

A Molecular Level Understanding of Template Effects in Ionic Liquids

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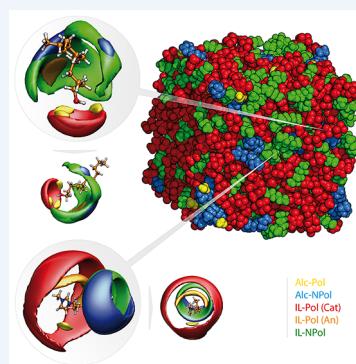
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Supporting Information

CONSPECTUS: The structure-directing or template effect has been invoked several times for ionic liquids to explain the different outcome in material synthesis, namely, different scaffolds or geometrical arrangements with varying ionic liquids. It is obvious to assume that such an effect can originate from the most likely complex microstructure, being present within the ionic liquid itself. In that regard, ionic liquids have already been shown to undergo a nanosegregation into polar and nonpolar phases, which is commonly known and denoted as microheterogeneity.

In order to provide detailed insight on the molecular level and to understand the effects rising from this structuring, we performed molecular dynamics simulations on selected very simple model systems composed of 1-alkyl-3-methylimidazolium bis-(trifluoromethylsulfonyl)imide, considering ethyl, butyl, hexyl, and octyl side chains attached to the cations, mixed with either *n*-dodecanol or *n*-butanol. By analyzing snapshots of the simulation boxes and calculating spatial distribution functions, we can visualize that with increasing side chains, the systems show considerable nanosegregation into polar and nonpolar domains. Combined angular and distance distribution functions show that in case of the nanosegregating systems the side chains of the cations are preferentially arranged in a parallel fashion, which indicates a micelle-like structure for the ionic liquids. The alcohol molecules participate in and are, therefore, influenced by this microheterogeneity. It can be shown that in the case of the short IL alkyl side chains, the self-aggregation of the nonpolar units of the alcohols is much stronger, while for the long chain cations, the nonpolar entities of the alcohols are most often connected to the nonpolar units of the ionic liquids. Using our domain analysis tool, we can quantify these observations by tracking the number, size, and shape of the polar and nonpolar entities present in the different investigated systems. The aforementioned combined angular-distance distribution functions reveal a structure-directing effect of the ionic liquids on the alcohol molecules within our simple model systems. The ionic liquids act as template and order the alcohol molecules according to their own structure, resulting in a parallel alignment of the alkyl side chains of the alcohols and ionic liquid cations, with both polar groups being at the same side. These observations show that the microheterogeneous structure of ionic liquids can indeed be applied to order substrates with respect to each other or, for example, to catalysts in a predetermined fashion, opening new possibilities for explaining or enhancing selectivities of chemical reactions in ionic liquids.



1. INTRODUCTION

As opposed to traditional molten salts,^{1–4} ionic liquids (ILs)^{5,6,7–8} possess polar and nonpolar moieties, which in many cases results in a distinct structural ordering. Resulting from this polar–nonpolar nature (one has to be careful here not to associate electrostatic forces with the polar part and dispersive forces with the nonpolar part; both parts have electrostatic and dispersive portions just differently weighted⁴), and the underlying balance between weak and Coulombic interactions, many ILs form nanosegregated structures, that is, microheterogeneity (MH).^{3,9–15} Hence, the term “supramolecular fluids” has been coined by Dupont to describe supraionic aggregates observed in ILs.² These features of ILs point to a different view than simply considering them as solvents; namely, it highlights their ability to act as structure-directing agents or templates.¹⁶ Such effects have been discussed extensively for standard supramolecular systems.¹⁷

Traditionally, the template effect is described as the template organizing other components of a system and allowing for

product formation that would not form as easily or at all in the absence of the template.¹⁸ This is accompanied by chemical reactions, in which significant spatial, topological, or geometric control is achieved, where the structural information stored in the template is transferred to the product. It has been pointed out repeatedly that a template works as an “entropic sink”, due to the introduction of the aforementioned increased ordering within the given system.¹⁹ One prominent example is the template-assisted synthesis of rotaxanes.²⁰ Vögtle and co-workers²⁰ have discussed the mechanism of threading a macrocycle wheel onto an axle to proceed via a pseudo- or semirotaxane complex, in which the guest is fixed by hydrogen bonds inside the host cavity. The preorganization of the axle enables a further reaction of the reactive groups at the end of the axle to form stoppers and thus a full rotaxane molecule.

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Template or structure-directing effects in ILs¹⁶ have been suggested especially in the field of inorganic material synthesis.^{16,21–23}

It was reported that the IL ions incorporate into the forming solid state product during the synthesis, and therefore through directing the structure new materials can be obtained.²³ Evidence for this phenomenon was found during the synthesis of three-dimensional iodometallate networks like $\text{GeI}_4\text{--I}^-$ and $[\text{Bu}_3\text{MeN}]_3[\text{cis-Bi}_3\text{I}_{12}]$, using ILs with asymmetrically substituted and sterically demanding cations.^{24,25} ILs recently have found increasing use as reaction media in the synthesis of zeolite-analogous framework compounds and metal–organic frameworks. In contrast to their conventional synthesis, which was performed under hydro- and solvothermal conditions via suitable templates, Morris et al. proposed a so-called “ionothermal synthesis” in ILs.^{21,22} For this method, IL solvents with large organic cations are used, which can directly act as template to guide the synthesis pathway. Liquid clathrate formation, occurring upon mixing ILs with aromatic hydrocarbons, presents another example where template effects might play a role.^{26–28} Liquid clathrates are generally considered to be liquid yet localized host–guest complexes formed by associative interactions between salt ions and aromatic molecules.

The first step toward understanding such complicated effects lies in understanding the nature of the IL itself. As mentioned already, microheterogeneity can be considered as a self-organization of the IL and thus could be highly relevant for the IL playing a role as a template. Several studies have contributed to the understanding of MH.^{3,9–15} MH shows a distinct dependence on the length of the side chains at the IL ions, typically attached to the cation. Although the side chains tend to aggregate already at the shortest applied ethyl groups,^{11,15} these aggregates are generally very small. It was observed by theory^{9–11} and later by experiments¹² that increasing the length of the side chain on the cation to longer than a butyl group results in the formation of a continuous nonpolar microphase that stretches through the whole system. Interestingly, an influence of the anion has also been observed on the aggregation of the cationic side chains.^{13,15} Naturally, functionalizing the side chains influences the MH. For instance, side chain perfluorination increases the segregation behavior compared to their parent alkyl side chain.^{13–15} Considering the tendency of fluoruous groups to segregate into a separate domain from both polar groups and hydrocarbons, fluorination opens the possibility to build even three microphases. By attaching long perfluorinated side chains to the anions, while having cations with large alkyl groups, Triolo and co-workers,²⁹ and later Rebelo and co-workers created such “triphylic” ionic liquids.³⁰ In a combined theoretical and experimental study, we have shown that the triphilicity can even be tuned by mixing ILs with alkyl and perfluoroalkyl side chains at the cations with different molar fractions.¹⁴

All the information above points to the existence of supramolecular structures in ionic liquids, which may be tuned through changing the components of the liquid. Since such features generally infer the possibility of template effects, and as described above there are indeed some scattered information on such phenomena in ILs, we will aim here to investigate this issue in detail theoretically. For such purposes, theoretical methods are ideal tools, since they allow direct insight into the microscopic level picture,³ providing, therefore, an in-depth understanding of the governing structural features.

We investigate the possibility of template effects of ILs on solute alcohol molecules, thus for very simple model systems.

Alcohol–IL mixtures have been studied in detail already.^{31–34} In various methanol–IL mixtures both theoretical^{31,32} and experimental^{32,33} results show that this small alcohol molecule interacts mainly with the polar part of the IL, in particular through hydrogen bonds with the anions. At higher methanol concentrations and in case of the weak hydrogen bond acceptor bis(trifluoromethylsulfonyl)imide ILs, the alcohol molecules tend to form larger clusters in the liquid through the strong methanol–methanol hydrogen bonds.³² On the other hand, hydrocarbons, such as *n*-hexane, tend to interact mainly with the alkyl groups of the IL.³¹ Accordingly, aliphatic alcohols can be expected to interact mainly with the polar, the nonpolar, or both microphases in a microheterogeneous IL, depending on the length of the side chains of the alcohol and the IL. Recent calorimetric experiments indirectly support this idea.³⁴

Therefore, in this work, we apply molecular dynamics simulations on model systems composed of the imidazolium based ILs 1-alkyl-3-methylimidazolium bis-(trifluoromethylsulfonyl)imide considering ethyl, butyl, hexyl, and octyl side chains attached to the cation ($[\text{C}_x\text{C}_1\text{Im}][\text{NTf}_2]$, $x = 2, 4, 6, 8$) mixed with either *n*-dodecanol or *n*-butanol in a ratio of 5:1 ion pairs of the IL to alcohol molecules (cf. Supporting Information for more details).

2. ANALYZING MOLECULAR DYNAMICS SIMULATIONS

Molecular dynamics simulations generate a large data file, that is, the trajectory, which contains for each of the discretized time steps the configuration with atomic positions and velocities of the simulated system.³⁵ This amount of data needs to be processed during the analysis and turned into chemically meaningful data, where the orientation of the molecules, as well as their movements can be shown. Our open source software TRAVIS³⁶ makes it possible to extract data beyond the regular analysis, and the supramolecular structure of the liquid can also be quantified. Below a few details are given regarding this function; more information on the analyses can be found in ref 36. The full simulation details of the present work are given in the Supporting Information.

The dissection of the liquid into domains is initiated by defining their building blocks, that is, subsets.¹⁵ These subsets can be functional groups or parts of the molecules or complete molecular entities. Then a radical Voronoi tessellation is performed, where all atoms are considered as Voronoi sites (i.e., points around which the Voronoi polyhedra are constructed). In this approach, the van der Waals radii are used to define borders, and thus volumes and surfaces for each atom, creating the atomic Voronoi cells, which will sum up to the cells of each subset. Those kind of subsets, which we initially defined to be building blocks of the same chemical nature (e.g., alkyl groups), belong to the same domain (e.g., nonpolar domain) if their cells share a common face. This allows us to obtain the average number of each kind of domain present in the liquid, which we call in this paper domain count, N_{Dom} . Any value for N_{Dom} that is smaller than the total number of the particular subsets that constitute it represents a certain aggregation in the system. If this domain count is one, it means that the subsets are forming a single, continuous microphase that stretches through the liquid. Since the Voronoi tessellation defines surfaces for the subsets, one can also calculate how

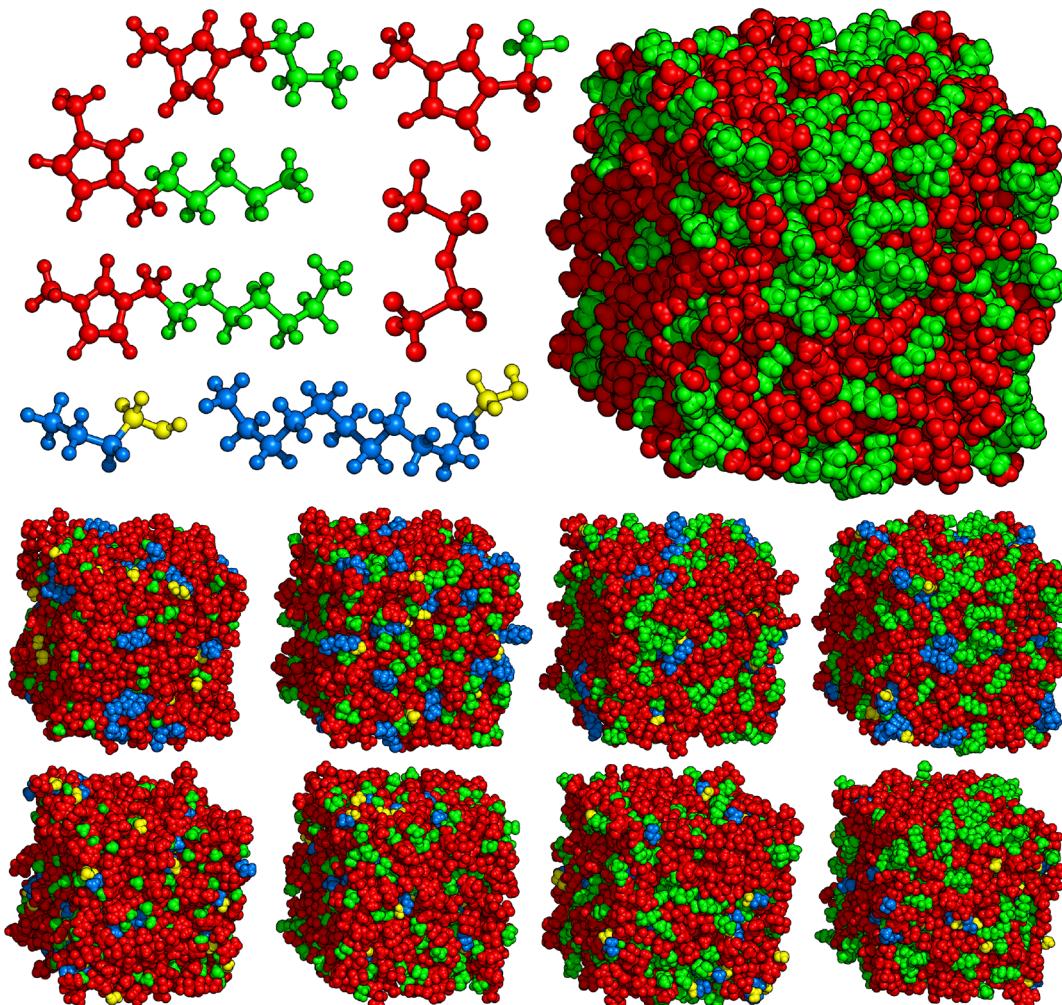


Figure 1. Snapshots of the simulated systems illustrating possible microheterogeneities. In the upper right snapshot, we distinguish only between polar (red) and nonpolar (green) subsets in the *n*-dodecanol in $[C_8C_1\text{Im}][\text{NTf}_2]$ system. For the eight snapshots below red indicates polar units of the ILs (P-IL), green indicates nonpolar units of the ILs (N-IL), yellow indicates polar units of the alcohols (P-A), and blue indicates nonpolar units of the alcohols (N-A). The upper four snapshots represent the systems composed of *n*-dodecanol in $[C_xC_1\text{Im}][\text{NTf}_2]$ with $x = 2$ (left) to $x = 8$ (right), and the lower ones represent the *n*-butanol containing analogues.

much of the surface of each subset is covered by any of the subsets in the system. It is worth mentioning here that we applied successfully the radical Voronoi tessellation beside the domain analysis, also in calculating partial atomic charges in systems with significant charge transfer³⁷ and with respect to the calculation of vibrational spectra,^{38–40} that is, for the discussion of the microscopic structure in systems with a strong dynamic network of intermolecular interactions, such as ILs.

3. OBSERVING THE TEMPLATE EFFECT IN IONIC LIQUIDS

The visual inspection of the simulated systems already shows some highly important information regarding the microheterogeneity (MH) and the template effect. Figure 1 shows a snapshot of each simulated system. First we focused on the MH in total, regardless of whether the alkyl side chains or the polar groups are from the alcohol or from the IL (see top right of Figure 1). It is clearly visible that in case of the long side chains the polar (red) and nonpolar groups (green) are segregated in the liquid, forming a highly microheterogeneous structure. The template effect of the IL should lie in the arrangement of the alcohol molecules within this mesoscopic

structure. Distinguishing the side chains of the alcohol molecules and the IL cations, as well as the polar moieties of the alcohol and the IL, shows interesting trends.

It is apparent that the polar units of the alcohol (yellow) are always connected to the polar components of the ILs (at least half a solvent shell is formed), showing in agreement with the previous studies^{31–34} the strong interactions between the polar components through hydrogen bonding; see also the spatial distribution functions (SDFs) in Figure 2 and the discussion below. For the side chains of the alcohols (blue), it is clearly visible that the self-aggregation is much stronger for *n*-dodecanol than for *n*-butanol, due to the difference in the length of the alkyl groups. Moreover, while the self-aggregation of the alcohols' nonpolar units is clearly observable in case of the ILs with shorter side chains (Figure 1 left), in case of longer cationic side chains (Figure 1 right), these blue units are dispersed, and they interact with the nonpolar moieties of the IL rather than with each other. The clustering of alcohols has been observed before for ILs with short side chains,³² but this was originated from hydrogen bonding in methanol, and here, we observe the aggregation due to the long side chains of the alcohols in short side chain-ILs and the disruption of the

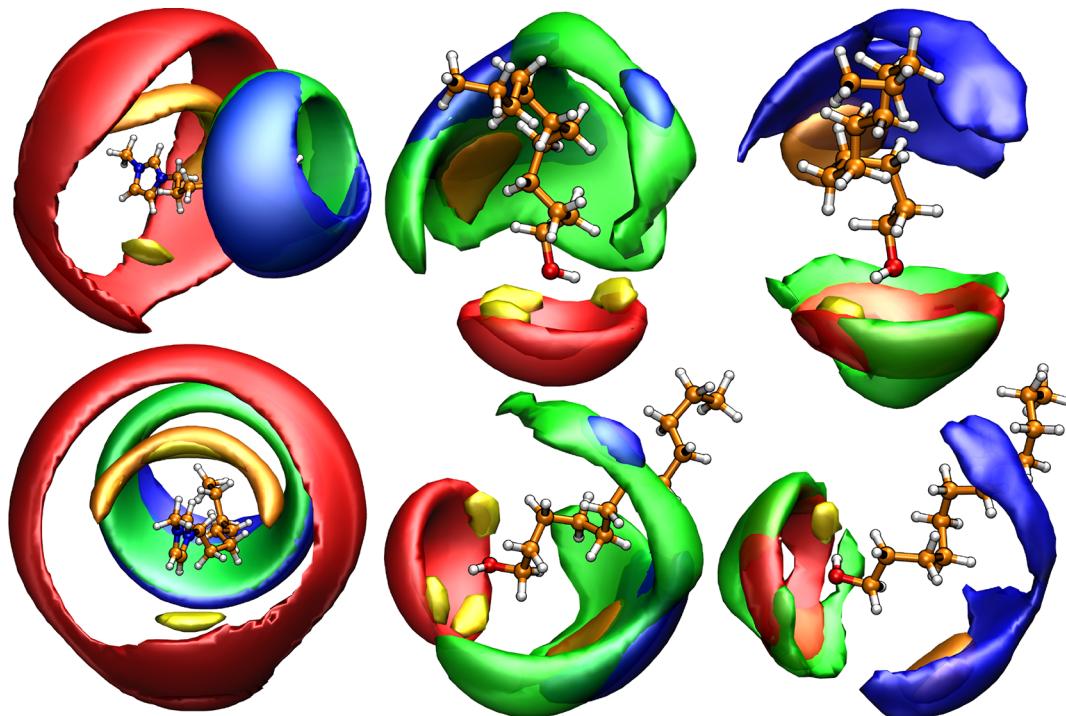


Figure 2. SDFs for components around the $[C_8C_1\text{Im}]^+$ cation (left panels), the *n*-dodecanol alcohol in $[C_8C_1\text{Im}][\text{NTf}_2]$ (middle panels), and the *n*-dodecanol alcohol in $[C_2C_1\text{Im}][\text{NTf}_2]$ (right panels). Colors were chosen similar to the colors for the snapshots, but here we distinguished between the anion and cation of the P-IL domain (cf. Figure 1: P-IL cation, red; P-IL anion, orange; N-IL, green; P-A, yellow; N-A, blue).

alcohol's self-aggregation in long side chain-ILs. This indicates a possible template effect in long alkyl side chain ILs, in which the alkyl moieties of the alcohols are aligned according to the order within the IL side chains, instead of self-aggregation.

Although the snapshots showed a clear indication that a template effect might be present in the hereby investigated systems, the structure has to be characterized in a systematic and quantitative manner and averaged over the course of the full simulations to prove this phenomenon. We first performed a detailed Voronoi and domain analysis, as described in the previous section.

Table 1 lists the number of domains, N_{Dom} , formed by the different subsets. It can be seen for $[C_2C_1\text{Im}][\text{NTf}_2]$ that, in agreement with the conclusions from the snapshots, the polar subsets (P) form a single domain, which shows that the alcohol

molecules are interacting through their hydroxyl group with the polar part of the ionic liquid. The nonpolar components (N), on the other hand, show a high number of domains, indicating that the ethyl side chains of the IL cations are not long enough to form larger structural units than small clusters in the liquid. By the increase of the IL's side chain length, the number of nonpolar mesoscopic units drops rapidly, showing a progressive growth of the alkyl islands in the liquid. This is in good accordance with the typical behavior of such ILs.^{3,9–15} Interestingly, although the number of polar domains is 1.0 in almost all systems, in case of the *n*-dodecanol in $[C_8C_1\text{Im}][\text{NTf}_2]$ simulation, it rises to a value of 1.1. This finding can be explained by the—compared to the other systems—extensive interaction between the N-A and N-IL subsets, which overcome the attraction of the hydroxyl moiety to the polar units of the IL, occasionally albeit rarely pulling the alcohol molecule out of the vicinity of the polar domain completely, splitting thereby the single polar domain into two entities.

Considering the functional groups of the alcohol molecules separately from those of the IL, an interesting trend can be observed. The domain counts of the P-A subsets, are barely influenced by the increase in the alcohol or IL side chains. The N_{Dom} values are in all cases between 40 and 43. This indicates that the 50 alcohol molecules are embedded in the liquid almost always separately from each other, and hydrogen bonds between them are relatively rare. Interestingly, the N-A subsets show a completely different behavior. Upon the increase of the side chain length, the *n*-dodecanol aggregates decrease in size significantly, as the domain counts almost double, showing the exact opposite change compared to the IL's N-IL subsets. For *n*-butanol, the changes are not that dramatic, but their dissociation is nevertheless notable. These findings confirm the picture obtained from the snapshots above: The nonpolar alcohol subsets (N-A) stick together when the N-IL part is

Table 1. Domain Analysis for Different ILs $[C_xC_1\text{Im}][\text{NTf}_2]$ Mixed Together with Alcohols $H_{2y+1}\text{C}_y\text{OH}^a$

IL	ALC	N_{Dom}					
		P (500)	N (300)	P-IL (500)	N-IL (250)	P-A (50)	N-A (50)
$x = 2$	$y = 12$	1.0	50.5	1.0	136.4	40.5	7.7
$x = 4$	$y = 12$	1.0	5.5	1.0	29.0	40.9	10.0
$x = 6$	$y = 12$	1.0	1.5	1.0	4.8	41.7	12.3
$x = 8$	$y = 12$	1.1	1.1	1.0	1.6	41.6	13.6
$x = 2$	$y = 4$	1.0	81.4	1.0	126.4	40.2	31.9
$x = 4$	$y = 4$	1.0	7.7	1.0	19.6	41.7	34.9
$x = 6$	$y = 4$	1.0	1.9	1.0	2.9	41.3	34.3
$x = 8$	$y = 4$	1.0	1.2	1.0	1.3	42.4	36.3

^aThe number of domains N_{Dom} emanating from the different subsets P, N, P-IL, N-IL, P-A, and N-A are shown. The maximal N_{Dom} values for each subset are shown in parentheses after the subset names.

Table 2. Surface Coverage from Voronoi Analysis for Different ILs $[C_xC_1Im][NTf_2]$ Mixed Together with Alcohols $H_{2y+1}C_yOH^a$

IL	ALC	P-IL	N-IL	P-A	N-A	P-IL	N-IL	P-A	N-A
P-IL coverage									
$x = 2$	$y = 12$	74.6	14.0	2.1	9.3	85.2	5.2	1.5	8.0
$x = 4$	$y = 12$	67.1	22.8	1.9	8.1	75.2	14.1	1.6	9.1
$x = 6$	$y = 12$	62.8	28.1	1.8	7.3	66.8	22.3	1.5	9.5
$x = 8$	$y = 12$	60.1	31.7	1.7	6.4	58.9	30.2	1.4	9.5
$x = 2$	$y = 4$	78.9	14.6	2.4	4.2	89.1	5.7	1.7	3.4
$x = 4$	$y = 4$	70.1	24.0	2.2	3.7	79.3	15.2	1.8	3.7
$x = 6$	$y = 4$	65.1	29.6	2.0	3.3	70.4	24.2	1.7	3.7
$x = 8$	$y = 4$	61.7	33.5	1.9	3.0	62.2	32.6	1.6	3.6
P-A coverage									
$x = 2$	$y = 12$	54.6	6.4	2.8	36.1	63.8	9.0	9.6	17.6
$x = 4$	$y = 12$	49.3	12.1	2.8	35.7	55.0	18.8	9.5	16.7
$x = 6$	$y = 12$	46.6	15.9	2.6	34.9	49.3	27.0	9.3	14.4
$x = 8$	$y = 12$	44.1	19.0	2.7	34.2	43.4	34.5	9.1	13.0
$x = 2$	$y = 4$	60.6	7.3	2.9	29.2	67.8	9.1	18.5	4.6
$x = 4$	$y = 4$	55.4	13.5	2.4	28.6	59.7	18.3	18.1	4.3
$x = 6$	$y = 4$	50.7	17.8	2.6	28.9	52.6	25.1	18.3	4.0
$x = 8$	$y = 4$	47.7	21.5	2.3	28.5	47.7	30.9	18.1	3.6
N-A coverage									

^aIt is distinguished between the subsets P-IL, N-IL, P-A, and N-A.

small, and they are more dispersed when the ILs become more microheterogeneous, that is, more connected in the N-IL part.

Creating the Voronoi cells in the system at each step of the simulation not only allows the domain analysis but also provides valuable information on the neighborhood of each subset and the interaction surfaces between the corresponding moieties. The average percentages that the different groups cover from the surface of each subset are shown in **Table 2** (note that each pair of subsets that are covalently bound to each other show, of course, some interaction surface; for example, N-IL possesses a high coverage by P-IL, which partly stems from the covalent bond between them). Apparently, for every subset, the coverage by N-IL increases by the increasing length of the cationic side chain, while the coverage by P-IL decreases. This indicates an increasing microheterogeneity and therefore confirms the conclusions from **Table 1**. Furthermore, in accordance with the results from the domain analysis, the surface coverages corresponding to the alcohol–alcohol interactions, especially between the alcohols’ alkyl chains, the coverages show a monotonous decreasing trend upon increasing the length of the cationic side chain; instead, the N-A subsets are covered more by the N-IL units. This further emphasizes that the alcohol molecules are pulled to the N-IL microphases, and the solvation of the alcohol molecules will be switched from the other alcohol molecules to the solvent when changing the structure of the IL.

After having seen how the embedding of the alcohol in the IL changes as the microheterogeneous structure of the solvent is altered, we focused on understanding how the local environment of the solute molecules differ in the present set of ILs. To observe the spatial, three-dimensional distribution of the previously defined subsets around the ions and molecules in the system, we created the spatial distribution functions (SDFs). In **Figure 2**, we illustrate the solvation of the $[C_8C_1Im]^+$ cation (left) and *n*-dodecanol in $[C_8C_1Im][NTf_2]$ (middle), and the *n*-dodecanol in $[C_2C_1Im][NTf_2]$ (right). For more detailed information on the SDF generation, including isovalue ranges (I_{min} – I_{max}) and chosen isovales I for SDF isosurfaces, see **Table S2** and the corresponding description in the Supporting Information.

In accordance with the microsegregation observed above, the SDFs around the cations clearly show the local distinction between the polar (yellow, orange, and red) and nonpolar (green and blue) subsets: The cationic imidazolium headgroup apparently attracts the polar moieties, while the nonpolar subsets are located around the side chain. The SDFs of the polar groups show the expected orientation around the cation. The anion (orange) and the alcohol’s polar groups (yellow) are mostly located in the close proximity of the ring hydrogen atoms. The further cations are arranged in the second solvent shell, completing the network of ions of the IL solvent. It is interesting to observe that the paths that represent the spatial distribution of side chains from the alcohols and the IL cations around the cations do almost completely overlap, suggesting the lack of significant selection between these moieties by the IL cation.

The SDFs around the alcohol molecules also shows some intriguing details regarding their solvation in the IL. The polar–polar interaction between the alcohol molecules is clearly visible in the three yellow spots at the hydroxyl group in the $[C_8C_1Im][NTf_2]$ solvent (**Figure 2**, middle). Such an interaction is also present in the IL $[C_2C_1Im][NTf_2]$, but not as pronounced (**Figure 2**, right). It is interesting to see that these weak hydrogen bond acceptor anions do not often form a hydrogen bond with the alcohol, as the orange spots are missing at these locations. Instead, the anions occupy the positions around the carbon atoms that are adjacent to the hydroxyl group. It seems possible that the interaction between the anion and the alcohol molecule is weak, and the polar IL–alcohol interplay is dominated by the hydrogen bond between the cation as donor and the alcohol as acceptor. In this case, the occurrence of the anions in these positions is mostly due to the interaction with the IL cation, being in a hydrogen bond with the solute. The most important finding here concerns, however, the nonpolar–nonpolar interactions in the solvation. In agreement with the observations above, in $[C_2C_1Im][NTf_2]$, the alkyl group of the alcohol is predominantly interacting with other alcohol side chains, indicating a certain self-aggregation. However, in $[C_8C_1Im][NTf_2]$, the cationic side chains form an overwhelming shell around the alcohol. This underlines the

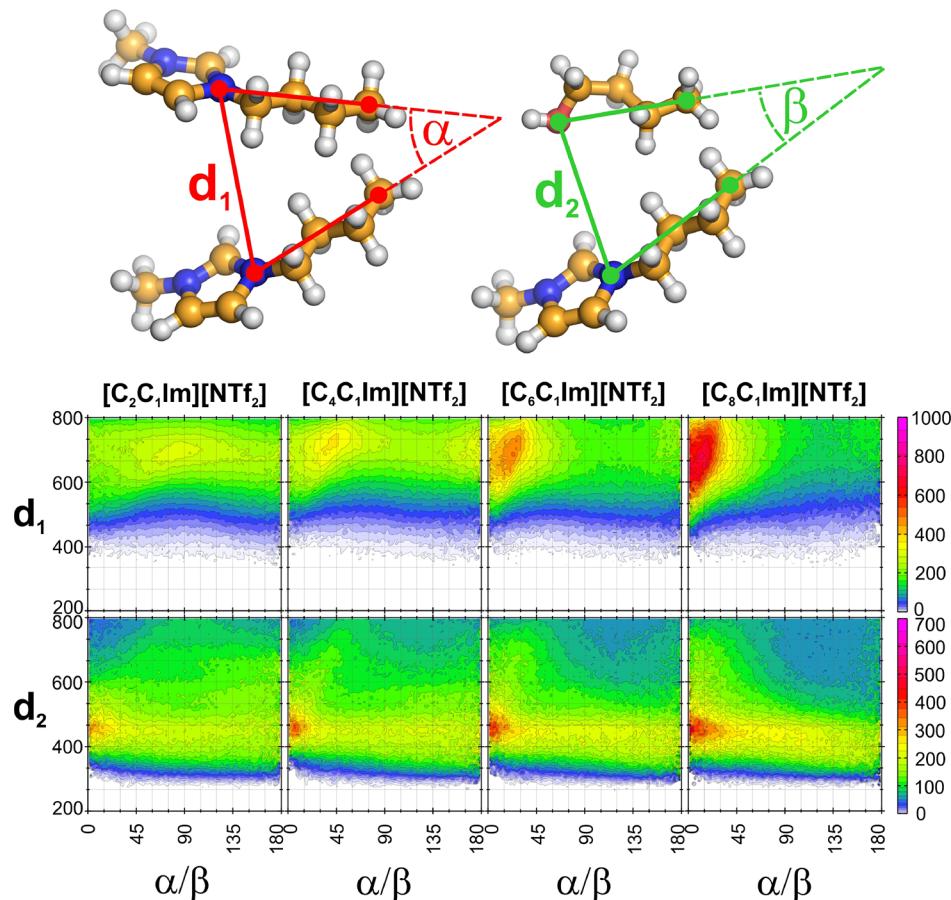


Figure 3. Combined angular (y-axis, degrees) and distance (x-axis, pm) distribution functions that show the alignment of the cations with respect to each other (above) or the alcohols with respect to the cations (below) as a function of the distance for the mixtures of *n*-butanol and $[\text{C}_x\text{C}_1\text{Im}][\text{NTf}_2]$ ILs.

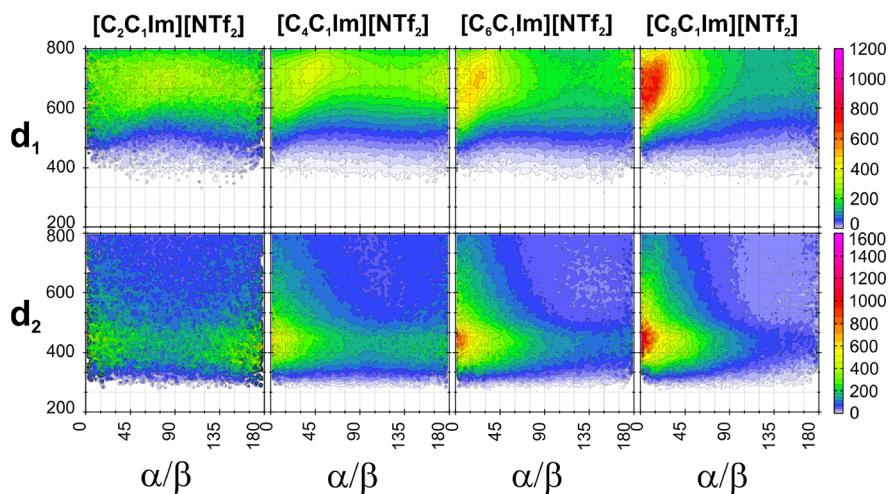


Figure 4. Combined angular (y-axis, degrees) and distance (x-axis, pm) distribution functions that show the alignment of the cations with respect to each other (above) or the alcohols with respect to the cations (below) as a function of the distance for the mixtures of *n*-dodecanol and $[\text{C}_x\text{C}_1\text{Im}][\text{NTf}_2]$ ILs. The description of d_1 and d_2 can be seen in Figure 3 for the analogous *n*-butanol-IL mixtures.

increasing importance of the cation–alcohol interactions with the introduction of longer side chains in the cation, which opens the possibility of enforcing the distinct structure of the liquid on the alcohol itself. Having seen the changes in the mesoscale structure and in the solvation of alcohols in ILs, we will now focus on exploring how much the structure of the solvent is actually transferred into the solute in these particular

cases, to see if the change in the solvent might indeed have a structure directing effect.

Angles were calculated for vectors defined along the alkyl side chains of the cations and distances were taken between the nitrogen atoms of the imidazolium rings, carrying the side chains. Lower panels consider angles defined by vectors along the alkyl side chains of the cations and the alkyl chains of the

alcohols. Distances are measured between the nitrogen atoms of the imidazolium rings and the oxygen atoms of the alcohols.

To observe if the microscopic order of the liquid, that is, the orientation of the cations with respect to each other in the microheterogeneous structure of the IL, is transferred or enforced on the alcohol molecules, we employed combined distribution functions (CDFs), shown in Figures 3 and 4. Here, we plot the mutual occurrence (shown by the color gradient and scaled individually for one row of plots) of two measures, in this case the distance between two entities (d_1 , pm, for upper plots, distances taken between nitrogen atoms of the imidazolium rings; d_2 , pm, for lower plots, distances taken between nitrogen atoms of the imidazolium rings and oxygen atoms of the alcohols) and their relative orientation (α , degrees, for upper plots, angles calculated for vectors defined along alkyl side chains of the cations; β , degrees, for lower plots, angles constructed by vectors along alkyl side chains of the cations and alkyl chains of the alcohols). From the plots that correspond to the cation–cation distances and orientations, that is, the upper row of plots in Figures 3 and 4, it is apparent that the nearby cations (thus, where the distance is low) change their alignment when the side chain increases in length. In case of the shorter cationic side chains (ethyl and butyl), the cations arrange mostly randomly next to each other. In the case of the longer chains (hexyl and octyl), however, where the microheterogeneity is more and more expressed, the neighboring cations order more in a parallel fashion, as a distinct maximum arises at low distances and parallel orientations. This is the first direct proof for the qualitative description of microheterogeneous ILs being similar to surfactants in forming a nonspherical micelle-like structure. The similarity in the cation–cation orientations regardless of the alcohol chain length is also clearly visible, suggesting that the IL and not the alcohol determines the structure.

Apparently, the aforementioned order is transferred also to the cation–alcohol orientations: While in case of the shorter side chains, the alcohols orient mostly randomly next to the cations, in the microheterogeneous ILs, the alcohol–cation pairs clearly align in a parallel fashion next to each other. Considering the observations from the domain analysis, the present results show that while the polar hydroxyl group of the alcohol often anchors in the polar microphase, the side chains are pointing into the nonpolar domain in a highly ordered way. Clearly, this parallel alignment produces a higher maximum for *n*-dodecanol, showing that its longer side chain makes it easier to control its ordering in the liquid. It is interesting to point out, however, that although butyl groups on the cations are too short to form a well-defined continuous domain that stretches through the liquid, the butyl side chain of the *n*-butanol can be incorporated in the microheterogeneity of the ILs, and therefore this chain is apparently already long enough for the alcohol to incorporate in the structural order of the IL. Thus, according to the CDFs the distinct structural order of microheterogeneous IL, described by the domain analysis and the cation–cation orientation CDFs, is strongly transferred into the orientation of the alcohol solutes in them, showing the presence of unambiguous template effects in ILs. This is, to our knowledge, the first time when such effects are proven in these highly applied solvents, which will expectedly lead the focus of experimental studies more to structure-directed synthesis in ILs.

4. CONCLUSION

In the present contribution, we applied selected analyses to classical molecular dynamics trajectories in order to observe template effects in ionic liquids (ILs). In our very simple model system, we dissolved two alcohols, *n*-butanol and *n*-dodecanol, in 1-alkyl-3-methylimidazolium bis(trifluoromethylsulfonyl)-imide ILs, where the alkyl side chains were varied from ethyl to butyl, hexyl, and octyl groups. The analyses all show the increasing segregation of the nonpolar from polar moieties as the side chain becomes longer and indicate that the IL cations are oriented in a specific, parallel way. While the alcohol molecules tend to aggregate in the ILs with shorter side chains, they are more and more dispersed in the liquid upon moving toward the ILs having longer alkyl tails. Thus, they can be considered to dissolve in the nonpolar IL microphase. Most importantly, not only their association but also their orientation changes with the different degree of microheterogeneity of the liquid, and the increasing order of the longer side chain ILs is imprinted in their alignment in the liquid. In particular, the polar part of the alcohol molecules mostly anchors to the polar microphase of the IL through strong polar–polar interactions, while the side chain of the alcohol stretches out parallel to the alkyl group of the IL cation. Interestingly, this behavior changes in degree but does not dissipate when exchanging the *n*-dodecanol to *n*-butanol, despite the shortness of the side chain. Instead, the behavior seems to be determined primarily by the structure of the IL itself, which serves as a highly structured template for the orientation of the solutes.

The observed transfer of order from the solvent to the solutes has tremendous practical consequences for the application of ILs, as apparently we can, by the simple change of the solvent, manipulate the orientation of reactants, or otherwise valuable molecules. We can, thus, make molecules assume a certain conformation or collide in the solution in a certain manner, which can definitely enhance some chemical processes in the liquid, while suppressing others, as it has been seen from the many examples in literature with other kinds of template effects in chemistry. Being aware of these template effects will not only aid us to interpret regioselectivities of reactions in ILs that has already been experimentally explored but will also enable us to consciously design solvent systems for reactions with the purpose of being more selective. It will be particularly interesting to see in the close future if the mesoscopic structure of the liquid can be imprinted directly into the morphology of (organic) polymers. Stereoselectivity and chirality are also highly interesting topics in that manner, since by introducing chiral microheterogeneous ILs template effects might increase the efficiency of the synthesis of the desired products.

■ ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: [10.1021/acs.accounts.7b00436](https://doi.org/10.1021/acs.accounts.7b00436).

Description of the investigated systems and details of the simulations, spacial distribution functions, domain analysis, angular distribution functions, and radial distribution functions and number integrals ([PDF](#))

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Notes

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