Parameterization of Electrostatic Interactions for Molecular Dynamics Simulations of Heterocyclic Polymers

Victor M. Nazarychev,[1] Sergey V. Larin,[1] Alexander V. Yakimansky,[1,2] Natalia V. Lukasheva,[1] Andrey A. Gurtovenko,[1,3] Iosif V. Gofman,[1] Vladimir E. Yudin,[1,4] Valentin M. Svetlichnyi,[1] Jose M. Kenny,[1] Sergey V. Lyulin[1,3]

[1]Institute of Macromolecular Compounds, Russian Academy of Sciences, Bolshoi pr. 31 (V.O.), St. Petersburg, 199004, Russia
[2]Saint-Petersburg National Research University of Information Technologies, Mechanics, and Optics, Kronverkskii pr., 49, St. Petersburg, 197101, Russia
[3]Department of Physics, St. Petersburg State University, Ul'yanovskaya str. 1, Petrodvorets, St. Petersburg, 198504, Russia
[4]St.Petersburg State Polytechnic University, Polytechnicheskaya str. 29, St.Petersburg, 195251, Russia
Correspondence to: S. V. Lyulin (E-mail: s.v.lyulin@gmail.com)

Received 16 November 2014; revised 9 February 2015; accepted 27 February 2015; published online 30 March 2015
DOI: 10.1002/polb.23715

ABSTRACT: The paper focuses on the problem of electrostatic interactions in molecular dynamics simulations of thermal properties of heterocyclic polymers. The study focuses on three thermoplastic polyimides synthesized on the basis of 1,3-bis-(3′,4-dicarboxyphenoxy)benzene (dianhydride R) and three diamines: 4,4′-*bis*-(4″-aminophenoxy) diphenylsulfone (diamine BAPS), 4,4′-*bis*-(4″-aminophenoxy) biphenyl (diamine BAPB), and 4,4′-*bis*-(4″-aminophenoxy) diphenyloxide (diamine BAPO). In the molecular dynamics simulations these polyimides were described by the Gromos53a5 force field. To parameterize the electrostatic interactions four methods of calculating the partial atomic charges were chosen: B3LYP/6–31G*(Mulliken), AM1(Mulliken), HF/6–31G*(Mulliken), and HF/6–31G*(ChelpG). As our parameterization is targeted to reproduce thermal properties of the thermoplastic polyimides, the choice of proper partial charges was finalized on a basis of the closest match between computational and experimental data for the thermal expansion coefficients of the polyimides below glass transition temperatures. Our finding clearly show that the best agreement with experimental data is achieved with the Mulliken partial atomic charges calculated by the Hartree-Fock method with 6–31G* basis set. Furthermore, in addition to the thermal expansion coefficients this set of partial atomic charges predicts an experimentally observed relationship between glass transition temperatures of the three polyimides under study: $T_g^{\text{R-BAPS}} > T_g^{\text{R-BAPB}} > T_g^{\text{R-BAPO}}$. A mechanism behind the change in thermal properties upon the change in the chemical structure in considered polyimides may be related to an additional spatial ordering of sulfone groups due to dipole-dipole interactions. Overall, the modified force-field is proved to be suitable for accurate prediction of thermal properties of thermoplastic polyimides and can serve as a basis for building up atomistic theoretical models for describing other heterocyclic polymers in bulk. © 2015 Wiley Periodicals, Inc. J. Polym. Sci., Part B: Polym. Phys. **2015**, *53*, 912–923

KEYWORDS: computer modeling; electrostatic interactions; glass transition; molecular dynamics; partial charges; polyimides; quantum chemistry

INTRODUCTION Polyimides (PIs) belong to the class of thermally stable heterocyclic polymers widely used in various branches of industry as heat-resistant chemically stable compounds with an increased strength. The domain of application of polyimide-based materials is very broad: they are employed in the production of lightweight heat-resistant constructions, gas-separating membranes, dielectric films, flexible printed circuit boards, advanced composites, etc.[1,2] An important feature of these compounds is that their thermal, electric and mechanical properties may vary considerably even upon an insignificant change in their chemical structure.[3–14]

Presently, the development of new polyimide-based materials with improved operational characteristics is extremely important for different applications. However, a traditional path for the creation of novel polymer compounds requires, as a rule, an expensive chemical synthesis followed by laborious experimental investigations. Molecular dynamics (MD) simulations represent an efficient alternative to chemical syntheses, making it possible to reduce both time and material resources and not only to interpret experimental investigation results at the molecular level but also to predict properties of novel polymer compounds before their synthesis. Furthermore, the MD method implemented into fully

Additional Supporting Information may be found in the online version of this article.

atomic models allows the effect of slight changes in the chemical structure of bulk PIs to be taken into account in order to optimize the performance of polyimide-based materials.[15–26]

Prior to MD investigations of polymer physical properties, potential functions of all interatomic interactions in the system under investigation, i.e., its "force field," should be defined. In a general case, the "force field" includes descriptions of both covalent (chemical bonds, bond angles, torsion angles) and noncovalent (excluded volume and electrostatic) interactions. Accounting for long-range electrostatic interactions (EI), which reproduce various quantum effects at the classical description level for neutral systems, is the most resource-intensive approach. Interatomic EI are usually described by Coulomb potential with certain effective partial charges assigned to all atoms, characterizing molecular electron density localizations.

Since partial atomic charge values cannot be measured experimentally and are, therefore, calculated by quantum-chemical methods, a correct parameterization of EI is nowadays one of the main problems of computer simulations. At the same time, these methods, based mainly on numerical solutions of the multielectron Schrödinger equation, involve many approximations and/or initial parameters and suffer from drawbacks of any computational procedure: the calculation results are strongly dependent on fine details of the calculation method.[27,28] Therefore, for an adequate presentation of EI in computer simulations, it is crucially important to define correctly the calculation method for partial atomic charges which would make it possible to reproduce accurately the polymer characteristics.

Computer simulations of such polymers as polyethylene, polystyrene, etc., which are less polar than heterocyclic polymers, are commonly performed with no account for EI.[29,30] This is caused by the fact that partial charges of carbon and hydrogen atoms in these polymers are rather low, and the contribution from EI to the system potential energy is negligible. However, the presence of heteroatoms (oxygen, nitrogen, sulfur) with higher values of partial charges in the structure of the thermally stable PIs makes necessary the account for EI. It was shown by us earlier[31–33] that EI are essential for PIs containing sulfone groups, and they may be responsible for an improvement of the polyimide thermal properties. Most papers devoted to simulations of heat-resistant PIs that take into account EI may be divided into two groups. In the first group, encoded (licensed) force fields with fixed values of partial atomic charges are used. For instance, an encoded force field Compass within the commercial Materials Studio package is often used for MD studies of diffusion of small molecules through polyimide films.[21–23] In these works, the initial configuration is generated by means of the Amorphous Cell module, applying the stochastic Monte-Carlo method that may give rise to some structural artifacts such as overlaps and entanglements between heterocycles and aromatic rings.[31–35] However, as it was shown earlier[31] the reproduction of the experimental density value in simulations does not ensure that the system is equilibrated. Characteristic density relaxation times for PIs under study do not exceed 10 ns.[36] However, in order to equilibrate PI R-BAPS with a polymerization degree $N_\mathrm{p} = 8$, even at high temperature around 600 K, simulations on a microsecond scale are required, corresponding to displacements of the center of masses of an individual macromolecule to distances comparable to its own sizes.[31] These simulation times are nowadays inaccessible for studies of systems, consisting of tens of thousands atoms by means of the Materials Studio package. Moreover, the room temperature density of a polymer sample prepared by cooling from the melt depends on the cooling rate, and may, therefore, differ from experimental values even in the equilibrium system.[31,32,36]

In the approach reported in the second group of papers, EI are parameterized by means of quantum-chemical calculations. However, we would like to emphasize that any force field based on classical mechanics is inherently semiempirical and may only validated by a direct comparison with a limited set of experimental data obtained, as a rule, for rather small molecules.[37] If a selected force field is further used for polymers with recalculated EIs, one should, in principle, reevaluate the quality of the chosen force filed for the system under consideration based, again, on a direct experimental validation. This means that some parameters of the original force field might need to be readjusted for the particular system. Instead of that, many authors use high-level quantum chemical calculations (e.g., MP2) to recalculate partial charges for a new molecule, inserting them further in the chosen force field with neither a recalculation of other force field parameters nor a proper experimental validation. The main idea of our study is an attempt to check whether the better quantum chemical methods for calculations of partial atomic charges provide the better reproduction of thermal properties for the studied set of thermoplastic PIs with close chemical structures among them.

In a number of studies, thermal properties of PIs are simulated[15–17] with the use of force fields of the TRIPOS family.[38,39] For each individual compound, the values of partial atomic charges are calculated by density functional theory (DFT) or Hartree-Fock (*ab initio*) methods. The initial sample configuration is generated in these works by means of a modified Monte-Carlo method. During the equilibration, not exceeding tens of nanoseconds, the reproduction of the experimental polymer density value was attempted.

In this work, we have used quantum-chemical calculations to parameterize EI within force field. The parameterization result is validated if experimental values of thermal characteristics are reproduced by computer simulations of the PIs under study. To this aim, a multiscale computer simulation was performed, consisting of quantum-chemical calculations and atomistic molecular dynamics over a microsecond timescale. Four quantum-chemical methods for calculations of partial atomic charge values were selected in order to

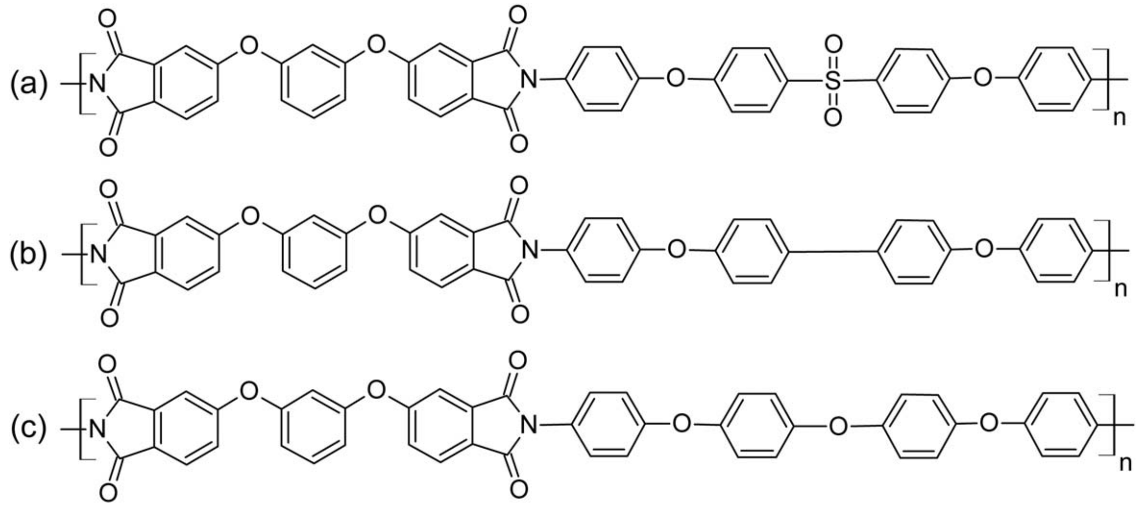

FIGURE 1 Chemical structures of the studied PIs: (a) R-BAPS, (b) R-BAPB, (c) R-BAPO.

parameterize further EI within the atomistic molecular dynamics approach. Reliabilities of parameterizations with partial atomic charge values calculated by means of the selected methods were estimated via a comparison of experimental and calculated thermal characteristics of the studied heterocyclic polymers. The computer MD simulation was carried out using the Gromacs package[40,41] with the Gromos53a5 force field[37] that proved to be successful upon investigations of thermal properties of heterocyclic polymers.[31–36]

The paper is organized as follows. In the first part, thermoplastic PIs are discussed, and the necessity to study the chemical structure effects on their thermal properties is substantiated. In the second part, the experimental procedure used to measure thermal properties of PIs is described. After that, the methodology of computer simulation is described; it includes calculation of partial atomic charges for the parameterization of EI and simulation of primary thermal properties (glass transition temperature, T_g, and thermal expansion coefficient, CTE) using atomistic models. Then, the obtained results are compared and discussed. Finally, the main conclusions are claimed and some practical recommendations are suggested with respect to studies of thermal properties of heterocyclic polymers.

INVESTIGATION OBJECTS

Modern chemical synthesis methods make it possible to obtain PIs, combining thermoplasticity with high T_g values. For example, the synthesis of thermoplastic PIs based on 1,3-bis-(3',4-dicarboxyphenoxy)benzene (dianhydride R) and two diamines: 4,4'-*bis*-(4''-aminophenoxy)diphenylsulfone (diamine BAPS) [Fig. 1(a)] and 4,4'-*bis*-(4''-aminophenoxy) biphenyl—(diamine BAPB) [Fig. 1(b)] has been widely reported.[9–11]

The presence of the sulfone group in the diamine component of polyimide R-BAPS leads to an increase in its T_g value by 14 K as compared with R-BAPB.[36] Even more pronounced variations of thermal properties are observed for commercial EXTEM™ and ULTEM™ PIs (SABIC Innovative Plastics):[22,42–45] replacing the diphenylsulfone (DPS) fragment for a meta-phenylene moiety in the diamine component leads to about 40 K increase in the T_g value of EXTEM™ compared with that of ULTEM™.[44,45]

Changes in the glass transition temperature of PIs upon variations of their chemical structure may be attributed to two factors: differing flexibilities of repeating units of PIs and possible contributions from dipole-dipole interactions, particularly those caused in our case by polar sulfone groups. Using the virtual bond formalism under the free-rotation approximation, persistent lengths of R-BAPS and R-BAPB PIs were earlier estimated to be 0.99 and 1.32 nm, respectively.[36] A decrease in the persistent length value should give rise to an increase of the polymer chain flexibility and, hence, to a reduction in the T_g value. However, this conclusion contradicts the earlier obtained experimental relation of T_g values: $T_g^{\text{R-BAPS}} > T_g^{\text{R-BAPB}}$.[36]

In order to establish the mechanism behind the observed changes in the thermal properties of PIs, we investigated the effects of the aforementioned possible contributions (variations in the polymer chain flexibility and changes in dipole-dipole interactions upon inserting sulfone group into the diamine fragment). Thus, replacing oxygen atom for sulfone group in the repeat unit of R-BAPS PI reduces dipole-dipole interactions, causing no significant influence on the polymer chain flexibility. Therefore, it was suggested to simulate the thermal properties of a novel PI R-BAPO (based on dianhydride R and diamine 4,4'-*bis*-(4''-aminophenoxy)diphenyloxide), Figure 1(c), which was further synthesized and studied experimentally. Its flexibility was estimated in our earlier study.[34] The average persistent length value for a freely jointed chain model of the R-BAPO amounted to ~1.17 nm that is close to the corresponding value for R-BAPS.

Thus, comparing the simulation results for R-BAPB and R-BAPO PIs, containing no polar sulfone groups, would allow us to study the chain flexibility effects on the thermal properties of PIs. On the other hand, comparing the thermal properties of R-BAPO and R-BAPS PIs would make it possible to establish the role of the electrostatic interactions.

METHODS

As it was mentioned above in the Introduction, a correct account for EI within atomistic force fields in the MD method is, nowadays, a nontrivial task due to the impossibility of a direct comparison of calculated partial atomic charges with experimental data.[27,28] Partial atomic charges are calculated by means of quantum-chemical methods from electronic orbital populations or electrostatic surface potential (ESP)[27,28] and used further in MD force fields.[14–18]

Parametrization of EI in Atomistic MD Simulation

To parameterize EI in molecular dynamics simulation we used 4 different methods to calculate partial charges: B3LYP/6–31G*(Mulliken), AM1(Mulliken), HF/6–31G*(Mulliken), and HF/6–31G*(ChelpG); the methods differ in both the level of theory and the method of analysis of the electron density distribution. The presence of the sulfone group in the diamine fragment of the repeat unit of PI R-BAPS may be the main reason of changes in its thermal characteristics compared with the other two PIs. Calculated partial charges for sulfur and oxygen atoms in the sulfone group differ significantly for all considered methods.

We did not use highly accurate configuration interactions and coupled clusters methods[27,28] as their application for calculations of partial atomic charges of our targets (repeat units of the studied PIs) is presently inaccessible due to formidably high computation facilities required to simulate systems of $\sim$90 atoms at so difficult to implement theoretical approach.

In addition to three methods chosen for the calculation of partial atomic charges with the use of the Mulliken approach, the method HF/6–31G*(ChelpG) was also considered. The method ChelpG defines partial atomic charges based on the calculated electrostatic potential, and in this respect, it is similar to the method RESP widely used to parameterize EI. Thus, including the HF/6–31G* (ChelpG) method for the parameterization of EI would elucidate the effect of the approach used for the electron density distribution analysis (ChelpG vs. Mulliken) on the polymer thermal characteristics determined by the MD simulation method.

To parameterize EI, partial atomic charge values were calculated for all PIs under study, R-BAPS, R-BAPB, and R-BAPO, with the use of four methods mentioned above. The calculations were performed for dimeric fragments of these PIs, consisting of 172, 166, and 168 atoms for R-BAPS, R-BAPB, and R-BAPO, respectively. Geometry of these dimeric fragments was optimized for several initial configurations (up to three configurations, depending on the method of calculation of partial atomic charges). The lowest energy configurations were used for calculations of atomic charges for all three studied PIs by the methods HF/6–31G*(Mulliken), HF/6–31G*(ChelpG), AM1(Mulliken), using Gaussian 09W[46] program package, and B3LYP/6–31G* (Mulliken), using Turbomole program.[47] Additionally, partial atomic charges for the PI R-BAPS were calculated by the method HF/6–31G*(Mulliken),[31,32,35] using Firefly PC Gamess program package.[48] Gaussian09W and Firefly programs gave similar results for atomic charges at sulfur and oxygen atoms in the sulfone group. Therefore, EI for the PI R-BAPS were parameterized with the charges calculated by the program Firefly PC Gamess for a consistency with the approach used in our previous papers.[31,32,35]

We would like to emphasize that calculations of partial charges in vacuum do not correspond completely to the experimental conditions due to the difference in the dielectric permittivity value. Moreover, using the calculated partial charges at a classical mechanics level in any case represents a rather rough approximation to real interactions. Disadvantages of quantum chemical methods are often related to an incorrect treatment of dispersion interactions, corresponding to the excluded volume interactions at the classical level and torsional potentials (the influence of electrostatic interactions on the torsional angles distribution is discussed below). Therefore, the parameterization of electrostatic interactions should be considered as a semi-empirical approach. In this case, partial charges calculated in vacuum (in gas phase) may serve as a first approximation if systems under considerations are not characterized by relatively strong specific interactions with their surroundings. Moreover, in considered polyimide, such specific interactions are not too essential.

Upon the “transfer” of partial atomic charge values into the force field, partial charges of hydrogen atoms, terminating the dimeric chain fragments, were divided equally between carbon atoms of heterocycles and aromatic rings arranged at both ends of the repeating unit.

ATOMISTIC MD WITH THE ACCOUNT FOR ELECTROSTATIC INTERACTIONS

Computer Model

The procedure for building an equilibrium sample state was described in details earlier.[31–36] Computer simulations were performed with the Gromos53a5 force field[37] implemented into the program package Gromacs.[40,41] The procedure of building the initial system configuration consisted of several steps. First, 27 partially folded polymer chains with the degree of polymerization $N_\mathrm{p} = 8$, corresponding to the polymer regime onset[31–36] were placed randomly into a cubic cell in a way to avoid overlaps with each other,[31,32] and the compression and annealing procedure was applied.[31–36] The system equilibration was conducted at temperature 800 K with the simulation time step of 1 fs. This set of parameters has been already successfully used for similar simulations. The inclusion of EI results in a sharp decrease of the mobility of polymer chains even at high temperatures (~600 K): times required for a displacement of their centers of masses to distances comparable to their own sizes amount to ~100 μs.[31,32] Therefore, the initial samples were equilibrated in the absence of EI.[31] However, it was shown earlier that, even in this case, simulations should be performed over microsecond timescales[31] (one simulation of such a system for 1 μs requires about 3 weeks of a continuous work of 64 processors of the supercomputer "Lomonosov").

The samples under investigation were equilibrated using a preliminary simulation of 2 μs at the temperature 800 K. The equilibration time at this temperature exceeds several times the diffusion time of the center of masses of individual polyimide chain to distances comparable to its own dimensions characterized by the gyration radius. The system was considered to be equilibrated when average values of the gyration radius for individual polymer chains leveled off.[31–35] Once the equilibrium was reached, a basic 1 μs simulation was performed, instantaneous configurations of the system being saved every 100 ns. The selected 11 instantaneous states were used as initial states for calculation of thermal properties.

Calculations of CTE and T_g Values

Experimental Measurements of CTE and T_g Values

All details of chemical synthesis of PI R-BAPO can be found in Supporting Information.

CTE values were determined by means of the following approach. Initially, linear thermal expansion coefficients (LCTE) were measured by the method of linear dilatometry, using a TMA 402 F3 Hyperion (NETZSCH, Germany) thermomechanical analyzer. A cylindrical sample was first cooled down to 223 K, then heated up to 438 K with the heating rate 5 K/min, and cooled again down to 303 K. During the tests, variations of the sample length caused by the indicated temperature changes were measured. The temperature dependence of the volumetric thermal expansion coefficient CTE were recalculated from the experimental LCTE values as described in ref. 32.

The T_g values for the three PIs under study in this work were calculated using two experimental techniques: dynamic mechanical analysis (DMA) and differential scanning calorimetry (DSC). In order to determine T_g by means of DMA, temperature dependences of the dynamic storage modulus, E′, and loss modulus, *E*″, were measured in the temperature range 303 to 623 K on a DMA 242 C/1/F (NETZSCH, Germany), straining film samples with frequency 1 Hz and deformation amplitude 0.1%. The T_g values were estimated from peak temperatures for *E*″ or mechanical loss tangent (tgδ) measured at a heating rate of 5 K/min. Glass transition temperatures of R-BAPS, R-BAPB, and R-BAPO film samples with a weight 3 to 4 mg were determined on a DSC 204 F1 Phoenix calorimeter (NETZSCH, Germany) under argon atmosphere with a heating rate of 5 K/min. The T_g value was determined as the inflexion point on the thermogram (Fig. 7S, Supporting Information).

Calculations of CTE and T_g Values in MD Simulation

Before the cooling procedure, the simulations of the 11 samples of each polymer were continued for more than 100 ns[31,32] with the use of the four selected sets of partial atomic charges (Tables 1S–3S in Supporting Information), EI being taken into account by means of the Particle Mesh Ewald (PME) method.[31,32,35,49]

CTE values for R-BAPS, R-BAPB, and R-BAPO polyimide samples were calculated from the temperature dependences of the density obtained during a stepwise cooling procedure from 800 to 290 K at the cooling rate $\gamma = 1.5 \times 10^{11}$ K/min.[31] In order to extract the neat effect of electrostatic interactions, systems with zero partial atomic charges were also subjected to the cooling procedure. At every cooling step, constant temperature and pressure values were maintained, employing Berendsen thermostat and barostat ($\tau_t = 0.1$ ps, $\tau_p = 0.5$ ps). The total simulation time of all investigated PIs at different methods of accounting for electrostatic interactions amounted to approximately 47 μs.

The CTE, β, was calculated from the temperature dependence of the polymer sample density via the following finite-difference relation:

$$\beta = \rho_1^{-1}\left(\frac{(\rho_2-\rho_1)}{(T_2-T_1)}\right)_{\mathrm{P}}, \tag{1}$$

where ρ_1 and ρ_2 are density values for a polymer sample calculated at the temperatures T_1 and T_2, respectively.

RESULTS AND DISCUSSIONS

The Effect of EI on CTE Values

In Figure 2, CTE calculation results for three PIs under investigation obtained by four selected EI parameterization methods (B3LYP/6–31G*(Mulliken), AM1(Mulliken), HF/6–31G*(Mulliken), and HF/6–31G*(ChelpG)) and without EI (zero partial atomic charges) are shown together with the experimental CTE values.

The analysis of the obtained results (Fig. 2) shows that CTE values for all investigated PIs fluctuate in the glassy state. Therefore, for the sake of comparison of computer simulation results with experimental values CTE values averaged over the range from 300 K to 410 K were chosen to compare the computer simulation results with the experimental values (are reported in Table 1).

The parameterization of EI by B3LYP/6–31G*(Mulliken) quantum-chemical methods brings about the worst results: CTE values for all three PIs exceed significantly experimental ones. Similar considerations can be given for the results obtained with no account for EI. This may be due to the fact that partial charge values at sulfur and oxygen atoms in the sulfone group are in this case the lowest among all four selected methods of EI parameterization.

CTE values calculated with EI parameterized by AM1(Mulliken) quantum-chemical method exceed experimental values for all three PIs, although the calculated CTE value for the PI R-BAPS is rather close to the experimental one. However, AM1(Mulliken) partial charges at sulfur and oxygen atoms of the sulfone group are unrealistically high, +2.9 and −0.9, respectively.[36]

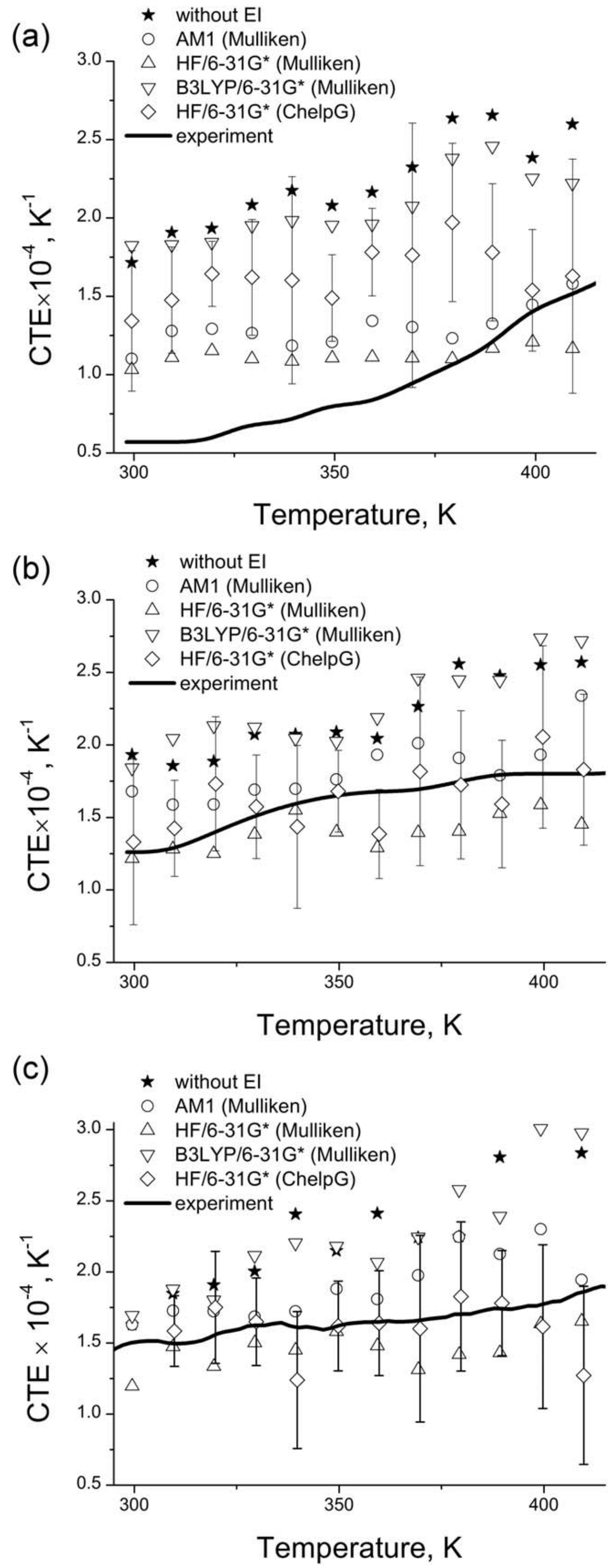

FIGURE 2 Temperature dependences of CTE for R-BAPS (a), R-BAPB (b), and R-BAPO (c) PIs with EI parameterized by AM1(Mulliken) (open circles) HF/6–31G* (Mulliken) (open triangles), B3LYP/6–31G*(Mulliken) (open inverted triangles), HF/6–31G*(ChelpG) (open diamonds) methods and without EI (black asterisks). Experimental CTE values are shown by black solid curves. Typical values of error bars are shown for HF/6-31G*(ChelpG) method.

The results obtained by the method HF/6–31G*(ChelpG), do not reproduce the experimentally observed difference between CTE values for the three investigated PIs. However, this method provides CTE values most close to experimental ones for R-BAPB and R-BAPO PIs, containing no sulfone group in their chemical structures.

The method HF/6–31G*(Mulliken) used to parameterize EI made it possible to calculate the most accurate CTE value for the PI R-BAPS. Moreover, this method, like the AM1(Mulliken) one, allows the relation between experimental CTE values for the three investigated PI to be reproduced qualitatively.

One of the advantages of the molecular dynamics method is the possibility to get insight into the dynamic properties of the systems under discussion. The study of the local orientation dynamics is of special interest for revealing links between the chemical structure of polymers and their glass transition temperatures. The corresponding results will be presented in our forthcoming publication. In the present work, the mobility of individual polyimide chains as a whole at temperatures above the glass transition temperature and the dependence of this mobility on the method of calculation of partial charges are explored. To this end, the time dependence of the mean square displacement of the center of mass $<\Delta r^2_{\mathrm{com}}(t)>$ of individual molecules of the studied polyimides (averaged over all molecules in a sample under study and over 11 initial configurations) was calculated at the temperature 600 K:

$$<\Delta r^2_{\mathrm{com}}(t)> = < \left(\overrightarrow{r}(t_1)-\overrightarrow{r}(t_2)\right)^2 > \tag{2}$$

where $\overrightarrow{r}(t_1)$ is the radius-vector of the center of mass of a selected molecule at the time moment t_1. The averaging was carried out over all time moments t_1 and t_2 differing by the value $t=t_2-t_1$. The results are presented in Figure 3. It is seen that $<\Delta r^2_{\mathrm{com}}(t)>$ curves reach a diffusion regime after ∼40 ns.

Comparing the data presented in Figure 3 with the CTE values (Table 1) leads to the following conclusion: smaller mobility of individual chains as a whole correlates with smaller CTE value. The use of rather high HF/6–31G* (Mulliken) and AM1(Mulliken) partial charges at sulfur and oxygen atoms in the sulfone groups of PI R-BAPS enhances electrostatic interactions between polymer chains, decreasing their translational mobility and slowing down their diffusion. This fact is finally revealed in the calculated thermal properties.

TABLE 1 Averaged CTE Values in the Range 300 to 410 K for the Considered Polymers Below T_g Calculated with and Without EI

Method of Calculation of Partial Atomic Charges	CTE × 10^4 1/K		
	R-BAPS	R-BAPB	R-BAPO
HF/6–31G* (Mulliken)	1.12	1.39	1.46
HF/6–31G* (ChelpG)	1.66	1.66	1.58
AM1 (Mulliken)	1.30	1.83	1.90
B3LYP/6–31G* (Mulliken)	2.06	2.27	2.26
Without EI	2.22	2.20	2.31
Experiment	0.90	1.60	1.66

The Effect of EI on Calculated T_g Values

A question arises on the reason for a large difference between CTE values for the PI R-BAPS calculated with EI parameterized with partial atomic charges provided by HF/6–31G*(Mulliken) and HF/6–31G*(ChelpG) methods. To answer this question, we calculated glass transition temperatures and compared the results with the corresponding experimental data.

In Table 2, experimental T_g values obtained by various methods are presented. All the data involved into these calculations (temperature dependences of the loss modulus (E''), mechanical loss tangent (tgδ), and specific heat capacity) are presented in the Supporting Information (Figs. 5S–7S).

The analysis of the data presented in Table 2 shows that all three experimental methods provide close T_g values. For the investigated PIs, the following qualitative relation is observed:

$$T_g^{\text{R-BAPS}} > T_g^{\text{R-BAPB}} > T_g^{\text{R-BAPO}}. \tag{3}$$

In order to determine T_g values from the results of the computer simulations, temperature dependences of the density $\rho(T)$ were built for all three PIs (without EI and with EI parameterized by HF/6–31G*(Mulliken) and HF/6–31G*(ChelpG) partial atomic charges). The T_g was calculated as the crossing point of two straight lines, approximating $\rho(T)$ at high and low temperatures (Fig. 4).

The results reported in Figure 4(a) evidence that the T_g values calculated with no account for EI have almost the same value of $T_g = 470 \pm 8$ K for all investigated PIs. These data agree well with our previous studies[31,32] where it was shown that EI should be taken into account for T_g values of R-BAPS and EXTEM$^{\text{TM}}$ PIs to be correctly calculated.

The analysis of the results obtained with EI parameterized by HF/6–31G*(Mulliken) partial atomic charges [Fig. 4(b)] shows that, for the chosen cooling rate, the system cooling procedure should be carried out in the temperature range from 800 to 290 K.[32] This is caused by the fact that the temperature dependence of the density $\rho(T)$ for the PI R-BAPO in the range from 290 to 600 K lies above that for the polyimide R-BAPB, leading to a wrong relation between T_g values for these polyimides due to an incorrect approximation of $\rho(T)$ in the high-temperature range. At temperatures above

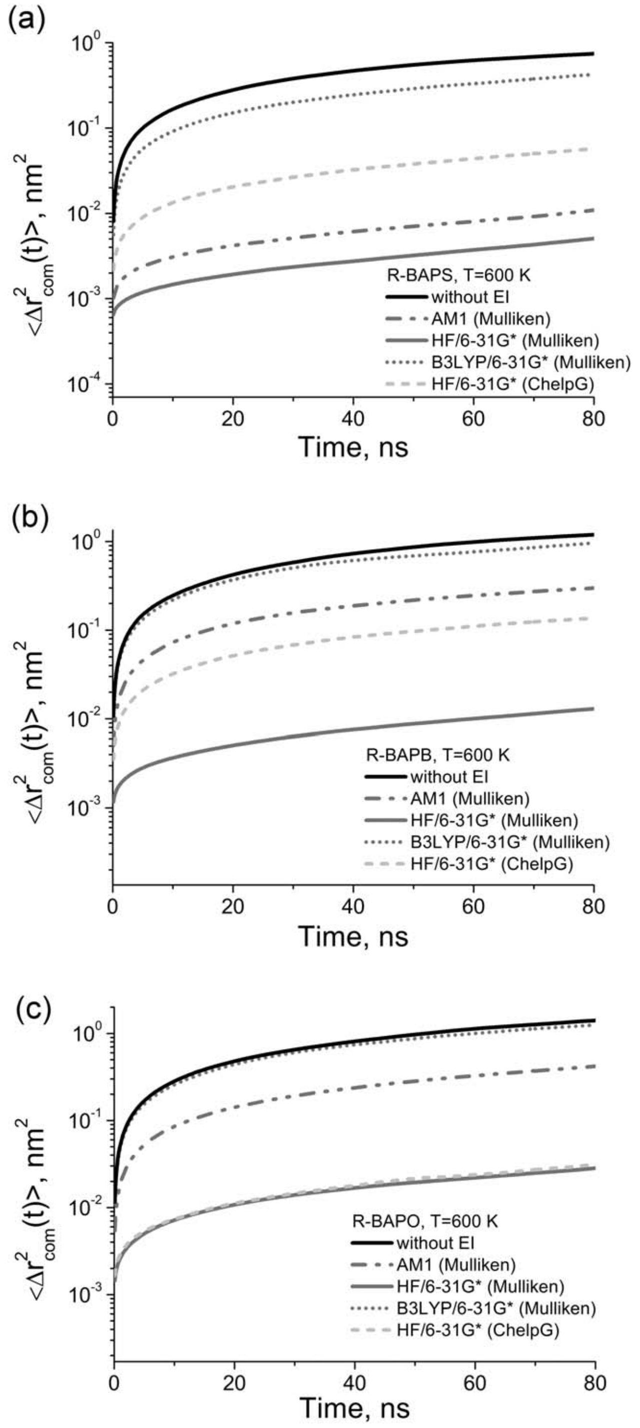

FIGURE 3 Time dependence of the mean square displacement $<\Delta r^2_{\text{com}}(t)>$ for the center of mass of R-BAPS (a), R-BAPB (b), and R-BAPO (c) PIs chain with EI parameterized by AM1(Mulliken) (gray dashed line) HF/6–31G* (Mulliken) (gray solid line), B3LYP/6–31G*(Mulliken) (gray dotted line), HF/6–31G*(ChelpG) (gray dash dot line) methods and without EI (black solid line)

TABLE 2 Values of T_g Measured by Different Experimental Methods

	Experimental Values		
Polymer	T_g (E''), K	T_g ($t_g\delta$), K	T_g (DSC), K
R-BAPO	450	455	462
R-BAPB	478	482	485
R-BAPS	496	499	499

600 K, the density value for R-BAPO is below that for R-BAPB [Fig. 4(b)]. Moreover, it should be stressed that HF/6–31G*(Mulliken) parameterization of EI, in contrast to HF/6–31G*(ChelpG) [Fig. 4(c)], allows the relation between experimental T_g values for all three PIs to be reproduced correctly by computer simulations.

Extrapolation of the simulated T_g values to the experimental cooling rates represent a special interest; for HF/6–31G*(Mulliken) parameterization of EI after such extrapolation we can reproduce[32] an excellent agreement of simulated T_g value with the experimental value for R-BAPS PI.

Thus, it was found that only the HF/6–31G*(Mulliken) approach for parameterization of electrostatic interactions allows reproducing the thermal properties of the considered PIs without changes of other force field parameters. However, an enhancement of electrostatic interactions due to the presence of rather high partial charges may affect some force field parameters, in particular, internal rotation barrier values implemented into the torsional potentials.[50,51] Therefore, the influence of changes of EIs on the parameters that describe torsional angles in Gromos53a5 force field was additionally studied.

To analyze the effect of EI parameterization on structural properties of thermoplastic polyimides and to reveal the mechanism of changes in thermal properties of PIs occurred upon introducing sulfone groups into their repeat units, pair distribution functions $g_{AB}(r)$ for sulfur atoms of sulfone groups of the PI R-BAPS repeat unit were calculated (partial charges at the atoms of sulfone groups are the most sensitive to a particular method of the electron density distribution analysis). The pair distribution function was calculated via the following equation:

$$g_{AB}(r)=\frac{1}{N_A\rho_B}\sum_{i\in A}^{N_A}\sum_{j\in B}^{N_B}\frac{\delta\left(r_{ij}-r\right)}{4\pi r^2}, \qquad (4)$$

where ρ_B is the average density of type B atoms around atoms A, N_A and N_B are the numbers of atoms A and B components, respectively, r_{ij} is the distance between two atoms of A and B components, δ is the Kronecker symbol.

Of special interest is the question why the HF/6–31G* (ChelpG) parameterization of EI interactions is inferior with respect to the HF/6–31G* (Mulliken) one. In Figure 5, the results of calculations of $g_{S\text{-}S}(r)$ pair distribution function for both EI parameterization methods at temperatures 800 K (melt) and 290 K (glass) are presented.

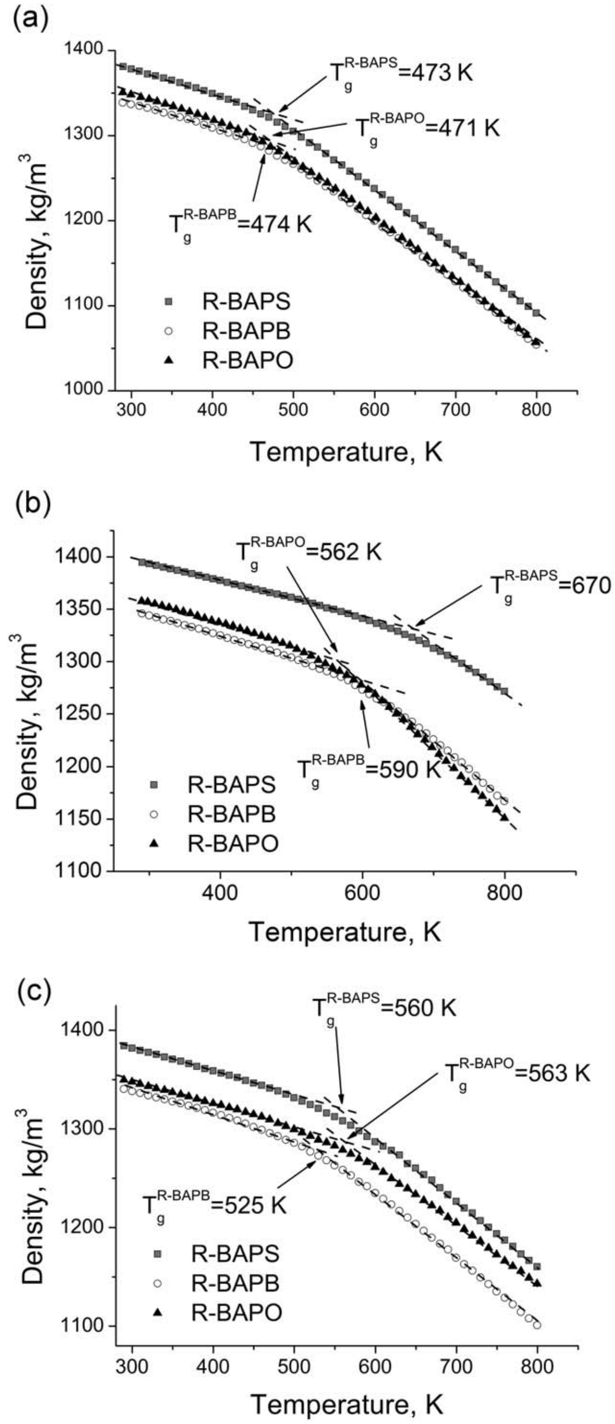

FIGURE 4 Temperature dependences of the density for three PIs under investigation during the cooling procedure from 800 to 290 K without EI (a) and with EI parameterized by HF/6–31G*(Mulliken) (b) and HF/6–31G*(ChelpG) (c) partial atomic charges. The error in the calculated T_g values for all investigated PIs obtained with all three indicated EI parameterizations was ~8 K.

The obtained results for the selected EI parameterization methods (Fig. 5) show that at high temperatures ($T = 800$ K) only one well-pronounced maximum of the pair distribution

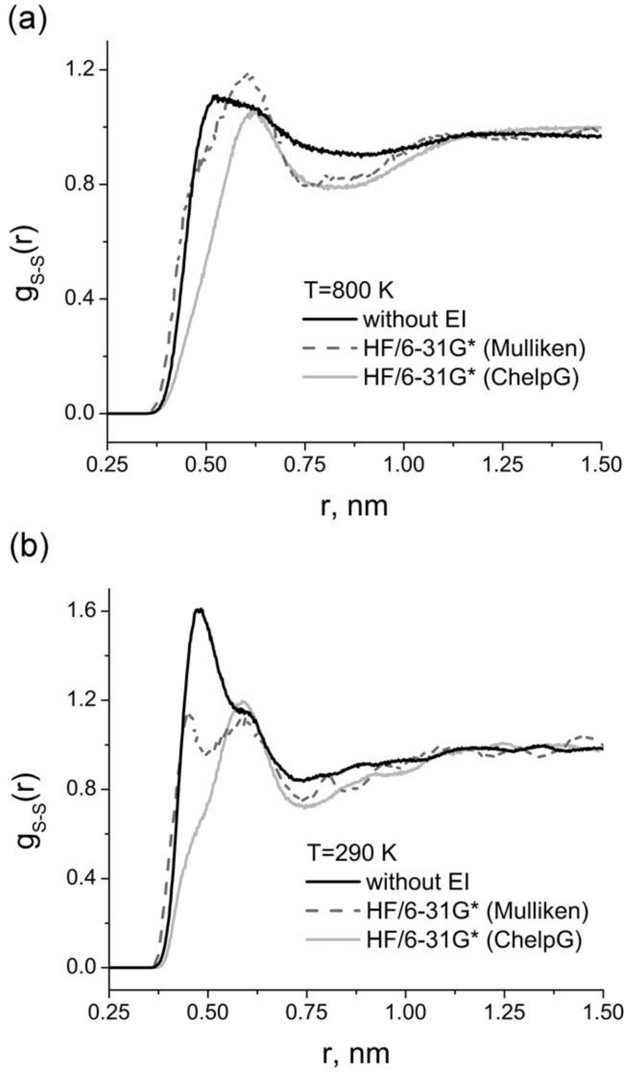

FIGURE 5 Pair distribution function $g_{\text{s-s}}(r)$ calculated between sulfur atoms for PI R-BAPS at $T = 800$ K (a) and $T = 290$ K (b) without EI and with EI parameterized by HF/6–31G* (Mulliken) and HF/6–31G*(ChelpG) methods.

function is observed which is typical for liquids. However, the positions and heights of the maxima do not coincide for different EI parameterization methods. The shortest distance between sulfur atoms is observed for systems without EI. Positions of the maxima for systems with HF/6–31G* (Mulliken) and HF/6–31G* (ChelpG) parameterized EI are almost the same, but the maximum of the pair distribution function is higher for the former than for the latter case.

At temperatures below T_g ($T = 290$ K), multiple maxima are observed in the radial distribution for the system with HF/6–31G* (Mulliken) parameterized EI, indicating the presence of a spatial ordering of sulfur atoms. The formation of stable three-dimensional structures of sulfur atoms may reflect a molecular mechanism responsible for an increase of the glass transition temperature for PI R-BAPS as compared with the other two investigated polyimides: the presence of polar sulfone groups results in an additional structural ordering due to an essential contribution of dipole-dipole interactions.

A much better agreement of the calculated thermal properties with the experimental data for the HF/6–31G* (Mulliken) parameterization of EI implies that this method of calculation of partial atomic charges is the most adequate for the selected force field. However, for partial atomic charges to be included into a force field, a revision of all remaining interaction parameters, first of all those related to internal rotations, is often required.

The distribution of torsion angles may be recalculated directly from computer simulations both for systems with HF/6–31G* (Mulliken) atomic charges and without accounting for EIs. The torsional potential for a dihedral angle in the Gromos 53a5 force field is described by a simple periodic function:[40,41]

$$U(\varphi)=k_{\text{dih}}(1+\cos(n\varphi-\varphi_{\text{s}})), \tag{5}$$

where k_{dih} is the force constant, φ_{s} is an equilibrium value of the torsional angle, and n is the parameter that defines the number of potential barriers. It should be noted that using this kind of potential makes it possible to reproduce correctly only internal rotations with equal heights of all energy barriers.

To analyze the influence of partial charges, we recalculated the distribution $P(\varphi)$ for different torsional angles of the considered systems with and without electrostatic interactions for the well-equilibrated samples with the use of the GROMACS routine g_angle. The resulting distributions were compared with those provided by the original force field. To recalculate the original $P(\varphi)$ from the potential energy, (5) the Boltzmann inversion method was used:

$$P(\varphi)=Z^{-1}\exp[-\beta U(\varphi)], \tag{6}$$

where $Z=\int_{-180}^{180}\exp[-\beta U(\varphi)]d\varphi$ is the partition function, $\beta=1/k_{\text{B}}T$, Boltzman constant is defined as $k_B=8.314\cdot10^{-3}\text{kJmol}^{-1}\text{K}^{-1}$ in the units used in GROMACS package.[40,41] The final distribution $P(\varphi)$ is normalized by following manner:

$$\int_{-180}^{180}P(\varphi)d\varphi=1. \tag{7}$$

A typical comparison of the results for most important torsional angles (Fig. 6), involving rather polar sulfone groups in R-BAPS polyimide, are shown in Figure 7 at $T = 800$ K (for others considered distributions, the results were found to be qualitatively the same).

As it is shown in Figure 7, the accounting for electrostatic interactions leads to negligible changes in the calculated torsional angle distribution as compared with that for the system without partial charges. However, both mentioned distributions are clearly distinguished from the original one provided by the force field. This may be due to the fact that

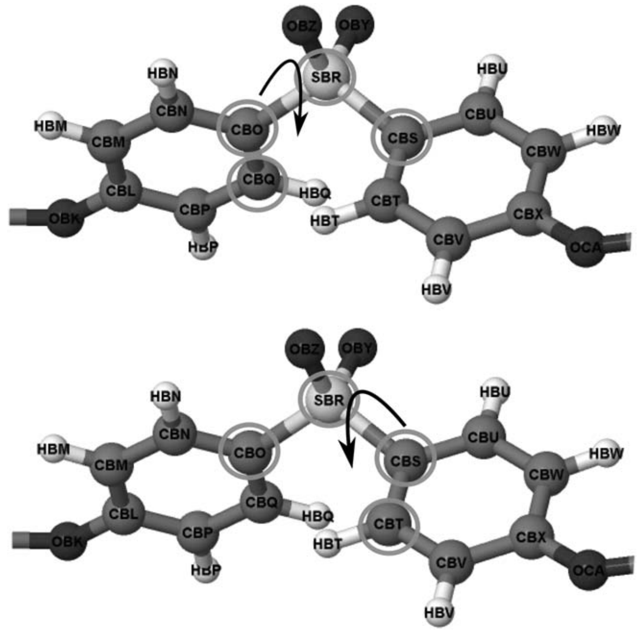

FIGURE 6 Torsional angles related to the highest charges of the sulfone group in a R-BAPS polyimide.

the Gromos53a5 force field is not initially designed for bulk polymer systems so that the observed effect is caused by an essential contribution of volume interactions. A detailed study of the effect of the molecular weight of PIs on their thermal properties is currently in progress, and the results will be published in forthcoming papers. Fortunately, the positions of $P(\varphi)$ maxima are virtually unaffected by the consideration of the electrostatic interactions.

Many authors have reported that using the HF/6–31G* approach for the parameterization of EIs is not suitable even for simplest polymers as polyethylene. The fact that the Mulliken scheme of the calculation of partial charges combined with this approach provides the best results for the calculated thermal properties could be explained as followings. If a polarizable force field is not used for PIs, often charge rescaling schemes have been shown to be successful, for example for ionic liquids.[52] Sometimes, Mulliken charges may be interpreted as rescaled real charges. Another explanation may be based on an occasional proximity of gas-phase Mulliken partial charges to 'real' charges in the bulk phase. Moreover, partial charges may affect not only torsional parameters but also Lennard-Jones ones. However, verification of these ideas needs additional resource-consuming simulations which will be carried out in the future. According to the obtained results, it can be concluded that increasing the level of quantum-chemical calculations of partial atomic charges to parameterize electrostatic interactions in the studied thermoplastic PIs with polar groups is not necessarily accompanied by an improvement of the reproduction of corresponding experimental thermal properties, since the force field as a whole may get unbalanced and needs to be readjusted.

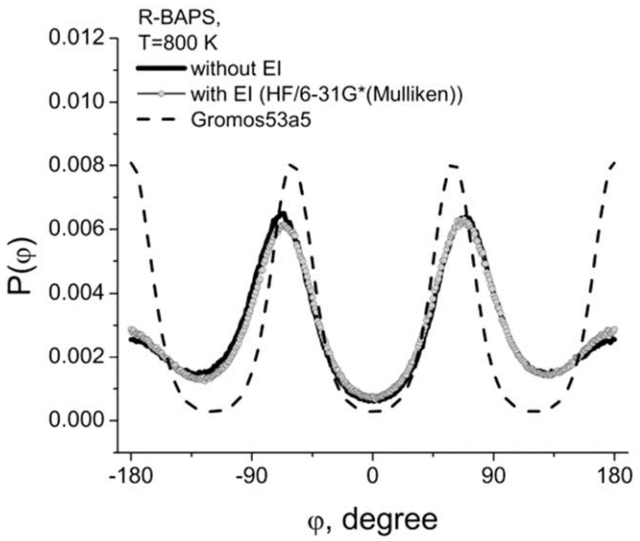

FIGURE 7 Averaged distribution $P(\varphi)$ of torsional angles shown in Figure 6.

Thus, an importance of electrostatic interactions for a correct reproduction of thermal properties of the studied PIs was established (Table 3) which is helpful for a better understanding of structure-properties relationships for thermoplastic polymers. Correlations between the density, energy of electrostatic interactions and T_g values for the considered PIs were found. It was shown that an increase in the chain flexibility, which is accompanied by a certain decrease in T_g, is less important than an increase in electrostatic interactions, as it is highlighted in Table 3.

CONCLUSIONS

In the present work, multi-scale computer simulations, combining molecular dynamics on a microsecond time scale with quantum-chemical calculations, were performed with the aim to parameterize EI in the Gromos53a5 force field for investigations of the thermal properties of heterocyclic polymers.

The performance of four selected EI parameterization methods was evaluated by the quality of the reproduction of experimental CTE values for R-BAPS, R-BAPB, and R-BAPO PIs in their glassy states by the atomistic MD simulation method. Surprisingly, a reasonable qualitative agreement between CTE values for the three PIs and a quantitative agreement with the

TABLE 3 Average Values of the Persistence Length(<a>).[34,36] Calculated T_g Values, Energies of Electrostatic Interactions E_{Coulomb} and Densities of the Studied PIs at $T = 800$ K

PI	<a> (nm)	T_g (K) Simulated/ Experimental Value	E_{Coulomb} (kJ/mol)	Density (kg/m^3)
R-BAPS	0.99	670/496	821.0	1271.6
R-BAPB	1.32	590/478	165.6	1167.1
R-BAPO	1.17	562/450	−1531.6	1150.9

experimental data was achieved when EI were parameterized using the HF/6–31G*(Mulliken) method for the calculation of atomic partial charges instead of using a more exact ChelpG approach. Moreover, using HF/6-31G*(Mulliken) allowed a confirmation of the experimentally observed qualitative relation $T_g^{\text{R-BAPS}} > T_g^{\text{R-BAPB}} > T_g^{\text{R-BAPO}}$. Computer simulations without EI showed identical values of CTE ($\text{CTE}^{\text{SIM}}_{\text{R-BAPS}} = \text{CTE}^{\text{SIM}}_{\text{R-BAPB}} = \text{CTE}^{\text{SIM}}_{\text{R-BAPO}}$) and $T^{\text{SIM}}_{g\text{R}-\text{BAPS}} = T^{\text{SIM}}_{g\text{R}-\text{BAPB}} = T^{\text{SIM}}_{g\text{R}-\text{BAPO}}$, contradicting experimental data. These results provide reasons to state that sulfone groups introduced into the diamine component of PIs cause rather strong intra- and intermolecular EI which may essentially improve polyimide thermal properties.

It should also be noted that the HF/6–31G*(Mulliken) method of the calculation of partial atomic charges is superior with respect to HF/6–31G*(ChelpG) one in the degree of reproduction of experimental data, despite the fact that the latter belongs to the most accurate methods of ESP surface calculation. Probably, using of HF/6–31G*(ChelpG) approach needs additional fine tuning of others force field parameters.

ACKNOWLEDGMENTS

This study has been supported by the Russian Ministry of Education and Science within State Contract No. 14.Z50.31.0002. The simulations were carried out with the use of the computational resources of the Institute of Macromolecular Compounds, Russian Academy of Sciences, and the Chebyshev and Lomonosov supercomputers at Moscow State University. The work was partially supported by the Government of the Russian Federation (Grant 074-U01) (A.V. Yakimansky). The authors are grateful to Nikolay Perov (Enikolopov Institute of Synthetic Polymeric Materials, Russian Academy of Sciences) for the help in the LCTE measurements.

REFERENCES AND NOTES

1 M. I. Bessonov, M. M. Koton, V. V. Kudryavtsev, L. A. Laius, Polyimides—Thermally Stable Polymers; Plenum: New York, **1987**.

2 M. K. Ghosh, K. L. Mittal, Polyimides: Fundamentals and Applications; Marcel Dekker: New York, **1996**.

3 D.-J. Liaw, K.-L. Wang, Y.-C. Huang, K.-R. Lee, J.-Y. Lai, C.-S. Ha, *Prog. Polym. Sci.* **2012**, *37*, 907–974.

4 T. Yasuda, S. Nakamura, Y. Honda, K. Kinugawa, S.-Y. Lee, M. Watanabe, *ACS Appl. Mater. Interfaces* **2012**, *4*, 1783–1790.

5 Y. Dai, M. D. Guiver, G. P. Robertson, Y. S. Kang, K. J. Lee, *Macromolecules* **2003**, *36*, 6807–6816.

6 S. Neyertz, D. Brown, A. Douanne, C. Bas, N. D. Albe, *J. Phys. Chem. B* **2002**, *106*, 4617–4631.

7 R. Pan, X. Liu, A. Zhang, Y. Gu, *Comput. Mater. Sci.* **2007**, *39*, 887–895.

8 M. Hegde, U. Lafont, B. Norder, S. J. Picken, E. T. Samulski, M. Rubinstein, T. Dingemans, *Macromolecules* **2013**, *46*, 1492–1503.

9 V. E. Yudin, V. M. Svetlichnyi, G. N. Gubanova, A. L. Didenko, T. E. Sukhanova, V. V. Kudryavtsev, S. Ratner, G. Marom, *J. Appl. Polym. Sci.* **2002**, *83*, 2873–2882.

10 V. E. Yudin, V. M. Svetlichnyi, A. N. Shumakov, D. G. Letenko, A. Y. Feldman, G. Marom, *Macromol. Rapid Commun.* **2005**, *26*, 885–888.

11 V. E. Yudin, G. M. Divoux, J. U. Otaigbe, V. M. Svetlichnyi, *Polymer* **2005**, *46*, 10866–10872.

12 M. J. M. Abadie, A. L. Rusanov, Practical Guide to Polyimides; Smithers Rapra Technology Limited: Shawbury, **2007**.

13 D. Hofmann, L. Fritz, J. Ulbrich, D. Paul, *Comput. Theor. Polym. Sci.* **2000**, *10*, 419–436.

14 S. Neyertz, D. Brown, *Macromolecules* **2004**, *37*, 10109–10122.

15 S. Neyertz, *Macromol. Theor. Simul.* **2007**, *16*, 513–524.

16 S. Pandiyan, D. Brown, S. Neyertz, N. F. A. van der Vegt, *Macromolecules* **2010**, *43*, 2605–2621.

17 E. Pinel, D. Brown, C. Bas, R. Mercier, N. D. Albe, S. Neyertz, *Macromolecules* **2002**, *35*, 10198–10209.

18 Y. Yani, M. H. Lamm, *Polymer* **2009**, *50*, 1324–1332.

19 P. V. Komarov, Y.-T. Chiu, S.-M. Chen, P. Reineker, *Macromol. Theor. Simul.* **2010**, *19*, 64–73.

20 P. V. Komarov, I. V. Mikhailov, Y.-T. Chiu, S.-M. Chen, P. G. Khalatur, *Macromol. Theor. Simul.* **2013**, *22*, 187–197.

21 M. Heuchel, D. Hofmann, *Desalination* **2002**, *144*, 67–72.

22 J. Xia, S. Liu, P. K. Pallathadka, M. L. Chng, T.-S. Chung, *Ind. Eng. Chem. Res.* **2010**, *49*, 12014–12021.

23 D. Hofmann, L. Fritz, J. Ulbrich, C. Schepers, M. Bo, *Macromol. Theor. Simul.* **2000**, *327*, 293–327.

24 D. Qi, J. Hinkley, G. He, *Model. Simul. Mater. Sci. Eng.* **2005**, *13*, 493–507.

25 S.-H. Tzeng, J.-L. Tsai, *J. Reinf. Plast. Compos.* **2011**, *30*, 922–931.

26 J.-S. Gao, S.-C. Shiu, J.-L. Tsai, *J. Compos. Mater.* **2012**, *47*, 449–458.

27 D. Young, Computational Chemistry: A Practical Guide for Applying Techniques to Real World Problems; John Wiley & Sons: New York, **2004**.

28 J. B. Foresman, A. E. Frisch, Exploring Chemistry with Electronic Structure Methods; Gaussian Inc.: Pittsburgh, **1996**.

29 A. V. Lyulin, M. A. J. Michels, *Macromolecules* **2002**, *35*, 1463–1472.

30 A. V. Lyulin, N. K. Balabaev, M. A. J. Michels, *Macromolecules* **2002**, *36*, 8574–8575.

31 S. V. Lyulin, A. A. Gurtovenko, S. V. Larin, V. M. Nazarychev, A. V. Lyulin, *Macromolecules* **2013**, *46*, 6357–6363.

32 S. V. Lyulin, S. V. Larin, A. A. Gurtovenko, V. M. Nazarychev, S. G. Falkovich, V. E. Yudin, V. M. Svetlichnyi, I. V. Gofman, A. V. Lyulin, *Soft Matter* **2014**, *10*, 1224–1232.

33 S. G. Falkovich, S. V. Lyulin, V. M. Nazarychev, S. V. Larin, A. A. Gurtovenko, N. V. Lukasheva, A. V. Lyulin, *J. Polym. Sci. Part B: Polym. Phys.* **2014**, *52*, 640–646.

34 V. M. Nazarychev, S. V. Larin, N. V. Lukasheva, A. D. Glova, S. V. Lyulin, *Polym. Sci. Ser. A* **2013**, *55*, 570–576.

35 S. V. Larin, S. G. Falkovich, V. M. Nazarychev, A. A. Gurtovenko, A. V. Lyulin, S. V. Lyulin, *RSC Adv.* **2014**, *4*, 830–844.

36 S. V. Lyulin, S. V. Larin, A. A. Gurtovenko, N. V. Lukasheva, V. E. Yudin, V. M. Svetlichnyi, A. V. Lyulin, *Polym. Sci. Ser. A* **2012**, *54*, 631–643.

37 C. Oostenbrink, A. Villa, A. E. Mark, W. F. van Gunsteren, *J. Comput. Chem.* **2004**, *25*, 1656–1676.

38 D. Brown, The gmq User Manual Version 5; **2013**. Available at: http://www.lmops.univ-savoie.fr/brown/gmq.html. Accessed on 20 March, 2015.

39 M. Clark, *J. Comput. Chem.* **1989**, *10*, 982–1012.

40 D. Van Der Spoel, E. Lindahl, B. Hess, G. Groenhof, A. E. Mark, H. J. C. Berendsen, *J. Comput. Chem.* **2005**, *26*, 1701–1718.

41 B. Hess, C. Kutzner, D. van der Spoel, E. Lindahl, *J. Chem. Theory Comput.* **2008**, *4*, 435–447.

42 Y. Wang, L. Jiang, T. Matsuura, T. S. Chung, S. H. Goh, *J. Membr. Sci.* **2008**, *318*, 217–226.

43 N. Peng, T.-S. Chung, M. L. Chng, W. Aw, *J. Membr. Sci.* **2010**, *360*, 48–57.

44 http://www.sabic-ip.com/gep/en/ProductsAndServices/SpecialtyAdditivesandIntermediatesProductPages/ultempeiresinsadditives.html. Accessed on 20 March, 2015.

45 http://www.sabic-ip.com/gep/en/ProductsAndServices/SpecialtyAdditivesandIntermediatesProductPages/extemthermoplasticpolyimideresins.html. Accessed on 20 March, 2015.

46 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian 09, Gaussian Inc, Inc.: Wallingford CT, **2009**.

47 TURBOMOLE V6.4 2012, a Development of University of Karlsruhe and Forschungszentrum Karlsruhe GmbH, 1989–2007, TURBOMOLE GmbH, since **2007**. Available from www.turbomole.com. Accessed on 20 March, 2015.

48 A. A. Granovsky, Firefly Version 7.1.G. Available at: http://classic.chem.msu.su/gran/firefly/index.html. Accessed on 20 March, 2015.

49 T. Darden, D. York, L. Pedersen, *J. Chem. Phys.* **1993**, *98*, 10089–10092.

50 J. B. Klauda, B. R. Brooks, A. D. MacKerell, R. M. Venable, R. W. Pastor, *J. Phys. Chem. B* **2005**, *109*, 5300–5311.

51 S. W. I. Siu, K. Pluhackova, R. A. Bockmann, *J. Chem. Theory Comput.* **2012**, *8*, 1459–1470.

52 F. Dommert, K. Wendler, R. Berger, L. Delle Site, C. Holm, *Chem. Phys. Chem.* **2012**, *13*, 1625–1637.