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The OPLS Potential Functions for Proteins. Energy Minimizations for Crystals of Cyclic Peptides and Crambin

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Abstract: A complete set of intermolecular potential functions has been developed for use in computer simulations of proteins in their native environment. Parameters are reported for 25 peptide residues as well as the common neutral and charged terminal groups. The potential functions have the simple Coulomb plus Lennard-Jones form and are compatible with the widely used models for water, TIP4P, TIP3P, and SPC. The parameters were obtained and tested primarily in conjunction with Monte Carlo statistical mechanics simulations of 36 pure organic liquids and numerous aqueous solutions of organic ions representative of subunits in the side chains and backbones of proteins. Bond stretch, angle bend, and torsional terms have been adopted from the AMBER united-atom force field. As reported here, further testing has involved studies of conformational energy surfaces and optimizations of the crystal structures for four cyclic hexapeptides and a cyclic pentapeptide. The average root-mean-square deviation from the X-ray structures of the crystals is only 0.17 Å for the atomic positions and 3% for the unit cell volumes. A more critical test was then provided by performing energy minimizations for the complete crystal of the protein crambin, including 182 water molecules that were initially placed via a Monte Carlo simulation. The resultant root-mean-square deviation for the non-hydrogen atoms is still ca. 0.2 Å and the variation in the errors for charged, polar, and nonpolar residues is small. Improvement is apparent over the AMBER united-atom force field which has previously been demonstrated to be superior to many alternatives.

Computer simulations are undoubtedly destined to become an increasingly important means for investigating the structures and dynamics of biomolecular systems.[1] At the heart of such theoretical calculations are the force fields that describe the interatomic interactions and the mechanics of deformations of the molecules.[2] There is also little doubt that there will be a continual evolution in force fields with added complexity and improved performance paralleling the availability of computer resources. Our own efforts in this area over the last few years have resulted in the OPLS potential functions for proteins whose development and performance are summarized here. These potential functions have a simple form and they have been parametrized directly to reproduce experimental thermodynamic and structural data on fluids. Consequently, they are computationally efficient and their description of proteins in solution or crystalline environments should be superior to many alterantives that have been developed with limited condensed-phase data. The latter point is pursued here primarily through calculations on the crystal structures for four cyclic hexapeptides, a cyclic pentapeptide, and the protein crambin. Improvements are apparent in comparison to the AMBER united-atom force field[3] which has previously been shown to be superior to many alternatives.[4]

Parametrization

The peptide residues of proteins contain readily identifiable organic subunits such as amides, hydrocarbons, alcohols, thioethers, etc. In view of this and since data are available on the corresponding pure organic liquids, our approach to developing a force field for proteins was to build it up from parameters demonstrated to yield good descriptions of organic liquids. Ultimately, the force field would need to treat both intramolecular terms for bond stretches, angle bends, and torsions, as well as the intermolecular and intramolecular nonbonded interactions. The latter are generally accepted to be the most difficult part of the problem and have been our focus.[3] A simple, computationally efficient form was chosen to represent the nonbonded interactions through Coulomb and Lennard-Jones terms interacting between sites centered on nuclei (eq 1). Thus, the intermolecular inter-

$$\Delta E_{ab} = \sum_{i}^{\text{on a}} \sum_{j}^{\text{on b}} (q_i q_j e^2/r_{ij} + A_{ij}/r_{ij}^{12} - C_{ij}/r_{ij}^{6}) \qquad (1)$$

action energy between molecules a and b is given by the sum of interactions between the sites on the two molecules. The nonbonded contribution to the intramolecular energy is evaluated with the same expression for all pairs of sites separated by more than three bonds. In the OPLS (optimized potentials for liquid simulations) model, each atomic nucleus has an interaction site, except CH_n groups are treated as united atoms centered on the carbon. It is important to note that in this model *no special functions were*

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Table I. Liquids Simulated with the OPLS Potential Functions

liquid	T (°C)	ref	liquid	T (°C)	ref
$HCONH_2$	25	5	pyrrole	25	9
$HCON(CH_3)_2$	25, 100	5	pyridine	25	9
$CH_3CONHCH_3$	100	5	CH_4	−161	10
CH_3OH	25	6	C_2H_6	−89	10
C_2H_5OH	25	6	C_3H_8	−42, 25	10
n-C_3H_7OH	25	6	n-C_4H_{10}	−0.5, 25	10
i-C_3H_7OH	25	6	i-C_4H_{10}	25	10
t-C_4H_9OH	25	6	n-C_5H_{12}	25	10
CH_3SH	6	7	i-C_5H_{12}	25	10
C_2H_5SH	25	7	neo-C_5H_{12}	25	10
$(CH_3)_2S$	25	7	c-C_5H_{10}	25	10
$C_2H_5SCH_3$	25	7	n-C_6H_{14}	25	10
$(C_2H_5)_2S$	25	7	$CH_3CH_2CH{=}CH_2$	25	10
CH_3SSCH_3	25	7	t-$CH_3CH{=}CHCH_3$	25	10
$(CH_3)_2O$	−25	8	C-$CH_3CH{=}CHCH_3$	25	10
$C_2H_5OCH_3$	25	8	$(CH_3)_2C{=}CH_2$	25	10
$(C_2H_5)_2O$	25	8	benzene	25	10
THF	25	8	$CH_3CO_2CH_3$	25	8

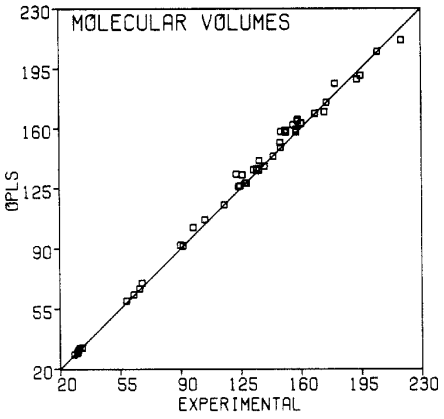

Figure 1. Comparison of computed and experimental volumes per molecule in Å^3 for the liquids in Table I and TIP4P water.

found to be needed to describe hydrogen bonding and there are no additional interaction sites for lone pairs. Another important point is that standard combining rules are used for the Lennard-Jones interactions such that $A_{ij} = (A_{ii}A_{jj})^{1/2}$ and $C_{ij} = (C_{ii}C_{jj})^{1/2}$. The A and C parameters may also be expressed in terms of Lennard-Jones σ's and ϵ's as $A_{ii} = 4\epsilon_i\sigma_i^{12}$ and $C_{ii} = 4\epsilon_i\sigma_i^6$.

The OPLS parameters for the 20 neutral peptide residues reported here were obtained primarily via Monte Carlo simulations for the 36 organic liquids listed in Table I.[5-10] Standard geometries were used for the molecules with fixed bond lengths and bond angles, though torsional motion was included, as described in detail elsewhere.[5-10] Particular emphasis was placed on reproducing the experimental densities and heats of vaporization for the liquids. In view of the simplicity of the functional form (eq 1), the accord with the experimental data is remarkable as illustrated in Figures 1 and 2; the average deviation between the experimental data and the theoretical results is less than 3%. The structural results for the liquids were also shown to be in accord with available experimental data including vibrational spectroscopy and diffraction data for formamide, dimethylformamide (DMF), methanol, ethanol, 1-propanol, 2-methyl-2-propanol, methane, ethane, neopentane, and benzene. The hydrogen bonding in the alcohols, thiols, and amides is well-represented by the OPLS potential functions. It should be noted that the number of unique parameters has been kept to a minimum.[5-10] Thus, only 12 different CH_n groups are used to describe all alkanes, alkenes,

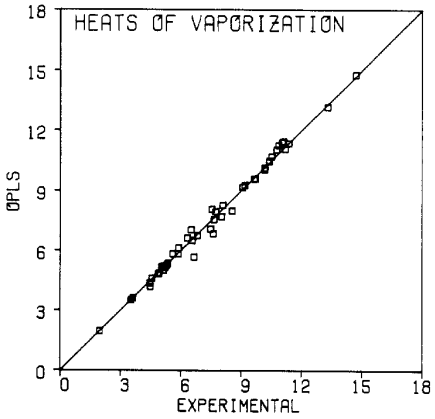

Figure 2. Comparison of computed and experimental heats of vaporization in kcal/mol for the liquids in Table I and TIP4P water.

and benzene,[10] and, for example, the parameters for the OH groups in all alcohols[6] and the carbonyl groups in all amides are the same.[5]

The parametrization for the neutral residues also entailed careful consideration of the interactions between the organic fragments and a water molecule. The water model used in conjunction with the OPLS potentials was TIP4P,[11,12] though the TIP3P[11] or SPC[13] models yield very similar results. For most purposes, these three alternatives may be considered to be interchangeable, though the slightly more complicated TIP4P model gives a better description of the angular variation of hydrogen bond energies. Complexes of a water molecule with amides, ethers, esters, alcohols, thiols, sulfides, azoles, and azines were studied with the OPLS potentials as well as ab initio molecular orbital calculations primarily with the 6-31G(d) basis set.[14] The trends in the ab initio findings for the hydrogen bond strengths and geometries are well reproduced by the OPLS results.[5-9,15] Furthermore, Monte Carlo simulations were carried out for dilute aqueous solutions of formamide,[15] N-methylacetamide (NMA),[15] DMF,[15] methanol,[16] and seven alkanes.[17] For the amides, experimental structural data are limited; however, the computed numbers of amide–water hydrogen bonds are reasonable and the computed heats of hydration, ca. −20 kcal/mol, are in the correct range.[15] Similarly, the hydration of methanol appears reasonable and the computed difference in free energies of hydration for methanol and ethane, 6.75 ± 0.2 kcal/mol, is in excellent accord with the experimental value, 6.93 kcal/mol.[16] The free energy calculations are a powerful diagnostic tool, but very demanding on computer resources.[16] The results for the hydrophobic hydration of the alkanes also revealed no aberrations and yielded pleasing correlations between numbers of water molecules in the first hydration shells and experimental enthalpies and entropies of hydration.[17]

The parametrization for the five charged protein residues, Asp, Glu, Hip (protonated His), Lys, and Arg, and terminal ammonium and carboxylate groups required a somewhat different approach. Since corresponding pure organic liquids cannot be construed in these cases, the emphasis was placed on comparisons with ab initio results for ion–molecule complexes and on Monte Carlo simulations for hydrated ions. Specifically, parameters for Lys, Glu, Asp and the charged terminal groups were developed through a

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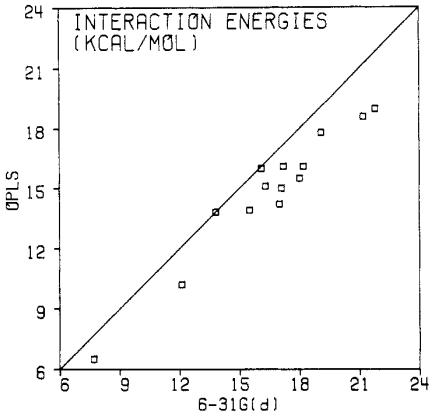
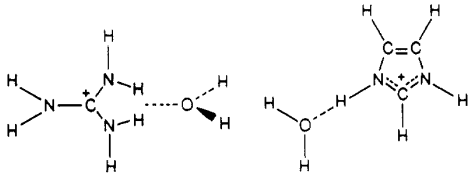


Figure 3. Comparison of interaction energies (kcal/mol) for ion–water complexes obtained with the OPLS potential functions and ab initio 6-31G(d) calculations.

general study of the hydration of ammonium and carboxylate ions.[18] Ab initio calculations were carried out with the 6-31G(d) basis set for low-energy forms of complexes between water and NH_4^+, $CH_3NH_3^+$, and $HCOO^-$.[18,19] The OPLS parameters were chosen to reproduce the resultant optimal geometries and interaction energies, which are also in good accord with gas-phase experimental data.[18,19] In addition, the OPLS parameters were required to yield good agreement with experimental heats of hydration for NH_4^+, $CH_3NH_3^+$, $(CH_3)_4N^+$, $HCOO^-$, and CH_3COO^-.[18] This was demonstrated through Monte Carlo simulations for the five ions in dilute aqueous solution.[18] The structural results were also shown to mirror experimental estimates of hydration numbers for the ammonium and carboxylate groups in Lys, Glu, and Asp from NMR studies of frozen polypeptide solutions.[18,20]

Recently, the OPLS parameters for Arg and Hip have been obtained by fitting to ab initio 6-31G(d) results for complexes of water with guanidinium ion and protonated imidazole.[21] The principal concern was the charge distributions for the ions since the Lennard-Jones parameters were adopted from standard values for nitrogen and carbons (all explicit hydrogens have $\sigma = \epsilon = 0$ in the OPLS potentials). The accord between the OPLS and 6-31G(d) results for low-energy geometries is uniformly good. For example, the OPLS optimal interaction energy and CO distance for **1** are 16.1 kcal/mol and 3.33 Å, whereas the 6-31G(d) values with fixed water and guanidinium geometries are 18.2 kcal/mol and 3.41 Å. And, for **2**, the OPLS predictions for the interaction energy and NO distance are 16.0 kcal/mol and 2.72 Å versus the



1 **2**

6-31G(d) values of 16.1 kcal/mol and 2.85 Å. In general, the accord between the OPLS and 6-31G(d) results is good as illustrated in Figures 3 and 4 for 14 low-energy geometries of water with NH_4^+, $CH_3NH_3^+$, $HCOO^-$, guanidinium ion, and protonated imidazole. The OPLS interaction energies are deliberately designed to be less than the 6-31G(d) results, since the latter are typically somewhat greater than the limited experimental data.[18,19] At this time, fluid simulations have not been executed for guanidinium ion or protonated imidazole in water. Experimental thermodynamic data do not appear to be available in these cases.

The OPLS parameters obtained in this way for 25 common peptide residues and both neutral and charged terminal residues

Table II. OPLS Atom and Group Assignments for Proteins[a]

residue	atom or group	type	residue	atom or group	type
			Main Chains		
Gly	N	3	Ala	N	3
	H(N)	4		H(N)	4
	CH_2^α	5		CH^α	6
	C	1		C	1
	O	2		O	2
Pro	N	3	Aib	N	3
	CH^α	14		H(N)	4
	C	1		C^α	64
	O	2		C	1
				O	2
			Side Chains		
Ala	CH_3^β	7	Val	CH^β	8
Aib	CH_3^β	65		CH_3^γ	7
Pro	CH_2^β	9	Leu	CH_2^β	9
	CH_2^γ	9		CH^γ	8
	CH_2^δ	15		CH_3^δ	7
Ile	CH^β	8	Phe	CH_2^β	9
	CH_2^γ	9		C^γ	11
	CH_3^γ	7		CH^δ	11
	CH_3^δ	10		CH^ϵ	11
				CH^ζ	11
Ser	CH_2^β	22	Cys	CH_2^β	31
	O^γ	23		S^γ	32
	H^γ	24		H^γ	33
Thr	CH^β	25	Met	CH_2^β	9
	O^γ	23		CH_2^γ	34
	$H^\gamma(O)$	24		S^δ	35
	CH_3^γ	7		CH_3^ϵ	36
Tyr	CH_2^β	9	Cystine	CH_2^β	37
	C^γ	11		S^γ	38
	CH^δ	11	Hyp	CH_2^β	9
	CH^ϵ	11	(Pro-OH)	CH^γ	25
	C^ζ	26		CH_2^δ	15
	O^η	23		O^δ	23
	H^η	24		$H^\delta(O)$	24
Asn	CH_2^β	9	Gln	CH_2^β	9
	C^γ	1		CH_2^γ	9
	O^δ	2		C^δ	1
	N^δ	12		O^ϵ	2
	$H^\delta(N)$	13		N^ϵ	12
				$H^\epsilon(N)$	13
Asp	CH_2^β	16	Glu	CH_2^β	9
	C^γ	17		CH_2^γ	16
	O^δ	18		C^δ	17
				O^ϵ	18
His	CH_2^β	9	Hip	CH_2^β	9
	C^γ	45	(His-H^+)	C^γ	49
	N^δ	40		N^δ	46
	$H^\delta(N)$	41		$H^\delta(N)$	47
	CH^δ	44		CH^δ	49
	CH^ϵ	43		CH^ϵ	48
	N^ϵ	42		N^ϵ	46
				$H^\epsilon(N)$	47
Trp	CH_2^β	9	Arg	CH_2^β	9
	C^γ	50		CH_2^γ	57
	CH^δ	45		CH_2^δ	56
	C^δ	50		N^ϵ	54
	N^ϵ	40		$H^\epsilon(N)$	55
	$H^\epsilon(N)$	41		C^ζ	53
	C^ϵ	45		N^η	51
	CH^ϵ	11		$H^\eta(N)$	52
	CH^ζ	11	Hyl	CH_2^β	9
	CH^η	11	(Lys-OH)	CH_2^γ	9
Lys	CH_2^β	9		CH^δ	25
	CH_2^γ	9		O^ϵ	23
	CH_2^δ	9		$H^\epsilon(O)$	24
	CH_2^ϵ	19		CH_2^ϵ	19
	N^ζ	20		N^ζ	20
	$H^\zeta(N)$	21		$H^\zeta(N)$	21

[a] Nomenclature for atoms: ref 22.

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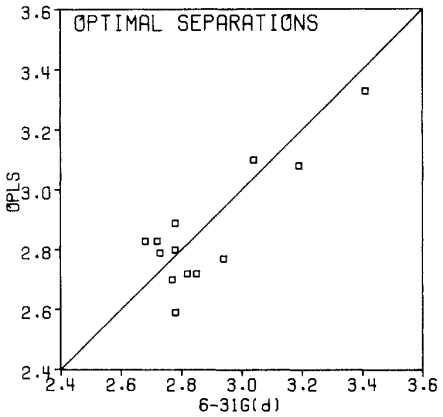


Figure 4. Comparison of optimal separations in Å for ion–water complexes obtained with the OPLS potential functions and ab initio 6-31G(d) calculations.

Table III. OPLS Atom and Group Assignments for Terminal Residues

residue	atom or group	type
	Charged Termini	
$H_3N^+CHRC{=}O$	N	20
	H(N)	21
	CH^{α}	29
	CH_2^{α} (R=H)	27
	C	1
	O	2
$NHCHRCO_2^-$	N	3
	H(N)	4
	CH^{α}	30
	CH_2^{α} (R=H)	28
	C	17
	O	18
	Neutral Termini	
$NHCHRC(O)OCH_3$	N	3
	H(N)	4
	CH^{α}	60
	CH_2^{α} (R=H)	61
	C	58
	O	59
	$O(CH_3)$	62
	CH_3	63
$CH_3C(O)(NHCHRC(O))$	CH_3	7
	C	1
	O	2
$(NHCHRC(O))NHCH_3$	N	3
	H(N)	4
	CH_3	39

are summarized in Tables II–IV. The atom and CH_n group type assignments are given in Tables II and III with use of standard notation,[22] while the actual charges and Lennard-Jones parameters are in Table IV. In all, 65 unique atom and group types are designated, though the number of unique sets of Lennard-Jones parameters is only 19. For reference, the parameters for the TIP4P, TIP3P, and SPC models for water are provided in Table V with use of consistent units. It should be noted that the side chains are each charge balanced to a net charge of 0, +1 or −1. The only charged side chains are for Asp, Glu, Hip, Lys, and Arg. Also, all residues use the Ala backbone except Gly, Pro, and Aib.

Further testing of the OPLS potentials then ensued after incorporation into the AMBER program.[3]

Merger with AMBER

In order to provide a complete energetic description of biomolecular systems, the intramolecular terms for bond length and bond angle variations as well as the torsions and nonbonded terms need to be included. Since substantial work has been done on the former items by others,[2,3] merger of the OPLS nonbonded potential functions and the local vibration and torsional functions from another force field could be considered. AMBER[3] was chosen because it is widely used and because of its documented success in comparison to 15 other force fields for calculations of the crystal structures of 3 cyclic hexapeptides, though we recognize that the test was limited since only Gly and Ala residues were represented.[4]

The bond stretch and angle bend terms in AMBER are quadratic, while the torsional potentials consist of a cosine term

(22) IUPAC–IUB Commission on Biochemical Nomenclature: *Biochemistry* **1970**, *9*, 3471.

Table IV. OPLS Parameters for Proteins

type	q	σ, Å	ϵ, kcal/mol
1	0.500	3.750	0.105
2	−0.500	2.960	0.210
3	−0.570	3.250	0.170
4	0.370	0.0	0.0
5	0.200	3.800	0.118
6	0.200	3.800	0.080
7	0.0	3.910	0.160
8	0.0	3.850	0.080
9	0.0	3.905	0.118
10	0.0	3.905	0.175
11	0.0	3.750	0.110
12	−0.850	3.250	0.170
13	0.425	0.0	0.0
14	0.285	3.800	0.080
15	0.285	3.800	0.118
16	−0.100	3.905	0.118
17	0.700	3.750	0.105
18	−0.800	2.960	0.210
19	0.310	3.905	0.118
20	−0.300	3.250	0.170
21	0.330	0.0	0.0
22	0.265	3.905	0.118
23	−0.700	3.070	0.170
24	0.435	0.0	0.0
25	0.265	3.850	0.080
26	0.265	3.750	0.110
27	0.310	3.800	0.118
28	0.100	3.800	0.118
29	0.310	3.800	0.080
30	0.100	3.800	0.080
31	0.180	3.905	0.118
32	−0.450	3.550	0.250
33	0.270	0.0	0.0
34	0.235	3.800	0.118
35	−0.470	3.550	0.250
36	0.235	3.800	0.170
37	0.300	3.800	0.118
38	−0.300	3.550	0.250
39	0.200	3.800	0.170
40	−0.570	3.250	0.170
41	0.420	0.0	0.0
42	−0.490	3.250	0.170
43	0.410	3.750	0.145
44	0.100	3.750	0.145
45	0.130	3.750	0.145
46	−0.540	3.250	0.170
47	0.460	0.0	0.0
48	0.500	3.750	0.145
49	0.330	3.750	0.145
50	−0.055	3.750	0.145
51	−0.800	3.250	0.170
52	0.460	0.0	0.0
53	0.640	2.250	0.050
54	−0.700	3.250	0.170
55	0.440	0.0	0.0
56	0.310	3.905	0.118
57	0.070	3.905	0.118
58	0.550	3.750	0.105
59	−0.450	2.960	0.210
60	0.250	3.800	0.080
61	0.250	3.800	0.118
62	−0.400	3.000	0.170
63	0.250	3.800	0.170
64	0.200	3.800	0.050
65	0.0	3.960	0.145

Table V. Parameters for Water Models

model	geometry	site	q	σ, Å	ϵ, kcal/mol
TIP4P[a]	r(OH) = 0.9572 Å	O	0.0	3.15365	0.1550
	r(OM) = 0.1500 Å	H	0.520	0.0	0.0
	∠HOH = 104.52°	M	−1.040	0.0	0.0
TIP3P[a]	r(OH) = 0.9572 Å	O	−0.834	3.15061	0.1521
	∠HOH = 104.52°	H	0.417	0.0	0.0
SPC[b]	r(OH) = 1.0000 Å	O	−0.820	3.16557	0.1554
	∠HOH = 109.47°	H	0.410	0.0	0.0

[a] Reference 11. [b] Reference 13.

Table VI. Relative Energies for Conformations of Butane[a]

method	gauche	cis	ref
AMBER/OPLS	1.03	7.08	this work
AMBER—normal	0.89	6.97	this work
AMBER—big	0.37	5.56	this work
AMBER—all atom	0.58	4.57	24
MM2	0.88	4.73	25
MP3/6-311G** + ZPE	0.7	6.0	26
Raman, gas phase	0.89	4.52	27
IR, gas phase	0.97		28
ED, gas phase	0.65	3.6	29

[a] Energies relative to the trans conformer in kcal/mol.

plus the 1,4-nonbonded interaction, both Coulombic and Lennard-Jones. Thus, the torsional potentials are affected by the choice of nonbonded parameters. Furthermore, the 1,4-nonbonded interactions are scaled in AMBER by dividing by factors SCNB and SCEE for the Lennard-Jones and Coulombic terms, respectively. The default value for SCEE is 2.0 and has been used in all calculations reported here. The default value for SCNB is also 2.0 when the "normal" AMBER nonbonded parameters are used.[3] However, in the note added in proof in ref 3, an alternative set of "big" parameters was proposed for CH, CH_2, and CH_3 united atoms adopted from the TIPS potentials.[23] In this case, the recommended SCNB is 8.0.[3] For the purpose of merging the OPLS and AMBER force fields in an uncomplicated manner, it was necessary to readdress the best choices for SCNB and SCEE. This was done by choosing values that gave reasonable agreement between results for conformational surfaces with AMBER/OPLS and "normal" AMBER. These tests are summarized in the next section, followed by more significant tests of the two force fields on crystal structures.

The calculations were executed by using a modified version of AMBER 2.0 on a Microvax II computer in our laboratory. Complete geometry optimizations were carried out with the conjugate gradients procedure.[3] All of the calculations employed a dielectric constant of 1 for evaluating the electrostatic energy. This is the proper choice since the OPLS parameters have been derived in this way and are intended for use on condensed-phase systems.

Conformational Results

Conformational energy surfaces were computed for butane, methyl ethyl ether, and two dipeptides. These calculations indicated that for AMBER/OPLS acceptable choices for SCEE and SCNB are 2.0 and 8.0, i.e., the same as for "big" AMBER.[3] All results for AMBER/OPLS reported here use these values.

For butane, the energies of the gauche and cis conformers relative to trans are listed in Table VI. The AMBER/OPLS and normal AMBER results are similar; the gauche − trans energy difference is on the high side of the range of experimental values[27-30] and of the best available ab initio result.[26]

Table VII. Relative Energies for Conformations of Methyl Ethyl Ether[a]

method	gauche	cis	ref
AMBER/OPLS	1.5	8.7	this work
AMBER—normal	1.6	9.4	this work
AMBER—big	1.6	8.9	this work
AMBER—all atom	1.4	5.3	24
MM2	1.8	4.5	31
4-31G	2.0	7.3	32
IR, gas phase	1.5		33
ED, gas phase	1.2		34

[a] Energies relative to the trans conformer in kcal/mol.

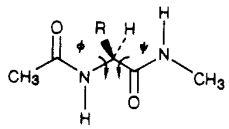
Table VIII. Relative Energies and Torsional Angles (Φ, Ψ) for Conformations of *N*-Acetylglycine *N*-Methylamide

method	C_7	C_5[b]	α	ref
AMBER/OPLS	0.0 (82, −67)	1.7		this work
AMBER—normal	0.0 (77, −64)	3.2	4.1 (66, 35)	3
AMBER—all atom	0.0 (75, −65)	3.3	4.1 (60, 39)	3
UNICEPP	0.0 (83, −76)	0.9	1.2 (71, 52)	35
ECEPP/2	0.0 (79, −73)	1.2	1.2 (73, 74)	36
4-21G	0.0 (83, −71)	0.8		37
PCILO	0.0 (80, −40)	2.0		38
IR, NMR (CCl_4)	(75, −50)			39
X-ray (crystal)	(109, −21)			40

[a] Energies in kcal/mol, angles (Φ and Ψ) in deg. [b] The C_5 conformation has $\Phi = \Psi = 180°$.

The corresponding results for methyl ethyl ether are summarized in Table VII. The AMBER/OPLS and normal AMBER results are again similar; the predicted gauche − trans energy differences are also close to the experimental findings.[33,34]

The two standard dipeptides that were studied are *N*-acetylglycine *N*-methylamide (GA) and *N*-acetylalanine *N*-methylamide (AA). Rough energy maps were constructed by varying Φ and ψ in 30° intervals between −180° and 180°. The local energy



GA: R=H
AA: R=CH_3

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