

Research paper

# Evaluation of COSMO-RS for solid–liquid equilibria prediction of binary eutectic solvent systems

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## Abstract

For the design of eutectic solvents (ESs, usually also known as deep eutectic solvents), the prediction of the solid–liquid equilibria (SLE) between candidate components is of primary relevance. In the present work, the SLE prediction of binary eutectic solvent systems by the COSMO-RS model is systematically evaluated, thereby examining the applicability of this method for ES design. Experimental SLE of such systems are first collected exhaustively from the literature, following which COSMO-RS SLE calculations are accordingly carried out. By comparing the experimental and predicted eutectic points (eutectic temperature and eutectic composition) of the involved systems, the effects of salt component conformer and COSMO-RS parameterization as well as the applicability for different types of components (specifically the second component paired with the first salt one) are identified. The distinct performances of COSMO-RS SLE prediction for systems involving different types of components are further interpreted from the non-ideality and fusion enthalpy point of view.

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**Keywords:** Eutectic solvents; Solid-liquid equilibria prediction; COSMO-RS; Calculation options; Applicability for component types

## 1. Introduction

Due to the growing awareness of the impacts of solvents on energy usage and environmental pollution, the replacement of conventional organic solvents with more sustainable solvents has been a burgeoning focus of both the research community and the chemical industry [1–7]. One such example is eutectic solvents (ESs), which are in many cases also coined as deep eutectic solvents (DESS) considering the large freezing temperature ( $T_f$ ) depression of the mixtures relative to the  $T_f$  of their pure components. ESs have many attractive properties such as broad liquidus range, low vapor

pressure, and easily tunable character, rendering them as analogous to ionic liquids (ILs). More interestingly, ESs could usually be less toxic, easier to prepare, and less expensive than ILs [8–10]. These advantages have brought ESs into the limelight as neoteric solvents in diverse applications, such as separations, catalysis, electro-deposition, and so on [10–18].

Despite being widely explored, the selection of ESs for a specific application still relies strongly on the experimental trial-and-error method. However, as a huge diversity of potential components with different ratios theoretically lead to a limitless ES space, this method not only is time-consuming and costly but also can barely reach the optimal ES system. For fast ES screening, there are a few studies that employ the COSMO-based activity coefficient models to quickly estimate the thermodynamic properties (e.g., liquid–liquid equilibria, activity coefficient, Henry's law constant) of ES-involved

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systems [12,19–24]. Nevertheless, such studies generally covered only a small number of ESs that have been either experimentally reported or hypothetically combined from commonly-used components, most frequently in fixed compositions (e.g., 1:1, 1:2, 1:3, among others). In this context, reliable methods that could guide the search of ES components over a much larger molecular space and the determination of optimal component ratio are highly desirable.

To preselect ES components, Alhadid et al. [25] proposed an approach to predict the eutectic temperature of binary systems based on the melting enthalpy estimation and the unitary activity coefficient assumption. This approach allows the qualitative estimation of eutectic behavior of binary systems, where the components to be considered have to share the same chemical functionality (i.e., the same type and number of functional groups). Very recently, our group [26] proposed a quantitative correlation between the  $T_f$  depression of choline chloride (ChCl) based ESs and the COSMO-RS derived molecular descriptors of their second components (in many cases could be denominated as hydrogen bond donors, HBDs, according to their role in ES), which is further applied to screen novel ESs from a large number of combinations of ChCl and potential HBDs. This correlation applies only to ChCl-based ESs due to the limitation of available experimental data and cannot directly estimate the eutectic temperature ( $T_e$ ) due to unknown eutectic compositions ( $x_e$ ) for novel component combinations. To design pharmaceutical eutectic solvents, Abranches et al. [27] estimated the solid–liquid equilibria (SLE) prediction by COSMO-RS for 35 ChCl based binary systems and then experimentally validated with four pharmaceutical compounds (aspirin, ibuprofen, ketoprofen, and paracetamol) as the second component paired with ChCl. Earlier, Silva et al. [28] also estimated and tuned the COSMO-RS model for the SLE prediction of systems comprising ChCl and sugars.

Among these above methods, the prediction of SLE by COSMO-RS is the most straightforward as the SLE phase diagram could not only provide the information of eutectic point ( $T_e$  and  $x_e$ ) but also suggest a feasible  $x$  range satisfying the operating requirement for a given task (as illustrated in Fig. 1). Due to the fully predictive character of this activity

coefficient model, the SLE prediction by COSMO-RS is potentially applicable to any system, provided that the fusion properties of individual components are known. However, so far, only very few previous studies have evaluated the COSMO-RS SLE prediction, where limited characteristics of ES systems are covered and the tested model parameterizations vary from case to case [27–29]. Therefore, to better examine the applicability of this method for ES design, a systematic evaluation of COSMO-RS for the SLE prediction of eutectic systems is of great significance.

Considering the aforementioned aspects, this work systematically evaluates the SLE prediction performance of COSMO-RS for binary ES systems. Experimental SLE data of such systems are compiled exhaustively from the open literature, and then COSMO-RS SLE calculations are performed for the collected systems. Based on the obtained results, the effects of different characteristics of binary systems (conformer and type of components) and COSMO-RS parameterizations are compared. Additionally, the ES systems that COSMO-RS presents distinct SLE prediction performances are analyzed, aiming to shed some light on the applicability of the method.

## 2. Fundamentals

### 2.1. Experimental database collection

Although ESs have been extensively studied in the past years, most of the related works are only application-centered, where the SLE phase diagrams of ES systems are not concerned. As a result, only 118 phase diagrams of binary ES systems (with multiple data points showing the eutectic behavior) are compiled after literature review. Moreover, for a large proportion of the systems, one can hardly judge the eutectic point directly as the reported SLE only cover a few data points on the liquidus curve and neglect the solidus line. To derive the eutectic point for such systems, the method suggested by Abranches et al. [27] is utilized. Specifically, the two separate liquidus curves are regressed linearly and then extrapolated to determine the eutectic point by their intersection. In some cases, only the data closer to the eutectic point are used in the regression, depending on the tendency of the whole liquidus curve. All the 118 collected ES systems with their extrapolated eutectic points as well as the references are tabulated in Table S1 (Supporting Information).

### 2.2. SLE prediction by COSMO-RS

COSMO-RS proposed by Klamt et al. [30,31] is a predictive model for the thermodynamic properties of liquids and liquid mixtures. A standard COSMO-RS calculation only requires the surface charge density profiles (also known as  $\sigma$ -profiles) of the involved molecules, which gives the relative amount of surface with polarity  $\sigma$  of a molecule. By integrating the  $\sigma$ -profile with a fast and accurate statistical thermodynamic approach, the chemical potential of compound  $i$  in

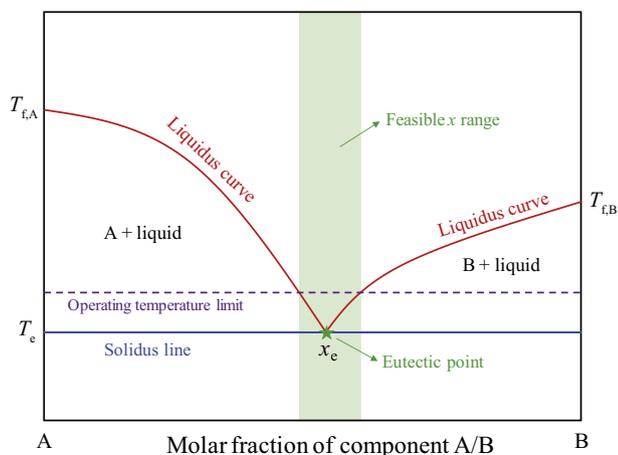


Fig. 1. Illustration of a two-component SLE diagram and its usefulness for ES screening.

solvent or solvent mixture  $S(\mu_i^S)$  can be computed, and following that, a wide variety of thermodynamic properties are predictable. For example, the activity coefficient ( $\gamma_i^S$ ) can be calculated as:

$$\gamma_i^S = \exp\left\{\frac{\mu_i^S - \mu_i^i}{RT}\right\} \quad (1)$$

where  $\mu_i^i$  is the chemical potential of pure compound  $i$ . For a more detailed introduction of the COSMO-RS theory, one can refer to [30,31].

In this work, the software package COSMOthermX (Version 19.0) is adopted for the COSMO-RS SLE calculation. With the *Solid-Liquid* option, COSMOthermX offers the possibility to search for SLE based on the following phase equilibrium condition:

$$\mu_i^i - \Delta G_{fus}(T) = \mu_i^S + RT \ln(x_i) \quad (2)$$

For the SLE of a solid compound  $i$  with a solvent,  $\Delta G_{fus}$  (the Gibbs free energy of fusion of the compound) is taken into account on the left-hand side of Eq. (2) for the solid phase. A temperature dependent Gibbs free energy of fusion can be calculated from pure compound data, that is, the melting temperature ( $T_m$ ) and the enthalpy or entropy of fusion ( $\Delta H_{fus}$  or  $\Delta S_{fus}$ ) as:

$$\Delta G_{fus}(T) = \Delta H_{fus} \left(1 - \frac{T}{T_m}\right) - \Delta Cp_{fus}(T_m - T) + \Delta Cp_{fus} T \ln \frac{T_m}{T} \quad (3)$$

$$\Delta G_{fus}(T) = \Delta S_{fus}(T_m - T) - \Delta Cp_{fus}(T_m - T) + \Delta Cp_{fus} T \ln \frac{T_m}{T} \quad (4)$$

The heat capacity upon melting  $\Delta Cp_{fus}$  is the difference between the molar heat capacity of compound  $i$  in the liquid and solid phases. When the equilibrium temperature is not far from the  $T_m$  of pure compound, the last two  $\Delta Cp_{fus}$  involved terms in Eqs. (3) and (4) are negligible in comparison to the  $\Delta H_{fus}$  involved term, and thus can be optionally selected (or neglected as such data are in many cases unavailable). Combining the above equations, the calculation of SLE of eutectic systems can be simplified as:

$$\ln x_i^L \gamma_i^L = -\frac{\Delta H_{fus,i}}{RT} \left(1 - \frac{T}{T_{m,i}}\right) \quad (5)$$

For a binary system, the solubility curves (liquidus curves) of the two components are calculated separately. The eutectic point where the two solubility curves meet can be automatically determined with the SLE suboption *OPT\_EUTECTIC*. The SLE calculation in the COSMOthermX assumes that there is a simple eutectic point in the phase diagram of a binary system, by which complicated systems with several phase transitions in the solid state cannot be assessed. The computation time of COSMO-RS for SLE depends on the specified temperature search range and step. In a typical run in our work, for instance, given the temperature range of 200–500 K

and a temperature search step of 10 K, the SLE calculation of a system including the estimation of eutectic point can be done in less than 1 min on a common personal computer (Intel Core i7-6700 CPU @3.40 GHZ).

From the above, the only required input except pure component fusion properties ( $T_m$  and  $\Delta H_{fus}$  or  $\Delta S_{fus}$ ) for SLE prediction by COSMO-RS is the  $\sigma$ -profiles of components. The current COSMObase of COSMOthermX already covers the  $\sigma$ -profiles of several thousands of conventional molecules and hundreds of cations and anions of ILs. In addition, the  $\sigma$ -profiles of new compounds can be conveniently obtained from standard quantum chemical calculations. For all the binary ES systems collected in this work, 51 conventional non-salt components and 18 salt components are involved, which are summarized in Table S2 (Supporting Information) along with their fusion properties experimentally measured in the literature. The  $\sigma$ -profiles of all the involved non-salt components except fructose are directly taken from the COSMObase. For fructose and the involved salt components, their  $\sigma$ -profiles are generated by quantum chemical calculations using the Gaussian 09 software package (Version D.01) [32]. It is worth mentioning that there are two common approaches for representing salt component in COSMO-RS, one is the electro-neutral mixture of cations and anions (C + A), and the other is a single non-dissociated ion pair (CA). As Abranches et al. [27] have proved that the CA approach greatly surpasses the C + A approach for SLE prediction by COSMO-RS with 35 ChCl-based ES systems, the latter is selected for representing salt components in this study. A typical run to generate the CA  $\sigma$ -profile of a salt component is as follows: (1) different anion locations around the cation are taken into account as initial configuration, and geometric optimizations of them are carried out at the B3LYP/6-31++G\*\* theoretical level in the ideal gas phase; (2) vibrational frequency analysis is conducted to ensure that the optimized configuration is in global energy minimum; (3) the COSMO files of the stable conformers are acquired based on single-point quantum COSMO calculation using the BP86/TZVP level of theory.

### 3. Results and discussion

Among the 118 collected binary systems in Table S1 (Supporting Information), 82 of them are combinations of a salt component and a non-salt component, 12 of them are based on two salts, and 24 of them are based on two non-salt components. As classified in Table S2 (Supporting Information), the 51 involved non-salt components cover molecular types of carboxylic acids (fatty, poly-, and  $\alpha$ -hydroxy-), sugars, fatty alcohols, polyols, phenols, pharmaceutical compounds, among others; among the 18 involved salt components, ChCl,  $[N_{nnnn}]Cl$  ( $n = 1-4$ ), and  $[N_{nnnn}]Br$  ( $n = 2-6$ ) appear in different types of binary systems, and the rest salts present in two salt systems. Based on this database, this work evaluates the COSMO-RS SLE prediction for these ES systems from three aspects: (1) effect of salt component conformer, (2) effect of COSMO-RS parameterization, and (3) applicability for component types (specifically the second

component paired with a salt one in ES), respectively. The first two aspects can suggest suitable options for COSMO-RS SLE calculation while the third aspect can distinguish the applicable range of this method.

### 3.1. Effect of salt component conformer

As different initial configurations of cation–anion may result in distinct conformers of salt component, it is of great importance to know whether COSMO-RS SLE calculation should specifically take account of the conformer effect in this respect. The 51 ChCl-based eutectic systems are taken for the evaluation, considering ChCl (treated as the first component) is paired widely with different types of second components (non-salts or salts) in the collected binary SLE database. In the cases that ChCl is paired with non-salt HBD components, it can usually be referred as hydrogen bond acceptor (HBA) according to its role in ES.

From varying initial locations of chloride anion around choline cation, three distinct conformers of ChCl are obtained, as shown in Fig. 2 with their COSMO surfaces and  $\sigma$ -profiles. In the HBA region ( $\sigma > 0.01 \text{ e } \text{\AA}^{-2}$ ) of  $\sigma$ -profiles, the peaks of conformer 1 and conformer 3 move marginally leftward and are higher in comparison to those of conformer 2. The reason is that the surfaces of chloride and the hydrogen of the hydroxyl group of choline overlap to some extent in conformer 2, bringing down the number of positive  $\sigma$  surfaces and also decreasing the  $\sigma$  value of remaining surfaces. Moreover, the  $\sigma$ -profiles of conformer 1 and conformer 3 also present a small peak in the HBD region ( $\sigma < -0.01 \text{ e } \text{\AA}^{-2}$ ) around  $-0.017 \text{ e } \text{\AA}^{-2}$  due to the exposure of the hydrogen of the hydroxyl group of choline. In the non-polar region ( $-0.01 \text{ e } \text{\AA}^{-2} < \sigma < 0.01 \text{ e } \text{\AA}^{-2}$ ), the  $\sigma$ -profiles of the three conformers also deviates slightly from each other in peak height and location. All such differences in the  $\sigma$ -profiles of the three conformers imply their non-negligible effect on SLE prediction.

With the obtained three conformers, the SLE of the 51 ChCl-based systems are calculated by COSMO-RS based on

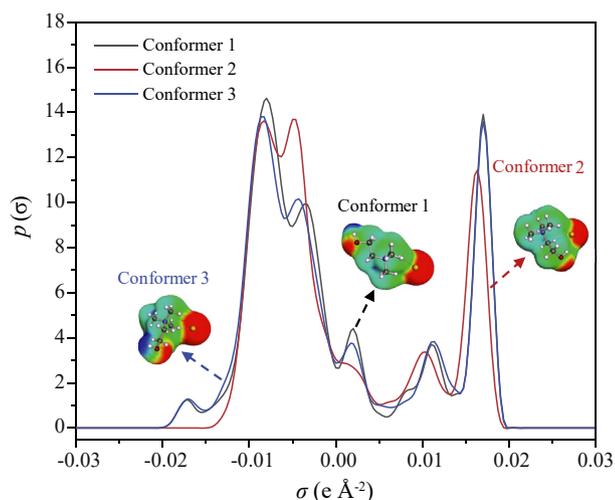


Fig. 2. Three different conformers of ChCl with the cation and anion optimized as a whole.

each individual conformer as well as the simultaneous selection of three conformers. The predicted eutectic point, whichever case it is obtained, is tabulated in Table S1a (Supporting Information). It turns out that COSMO-RS only finds the eutectic point for 30–33 of the 51 ChCl-based systems (predictable cases), depending on the different conformers and parameterizations employed for the SLE calculation; for the rest systems, COSMO-RS cannot find a eutectic point and output “optimization leads to unreasonable temperature value” (unpredictable cases). Fig. 3 exemplifies the two distinct cases with ChCl: urea [8] and ChCl: citric acid [33] as representative binary systems, respectively, where the COSMO-RS predictions obtained by selecting all three ChCl conformers simultaneously and under the BP\_TZVP\_19 parameterization are used for illustration. As seen, despite of a certain deviation from experimental data, the two calculated liquidus curves in the SLE of ChCl: urea evolve regularly and intersect, leading to the predicted eutectic point. In contrast, in the SLE of ChCl: citric acid, the two calculated liquidus curves deviate strongly from the experimental data in the high concentration region, specifically with the molar fraction of citric acid from 0.25 to 0.75, which are not crossed until 100 K. In the following, only the binary systems with eutectic point predictable by COSMO-RS are used to evaluate the effect of ChCl conformers. The differences in the systems that COSMO-RS can and cannot find the eutectic point will be discussed later in Section 3.3.

Fig. 4 compares the experimentally determined  $T_e$  and  $x_e$  with the COSMO-RS predictions based on different conformer options under BP\_TZVP\_19 parameterization. From Fig. 4, different conformers lead to very distinct  $T_e$  for many of the involved systems (as seen from the points sharing the same experimental  $T_e$  in Fig. 4a), and this finding also holds true in terms of  $x_e$  in Fig. 4b. In some special cases, namely ChCl: glycolic acid, ChCl: oxalic acid, and ChCl: glutaric acid, the eutectic point is only found with one of the conformer options (see details in Table S1a, Supporting Information). These observations clearly demonstrate the significant effect of ChCl conformer on SLE prediction by COSMO-RS. Quantitatively, there exists at least one conformer that can result in a  $T_e$  prediction deviating within  $\pm 50 \text{ K}$  with respect to the experimental data (an empirical threshold for acceptable  $T_e$  prediction considered here) for 26 of the predictable systems (distributing almost evenly around the diagonal). For these systems, the mean deviation ( $MD$ ) and coefficient of determination ( $R^2$ ) obtained by different conformer options are calculated, which are in the range of 14.03–16.84 K and 0.8383–0.8709, respectively. Such a quantitative prediction performance for  $T_e$  is acceptable, considering the fully predictive character of COSMO-RS. Meanwhile, although conformer 2 presents a slightly superior overall performance for  $T_e$  prediction ( $R^2 = 0.8709$  and  $MD = 14.03 \text{ K}$ ), the best conformer, that is the one with the  $T_e$  prediction closest to the diagonal, varies from case to case. In consequence, the option of selecting all three conformers simultaneously gives rise to an  $MD$  (15.11 K) and  $R^2$  (0.8679) very close to those of conformer 2 due to moderate  $T_e$  predictions for different

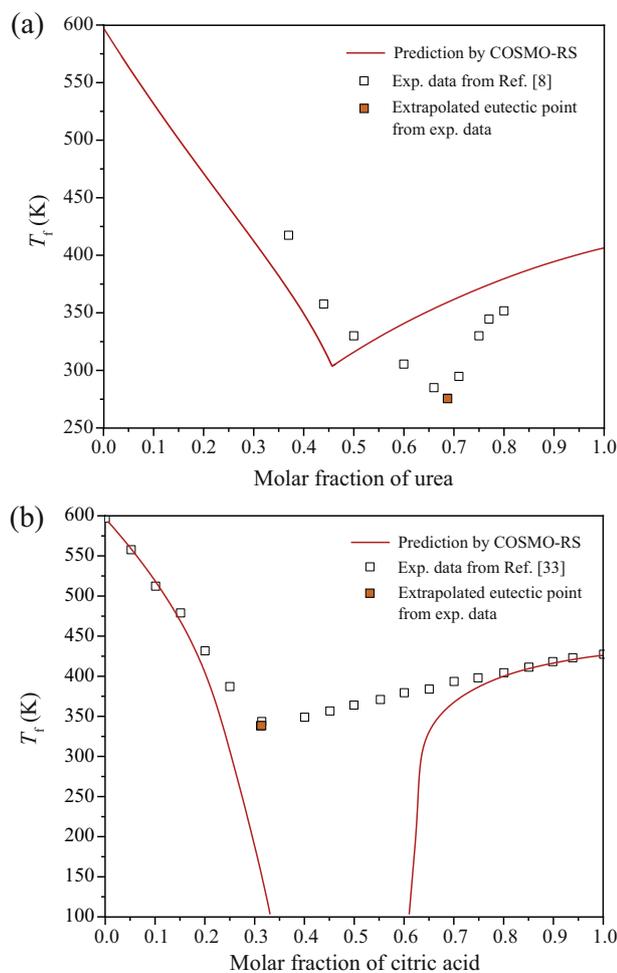


Fig. 3. Experimental and COSMO-RS (all conformers selected, BP\_TZVP\_19) predicted SLE diagrams of ChCl: urea (a) and ChCl: citric acid (b).

systems. Regarding  $x_e$ , the predictions are both qualitatively and quantitatively rough as the data points distribute broadly and only few of them locate in a close range to the diagonal.

Indicated by the example of ChCl-based systems, the salt component conformer can have a significant effect on the SLE prediction performance by COSMO-RS. For the predictable systems, the  $T_e$  prediction is acceptable despite of some outliers whereas the  $x_e$  prediction is generally rough. Straightforwardly, if the non-salt component in ES also possesses notably distinct conformers, a non-negligible effect on the SLE prediction result could also be inferred. It is recommended to select different possible component conformers for general evaluation and consider the effect of conformers in specific cases.

### 3.2. Effect of COSMO-RS parameterization

The COSMOthermX (Version 19.0) provides a new parameterization BP\_TZVP\_19, wherein the unit conversions and fundamental physical constants (Avogadro constant  $N_A$ , Boltzmann constant  $k$ , Elementary charge  $e$ , Electron mass  $m_e$ ,

Planck constant  $h$ , and Electric constant  $\epsilon^0$ ) were updated according to the latest NIST/CODATA recommendations [30]. However, in the very few previous works on COSMO-RS SLE prediction, only different versions of older parameterizations have been used [27–29]. Therefore, it is of high interest to compare the predictions obtained under different parameterizations (including the latest BP\_TZVP\_19), thereby identifying whether there is a best one for SLE calculation of ES systems.

In this work, two previous parameterizations BP\_TZVP\_C30\_1601 and BP\_TZVP\_C30\_1701 are selected for comparison with the latest BP\_TZVP\_19 (in the following abbreviated as TZVP\_16, TZVP\_17, and TZVP\_19, respectively). In addition to the ChCl-based binary systems, the 67 non-ChCl-based ones (Table S1b, Supporting Information) are further calculated under these three parameterizations. The possible conformers for the involved components in each system are all selected in the SLE calculation, as suggested above. As a result, COSMO-RS predicts the eutectic point for 63, 66, and 65 of the 67 non-ChCl-based systems based on the parameterization of TZVP\_16, TZVP\_17 and TZVP\_19, respectively. All the ChCl-based and non-ChCl-based systems that COSMO-RS finds the eutectic point are combined for evaluating the effect of different parameterizations.

As shown in Fig. 5, the COSMO-RS predicted  $T_e$  and  $x_e$  in most cases only change slightly with different parameterizations. For instance, except 7 of the overall 95–97 predictable systems (see detailed data in Table S1, Supporting Information), the deviations between predicted  $T_e$  under different parameterizations are less than  $\pm 10$  K (mostly within  $\pm 5$  K) for the other systems. Again, a deviation threshold of  $\pm 50$  K (as noted in Section 3.1) is employed to assess the quantitative prediction performance for  $T_e$  under different parameterizations. Subtracting the 13–15 outliers, the  $MD$  and  $R^2$  between experimental and predicted  $T_e$  under different parameterizations for the rest cases are in a close range of 10.57–11.57 K and 0.8224–0.8423, respectively, where the results from TZVP\_17 are marginally better than those from the TZVP\_16 and TZVP\_19. For  $x_e$ , the predictions under different parameterizations are even closer for most of the systems, as evidenced by the strong overlaps in each case in Fig. 5b. However, a very broad distribution of the predicted  $x_e$  is again observed along the diagonal with respect to their experimental counterparts.

To summarize, the different parameterizations have a minor effect on the eutectic point prediction by COSMO-RS, which all lead to acceptable  $T_e$  prediction in many cases but generally rough  $x_e$  prediction. Nevertheless, TZVP\_17 has slightly better performance for  $T_e$  prediction than TZVP\_16 and TZVP\_19, and could be considered as a prior parameterization.

### 3.3. Applicability for component types

When looking into the systems that COSMO-RS predicts  $T_e$  poorly (i.e., the outliers in Figs. 4a and 5a) and that COSMO-RS cannot predict the eutectic point (Table S1, Supporting Information), they are all combinations of a salt (treated as the

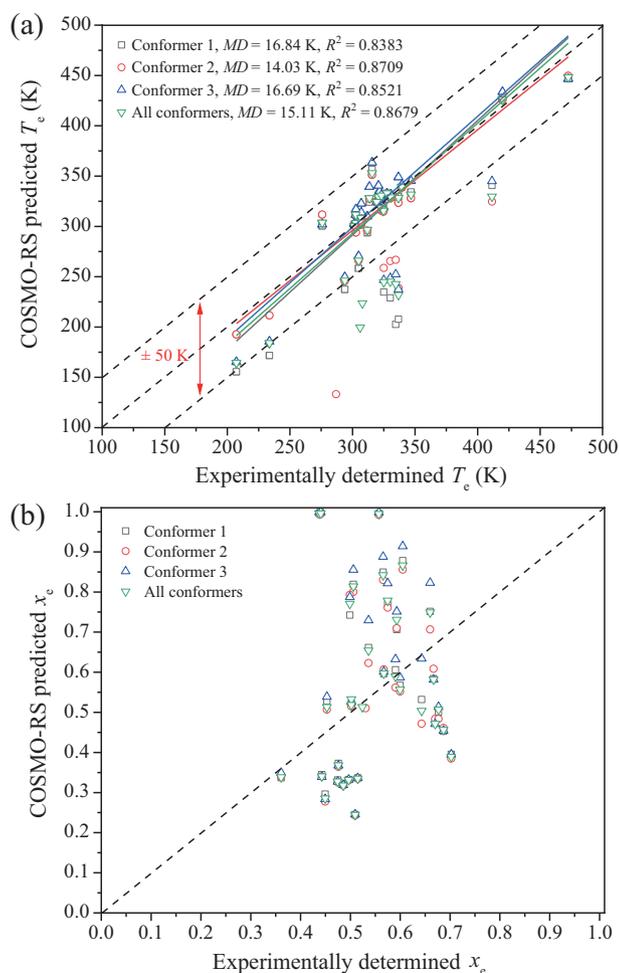


Fig. 4. Effect of ChCl conformers on the COSMO-RS (BP\_TZVP\_19) predicted  $T_e$  (a) and  $x_e$  (b) of the involved eutectic systems.

first component) and a second component of limited types. This finding motivates us to further evaluate in detail the applicability of COSMO-RS SLE calculation for salt-involved systems pairing different types of second components.

First, for all the salt-involved systems that COSMO-RS finds the eutectic point, the COSMO-RS predictions (TZVP\_17, all conformers selected) are compared with their experimental counterparts in Fig. 6 according to the types of the second component. As seen in Fig. 6a, among the 15 outliers of the  $T_e$  deviation threshold, seven, four, and two are based on the second component of polycarboxylic acids, sugars, and polyols, respectively. The remaining two outliers are based on the second component of fatty carboxylic acids and salts, respectively. The one outlier of fatty carboxylic acid may result from experimental deviation as the  $T_e$  predictions for 22 of 23 similar binary systems fall within the  $\pm 50$  K deviation threshold. The one outlier of salt may be ascribed to the double salt IL character (not simple ‘mixture’ of two ILs) of the systems [34–36], which can also be suggested by the four similar systems that COSMO-RS cannot predict the eutectic point. Except the above, the  $T_e$  for the systems

comprising the second component of fatty carboxylic acids (22 of 23 systems), aromatic carboxylic acids (4 systems), fatty alcohols (9 systems), pharmaceutical compounds (4 systems), and others (2 systems, specifically referring to urea and 2,4,6-trimethylphenol here) are reasonably predicted. Regarding  $x_e$ , no clear dependency of the predictions on the component type is observed (Fig. 6b) because overall only rough estimations are obtained in this respect.

Second, for all the 21 (19 of them are ChCl-based ones) systems that COSMO-RS cannot predict the eutectic point, eleven, six, and four are based on the second component of poly- $\alpha$ -hydroxy-/aromatic carboxylic acids, phenolic compounds, and salts, respectively. That is to say, there seems to be a clear dependency on the types of the second component for the salt-involved systems whose eutectic points can or cannot be found by COSMO-RS. Meanwhile, the second component types of polycarboxylic acids and salts in the unpredictable cases also coincide with those involved in the outliers in the predictable cases, which generally indicate poor applicability of COSMO-RS SLE calculation for such systems.

To provide some insights into the distinct SLE prediction performances for salt-involved systems pairing different types of second components, all the ChCl-based systems are analyzed from the non-ideality and fusion enthalpy point of view. Here, only the ChCl-based systems are selected to allow for a fair applicability analysis. Except the double salt systems that have already been discussed above, all the other ChCl-based systems are employed in this analysis. The infinite dilution activity coefficient ( $\gamma^\infty$ ) of the second component in ChCl at 298.15 K is calculated by COSMO-RS as a rough indication for the non-ideality of different systems. As compared in Fig. 7, all the systems that COSMO-RS cannot find the eutectic point or predict  $T_e$  poorly (outliers of the  $\pm 50$  K deviation threshold) are generally located in the lower left corner, which refers to strong negative non-ideality of the involved systems and/or low fusion enthalpy of the second components. In contrast, when the systems have no strong negative non-ideality (close to ideality or with positive non-ideality to some extent) and/or comprise second components of high fusion enthalpy, that is, the upper right region of Fig. 7, the  $T_e$  of systems are reasonably predicted. Combining this interesting finding with the distinct SLE prediction results, the systems that COSMO-RS cannot find the eutectic point or can only predict  $T_e$  poorly could be ascribed to an overestimation of the negative non-ideality. From the SLE equation in Eq. (5), the overestimation of the negative non-ideality (predicting lower activity coefficient) will lead to a lower  $T_e$ , as can be seen in Figs. 4–6 that most of the outliers are below the threshold of  $-50$  K. Such an effect of activity coefficient underestimation becomes greater when the component is of low fusion enthalpy, which may account for the eutectic point unpredictable cases.

From the above analysis, it can be inferred that the applicability of COSMO-RS SLE calculation for salt-involved systems pairing different types of second component essentially lies in the differences in the estimated system non-

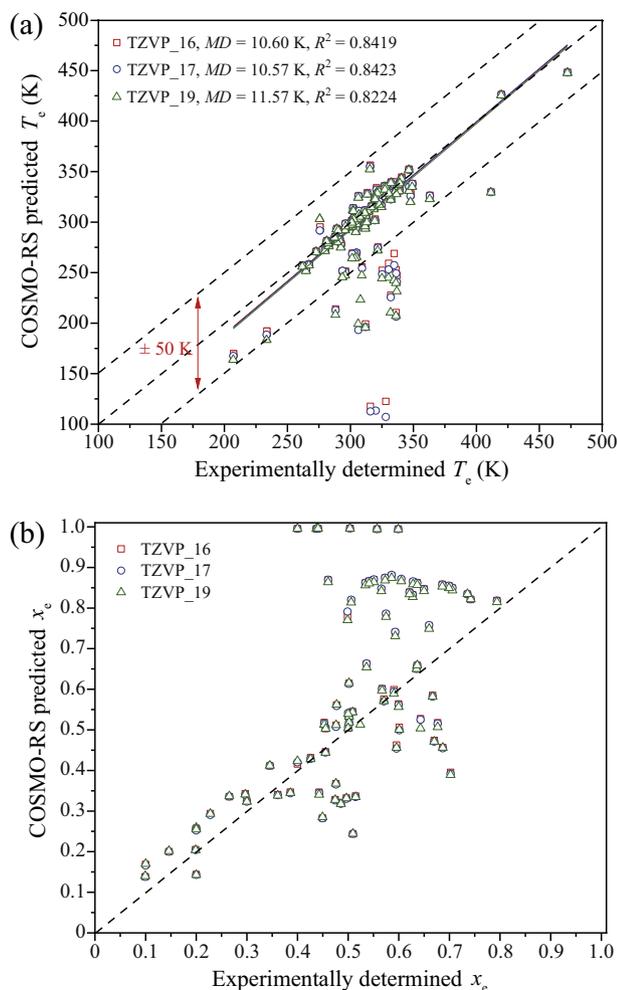


Fig. 5. Effect of COSMO-RS parameterization on the predicted  $T_c$  (a) and  $x_c$  (b) of all involved eutectic systems.

ideality and fusion enthalpy of the second component, not simply in the component types. A good evidence is the systems of ChCl + phenolic compounds, as marked with superscripts 1–7 in Fig. 7: (1) when the second component is 2,4,6-trimethylphenol, the COSMO-RS predicted  $T_c$  (311.32 K) is quite reasonable (exp. value is 307.06 K) due to a low negative non-ideality ( $\ln\gamma^\infty = -0.44$ ) and a fusion enthalpy of 21.41 kJ mol<sup>-1</sup>; (2) when the second component is 3,4-dimethylphenol, hydroquinone, resorcinol, phenol, *o*-cresol, and 2,3-xylenol, the eutectic point is even not found due to a stronger negative non-ideality ( $\ln\gamma^\infty$  in the range of  $-9.77$  to  $-3.04$ ) and a lower fusion enthalpy (except 27.11 kJ mol<sup>-1</sup> for hydroquinone, 11.51–21.02 kJ mol<sup>-1</sup> for the others). This conclusion is also well supported by the reasonable predictions for the 24 systems comprising two non-salt components ( $MD$  of  $T_c$  prediction is 3.93 K, see detailed data in Table S1b, Supporting Information) as such systems, mostly thymol or menthol + fatty carboxylic acids or alcohols, are generally of

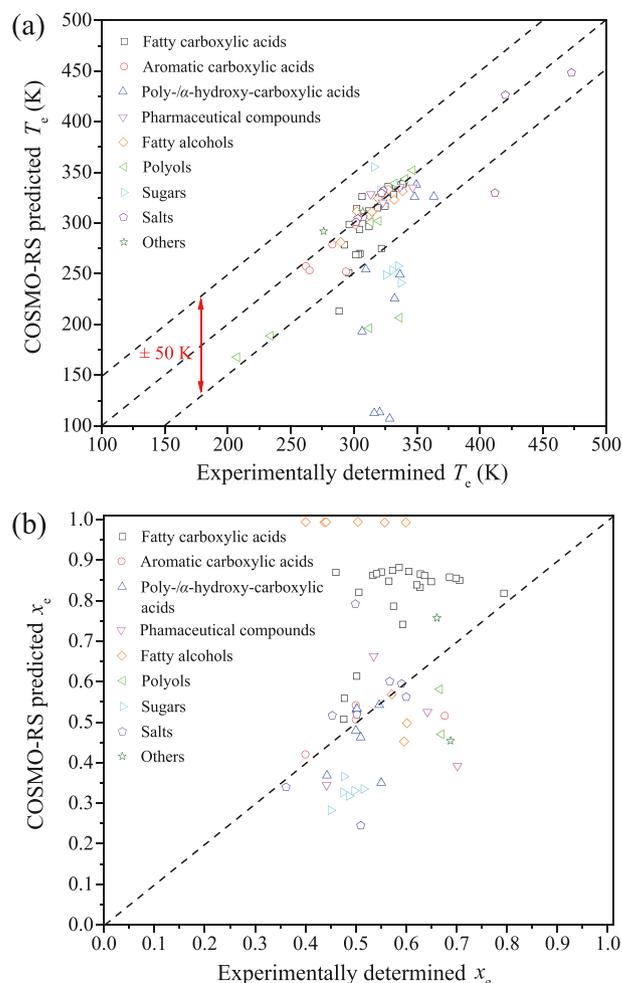


Fig. 6. Comparison of the experimental and COSMO-RS predicted  $T_c$  (a) and  $x_c$  (b) of all salt-involved systems according to the types of the second component.

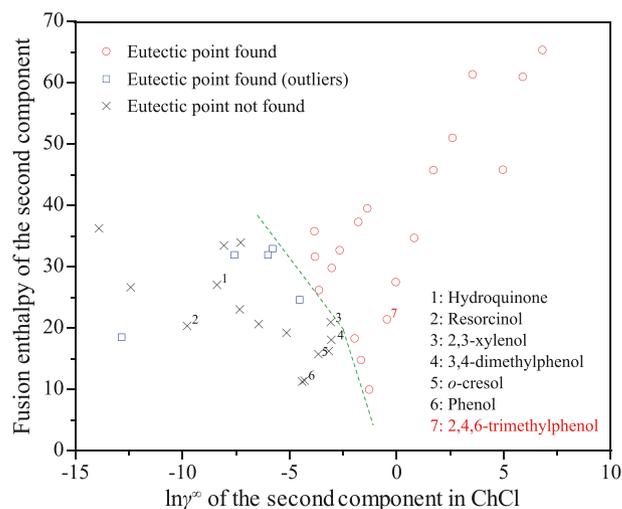


Fig. 7. Analysis of different ChCl-based systems that COSMO-RS presents distinct  $T_c$  prediction performance (each point corresponds to an individual second component).

low negative non-ideality. It is worth mentioning that whether a ES system possesses negative non-ideality is proposed as the criterion to seriously differentiate a simple ES from a true DES by several researchers [37].

On the whole, the COSMO-RS SLE prediction performance for salt-involved systems shows a dependency on the types of the second component. In the cases such as poly-/ $\alpha$ -hydroxy-carboxylic acids, phenolic compounds, and sugars, COSMO-RS cannot or can only poorly predict the eutectic point. By contrast, in the cases such as fatty/aromatic carboxylic acids, fatty alcohols, pharmaceutical compounds, and others, the  $T_e$  prediction is generally reasonable. Such distinct applicability for different types of the second component in ChCl-based systems could be generally distinguished from the system non-ideality and component fusion enthalpy point of view. These findings could be helpful to estimate the potential applicability of COSMO-RS SLE calculation for novel binary systems.

#### 4. Conclusions

In this work, the SLE prediction performance of COSMO-RS for binary eutectic systems is systematically evaluated. Experimental SLE of 118 eutectic systems are collected from the literature, covering different system characteristics and various component types. The comparison of experimental and predicted results demonstrates that the salt component conformers have a significant effect while the different parameterizations have only a slight effect on the SLE prediction by COSMO-RS. Correspondingly, the simultaneous selection of different possible conformers and the TZVP\_17 parameterization are recommended as a prior option for the COSMO-RS SLE calculation. It is found that COSMO-RS give acceptable predictions in many cases on the eutectic temperature but generally presents very rough predictions on the eutectic composition. Such a performance allows the usage of COSMO-RS for the screening of eutectic systems as the selection of component combinations from almost limitless candidates is much more challenging than the determination of  $x_e$ . Once the component combination is selected,  $x_e$  including a feasible composition range meeting a specific temperature requirement could be assessed by experiments. Moreover, the eutectic point prediction by COSMO-RS shows distinct applicability for systems involving different components, which could be reasonably distinguished from the perspectives of non-ideality and fusion enthalpy. The present evaluation could offer useful guidance for developing ES design method based on COSMO-RS in future work. When more experimental SLE data are available, a task-specific fine-tuning of the COSMO-RS parameters could also be attempted to further improve the prediction performance of this model.

#### Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.gee.2020.11.020>.

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