

The Entropy of Deep Eutectic Solvent Formation

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Abstract: The standard entropies $S_{298^\circ\text{E}}$ of deep eutectic solvents (DESs), which are liquid binary mixtures of a hydrogen bond acceptor component and a hydrogen bond donor one, are calculated from their molecular volumes, derived from their densities or crystal structures. These values are compared with those of the components—pro-rated according to the DES composition—to obtain the standard entropies of DES formation $\Delta_f S$. These quantities are positive, due to the increased number and kinds of hydrogen bonds present in the DESs relative to those in the components. The $\Delta_f S$ values are also compared with the freezing point depressions of the DESs $\Delta_{\text{fus}} T/\text{K}$, but no general conclusions on their mutual relationship could be drawn.

Keywords: deep eutectic solvent (DES); molecular volume; standard entropy; hydrogen bonding

1. Introduction

Deep eutectic solvents (DESs) are a response to the search for neoteric reaction media that are “green” and readily made from inexpensive ingredients. Such solvents should conform to the requirements from “green” solvents, namely, that waste is prevented in their synthesis and processing, no toxic materials should result from the process, materials or processes that are hazardous are avoided, renewable feedstock are preferred, catalysts are preferable to stoichiometric reagents, and degradable products and reagents are preferred, as are minimal quantities of recyclable solvents.

DESs are binary mixtures that are liquid at ambient conditions and freeze (or form glasses) at temperatures considerably below those at which the ingredients do. They exhibit a network of hydrogen bonds between an acceptor (generally a salt, but not necessarily) and a donor, and are able to dissolve a great variety of solutes. The question arises as to why these eutectics have such relatively low freezing (glass formation) points. Examples of the freezing point depression of DESs relative to the composition-pro-rated values of the components are the 1:2 eutectic of choline chloride and urea, $\Delta_{\text{fus}} T/\text{K} = 178$ [1] and the 1:1 eutectic of lithium iodide dihydrate and water, $\Delta_{\text{fus}} T/\text{K} = 116$ [2]. A partial answer, at least, to this query that has been suggested is the significant impact of the many different types of H-bonds existing in the DESs that could be expected to increase the entropy of the system, and thus favor eutectic formation [3].

In the present study the standard entropies of DESs at 298.15 K and ambient pressure are calculated from data in the literature and compared with those of the components, pro-rated according to the DES composition, to obtain the standard entropies of formation $\Delta_f S$.

The question of whether and how the entropies of formation of the DESs affect the melting properties of the DESs is explored.

2. The Data

The standard molar entropies of a DES (subscript _E) relative to its hydrogen bond acceptor (subscript _A) and donor (subscript _D) components can be estimated from their molecular volumes according to Jenkins and Glasser [4–7]. This method has been applied by some authors to the

DESs [8,9] and is used in the present paper, too. The molecular volumes are obtained from the densities according to

$$M/\rho N_A = 1.6605 \times 10^{-3} [(M/\text{g mol}^{-1})/(\rho/\text{g cm}^{-3})] = v_m/\text{nm}^3 \quad (1)$$

where M is the molar mass of the DES or its component, ρ is its density, and v_m is its molecular (formula unit) volume. DESs are treated as ionic liquids and, following Glasser [6], the expression employed for its standard molar entropy at 298.15 K and ambient pressure, $S_{298^\circ\text{E}}$, is

$$S_{298^\circ\text{E}}/\text{J K}^{-1} \text{ mol}^{-1} = 1246.5(v_{m\text{E}}/\text{nm}^3) + 29.5 \quad (2)$$

The freezing points and the densities at 298.15 K of the DESs are taken from the author's book [2] where they are annotated. For organic components that are solid at 298 K, the standard molar entropy is, according to Glasser and Jenkins [5],

$$S_{298^\circ}/\text{J K}^{-1} \text{ mol}^{-1} = (774 \pm 21)(v_m/\text{nm}^3) + (57 \pm 6) \quad (3)$$

whereas for liquid components the values are [5]

$$S_{298^\circ}/\text{J K}^{-1} \text{ mol}^{-1} = (1133 \pm 7)(v_m/\text{nm}^3) + (44 \pm 2) \quad (4)$$

Hence, for the components before forming the eutectic solvent the sum of the entropies is

$$\Sigma_{\text{A+D}} S_{298^\circ}/\text{J K}^{-1} \text{ mol}^{-1} = x_{\text{A}} S_{198^\circ\text{A}}/\text{J K}^{-1} \text{ mol}^{-1} + x_{\text{D}} S_{198^\circ\text{D}}/\text{J K}^{-1} \text{ mol}^{-1} \quad (5)$$

The crucial quantity for the calculation of the entropy of a component of the DES is its density ρ , from which its molecular volume v_m is derived in the manner of Equation (2). The densities and temperatures of fusion of some of the components of the DESs, not available in the Handbook [10], are from [11–17]. The crystal structures of some of the components, from which the molecular volumes are calculated as $v_m = v_{\text{uc}}/Z$, where v_{uc} is the unit cell volume and Z the number of formula units per unit cell, are from [18–24]. In the cases of unconventional DESs based on salt hydrates and water as components [25], the standard molar entropy of the DES is calculated using Equations (1) and (2) as for the conventional ones, but for the solid hydrates the value of $v_{m\text{A}}$ is better obtained from the unit cell volumes of the crystalline salt hydrates per formula unit [26] rather than from the salt density. For the salt hydrate/water DESs the standard molar entropy of the hydrogen bond donor liquid water at 298.15 K is $69.91 \text{ J K}^{-1} \text{ mol}^{-1}$ [27]. The standard entropies of formation of the DES are then calculated by

$$\Delta_{\text{f}}S = S_{298^\circ\text{E}} - \Sigma_{\text{A+D}} S_{298^\circ\text{E}} \quad (6)$$

The freezing point depression of a DES relative to its hydrogen bond acceptor and donor components is

$$\Delta_{\text{fus}}T/\text{K} = x_{\text{A}}(T_{\text{fusA}}/\text{K}) + x_{\text{D}}(T_{\text{fusD}}/\text{K}) - T_{\text{fusE}}/\text{K} \quad (7)$$

Note that the difference in Equation (7) has the opposite form from that in Equation (6) in order to have positive values for the depression.

Table 1 is a representative list of the compositions of conventional deep eutectic solvents consisting of a quaternary ammonium salt hydrogen bond acceptor with a polyol, amide, or carboxylic acid hydrogen bond donor. Also listed are the mole fractions of the hydrogen bond accepting component, x_{A} ; the temperature of fusion of the eutectic, T_{fus} ; the freezing point depression according to Equation (7), $\Delta_{\text{fus}}T$; the molecular volume according to Equation (2), $v_{m\text{E}}$; the molar entropy, S_{E} ; the entropy sum of the ingredients according to Equation (6), $\Sigma_{\text{A+D}}S$; and the molar entropy change on formation, $\Delta_{\text{f}}S$. Although DESs based on quaternary phosphonium salts with various hydrogen bond donors are an important class of conventional DESs, no density or crystal structure data for their hydrogen bond

acceptor components could be found; hence, they are not included in Table 1. Table 2 is a similar list for unconventional DESs consisting of a zwitterionic or a hydroxylic acceptor and a carboxylic acid donor or DESs consisting of a salt hydrate with water.

Table 1. Representative conventional deep eutectic solvents: their composition, x_A ; temperature of fusion, T_{fus} ; freezing point depression, $\Delta_{fus}T$; molecular volume, v_m ; molar entropy, S_E ; the entropy sum of the ingredients, $\Sigma_{A+D}S$; and the molar entropy change on formation, $\Delta_f S$.

| HB Acceptor | HB Donor | x_A | T_{fus}/K | $\Delta_{fus}T/K$ | v_m/nm^3 | $S_E/J\ K^{-1}\ mol^{-1}$ | $\Sigma_{A+D}S/J\ K^{-1}\ mol^{-1}$ | $\Delta_f S/J\ K^{-1}\ mol^{-1}$ |
|------------------------|--------------------|-------|-------------|-------------------|------------|---------------------------|-------------------------------------|----------------------------------|
| Choline chloride | urea | 0.333 | 285 | 178 | 0.3599 | 452 | 145 | 307 |
| | trifluoroacetamide | 0.333 | 229 | 193 | 0.4088 | 507 | 173 | 334 |
| | ethylene glycol | 0.333 | 207 | 158 | 0.3921 | 488 | 167 | 321 |
| | glycerol | 0.333 | 233 | 153 | 0.4510 | 549 | 189 | 360 |
| | glucose | 0.667 | 288 | 235 | 0.5569 | 675 | 205 | 469 |
| | phenol | 0.250 | 253 | 126 | 0.6414 | 771 | 180 | 591 |
| | o-cresol | 0.250 | 249 | 123 | 0.6759 | 810 | 193 | 617 |
| | levulinic acid | 0.250 | 262 | 113 | 0.7188 | 851 | 192 | 659 |
| | malonic acid | 0.500 | 217 | 276 | 0.2889 | 371 | 172 | 199 |
| Tetramethylammonium Cl | lactic acid | 0.333 | 204 | 246 | 0.4217 | 555 | 154 | 401 |
| | lactic acid | 0.333 | 204 | | 0.5179 | 675 | 187 | 488 |
| Tetraethylammonium Br | ethylene glycol | 0.200 | 249 | 258 | 0.6564 | 788 | 168 | 620 |
| Tetrapropylammonium Br | ethylene glycol | 0.200 | 250 | 63 | 0.7535 | 898 | 188 | 710 |
| Tetrabutylammonium Br | levulinic acid | 0.200 | 273 | 49 | 1.1811 | 1382 | 241 | 1141 |
| | malonic acid | 0.500 | 255 | 49 | 0.7472 | 960 | 298 | 662 |

Table 2. Representative nonconventional deep eutectic solvents: their composition, x_A ; temperature of fusion, T_{fus} ; freezing point depression, $\Delta_{fus}T$; molecular volume, v_m ; molar entropy, S_E ; the entropy sum of the ingredients, $\Sigma_{A+D}S$; and the molar entropy change on formation, $\Delta_f S$.

| HB Acceptor | HB Donor | x_A | T_{fus}/K | $\Delta_{fus}T/K$ | v_m/nm^3 | $S_E/J\ K^{-1}\ mol^{-1}$ | $\Sigma_{A+D}S/J\ K^{-1}\ mol^{-1}$ | $\Delta_f S/J\ K^{-1}\ mol^{-1}$ |
|---|-------------------|-------|-------------|-------------------|------------|---------------------------|-------------------------------------|----------------------------------|
| Betaine | glycolic acid | 0.333 | 237 | 146 | 0.117 | 175 | 140 | 35 |
| | lactic acid | 0.500 | 298 | 92 | 0.144 | 208 | 164 | 44 |
| | phenylacetic acid | 0.333 | 266 | 118 | 0.186 | 261 | 204 | 57 |
| menthol | acetic acid | 0.500 | 265 | 34 | 0.1551 | 222 | 218 | 4 |
| | lactic acid | 0.333 | 212 | 108 | 0.1485 | 214 | 196 | 18 |
| | dodecanoic acid | 0.667 | 288 | 26 | 0.2604 | 354 | 293 | 61 |
| Glucose | citric acid | 0.500 | 283 | 141 | 0.213 | 295 | 206 | 89 |
| | tartaric acid | 0.500 | 255 | 178 | 0.188 | 263 | 186 | 77 |
| Octanoic acid | dodecanoic acid | 0.750 | 282 | 15 | 0.2916 | 392 | 274 | 118 |
| CaBr ₂ ·6H ₂ O | water | 0.695 | 251 | 48 | 0.2255 | 310 | 306 | 4 |
| Ca(ClO ₄) ₂ ·6H ₂ O | water | 0.548 | 198 | 117 | 0.4654 | 609 | 322 | 287 |
| KF·2H ₂ O | water | 0.242 | 233 | 50 | 0.2587 | 351 | 91 | 260 |
| KOH·H ₂ O | water | 0.488 | 208 | 127 | 0.1270 | 187 | 93 | 94 |
| LiNO ₃ ·3H ₂ O | water | 0.171 | 250 | 76 | 0.3170 | 424 | 96 | 328 |
| LiI·2H ₂ O | water | 0.670 | 204 | 116 | 0.1692 | 240 | 146 | 94 |
| MgBr ₂ ·6H ₂ O | water | 0.472 | 230 | 121 | 0.4112 | 542 | 224 | 318 |
| Mg(ClO ₄) ₂ ·6H ₂ O | water | 0.582 | 204 | 159 | 0.4937 | 644 | 332 | 312 |

3. Discussion

The standard entropies $S_{198^\circ E}$ of the DESs in Table 1 are commensurate with those obtained by other workers [8,9] on the same premise shown in Table 3. The standard entropies of formation of DESs shown in Table 1 are also in good agreement with values calculated quantum-chemically [28] and also shown in Table 3 (the negative signs on two of the values in [27] are mistakes). The entropy changes on formation of the DESs are positive in all the cases treated. They are, on the whole, larger where the hydrogen bond acceptor component is a quaternary ammonium salt (Table 1) or a salt hydrate (Table 2) than for those organic DESs where this component is neutral (Table 2). This difference cannot be attributed in the cases of the neutral acceptor components to the use of Equation (2) for the nonionic eutectic liquids rather than Equation (4) for organic liquids, the slopes with respect to v_m being commensurate. The formation of the liquid DES involves an increase in entropy that may be related to the increase in the kinds and numbers of hydrogen bonds that can be formed in the binary mixtures relative to the ingredients, even if the latter are liquid themselves. Note that for the salt hydrates at least one of the ions is a strong water structure maker, even when the counter ion is a structure breaker, so that more hydrogen bonds are formed in their concentrated aqueous solutions composing the DESs.

Table 3. Some deep eutectic solvents reported in the literature: their composition, x_A ; molecular volume, v_m ; molar entropy, S_{E298° ; or molar entropy of formation, $\Delta_f S$.

| HB Acceptor | HB Donor | x_A | v_m/nm^3 | $S_{E298^\circ}/\text{J K}^{-1} \text{mol}^{-1}$ | $\Delta_f S/\text{J K}^{-1} \text{mol}^{-1}$ |
|-----------------------|--------------------------------|-------|-------------------|--|--|
| Choline chloride | urea | 0.333 | | | 301 [27] |
| | ethylene glycol | 0.333 | | | 333 [27] |
| | malonic acid | 0.500 | | | 160 [27] |
| | propanoic acid | 0.333 | 0.4445 | 584 [9] | |
| | chloroacetic acid | 0.333 | 0.4269 | 562 [9] | |
| | trichloroacetic acid | 0.333 | 0.5302 | 690 [9] | |
| | <i>p</i> -toluenesulfonic acid | 0.333 | 0.6469 | 836 [9] | |
| Tetrabutylammonium Cl | ethylene glycol | 0.333 | 0.6751 | 871 [8] | |
| | polyethylene glycol | 0.333 | 1.6619 | 2101 [8] | |
| | propanoic acid | 0.333 | 0.7327 | 942 [8] | |
| | phenylacetic acid | 0.333 | 0.8785 | 1124 [8] | |

It is futile to try to analyze the contributions to the total entropy of the eutectic mixture in terms of the translational, rotational, and vibrational modes of the components. These modes are generally unknown for the pure components, and all that can be said about the eutectic mixture is that the translational entropy should be reduced relative to the components in view of the more extensive hydrogen bonded network characteristic of the eutectic mixture.

The data listed in Tables 1 and 2, being representative but not comprehensive, permit qualitative conclusions only to be drawn about the freezing point depressions $\Delta_{\text{fus}} T$ of the various kinds of DESs and the entropy changes of formation of the DESs from the components $\Delta_f S$. The latter quantities are positive in all the cases, but for the conventional DESs in Table 1, $\Delta_{\text{fus}} T$ diminishes with increasing $\Delta_f S$ values, whereas for the unconventional DESs in Table 2, it increases in this direction, more for the nonionic organic DESs than for the aqueous salt hydrate DESs, but the scatter in all the cases is appreciable.

In conclusion, the question posed in the introduction—whether the entropies of the DESs compared with those of their components affects the melting properties of the DESs—cannot be answered on the basis of the data presented here. It is doubtful if a more comprehensive collection of data would be helpful in this respect, as an important obstacle in the exploration of this direction is the lack of adequate density or crystal structure data for the solid component involved in the formation of many DESs.

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References

- 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. [\[CrossRef\]](#)
- Marcus, Y. *Deep Eutectic Solvents*; Springer: Berlin, Germany, 2018, in press.
- Ashworth, C.R.; Matthews, R.P.; Welton, T.; Hunt, P.A. Doubly ionic hydrogen bond interactions within the choline chloride-urea deep eutectic solvent. *Phys. Chem. Chem. Phys.* **2016**, *18*, 18145–18160. [\[CrossRef\]](#) [\[PubMed\]](#)
- Jenkins, H.D.B.; Glasser, L. Standard entropies, S_{0298} , values from volume or density. 1. Inorganic materials. *Inorg. Chem.* **2003**, *42*, 8702–8708. [\[CrossRef\]](#) [\[PubMed\]](#)
- Glasser, L.; Jenkins, H.D.B. Standard entropies, S_{0298} , values from volume or density. Part II. Organic liquids and solids. *Thermochim. Acta* **2004**, *414*, 125–130. [\[CrossRef\]](#)
- Glasser, L. Lattice and phase transition thermodynamics of ionic liquids. *Thermochim. Acta* **2004**, *421*, 87–93. [\[CrossRef\]](#)
- Glasser, L.; Jenkins, H.D.B. Volume-based thermodynamics: A prescription for its application and usage in approximation and prediction of thermodynamic data. *J. Chem. Eng. Data* **2011**, *58*, 874–880. [\[CrossRef\]](#)
- Su, H.-Z.; Yin, J.-M.; Liu, Q.-S.; Li, C.-P. Properties of four deep eutectic solvents: Density, electrical conductivity, dynamic viscosity, and refractive index. *Acta Phys. Sin.* **2015**, *31*, 1468–1473.

9. Cui, Y.; Li, C.; Yin, J.; Li, S.; Jia, Y.; Bao, M. Design, synthesis and properties of acidic deep eutectic solvents based on choline chloride. *J. Mol. Liq.* **2017**, *236*, 338–343. [[CrossRef](#)]
10. Lide, D. (Ed.) *Handbook of Chemistry and Physics*, 82nd ed.; CRC Press: Baton Rouge, FL, USA, 2001/2002.
11. Coker, T.G.; Ambrose, J.; Janz, G.J. Fusion properties of some ionic quaternary ammonium compounds. *J. Am. Chem. Soc.* **1970**, *92*, 5293–5297. [[CrossRef](#)]
12. Cardellini, P.; Tiecco, M.; Germani, R.; Cardinali, G.; Corte, L.; Roscini, L.; Spreti, N. Novel zwitterionic deep eutectic solvents from trimethylglycine and carboxylic acids: Characterization of their properties and their toxicity. *RSC Adv.* **2014**, *4*, 55990–56002. [[CrossRef](#)]
13. Ribeiro, B.D.; Florindo, C.; Iff, L.C.; Coelho, M.A.Z.; Marrucho, I.M. Menthol-based eutectic mixtures: Hydrophobic low viscosity solvents. *ACS Sustain. Chem. Eng.* **2015**, *3*, 2469–2477. [[CrossRef](#)]
14. Craveiro, R.; Aroso, I.; Flamma, V.; Carvalho, T.; Viciosa, M.T.; Dionisio, M.; Barreiros, S.; Reis, R.L.; Duarte, A.R.C.; Paiva, A. Properties and thermal behavior of natural deep eutectic solvents. *J. Mol. Liq.* **2016**, *215*, 534–540. [[CrossRef](#)]
15. Altamash, T.; Nasser, M.S.; Elhamarnah, Y.; Magzoub, M.; Ullah, R.; Qiblawey, H.; Aparicio, S.; Atilhan, M. Gas solubility and rheological behavior study of betaine and alanine based natural deep eutectic solvents (NADES). *J. Mol. Liq.* **2018**, *256*, 286–295. [[CrossRef](#)]
16. Florindo, C.; Romero, L.; Rintoul, I.; Branco, L.C.; Marrucho, I.M. From phase change materials to green solvents: Hydrophobic low viscous fatty acid-based deep eutectic solvents. *ACS Sustain. Chem. Eng.* **2018**, *6*, 3888–3895. [[CrossRef](#)]
17. Verma, R.; Banerjee, T. Liquid–Liquid extraction of lower alcohols using menthol-based hydrophobic deep eutectic solvents: Experimental and COSMO-SAC predictions. *Ind. Eng. Chem. Res.* **2018**, *57*, 3371–3381. [[CrossRef](#)]
18. Zalkin, A. The crystal structure of tetra-n-propyl ammonium bromide. *Acta Crystallogr.* **1957**, *10*, 557–560. [[CrossRef](#)]
19. Senko, M.E.; Tempelton, D.H. Unit cells of choline halides and structures of choline chloride. *Acta Crystallogr.* **1960**, *13*, 281–285. [[CrossRef](#)]
20. Pistorius, C.W.F.T.; Gibsdon, A.A.V. Disorder and polymorphism of tetramethylammonium chloride. *J. Solid State Chem.* **1973**, *8*, 126–131. [[CrossRef](#)]
21. Ralle, M.; Bryan, J.C.; Habenschuss, A.; Wunderlich, B. Low-temperature phase of tetraethylammonium bromide. *Acta Crystallogr.* **1997**, *C53*, 488–490. [[CrossRef](#)]
22. Staples, R.J. Crystal structure of anhydrous tetraethylammonium chloride, $[(\text{CH}_3\text{CH}_2)_4\text{N}]\text{Cl}$. *Z. Kristallogr. NCS* **1999**, *214*, 231–232.
23. Viertorinne, M.; Valkonen, J.; Pitkanen, I.; Mathlouthi, M.; Nurmi, J. Crystal and molecular structure of anhydrous betaine, $(\text{CH}_3)_3\text{NCH}_2\text{CO}_2$. *J. Mol. Struct.* **1999**, *477*, 23–29. [[CrossRef](#)]
24. Elsegood, M.R.J. Tetra-n-butylammonium bromide: A redetermination at 150 K addressing the merohedral twinning. *Acta Crystallogr.* **2011**, *67*, o2599. [[CrossRef](#)] [[PubMed](#)]
25. Marcus, Y. Unconventional deep eutectic solvents: Aqueous salt hydrates. *ACS Sustain. Chem. Eng.* **2017**, *5*, 11780–11787. [[CrossRef](#)]
26. Marcus, Y.; Jenkins, H.D.B. Standard absolute entropy, S_{298}° , of salt hydrates from volumes and hydrate numbers and the thermodynamic difference rule. *Chem. Phys. Lett.* **2018**, submitted.
27. Wagman, D.D.; Evans, W.H.; Parker, V.B.; Schumm, R.H.; Nuttall, R.L. The NBS tables of chemical thermodynamic properties. *J. Phys. Chem. Ref. Data* **1982**, *18*, 1807. [[CrossRef](#)]
28. Wagle, D.V.; Deakyne, C.A.; Baker, G.A. Quantum chemical insight into the interactions and thermodynamics present in choline chloride based deep eutectic solvents. *J. Phys. Chem. B* **2016**, *120*, 6739–6746. [[CrossRef](#)] [[PubMed](#)]

