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Letter

Assessing Melting and Solid−Solid Transition Properties of Choline Chloride via Molecular Dynamics Simulations

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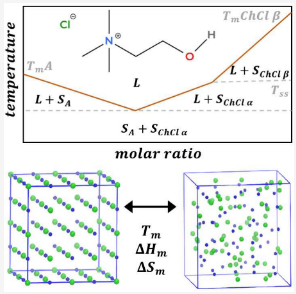
ABSTRACT: Choline chloride (ChCl) is used extensively as a hydrogen bond donor in deep eutectic solvents (DESs). However, determining its melting properties experimentally is challenging due to decomposition upon melting, leading to widely varying literature values. Accurate melting properties are crucial for understanding the solid−liquid phase behavior of ChCl-containing DESs. Here, we employ molecular dynamics simulations to compute the phase transitions of ChCl, testing a variety of atomistic force fields. We find that the results are sensitive to the choice of force field, but a melting temperature of 627 K and a melting enthalpy of 7.8 kJ/mol seem most reasonable, in good agreement with some literature values. We suggest these as the likely melting properties of ChCl, though the results are tentative due to limited experimental data for the liquid ChCl phase.



Deep eutectic solvents (DESs) are a class of materials prepared by physically mixing two or more (usually) solid precursors, typically a hydrogen bond donor (HBD) and a hydrogen bond acceptor (HBA).[1] These precursors establish a eutectic solid−liquid equilibrium (SLE), resulting in a significant reduction of the melting point relative to their pure components, thereby producing a liquid solvent without the need for any synthesis step. As such, DESs broaden the range of available solvents by enabling the use of solid compounds in liquid form, finding numerous applications in areas such as catalysis,[2] carbon dioxide capture,[3] and extraction processes.[4] Furthermore, because they are mixtures, the physicochemical properties of DESs can be easily tuned by changing the nature and relative compositions of their precursors.

(2-Hydroxyethyl)trimethylammonium chloride, commonly referred to as choline chloride (ChCl), is the most common HBA used in formulating a DES.[1] Its widespread use can be attributed to its availability, low cost, biocompatibility, biodegradability, and overall green character.[5,6] The (predicted) low melting enthalpy of ChCl enhances the melting temperature depression of ChCl-based DESs, facilitating the formation of liquid solvents at room temperature despite its high melting temperature (thought to be above 597 K).[1]

Measuring and analyzing the SLE behavior of DESs is crucial to understanding their operating windows and the intermolecular interactions established in the liquid phase.[7,8] When the melting properties of the pure precursors are known, SLE data can be used to determine the activity coefficients and excess Gibbs energies. These properties provide insights into the solubility, stability, and interactions of the components within DESs. This is relevant in the distinction between a eutectic solvent and a DES, the latter of which is characterized by negative deviations from thermodynamic ideality.[1]

Despite the advantages of studying the SLE behavior noted above, the melting properties of many DES precursors are not readily available. This is the case for ChCl, which decomposes upon melting, making the direct experimental measurement of its melting properties difficult. To address this issue, indirect methods have been proposed. Fernandez et al.[9] reported a melting temperature of 597 K and a melting enthalpy of 4.3 kJ/mol. This work used experimental SLE data for binary mixtures of ChCl and other ionic compounds, which exhibited a near-ideal thermodynamic behavior. Thus, assuming activity coefficients close to unity, the melting properties of ChCl could be extracted from the SLE data.

In contrast, Vilas-Boas et al.[10] estimated the melting enthalpy of ChCl to be 7.7 kJ/mol (almost double the value reported by Fernandez et al.[9]). Their method relied on experimental solubility data of ChCl in water, along with modeling via the PC-SAFT equation of state[11] and the COSMO-RS thermodynamic model.[12] Offering yet a different perspective, van den Bruinhorst et al.[13] conducted direct experimental measurements of ChCl melting using fast scanning calorimetry combined with X-ray crystallography and optical microscopy. This approach, which potentially avoids the decomposition of ChCl, yielded a melting temperature and enthalpy estimates of approximately 678 K and 13.8 kJ/mol, respectively. These are both significantly

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higher than the values reported by Vilas-Boas et al.[10] and Fernandez et al.[9]

Inspired by the conflicting views listed above, this work aims to determine the melting properties of ChCl by using molecular dynamics (MD) simulations. We use the pseudo-supercritical path (PSCP) method[14,15] and evaluate several different classical force fields. Another goal is to computationally determine the solid−solid transition properties of ChCl, which are well-established experimentally. This is relevant, given the limited studies of polymorph phase transitions in the MD literature.[16,17] The PSCP methodology along with full simulation details are described in section S.I. of the Supporting Information.

Under standard atmospheric pressure, crystalline ChCl exists in forms α and β, depending on the temperature. Form α is stable at temperatures below 352 K, while form β prevails above this threshold.[18] Figure 1 illustrates the unit cells of both polymorphs. Form α adopts an orthorhombic structure with space group $P2_12_12_1$, characterized by the lattice parameters $a \neq b \neq c$ and $\alpha = \beta = \gamma = 90°$.[19,20] In contrast, form β exhibits a disordered face-centered cubic (fcc) structure with space group $Fm3m$, having lattice parameters $a = b = c$ and $\alpha = \beta = \gamma = 90°$.[21]

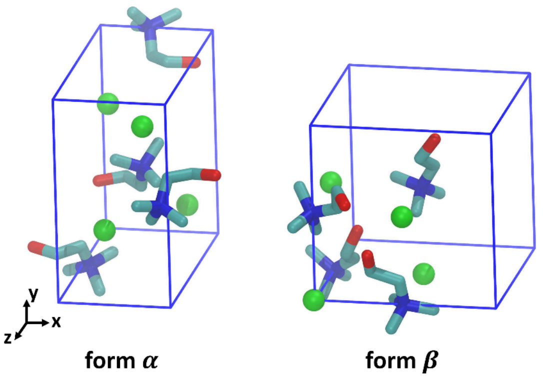

Figure 1. Choline chloride forms α and β unit cells.[20,21] The hydrogen atoms are omitted for clarity.

Due to the disordered nature of form β, precise atomic positions within the unit cell have not been well-defined in the literature. For our simulations, we applied the approximate model described by Petrouleas et al.,[21] where the chloride and nitrogen atoms are positioned at 0, 0, 0 and 1/2, 1/2, 1/2, respectively, corresponding to the fcc lattice. The carbon and oxygen atoms are positioned in a disorderly manner, rotating around axes that pass through the nitrogen atom. The study by Petrouleas et al.[21] provided a set of probable positions for these atoms, which allowed us to establish a unit cell configuration. The atomic positions of the unit cell are given in section S.II.

There are no agreed upon force fields for modeling the solid and liquid phases of ChCl, nor do we expect that ab initio-based force fields are accurate enough to capture the subtle interactions responsible for small differences in melting temperature and enthalpy.[22] We therefore evaluated five different classical force fields (GAFF-DES, OPLS-DES, GAFF, OPLS, and CHARMM)[23−27] along with three charge scaling factors (1.0, 0.9, and 0.8), resulting in a total of 15 combinations. The charge scaling factors account for polarization in an approximate way. Their validation consisted of comparing computed average lattice parameters and densities of the crystalline polymorphs with experiments. The results are shown in Figure 2 for form α at 295 K and form β at 358 K. Additional data are available in section S.III.

The computed densities depend on the combination of the force field and charge scaling factor, with deviations from experiments of up to 13.3% across all cases. Larger charge scaling reduces solid densities due to a decrease in cohesive energies induced by reduced Coulombic interactions.

The lattice parameters also depend on the force field and the charge scaling factor. For form α, GAFF-DES and GAFF predict the lattice parameters within 8% of experiments, depending on the charge scaling. In comparison, OPLS-DES and OPLS have deviations of up to 19% for a. CHARMM has

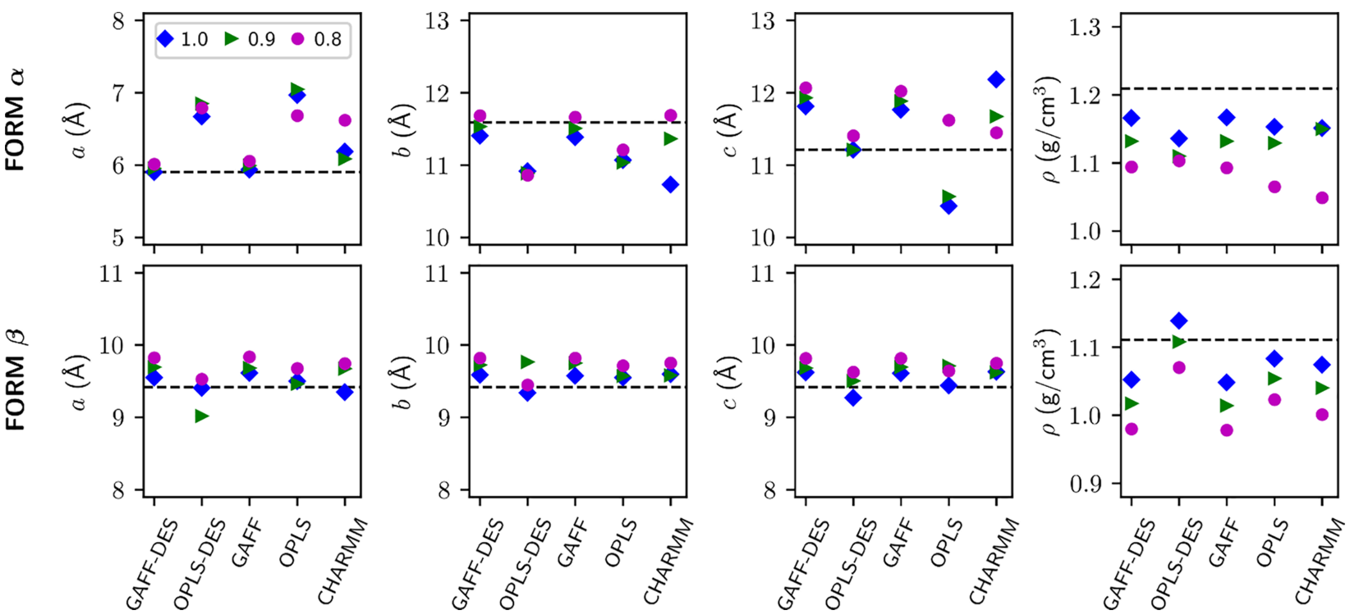

Figure 2. Computed average lattice parameters and densities of ChCl form α at 295 K and form β at 358 K for different force fields and charge scaling factors. Horizontal lines represent experimental values.[19,21]

deviations of 4% or less in a when a charge scaling factor of 0.9 is used. For form β, all of the force fields preserve the fcc structure. A cubic shape is maintained, with a, b, and c being around 5% of each other and the average box angles staying close to 90°.

Given these varying results, we selected force fields and charge scaling factors that describe the polymorph structures reasonably well, based on the criterion that the computed lattice parameters and densities differ by less than 6% from experiments. The three combinations meeting this criterion for both polymorphs are GAFF-DES with a scaling of 1.0, GAFF with a scaling of 1.0, and CHARMM with a scaling of 0.9. We describe the results obtained using these three force field combinations below; results using the other combinations are provided in the Supporting Information.

To further assess the performance of the three selected force fields, the solid−solid transition between forms α and β was examined, given its well-documented properties. The results are summarized in Table 1. Test simulations were carried out to choose the proper simulation conditions, as detailed in section S.IV. Additional data are available in section S.V.

Table 1. Computed Solid−Solid Transition Properties of ChCl Compared with Experimental Data[a]

	charge scaling	T_{ss} (K)	ΔH_{ss} (kJ/mol)	ΔS_{ss} (J/mol/K)
Expt. 18		352.3(1)	16.4(7)	47(2)
GAFF-DES	1.0	348(5)	17.4(4)	50(1)
GAFF	1.0	358(4)	20.3(5)	57(2)
CHARMM	0.9	347(5)	15.2(4)	44(1)

[a]Numbers within parentheses indicate the statistical uncertainty in the last digit.

Table 1 shows that all three force fields do a reasonable job of capturing the $\alpha \rightarrow \beta$ transition. The transition temperatures deviate less than 2% from experiments for all cases. The transition enthalpies for GAFF-DES and CHARMM deviate less than 7%, while GAFF has a larger variation of 24%.

An investigation of form β was performed to study its disordered structure. We studied the mean squared displacement (MSD) and radial pair distribution function (RDF) of ChCl atoms at 358 K. The results are shown in Figure 3 for the selected force field combinations. Additional data are available in section S.VI.

We observe a low mobility of nitrogen and chloride atoms, resulting in a nearly flat MSD versus time. In contrast, the carbon and oxygen atoms exhibit a higher mobility, leading to a more noticeable change in the MSD over time. The analysis focuses on the carbon atom directly bonded to the oxygen atom, as these are the ones where Petrouleas et al.[21] observed the most pronounced disorder. At longer times, the MSDs stabilize, indicating that rotational motion of the atoms dominates, and translational motion is still constrained by the crystal lattice.

Similarly, the RDFs show periodicity in the arrangement of the nitrogen and chloride atoms. This periodicity is absent in the carbon−carbon and oxygen−oxygen RDFs, where the increased mobility causes a loss of long-range structural order. Consequently, they become less correlated with each other, and the RDF approaches the bulk value (RDF = 1) at about 10 Å. Simulations using all three force fields show similar results, and all effectively capture the disordered nature of form β.

Based on the excellent performance of the three force fields in describing the ChCl polymorphs, including the disordered structure in form β and the solid−solid phase transition, the solid−liquid phase transition (melting) of ChCl was studied next. The results are shown in Table 2. Additional data are available in section S.VII. During the simulations, form β was used for the solid phase, as it represents the stable state before experimental melting.

Table 2 shows that the results using GAFF-DES and GAFF with full charge significantly overestimate all three literature melting temperatures. On the other hand, the melting temperature computed with CHARMM falls in between the different literature values. All three force fields predict melting enthalpies and entropies that are lower than those reported by van den Bruinhorst et al.,[13] while CHARMM is in near perfect

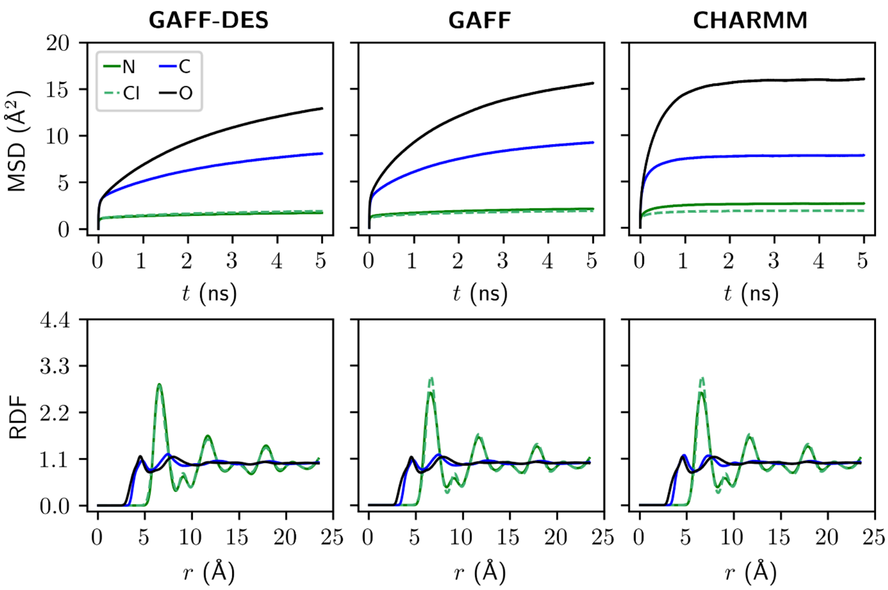

Figure 3. Computed MSD and intermolecular RDF for oxygen−oxygen, carbon−carbon, nitrogen−nitrogen, and chloride−chloride atoms in ChCl form β at 358 K (GAFF-DES, scaling 1.0; GAFF scaling 1.0; CHARMM scaling 0.9). Data for the nitrogen and chloride atoms are nearly identical.

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Table 2. Computed Melting Properties of ChCl Form β along with Literature Values[a]

	charge scaling	T_m (K)	ΔH_m (kJ/mol)	ΔS_m (J/mol/K)
Lit. 9		597(7)	4.3(6)	7.2(9)
Lit. 10		597(7)	7.7(1)	12.9(4)
Lit. 13		687(9)	13.8(3)	20.1(5)
GAFF-DES	1.0	759(4)	11.0(5)	14.5(7)
GAFF	1.0	748(4)	10.9(4)	14.6(5)
CHARMM	0.9	627(6)	7.8(7)	12.4(9)

[a]Numbers within parentheses indicate the statistical uncertainty in the last digit.

agreement with the melting enthalpy and entropy of Vilas-Boas et al.[10]

Given these results, we are left with the following question: What are the true melting temperature, enthalpy, and entropy of ChCl? The results are not clear-cut. The three force fields examined in Table 2 all do a reasonable job modeling the solid phase of ChCl. A direct comparison with experiments in the liquid phase is not possible, however, due to the lack of experimental data. Given the fact that the GAFF-DES and GAFF models both significantly overestimate the melting temperature for all three literature studies, while the CHARMM model gives more reasonable values, we believe the CHARMM model is likely the most accurate. Assuming this to be the case, the present study predicts the melting temperature of ChCl to be 627 K, and the melting enthalpy and entropy to be 7.8 kJ/mol and 12.4 J/mol/K, respectively. These results most closely match the literature values reported by Vilas-Boas et al.[10] We note that this conclusion is tentative due to the difficulty of modeling SLE, although we believe that this study provides important insights into the SLE of ChCl and is valuable in guiding further understanding and design of DES systems.

■ ASSOCIATED CONTENT

Data Availability Statement

The data supporting this article have been included as part of the Supporting Information. The data analysis scripts are available at github.com/atoms-ufrj/CHCL-article-2024.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.jpclett.4c03051.

Details on the methodology and simulations; atomic positions of the unit cell of form β; numerical values of the lattice parameters and densities of forms α and β; additional results of mean squared displacement and radial distribution function of form β; initial analysis of the phase transitions of ChCl; additional results on melting and solid−solid transition properties (PDF)

Transparent Peer Review report available (PDF)

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Notes

The authors declare no competing financial interest.

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