COMMENTS

Comment on "On the Accuracy of Force Fields for Predicting the Physical Properties of Dimethylnitramine"

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Zheng and Thompson have recently reported a comparison of three atomistic force fields for prediction of physical properties of dimethylnitramine (DMNA) from molecular dynamics (MD) simulations.[1] Specifically, they compared the rigid molecule force field by Sorescu, Rice, and Thompson (SRT);[2] the generalized AMBER- (with partial charges assigned by Zheng and Thompson); and a fully atomistic quantum chemistry (QC)-based force field developed by Smith, Bharadwaj, Bedrov, and Ayyagari (SBBA)[3] for prediction of unit cell parameters, bulk modulus, and melting temperature for crystal DMNA, as well as volumetric properties of liquid DMNA. The authors found that simulations using the SBBA force field predict DMNA properties that significantly deviate from experimental data. This was particularly apparent for the melting temperature of DMNA, which was found to be ∼70 K lower than the experimental value. The two other force fields investigated overestimated the melting temperature of DMNA, but to a lesser extent. In an attempt to improve prediction of the DMNA melting temperature, Zheng and Thompson have adjusted the AMBER dihedral potential, arguing that the original potential predicts dihedral barriers that are off a factor of ∼3 from predictions of QC calculations and experiments.

In this comment, we show that (1) simulations using the SBBA force field predict physical properties of crystal DMNA in very good agreement with experiment, including melting temperature; (2) the interpretation of Zheng and Thompson of conformational properties using SBBA and AMBER force fields are incorrect; and (3) the AMBER and AMBER-modified force fields do not provide an adequate description of DMNA conformational properties.

SBBA Force Field. To make sure that parameters published in the original SBBA force field manuscript[3] are consistent with those that were used in the simulations described below, we have set up input files for DNMA simulations from scratch using information provided in the original force field reference. It is necessary to point out that in the original force field paper, it was implicit that intramolecular nonbonded (van-der-Waals and Coulomb) interactions are excluded between atoms separated by one or two bonds and are included without any scaling for those that are separated by three (the so-called 1−4 interactions) and more bonds. The former is a standard practice in atomistic MD simulations, whereas the latter (the scaling factor for the 1−4 nonbonded interactions) can depend on a particular force field. Incorrect implementation of the 1−4 intramolecular

interactions[4] in Zheng and Thompson's work for the SBBA force field resulted in poor predictions of DMNA properties for this force field.

MD Simulations of Liquid DMNA. MD simulations in the NPT ensemble have been run for the system of 160 molecules at 400 K and atmospheric pressure. Zheng and Thompson have reported that for liquid DMNA, they obtained a density of 1.16 g/cm^3 from simulations using the SBBA force field. They acknowledged that this value is about 8% higher than the value predicted from the original SBBA force field paper[3] using the same thermodynamic conditions and also significantly higher than the estimated experimental value. Zheng and Thompson have speculated that observed inconsistency might be attributed to slightly different simulations parameters (e.g., number of DMNA molecules) used in their work and in ref 3. Our simulations using the same simulation parameters (number of molecules and cutoff radius) as in the Zheng and Thompson work predict a density of liquid DMNA to be 1.07 g/cm^3, which is consistent with value reported in ref 3 as well as with the experimental value of 1.1 g/cm^3.

Simulations of DMNA Crystal Using the SBBA Force Field. Because Zheng and Thompson have incorrectly implemented the SBBA force field (as illustrated by an inconsistent prediction of the liquid properties), the results reported by Zheng and Thompson from simulations of crystalline DMNA using the SBBA force field are also incorrect.[4] We therefore performed our own simulations of crystal DMNA. A DMNA crystal consisting of 160 molecules arranged in the super cell with $4 \times 4 \times 5$ unit cells was utilized in our simulations. A 10-Å cutoff was used for all nonbonded interactions. The Ewald summation was used to take into account long-range electrostatic interactions. A combined MD−Monte Carlo simulation protocol was used to simulate the crystal as described elsewhere.[5] Bonds were constrained to a fixed length, and all other intramolecular degrees of freedoms were integrated according to intramolecular and intermolecular forces given by the force field. To predict the melting temperature of the DNMA crystal, we used the same approach as Zheng and Thompson and introduced random molecular voids into the system.[6] In this approach, the apparent melting temperature for each system is determined by a brute force heating of the crystal and monitoring the system volume and molecular mean-squared displacements (MSD). The temperature at which the volume and MSD increase sharply is identified as an apparent melting temperature for a given system. Simulations of several systems with different number of molecular voids provide dependence of apparent melting temperature on the number of molecular voids in the crystal. A thermodynamic melting temperature is defined by the plateau region in the dependence of the apparent melting temperature versus number of voids. We have conducted simulations with the number of voids ranging from 0 to 25 in the temperature range of 295−450 K with 5° increments. Each simulation run was over 2 ns of MD simulation with a 1-fs integration time step intermitted every 1 ps with 1000 MC trials of cell shape and volume changes.

In Table 1, we report crystal DMNA unit cell parameters, density and bulk modulus data obtained from our simulations

Comments

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TABLE 1: Lattice Parameters and Density and Bulk Modulus for DMNA Crystal at 295 K Predicted from Simulations Using the SBBA Force Field and from Experiments[6]

|	SBBA	experiment
a (Å)	6.66	6.59
b (Å)	6.51	6.50
c (Å)	6.06	6.13
α (deg)	90.00	90.00
β (deg)	123.76	123.13
γ (deg)	90.02	90.00
density (g/cm^3)	1.31	1.36
bulk modulus (GPa)	5.40	6.5 ± 0.3

using the SBBA force field at 295 K and atmospheric pressure. The values obtained from our simulations are in much better agreement with experiment than those reported by Zheng and Thompson. In Figure 1, we show computed apparent melting temperatures as a function of the number of voids in the system. The apparent melting temperatures obtained from our simulations are significantly different from those obtained by Zheng and Thompson. For the system with no voids, our simulations predict a stable crystal phase up to 420 K, which is ∼60° higher than that reported by Zheng and Thompson. Moreover, we find that the plateau region, which has been associated with thermodynamic melting temperature, is ∼330 K, which is in excellent agreement with experiment (331 K).[7] Our simulations illustrate that the SBBA force field provides a better prediction of physical properties of crystalline DMNA than the SRT and AMBER force fields as reported by Zheng and Thompson.

Conformational Properties of DMNA. Using molecular mechanics (MM) calculations, we have also investigated the relative conformational energies of a single DMNA molecule in vacuum associated with rotation and inversion of the NO$_2$ group. In these calculations, the C$-$N$-$N$-$O dihedral or C$-$N$-$C$-$N* out-of-plane deformation has been constrained in the desired orientation, whereas all other molecular degrees of freedom were minimized by MM.

In their discussion of the ability of AMBER and SBBA force fields to reproduce conformational properties of DMNA, Zheng and Thompson have made an oversimplification that provided them with the wrong conclusions. Namely, the authors assumed that the force constant, K^T, in intrinsic dihedral potential for a given torsion (e.g., C$-$N$-$N$-$O) can be used to estimate the molecule conformational energy as a function of the rotation around that dihedral. Following this approach, Zheng and
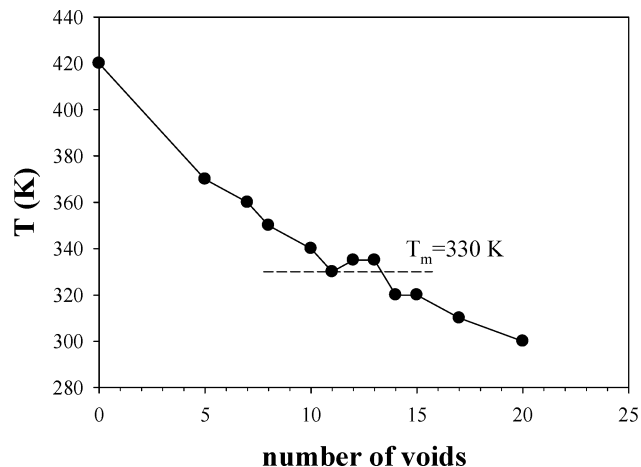
Figure 1. An apparent melting temperature of DMNA crystal as a function of the number of molecular voids in the supercell (160 molecules). Dashed line indicates the thermodynamic melting temperature.
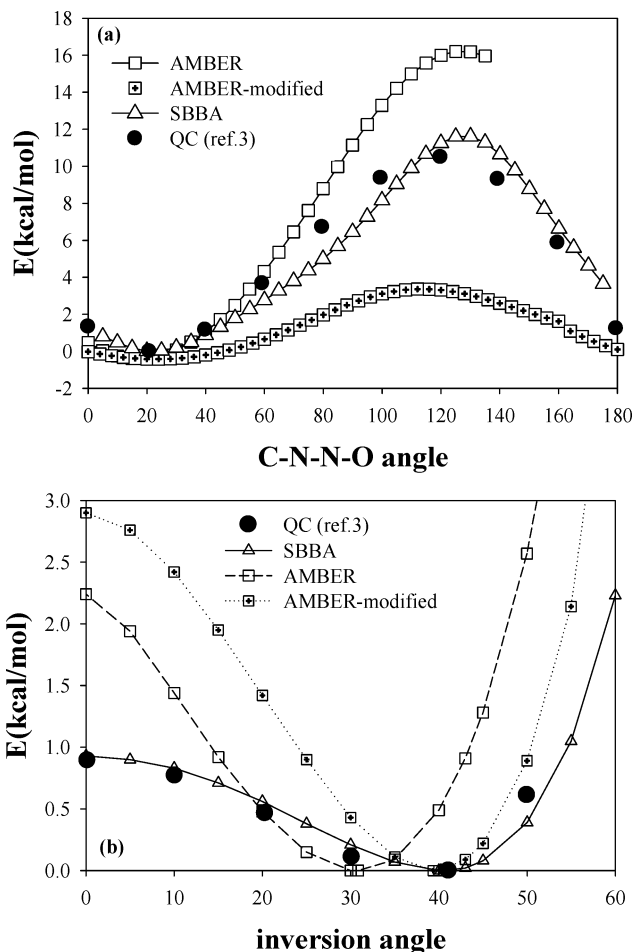
Figure 2. MM calculations using the SBBA, AMBER, and AMBER-modified force fields and high level QC calculations for (a) DMNA conformational energies as a function of CNNO dihedral angle and (b) inversion potential for DMNA molecule as a function of the out-of-plane angle, defined as an angle between the N$-$N bond and the C$-$N$-$C bend.

Thompson found that both the AMBER and SBBA force fields predict conformational barriers for rotation around the H$-$C$-$N$-$N and C$-$N$-$N$-$O dihedrals that are significantly different from QC calculations or experimental data. For example, Zheng and Thompson estimated the barrier for the rotation of the NO$_2$ group around the N$-$N bond using the SBBA force field to be 141.4 kJ/mol, whereas QC calculations from ref 3 predicted a barrier value of 44.3 kJ/mol. We would like to point out that ref 3 has clearly demonstrated excellent agreement between DMNA conformational energies for rotation of NO$_2$ (C$-$N$-$N$-$O dihedral angle) obtained from MM using the SBBA force field and from high-level QC calculations. In their simplified estimation of conformational energies, Zheng and Thompson have not taken into account contributions of other intramolecular interactions, such as intramolecular van-der-Waals and Coulomb interactions or contributions from bond, bend, and other dihedrals deformations, all of which can provide significant contribution to the relative conformational energy of DMNA molecule. Moreover, in the SBBA force field, the C$-$N$-$N$-$O dihedral potential has multiple folds, the contribution of which also has not been taking into account by Zheng and Thompson.

AMBER Force Field. Unlike the SBBA force field, which has been parametrized for DMNA explicitly, the generic AMBER force field has not been developed or applied for this compound previous to the work of Zheng and Thompson. To apply the AMBER force field, Zheng and Thompson had to

assign partial atomic charges by applying the restrained electrostatic potential fit method using MP2/6-31** level QC calculations on DMNA. We have conducted a MM drive around the C−N−N−O dihedral for the AMBER and AMBER-modified (reduced force constants for C−N−N−O and H−C−N−N dihedrals) force fields developed by Zheng and Thompson. Conformational energies of DMNA as a function of C−N−N−O dihedral angle are shown in Figure 2a. The rotational barrier around this dihedral is noticeably larger for the AMBER force field and significantly lower for the AMBER-modified force field than for those obtained from high-level QC calculations and from MM calculations using the SBBA force field.[3]

Another important conformational characteristic of DMNA is its ability to undergo an inversion about the amine nitrogen. QC calculations showed that the ground state geometry for the DMNA molecule does not have planar alignment of heavy atoms (N, C, O). Instead, a tilted geometry with C_s symmetry has the lowest energy, whereas the planar C_{2v} geometry is a saddle point with an inversion barrier of ∼0.9 kcal/mol.[3] Using MM calculations, we have determined the energies (Figure 2b) for the NO_2 group inversion using AMBER and AMBER-modified force fields used by Zheng and Thompson and compared those with results predicted from the SBBA force field and QC calculations.[3] The AMBER and AMBER-modified force fields predict an inversion barrier of 2.2 and 2.8 kcal/mol, respectively, which are significantly higher than the QC and SBBA force field value (0.9 kcal/mol).

References and Notes

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