

## The Structure of Liquid Benzene

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Received January 17, 2006

**Abstract:** The interactions of aromatic groups have been identified as playing a crucial role in many systems of interest. Unfortunately, conventional atom-centered force fields provide only an approximate representation of these molecules owing to their failure to consider the quadrupole moment arising from the  $\pi$  electrons. In this paper the structure of liquid benzene, the prototypical aromatic system, is investigated using a novel approach to Monte Carlo simulation, parametrized against experimental thermodynamic data, which incorporates an explicit representation of the aromatic  $\pi$  electrons. In contrast to previous simulations of liquid benzene it is found that a perpendicular arrangement of benzene molecules is preferred to a parallel arrangement. This result is in good agreement with experimental data.

### Introduction

In recent years interactions involving aromatic residues have been shown to be of crucial significance in a number of important problems including protein–ligand binding,<sup>1,2</sup> the determination of protein structure,<sup>3</sup> and DNA base stacking.<sup>4</sup> As the realization of the importance of aromatic interactions grows, so too does the requirement for accurate model potentials which can reproduce these experimental observations. The charge separation model of Hunter and Sanders<sup>5</sup> is one such model and has received much attention as a simple and physically reasonable method for modeling these interactions. It represents the aromatic  $\pi$  electrons as a series of explicit points lying in two planes above and below the aromatic C atoms. While it has been successfully applied in a variety of situations, varying from porphyrin rings<sup>5</sup> to aromatic amino acids<sup>6</sup> and molecular clips,<sup>7</sup> it has not been used to investigate the nature of molecular liquids such as benzene. As the prototypical case of the aromatic interaction,

a thorough understanding of the characteristics of the benzene molecule is essential if we are to progress to modeling more complicated systems involving aromatic interactions. Here we present such an application, giving an improved parametrization of the model which reproduces the experimental properties of liquid benzene as well as providing insights into the intermolecular geometries that give rise to these properties at a molecular level.

### Background

Although the isolated benzene dimer has received much attention, both theoretically and experimentally, there is still much debate as to the true structure of its global energy minimum. The two candidates are those structures that would be anticipated given the quadrupolar nature of the benzene molecule: a parallel displaced (PD) structure and a T-shaped (TS) structure in which one molecule lies perpendicular to the second, forming a hydrogen bond to the  $\pi$  system. In reality this is not a hydrogen bond in the conventional sense; when the dimer is formed, the C–H bond length shortens to allow for the maximization of the favorable quadrupole–quadrupole interactions. As such, it has been termed an ‘anti-hydrogen bond’.<sup>8</sup>

In the early days of theoretical calculations on the benzene dimer, it was generally believed that the structure of the dimer was T-shaped<sup>9,10</sup> or a slightly distorted T-shaped

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structure.<sup>11</sup> As new experimental evidence came to light,<sup>12</sup> the structure of the benzene dimer received new focus, and, performing calculations at the MP2/6-31+G\* level of theory, Hobza et al.<sup>13</sup> identified that the parallel displaced structure was actually an energetic minimum and that it even lay lower in energy than the T-shaped structure. Jaffe and Smith,<sup>14</sup> again working with the MP2 theory, also favored the PD structure, concluding that the TS structure was not in fact a minimum at all but rather a saddle point on the transition between two parallel displaced structures. The complexity of the problem was well illustrated when, within a few months, Hobza et al.<sup>15</sup> presented a study using the CCSD(T) theory, which concluded that both the PD and TS structures were true minima, and almost isoenergetic, but with the TS structure lying marginally lower in energy. Since this time, the debate had bounced back and forth between the two competing structures, Gonzalez and Lim<sup>16</sup> concluded that the TS dimer is marginally lower in energy than the PD dimer, although their work was limited by the small size of their basis sets. Hobza et al. used CCSD(T) calculations to parametrize the NEMO model,<sup>17</sup> suggesting that only one minimum, a TS structure, is present and that the PD structure is actually a transition state.<sup>18</sup> Tsuzuki et al.<sup>19,20</sup> have concluded that the two dimer structures are approximately isoenergetic,<sup>19</sup> though CCSD(T) calculations reveal that the PD structure is slightly lower in energy.<sup>20</sup> The authors conclude, however, that these calculations are likely to overestimate the attraction in the PD case and that, in reality, the TS structure may be lower in energy. The most recent and rigorous calculations on this system by Sinnokrot et al.,<sup>21,22</sup> performed using CCSD(T), also conclude that the two dimer structures are isoenergetic.

The results from experimental studies on the benzene dimer are just as inconclusive as those from theoretical calculations. The earliest experimental studies were performed using molecular beams and concluded that the benzene dimer is polar.<sup>23,24</sup> The authors interpreted this to mean that the molecules adopt a T-shaped arrangement, as is found in the solid.<sup>25</sup> This view was also backed up by experiments performed using resonant two photon ionization (R2PI) techniques,<sup>26</sup> ionization-detected stimulated Raman spectroscopy (IDSRS),<sup>27,28</sup> and rotational spectroscopy.<sup>29</sup>

The experimental evidence favoring the TS dimer, however, is far from conclusive. Various vibronic spectra of isotopically substituted benzenes have been measured;<sup>30–33</sup> all of these studies conclude that the structure of the dimer is symmetric, precluding the TS structure, but not the PD structure, which has been suggested by Bernstein et al.<sup>30,31</sup> Additionally, Schlag et al. have proposed from these results a 'V-shaped' dimer structure.<sup>32,33</sup> In addition to the IDSRS experiments performed by Henson et al.,<sup>27,28</sup> the same technique has been used by Ebata et al.,<sup>34</sup> who came to the conclusion that two isomers exist, having center of mass separations of 3.6 Å and 5.0 Å, which would correspond to the PD and TS dimers, respectively. The conclusion that more than one dimer structure is present was also reached by Scherzer et al.,<sup>12</sup> who found that at least two dimers exist.

It is clear that the theoretical and experimental study of the benzene dimer has given results for its structure which

are, thus far, inconclusive. However, there are some broad conclusions that can be drawn: 1. The PD and TS structures lie very close in energy. 2. The potential energy surface for the benzene dimer is very flat in the region around the minima.<sup>19,35</sup> 3. In reality the benzene dimer is likely to be highly fluxional, constantly moving between the two structures.<sup>21</sup>

Although the structure of the benzene dimer has received much attention, and the structure of solid benzene is well defined,<sup>25</sup> what is less well understood is the structure of the liquid phase of benzene. Atom-centered force field simulations have suggested that the liquid is comprised of well-defined solvation spheres around each molecule but that within each sphere there is either no orientational preference for the individual molecules<sup>36</sup> or a very slight preference for the orthogonal arrangement.<sup>37</sup> Evidence from X-ray diffraction<sup>38</sup> and neutron scattering<sup>39</sup> experiments, however, as well as recent experimental results<sup>40</sup> from optical Kerr effect spectroscopy<sup>41</sup> all conclude that the local ordering in liquid benzene is perpendicular.

Conventional all atom force fields perform well in many situations, for example in the reproduction of the dipole moment of molecules, but actually provide a poor description of the electronic distribution in the benzene molecule. In benzene, the delocalized  $\pi$  orbitals above and below the plane of the ring contain substantial amounts of electron density that give rise to a quadrupole moment, the first nonzero multipole moment present in the benzene molecule. This quadrupole moment is completely neglected by atom-centered approaches. Hunter and Sanders<sup>5</sup> proposed that this charge distribution could be accounted for by placing two points above and below each C atom in the ring, each having a negative charge but no volume, to represent the  $\pi$  electrons. This approach, termed charge separation, has been applied widely for the inclusion of lone pairs in, for example, water<sup>42</sup> and sulfur in proteins<sup>43</sup> and has been found to perform well.

In this work we will begin by presenting a brief study of the benzene dimer, which will illustrate the effect of the charge separation model on a simple aromatic system. We will then move on to consider the case of liquid benzene and examine how the new model affects previous ideas on the structure of the liquid at a molecular level.

## Methods

**Ab Initio Calculations.** In parametrizing their model Hunter and Sanders<sup>5</sup> proposed that each C atom would contribute one electron to the  $\pi$  system, meaning that each  $\pi$  point would have a charge,  $q_\pi$ , of  $-0.50$  e. The value of the separation between the nuclear site and the  $\pi$  point,  $\delta$ , was determined by fitting to the gas-phase quadrupole moment of the benzene molecule, to give a value of 0.47 Å.

To consider the effect of charge separation on the benzene dimer we adopted a different approach, parametrizing the model via a comparison with ab initio data. Tran et al.<sup>44</sup> identified 10 minimum energy conformations of the benzene dimer, labeled a–j. The energies of these structures were recalculated at the MP2/6-311+G\*\* level of theory. Although CCSD(T) methods have become the de facto method of choice for benzene dimer calculations, it has been shown<sup>45</sup>

that MP2 methods employing medium sized basis sets give very good results, due to a fortuitous cancellation of errors, at much reduced computational cost. All ab initio calculations were performed using the Gaussian98<sup>46</sup> program, and all calculated energies were corrected for basis set superposition error (BSSE)<sup>47</sup> using the counterpoise method.<sup>48</sup>

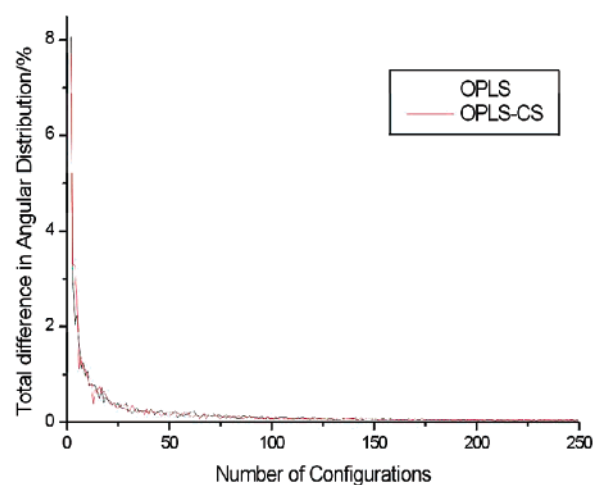
With the ab initio energies calculated, the equivalent energies were calculated for the same 10 structures using a charge separation force field in which the values of  $q_\pi$  and  $\delta$  were varied from 0 to  $-2e$  and 0 to 1 Å, respectively. The ability of the force field to reproduce the ab initio calculated energies at each set of parameters was measured via eq 1.

$$\Delta E = \sum_{n=a}^j (E_n^{\text{MP2}} - E_n^{\text{CS}})^2 \quad (1)$$

**Monte Carlo Calculations.** Previous studies have found that parametrizing force fields by fitting to ab initio data in vacuo is inappropriate for modeling condensed phases in general<sup>49</sup> and aromatic interactions in solution in particular,<sup>50</sup> and this observation was found to hold true in this case, with the ab initio derived parameters performing poorly for the case of the liquid simulations (results not shown). To surmount this problem when parametrizing the original OPLS all atom model for liquid simulations of benzene Jorgensen and Severance<sup>54</sup> fitted their parameters to experimental thermodynamic and structural data. In this instance, a similar approach has been adopted, with the additional constraint that the model must reproduce the experimental value of the benzene quadrupole moment.

Because OPLS is an effective potential, any properties not explicitly accounted for in the model will have been ‘mixed into’ the model during the parametrization process. This means that rather than just adding extra points so that they reproduce the correct quadrupole moment, it is necessary to reexamine all of the parameters within the system. To do this we have followed a methodology similar to that used in the parametrization of the TIP5P<sup>42</sup> water model. The bond lengths and angles used are the experimentally derived values for the isolated benzene molecule.<sup>54</sup> To these we then add a series of charge and van der Waals parameters. The charge parameters are subject to the constraints that the individual molecules must be charge neutral and that  $q_\pi = -q_H$  where  $q_\pi$  and  $q_H$  are the charges on the  $\pi$  electron points and H atoms, respectively.  $q_\pi$  and  $\delta$  were then varied systematically along with the van der Waals parameters,  $\sigma$  and  $\epsilon$ , until the models give the minimum deviation from experimental thermodynamic results. For the purpose of parametrization a series of Monte Carlo simulations including 267 benzene molecules in the NPT ensemble (with  $P=1$  atm and  $T=298$  K) was performed. Each simulation consisted of  $6.0 \times 10^7$  steps of equilibration followed by  $6.0 \times 10^7$  steps of averaging.

With the necessary parameters in place three Monte Carlo simulations of liquid benzene were performed. The first treated the benzene molecules using a 12 site model, the OPLS all atom potential<sup>51</sup> (denoted OPLS), the second used a 24 site model consisting of the OPLS all atom potential



**Figure 1.** Convergence of angular distributions.

modified in such a way as to incorporate the  $\pi$  electron points of the charge separation model (denoted OPLS-CS), and the third used the original charge separation model of Hunter and Sanders (HS). All simulations were performed using BOSS version 4.2;<sup>52</sup> in the OPLS simulation the standard OPLSAA parameters were used, in the OPLS-CS simulation the OPLSAA parameters were modified so as to incorporate the  $\pi$  parameters described above, and in the HS simulation the parameters used were those obtained in the original work by Hunter and Sanders.<sup>5</sup> In all cases a system consisting of 267 benzene molecules was used in simulations that were run in the NPT ensemble with  $T = 298$  K and  $P = 1.0$  atm. The simulations were begun from a configuration in which all of the benzene molecules were arranged in a parallel fashion, and in all simulations  $4 \times 10^6$  equilibration steps were performed followed by  $2.5 \times 10^8$  steps of averaging. The orientational distributions shown in Figure 7 were calculated as the average of configurations extracted from the simulation every  $1 \times 10^6$  steps, which was found to be sufficient for the angular distributions to have converged to their limiting values (Figure 1).

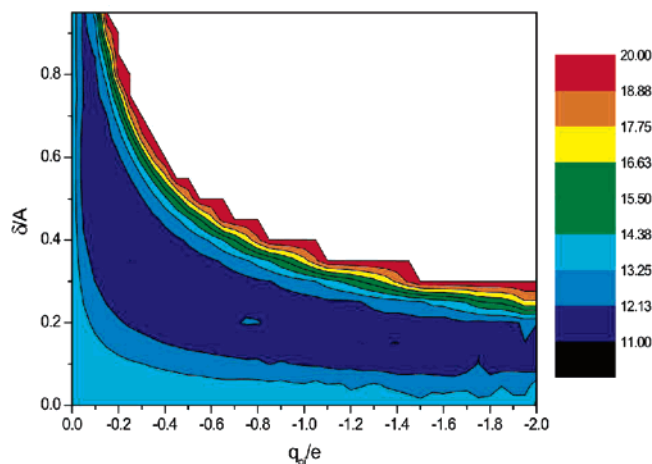
## Results and Discussion

**Benzene Dimer: Ab Initio Calculations.** The results of the parametrization against ab initio data can be seen in Figure 2.

From this we can see that the best parameter values lie some way from those of an all atom force field at  $q_\pi = 0e$ ,  $\delta = 0$  Å and also from those used by Hunter and Sanders at  $q_\pi = -0.5e$  and  $\delta = 0.47$  Å. The values obtained from this parametrization are  $q_\pi = -0.30e$  and  $\delta = 0.30$  Å.

It has previously been shown that atom-centered force fields perform badly when modeling T-shaped structures of the benzene dimer.<sup>16</sup> As an illustration of the improvement that can be brought about via the use of the charge separation model Figure 3 shows potential energy surfaces calculated for the region around the T-shaped minimum. In all cases, the surfaces have been calculated by keeping the  $z$  separation of the molecules fixed at their equilibrium separation of 4.9 Å<sup>22</sup> and scanning over the  $x$  and  $y$  directions, calculating the energy every 0.2 Å.





**Figure 2.** Parametrizing the CS model against ab initio data.

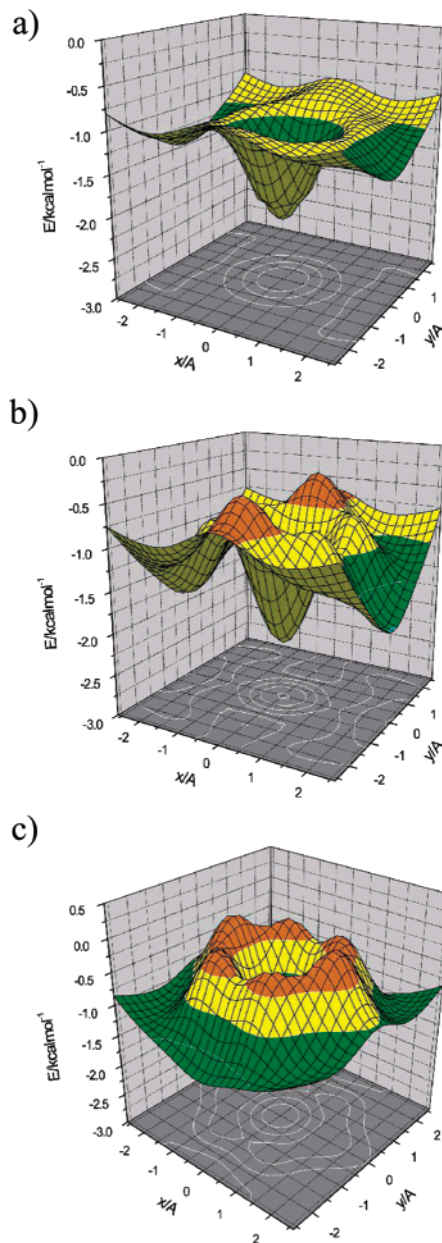
The general shape of the surface produced using the charge separation model is much closer to the ab initio surface than is the surface calculated using an all atom approach. Although the agreement between the charge separation and ab initio surfaces is not quantitative, the charge separation model does give qualitatively correct results. Since the objective of this work is not the accurate reproduction of benzene dimer energies, we have not chosen to refine this model further but have rather considered these data to be evidence that the use of explicit points to represent aromatic  $\pi$  electrons can improve the representation of the benzene molecule. As such, rather than providing a definitive solution to the problem, these calculations demonstrate the potential of the charge separation approach, and recommend it for further study.

### Liquid Benzene: Monte Carlo Simulations

From the initial simulations performed, a set of parameters was determined as the best OPLS-CS model. These values are listed in Table 1, and the comparison with the thermodynamic data from experiment can be seen in Table 2.

The agreement between the OPLS-CS calculated and experimental values is generally at least as good as that of the OPLS model and offers a large improvement in terms of the reproduction of the quadrupole moment of the molecule. Of all the models employed, the Hunter and Sanders model performs worst in reproducing the experimental thermodynamic properties of the liquid, providing a good representation of the quadrupole moment but overestimating the attraction between the molecules. That this model performs badly is perhaps no great surprise. It was never developed with the simulation of liquids in mind and indeed was not intended to treat benzene at all, actually being developed for the treatment of porphyrins.<sup>5</sup>

As a first measure of the structure of the liquid we can consider the center of mass radial distribution functions,  $g_{\text{CMCM}}(r)$  (Figure 4). These distributions provide little information about the detailed structure within the liquid but do provide information on the size and number of molecules within the first solvation shell. Furthermore, by comparing the calculated values to experimental results obtained from neutron diffraction,<sup>39</sup> we can begin to judge the quality of



**Figure 3.** Potential energy surface around the T-shaped minimum, calculated using (a) MP2/6-311+G\*\*, (b) the CS model, and (c) an all atom potential.

our potentials. In this case, both the OPLS and OPLS-CS models perform reasonably well in terms of reproducing the general shape and position of the distribution, with the OPLS-CS model more accurately predicting the height of the first peak and the OPLS model its slope.

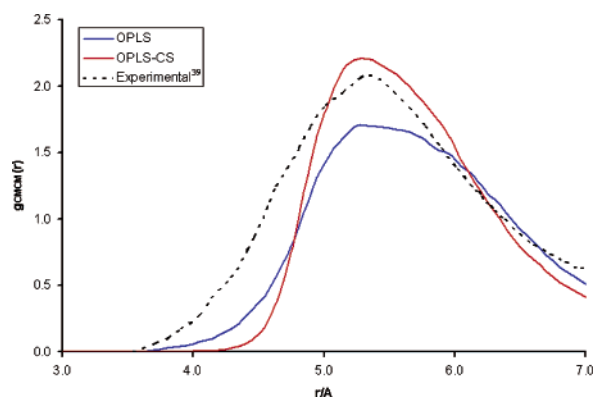
The relative orientation of molecules in liquid benzene can be analyzed more closely via consideration of the constituent radial distribution functions,  $g(r)$ . The experimental  $g(r)$  have been determined by X-ray diffraction,<sup>38</sup> and the same functions have also been calculated as a result of several simulations using Monte Carlo<sup>54</sup> and molecular dynamics<sup>35,37,55,56</sup> techniques. In this study we have calculated the radial distribution functions using both the OPLS and OPLS-CS potentials, with  $g_{\text{CC}}(r)$  also evaluated for the HS model. The calculated  $g(r)$  are shown in Figure 5.

**Table 1.** Parameters Used in OPLS-CS and OPLS Benzene Models

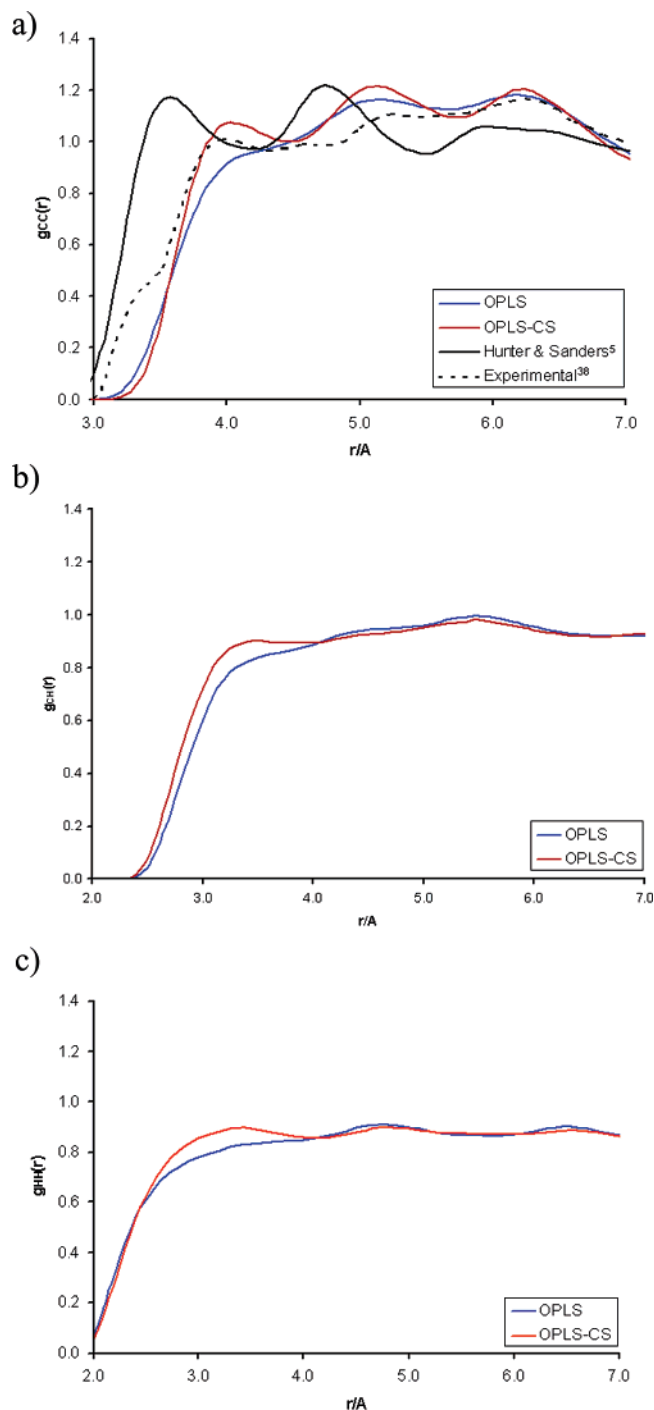
parameter	OPLS-CS	OPLS
$R_{CC}/\text{\AA}$	1.40	1.40
$R_{CH}/\text{\AA}$	1.08	1.08
$\delta/\text{\AA}$	0.90	n/a
$\theta_{CCC}/^\circ$	120.0	120.0
$\theta_{CCH}/^\circ$	120.0	120.0
$\theta_{CC\pi}/^\circ$	90.0	n/a
$\Psi_{CCCC}/^\circ$	0.0	0.0
$\Psi_{CCCH}/^\circ$	180.0	180.0
$\Psi_{CC\pi\pi}/^\circ$	90.0/−90.0	n/a
$q_C/e$	0.1435	−0.115
$q_H/e$	0.1435	0.115
$q_\pi/e$	−0.1435	n/a
$\sigma_C/\text{\AA}$	3.69	3.55
$\sigma_H/\text{\AA}$	2.52	2.42
$\epsilon_C/\text{kcalmol}^{-1}$	0.07	0.07
$\epsilon_H/\text{kcalmol}^{-1}$	0.03	0.03

**Table 2.** Thermodynamic Properties of Liquid Benzene

	OPLS	OPLS-CS	HS	experiment <sup>54</sup>
quadrupole/ $ea_0^2$	0.00	−6.7	−6.4	−6.7 <sup>53</sup>
dipole/ $ea_0$	0.00	0.00	0.00	0.00
density/ $\text{g cm}^{-3}$	0.865	0.872	0.997	0.874
$\Delta H_{vap}/\text{kcalmol}^{-1}$	7.89	7.58	25.50	8.09
$C_p/k_B$	15.0	15.9	10.91	15.5
molecular volume/ $\text{\AA}^3$	149.8	148.7	130.1	148.4

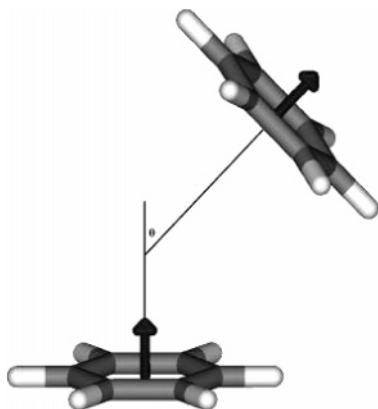
**Figure 4.**  $g_{CMCM}(r)$  for liquid benzene.

Of these radial distribution functions, the most useful in terms of elucidating structural information is  $g_{CC}(r)$ . The HS model performs poorly in reproducing the experimental  $g_{CC}(r)$ , the first peak is found at too small a distance, and the height of the peaks is far larger than that observed experimentally. The model seems to be predicting an excessively solidlike structure. Although the OPLS potential provides a reasonable reproduction of the experimental data, the first peak in the experimental  $g_{CC}(r)$  is not well reproduced, instead being merged into the second peak. With the OPLS-CS model, however, we see a better reproduction of this first peak within the experimental  $g_{CC}(r)$ . It follows that this difference in the  $g_{CC}(r)$  values must be related to a structural difference within the liquid. To investigate this difference, we have performed a geometrical analysis on the results of

**Figure 5.** Radial distribution functions for liquid benzene: (a)  $g_{CC}(r)$  (b)  $g_{CH}(r)$ , and (c)  $g_{HH}(r)$ .

these two simulations. For each molecule within the system, we have extracted the coordinates of every molecule that lies within the first solvation shell, defined by analysis of  $g_{CMCM}(r)$  as having an intermolecular centroid distance less than 7.7  $\text{\AA}$ , and then for each pair of molecules calculated the angle between the vectors normal to the planes of the two rings (Figure 6). The resulting orientational distributions can be seen in Figure 7.

While the OPLS simulation gives a sinusoidal distribution, indicating that there is an isotropic arrangement of molecules and hence no preference for either of the two energetic minima, the OPLS-CS distribution deviates significantly from



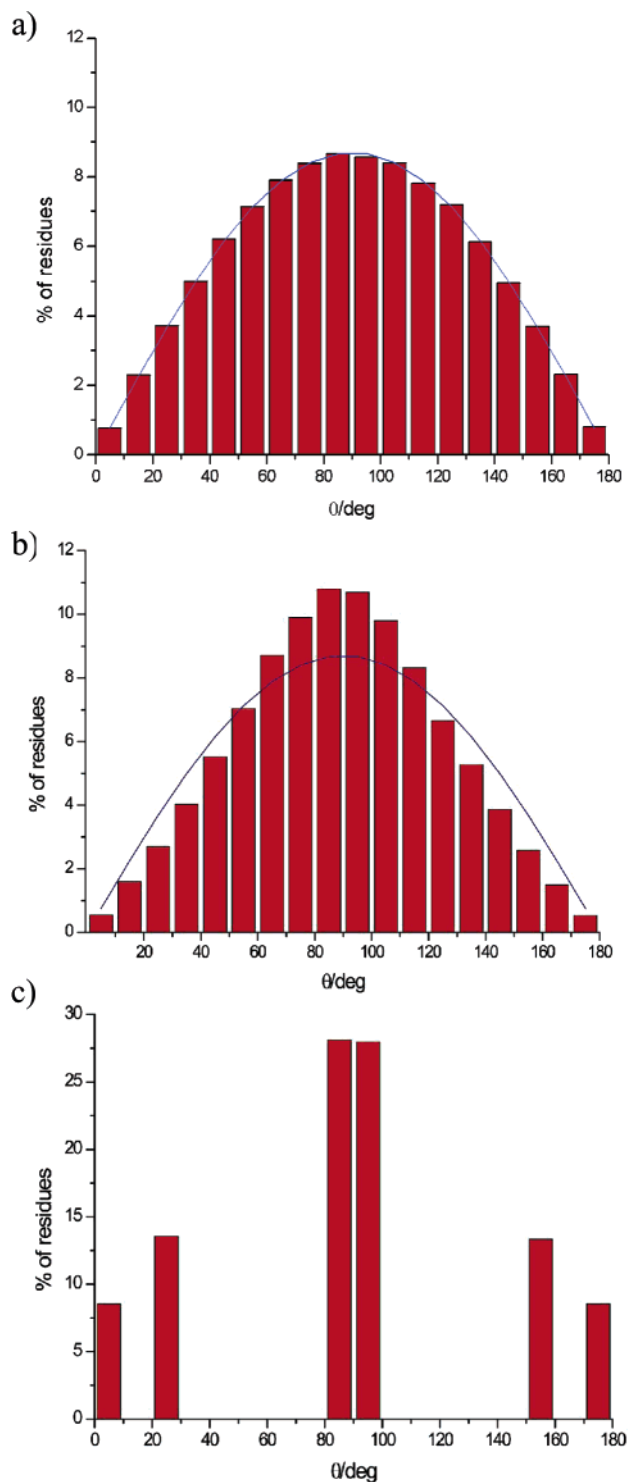
**Figure 6.** Calculation of  $\theta$ , the angle between the normals to two benzene molecules.

the sinusoidal shape, revealing a preference for the orthogonal arrangement over the parallel arrangement, in effect the OPLS-CS model predicts a much more solidlike structure than does the OPLS (Figure 7). This idea, that the orthogonal arrangement is preferred, can also be seen in the first solvation shell of a molecule taken from the simulation (Figure 8).

It is informative to consider both the radial and orientational distributions as sources of structural information, and the process can be refined further via the consideration of angular distribution functions (Figure 9), which consider simultaneously both the radial and orientational dependence of the molecular structure.

The first peak in  $g(r, \theta)$  represents the first solvation shell of the molecule, and it is clear to see that in the OPLS simulations, there is a small preference for a perpendicular arrangement of the molecules. This result is in good agreement with angular distribution functions calculated from previous simulations using atom-centered potentials.<sup>36,57,58,59</sup> In contrast,  $g(r, \theta)$  obtained from the OPLS-CS simulations shows a clear preference for the perpendicular arrangement of molecules within the first solvation shell.

Such a result has been predicted theoretically for quadrupolar fluids. Streett and Tildesley<sup>60</sup> performed molecular dynamics simulations on an idealized diatomic liquid, both with and without the inclusion of quadrupole-quadrupole interactions. When these interactions were omitted from their simulation, it was found that the molecules exhibited no orientational preference. Once quadrupolar interactions were switched on, however, the structure of the liquid showed a clear preference for a T-shaped orientation of the molecules. In the case of benzene, conventional all atom force fields do not account for the quadrupole moment that arises from the  $\pi$  electron clouds above and below the plane of the ring. By incorporating the charge separation model we have reproduced this quadrupole moment within the benzene molecule, and the theoretically predicted behavior has been recovered. Such a result has also been seen in the case of liquid bromine, where Monte Carlo simulations including quadrupolar interactions were found to predict more accurately experimental results than those without, and also favored a T-shaped arrangement of the molecules.<sup>61</sup> Furthermore, Brown and Swinton<sup>62</sup> found that in the prediction

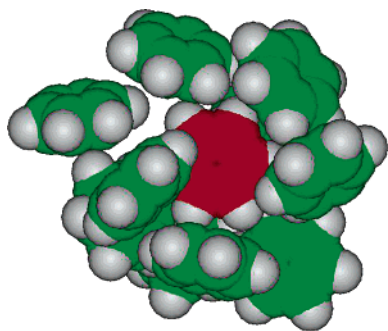


**Figure 7.** Angular distributions of benzene molecules within the first solvation shell of benzene, obtained from (a) the OPLS and (b) OPLS-CS simulations as well as (c) solid benzene.<sup>25</sup>  $0^\circ$  corresponds to a parallel structure and  $90^\circ$  to a perpendicular structure.

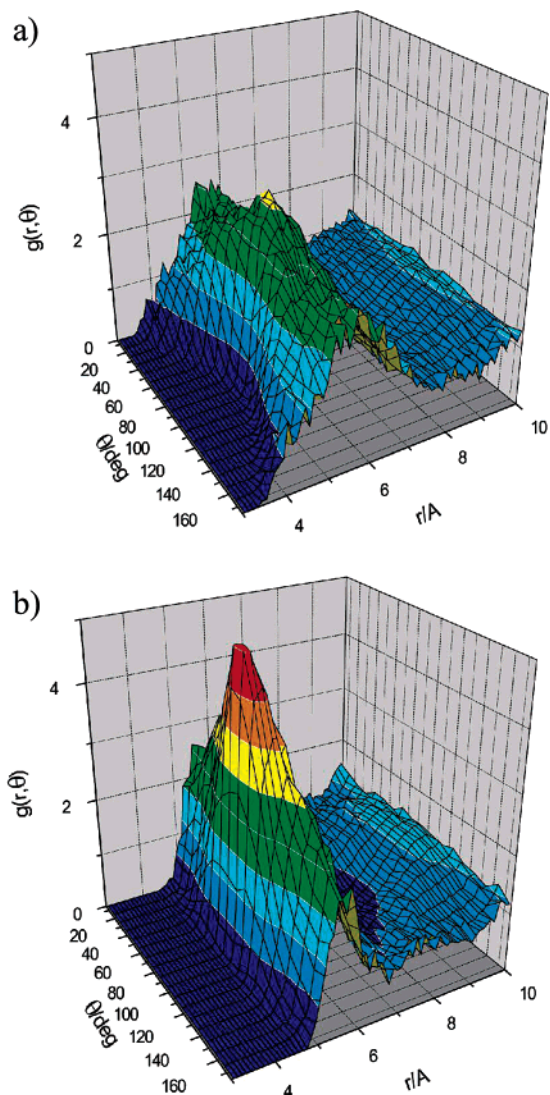
of the structures of solid benzene and hexafluorobenzene, the quadrupole moment was the most important factor.

These results, when combined with the experimental data available, support the view that the structure of liquid benzene is well ordered with an orthogonal arrangement of benzene molecules existing wherever possible. The parallel





**Figure 8.** First solvation shell of a single benzene molecule (in red), taken from the OPLS-CS simulation.



**Figure 9.** Angular distribution functions: (a) OPLS and (b) OPLS-CS.

displaced structure still features in the liquid phase but is less common than previously believed.

These results are also in good agreement with a variety of other condensed phase results, in which it has been found that aromatic–aromatic interactions tend to favor the T-shaped structure over the parallel displaced structure. Examples of such cases include solid benzene, in which 8 out of the 12 nearest neighbors of any molecule are found to be

orthogonal,<sup>25</sup> and proteins,<sup>63</sup> in which aromatic–aromatic interactions are believed to be an important factor in the determination of the structure a protein adopts.<sup>64</sup>

Although this study suggests that the effect of including the quadrupole moment of the benzene molecule is significant, we must be aware of the fact that OPLS-CS (like OPLS) is an effective potential. While the basis of the OPLS model is physical, for example using experimental geometries, the simplicity of the model means that fitting to experimental data is necessary if we are to achieve an accurate reproduction of experimental data, and the model becomes an ‘effective’ potential. The result of this is that the original physical characteristics lose their precise meanings, and any properties not explicitly accounted for are ‘mixed into’ the model. In the case of the OPLS-CS model, one of the physical properties that we originally considered was the quadrupole moment of benzene, and it follows that the parametrization process will have resulted in the ‘mixing in’ of other properties into this term. Thus, although the only physical addition we have made to the model is that of the quadrupole moment, the effects that we are seeing may also be arising from properties other than the quadrupole. This, however, is a problem inherent to any effective potential and the ability of the OPLS-CS potential to reproduce the thermodynamic data gives us confidence that it is a reasonable potential, but it is important to be aware of the possibility that some of the effects that we observe may not be due entirely to the inclusion of the quadrupole.

When considering potentials for simulation of a molecular liquid, it is wise to be aware of the development of potential functions for liquid water, by far the most intensively studied of all molecular liquids. For 20 years from the early 1980s simple three site models of water, such as TIP3P,<sup>65</sup> were the methods of choice for molecular mechanics simulation. In 2000 Mahoney and Jorgensen<sup>42</sup> demonstrated that a physically intuitive 5 site model (with the extra sites located at the O lone pair sites) offered a considerable improvement in terms of the reproduction of both thermodynamic and structural data. Water models have also increased significantly in both sophistication and accuracy via the inclusion of, for example, polarizability<sup>66</sup> or diffuse charges<sup>67</sup> into the potential. Over the same period the models of aromatic groups available within the commonly used force fields has remained at the level of an all atom potential. We would acknowledge that there is still work to be done before the available models of benzene reach the same level of sophistication as those of water but view this work as a necessary step toward that goal and a step that is readily compatible with existing molecular mechanics methodologies.

## Conclusions

The charge separation model of Hunter and Sanders<sup>5</sup> has been reparametrized to model the liquid phase of benzene by fitting to experimental thermodynamic data. This model has then been applied to the study of the structure of liquid benzene via Monte Carlo simulation and has been shown to offer a better reproduction of experimental results than a conventional all atom force field. The charge separation

model indicates that the structure within the first solvation shell of liquid benzene is largely perpendicular, in agreement with several experimental studies but in contrast to previous molecular mechanics based calculations.

The agreement between the experimental and calculated results, though improved, is still not perfect, and, if we have learned from the case of water, models of increasing sophistication will be required before we can truly hope to model the full range of aromatic interactions with complete confidence. This work might be considered to be only a first step toward that goal, but the development of a new force field that demonstrates an improved ability to treat the interactions of aromatic molecules bodes well for the study of many important biological systems.

**Acknowledgment.** C.M.B. thanks the National Foundation for Cancer Research for funding and Prof. W. L. Jorgensen for his generous provision of the BOSS program.

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CT060024H