
		30	-3.52 (0.05)	0.09 (0.06)	2.35 (0.06)	5.17 (0.10)	0.29 (0.09)	0.58 (0.01)	35	0.99	1572

7	$[Ch^+][Cl^-]$: 2 (1,3-BD)	40	-3.62 (0.06)	0.15 (0.06)	2.35 (0.07)	5.03 (0.11)	0.36 (0.10)	0.55 (0.02)	35	0.99	1216
		50	-3.52 (0.06)	0.08 (0.06)	2.32 (0.07)	4.90 (0.11)	0.25 (0.09)	0.53 (0.01)	36	0.99	1234
8	$[Ch^+][Cl^-]$: 2 (2,3-BD)	30	-3.35 (0.06)	0.17 (0.06)	2.41 (0.07)	5.19 (0.11)	0.42 (0.09)	0.55 (0.02)	36	0.99	1385
		40	-3.35 (0.06)	0.18 (0.06)	2.33 (0.07)	4.92 (0.11)	0.40 (0.09)	0.51 (0.01)	36	0.99	1301
		50	-3.41 (0.06)	0.19 (0.06)	2.31 (0.07)	4.74 (0.11)	0.38 (0.09)	0.48 (0.02)	36	0.99	1151
9	$[Ch^+][Cl^-]$: 2 (1,6-HD)	30	-3.28 (0.06)	0 (0)	2.18 (0.07)	5.18 (0.11)	0.29 (0.09)	0.69 (0.01)	38	0.99	1424
		40	-3.28 (0.05)	0 (0)	2.11 (0.06)	4.89 (0.09)	0.30 (0.08)	0.63 (0.01)	38	0.99	1720
		50	-3.28 (0.05)	0 (0)	2.09 (0.06)	4.67 (0.09)	0.28 (0.08)	0.58 (0.01)	38	0.99	1632
10	$[Ch^+][Cl^-]$: 4 (1,6-HD)	30	-3.25 (0.06)	0 (0)	2.23 (0.07)	5.19 (0.10)	0.33 (0.09)	0.73 (0.02)	38	0.99	797
		40	-3.27 (0.06)	0 (0)	2.16 (0.06)	4.91 (0.09)	0.31 (0.08)	0.68 (0.01)	38	0.99	854
		50	-3.29 (0.05)	0 (0)	2.11 (0.06)	4.59 (0.09)	0.29 (0.08)	0.61 (0.01)	38	0.99	652
11	$[Ch^+][Cl^-]$: 2 LvA	30	-3.32 (0.06)	0.27 (0.06)	2.59 (0.07)	4.79 (0.11)	0.37 (0.09)	0.50 (0.02)	37	0.99	1151
		40	-3.34 (0.05)	0.22 (0.06)	2.54 (0.07)	4.50 (0.11)	0.34 (0.09)	0.47 (0.02)	37	0.99	1306
		50	-3.32 (0.05)	0.26 (0.05)	2.44 (0.06)	4.21 (0.10)	0.36 (0.08)	0.43 (0.01)	37	0.99	1525
12	$[Ch^+][Cl^-]$: MA	30	-3.37 (0.09)	0.39 (0.10)	2.74 (0.10)	4.70 (0.16)	0.72 (0.16)	0.34 (0.02)	29	0.99	501
		40	-3.24 (0.08)	0.44 (0.09)	2.54 (0.10)	4.23 (0.16)	0.72 (0.15)	0.28 (0.02)	29	0.99	452
		50	-3.07 (0.08)	0.46 (0.09)	2.33 (0.09)	3.76 (0.15)	0.71 (0.14)	0.24 (0.02)	29	0.99	406
13	$[Ch^+][Cl^-]$: 2 MA	30	-3.82 (0.09)	0.34 (0.10)	2.69 (0.12)	4.80 (0.17)	1.31 (0.17)	0.42 (0.02)	31	0.99	610
		40	-3.63 (0.08)	0.31 (0.09)	2.64 (0.09)	4.50 (0.15)	1.06 (0.15)	0.36 (0.02)	31	0.99	556
		50	-3.68 (0.08)	0.32 (0.09)	2.59 (0.09)	4.36 (0.15)	1.02 (0.15)	0.33 (0.02)	31	0.99	544
14	$[Ch^+][Cl^-]$: 2 Ace	30	-3.48 (0.07)	0.22 (0.09)	2.21 (0.10)	4.80 (0.15)	0.46 (0.13)	0.52 (0.02)	34	0.99	661
		40	-3.49 (0.07)	0.25 (0.08)	2.16 (0.09)	4.61 (0.14)	0.47 (0.12)	0.48 (0.02)	34	0.99	710

		50	-3.42 (0.06)	0.27 (0.07)	2.18 (0.08)	4.45 (0.12)	0.47 (0.11)	0.43 (0.02)	34	0.99	808
15	$[Ch^+][Cl^-]$: 2 U	30	-3.56 (0.14)	0.49 (0.15)	2.43 (0.16)	4.38 (0.25)	0.90 (0.23)	0.34 (0.04)	32	0.98	185
		40	-3.12 (0.11)	0.51 (0.12)	2.16 (0.13)	3.58 (0.20)	1.05 (0.18)	0.23 (0.03)	32	0.98	217
		50	-2.65 (0.10)	0.56 (0.10)	1.81 (0.11)	2.89 (0.18)	0.84 (0.15)	0.16 (0.02)	31	0.98	202
16	$[Ch^+][Cl^-]$: 2 Iso	30	-3.81 (0.07)	0.38 (0.08)	2.76 (0.09)	4.97 (0.14)	0.64 (0.12)	0.46 (0.02)	34	0.99	970
		40	-3.56 (0.06)	0.35 (0.07)	2.60 (0.08)	4.54 (0.12)	0.51 (0.10)	0.40 (0.02)	34	0.99	1065
		50	-3.68 (0.07)	0.42 (0.07)	2.53 (0.09)	4.35 (0.13)	0.59 (0.12)	0.37 (0.02)	34	0.99	820
17	$[Ch^+][Ace^-]$: 4 (1,4-BD)	30	-3.38 (0.05)	0 (0)	2.28 (0.07)	5.51 (0.10)	0.37 (0.09)	0.64 (0.01)	35	0.99	1585
		40	-3.36 (0.05)	0 (0)	2.19 (0.07)	5.18 (0.10)	0.40 (0.08)	0.59 (0.01)	36	0.99	1456
		50	-3.38 (0.05)	0 (0)	2.13 (0.06)	4.90 (0.10)	0.39 (0.08)	0.56 (0.01)	35	0.99	1318
18	$[Ch^+][Ace^-]$: 4 TEG	30	-3.08 (0.07)	0 (0)	2.25 (0.09)	5.13 (0.13)	0 (0)	0.70 (0.01)	34	0.99	882
		40	-3.09 (0.06)	0 (0)	2.18 (0.07)	4.84 (0.11)	0 (0)	0.65 (0.01)	35	0.99	1119
		50	-3.11 (0.05)	0 (0)	2.12 (0.07)	4.59 (0.10)	0 (0)	0.61 (0.01)	35	0.99	1203

[a] *n*, number of probes subjected to multiple linear regression analysis; [b] R^2, correlation coefficient;
[c] *F*, Fisher F-statistic

Table 2. System constants for DESs comprised of $[N_{4444}^+][Cl^-]$ salt as HBA and TEG and Gly HBDs. See Figure 1 for names, explanation of abbreviations, and chemical structures of all HBAs and HBDs.

No.	DES	Temp. (°C)	System constants								
			c	*e*	*s*	*a*	*b*	*l*	*n* [a]	R^2 [b]	*F* [c]
19	4 $[N_{4444}^+][Cl^-]$: TEG	30	-3.38 (0.09)	-0.23 (0.09)	2.76 (0.12)	7.99 (0.18)	-0.46 (0.15)	0.81 (0.02)	35	0.99	815
		40	-3.36 (0.09)	-0.18 (0.08)	2.63 (0.11)	7.57 (0.16)	-0.46 (0.13)	0.76 (0.02)	35	0.99	905
		50	-3.38 (0.08)	-0.17 (0.07)	2.56 (0.10)	7.23 (0.14)	-0.47 (0.12)	0.71 (0.02)	35	0.99	1003
20	3 $[N_{4444}^+][Cl^-]$: TEG	30	-3.32 (0.08)	-0.18 (0.08)	2.72 (0.10)	7.75 (0.16)	-0.46 (0.13)	0.79 (0.02)	35	0.99	1006
		40	-3.34 (0.07)	-0.17 (0.07)	2.64 (0.09)	7.37 (0.14)	-0.45 (0.12)	0.75 (0.02)	35	0.99	1124
		50	-3.30 (0.07)	-0.12 (0.07)	2.51 (0.08)	6.95 (0.13)	-0.45 (0.11)	0.70 (0.02)	35	0.99	1237
21	2 $[N_{4444}^+][Cl^-]$: TEG	30	-3.33 (0.08)	-0.19 (0.08)	2.69 (0.10)	7.30 (0.15)	-0.42 (0.12)	0.79 (0.02)	35	0.99	1052
		40	-3.30 (0.07)	-0.17 (0.07)	2.57 (0.09)	6.92 (0.13)	-0.44 (0.11)	0.75 (0.02)	35	0.99	1194
		50	-3.32 (0.07)	-0.13 (0.06)	2.48 (0.08)	6.58 (0.12)	-0.42 (0.10)	0.70 (0.02)	35	0.99	1190
22	$[N_{4444}^+][Cl^-]$: TEG	30	-3.24 (0.06)	-0.11 (0.06)	2.59 (0.08)	6.25 (0.11)	-0.32 (0.10)	0.75 (0.01)	35	0.99	1460
		40	-3.24 (0.06)	-0.10 (0.05)	2.51 (0.07)	5.93 (0.10)	-0.31 (0.09)	0.71 (0.01)	35	0.99	1603
		50	-3.22 (0.05)	-0.06 (0.05)	2.38 (0.07)	5.56 (0.10)	-0.29 (0.09)	0.66 (0.01)	35	0.99	1508
23	$[N_{4444}^+][Cl^-]$: 3 Gly	30	-3.41 (0.05)	0.12 (0.05)	2.41 (0.06)	5.08 (0.09)	0.17 (0.08)	0.66 (0.01)	35	0.99	1945
		40	-3.41 (0.05)	0.12 (0.04)	2.35 (0.06)	4.81 (0.09)	0.17 (0.07)	0.61 (0.01)	35	0.99	2031
		50	-3.41 (0.04)	0.12 (0.04)	2.27 (0.05)	4.53 (0.08)	0.16 (0.07)	0.58 (0.01)	35	0.99	2219
24	$[N_{4444}^+][Cl^-]$: 4 Gly	30	-3.26 (0.05)	0.11 (0.06)	2.20 (0.07)	4.76 (0.10)	0.28 (0.09)	0.64 (0.01)	34	0.99	1519
		40	-3.25 (0.04)	0.14 (0.05)	2.12 (0.05)	4.45 (0.08)	0.30 (0.07)	0.59 (0.01)	34	0.99	2112
		50	-3.22 (0.04)	0.17 (0.05)	2.03 (0.05)	4.15 (0.08)	0.28 (0.07)	0.54 (0.01)	34	0.99	1831
25	$[N_{4444}^+][Cl^-]$: 5 Gly	30	-3.48 (0.05)	0.24 (0.05)	2.36 (0.06)	4.90 (0.09)	0.57 (0.08)	0.58 (0.01)	36	0.99	1904
		40	-3.47	0.23	2.30	4.61	0.55	0.54	36	0.99	1716

		(0.05)	(0.05)	(0.06)	(0.09)	(0.08)	(0.01)			
	50	-3.56	0.20	2.28	4.46	0.51	0.51	36	0.99	1584
		(0.05)	(0.05)	(0.06)	(0.10)	(0.08)	(0.01)			

[a] *n*, number of probes subjected to multiple linear regression analysis; [b] R^2, correlation coefficient;
[c] *F*, Fisher F-statistic

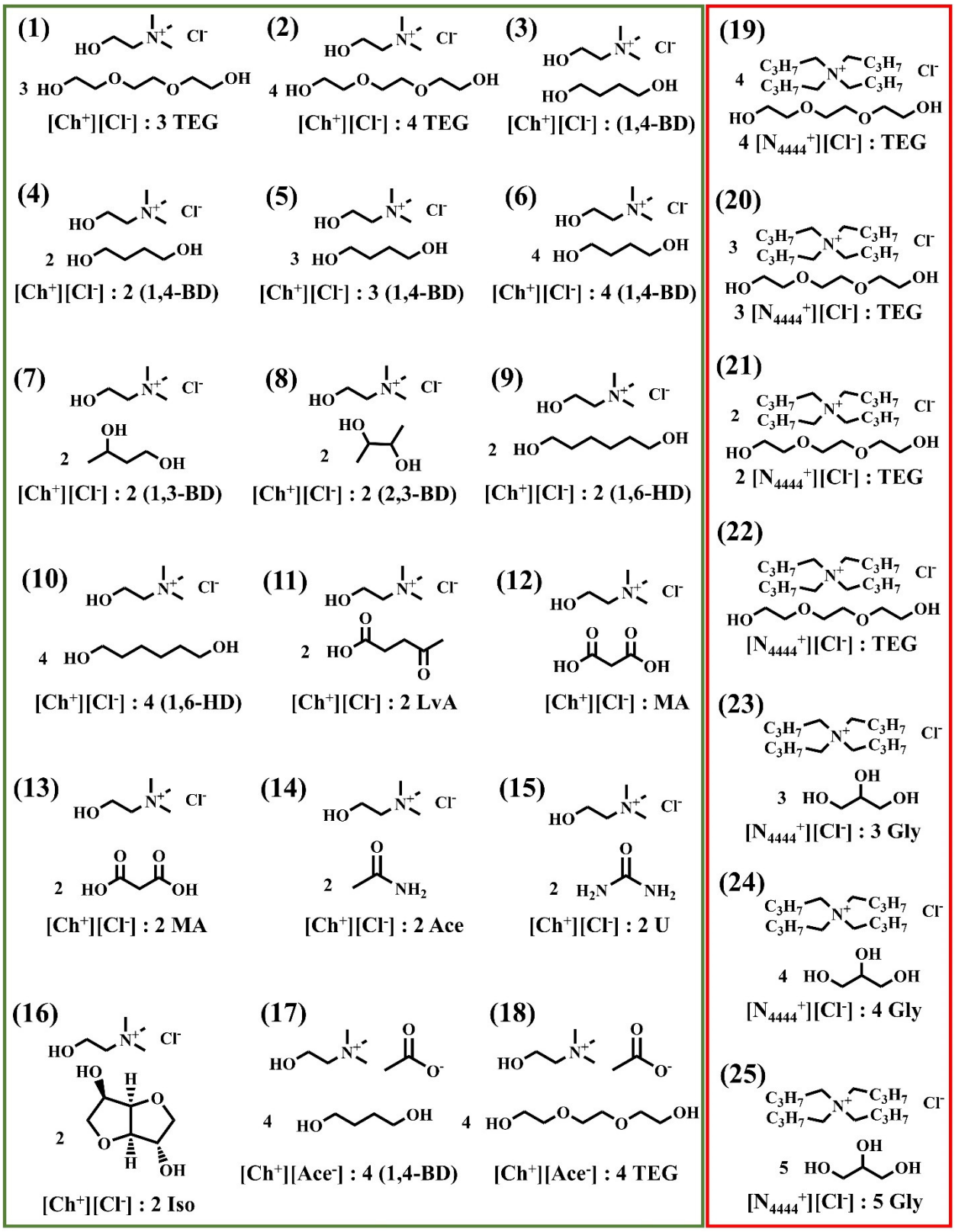


Figure 1: Chemical structures, abbreviations, and numbering scheme used for the DESs examined in this study. Abbreviations: triethylene glycol (TEG); 1,4-butane diol (1,4-BD); 1,3-butane diol

(1,3-BD); 2,3-butane diol (2,3-BD); 1,6-hexane diol (1,6-HD); levulinic acid (LvA); malonic acid (MA); acetamide (Ace); urea (U); isosorbide (Iso); glycerol (Gly); choline chloride ($[Ch^+][Cl^-]$); choline acetate ($[Ch^+][Ace^-]$); and tetrabutylammonium chloride ($[N_{4444}^+][Cl^-]$).

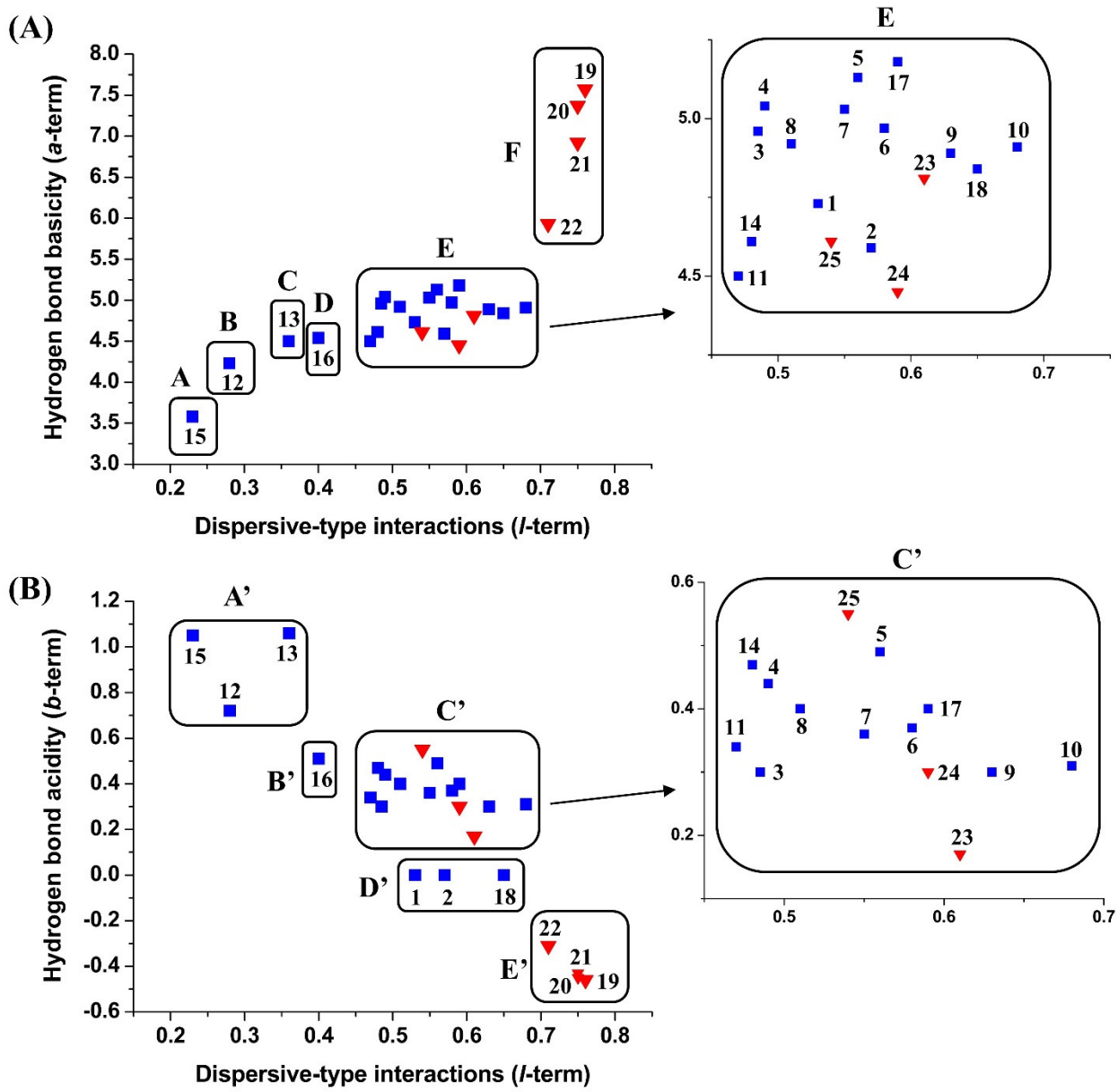


Figure 2: Plot illustrating the relation of (A) hydrogen bond basicity versus dispersive-type interactions and (B) hydrogen bond acidity versus dispersive-type interactions at 40 °C for the 25 DESs evaluated in this study and grouped together using *k*-means clustering. $[N_{4444}^+][Cl^-]$ DESs are represented by (▼) and $[Ch^+][Cl^-]$ and $[Ch^+][Ace^-]$ DESs are represented by (■). **1**, $[Ch^+][Cl^-]$: 3 TEG; **2**, $[Ch^+][Cl^-]$: 4 TEG; **3**, $[Ch^+][Cl^-]$: (1,4-BD); **4**, $[Ch^+][Cl^-]$: 2 (1,4-BD); **5**, $[Ch^+][Cl^-]$: 3 (1,4-BD); **6**, $[Ch^+][Cl^-]$: 4 (1,4-BD); **7**, $[Ch^+][Cl^-]$: 2 (1,3-BD); **8**, $[Ch^+][Cl^-]$: 2 (2,3-BD); **9**, $[Ch^+][Cl^-]$: 2 (1,6-HD); **10**, $[Ch^+][Cl^-]$: 4 (1,6-HD); **11**, $[Ch^+][Cl^-]$: 2 LvA; **12**, $[Ch^+][Cl^-]$: MA; **13**, $[Ch^+][Cl^-]$: 2 MA; **14**, $[Ch^+][Cl^-]$: 2 Ace; **15**, $[Ch^+][Cl^-]$: 2 U; **16**, $[Ch^+][Cl^-]$: 2 Iso; **17**, $[Ch^+][Ace^-]$: 4 (1,4-BD); **18**, $[Ch^+][Ace^-]$: 4 TEG; **19**, 4 $[N_{4444}^+][Cl^-]$: TEG; **20**, 3 $[N_{4444}^+][Cl^-]$: TEG; **21**, 2 $[N_{4444}^+][Cl^-]$: TEG; **22**, $[N_{4444}^+][Cl^-]$: TEG; **23**, $[N_{4444}^+][Cl^-]$: 3 Gly; **24**, $[N_{4444}^+][Cl^-]$: 4 Gly; and **25**, $[N_{4444}^+][Cl^-]$: 5 Gly.

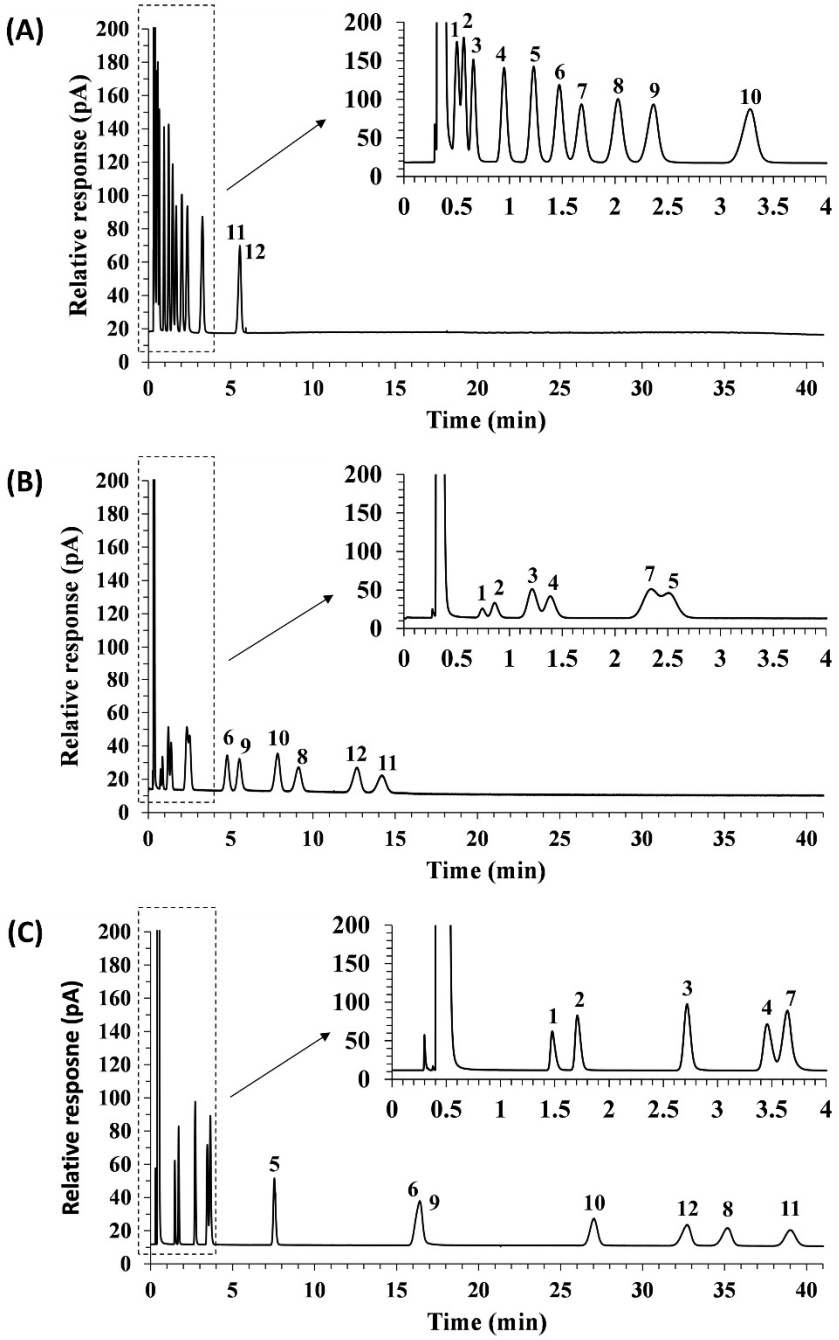


Figure 3: Chromatographic separation of 12 probe molecules on the (A) $[Ch^+][Cl^-]$: 2 MA, (B) $[Ch^+][Cl^-]$: 2 (1,6-HD), and (C) $[N_{4444}^+][Cl^-]$: TEG DES stationary phases at 50 °C. Analytes: 1, methanol; 2, ethanol; 3, 2-butanol; 4, 1-propanol; 5, 1-butanol; 6, 1-pentanol; 7, cyclohexanone; 8, 1-hexanol; 9, benzaldehyde; 10, benzonitrile; 11, cyclohexanol; and 12, acetophenone.

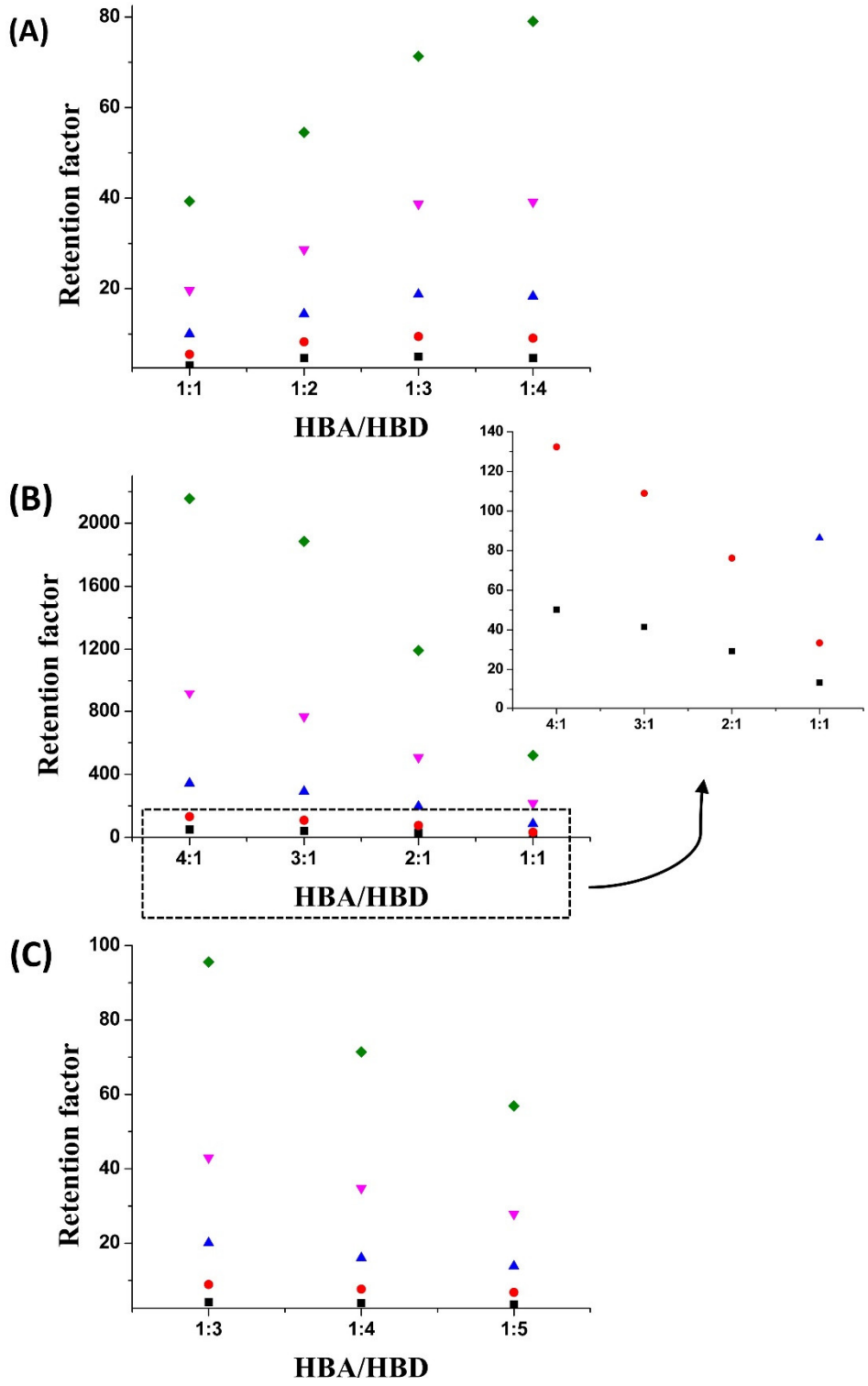
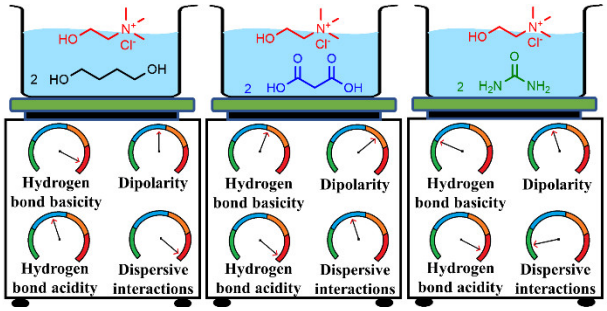


Figure 4: Plot illustrating the change in retention factor of straight-chain alcohols at 30 ℃ as a function of HBA/HBD molar ratio for (A) DES system comprised of $[Ch^+][Cl^-]$ HBA and 1,4-BD HBD, (B) DES system composed of $[N_{4444}^+][Cl^-]$ HBA and TEG HBD, and (C) DES system comprised of $[N_{4444}^+][Cl^-]$ HBA and Gly HBD. Analytes: ethanol (▪), 1-propanol (•), 1-butanol (▲), 1-pentanol (▼), and 1-hexanol (◆).

TOC Image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N+
Cl-
2 HO
OH
Hydrogen bond basicity
Dipolarity
Hydrogen bond acidity
Dispersive interactions
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Cl-
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Hydrogen bond basicity
Dipolarity
Hydrogen bond acidity
Dispersive interactions
HO
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Hydrogen bond basicity
Dipolarity
Hydrogen bond acidity
Dispersive interactions