Development of a force field for molecular simulation of the phase equilibria of perfluoromethylpropyl ether

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A first step towards the development of a general, realistic potential model for perfluoroether compounds has been to parameterize a united atom model for a short chain perfluoroether perfluoromethylpropyl ether ($CF_3CF_2CF_2OCF_3$). The potential model takes the usual form in which separate bond bending and torsional terms describe the intramolecular interactions with the addition of van der Waals and electrostatic terms to describe the non-bonded interactions. *Ab initio* quantum calculations have been carried out to obtain the partial charges and intramolecular torsional and bending potentials. Phase equilibrium data were then used to optimize the van der Waals interaction parameters through Gibbs ensemble Monte Carlo simulations. The resulting model reproduces vapour–liquid equilibrium densities, the critical temperature and the critical density of perfluoromethylpropyl ether, in good agreement with those from experiment.

1. Introduction

In the past decade, perfluoroethers have attracted interest from a wide range of communities because of their importance in a number of applications and research areas. Perfluoropolyethers, and perfluorocarbons in general, have a unique combination of physical and chemical properties which makes them suitable for a wide range of potential applications in the medical, biotechnology, electronic, and oil and gas industries [1, 2]. Perfluoropolyethers are extremely unreactive, non-toxic, non-flammable fluids, making them excellent candidates as high performance lubricants [3–5]. For example, Fomblin® and Krytox® are widely used as lubricants for magnetic recording media because of their low vapour pressure, oxidative stability, and relatively stable structures [6–8]. In the pharmaceutical and biomedical industries, perfluoropolyethers have attracted a lot of attention because of their chemical and biochemical inertness. This inertness, when combined with their high solubility of oxygen and other respiratory gases, has led to a number of applications, such as, blood plasma substitutes, eye fluid, infusion fluid in the treatment of burns, and in cosmetics [1]. Additionally, several simple perfluoroethers can be used as potential CFC substitutes [9]. A particularly topical example is the possible use of functionalized perfluoropolyethers as surfactants that can form microemulsions which disperse water in supercritical carbon dioxide [10–12], helping to make CO_2 a more versatile replacement solvent in the chemical and related industries.

Thus, it would be of great value to be able to model perfluoropolyethers with molecular simulation techniques. While the thermophysical properties (including phase equilibrium and rheology) of hydrocarbons have been examined extensively through molecular simulation, and numerous force fields have been proposed in the literature [13–17], simulation studies and force field development for perfluorinated compounds are much less advanced [18, 19]. Essentially, previous work for perfluoro compounds has been for perfluoroalkanes, and has focused on modelling the solid phase diagram of PTFE using explicit atom models to describe the helical nature of the carbon backbone (see, e.g. [13, 20–23]). In the early 1990s, in a study of the properties of liquid supported monolayers of long chain amphiphilic molecules, Rice and coworkers [24–26] developed a united atom model for CF_3 and CF_2 groups in per-

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fluorinated amphiphiles. However, their potential was based on those used for hydrocarbons and solid state data for perfluoroalkanes, therefore perhaps it is not surprising that this model was found to perform poorly in phase equilibrium studies of liquid perfluoroalkanes [27, 28].

Generally, it is well recognized that the applicability of a potential model or force field lies in its parametrization. Hence, in order to obtain accurate predictions of the thermophysical properties of perfluoroethers from simulation, it is our goal to develop an accurate potential model that is fitted to liquid state thermodynamic properties in addition to *ab initio* calculations. To date, no potential model has been developed specifically for perfluoropolyethers. Although Koike [29] has performed molecular dynamics simulations of confined branched and linear perfluoropolyethers using the consistent valence force field [30] potential model, this model was developed for the study of proteins and their binding to active sites, and has not been tested for phase equilibrium or bulk transport properties.

We propose a united atom model for perfluoromethyl propylether, which we show to reproduce accurately experimental phase equilibrium data. We chose to develop a united atom model over an explicit atom approach for two main reasons. First, we anticipate that a united atom model will be successful in the prediction of such properties for perfluoroethers because united atom models have proved to be accurate in the determination of phase equilibria for a wide variety of substances, such as hydrocarbons [13, 31], perfluorocarbons [18, 24, 25], alkenes [32, 33], alcohols [34], and thiols [35]. On the other hand, a united atom model might not be expected to be quite so successful for predicting transport properties. Second, a united atom model is computationally more efficient than explicit atom models. Normally, for a fixed number of molecules, the computational cost of a molecular simulation scales as N^2, where N is the total number of sites. For molecules such as alkanes, ethers, and their perfluoro counterparts, the number of sites in an explicit atom model is about three times that of a united atom model. Therefore, simulation with an explicit atom model is about nine times more expensive than with a united atom model. Figure 1 shows the grouping of the united atom model for perfluoromethylpropylether in this work.

2.   Methods

The force field we propose consists of bond angle bending terms E_{ba}, a torsional term $E_{torsion}$ and terms to describe the van der Waals E_{vdW} and electrostatic interactions E_{es}, with the total energy being given by the sum of these contributions:

$$E = E_{ba} + E_{torsion} + E_{vdw} + E_{es}. \qquad (1)$$

In the parametrization of this force field, two different types of calculation were performed, *ab initio* quantum mechanical calculations and classical Gibbs ensemble Monte Carlo simulations [36]. The intramolecular potential terms of equation (1) are crucial to determining the conformation of the molecule. Hence, although they do not have a predominant impact on the thermodynamic properties of the system, they do significantly impact transport and spectroscopic properties; however, we were unable to find any transport or spectroscopic experimental data with which to test this force field. Luckily, to a large degree, thermodynamic properties are determined mainly by the electrostatic interactions, represented by partial charges on the atomic sites, and the van der Waals interactions, which in our model we describe through Lennard-Jones site–site potentials. For that, experimental data for the phase envelope of perfluoromethylpropyl ether is available in the literature and was used in the fitting procedure. In the rest of this section, methods for obtaining the potentials will be described briefly.

2.1.   *Geometry optimization and single point energy calculation*

The electronic structure calculations were used to obtain the optimized geometry of the perfluoro methyl propyl ether molecule, which provided us with the equilibrium bond lengths, bond angles, and dihedral angles. All the calculations were performed exclusively with Gaussian 98® [37] using the restricted Hartree–Fock method and the cc-pvdz basis set (RHF/cc-pvdz). For single-point energy calculations, the second-order Möller–Plesset, MP2, method was applied with the same basis set.

2.2.   *Bond stretching and bond bending*

As in many other united atom models [18, 24, 25], the bond lengths in this model were fixed at their equilibrium positions. Bending potentials were described by simple harmonic functions of the form

$$E_{ba} = \sum_{angles} K_\theta (\theta - \theta_{eq})^2,$$

where θ is the bond angle. The equilibrium bond angles θ_{eq}, were obtained by geometry optimization calculations as described previously. Then each bond angle was perturbed from its equilibrium value one by one while keeping the rest of the geometry parameters fixed. The energy difference between the perturbed and equilibrium geometries was then calculated and used to infer the bond-bending constant K_θ.

2.3. *Torsional potentials*

As seen in figure 1, there are two dihedral angles in the perfluoromethylpropyl ether molecule: D1 is the angle about the central bond in CCCO, and D2 is the angle about the central bond in CCOC. When parametrizing the torsional potential of chain molecules, the independence between different dihedral angles is a common simplifying assumption. However, we note that with this assumption the resulting potential model will not necessarily reproduce the *ab initio* results in terms of optimized geometries. Since the model being developed in this work is focused on applications to phase equilibrium, we do not expect this to have a significant impact, and hence independence of the dihedral angles was assumed. To obtain the torsional potentials, partial optimizations on the geometry of the molecule were carried out to generate the potential energy as a function of dihedral angle. During this process, the target dihedral angle was frozen at a predetermined angle, and the remaining degrees of freedom in the molecule were allowed to relax. This approach is justified because the torsional motions have lower frequencies than the bending motions; thus, the other atoms should be allowed to have time to adjust to the change in dihedral angle. To obtain the potential energy profile, such partial optimizations were performed for each dihedral angle from 0 to 180° in increments of 15°. The resulting potential energy profile for each dihedral angle ϕ was then fitted to a 7th order polynomial equation in $\cos \phi$ as follows:

$$E_{\text{torsion}} = \sum_{\text{Di}} \sum_{j=0}^{7} a_{\text{Di},j} \cos^j \phi,$$

where Di identifies dihedral angles.

2.4. *Partial charges*

The determination of partial charges is more complicated than the other terms in the potential model because the partial charge is not a measurable property that can be obtained directly by operating on the wavefunctions. Population analysis methods such as the Mulliken method [38] tend to generate unreliable results due to the simplifications used in such methods and can be, in the case of Mulliken charges, very basis-set dependent [39]. An alternative approach is to fit the point charges at pre-selected positions to the electrostatic potential surface generated by *ab initio* calculation [40–43]. The partial charges thus obtained can be very conformation-dependent, because of the statistical poor-behaviour of deeply buried charges [44], since generally the closest predetermined grid points to the buried sites are closer to other sites. Hence, it could require a significant change in the resulting partial charges on those buried
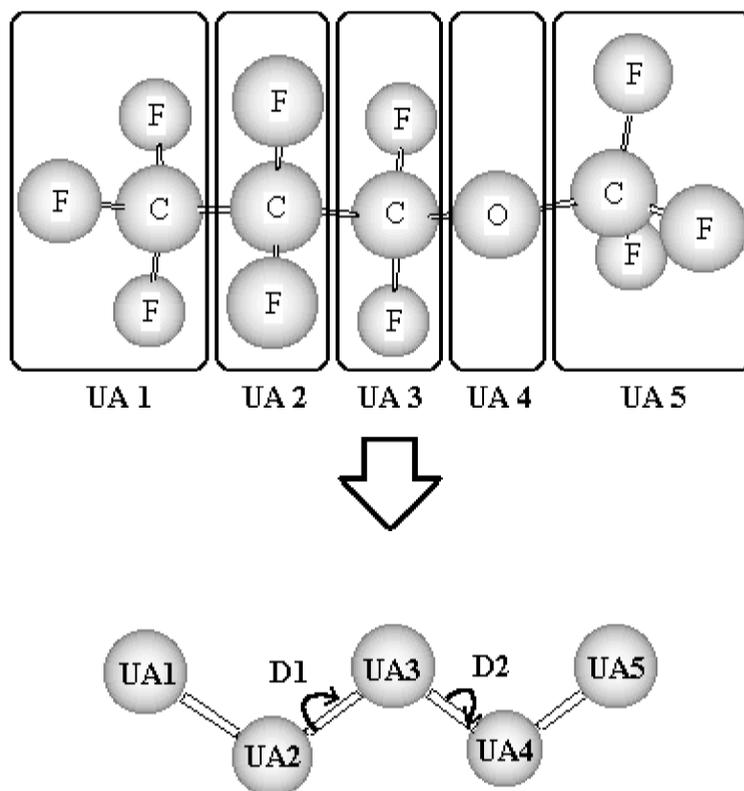

Figure 1. Perfluoromethylpropyl ether, the grouping of the united atom, and the assignment of the two dihedral angles.

sites just to achieve a small improvement in the optimization. However, neglecting the conformational dependence of the partial charges can lead to severe errors in a molecular simulation [45]. One way to circumvent this problem while accounting for the conformational variance in partial charges is to carry out the fitting process at several different conformations and then weight the resulting partial charges using Boltzmann statistics [46], although other methods are available [44, 46–48].

In this work, we adopted the partial charges fitted to the quantum mechanically generated electrostatic potential with the Boltzmann factor weighting. During the calculations of the torsional potential energy profile, electrostatic potential charges q_i, for each atom were obtained with the Merz–Singh–Kollman [39, 49] algorithm at each different conformation. Weighted charges on each atom were calculated, using Boltzmann

weighting factors at 300 K corresponding to each conformation. These weighted charges were used to derive a single set of explicit-atom partial charges by averaging over conformations as follows:

$$\bar{q} = \frac{\sum_i q_i \exp\left(-\dfrac{E_i}{kT}\right)}{\sum_i \exp\left(-\dfrac{E_i}{kT}\right)},$$

where the summation is over all the conformations. The partial charges from each atom of a given united atom group were then summed to give the united atom partial charges for the molecule. It may be argued that Boltzmann averaging the potential derived charges for each conformation to get atomic charges, and then summing these to give united atom partial charges may not give

Table 1. Intra- and intermolecular potential model parameters for perfluoromethylpropyl ether.

	Model	Parameters
Bond length	fixed	C—C 1.536 Å C—O 1.360 Å

Bond bending potential	$E_{ba} = \sum_{angles} K_\theta (\theta - \theta_{eq})^2$	θ_{eq}: CCC 116.71°
		    CCO 109.13°
		    COC 121.69°
		K_θ (in kJ mol^{-1} rad^{-2}): CCC 428.32
		    CCO 455.89
		    COC 281.38

Torsional potential	$E_{torsion} = \sum_{Di} \sum_{i=0}^{7} a_i \cos^i(\phi)$	D1 (in kJ mol^{-1}): $a_0 = 6.5728$ $a_1 = -22.891$ $a_2 = 10.802$ $a_3 = 22.665$ $a_4 = -26.185$ $a_5 = 15.312$ $a_6 = 17.718$ $a_7 = -7.0944$ D2 (in kJ mol^{-1}): $a_0 = 8.4719$ $a_1 = 9.9988$ $a_2 = -12.342$ $a_3 = -49.346$ $a_4 = 21.799$ $a_5 = 111.320$ $a_6 = -3.3242$ $a_7 = -59.017$
Partial charges	$E_{es} = \dfrac{1}{4\pi\varepsilon_0} \dfrac{q_i q_j}{r}$	C—C—C—O—C $+0.08 - 0.11 + 0.20 - 0.42 + 0.25$

L-J potential	$E_{vdw} = 4\varepsilon \left[\left(\dfrac{\sigma}{r}\right)^{12} - \left(\dfrac{\sigma}{r}\right)^6 \right]$	σ: CF$_2$ 4.6 Å
		   CF$_3$ 4.6 Å
		   O 3.0698
		ε/k: CF$_2$ 30 κ
		   CF$_3$ 79 κ
		   O 125 κ

the best united atom partial charges. However, this is one practical solution to the problem, which *post facto* appears to give a useful result.

2.5. *LJ parameters*

Once the partial charges and intramolecular potentials had been obtained by the approaches described above, Gibbs ensemble Monte Carlo simulations were carried out to calculate the vapour and liquid densities at phase equilibrium. In the Gibbs ensemble Monte Carlo simulation, three different types of trial configuration, including particle motions (translation, rotation, and molecular conformation), volume change, and molecule exchange, were carried out in order to achieve equilibration of the temperature, pressure, and chemical potential between the simulated coexisting phases. The Lennard-Jones parameters for the CF_2 and CF_3 sites were taken from the model for perfluoroalkanes developed by Cui *et al*. [18], and the parameters for the oxygen were then adjusted to reproduce the experimentally measured phase diagram of perfluoromethylpropyl ether [50]. During the development of the model, the long range interactions from the partial charges on each site were calculated using the site–site reaction field method [51]. Electrostatic and Lennard-Jones interactions between intramolecular sites separated by 3 or fewer bonds were eliminated because of the assumption that all the interactions within such a distance were accounted for by the intramolecular potentials.

3. Results and discussion

In our discussion of the results we focus initially on our findings for the torsional potential and the partial charges, and then go on to discuss a comparison of Gibbs ensemble simulation results with experimental data for the phase envelope of perfluoromethylpropyl ether. The force field for perfluoromethylpropyl ether consisting of both intra- and intermolecular potentials is summarized in table 1.

Figure 2 shows the energy difference profiles for the dihedral angle, D1 (CCCO), calculated by the restricted Hartree–Fock and the second-order Möller–Plesset methods with the cc-pvdz basis set. Although the energies calculated by restricted Hartree–Fock and the second order Möller–Plesset methods differ from each other, the profiles generated by the two methods are very close. It is worth mentioning that the shape of the curve is more like that seen for the alkanes than that of the perfluoroalkanes [20], as we find undistorted minima at the *trans* and *gauche* positions. It may seem surprising to find that the curve is even closer to a simple cosine function than that for some alkanes. This may be due to the lack of hydrogen or fluorine atoms on the oxygen,

which eliminates the steric hindrance that complicates the details of the torsional potential.

Figure 3 shows similar profiles for the dihedral angle, D2 (CCOC), obtained using the same methods and basis set. Unlike those of D1, the energy difference profiles calculated from the restricted Hartree–Fock and the second-order Möller–Plesset methods are significantly different for the two methods. In this regard, our results are very similar to previous work by Stanton *et al*. [52] and Waltman [53] for the same dihedral angle. All three calculations, the two prior studies [52, 53] and that reported here, have distorted minima. Figure 4 shows a comparison between the torsional potential obtained by Waltman [53], using the restricted Hartree–Fock method, and that of this work, from which we note that the two D2 curves show a distorted minimum at the *gauche* position and at the *trans* position compared with the corresponding hydrogenated ethers. The results
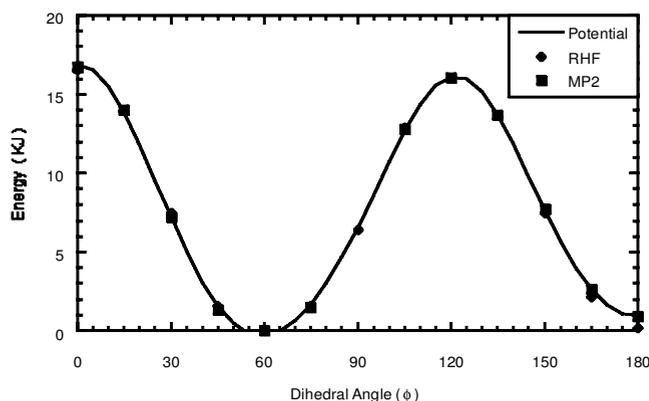
Figure 2. Energy profile of the dihedral angle D1 (CCCO), calculated by restricted Hartree–Fock and second-order Möller–Plesset methods with the cc-pvdz basis set, and generated by the torsional potential.
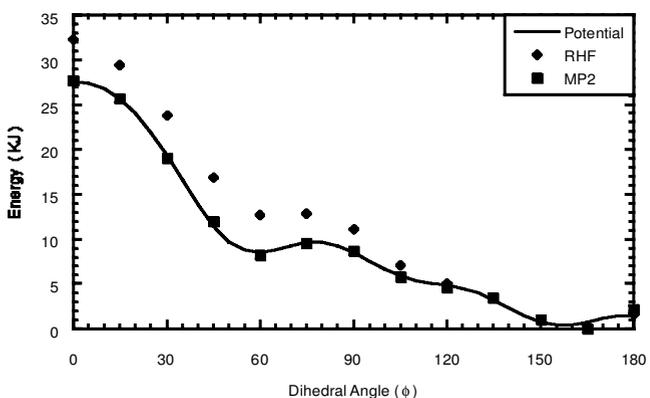
Figure 3. Energy profile of the dihedral angle D2 (CCOC), calculated by restricted Hartree–Fock and second-order Möller–Plesset methods with the cc-pvdz basis set, and generated by the torsional potential.
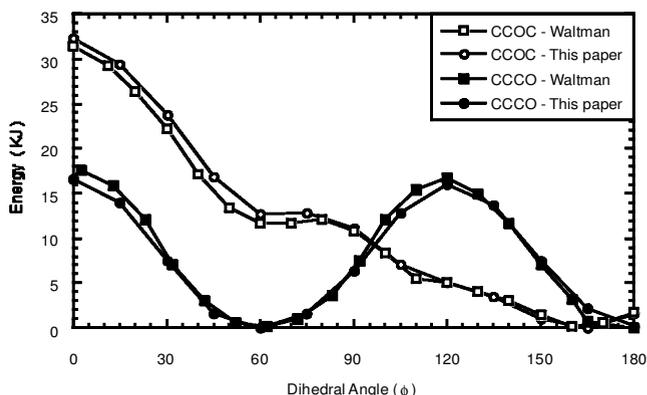
Figure 4. Comparison of torsional potentials obtained by Waltman [33] and in this work, both using the restricted Hartree–Fock method.
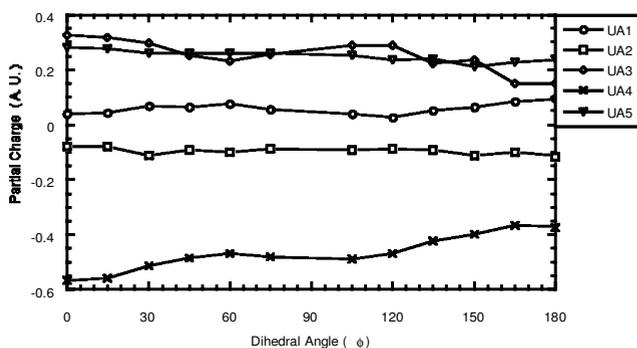

Figure 5. United atom partial charge profile of dihedral angle D1 (CCCO), calculated by the restricted Hartree–Fock method with the cc-pvdz basis set.

Figure 6. United atom partial charge profile of dihedral angle D2 (CCOC), calculated by the restricted Hartree–Fock method with the cc-pvdz basis set.

Figure 7. Phase diagram of perfluoromethylpropyl ether from simulation and experiment [50]. The solid and dotted lines are the rectilinear lines from simulation and experiment, respectively.

of this work and that of Waltman are only slightly different, which probably is due to the use of a different basis set (6-31G[d] in the case of Waltman).

Figures 5 and 6 present the calculated point charges at different values of the dihedral angle D1 and dihedral angle D2, respectively. As discussed in the previous section, electrostatic potential fitted charges can be non-transferable because of their conformation dependence; however, as seen in the figures, the conformation dependence for perfluoromethylpropyl ether is not large, and therefore it is not likely to be significant in this case. Therefore, Boltzmann averages were taken over the different conformations to give a single set of partial charges. Again, note that partial charges are not physical measurables of quantum mechanical calculations, but are calculated algorithmically.

Figure 7 shows a comparison of the phase envelope of perfluoromethylpropyl ether from experiment [50] and our simulation results using the force field developed in this work. From the figure we see that our simulations yield liquid densities that agree very well with the experi-
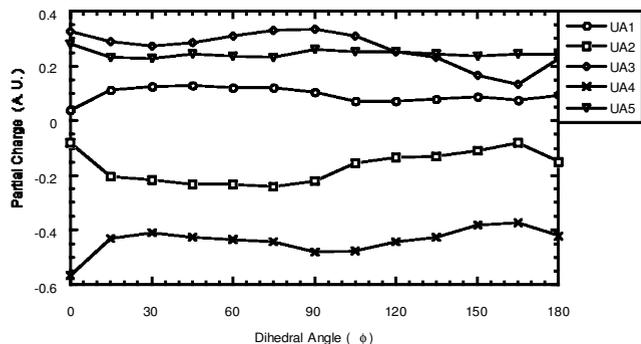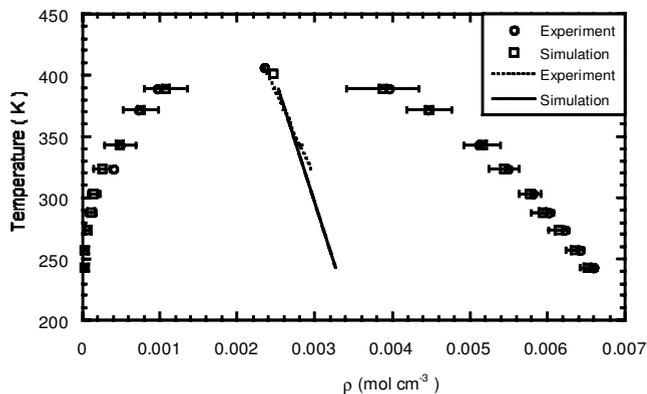
mental data. For the gas densities, the agreement is not quite so good, but is still acceptable considering that the only adjustable parameters are the Lennard-Jones parameters for oxygen. The original [50] mean-field fits of the experimental data [50] yielded a critical temperature of 391.7 K, which is significantly lower than that found by our scaling analysis of the experimental data [54], 405.8 K, or that predicted from the simulation reported in this paper, 401.1 K, with the same scaling analysis method. Using the same scaling analysis method, our simulation results yield a critical density of $0.0024 \, \text{mol} \, \text{cm}^{-3}$, which is very close to the experimental value, $0.0023 \, \text{mol} \, \text{cm}^{-3}$.

4. Conclusion

We have proposed a force field for a united atom model of perfluoromethylpropyl ether derived from *ab initio* quantum mechanical calculations and Gibbs ensemble Monte Carlo simulations reported here. Through the Gibbs ensemble Monte Carlo simulations we have shown that our united atom model accurately

reproduces the phase equilibrium properties of perfluoromethylpropyl ether, achieving good agreement with experimental data. Using the present potential as a cornerstone we are now working with other perfluoroether molecules to expand our set of parameters and test the transferability of the parameters to other perfluoroethers and longer polymer-like molecules. This will be the basis of a future publication and a further step towards an accurate potential model that can be used to study perfluoropolyether molecules of industrial interest.

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