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Insight into Structure and Stability of DNA in Ionic Liquids from Molecular Dynamics Simulation and Experimental Studies

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SUPPORTING INFORMATION

1. Details Parameterization of ILs

MD simulation was started by performing a careful parameterization of new 1,3-dialkylimidazolium bromide ILs. ILs' cations used in this study were modeled using united-atom (UA) description only for alkyl chains of CH_2 and CH_3 group. The hydrogen atoms in imidazole ring were modeled using all-atom (AA) description since these hydrogen is attached to the ring contains heavy atoms. Figure S1 shows three different alkyl chain lengths of cation used in this study. The geometry structures of cation were optimized in gas phase using the Hartree-Fock level with the basic set 6-31G(d). Partial atomic charges were calculated using Restrained Electrostatic Potential (RESP)[1] method based on electrostatic potentials obtained previously with the 6-31G(d) basis set calculated by GAMESS.[2] The charges were computed using a single step and were only distributed around the imidazolium ring of the cations including the hydrogen attached to the ring and carbon alkyl chains near to the imidazole ring. Bonded and non-bonded terms were derived from similar building blocks present in OPLS force field.

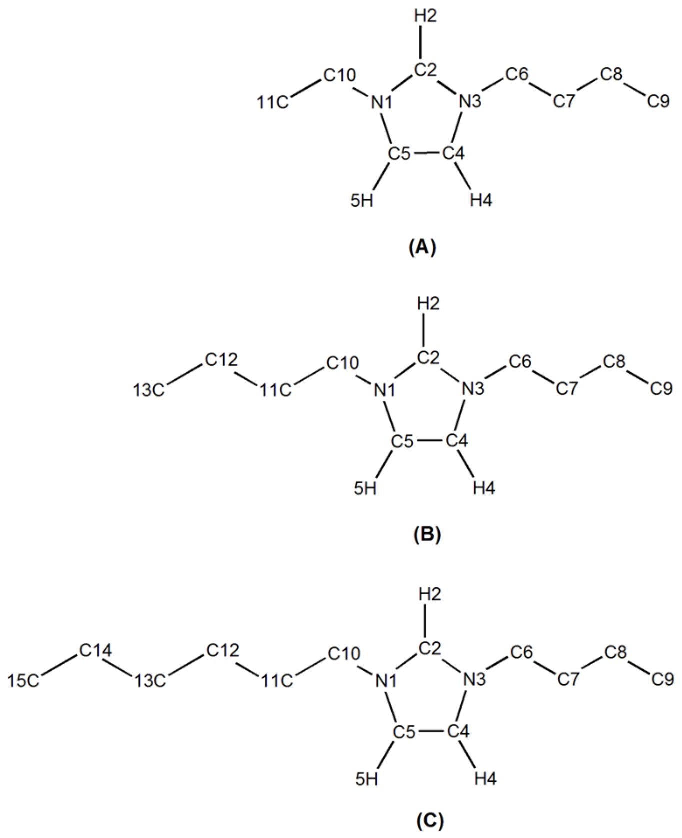

Figure S1. Schematic structure representation of (A) [C_2bim], B) [C_4bim] and C) [C_6bim] united atom (UA) molecular topology based on the OPLS FF.

The parameters for bromide anion (Br^-) are available in GROMACS OPLS force field and were used without any modification except for van der Waals (vdW) parameter. The σ shown in Table S1 has been modified because the simulated properties obtained (density and shear viscosity) using this number match with experimental data as possible. Meanwhile, the ε number is an original value obtained from OPLS force field database in GROMACS and was used without modification. It was reported that, the simulated properties of ILs were dependent on the van der Waals interactions and H-bonding of anion.[3] All ILs were parameterized to be used with the OPLS force field. These alkylimidazolium-based ILs couple with bromide anion was chosen because experiments of DNA in this type of ILs have previously been reported.[4]

Table S1. vdW parameters used for (Br^-) anion.

Atom	ε (kJ/mol)	σ (nm)
Br	0.3765	0.3699

2. Molecular Dynamics Simulation of Ionic Liquids

Molecular dynamic (MD) simulation of each ILs was performed in order to validate the force field used. The force fields was validated based on two main criteria namely density and viscosity. Therefore, the ILs were modeled in order to fit the experimental data as possible. The starting structure for ILs was assembled in a simulation box containing an equivalent amount of cation and anion. Total amount of 400 molecules were added randomly in a cubic box with dimension 4.0 x 4.0 x 4.0 nm using packmol.[5] Energy minimization of the ILs system was performed using steepest descent method following with conjugate gradients. 5000 steps were applied for each energy minimization with a time steps 0.2 fs. The other parameters used are similar to parameter for simulation of DNA. The MD simulation production for each ILs was simulated for 10 ns in isobaric-isothermal (NPT) where the number of particle, pressure and temperature were fixed. The first 5 ns were dedicated for the system to achieve equilibration and the properties for analysis were taken from the last 2 ns trajectory.

For density analysis, the initial configuration of cations and anions positions and box simulation vectors were rescaled in order to start the simulations of each ILs at the known density at 298.15 K obtained from experimental data. Viscosity of liquid materials can be calculated using various methods developed nowadays but we prefer to use perturbation method to calculate the shear viscosity. Perturbation is a more accurate method to calculate shear viscosity of model liquids and this method was reviewed by Hess.[6] The accuracy to obtain a shear viscosity increases if the dimension of simulation box increase along the *z*-axis. Therefore, the new box vectors were built with a new dimension 4.0 x 4.0 x 12.0 nm by replicating previously equilibrated system. A total amount of 600 molecules cation and 600 molecules anion in an extended box were energy minimized following the method previously described.

Non-equilibrium method was applied to the simulation by adding 0.02 nm ps^{-2} external periodic acceleration profile to the system. The ILs' systems were simulated at 298.15 K for 10 ns and the shear viscosity was calculated from a last 5 ns trajectory. The first 5 ns were used for system to obtain equilibration. A heat generated by the viscous friction was removed by coupling to a heat bath. The simulated density and viscosity are shown in Table S2 and were compared with experimental data. It is well known that self-diffusion coefficients are difficult to reproduce in simulations because they depend strongly on the force field employed and a 2- to 3- fold difference is often considered as reasonable agreement.[7]

Table S2. Results of density, shear viscosity and self-diffusion coefficient of ILs obtained at 298.15 K.

ILs	Density (g/cm^3)		Shear Viscosity (cP)		Self-diffusion Coefficient (D) (x 10^{-11} m^2/s)	
	sim	exp	sim	exp	D_{cation}	D_{anion}
$[C_2bim]Br$	1.229	1.248	250	199	1.83	1.31
$[C_4bim]Br$	1.173	1.190	1084	1052	1.65	1.81
$[C_6bim]Br$	1.135	1.143	1294	1180	1.47	1.07

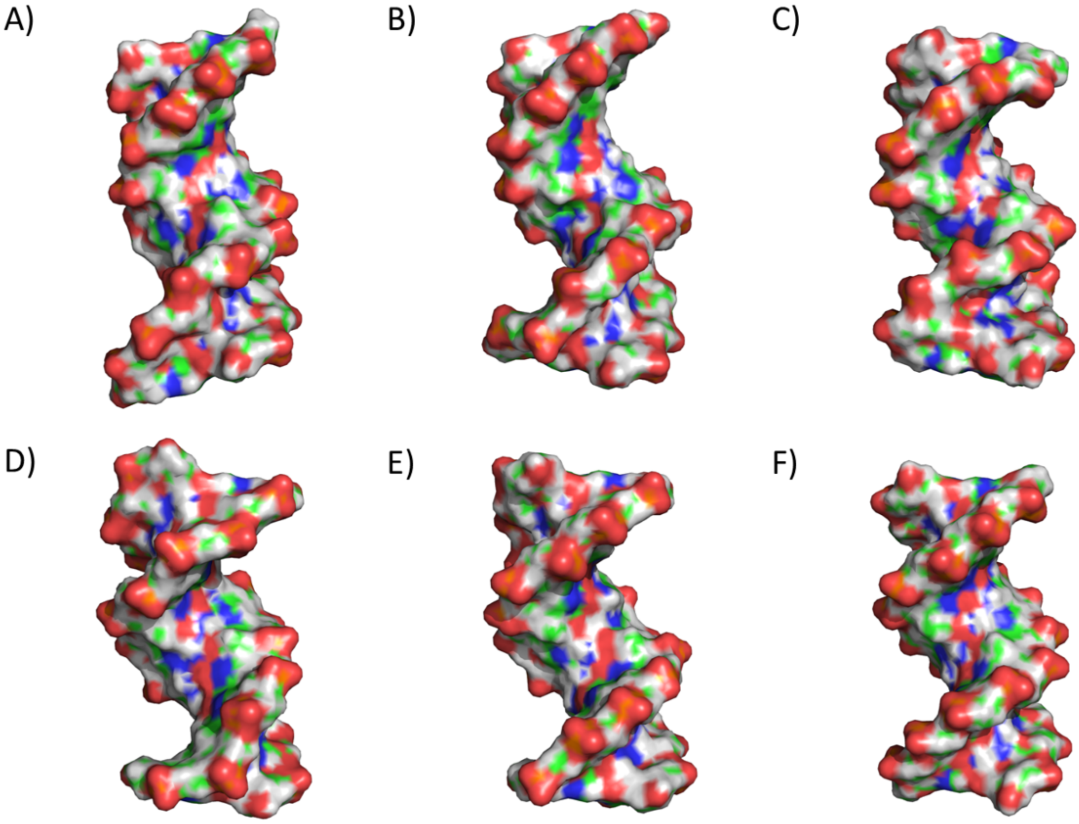

Figure SS1. DNA conformation obtained from last 10 ns simulation trajectories. A) Structure of DNA in pure water system; B) 25 % [C_4bim]Br; C) 50 % [C_4bim]Br; D) 75 % [C_4bim]Br; E) DNA in neat [C_4bim]Br and F) Initial crystal structure of Calf thymus DNA.

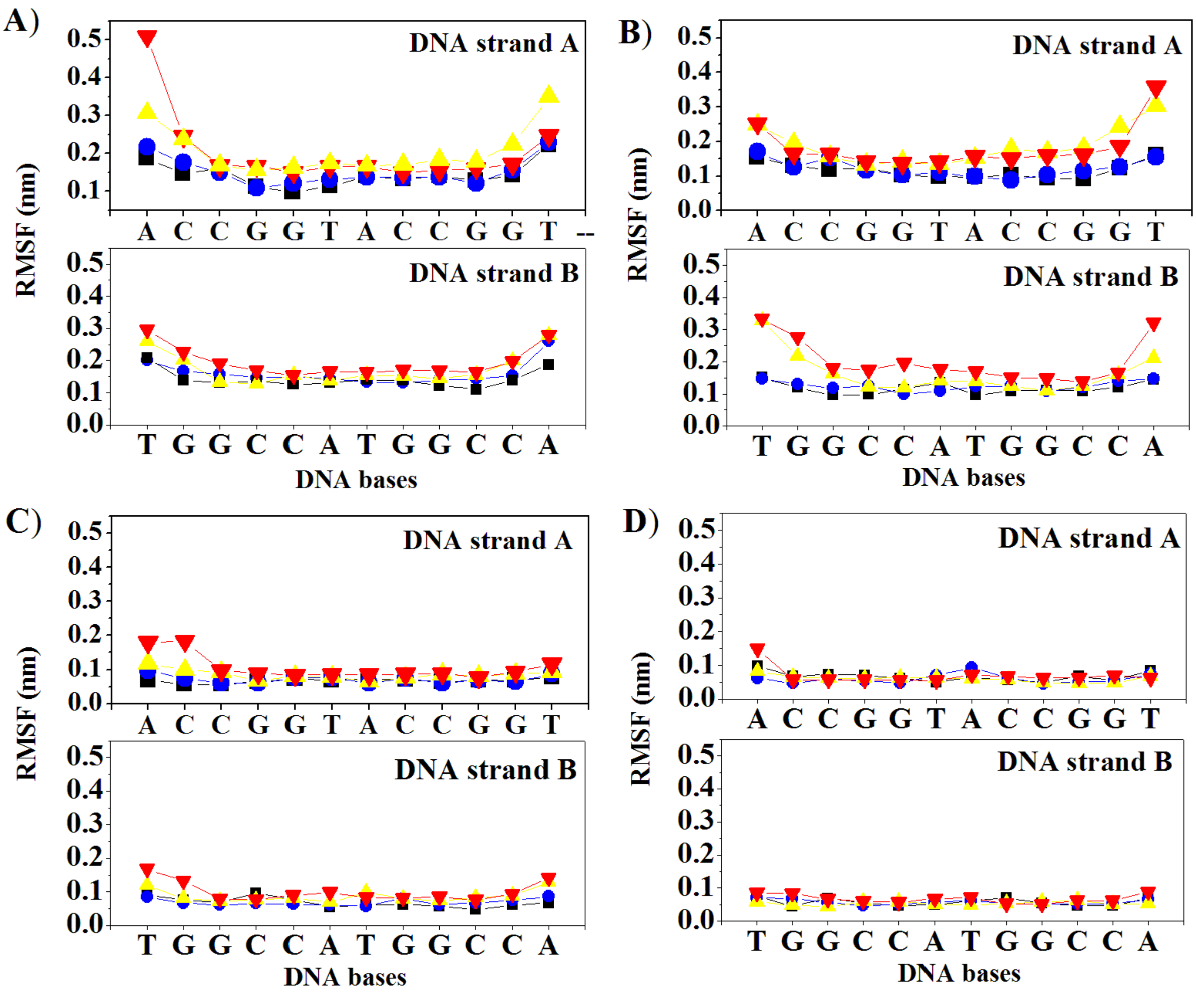

Figure SS2. RMSF of DNA bases (all heavy atoms) in different hydrated [C$_4$bim]Br systems including DNA in neat [C$_4$bim]Br at various temperatures. DNA in 25 % (w/w) [C$_4$bim]Br, (A); 50 %, (B); 75 %, (C) and neat [C$_4$bim]Br (D). Colour scheme are as follow: black, 298.15 K; blue, 323.15 K; yellow, 343.15 K and red, 373.15 K. Bases of DNA strand A pair with bases of DNA strand B with the following combination A-T and C-G pairs. RMSF averaged over the last 2 ns of MD simulation.

Table SS1. Average number of [C_4bim]Br ions and water molecules within 0.35 nm from the DNA surface at different temperatures. Data averaged from the last 2 ns of MD simulations.

[C_4bim]Br:H_2O (% w/w)	Temperature (K)	Average Number of Molecules		
		Cation	Anion	H_2O
0:100	298.15	-	-	356.7 ± 7.3
	323.15	-	-	347.8 ± 8.1
	343.15	-	-	336.0 ± 9.7
	373.15	-	-	310.9 ± 9.7
25:75	298.15	6.4 ± 1.9	0.4 ± 0.1	250.1 ± 9.8
	323.15	6.0 ± 2.6	0.5 ± 0.1	234.6 ± 10.6
	343.15	7.5 ± 1.8	0.5 ± 0.1	246.5 ± 9.0
	373.15	6.6 ± 2.0	0.5 ± 0.1	233.5 ± 11.2
50:50	298.15	9.7 ± 2.3	1.6 ± 0.8	205.5 ± 5.9
	323.15	8.9 ± 2.2	2.9 ± 1.4	196.1 ± 8.8
	343.15	10.6 ± 2.1	2.3 ± 1.3	185.9 ± 8.8
	373.15	8.3 ± 2.2	2.9 ± 1.4	175.0 ± 7.5
75:25	298.15	12.6 ± 2.2	5.1 ± 0.8	128.5 ± 4.1
	323.15	13.1 ± 1.9	4.7 ± 0.6	101.3 ± 3.1
	343.15	13.4 ± 2.2	7.2 ± 1.3	100.6 ± 3.1
	373.15	16.5 ± 2.8	7.2 ± 1.2	94.5 ± 3.8
100:0	298.15	14.9 ± 1.9	6.3 ± 0.6	-
	323.15	15.6 ± 2.0	8.5 ± 1.0	-
	343.15	15.6 ± 1.9	10.4 ± 0.9	-
	373.15	17.4 ± 2.6	14.3 ± 0.9	-

Table SS2. The calculated of interaction energies between different parts in the simulation systems. The contribution of electrostatic and van der Waals interactions are shown.

Interaction	Electrostatic energy (kcal/mol)	Van der Waals energy (kcal/mol)
Water – PO^-_4	-12.78 ± 2.12	+ 1.79 ± 0.87
$[C_4bim]^+$ – PO^-_4	- 46.55 ± 4.75	- 2.31 ± 2.49
Br^- – PO^-_4	+ 0.41 ± 0.17	+ 0.64 ± 0.36

Table SS3. Average hydrogen bonds formed between DNA bases and ILs' cations and anions at different temperatures. H-bonds are considered to occur when the distances between the donor and the acceptor is less than 0.35 nm is and the angle hydrogen-donor-acceptor is lower than 30°. The hydrogen bond is considered between a proton in an imidazolium ring and the DNA bases. Data is averaged over the last 2 ns of MD simulations.

System	$[C_4bim]Br:H_2O$ (% w/w)	Temperature (K)	Average H-bonds	
			Cation	Anion[a]
$[C_4bim]Br$	25:75	298.15	3.7 ± 1.7	0.1 ± 0.04
		323.15	3.9 ± 1.9	0.2 ± 0.04
		343.15	3.5 ± 1.8	0.2 ± 0.06
		373.15	3.9 ± 1.9	0.2 ± 0.07
	50:50	298.15	6.1 ± 2.2	0.8 ± 0.17
		323.15	6.1 ± 2.4	1.5 ± 0.16
		343.15	6.1 ± 2.4	1.2 ± 0.13
		373.15	6.7 ± 2.4	1.7 ± 0.12
	75:25	298.15	8.8 ± 2.5	3.9 ± 0.95
		323.15	9.5 ± 2.8	4.3 ± 1.03
		343.15	12.5 ± 3.0	6.2 ± 0.85
		373.15	11.8 ± 3.1	6.0 ± 1.26
	100:0	298.15	16.6 ± 3.3	6.9 ± 0.28
		323.15	16.5 ± 3.1	5.9 ± 0.12
		343.15	16.4 ± 3.3	8.7 ± 0.45
		373.15	17.4 ± 3.6	12.3 ± 1.18

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