Direct Derivation of van der Waals Force Field Parameters from Quantum Mechanical Interaction Energies

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van der Waals force field parameters are difficult to determine from only experimental data because of the insufficient data-to-parameter ratio, particularly for the diverse set of atom types necessary for force fields used in virtual ligand screening. We present a method which exploits the virtually unlimited number of ab initio calculations, as compared with experimental data, and does not have to rely on unphysical combination rules used by most force fields. Interaction energies of all pairs of molecules from a set of eight compounds at the MP2/d-aug-cc-pVDZ level with a counterpoise correction are used to simultaneously fit parameters in a buffered Lennard-Jones van der Waals potential for six atom types. The transferability of the parameters is demonstrated by the reproducibility of ab initio dimer energies for four molecules in a validation set. Next, sublimation energies of 14 alkanes and 11 nonalkane compounds are calculated using both our potential and the van der Waals potential from the MMFF94 force field. Whereas, except for a few outliers, calculations using our van der Waals potential accurately reproduce the experimental values, the MMFF94 values are systematically 30–40% too low. Finally, two possible effects contributing to the good agreement of the sublimation enthalpies calculated using our potential with experimental data are discussed: the increased basis set flexibility due to basis functions on adjacent bonded atoms and the systematic error resulting from the neglect of the intramolecular conformational energy in the calculation of the sublimation enthalpy.

1. Introduction

Most molecular simulation methods rely on force fields to calculate the energy of a molecular system. Force fields are a parametrization of the energy of a molecular system in terms of a relatively simple function of the conformational coordinates. Solvation may also be implicitly included by an additional term to yield the potential of mean force for a solvated system. An accurate and relatively simple force field is essential for a molecular simulation for it to yield an accurate result within a reasonable amount of time.

Force field parameters may be determined from experimental data, quantum mechanical (QM) calculations, or a combination of both. QM calculations can provide a much larger amount of data, for a more diverse range of compounds, than experimental data. This is especially important for a force field that is applicable to a diverse range of chemical functional groups since the experimental data may be sparse for compounds containing some of the groups. Another advantage is that the force field energies may be directly compared with the QM results. This is not the case with most experimental data since usually they must be compared with a thermodynamic average calculated using the force field. It is also difficult to investigate limitations and possible improvements to the functional form of the potential solely on the basis of experimental data because the data represents an average over an ensemble of conformations. Ultimately, however, the accuracy of a force field derived using QM data should be tested by its ability to reproduce experimentally measured quantities and some experimental input should be used to derive the force field parameters.

1.1. van der Waals Potentials in Force Fields.
Parameters for vdW interactions are arguably the most difficult parameters to derive in a force field because of both a lack of relevant experimental data to sufficiently constrain the parameters and the need for electron correlation and large basis sets for QM methods to accurately calculate the attractive dispersion contribution at small atomic separations. Although the vdW potential is not pairwise additive, even for three or more isolated atoms, it is usually approximated as a sum over pairwise contributions from atoms in the molecules which depends only on the separation of the atomic centers. A number of functional forms for the vdW potential have been used including the Lennard-Jones, Exp-6, Morse, and buffered-14–7[1] potentials. We use the buffered Lennard-Jones 6–12 (LJ) potential

$$E_{\text{vdW}}(i, j, r) = A_{ij}(r + d)^{-12} + B_{ij}(r + d)^{-6} \qquad (1)$$

since it is faster to calculate than other potentials and the buffer distance d prevents numerical overflows which interfere with minimization of the potential. The total vdW potential is a pairwise sum of $E_{\text{vdW}}(i, j, r)$ with i and j the atom types of the respective atoms. Another advantage of this potential function is that it is a linear function of the parameters A_{ij} and B_{ij}, which allows the use of linear regression rather than less reliable nonlinear global optimization techniques to fit the potential parameters. Besides the problem of fitting the large number of parameters in more complicated potential functions, such as those used for fitting experimental noble gas data, such potentials may not yield significantly greater accuracy due to comparable errors from the pairwise atom-centered approximation for the VdW potential.

Experimental data such as sublimation enthalpies, crystal geometries from X-ray diffraction data, and liquid properties

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such as the density, heat of vaporization, and self-diffusion coefficient may be used to constrain vdW potential parameters. Gas thermodynamic quantities are not particularly useful since the low density implies that each molecule is most likely far from its neighbors and hence the predicted values are relatively insensitive to the form of the attractive potential well at small separations. We chose to compare the vdW potential fit to QM calculations to sublimation enthalpies since they are sensitive to short-range intermolecular interactions and their prediction using the vdW and electrostatic potentials is less difficult and more accurate than for the other physical properties mentioned above. Although it is advantageous to eventually include all relevant experimental data, there are a number of difficulties with using the other data to study the force field vdW potential. The prediction of liquid properties using Monte Carlo (MC) or molecular dynamics (MD) methods requires intramolecular energy terms such as torsion angle energy terms to accurately reproduce thermodynamic quantities for flexible molecules. The same considerations apply to the prediction of the crystal cell parameters and atomic coordinates of X-ray structures, which have the additional difficulties of requiring a search for the global maximum of the potential energy function and thermal effects such as lattice expansion. After the intramolecular energy terms are included in the force field the comparison of MC calculations with liquid-state data should provide more constraints on the vdW potential.

There are a number of force fields with atom types covering diverse chemical functional groups that have been used successfully in molecular simulations. Although most of them use the Lennard-Jones 6−12 function for the vdW potential, they fit the parameters to experimental data using a number of different methods. One of the first force fields for proteins, ECEPP,[2] determined the r^{-6} coefficients using the Slater−Kirkwood approximation[3] with additive atomic polarizabilities and the r^{-12} ones by fitting to experimental X-ray crystal unit cell parameters. The OPLS force field[4] used liquid simulations almost exclusively to fit the vdW parameters. AMBER[5] also used liquid simulations compared with experimental densities and enthalpies of vaporization to fit the vdW parameters. The CHARMM force field[6] fit the vdW parameters to solvent simulations of heats of vaporization and densities and crystal simulations of sublimation enthalpies and lattice constants. The CVFF force field[7] used exclusively X-ray crystal structures and sublimation enthalpy data to fit the Lennard-Jones 6−9 vdW potential parameters, along with the novel Waldman−Hagler combination rules.[8] Finally, the MMFF94 force field[9,10] used a buffered 14−7 vdW potential with parameters determined from the Slater−Kirkwood approximation and several empirical relations along with atom polarizabilities, effective number of electrons, and scaling factors determined from experimental data.[1] MP4 calculations of methane and H_2 dimer interaction energies with large basis sets were then used to adjust the aliphatic hydrogen vdW parameters. To correct for excessive short-range intramolecular repulsion, the vdW potential for atoms separated by three bonds are scaled by a factor, which is usually 1/2, for all force fields mentioned here except CVFF, MMFF94, and certain atom types in CHARMM.

There have been several previous studies that used high-level ab initio calculations to either fit the vdW potential or investigate the orientational dependence of the intermolecular energy. MP2/6-311++G(2d,2p) interaction energies for dimers at different separations but fixed orientation were used to modify MM3/MM4 vdW parameters.[11] A systematic study of propane dimer intermolecular energies using Hartree−Fock, CCSD(T), and MP2 calculations with several basis sets up to cc-pVQZ was performed in ref 12 to compare their relative accuracy and the orientational dependence of the intermolecular energy. The authors of ref 13 used MP2 and CCSD(T) calculations with the cc-aug-pVQZ basis set on H_2, N_2, and O_2 dimers to investigate the orientational dependence of the intermolecular potential. Another work used MP2/6-311++G(2df,2pd) interaction energies for ethane molecules in 22 different relative orientations to examine how well different functional forms of the vdW potential reproduced these calculations.[14] Reference 15 used MP2 methanol dimer and trimer energies to derive parameters in an intermolecular potential including separate repulsion, dispersion, and polarization components. Finally, refs 16 and 17 used ab initio calculations of the interaction energy of a noble gas atom with either a methane molecule or fluorethanes and amines, respectively, to derive vdW potential parameters.

1.2. Combination Rules for van der Waals Potential Parameters. Because vdW potential parameters are usually derived solely from experimental data, which is insufficient to adequately constrain parameters for all atom type pairs, empirical relations, called combination rules, are used to reduce the number of parameters in the potential function. Combination rules relate the parameters in the vdW potential between atom types i and j with those between two atoms of type i and two atoms of type j. They are usually defined in terms of variables r^*_{ij} and ϵ_{ij}, the atomic separation and depth at the minimum of the vdW potential for atom types i and j, respectively. For example, one set of commonly used combination rules are the arithmetic mean for the minimum energy separation, $r^*_{ij} = (r^*_{ii} + r^*_{jj})/2$, and the geometric mean for the well depth, $\epsilon_{ij} = (\epsilon_{ii}\epsilon_{jj})^{1/2}$. However, Halgren demonstrated that the "cubic mean" rule $r^*_{ij} = (r^{*3}_{ii} + r^{*3}_{jj})/(r^{*2}_{ii} + r^{*2}_{jj})$ and an implicit combination rule based on the Slater−Kirkwood formula for ϵ_{ij} more accurately reproduced the potential minimum for dissimilar noble gas atoms.[1] Our primary motivation is to avoid the use of any combination rules by using QM data to determine vdW potential parameters. This is possible because of the significantly larger amount of QM data that may be calculated relative to the available experimental data to constrain the vdW parameters.

1.3. Overview. To study the accuracy and feasibility of determining vdW potential parameters from QM calculations we fit buffered LJ parameters for six atom types to MP2 interaction energies between rigid molecules in a training set of eight compounds. No combination rules are used. Since this is intended to be a proof of concept, we limit our study to only a small number of atom types. To be useful the vdW parameters should be transferable to molecules outside of our training set. This is investigated by comparing MP2 interaction energies between pairs of four molecules in the validation set, which are not included in the training set, with interaction energies calculated using the fit buffered LJ potential. Finally the sublimation enthalpies of 25 compounds, for which there are high-resolution X-ray crystal structures, are calculated using both the vdW potential fit to MP2 interaction energies and the MMFF vdW potential and compared with experimental data.

The following section describes the QM dimer interaction energy calculations used to fit the vdW potential parameters. Section 3 then discusses the results of the unrestrained linear regression fit to the QM dimer energies to obtain the vdW parameters. Next, in section 4, the transferability of the vdW potential parameters is tested by comparing the QM interaction energies for molecules in the validation set to the energies calculated using the fit vdW potential. Section 5 describes the

van der Waals Force Field Parameters

J. Phys. Chem. B, Vol. 107, No. 35, 2003 **9603**

TABLE 1: Atom Types for Which vdW Potential Function Parameters Were Derived and the Compounds Containing These Atom Types That Were Used To Derive the Parameters

atom type	description	compds
C_A	alkane C	ethane, propane
H_A	alkane H	ethane, propane
C_C	carbonyl C	formaldehyde, acetaldehyde
O_C	carbonyl O	formaldehyde, acetaldehyde
C_V	vinylic C	ethene, propene
O_E	ether O	dimethyl ether, methyl ethyl ether

TABLE 2: Comparison of Dipole Moments Calculated Using B3LYP/cc-pVDZ Merz−Singh−Kollman Charges with Experimental Gas-Phase Dipole Moments[a]

compd	exptl gas-phase dipole moment (D)	M−S−K dipole moment (D) (% error)
acetaldehyde	2.750 ± 0.006	$2.609\ (-5)$
acetone	2.88 ± 0.03	$2.748\ (-5)$
dimethyl ether	1.30 ± 0.01	$1.333\ (3)$
formaldehyde	2.332 ± 0.002	$2.170\ (-7)$
methoxyethylene	0.965 ± 0.002	$0.943\ (-2)$
methyl ethyl ether	1.17 ± 0.02	$1.204\ (3)$
methyl formate	1.77 ± 0.04	$1.783\ (7)$

[a] All experimental values are from ref 38.

method for calculating the sublimation enthalpies from crystal structures and the comparison of these values with experimental data to verify the accuracy of the vdW parameters. The selection of the sublimation enthalpy data is explained in the Appendix. Finally, the results are summarized and future extensions discussed in section 6.

2. Defining a Balanced Training Set of Quantum Mechanical Interaction Energies

The vdW parameters for six atom types, shown in Table 1, were determined. Atom types commonly occurring in small molecules were chosen, and polar hydrogen types were not included to avoid hydrogen bond interactions. This is because hydrogen bond terms in the force field may not be accurately represented by vdW and electrostatics terms alone and may require a different functional form to fit them accurately.

Dimer interaction energies between a training set of small molecules were used to derive the vdW parameters. This set is comprised of two compounds for each class: the alkanes ethane and propane; the aldehydes formaldehyde and acetaldehyde; the ethers dimethyl ether and methyl ethyl ether; the alkenes ethene and propene. The structures of these compounds were first optimized using MP2/6-31G**. All QM calculations in this paper were performed using Gaussian 98.[18] The conformation of each molecule was fixed to the optimized geometry, but their relative orientation in each dimer configuration was varied. Next atom-centered charges were calculated for the optimized structures using the Merz−Singh−Kollman[19,20] method with the B3LYP/cc-pVDZ electric potential. Since the vdW contribution to the interaction energy is the focus of this study, we do not attempt to derive consensus atomic charges. Also the known conformational dependence of these atomic charges[21,22] is unimportant for the fixed conformations considered in this study. As shown in Table 2, these charges accurately reproduce the gas phase dipole moments of several compounds used in this study, even without configurational averaging. Finally, the MP2/d-aug-cc-pVDZ dimer interaction energies were calculated using the counterpoise procedure to correct for basis set superposition error (BSSE).[23,24] The d-aug-cc-pVDZ basis set is constructed by adding two diffuse functions for each of s-, p-, and d-orbitals

present in the original cc-pVDZ correlation consistent basis set.[25] The additional diffuse functions were found necessary to accurately reproduce molecular and atomic polarizabilities[25] as well as the dispersion interactions of Ne_2 and Ar_2.[26]

Since low-energy conformations are the most important for molecular mechanics minimization of the energy function and also dominate thermodynamic averages calculated using MC or MD methods, we generate QM data that contain predominantly low-energy conformations. This was done by generating random dimer conformations with the MMFF94 vdW interaction energy E_{vdw}, expressed in kcal/mol, in the ranges $E_{vdw} < -0.4$, $-0.4 < E_{vdw} < -0.05$, $0.05 < E_{vdw} < 0.6$, and $0.6 < E_{vdw} < 1.2$ with the fraction of the total number of conformations 0.5, 0.26, 0.18, and 0.06, respectively. These fractions are proportional to the total Boltzmann weight W for the energy interval

$$W = \int_{E_{min}}^{E_{max}} \exp\left(-\frac{E}{kT}\right) dE \tag{2}$$

with $kT = 0.6$ kcal/mol and $E_{min} = -0.8$ kcal/mol as a nominal value for the lowest energy range. The energy range near zero, $|E| < 0.05$, was excluded, and the maximum separation between nearest atoms was restricted to be less than 5 Å to avoid generating many conformations with large separations which would only contribute to fitting the long-distance dispersion tail of the vdW potential rather than the desired region near the potential minimum. MP2/d-aug-cc-pVDZ interaction energies with the counterpoise BSSE correction were calculated for all possible pairs of the eight small molecules in Table 1. A total of 100 random conformations were generated for each dimer with less than 6 non-hydrogen atoms, and 50 conformations were generated for each of the remaining molecule pairs because of their longer computational time. The data for the molecule pairs with 50 conformations was then weighted by a factor of 2 in the subsequent linear regression fitting of the vdW potential parameters.

3. Simultaneous Unrestrained Fit of van der Waals Parameters to Quantum Mechanical Interaction Energies

3.1. Linear Regression Method. The vdW parameters A_{ij} and B_{ij} were determined simultaneously for all atom type pairs using a linear regression fit to the QM vdW energies $E_{vdw}^{QM} \equiv E_{int} - E_{el}$ with E_{int} the QM dimer interaction energy using the counterpoise procedure

$$E_{int} \equiv E_{1,2} - E_{1,2ghost} - E_{1ghost,2} \tag{3.3}$$

and the electrostatic energy determined from the set of atomic charges $q_i^{(I)}$ molecule I using

$$E_{el} \equiv 332.1 \sum_{i=1}^{N_1} \sum_{i=1}^{N_2} \frac{q_i^{(1)} q_j^{(2)}}{|\vec{r}_{ij}|} \tag{3.4}$$

with $\vec{r}_{ij} \equiv \vec{y}_j - \vec{x}_i$, a vector from the center of atom i in molecule 1 to atom j in molecule 2. The constant factor is chosen to give E_{el} in kcal/mol when distances are in Å and charges in units of the electronic charge.

The linear regression method minimizes the weighted sum of square residuals $\Sigma_i w_i[(E_{vdw}^{calc})_i - (E_{vdw}^{QM})_i]^2$ with the calculated intermolecular vdW energy defined as

$$E_{vdw}^{calc} \equiv \sum_{i=1}^{N_1} \sum_{j=1}^{N_2} E_{vdw}(type(1,i), type(2,j), |\vec{r}_{ij}|) \tag{3.5}$$
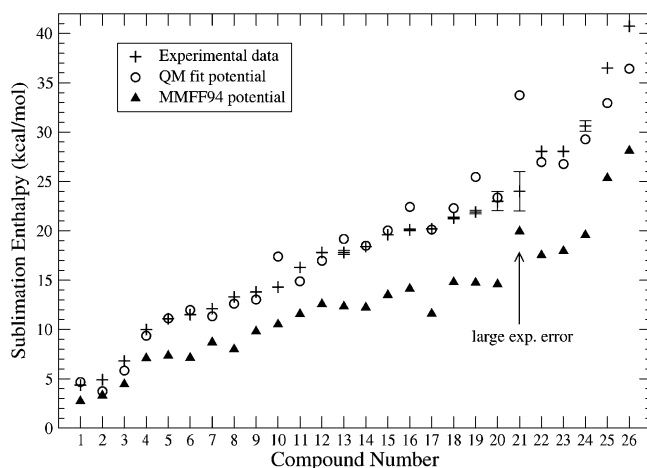
Figure 1. Experimental values ($+$) of the sublimation enthalpy, ΔH_{subl}, and values calculated using the vdW potential with Table 3 parameters ($\bigcirc$) and the MMFF94 vdW potential ($\blacktriangle$). Compounds are arranged in order of increasing experimental ΔH_{subl}, and the experimental errors are shown, when available. Refer to Table 5 for compound numbers and numerical values of ΔH_{subl}.

TABLE 3: vdW Parameters for the Buffered Lennard-Jones Potential of Eq 1 with $d = 0.1$ Å

atom types	$10^{-9} \times A_{ij}$ (cal Å^{12}/mol)	$10^{-5} \times B_{ij}$ (cal Å^6/mol)
C_A,C_A	2.073	-3.577
C_A,C_V	1.594	-1.671
C_A,C_C	1.184	-9.225
C_A,H_A	0.1312	-3.103
C_A,O_E	1.125	-2.954
C_A,O_C	1.130	-6.838
C_V,C_V	2.776	-3.843
C_V,C_C	1.684	-7.008
C_V,H_A	0.1892	-3.684
C_V,O_E	0.9739	-4.359
C_V,O_C	0.9354	-6.349
C_C,C_C	0.1849	-2.561
C_C,H_A	0.1014	-0.5390
C_C,O_E	0.5705	-7.764
C_C,O_C	0.7458	-8.938
H_A,H_A	0.003394	0.4518
O_E,H_A	0.03449	-1.609
O_C,H_A	0.03792	-1.101
O_E,O_E	0.5973	-2.733
O_E,O_C	0.3054	-2.995
O_C,O_C	0.1933	0.7579

where type(I, j) is the type of atom j in molecule I and $E_{vdw}(i, j, r)$ is the buffered LJ potential of eq 1 with $d = 0.1$ Å. $w_i = 2$ for molecule pairs for which 50 conformations were generated, and $w_i = 1$ for the remaining data to achieve equal importance of the QM data for all molecule pairs. The resulting best fit vdW parameters are given in Table 3. The fit residual average -2.31×10^{-3} kcal/mol and the residual standard deviation 0.134 kcal/mol, demonstrating that the derived vdW potential function fits the QM data quite well.

3.2. Sensitivity of Fit Parameters. It is useful to consider the vdW parameters for the alkane atom types C_A and H_A since they are effectively electrically neutral and are commonly occurring atom types. The well depths for the $C_A - C_A$ and $C_A - H_A$ vdW potentials are 0.0154 and 0.183 kcal/mol, respectively, and the $H_A - H_A$ potential has no minimum; i.e., it is purely repulsive with both A_{ij} and B_{ij} positive. This implies that most of the attractive vdW contribution between alkanes is due to $C_A - H_A$ terms. One explanation for the weakly attractive potential between C_A atoms is that the repulsion of bonded hydrogen atoms dominates the weakly attractive interaction between the C_A atoms and thus they are effectively shielded.

This is analogous to the difficulty in determining the atomic charges of buried atoms because of the insensitivity of the electrostatic potential outside the molecular surface to these charges.[21] It is not surprising that the fit $H_A - H_A$ potential is found to be purely repulsive since the well depth is expected to be small. Calculations on H_2 dimers show that although the vdW potential has a very shallow minimum, the best-fit buffered LJ potential has none. A potential with a minimum can be obtained by using a more complicated vdW potential function with more parameters; however, the increased accuracy is expected to be insignificant compared to other approximation errors such as those in the electrostatic term and the pairwise approximation to the vdW potential. Finally, we note that the T-statistics for the vdW parameters involving only alkane atom types C_A and H_A in the linear regression fit all have probability $p \leq 1.6 \times 10^{-2}$, indicating that none of the parameters may be neglected, i.e. set to zero, in the total vdW potential function. This result is is in contrast to that of ref 14 in which the $C_A - C_A$ vdW potential term was dropped because of the apparent insensitivity of the potential to the corresponding parameters.

The linear regression T-statistics for all of the vdW parameters have $p \leq 7.7 \times 10^{-2}$, most with p-values orders of magnitude lower than this, except for $p(A_{C_C,C_C}) = 0.63$, $p(B_{C_C,C_C}) = 0.45$, $p(B_{O_C,O_C}) = 0.41$, and $p(B_{C_C,H_A}) = 0.16$. The high p-values for B_{O_C,O_C} and B_{C_C,H_A} but not for the corresponding R^{-12} coefficients A_{O_C,O_C} and A_{C_C,H_A} indicates that a purely repulsive vdW potential for these atom types, with $B_{ij} = 0$ would still fit the MP2 dimer interaction energies well. This is reasonable considering that the $O_C - O_C$ potential is actually purely repulsive and the $C_C - H_A$ well depth is only 7.2×10^{-3} kcal/mol. The relatively high p-values for both $C_C - C_C$ vdW parameter T-statistics indicate that completely removing this term from the total vdW potential would still yield a reasonably close fit to the QM data. This may be due to the fact that C_C atoms have a large atomic charge so that the electrostatic contribution dominates the dimer interaction energy and that they are relatively inaccessible due to the repulsive potentials of nearby atoms such as O_C. MP2/d-aug-cc-pVDZ interaction energies between pairs of formaldehyde and acetaldehyde molecules with the carbonyl carbon atoms the closest atoms from each molecule were calculated at 0.1 Å intervals along a line connecting the type C_C atoms on each molecule. In all cases the interaction energy was a monotonically decreasing function of the atom separation indicating that the shallow or absent vdW potential minimum results from subtracting the relatively large repulsive electrostatic energy. Therefore, either the electrostatic energy alone is sufficient to reproduce the dimer interaction energy or a large approximation error in the electrostatic term yields a large error in the vdW potential term. We did not investigate setting the vdW potential terms with high p-values to zero, which should be done in a stepwise fashion, since this is best done after the total force field potential is determined.

4. Transferability of van der Waals Parameters

Next the transferability of the vdW parameters was studied by comparing QM vdW dimer interaction energies E_{vdw}^{QM} for molecules in a validation set with the values calculated using the buffered LJ potential E_{vdw}^{calc}. Four molecules were chosen for the validation set, acetone, ethanedial, methoxyethylene, and methyl formate, since they are reasonably small yet contain a variety of different atom types for which vdW parameters were derived. The combinations of chemical functional groups also differs from the molecules used to derive the vdW parameters providing a reasonable test of the transferability of these

van der Waals Force Field Parameters

J. Phys. Chem. B, Vol. 107, No. 35, 2003 **9605**

TABLE 4: Compounds for Which the Sublimation Enthalpies Were Calculated Using the Crystal Structure and Compared with the Experimental Values[a]

compd name	formula	CAS no.	CSD entry (ref)	T_{crys} (K)	T_{subl} (K)
		alkanes			
ethane	C_2H_6	74-84-0	ETHANE01 (39)	85	90
propane	C_3H_8	74-98-6	JAYDUI (40)	30	86
n-pentane	C_5H_{12}	109-66-0	PENTAN01 (40)	90	143
cyclohexane	C_6H_{12}	110-82-7	CYCHEX (41)	115	186
n-hexane	C_6H_{14}	110-54-3	HEXANE01 (40)	90	178
n-heptane	C_7H_{16}	142-82-5	HEPTAN02 (40)	90	183
n-octane	C_8H_{18}	111-65-9	OCTANE01 (40)	90	216
n-nonane	C_9H_{20}	111-84-2	QQQFAY01 (40)	90	219
adamantane	$C_{10}H_{16}$	281-23-2	ADAMAN02 (42)	283−303	278−368
cyclotetradecane	$C_{14}H_{28}$	295-17-0	CYTDEC (43)	116	285−290
tricyclo[8.2.2.2^{4,7}]hexadecane	$C_{16}H_{28}$	283-68-1	PIRFIF (44)	145	316−338
n-octadecane	$C_{18}H_{38}$	593-45-3	NOCTDC (45)	283−303	298
tricyclohexylmethane	$C_{19}H_{34}$	1610-24-8	LEPRON[†] (46)	283−303	301−321
tricyclohexylmethane	$C_{19}H_{34}$	1610-24-8	LEPRON01[‡] (46)	283−303	301−321
eicosane	$C_{20}H_{42}$	112-95-8	QQQCIM01 (47)	283−303	298
		nonalkanes			
ethylene	C_2H_4	74-85-1	ETHLEN10 (48)	85	79−104
1,3,5-trioxane	$C_3H_6O_3$	110-88-3	TROXAN (49)	283−303	298
dihydro-2,5-furandione	$C_4H_4O_3$	108-30-5	SUCANH (50)	283−303	290−311
dimethyl oxalate	$C_4H_6O_4$	553-90-2	DMEOXA01 (51)	283−303	268−298
1,4-dioxane	$C_4H_8O_2$	123-91-1	CUKCIU10 (52)	279	284.1
1,4-cyclohexanedione	$C_6H_8O_2$	637-88-7	CYHEXO (53)	133	289
2,5-dimethyl-1,4-benzoquinone	$C_8H_8O_2$	137-18-8	DMEBQU01 (54)	283−303	273−293
endo-5-norbornene-2,3-dicarboxylic anhydride	$C_9H_8O_3$	129-64-6	NBORAN10 (55)	283−303	298
1-adamantyl methyl ketone	$C_{12}H_{18}O$	1660-04-4	PUSDEM (56)	220	287−305
18-crown-6	$C_{12}H_{24}O_6$	17455-13-9	HOXOCD (57)	283−303	298
dicyclohexyl peroxalate	$C_{14}H_{22}O_6$	1561-49-5	SEGROL (58)	153	293−313

[a] CSD entry denotes the entry name of the crystal structure in the Cambridge Structural Database. T_{crys} and T_{subl} are the temperatures at which the X-ray crystal structure was determined and the sublimation enthalpy was measured, respectively. 283−303 denotes room temperature for T_{crys}. [†] and [‡] indicate the monoclinic and orthorhombic polymorphs of tricyclohexylmethane, respectively. The crystal structure for 1,4-dioxane is the phase I polymorph that exists above 278 K.

parameters to other molecules. As for the QM data used to derive the vdW parameters, the structures were first optimized using MP2/6-31G**, Merz−Singh−Kollman atomic point charges calculated, and E_{vdw}^{QM} calculated using MP2/d-aug-cc-pVDZ with the counterpoise procedure. The optimized structures were used for each molecule and their relative orientations chosen at random. Since the vdW potential parameters were derived in such a way as to best reproduce the most attractive portion of the potential function rather than the repulsive interaction at small separations, the error in the calculated vdW energy is expected to be correspondingly larger when E_{vdw}^{QM} is large. This also occurs because the vdW interaction energy for two molecules is dominated by the contribution of the closest approaching atoms and the steep slope of the repulsive region of the potential yields large errors. Because of this effect, conformations with E_{vdw}^{QM} in three energy ranges were generated: $E_{vdw}^{QM} < -0.6$; $-0.6 < E_{vdw}^{QM} < -0.05$; $0.05 < E_{vdw}^{QM} < 0.6$. A total of 20 random conformations for pairs of each molecule in a given energy range were generated; i.e., a total of 60 conformations were generated for each molecule pair. The comparison between E_{vdw}^{calc} and E_{vdw}^{QM} is show in Table 6.

The error in E_{vdw}^{calc} in a particular energy range is comparable for all four molecules. It is also evident that the error is lowest for the two energy ranges with $E_{vdw}^{QM} < 0.0$. This is expected since the QM data used to derive the parameters was chosen so as to most accurately reproduce the low energy portion of the vdW potential. The error for the energy range $-0.6 < E_{vdw}^{QM} < -0.05$ is lower than for $E_{vdw}^{QM} < -0.6$ because the average magnitude of the interaction energy is corresponding smaller. Errors in the calculation of the electrostatic interaction energy due to the approximation of using atom-centered charges also contribute to the error in E_{vdw}^{calc}, as we discuss next.

Since the vdW energy $E_{vdw} = E_{int} - E_{el}$ is defined to be the difference between the intermolecular interaction energy and the electrostatic energy, the approximation error in the atomic point charge model for E_{el} propagates to the fit E_{vdw}. We investigated the effect of this approximation error by repeating the fitting procedure for the vdW potential parameters with the inclusion of atomic dipoles. The fit residual average for the vdW parameters was reduced to 1.92×10^{-3} kcal/mol, and the residual standard deviation was reduced to 0.112 kcal/mol, indicating that the improved electrostatic model does indeed yield a better fit to the QM interaction energies. Also the deviation between the vdW energy calculated using this fit potential and the QM values for the four molecules in the validation set was also reduced in most cases. These results indicate that a portion of the error in the vdW potential is due to the relatively simple atomic point charge model for electrostatics. However, we decided that the increased computational demands of including atomic dipoles, as well as potential problems with their transferability and conformational dependence, does not outweigh the modest improvement in predicting nonbonded interaction energies.

5. Comparison with Experimental Sublimation Enthalpy Data

5.1. Theoretical Model for Calculating Sublimation Enthalpy. The sublimation enthalpy, ΔH_{subl}, may be calculated using

$$\Delta H_{subl} = \Delta E_{inter}^{conf} + \Delta E_{inter}^{vib} + \Delta E_{intra}^{conf} + \Delta E_{intra}^{vib} + PV \quad (5.6)$$

with the common approximations that the change in intramolecular vibrational energy $\Delta E_{intra}^{vib} = 0$, $\Delta E_{inter}^{vib} = (3nRT -$

TABLE 5: Experimental Sublimation Enthalpies and the Deviations of the Values Calculated Using the Buffered Lennard-Jones Potential with the Parameters of Table 3 and the Values Calculated Using the MMFF94 vdW Potential

compd no.	compd name	exptl ΔH_{subl} (kcal/mol) (ref)	Table 3 params calcd ΔH_{subl} − exptl ΔH_{subl} (kcal/mol) (% deviation)	MMFF94 calcd ΔH_{subl} − exptl ΔH_{subl} (kcal/mol) (% deviation)
		Alkanes		
2	ethane	4.90 (59)	−1.15 (−23)	−1.58 (−32)
3	propane	6.81 (59)	−0.980 (−14)	−2.36 (−35)
4	*n*-pentane	10.0 (59)	−0.632 (−6.3)	−2.91 (−29)
5	cyclohexane	11.1 (59)	0.0319 (0.29)	−3.75 (−34)
7	*n*-hexane	12.1 (59)	−0.756 (−6.2)	−3.40 (−28)
9	*n*-heptane	13.8 (59)	−0.765 (−5.5)	−4.00 (−29)
11	*n*-octane	16.3 (59)	−1.42 (−8.7)	−4.74 (−29)
12	*n*-nonane	17.8 (59)	−0.836 (−4.7)	−5.23 (−29)
10	adamantane	14.3 (60)	3.09 (22)	−3.79 (−27)
18	cyclotetradecane	21.3 ± 0.1 (61)	0.998 (4.7)	−6.50 (−31)
19	tricyclo[8.2.2.2^{4,7}]hexadecane	21.9 ± 0.2 (62)	3.55 (16)	−7.16 (−33)
25	*n*-octadecane	36.5 (63)	−3.56 (−9.8)	−11.16 (−31)
22	tricyclohexylmethane	28.06 (60)	−1.10 (−3.9)	−10.5 (−38)
23	tricyclohexylmethane	28.06 (60)	−1.29 (−4.6)	−10.1 (−36)
26	eicosane	40.73 (63)	−4.312 (−11)	−12.6 (−31)
		Nonalkanes		
1	ethylene	4.37 (60)	0.311 (7.0)	−1.63 (−37)
8	1,3,5-trioxane	13.3 (64)	−0.691 (−5.2)	−5.30 (−40)
15	dihydro-2,5-furandione	19.6 (64)	0.436 (2.2)	−6.10 (−31)
13	dimethyl oxalate	17.8 ± 0.2 (65)	1.37 (7.7)	−5.46 (−31)
6	1,4-dioxane	11.5 (see text)	0.468 (4.1)	−4.37 (−38)
17	1,4-cyclohexanedione	20.2 (64)	−0.0702 (0.35)	−8.60 (−43)
14	2,5-dimethyl-1,4-benzoquinone	18.4 (66)	0.0862 (0.47)	−6.17 (−34)
20	*endo*-5-norbornene-2,3-dicarboxylic anhydride	23 ± 0.98 (67)	0.373 (1.6)	−8.41 (−37)
16	1-adamantyl methyl ketone	20.1 ± 0.1 (68)	2.33 (12)	−5.97 (−30)
24	18-crown-6	30.62 ± 0.55 (69)	−1.36 (−4.4)	−11.1 (−36)
21	dicyclohexyl peroxalate	24.0 ± 2.0 (70)	9.75 (41)	−4.05 (−17)

TABLE 6: Comparison of the Dimer vdW Interaction Energies Calculated Using the Fit vdW parameters and the QM MP2/d-aug-cc-pVDZ results[a]

compd name; atom types	min E_{vdw}^{QM}	max E_{vdw}^{QM}	rmsd E_{vdw}^{calc}	ave E_{int}^{QM}	std E_{int}^{QM}	min E_{int}^{QM}	max E_{int}^{QM}
acetone; C_A, C_C, H_A, O_C		−0.6	0.146	−1.25	0.751	−2.37	0.211
	−0.6	−0.05	0.0492	−0.374	0.316	−1.01	0.145
	0.05	0.6	0.373	0.347	1.20	−1.39	3.85
ethanedial; C_C, H_A, O_C		−0.6	0.294	−0.778	0.990	−2.95	0.907
	−0.6	−0.05	0.155	−0.130	0.537	−1.08	0.996
	0.05	0.6	0.521	0.458	1.11	−1.88	1.93
methoxyethylene; C_A, C_V, H_A, O_E		−0.6	0.147	−1.09	0.457	−2.13	−0.308
	−0.6	−0.05	0.0608	−0.304	0.173	−0.880	−0.0282
	0.05	0.6	0.538	0.463	0.393	−0.484	0.987
methyl formate; C_A, C_C, H_A, O_C, O_E		−0.6	0.237	−1.04	0.496	−2.17	−0.294
	−0.6	−0.05	0.097	−0.272	0.376	−1.01	0.351
	0.05	0.6	0.481	0.281	0.733	−1.22	1.23

[a] 20 random conformations with QM vdW energies between indicated minimum and maximum values were used. The root-mean-squared deviation (rmsd) of the calculated vdW energy from the QM value is given. The average, standard deviation, and minimum and maximum of the QM interaction energy values are also shown.

$6nRT) = -3nRT$,[27] and the ideal gas equation is used for the last term. The approximation that the change in the intramolecular conformational energy upon going from the crystalline to gas phase $\Delta E_{intra}^{conf} = 0$ was also used to calculate the sublimation enthalpies in Table 5. The implications of this approximation are discussed later in this section. Since the intermolecular conformational energy in the gas phase is small $\Delta E_{inter}^{conf} = -E_{vdw}^{crys} - E_{el}^{crys}$. The sublimation enthalpy is then calculated using eq 6 with these approximations:

$$\Delta H_{subl} = -E_{vdw}^{crys} - E_{el}^{crys} - 2nRT \qquad (5.7)$$

E_{el}^{crys} was calculated using B3LYP/cc-pVDZ Merz−Singh−Kollman atomic charges derived for an isolated molecule in the crystal conformation, and lattice sums were evaluated using Ewald summation with a conducting boundary term as imple-

mented in the program GULP.[28] Atomic charges were averaged over symmetry-related atoms. E_{vdw}^{crys} was calculated by summing the vdW interaction potential between a central molecule and all symmetry-related molecules with at least one atomic center within 10 Å of the nearest atom center of the central molecule and multiplying this by a factor of 1/2 to compensate for double counting of the intermolecular interactions. Both the buffered LJ potential with the fit parameters of Table 3 and the MMFF94 vdW potential of ref 1 were used to calculate this term to compare their accuracy.

5.2. Comparison Results. Table 5 shows the experimental sublimation enthalpies and deviations between ΔH_{subl} values calculated using either the buffered LJ potential with the parameters of Table 3 or the MMFF94 vdW potential and the corresponding experimental values. These experimental and calculated sublimation enthalpy values are also plotted for

van der Waals Force Field Parameters

J. Phys. Chem. B, Vol. 107, No. 35, 2003 **9607**

comparison in Figure 1. It is apparent that whereas the vdW potential fit to the MP2 calculations yield ΔH_{subl} values close to the experimental values, except for a few outliers, the MMFF94 vdW potential gives values about 30−40% too low. This indicates that the attractive portion of MMFF94 vdW potential function is too shallow; i.e., the energy is too high. The fact that ΔH_{subl} values for adamantane and dicyclohexyl peroxalate calculated using the buffered LJ potential are too high and the MMFF94 values are also higher than the overall systematic error mentioned above indicates that there may be an error in the experimental measurement. One simple method to correct for the systematic error in the MMFF94 sublimation enthalpy values is to multiply the vdW potential by a constant. If this constant is determined by minimizing the rms deviation between the calculated and experimental ΔH_{subl} values for all compounds in Table 5, except the outlier dicyclohexyl peroxalate, i.e. using linear regression, it is found to be 1.49 for the MMFF94 values. Using the same procedure to determine the multiplicative constant our the buffered LJ potential gives a factor of 1.02, indicating a lack of systematic error in the MP2 fit parameters. Of course, it is not yet known whether scaling the MMFF94 vdW potential by 1.49 will improve the accuracy of the ΔH_{subl} calculation for molecules with atom types not considered here. It is interesting to note that the authors of ref 30 similarly concluded that MMFF94 C−C and C−H non-bonded interactions were too weak, on the basis of a comparison of liquid simulation results with experimental data, and suggested the scaling of a vdW potential parameter to correct this.

5.3. Factors Contributing to Accurate Prediction of Sublimation Enthalpy Values. Actually the close agreement between the sublimation enthalpy values calculated using the buffered LJ potential fit to MP2 results and the experimental values is somewhat unexpected because of the reduced attractive well depths, compared with experimental values, for noble gas dimers calculated using the same quantum method and basis set. MP2/d-aug-cc-pVDZ calculations reproduce, on the average, only about half of the experimentally determined well depth between noble gas dimers. Noble gas dimers offer the only examples of a vdW interaction without the added complications of electrostatic interactions and corrections to the pairwise atom-centered potential and have been used as a basis for determining more general vdW potentials.[1] There are two possible explanations for the accuracy of the sublimation enthalpy calculations. One is that the basis functions centered on adjacent bonded atoms act as higher angular symmetry basis functions and that this more flexible basis set more accurately reproduces the dispersion interaction between molecules. This is plausible since large basis sets with higher angular momentum functions are necessary to accurately calculate the dispersion energy.[26] Additional evidence for this effect is provided by the high level ab initio calculation of propane dimer interaction energies in ref 12. The authors found that the MP2 propane dimer well depth calculated with a smaller basis set than used in this study, aug-cc-pVDZ, was lower than the MP2 complete basis set limit result by only 14%. This paper also demonstrated that the MP2 perturbative approximation was adequate to accurately reproduce the propane dimer dispersion energy since the MP2/aug-cc-pVDZ well depth differed from MP4 and CCSD(T) results calculated with the same basis set by only 1.7 and 3.0%, respectively. Thus it appears that the dispersion contribution to the interaction energy of molecules is more accurately reproduced than for isolated noble gas atoms, for the same level of ab initio theory and the same basis set. The second contribution to the apparent accuracy of the sublimation

enthalpy calculation by the MP2 fit vdW potential is the neglect of the intramolecular conformational energy change ΔE_{intra}^{conf} in the calculation of the sublimation enthalpy using eq 7. If the approximation is made that only the lowest energy molecular conformation in the gas-phase contributes to ΔE_{intra}^{conf}, then since gas phase conformation clearly has lower energy than the crystal phase one $\Delta E_{intra}^{conf} < 0$. If this value for ΔE_{intra}^{conf} were included it would systematically lower the calculated sublimation enthalpy values and the MP2 fit vdW potential would appear to be too repulsive. However, this would also make the MMFF94 sublimation enthalpy values deviate even more from the experimental results. There are a number of problems with estimating ΔE_{intra}^{conf}. Direct use of a force field to calculate ΔE_{intra}^{conf} would give consistently too large of a value because errors in the force field equilibrium bond lengths and angles would yield large conformational energies for these relatively stiff degrees of freedom. One could also attempt to calculate ΔE_{intra}^{conf} using QM methods by subtracting the energy of the molecule in the crystal structure conformation from the geometry-optimized energy. However, uncertainties in the hydrogen atom positions in the X-ray crystal structure may cause large errors. Even bond angles for hydrogen atoms vary significantly between structures as may be seen by superimposing crystal structures for the same compound and space group. Since the hydrogen atom degrees of freedom contribute significantly to the total intramolecular conformational energy and also since using the QM-optimized geometry for the gas phase conformation gives a systematic overestimation of ΔE_{intra}^{conf}, it is difficult to calculate it accurately, even using high-level ab initio methods. Whereas the increased basis set flexibility for molecules, discussed above, implies that the vdW potentials for molecules are, in fact, more accurate than expected from noble gas atom calculations, the neglect of ΔE_{intra}^{conf} represents a systematic error in the calculation of sublimation enthalpies and should eventually be corrected. Comparison of liquid simulation results with experimental data should provide an independent method to determine whether the vdW potential function needs to be corrected by, for example, a multiplicative scaling factor to correct for errors in the QM calculation of the interaction energies.

6. Discussion and Conclusions

We found that a simple vdW potential function, the buffered LJ potential, with parameters unconstrained by artificial combination rules and fit to ab initio dimer energies is accurate and transferable, as demonstrated by the good agreement with experimental sublimation enthalpy data and ab initio dimer energies for validation set molecules, respectively. Comparison with validation set dimer energies also revealed that the vdW potential is more accurate for lower energy conformations, as expected from the bias toward lower energy conformations in the training set interaction energies used to derive the vdW potential parameters. This bias was introduced exactly for this reason since low-energy conformations are the most important for molecular mechanics energy minimization and MC and MD calculations of thermodynamic averages. Overall, these results indicate that ab initio calculations may be used along with experimental data to provide enough constraints to determine vdW potential parameters without resorting to empirical combination rules. Finally, we note that our procedure to determine van der Waals parameters is objective, in the sense that the fitting procedure does not contain constraints imposing unsubstantiated beliefs of physical reasonableness on the parameters,

and also is a simultaneous fit of all parameters so that it may be easily automated.

Although we chose the training set molecules to isolate the vdW component of the energy as much as possible, other energy terms must eventually be included. The next steps in including these results in a complete force field are to introduce more atom types, to derive consensus atom charges, and to include intramolecular terms so that force field calculations may be compared with other experimental data, such as liquid-state properties. It is also useful to examine the accuracy of MP2 dimer energy calculations with smaller basis sets since atom types such as an aromatic carbon will require dimer calculations with larger molecules than used here and so may use significantly more computational time. In addition, a hydrogen bond energy term should be included in the force field so that atom types that form a strong hydrogen bond may be added to the vdW potential. Since electrostatic potentials, torsional energies, and hydrogen bonding energies are adequately reproduced using less computationally expensive quantum methods, such as Hartree−Fock or density functional methods, and smaller basis sets than used here for determining the vdW potential, it is advantageous to use ab initio calculations extensively to derive these terms as well.

Appendix: Sublimation Enthalpy Experimental Data

Compounds that contain only the atom types listed in Table 1 and for which there is reliable X-ray crystal structures and sublimation data were included. The X-ray crystal structures were required to have coordinates for all atoms, no errors, and an R-factor less than 0.1. All structures were obtained from the Cambridge Structural Database.[31] Also compounds for which the X-ray structures and sublimation data were determined at temperatures differing by more than 250 °C were not included since thermal expansion of the crystal lattice causes significant errors in the calculation of the sublimation enthalpy using a structure determined at a much lower temperature. In cases where more than one X-ray structure was available, the one determined at a temperature closest to that of the sublimation data was used. The X-ray crystal structures and temperatures for both the crystal structure and sublimation enthalpy data are given in Table 4.

Since the available sublimation enthalpy of 8.51 kcal/mol from ref 32 for 1,4-dioxane was determined by a least-squares fit to the ln P versus $1/T$ graph and the Clausius−Clapeyron equation with only three points of vapor pressure data for the solid form from ref 33, it was considered unreliable. Instead it was calculated using the sum of the enthalpy of fusion (3.069 kcal/mol at 284.1 K)[34] and the enthalpy of vaporization (8.56 kcal/mol at 273 K)[35] extrapolated to a common temperature using the constant pressure molar specific heats of the liquid (34.89 cal/(mol K) at 291 K)[36] and the gas phases (20.15 cal/(mol K) at 273.15 K)[37] using

$$\Delta H_{vap}(T_2) = \Delta H_{vap}(T_1) + \int_{T_1}^{T_2}[C_{P,gas}(T) - C_{P,liq}(T)] \, dT \quad (8)$$

to give $\Delta H_{subl} = 11.5$ kcal/mol at 284.1 K.

References and Notes

(1) Halgren, T. *J. Am. Chem. Soc.* **1992**, *114*, 7827−7843.

(2) Momany, F.; Carruthers, L.; McGuire, R.; Scheraga, H. *J. Phys. Chem.* **1974**, *78*, 1595−1620.

(3) Slater, J.; Kirkwood, J. *Phys. Rev.* **1931**.

(4) Jorgensen, W.; Maxwell, D.; Tirado-Rives, J. *J. Am. Chem. Soc.* **1996**, *118*, 11225−11236.

(5) Cornell, W.; Cieplak, P.; Bayly, C.; Gould, I.; Merz, K.; Ferguson, D.; Spellmeyer, D.; Fox, T.; Caldwell, J.; Kollman, P. *J. Am. Chem. Soc.* **1995**, *117*, 5179−5197.

(6) MacKerell, A.; et al. *J. Phys. Chem. B* **1998**, *102*, 3586−3616.

(7) Ewig, C.; Thacher, T.; Hagler, A. *J. Phys. Chem. B* **1999**, *103*, 6998−7014.

(8) Waldman, M.; Hagler, A. *J. Comput. Chem.* **1993**, *14*, 1077−1084.

(9) Halgren, T. *J. Comput. Chem.* **1996**.

(10) Halgren, T. *J. Comput. Chem.* **1996**, *17*, 520−552.

(11) Allinger, N. L.; Durkin, K. *J. Comput. Chem.* **2000**, *21*, 1229−1242.

(12) Tsuzuki, S.; Uchimaru, T.; Mikami, M.; Tanabe, K. *J. Phys. Chem. A* **2002**, *106*, 3867−3872.

(13) Rozenbaum, V.; Mebel, A.; Lin, S. *Mol. Phys.* **2001**, *99*, 1883−1897.

(14) Rowley, R.; Yang, Y.; Pakkanen, T. *J. Chem. Phys.* **2001**, *114*, 6058−6067.

(15) Mooij, W.; van Duijneveldt, F.; van Duijneveldt-van de Rijdt, J.; van Eijck, B. *J. Phys. Chem. A* **1999**, *103*, 9872−9882.

(16) Hill, J. *J. Comput. Chem.* **1997**, *18*, 211−220.

(17) Chen, I.; Yin, D.; MacKerrell, A., Jr. *J. Comput. Chem.* **2002**, *23*, 199−213.

(18) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Salvador, P.; Dannenberg, J. J.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.9; Gaussian Inc.: Pittsburgh, PA, 2001.

(19) Singh, U.; Kollman, P. *J. Comput. Chem.* **1984**, *5*, 129−145.

(20) Besler, B.; Merz, K.; Kollman, P. *J. Comput. Chem.* **1990**, *11*, 431−439.

(21) Bayly, C.; Cieplak, P.; Cornell, W.; Kollman, P. *J. Phys. Chem.* **1993**, *97*, 10269−10280.

(22) Henchman, R. H.; Essex, J. *J. Comput. Chem.* **1999**, *20*, 483−498.

(23) Boys, S.; Bernardi, F. *Mol. Phys.* **1970**, *19*, 553.

(24) van Lenthe, J.; van Duijneveldt-van de Rijdt, J.; van Duijneveldt, F. *Adv. Chem. Phys.* **1987**, *69*, 521.

(25) Woon, D.; Dunning, T., Jr. *J. Chem. Phys.* **1994**, *100*, 2975−2988.

(26) Dunning, T., Jr. *J. Phys. Chem. A* **2000**, *104*, 9062−9080.

(27) Gavezzotti, A.; Ed. *Theoretical aspects and computer modeling of the molecular solid state*; The molecular solid state 1; J. Wiley: New York, 1997.

(28) Gale, J. *J. Chem. Soc., Faraday Trans.* **1997**, *93*, 629.

(29) Dick, B.; Overhauser, A. *Phys. Rev.* **1958**, *112*, 90.

(30) Kaminski, G.; Jorgensen, W. *J. Phys. Chem.* **1996**, *100*, 18010−18013.

(31) Allen, F.; Kennard, O. *Chem. Des. Autom. News* **1993**, *8*, 31−37.

(32) Chickos, J.; Acree, W., Jr. *J. Phys. Chem. Ref. Data* **2002**, *31*, 537−698.

(33) Stull, D. *Ind. Eng. Chem.* **1947**, *39*, 517.

(34) Domalski, E.; Hearing, E. *J. Phys. Chem. Ref. Data* **1996**, *25*, 1−525.

(35) Gallaugher, A.; Hibbert, H. *J. Am. Chem. Soc.* **1937**, *59*, 2521−2525.

(36) Roth, W.; Meyer, I. *Z. Electrochem.* **1933**, *39*, 35−37.

(37) Dorofeeva, O. *Thermochim. Acta* **1992**, *200*, 121−150.

(38) Weast, R. C.; Ed. *Chemical Rubber Company handbook of chemistry and physics*, 83rd ed.; CRC Press: Boca Raton, FL, 2002.

(39) van Nes, G.; Vos, A. *Acta Crystallogr., Sect. B* **1978**, *34*, 1947.

(40) Boese, R.; Blaeser, D.; Weiss, H. *Angew. Chem., Int. Ed.* **1999**, *38*, 988.

(41) Kahn, R.; Fourme, R.; Andre, D.; Renaud, M. *Acta Crystallogr., Sect. B* **1973**, *29*, 131.

(42) Donohue, J.; Goodman, S. *Acta Crystallogr.* **1967**, *22*, 352.

(43) Groth, P. *Acta Chem. Scand., Ser. A* **1976**, *30*, 155.

(44) Knobler, C.; Maverick, E.; Trueblood, K. *Acta Chim. Hung.* **1993**, *130*, 523−536.

(45) Nyburg, S.; Luth, H. *Acta Crystallogr., Sect. B* **1972**, *28*, 2992.

(46) Columbus, I.; Biali, S. *J. Org. Chem.* **1993**, *58*, 7029.

van der Waals Force Field Parameters

J. Phys. Chem. B, Vol. 107, No. 35, 2003 **9609**

(47) Nyburg, S.; Gerson, A. *Acta Crystallogr., Sect. B* **1992**, *48*, 103.

(48) van Nes, G.; Vos, A. *Acta Crystallogr., Sect. B* **1979**, *35*, 2593–2601.

(49) Busetti, V.; Mammi, M.; Carazzolo, G. *Z. Kristallogr., Kristallgeom., Kristallphys., Kristallchem.* **1963**, *119*, 310.

(50) Ehrenberg, M. *Acta Crystallogr.* **1965**, *19*, 698.

(51) Jones, G.; Cornell, B.; Horn, E.; Tiekink, E. *J. Crystallogr. Spectrosc. Res.* **1989**, *19*, 715.

(52) Buschmann, J.; Muller, E.; Luger, P. *Acta Crystallogr., Sect. C* **1986**, *42*, 873.

(53) Mossel, A.; Romers, C. *Acta Crystallogr.* **1964**, *17*, 1217.

(54) Hirshfeld, F.; Rabinovich, D. *Acta Crystallogr.* **1967**, *23*, 989.

(55) Destro, R.; Filippini, G.; Gramaccioli, C.; Simonetta, M. *Acta Crystallogr., Sect. B* **1969**, *25*, 2465.

(56) Homan, H.; et al. *J. Org. Chem.* **1997**, *62*, 8503.

(57) Dunitz, J.; Seiler, P. *Acta Crystallogr., Sect. B* **1974**, *30*, 2739–2741.

(58) Kosnikov, A.; Antonovskii, V.; Lindeman, S.; Struchkov, Y.; Zyat'kov, I. *Kristallografiya* **1988**, *33*, 875.

(59) Bondi, A. *Chem. Eng. Data* **1963**, *8*, 371.

(60) Stephenson, R.; Malanowski, S. *Handbook of the Thermodynamics of Organic Compounds*; Elsevier: New York, 1987.

(61) Magnus, A. *Z. Phys. Chem.* **1956**, *9*, 141.

(62) Shieh, C.; McNally, D.; Boyd, R. *Tetrahedron* **1969**, *25*, 3653–3665.

(63) Morawetz, E. *J. Chem. Thermodyn.* **1972**, *4*, 139–144.

(64) DeWit, H.; Miltenburg, J. V.; DeKruif, C. *J. Chem. Thermodyn.* **1983**, *15*, 651.

(65) Chickos, J. S.; Sabbah, R.; Hosseini, S.; Liebman, J. F. *Struct. Chem.* **1996**, *7*, 391–395.

(66) Coolidge, A.; Coolidge, M. *J. Am. Chem. Soc.* **1927**, *49*, 100–104.

(67) Rogers, F. E.; Quan, S. W. *J. Phys. Chem.* **1973**, *77*, 828–831.

(68) Abboud, J.; Jimenez, P.; Roux, M.; Turrion, C.; Lopez-Mardoningo, C.; Sanz, G. *J. Chem. Thermodyn.* **1992**, *24*, 217.

(69) Nichols, G.; Orf, J.; Reiter, S. M.; Chickos, J.; Gokel, G. W. *Thermochim. Acta* **2000**, *346*, 15–28.

(70) Rabinovich, I.; Tel'noi, V.; Terman, L.; Kirillova, A.; Razuvaev, G. *Dokl. Akad. Nauk SSSR* **1962**, *143*, 133.