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Quantum Mechanical Continuum Solvation Models for Ionic Liquids

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Abstract. The quantum mechanical SMD continuum universal solvation model can be applied to predict the free energy of solvation of any solute in any solvent following specification of various macroscopic solvent parameters. For three ionic liquids where these descriptors are readily available, the SMD solvation model exhibits a mean unsigned error of 0.48 kcal/mol for 93 solvation free energies of neutral solutes and a mean unsigned error of 1.10 kcal/mol for 148 water-to-IL transfer free energies. Because the necessary solvent parameters are *not* always available for a given ionic liquid, we determine average values for a set of ionic liquids over which measurements *have* been made in order to define a generic ionic liquid solvation model, SMD-GIL. Considering 11 different ionic liquids, the SMD-GIL solvation model exhibits a mean unsigned error of 0.43 kcal/mol for 344 solvation free energies of neutral solutes and a mean unsigned error of 0.61 kcal/mol for 431 water-to-IL transfer free energies. As these errors are similar in magnitude to those typically observed when applying continuum solvation models to ordinary liquids, we conclude that the SMD universal solvation model may be applied to ionic liquids as well as ordinary liquids.

Keywords: Partitioning; Implicit solvation; Green solvents; Solute-solvent interactions

Introduction

Over the course of the last 15 years, there has been a surge of interest in the use of ionic liquids as replacements for ordinary organic solvents otherwise used as media for chemical reactions and processes.¹⁻¹² Ionic liquids are molten salts with melting temperatures below about 100° C, i.e., they are constituted entirely of ions, and they exist in the liquid state at temperatures that are readily accessible, possibly including room temperature. Some factors motivating interest in ionic liquids include observed catalytic effects and/or enhanced stereoselectivity for chemical transformations, high conductivity, their essentially negligible volatility, and their generally high chemical and thermal stabilities (including non-flammability). In addition, ionic liquids are widely used for separations and processing and as lubricating, dispersing, and heat transferring agents. They have several characteristics that make them environmentally friendly, although a full evaluation of that aspect requires also considering their toxicity and their energy consumption properties.¹³ As the number of possible ionic liquids is vast, and as they offer unique opportunities for materials design, there is considerable interest in the development of *in silico* approaches to predict the solubility and partitioning of solutes in individual ionic liquids in order to facilitate the selection or design of optimal combinations of cationic and anionic constituents for specific applications.^{14,15} Solubility and partitioning may both be predicted from free energies of solvation,¹⁶⁻¹⁹ and solvation effects on chemical reaction rates can also be estimated from free energies of solvation;²⁰⁻²⁴ free energies of solvation and partitioning are the subjects of the present article.

Solubility and partitioning in ionic liquids, just as in ordinary liquids, is determined by dielectric polarization of the solvent and by specific interactions in the first solvation shell. Also similarly to ordinary liquids, ionic liquids influence chemical reactivity based on the degree to which they differentially stabilize (or destabilize) different regions of reaction coordinates associated with dissolved solutes.^{25,26} More generally, equilibrium coupling with a solvent may be regarded as generating a free

energy surface, with the solvated surface being generated for every set of solute coordinates by adding the free energy of solvation to the gas-phase energy associated with that set of coordinates.^{21,24} Given the powerful tools available for the generation of accurate gas-phase potential energy surfaces,²⁷ the similar development of accurate models for predicting free energies of solvation continues to be an important goal so that accurate predictions of chemical structure and reactivity in solution can be made.^{22,28-31}

In an effort better to understand the molecular nature of solvation effects in ionic liquids, linear solvation free energy relationships familiar from physical organic chemistry have been explored.³²⁻³⁹ In addition, a number of quantum and classical mechanical studies of solute-solvent (component) clusters have been reported, as have results from full condensed-phase simulations.^{9,40-63} To date, most theoretical modeling has been fully atomistic, that is, the ionic liquid is explicitly represented in cluster or periodic condensed-phase calculations, although some results have also been reported for a reference interaction site model (RISM) approach⁶⁴⁻⁶⁶ and from the statistical mechanical COSMO-RS model.^{67,68}

In this work, we explore the degree to which ionic liquid solvation effects can be reproduced with an *implicit* solvation model, also often referred to as a continuum solvation model.^{22,28-31} The SMx series of continuum solvation models have been demonstrated to provide excellent accuracy for the prediction of free energies of solvation for molecular neutral and ionic solutes in typical organic solvents.^{30,69,70} Importantly, the SMx models (with $x = 5-8$ or D) were designed to be universal, meaning that their application to *any* solvent is possible provided a user has measured or can estimate a handful of necessary solvent descriptors.^{30,71-78} We here demonstrate the extension of the SMD solvation model⁷⁷ to ionic liquids, and we show how that model may even be applied to ionic liquids where solvent descriptors are not available from experiment.

Computational Model

The SMD continuum solvation model has been described in detail elsewhere,⁷⁷ and we here recapitulate only those details critical to explaining its extension to ionic liquids as solvents. Like all SM_x models, the SMD model computes the 298 K free energy associated with transferring a solute from the gas phase, at 1 M concentration and behaving as an ideal gas, to a liquid solution, at 1 M concentration and behaving as though infinitely dilute.⁷⁹ The contributions to the free energy of solvation are divided in the SMD model into electrostatic and non-electrostatic components. The electrostatic component is computed from the polarized continuum model⁸⁰ (PCM) that self-consistently solves the Poisson equation for a nonhomogeneous medium to obtain the quantum mechanical solute charge distribution inside a molecular cavity; the calculation depends on an optimized set of cavity radii and requires the solvent dielectric constant.⁷⁷ (The medium is nonhomogeneous because the dielectric constant is unity inside the cavity, where polarization is treated explicitly, and is equal to the bulk dielectric constant outside the cavity, where polarization is treated by continuum methods.) The non-bulk-electrostatic component is computed assuming characteristic contributions proportional to the exposed surface areas of solute atoms. The proportionality constants (atomic and molecular surface tensions) depend semiempirically on a small group of *solvent* descriptors. These descriptors are the index of refraction (n), the macroscopic surface tension (γ), Abraham's hydrogen bond acidity and basicity parameters for the solvent when treated as a *solute* ($\Sigma\alpha_2^H$ and $\Sigma\beta_2^H$), the fraction of non-hydrogen atoms that are aromatic carbon atoms (ϕ), and the fraction of non-hydrogen atoms that are electronegative halogen atoms (ψ). The functions from which the atomic or group surface tensions are computed are invariant across solvents; the surface tensions change only as a result of changes in the macroscopic solvent descriptors, making the SMD model "universal" in the sense that it may be applied to any solvent for which the necessary descriptors are either known from measurement or may be conveniently estimated. In the

case of ϕ and ψ , only the molecular structure is required to determine necessary values, but the other solvent descriptors must be determined by experiment or modeling.

Table 1 lists solvent descriptors determined experimentally⁸¹⁻⁸⁹ for 12 ionic liquids. The cationic components of these liquids include EMIM, BMIM, HMIM, and OMIM (1-ethyl-, 1-butyl-, 1-hexyl-, and 1-octyl-3-methylimidazolium, respectively), M₃BAm (trimethylbutylammonium), and MBPy (4-methyl-*N*-butylpyridinium). The anionic components include BF₄, DCA (dicyanamidate), NTf₂ (bis(trifluoromethylsulfonyl)imide), OTf (trifluoromethylsulfonate), and PF₆. Note that dielectric constants for ionic liquids are typically determined by zero-frequency extrapolation of the solvent's complex dielectric function determined from dielectric spectroscopy in the megahertz/gigahertz regime.

Table 1. Macroscopic Solvent Descriptors for 12 Ionic Liquids ^a

Ionic liquid	ϵ	n	γ	ϕ	ψ
[BMIM][BF ₄]	11.70 ⁸¹	1.4215 ⁸⁶	67.07 ⁸⁷	0.2000	0.2667
[BMIM][NTf ₂]	11.52 ⁸⁵	1.4271 ⁸⁷	53.97 ⁸⁷	0.1200	0.2400
[BMIM][PF ₆]	11.40 ⁸¹	1.4090 ⁸⁷	70.24 ⁸⁷	0.1765	0.3529
[EMIM][BF ₄]	12.80 ⁸¹	1.4098 ⁸²	78.30 ⁸³	0.2308	0.3077
[EMIM][DCA]	11.00 ⁸⁴	1.5329 ⁸²	66.07 ⁸²	0.2308	0.0000
[EMIM][NTf ₂]	12.25 ⁸⁵	1.4225 ⁸⁶	56.13 ⁸³	0.1304	0.2609
[EMIM][OTf]	15.20 ⁸¹	-	56.42 ⁸³	0.1875	0.1875
[HMIM][NTf ₂]	12.70 ⁸⁴	1.4295 ⁸⁶	50.38 ⁸³	0.1111	0.2222
[HMIM][PF ₆]	8.90 ⁸¹	1.4165 ⁸⁶	62.47 ⁸⁷	0.1579	0.3158
[M ₃ BAm][NTf ₂]	-	-	-	0.0000	0.2609
[MBPy][BF ₄]	-	-	-	0.3125	0.2500
[OMIM][PF ₆]	7.50 ⁸⁸	1.4235 ⁸⁹	51.38 ⁸⁹	0.1429	0.2857

^a All descriptors are dimensionless except γ , which has units of cal mol⁻¹ Å⁻². Superscript numbers to the right of values are literature citations, not uncertainties.

Table 1 does not include Abraham $\Sigma\alpha_2^H$ and $\Sigma\beta_2^H$ values for any of the ionic liquids because; to the best of our knowledge, these values have not been measured. However, Kamlet and Taft hydrogen bonding parameters⁹⁰ α and β have been measured for several ionic liquids. We note that the distinction between these two sets of hydrogen

bonding parameters is that those of Abraham are determined from free energy data for a molecule acting as a *solute* while those of Kamlet and Taft are determined in other ways for a molecule when acting as a *solvent*. It is reasonable to expect that there might be an correlation between the two sets of scales of hydrogen bonding parameters, and we therefore we explored the degree to which Kamlet and Taft parameters might be used to predict Abraham parameters. In particular, we considered the 19 organic solvents listed in Table 2, for which both sets of parameters have been determined.⁹¹⁻⁹³

Table 2. Kamlet and Taft and Abraham Hydrogen Bond Acidity and Basicity Parameters ^a

Solvent	Kamlet and Taft		Abraham	
	α	β	$\Sigma\alpha_2^H$	$\Sigma\beta_2^H$
acetone	0.20	0.54	0.04	0.49
acetonitrile	0.35	0.37	0.07	0.32
<i>n</i> -butanol	0.79	0.88	0.37	0.48
<i>tert</i> -butanol	0.68	1.01	0.31	0.60
chlorobenzene	0.00	0.07	0.00	0.07
chloroform	0.44	0.00	0.15	0.02
cyclohexane	0.00	0.00	0.00	0.00
dichloromethane	0.04	-0.01	0.10	0.05
diisopropyl ether	0.00	0.49	0.00	0.41
1,4-dioxane	0.00	0.37	0.00	0.64
diphenyl ether	0.00	0.13	0.00	0.20
ethanol	0.83	0.77	0.37	0.48
hexane	0.07	0.04	0.00	0.00
methanol	1.05	0.61	0.43	0.47
2-propanol	0.76	0.95	0.33	0.56
pyridine	0.00	0.64	0.00	0.52
tetrahydrofuran	0.00	0.55	0.00	0.48
toluene	-0.21	0.08	0.00	0.14
triethylamine	0.00	0.71	0.00	0.79

^a All values are dimensionless. Data were taken from references⁹¹⁻⁹³.

We find a strong correlation between α and $\Sigma\alpha_2^H$ values ($R^2 = 0.94$) and a weaker, but still useful correlation between β and $\Sigma\beta_2^H$ values ($R^2 = 0.61$). Based on the respective correlating equations

$$\Sigma\alpha_2^H = 0.4098\alpha + 0.0064 \tag{1}$$

and

$$\sum \beta_2^H = 0.6138\beta + 0.0890 \quad (2)$$

we have a means to predict $\sum \alpha_2^H$ and $\sum \beta_2^H$ values for ionic liquids where only Kamlet and Taft parameters have been determined. We present those predictions in Table 3.

Table 3. Kamlet and Taft and Predicted Abraham Hydrogen Bond Acidity and Basicity Parameters ^a

Solvent	Kamlet and Taft		Abraham	
	α	β	$\sum \alpha_2^H$	$\sum \beta_2^H$
[BM ₂ IM][BF ₄]	0.402	0.363	0.171	0.312
[BM ₂ IM][NTf ₂]	0.381	0.239	0.163	0.236
[BMIM][BF ₄]	0.627	0.376	0.263	0.320
[BMIM][NTf ₂]	0.617	0.243	0.259	0.238
[BMIM][OTf]	0.625	0.464	0.263	0.374
[BMIM][PF ₆]	0.634	0.207	0.266	0.216
[BMIM][SbF ₆]	0.639	0.146	0.268	0.179
[bmpy][NTf ₂]	0.427	0.252	0.181	0.244

^a All values are dimensionless. Kamlet and Taft values were taken from reference.⁹¹ Abraham values were predicted from Kamlet and Taft data using eqs 1 and 2. BM₂IM is 1-butyl-2,3-dimethylimidazolium and bmpy is 1-butyl-1-methylpyrrolidinium (all other notations have been previously defined).

There are 3 ionic liquids in Table 3 for which all properties *other* than $\sum \alpha_2^H$ and $\sum \beta_2^H$ have been measured and are tabulated in Table 1, namely, [BMIM][BF₄], [BMIM][NTf₂], and [BMIM][PF₆]. Thus, the SMD universal solvation model can be applied without further consideration to make predictions for these three solvents using eqs 1 and 2 and the available Kamlet and Taft parameters.

For all of the other ionic liquids in Tables 1 and 3, either some solvent descriptor in Table 1 or the Kamlet and Taft hydrogen bonding parameters are missing. To address such cases, we define solvent-independent generic values for all of the solvent descriptors by averaging the various descriptors over all ionic liquids for which measurements *are* available. Thus, for ϵ the average is 11.50 over 10 ionic liquids, for n the average is

1.4300 over 9 ionic liquids, for γ the average is 61.24 cal mol⁻¹ Å⁻² over 10 ionic liquids, and for $\Sigma\alpha_2^H$ and $\Sigma\beta_2^H$ the averages are 0.229 and 0.265, respectively, over 8 ionic liquids (see Tables 1 and 3 for data). We note that other attempts to correlate macroscopic ionic liquid descriptors with various measured properties have been reported,⁹⁴⁻⁹⁷ and these may provide useful alternatives to estimating missing values in certain instances, but we will not explore these approaches here.

In the present study, we test three computational protocols based on the SMD solvation model. When all the necessary solvent descriptors for the ionic liquid under consideration are available from experiment (noting that for any ionic liquid studied here, we derive “experimental” $\Sigma\alpha_2^H$ and $\Sigma\beta_2^H$ values from their correlations with measured Kamlet-Taft α and β values using eqs 1 and 2, *vide supra*), we can perform “true” SMD calculations. In such calculations, the ionic liquid is treated no differently than any other liquid in terms of being amenable to application of the universal SMD model. Such calculations will be labeled here as SMD. We will also test the model in which all solvent descriptors except ϕ and ψ are set equal to the average (“generic”) values presented above; such calculations will be called SMD-GIL, where GIL implies Generic Ionic Liquid. Finally we test a practical compromise method in which we use any solvent descriptors that *are* available for the ionic liquid under consideration, and replace any missing ones with the generic parameters; this may be considered as a practical approximation to a proper SMD calculation, and in the present paper results obtained this way will be labeled SMD-PGP, where PGP denotes that we use Partial Generic Parameters. The philosophy of the SMD-PGP model is that any solvent descriptor that is not available from an experimental measurement shall be taken to be the average of that descriptor over all ionic liquids for which measurements *are* available.

Solute geometries and electronic structures were optimized using *Gaussian 09*⁹⁸ with the M06-2X⁹⁹ density functional and the MG3S¹⁰⁰ basis set for all molecules except for one iodine-containing molecule (iodomethane) for which the MIDI! basis set¹⁰¹ was

employed on all atoms. The SMD solvation free energies were computed at the M05-2X¹⁰²/6-31G(d,p)¹⁰³ level of theory using *Gaussian 03*¹⁰⁴ and the *GESOL* program.¹⁰⁵ The latter takes advantage of the external option of *Gaussian 03* in order to incorporate the SMD model in *Gaussian 03*. These results can be readily reproduced (see the Supporting Information) using the SMD model incorporated in *Gaussian 09*. Examples of appropriate *Gaussian 09* input files for SMD calculations are given in the Supporting Information. The Supporting Information also presents results of additional solvation energy calculations carried out using SMD/B3LYP¹⁰⁶⁻¹⁰⁹/6-31G(d,p), SMD/M06-2X/6-31G(d,p), SMD/M06-2X/MG3S, and SM8⁷⁶/M06-2X/6-31G(d,p). Note that the SM8 solvation model (tested here by using a locally modified version of *Gaussian 09*) is a self-consistent reaction field continuum solvation model based on the generalized Born approximation for the bulk electrostatic contribution to the free energy of solvation (see Ref⁷⁶ and references therein) whereas the SMD model utilizes the continuous charge density of the solute molecule.

We turn now to a summary of results from the SMD, SMD-PGP, and SMD-GIL models.

Results and Discussion

The available experimental data relevant to ionic liquids consist of partition coefficient measurements corresponding to free energies of transfer for various solutes between ionic liquids and water. In particular, we have 431 transfer free energies associated with 11 different ionic liquids (out of 12 ionic liquids introduced in Table 1) and water. For 344 out of 431 cases, the hydration free energy for the solute is also known experimentally. Therefore, one can compute the gas-to-ionic-liquid solvation free energy as

$$\Delta G_{\text{solv,IL}}^{\circ} = -2.303RT \log P_{\text{IL/S}} + \Delta G_{\text{solv,S}}^{\circ} \quad (3)$$

where $\Delta G_{\text{sol},X}^0$ is the 1 M standard-state free energy of solvation of the solute in either the ionic liquid ($X = \text{IL}$) or an ordinary solvent ($X = \text{S}$), respectively, R is the universal gas constant, T is the temperature in Kelvin, and $P_{\text{IL/S}}$ is the partition coefficient measured as concentration in the ionic liquid divided by concentration in the ordinary solvent.¹⁸ All data and references are provided in the Supporting Information. In this work the ordinary solvent S is always water, but the theory is general enough to be applied to organic liquids for future applications.

We present in Table 4 the predictions of the SMD, SMD-PGP, and SMD-GIL models for the 344 derived gas-to-IL solvation free energies. Again, the distinction is that for the SMD predictions, all of the necessary solvent descriptors for the ionic liquids involved are available from experiment (noting that for any ionic liquid studied here, we derive “experimental” $\Sigma\alpha_2^{\text{H}}$ and $\Sigma\beta_2^{\text{H}}$ values from the correlations with measure Kamlet and Taft α and β values using eqs. 1 and 2). Thus, the ionic liquid is treated no differently than any other liquid in terms of being amenable to application of the universal SMD model. There are three ILs for which a standard SMD calculation can be performed. For the remaining ionic liquids, for which at least one solvent descriptor (other than ϕ and ψ) is *not* available, we utilize the SMD-PGP protocol where any missing descriptors are replaced by the average values already noted above. Finally, the SMD-GIL protocol is applied to each ionic liquid in the table, irrespective of the availability of some solvent descriptors. SMD-PGP and SMD-GIL calculations are identical for the cases of $[\text{M}_3\text{BAm}][\text{NTf}_2]$ and $[\text{MBPy}][\text{BF}_4]$ because for these ionic liquids there are *no* measured values for any solvent descriptors other than ϕ and ψ , i.e., we *must* use entirely generic values. The corresponding water-to-IL transfer free energy data are presented in Table 5.

Table 4. Errors in Predicted Ionic Liquid Solvation Free Energies (kcal/mol) ^a

Ionic Liquid	N	SMD		SMD-PGP		SMD-GIL	
		MSE	MUE	MSE	MUE	MSE	MUE
[BMIM][BF ₄]	2	−0.08	0.20			−0.66	0.66
[BMIM][NTf ₂]	51	−0.37	0.45			0.07	0.33
[BMIM][PF ₆]	40	0.22	0.53			−0.31	0.61
[EMIM][BF ₄]	2			−0.86	0.86	−1.18	1.18
[EMIM][DCA]	48			−0.31	0.69	−0.29	0.65
[EMIM][NTf ₂]	37			−0.44	0.49	−0.13	0.30
[EMIM][OTf]	28			−0.41	0.51	0.02	0.34
[HMIM][NTf ₂]	54			−0.52	0.57	0.19	0.37
[HMIM][PF ₆]	2			2.23	2.23	1.85	1.85
[M ₃ BAm][NTf ₂]	42			−0.04	0.31	−0.04	0.31
[MBPy][BF ₄]	38			−0.28	0.39	−0.28	0.39
3 ILs	93	−0.11	0.48			−0.11	0.46
8 ILs	251			−0.32	0.52	−0.08	0.42
all 11 ILs	344			−0.26 ^b	0.51 ^b	−0.08	0.43

^a N is number of data in each ionic liquid, MSE is mean signed error, and MUE is mean unsigned error. ^b Over a combination of 93 SMD data and 251 SMD-PGP data

Table 5. Errors in Predicted Water-to-Ionic-Liquid Transfer Free Energies (kcal/mol) ^a

Ionic Liquid	N	SMD		SMD-PGP		SMD-GIL	
		MSE	MUE	MSE	MUE	MSE	MUE
[BMIM][BF ₄]	3	−1.71	1.78			−2.30	2.30
[BMIM][NTf ₂]	60	−0.10	0.56			0.33	0.54
[BMIM][PF ₆]	85	1.15	1.45			0.52	1.11
[EMIM][BF ₄]	3			−0.18	0.63	−0.54	0.71
[EMIM][DCA]	53			−0.24	0.59	−0.21	0.55
[EMIM][NTf ₂]	41			−0.26	0.55	0.05	0.47
[EMIM][OTf]	31			−0.27	0.30	0.15	0.27
[HMIM][NTf ₂]	63			−0.40	0.49	0.35	0.53
[HMIM][PF ₆]	6			1.09	1.18	0.64	0.99
[M ₃ BAm][NTf ₂]	48			0.06	0.40	0.06	0.40
[MBPy][BF ₄]	38			−0.16	0.30	−0.16	0.30
3 ILs	148	0.59	1.10			0.39	0.90
8 ILs	283			−0.19	0.47	0.06	0.46
all 11 ILs	431			0.08 ^b	0.69 ^b	0.17	0.61

^a See corresponding footnote in Table 5 ^b Over a combination of 148 SMD data and 283 SMD-PGP data

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4 Interestingly, the SMD model applied to [BMIM][BF₄], [BMIM][NTf₂], and
5 [BMIM][PF₆] leads to errors of about the same magnitude that SMD achieves for
6 ordinary solvents (Table 4). That is, the universality of the solvent model is not adversely
7 affected by the molten salt nature of the ionic liquid. As the average ionic liquid solvent
8 descriptors are quite close to those measured for these three solvents, the SMD-GIL
9 model performs very similarly to SMD and SMD-PGP, with the exception of
10 [BMIM][BF₄], for which only two data are available.
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18 With respect to the remaining eight ionic liquids in Table 4, the errors are quite
19 similar to those for the three already discussed. Interestingly, the results from the SMD-
20 GIL model are better than those from the SMD-PGP model. One way to interpret this
21 point would be to say that all of the ionic liquids considered here are more similar to one
22 another than is consistent with the variation in their macroscopic descriptors. However,
23 the MUE difference between the two models over all 11 ILs is less than 0.1 kcal/mol, so
24 it is difficult to assess this point in the absence of a collection of ionic liquids showing
25 substantially greater variation from the average in one or more solvent descriptors.
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35 There are some systematic trends that are worthy of note. For instance, when BF₄
36 is the anion, in two cases out of three, the MUE is equal in magnitude to the MSE,
37 meaning that every single prediction is in error in the same direction (in this case,
38 predicting too favorable a solvation free energy in the ionic liquid). When PF₆ is the
39 anion, the error seems to be systematically in the positive free energy direction, although
40 it is somewhat speculative to put too much weight on the only two data points measured
41 for [HMIM][PF₆]. Should more data be acquired in the relevant ionic liquids, it may be
42 possible to explore these points more closely.
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51 Turning to the case of transfer free energies, we see essentially the same trends
52 and systematic errors as those noted above for the solvation free energies. The predicted
53 MUEs for the water-to-IL transfer free energies are somewhat larger than are those for
54 the directly predicted solvation free energies, but they are still within the range of typical
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SMD errors. The increase in magnitude may reflect increasing diversity in the larger data set of transfer free energies.

Paulechka et al.¹¹⁰ measured the vapor pressure of [BMIM][NTf₂] from 458 to 517 K and derived an equation relating vapor pressure to temperature. If we extrapolate their equation to 298 K, and convert vapor pressure to free energy of (self) solvation according to¹⁸

$$\Delta G_{\text{solv,IL}}^{\circ} = -RT \ln \left(\frac{M_{\text{IL}} / M^{\circ}}{P_{\text{IL}} / P^{\circ}} \right) \quad (4)$$

where M_{IL} is the molarity of the ionic liquid (derived from its molecular weight and its density⁸⁷), P_{IL} is its vapor pressure, and M° and P° are the relevant standard state units, in this case, mol/L, we arrive at a self-solvation free energy of -22.0 kcal/mol. With the SMD solvation model at the M05-2X/6-31G(d,p) level of theory, we compute a value of -19.1 , which seems quite reasonable agreement given the use of a tight-ion-pair gas-phase structure in this instance. The gas-phase M06-2X/MG3S optimized molecular geometry of [BMIM][NTf₂] used in this calculation is given in the Supporting Information.

We also examined the free energies of transfer between ionic liquids and water of three steroid derivatives, namely dexamethasone, 5-dehydroepiandrosterone (DHEA), and progesterone (these solutes are in addition to the 149 solutes discussed above). Their molecular structures are depicted in Figure 1. Table 6 shows computed values of $\log P_{\text{IL/w}}$ corresponding to the free energy of transfer from water (w) to the ionic liquids [BMIM][PF₆], [HMIM][PF₆], or [OMIM][PF₆], and compares to available experimental data.⁸⁹ We employed the SMD and SMD-GIL computational protocols at the M05-2X/6-31G(d,p) level of theory as well as SM8/M06-2X/6-31G(d,p). We note that the values of $\log P_{\text{IL/w}}$ predicted for DHEA and progesterone are in satisfactory agreement with available experimental data but the $\log P_{\text{IL/w}}$ values for dexamethasone predict this steroid to favor water strongly over any of the tested ionic liquids, which is not consistent with

experiment, where small preferences for the ionic liquids are measured. The absolute solvation free energies predicted for dexamethasone in any of the ionic liquids or water are much more negative than are corresponding solvation free energies predicted for DHEA and progesterone. The SM8 solvation model predicts a $\log P_{\text{IL/w}}$ value for dexamethasone in somewhat better agreement with experiment than do SMD or SMD-GIL (see Table 6) because all SM8 predictions are between 1 and 2 log units more positive than the SMD predictions. Table 6 also presents the computed octanol–water logP values which are in better agreement with available experimental data¹¹¹ (within 0.5 log units) than the corresponding IL–water logP values. For solvation calculations in octanol we used the following values of octanol's descriptors: $\epsilon = 9.8629$, $n = 1.4295$, $\gamma = 39.01$, $\phi = \psi = 0$, $\Sigma\alpha_2^{\text{H}} = 0.37$, and $\Sigma\beta_2^{\text{H}} = 0.48$ (these values can be compared to those for the studied ionic liquids given in Table 1 and the text).

Figure 1. Molecular Structures of 3 Steroid Derivatives. Hydrogen atoms are white, carbon is grey, fluorine is cyan, and oxygen is red.

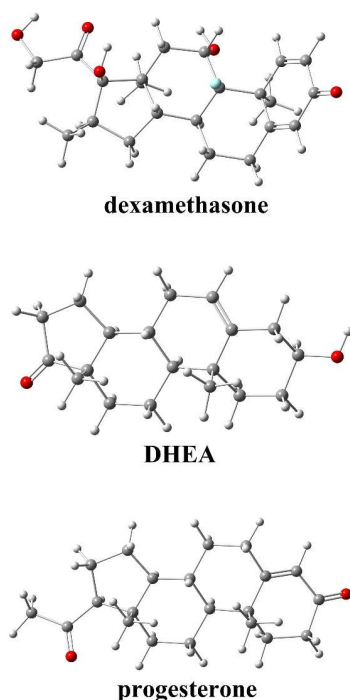


Table 6. Values of $\log P_{\text{IL/w}}$ for Three Steroid Derivatives ^a

Solute	Theory			Exp
	$\Delta G_{\text{sol},w}^{\circ}$	$\Delta G_{\text{sol},\text{IL}}^{\circ}$	$\log P_{\text{IL/w}}$	$\log P_{\text{IL/w}}$
[BMIM][PF ₆], SMD-GIL				
dexamethasone	-20.37	-18.43	-1.42	0.011 ± 0.008
DHEA	-10.01	-12.41	1.77	0.98 ± 0.09
progesterone	-9.19	-12.41	2.36	2.35 ± 0.13
[HMIM][PF ₆], SMD-GIL				
dexamethasone	-20.37	-18.35	-1.48	0.29 ± 0.02
DHEA	-10.01	-12.34	1.71	0.91 ± 0.14
progesterone	-9.19	-12.33	2.30	2.14 ± 0.35
[OMIM][PF ₆], SMD-GIL				
dexamethasone	-20.37	-18.30	-1.52	0.32 ± 0.08
DHEA	-10.01	-12.29	1.68	0.87 ± 0.08
progesterone	-9.19	-12.28	2.26	2.01 ± 0.14
[BMIM][PF ₆], SMD				
dexamethasone	-20.37	-17.14	-2.37	0.011 ± 0.008
DHEA	-10.01	-11.19	0.87	0.98 ± 0.09
progesterone	-9.19	-10.92	1.27	2.35 ± 0.13
[BMIM][PF ₆], SM8				
dexamethasone	-14.52	-13.38	-0.84	0.011 ± 0.008
DHEA	-6.48	-9.32	2.08	0.98 ± 0.09
progesterone	-6.62	-10.45	2.80	2.35 ± 0.13
<i>n</i> -octanol, SMD				
dexamethasone	-20.37	-22.17	1.32	1.83
DHEA	-10.01	-15.02	3.68	3.23
progesterone	-9.19	-14.71	4.04	3.87

^a The mean signed and the mean unsigned errors relative to experiment (Exp) in the $\log P$ values calculated over the nine SMD-GIL data are equal to -0.25 and 0.87 log units, respectively.

The SMD-GIL model is able qualitatively to predict the experimentally observed trends associated with increasing alkyl chain length of the imidazolium component of the ionic liquid. For example, proceeding from BMIM to HMIM to OMIM, observed partition coefficients and the computed SMD-GIL values somewhat decrease for DHEA and progesterone. The same trend is predicted by the SMD-GIL model. As more

experimental data become available, it will be interesting to explore whether such trends across multiple ionic liquids may be used to further refine the continuum models.

Concluding remarks

We have previously developed solvation models for predicting free energies of solvation and transfer for solutes in water and molecular (nonionic) organic solvents. The models differ from most other solvation models in that they include consistently optimized parameters for the first solvation shell as well as a treatment of bulk electrostatics^{30,70} and in that they are universal.⁷¹⁻⁷³ The solvation models are universal in the sense that they may be applied to any solvent for which a small set of solvent descriptors is available, in particular dielectric constant, refractive index, macroscopic surface tension, and Abraham-type acidity and basicity parameters. The present study shows that these models may be applied successfully to ionic liquids. Furthermore, we were able to obtain a set of generic parameters that yield high accuracy for solvation free energies of all tested ionic liquids, even those for which the actual solvent descriptors are not presently available. The latter result unveils a previously unappreciated universality in the solvation characteristics of ionic liquids, at least over the range studied here.

■ ASSOCIATED CONTENT

Supporting Information.

Reference data for water/ionic-liquid partitioning data and associated literature references, an extended table with errors in solvation and transfer free energies calculated by various methods, and Cartesian coordinates of tested solute molecules. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Graphical Abstract

