J. Phys. Chem. **1990**, *94*, 8897-8909 **8897**

DREIDING: A Generic Force Field for Molecular Simulations

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We report the parameters for a new generic force field, DREIDING, that we find useful for predicting structures and dynamics of organic, biological, and main-group inorganic molecules. The philosophy in DREIDING is to use general force constants and geometry parameters based on simple hybridization considerations rather than individual force constants and geometric parameters that depend on the particular combination of atoms involved in the bond, angle, or torsion terms. Thus all bond distances are derived from atomic radii, and there is only one force constant each for bonds, angles, and inversions and only six different values for torsional barriers. Parameters are defined for all possible combinations of atoms and new atoms can be added to the force field rather simply. This paper reports the parameters for the "nonmetallic" main-group elements (B, C, N, O, F columns for the C, Si, Ge, and Sn rows) plus H and a few metals (Na, Ca, Zn, Fe). The accuracy of the DREIDING force field is tested by comparing with (i) 76 accurately determined crystal structures of organic compounds involving H, C, N, O, F, P, S, Cl, and Br, (ii) rotational barriers of a number of molecules, and (iii) relative conformational energies and barriers of a number of molecules. We find excellent results for these systems.

I. Introduction

A great deal of progress has been made over the last two decades in developing force fields suitable for predicting the structures and dynamics of molecules. Examples include the MM2/MMP2 force fields of Allinger and co-workers,[2] which have been useful for a variety of organic and inorganic systems, the AMBER force field of Kollman and co-workers[3] for proteins and nucleic acids, and the CHARMM force field of Karplus and co-workers[4] for proteins and nucleic acids. In these specialized force fields, there are often subtle distinctions in force constants and geometric parameters for similar atoms in slightly different environments, and it is often not clear how to generalize for new atoms or new bond types. In order to facilitate prediction of structures for molecules where there are little or no experimental data, we have developed a generic approach to force fields using parameters that are deliberately restricted to very simple rules. This may lead to lower accuracy for a specialized subset of molecules but has the virtue of allowing reasonably accurate predictions to be made for novel combinations of elements. In this paper we discuss a simple generic force field, DREIDING, that we have found useful for predicting structures and dynamics of organic, biological, and main-group inorganic molecules.

II. The DREIDING Force Field

A. Atom Types. The elements of the DREIDING force field are the *atom types.* Atoms with the same atom type are treated *identically* in the molecular mechanics force field. Each atom type uses a five-character mnemonic label. The first two characters correspond to the chemical symbol (e.g., N_ is nitrogen, Te is tellurium), where elements with one letter have an underscore.

The third character indicates hybridization or geometry: 1 = linear (sp^1), 2 = trigonal (sp^2), and 3 = tetrahedral (sp^3). In addition, an sp^2 atom involved in a resonance situation (e.g., in an aromatic ring) is denoted R. Thus, ethane uses C_3, ethylene uses C_2, benzene uses C_R, while acetylene uses C_1.

The fourth character is used to indicate the number of implicit hydrogens (hydrogens that are not included explicitly in the calculations). Thus C_32 is a tetrahedral carbon with two implicit hydrogens. For describing folding of polyethylene polymer chains, we could ignore the hydrogens and use only C_32.

The fifth character is used to indicate alternate characteristics of the atom such as formal oxidation state.

The standard DREIDING atom types are listed in Table I along with various parameters. These rules are easy to program so that the force field types are assigned automatically from examining the topology of a structure.

The___HB type denotes a hydrogen atom capable of forming hydrogen bonds (see section II.I). The H_b is the bridging hydrogen of diborane.

B. Form of the Force Field. The potential energy for an arbitrary geometry of a molecule is expressed as a superposition of valence (or bonded) interactions (E_{val}) that depend on the specific connections (bonds) of the structure and nonbonded interactions (E_{nb}) that depend only on the distance between the atoms

$$E = E_{val} + E_{nb} \tag{1}$$

In DREIDING the valence interactions consist of bond stretch (E_B, two-body), bond-angle bend (E_A, three-body), dihedral angle torsion (E_T, four-body), and inversion terms (E_I, four-body)

$$E_{val} = E_B + E_A + E_T + E_I \tag{2}$$

while the nonbonded interactions consist of van der Waals or dispersion (E_{vdw}), electrostatic (E_Q), and explicit hydrogen bonds (E_{hb}) terms

$$E_{nb} = E_{vdw} + E_Q + E_{hb} \tag{3}$$

The forms of these terms are described next.

C. Bond Stretch. DREIDING describes the bond stretch interaction either as a simple harmonic oscillator

$$E = \tfrac{1}{2}k_e(R - R_e)^2 \tag{4a}$$

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(2) (a) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127. (b) Sprague, J. T.; Tai, J. C.; Yuh, Y.; Allinger, N. L. *J. Comput. Chem.* **1987**, *8*, 581. (c) Burkert, U.; Allinger, N. L.; *Molecular Mechanics*; American Chemical Society: Washington, DC, 1982; ACS Monograph 177.

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TABLE I: Geometric Valence Parameters for DREIDING

atom	bond radius R_I^0, Å	bond angle, deg	atom	bond radius R_I^0, Å	bond angle, deg
H_	0.330	180.0	Si3	0.937	109.471
H__HB	0.330	180.0	P_3	0.890	93.3
H_b	0.510	90.0	S_3	1.040	92.1
B_3	0.880	109.471	Cl	0.997	180.0
B_2	0.790	120.0	Ga3	1.210	109.471
C_3	0.770	109.471	Ge3	1.210	109.471
C_R	0.700	120.0	As3	1.210	92.1
C_2	0.670	120.0	Se3	1.210	90.6
C_1	0.602	180.0	Br	1.167	180.0
N_3	0.702	106.7	In3	1.390	109.471
N_R	0.650	120.0	Sn3	1.373	109.471
N_2	0.615	120.0	Sb3	1.432	91.6
N_1	0.556	180.0	Te3	1.280	90.3
O_3	0.660	104.51	I_	1.360	180.0
O_R	0.660	120.0	Na	1.860	90.0
O_2	0.560	120.0	Ca	1.940	90.0
O_1	0.528	180.0	Fe	1.285	90.0
F_	0.611	180.0	Zn	1.330	109.471
Al3	1.047	109.471			

or as the Morse function

$$E = D_e[e^{-(\alpha nR-R_e)} - 1]^2 \tag{5a}$$

The Morse function is a more accurate description since (5a) includes anharmonic terms near equilibrium (R_e) and leads to a finite energy (D_e) for breaking the bond. However, in many applications the starting geometry for new structures may be very approximate (say, obtained by sketching molecules on a graphics screen, which might lead to distances a factor of 10 too large or too small) and it is essential that the force field quickly adjust to the optimum geometry. Since the Morse function (5) leads to nearly zero forces for very large R and the harmonic function leads to increasingly large restoring forces as R is increased from R_e, we use the harmonic form as the default for DREIDING and denote calculations using the Morse form as DREIDING/M. In the latter case we use the harmonic function (4a) in the initial stage of geometry optimization and the Morse function (5a) for refined calculations.

Writing the force constant as

$$k_e = \left(\frac{\delta^2 E}{\delta R^2}\right)_{R=R_e} \tag{4b}$$

leads to

$$\alpha = \left[\frac{k_e}{2D_e}\right]^{1/2} \tag{5b}$$

for the Morse scale parameter.[5]

To predict the equilibrium bond distance R_{IJ}^0 for bond IJ, we assume additivity of bond radii

$$R_{IJ}^0 = R_I^0 + R_J^0 - \delta \tag{6}$$

where the bond radii R_I^0 are based on structural data of standard reference molecules and $\delta = 0.01$ Å. The bond radius R_J^0 is defined in terms of the experimental bond length[6,7] of atom J to CH_3 (or another single bond to carbon). The resulting radii are listed in Table I.

In DREIDING we set all energy parameters for single bonds to

$$K_{IJ}(1) = 700\ (\text{kcal/mol})/\text{Å}^2 \tag{7}$$

$$D_{IJ}(1) = 70\ \text{kcal/mol} \tag{8}$$

independent of I,J. [For cases where atoms of two different bond orders are bonded (e.g., C_3–C_2 bond of propane) the default is to use the parameters for a single bond.] This restriction to one force constant parameter and one bond energy is oversimplified; however, it is well-defined for any possible pair of atoms and leads to reasonably accurate equilibrium structures.

For a multiple bond with bond order n, the parameters are taken as

$$K_{IJ}(n) = nK_{IJ}(1) \tag{9a}$$

$$D_{IJ}(n) = nD_{IJ}(1) \tag{9b}$$

D. Angle Bend. For two bonds IJ and JK sharing a common atom, the three-body angle bend terms are all taken of the harmonic cosine form

$$E_{IJK} = \tfrac{1}{2}C_{IJK}[\cos\theta_{IJK} - \cos\theta_J^0]^2 \tag{10a}$$

where θ is the angle between bonds IJ and JK. The equilibrium angles θ_J^0 (see Table I) are assumed independent of I and K, and were obtained from standard reference structures of the parent hydrides.[6] Where the structural data were unavailable, the θ_J^0 were extrapolated from nearby elements in the same column of the periodic table.

The harmonic angle form

$$E_{IJK} = \tfrac{1}{2}K_{IJK}[\theta_{IJK} - \theta_J^0]^2 \tag{11}$$

is in common use but we prefer (10a) because (11) does not generally lead to zero slope as θ approaches 180°.

The C_{IJK} in (10a) is related to the force constant K_{IJK} by

$$C_{IJK} = \frac{K_{IJK}}{(\sin\theta_J^0)^2} \tag{10b}$$

For molecules with linear equilibrium geometries ($\theta_J^0 = 180°$), we replace (10a) with[28]

$$E_{IJK} = K_{IJK}[1 + \cos\theta_{IJK}] \tag{10'}$$

The force constants for all angle bend interactions are taken as

$$K_{IJK} = 100\ (\text{kcal/mol})/\text{rad}^2 \tag{12}$$

independent of I, J, and K.

E. Torsion. The torsion interaction for two bonds IJ and KL connected via a common bond JK is taken of the form

$$E_{IJKL} = \tfrac{1}{2}V_{JK}\{1 - \cos[n_{JK}(\varphi - \varphi_{JK}^0)]\} \tag{13}$$

where φ is the dihedral angle (angle between the IJK and JKL planes), n_{JK} is the periodicity (an integer), V_{JK} is the barrier to rotation (always positive), and φ_{JK}^0 is the equilibrium angle. The form of (13) is chosen so that the torsion energy is zero at the equilibrium angle and never negative. Because of symmetry (zero slope at 0° and 180°), the torsion potential must be a maximum or minimum at 0° and 180° and there are only discrete choices for φ_{JK}^0 (multiple of $180°/n_{JK}$). The parameters V_{JK}, n_{JK}, and φ_{JK}^0 are taken as independent of I and L.

The V_{JK} is taken as the *total* barrier after adding all possible I and L terms to the energy expression, but the energy is renormalized by the total number of terms having a common J and K. Thus, for a substituted ethane (involving C_3 for J and K) $V_{JK} = 2.0$ kcal/mol and the program uses a barrier of $V_{IJKL} = 2/9$ for each of the nine possibilities of I and L. Similarly, for a substituted ethylene, $V_{JK} = 45$ kcal/mol and the program uses $V_{IJKL} = 45/4$ for each of the four possibilities of I and L.

In DREIDING the torsional parameters are based on hybridization and are independent of the particular atoms involved.

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(5) The cubic term in the expansion of (5a) about $R = R_e$ is $k'_e \equiv (\delta^3 E/\delta R^3)_{R=R_e} = -3\alpha k_e$. For comparison, the MM2 force field[2] uses a cubic term $k'_e = -6k_e$, a value we would obtain if $D_e = k_e/8$. For $k_e = 700$, this would yield $D_e = 87.5$.

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The various standard cases are as follows:

(a) A dihedral single bond involving two sp^3 atoms (*J*,*K* = X_3)

$$V_{JK} = 2.0\ \text{kcal/mol},\quad n_{JK} = 3,\quad \varphi^0_{JK} = 180° \text{ (or } 60°) \tag{14}$$

(b) A dihedral single bond involving one sp^2 center and one sp^3 center {e.g., the C–C bond in acetic acid [$CH_3C(O)$–OH)]}: (*J* = X_2, X_R; *K* = X_3)

$$V_{JK} = 1.0\ \text{kcal/mol},\quad n_{JK} = 6,\quad \varphi^0_{JK} = 0° \tag{15}$$

(c) A dihedral double bond involving two sp^2 atoms (*J*,*K* = X_2)

$$V_{JK} = 45\ \text{kcal/mol},\quad n_{JK} = 2,\quad \varphi^0_{JK} = 180° \text{ (or } 0°) \tag{16}$$

(d) A dihedral resonance bond (bond order = 1.5) involving two resonant atoms (*J*,*K* = X_R)

$$V_{JK} = 25\ \text{kcal/mol},\quad n_{JK} = 2,\quad \varphi^0_{JK} = 180° \text{ (or } 0°) \tag{17}$$

(e) A dihedral single bond involving two sp^2 or resonant atoms[8] [e.g., the middle bond of butadiene] (*J*,*K* = X_2, X_R)

$$V_{JK} = 5\ \text{kcal/mol},\quad n_{JK} = 2,\quad \varphi^0_{JK} = 180° \tag{18}$$

(f) An exception to (e) is that for an exocyclic dihedral single bond involving two aromatic atoms [e.g., a phenyl ester or the bond between the two rings of biphenyl] (*J*,*K* = X_R)

$$V_{JK} = 10\ \text{kcal/mol},\quad n_{JK} = 2,\quad \varphi^0_{JK} = 180° \tag{19}$$

(g) For dihedrals involving one or two sp^1 atoms (X_1), monovalent atoms (F, Cl, Na, K, ...), or metals (Fe, Zn, ...)

$$V_{JK} = 0.0 \tag{20}$$

Elements of the oxygen column (column 16) having two single bonds are denoted as X_3; however, the rotational barriers are best understood by thinking of the atoms in terms of the s^2p^4 configuration, where two singly occupied p orbitals are used to make the two bonds (with a bond angle[6] of ~92° for S, Se, and Te and 104.5° for O), leaving a p line pair perpendicular to the bonds (the pπ lone pair). The pπ lone pair is stabilized by overlapping a singly occupied (bond) orbital on an adjacent center. As a result HSSH leads to an optimum torsion angle[6] of 90.4° as does crystalline HOOH (gas-phase HOOH has an optimum torsion angle of 111°). Thus

(h) A dihedral single bond involving two sp^3 atoms of the oxygen column (*J*,*K* = X_3 of column 16)

$$V_{JK} = 2.0\ \text{kcal/mol},\quad n_{JK} = 2,\quad \varphi^0_{JK} = 90° \tag{21}$$

[however, the interaction with an sp^3 atom of another column is given in eq 14 above].

(i) For dihedral bonds involving an sp^3 atom of the oxygen column with an sp^2 or resonant atom of another column, the pπ pair and the oxygen-like prefers to overlap the π orbitals of the sp^2 atom, leading to a planar configuration (*J* = X_3 of column 16, *K* = X_2,X_R)

$$V_{JK} = 2.0\ \text{kcal/mol},\quad n_{JK} = 2,\quad \varphi^0_{JK} = 180° \tag{22}$$

(j) An exception to the above principles is made for the case of a dihedral single bond involving one sp^2 atom (*J* = X_2, X_R) and one sp^3 atom (*K* = X_3) (for example, the single bond of propene). The problem here is that for a system such as propene there is a 3-fold barrier with the sp^3 center eclipsing the double bond, whereas for the CC bond, say, of acetate anion (CH_3–C–OO^-), the barrier should have 6-fold character [as in (15)]. To accommodate this we use (15) *unless I* is *not* an sp^2 center (X_2 or X_R); otherwise we use the following *I* ≠ X_2, X_R; *J* = X_2, X_R; *K* = X_3

$$V_{JK} = 2.0\ \text{kcal/mol},\quad n_{JK} = 3,\quad \varphi^0_{JK} = 180° \tag{23}$$

TABLE II: The van der Waals Parameters for DREIDING

atom	R_0 Å	D_0, kcal/mol	ζ	source
H	3.195	0.0152	12.382	*n*-hexane crystal[11a]
H__b	3.195	0.0152	12.382	interpolation
H_HB	3.195	0.0001	12.0	H_2O dimer
B	4.02	0.095	14.23	interpolation
C	3.8983	0.0951	14.034	Williams[11a]
N	3.6621	0.0774	13.843	Williams[11a]
O	3.4046	0.0957	13.483	Williams[11d]
F	3.4720	0.0725	14.444	Williams[11b]
Al	4.39	0.31	12.0	interpolation
Si	4.27	0.31	12.0	interpolation
P	4.1500	0.3200	12.0	P_4 crystal
S	4.0300	0.3440	12.0	S_8 crystal
Cl	3.9503	0.2833	13.861	Williams[11c]
Ga	4.39	0.40	12.0	interpolation
Ge	4.27	0.40	12.0	interpolation
As	4.15	0.41	12.0	interpolation
Se	4.03	0.43	12.0	interpolation
Br	3.95	0.37	12.0	interpolation
In	4.59	0.55	12.0	interpolation
Sn	4.47	0.55	12.0	interpolation
Sb	4.35	0.55	12.0	interpolation
Te	4.23	0.57	12.0	interpolation
I	4.15	0.51	12.0	interpolation
Na^+	3.144	0.5	12.0	DREIDING/A
Ca^{2+}	3.472	0.05	12.0	DREIDING/A
Fe^{2+}	4.54	0.055	12.0	DREIDING/A
Zn^{2+}	4.54	0.055	12.0	DREIDING/A
		Implicit Hydrogens		
C_R1	4.23	0.1356	14.034	benzene crystal
C_34	4.2370	0.3016	12.0	CH_4 crystal
C_33	4.1524	0.2500	12.0	interpolation
C_32	4.0677	0.1984	12.0	interpolation
C_31	3.9830	0.1467	12.0	interpolation

TABLE III: Valence Force Constants for DREIDING

bonds		
n = 1	*K* = 700 (kcal/mol)/Å^2	*D* = 70 kcal/mol
n = 2	*K* = 1400 (kcal/mol)/Å^2	*D* = 140 kcal/mol
n = 3	*K* = 2100 (kcal/mol)/Å^2	*D* = 210 kcal/mol
angles	*K* = 100 (kcal/mol)/rad^2	
inversions:		
X_2, X_R	*K* = 40(kcal/mol)/rad^2	$\Psi_0 = 0°$
*C*_31	*K* = 40(kcal/mol)/rad^2	$\Psi_0 = 54.74°$
X_3	*K* = 0	

The barriers in (14)–(23) are based roughly on values for the carbon row. They should generally decrease for other rows of the periodic table. However, we eschew such subtleties here.

F. Inversion. For an atom *I* bonded to exactly three other atoms, *J*, *K*, *L*, it is often necessary to include an energy term describing how difficult it is to force all three bonds into the same plane (inversion) or how favorable it is to keep the bonds in the same plane. Thus for planar molecules such as ethylene, the use of bond angle terms will not in general lead to the proper restoring force toward the planar configuration, and it is necessary to add an explicit four-body inversion term. Similarly for a nonplanar molecule such as ammonia (where the barrier to inversion is 6 kcal/mol), the constants used for bond angle terms may not lead to the correct inversion barrier, requiring an explicit four-body term to correctly describe the inversion energy. (In fact, for DREIDING the inversion barriers of NH_3, PH_3, etc., are well described without explicit inversion terms.)

A number of approaches have been adapted to describe such inversion terms. Denoting the angle between the *IL* bond and the *JIK* plane as Ψ, spectroscopists have often used the form

$$E^{s}_{\text{inv}}(\Psi) = \tfrac{1}{2}K_{\text{inv}}(\Psi - \Psi_0)^2 \tag{24}$$

[We define Ψ_0 so that it is zero for a normal planar molecule (where the projection of the *IL* bond onto the *JIK* plane points away from the bisector of the *IJ* and *IL* bonds).]

In the literature on biological simulations, it has been more common to use expressions in which the inversion is treated as if it were an (improper) torsion. Thus, the CHARMM force field[4] uses

$$E^{c}_{\text{inv}}(\phi) = \tfrac{1}{2}K_{\text{inv}}(\phi - \phi_0)^2 \tag{25}$$

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(8) For the exocyclic bond of an aromatic carbon to a heteroatom having a lone pair (e.g., NH_2, OH), the interaction of the lone pair with the ring leads to the N or O being described as N_R or O_R, so that (18) applies to the torsions involving this C_R–N_R or C_R–O_R dihedral.

TABLE IV: DREIDING Torsion Parameters for Equivalent Central Atoms

atom	n	V_{JJ}, kcal/mol	φ, deg
H_		0	
B_3	3	2.0	180
C_3	3	2.0	180
C_R	2	25.0	180
C_2	2	45.0	180
C_1		0	
N_3	3	2.0	180
N_R	2	25.0	180
N_2	2	45.0	180
N_1		0	
O_3	2	2.0	90
O_R	2	25.0	180
O_2		45.0	180
O_1		0	
F_		0	
Al3	3	2.0	180
Si	3	2.0	180
P_3	3	2.0	180
S_3	2	2.0	90
Cl		0	
Ga3	3	2.0	180
Ge	3	2.0	180
As3	3	2.0	180
Se3	2	2.0	90
Br		0	
In3	3	2.0	180
Sn3	3	2.0	180
Sb3	3	2.0	180
Te3	2	2.0	90
I_		0	
Na		0	
Ca		0	
Fe		0	
Zn		0	

TABLE V: Hydrogen Bond Parameters for DREIDING (Based on $(H_2O)_2$)

				water dimer		
convention for charges	Q_H for H_2O, e	R_{hb}, Å	D_{hb}, kcal/mol	E, kcal/mol	$R_{O\cdots O}$, Å	$\theta_{OH\cdots O}$ deg
experiment	0.33	2.75	4.0	6.13	2.94	176.1
gasteiger	0.21	2.75	7.0	−6.05	2.93	178.6
no charges[a]	0.00	2.75	9.0	−6.03	2.92	179.9

[a] DREIDING/A uses R_{hb} = 2.75 Å and D_{hb} = 9.5 kcal/mol.

where ϕ is the improper torsion angle of IJ with respect to KL using the JK pseudobond dihedral (the angle between the IJK and JKL planes). A second improper torsion approach (used in AMBER[3]) is to consider one bond (say, IL) as special and to write the energy as

$$E^{a}_{inv}(\theta) = \tfrac{1}{2}K_{inv}\{1 - \cos[n(\theta - \theta_0)]\} \tag{26}$$

where θ is the angle between JIL and KIL planes and $n = 2$ (for planar centers) or $n = 3$ (for tetrahedral centers). MM2 uses the form[2]

$$E_{inv}(\alpha) = \tfrac{1}{2}K_{inv}(\alpha - \alpha_0)^2 \tag{27}$$

where $\alpha = \Psi - \phi$.

Although the improper torsion formulations are easier to program, we prefer the spectroscopic inversion because of its close correspondence to chemical concepts. However, in order that the energy have zero slope for planar configurations ($\Psi \to 180°, 0°$), we replace (24) with the form

$$E^{d}_{IJKL} = \tfrac{1}{2}C_1(\cos\Psi - \cos\Psi^0_I)^2 \tag{28a}$$

where

$$C_I = K_I/(\sin\Psi^0_I)^2 \tag{28b}$$

and K_I is the force constant. For systems with planar equilibrium geometries ($\Psi^0_1 = 0°$) we replace (28a) with[28]

$$E_{IJKL} = K_I[1 - \cos\Psi_I] \tag{28c}$$

TABLE VI: Geometric Valence Parameters for DREIDING/A

atom	bond radius R^0_I, Å	bond angle, deg	atom	bond radius R^0_I, Å	bond angle, deg
H_	0.330	180.0	Al3	1.071	109.471
H___HB	0.330	180.0	Si3	0.937	109.471
C_3	0.770	109.471	P_3	0.890	109.471
C_R	0.700	120.0	S_31	1.04	97.2
C_2	0.670	120.0	S_3	1.01	104.2
C_1	0.602	180.0	Cl	0.997	180.0
N_3	0.700	109.471	Br	1.167	180.0
N_R	0.620	120.0	Na	0.97	90.0
N_2	0.620	120.0	Ca	0.99	90.0
N_1	0.388	180.0	Ti	1.31	90.0
O_3	0.660	109.471	Fe	1.305	90.0
O_R	0.660	120.0	Zn	1.280	109.471
O_2	0.560	120.0	Ru	1.305	90.0
F_	0.611	180.0			

TABLE VII: van der Waals Parameters for DREIDING/A[a]

atom	R_0, Å	D_0, kcal/mol	atom	R_0, Å	D_0, kcal/mol
H_	3.2000	0.0100	N_R	3.6950	0.1450
H___HB	2.4000	0.000	N_1	3.6950	0.1450
C_33	4.1800	0.3050	O_32	3.7100	0.4150
C_32	4.0800	0.2150	O_31	3.6100	0.3050
C_31	3.9800	0.1450	O_3	3.5100	0.2150
C_3	3.8800	0.0950	O_2	3.5100	0.2150
C_22	4.0800	0.2150	O_R	3.5100	0.2150
C_21	3.9800	0.1450	O_R1	3.6100	0.2150
C_2	3.8800	0.0950	F_	3.2850	0.3050
C_R2	4.0800	0.2150	Na	3.1440	0.5000
C_R1	3.9800	0.1450	Al3	4.6150	0.0650
C_R	3.8800	0.0950	Si3	4.4350	0.0950
C_11	3.9800	0.1450	P_3	4.2950	0.2150
C_1	3.8800	0.0950	S_31	4.2400	0.3050
N_33	3.9950	0.4150	S_3	4.1400	0.2150
N_32	3.8950	0.3050	Cl	3.9150	0.3050
N_31	3.7950	0.2150	Br	4.2150	0.3050
N_3	3.6950	0.1450	Ca	3.4720	0.0500
N_22	3.8950	0.3050	Ti	4.5400	0.0550
N_21	3.7970	0.2150	Fe	4.5400	0.0550
N_2	3.6950	0.1450	Zn	4.5400	0.0550
N_R2	3.8950	0.3050	Ru	4.5400	0.0550
N_R1	3.7950	0.2150			

[a] For X6 potentials, use ζ = 12.0000.

For nonplanar molecules the contribution of (28) to the barrier for inversion is

$$E_{bar} = 2C_I[\sin(\tfrac{1}{2}\Psi^0_I)]^2 \tag{28d}$$

For nonplanar geometries the inversion expression in (28) treats bond IL in a way slightly different from bonds IJ and IK, and hence in DREIDING we add together all three possible inversion terms with each weighted by a factor of 1/3.

The parameters in (28) are defined only for atoms that can make three bonds and we use force constants as follows:

(a) For all planar molecules (I = X_2,X_R)

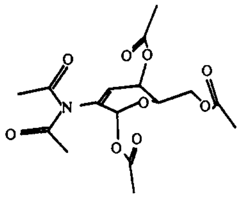
$$K_I = 40\ (\text{kcal/mol})/\text{rad}^2 \tag{29}$$

(b) For nonplanar molecules where the central atom is in the nitrogen column (I = X_3), we find that the angle terms account properly for the inversion barrier in XH_3 without the need for additional inversion terms. Thus with the harmonic cos θ angle term (10) NH_3 and PH_3 lead to barriers of 7.4 and 29.5 kcal/mol respectively, while the harmonic theta angle term (11) leads to 8.1 and 32.6, respectively. Since these values are both in reasonable agreement with experiment (6 and >30, respectively), we take $K_I = 0$ and ignore such inversion terms.

(c) For nonplanar molecules with four or more bonds, the angle interactions will normally prevent inversion of the center and we do not include explicit inversion terms. Although the energy $E(\Psi)$ should have the symmetry

$$E(-\Psi) = E(+\Psi) \tag{30}$$

it is sometimes useful to bias the calculations so that (30) is *not*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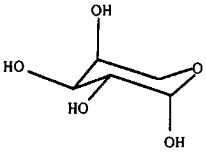
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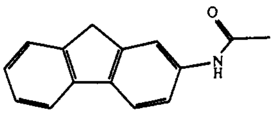
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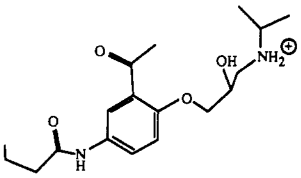
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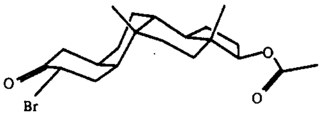
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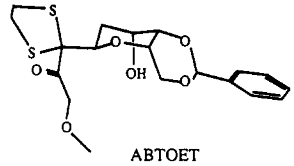
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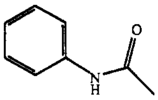
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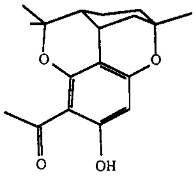
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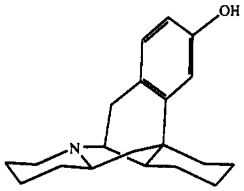
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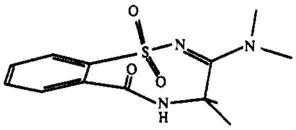
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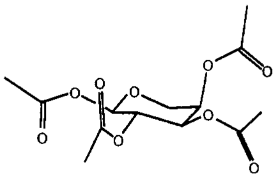
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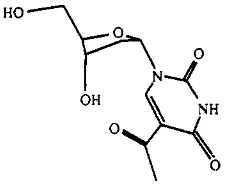
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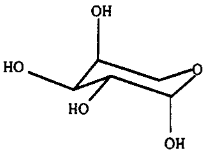
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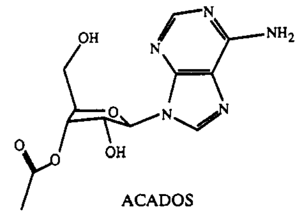
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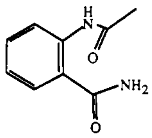
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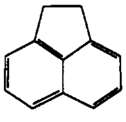
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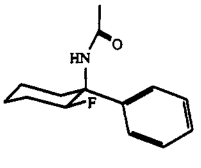
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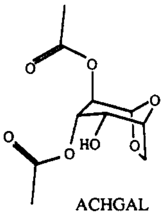
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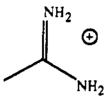
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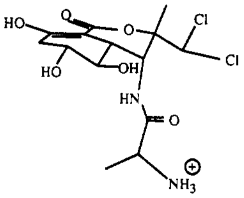
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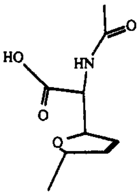
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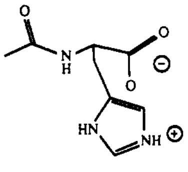
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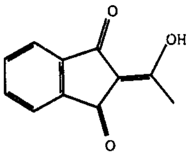
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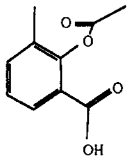
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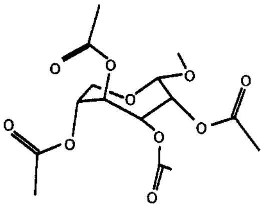
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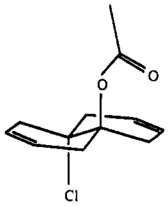
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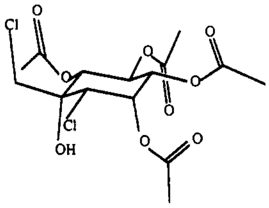
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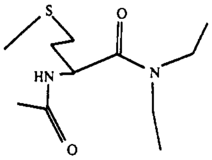
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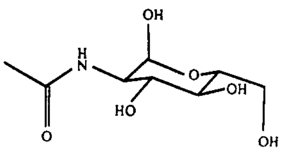
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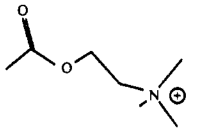
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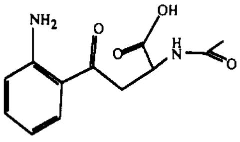
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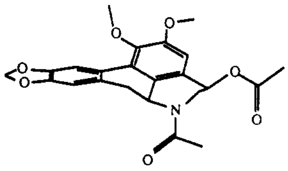
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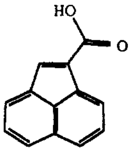
Figure 1. The 76 molecules studied in Tables VIII–X.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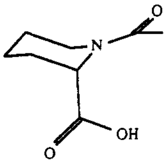
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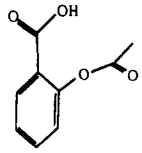
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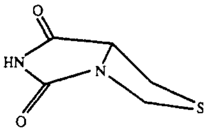
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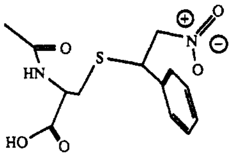
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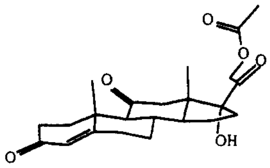
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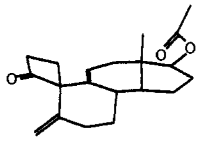
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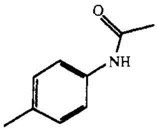
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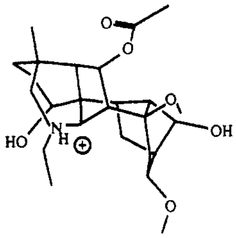
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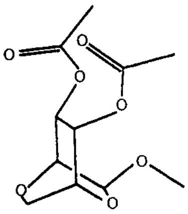
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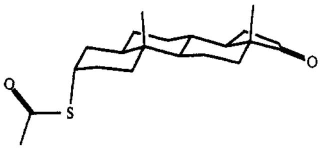
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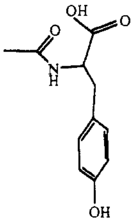
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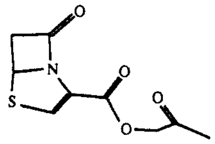
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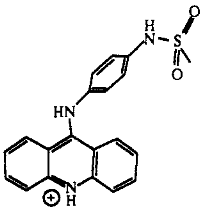
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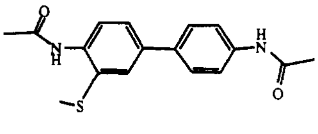
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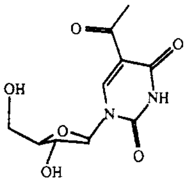
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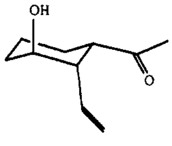
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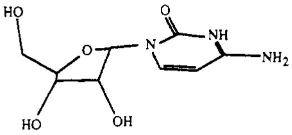
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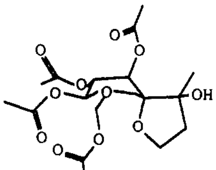
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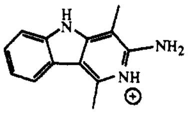
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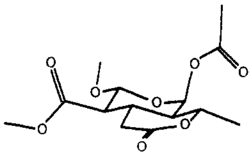
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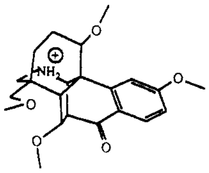
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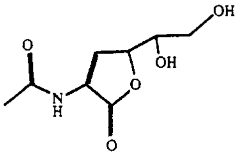
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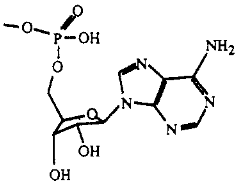
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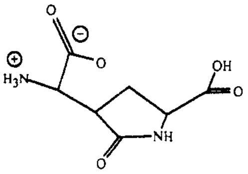
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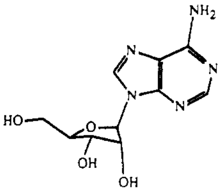
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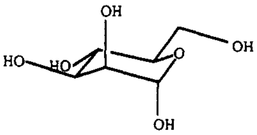
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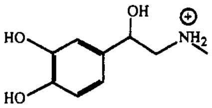
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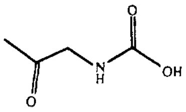
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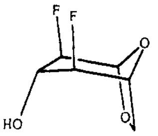
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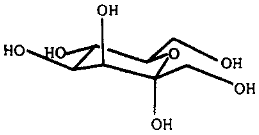
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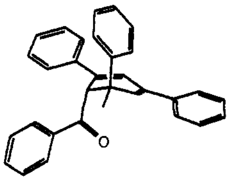
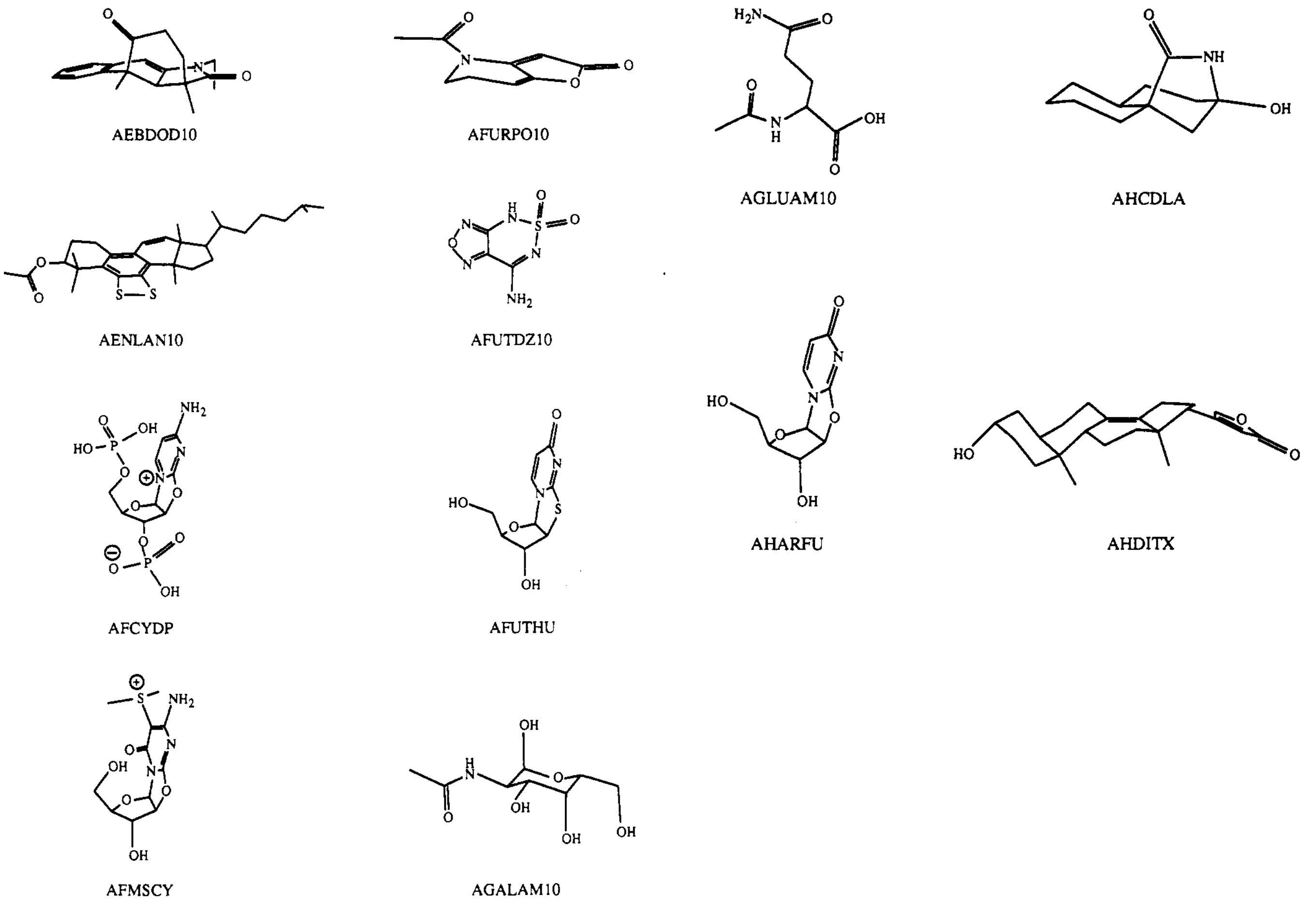

ADYPNL

Figure 1. Continued.



AEBDOD10

AENLAN10

AFCYDP

AFMSCY

AFURPO10

AFUTDZ10

AFUTHU

AGALAM10

AGLUAM10

AHARFU

AHCDLA

AHDITX

Figure 1. Continued.

satisfied. The most common example occurs when one wants to force a specific stereochemistry at a center while calculating structures or dynamics. To do this we use the form (24) where Ψ_0 is defined so as to be positive for the desired stereochemistry. In this case we use K_I = 40 kcal/mol to ensure retention of stereochemistry. This is particularly important when implicit hydrogens are used for the C_α atoms of amino acids (I = C_31).

G. Nonbonded Interactions. The two common expressions for describing van der Waals nonbonded interactions[9] are the Lennard-Jones 12-6 type expression (denoted LJ)

$$E^{LJ}_{vdw} = AR^{-12} - BR^{-6} \tag{31}$$

and the exponential-6 form (denoted X6)[10]

$$E^{X6}_{vdw} = Ae^{-CR} - BR^{-6} \tag{32}$$

The LJ form is simpler (two parameters rather than three) and faster to compute (eliminating a square root and an exponentiation); however, our experience is that the X6 form gives a somewhat better description of short-range interactions. Thus, DREIDING allows either form and our programs permit these forms to be interconverted. We consider the LJ as the default and use DREIDING/X6 to denote cases where the exponential-6 form is used.

In order to better compare (31) and (32), we rewrite them as

$$E^{LJ} = D_0[\rho^{-12} - 2\rho^{-6}] \tag{31'}$$

$$E^{X6} = D_0\left[\left(\frac{6}{\zeta - 6}\right)e^{\zeta(1-\rho)} - \left(\frac{\zeta}{\zeta - 6}\right)\rho^{-6}\right] \tag{32'}$$

where $\rho = R/R_0$ is the scaled distance, R_0 is the van der Waals bond length (Å), D_0 is the van der Waals well depth (kcal/mol), and ζ is a dimensionless scaling parameter. Given the R_0 and D_0 parameters for the LJ form, there are two reasonable choices for the scaling parameter ζ in X6: (a) ζ = 12.0 leads to X6 having exactly the same long-range attraction as the LJ form, and (b) ζ = 13.772 leads to a dimensionless force constant

$$\kappa = \frac{1}{D_e}\left(\frac{\delta^2 E}{\delta\rho^2}\right)_{R=R_0} \tag{33}$$

of κ = 72 for X6, which is exactly equal to the value for LJ. Thus, with ζ = 13.772, the X6 and LJ forms lead to the same description near R_0. Given the parameters for the X6 form there are two reasonable choices for converting to the LJ form: (c) use the same R_0 and D_0, leading to a similar description near R_0; (d) require that the coefficient of the long range (R^{-6}) term be exactly the same and require that the inner crossing point (E_{vdw} = 0) be at the same distance. This leads to simple equations

$$\gamma e^{\zeta(1-\gamma)} = 1 \tag{34a}$$

$$\frac{D_L}{D_X} = \frac{3\gamma}{2(\zeta - 6)} \tag{34b}$$

$$\frac{R_L}{R_X} = \left(\frac{\zeta}{3\gamma}\right)^{1/6} \tag{34c}$$

---

[9] (a) In order to truncate the sums over nonbonded interactions for large molecules (>1000 atoms), it is often convenient to replace (31), (32), or (37) with a function that goes smoothly to zero after some large cutoff distance (e.g., R_{cut} = 9.0 Å).[4a] However, in this paper we calculate all nonbond interactions. (b) Similarly for (38) we use no distance cutoffs. [The hydrogen bond angle θ_{DHA} is restricted to be larger than 90° (linear is 180°)].

[10] For sufficiently small R, (32) leads to a negative energy with $E \rightarrow -\infty$ as $R \rightarrow 0$. To avoid such unpleasant situations, we use a simple exponential $\tilde{A}\exp[-\tilde{C}R]$ for R below the inner inflection point of (32) (where the curvature becomes negative), with $\tilde{A}$ and $\tilde{C}$ matched to the values at the inflection point. For scale parameters $\zeta \geq 10$, this inflection point is far up the repulsive wall and not important.

TABLE VIII: Summary of Results for Various Options in the DREIDING Force Field

	bonds	harm.	Morse	harm.	harm.	harm.	harm.	
	angles	theta	theta	cosine	theta	theta	theta	
	vdw	LJ	LJ	LJ	x6	LJ	LJ	DREIDING/
	charges	no	no	no	no	$\epsilon = R$	$\epsilon = 1$	A
atoms, Å	rms	0.235	0.236	0.237	0.250	0.247	0.257	0.334
	avg	0.221	0.223	0.224	0.224	0.231	0.243	0.290
	max	1.953	1.942	1.944	2.026	1.988	3.501	2.483
bonds, Å	rms	0.035	0.036	0.035	0.033	0.035	0.035	0.036
	avg	0.009	0.011	0.009	0.003	0.009	0.009	0.004
	max	0.169	0.168	0.168	0.168	0.165	0.162	0.139
angles, deg	rms	3.237	3.221	3.356	3.065	3.255	3.310	3.674
	avg	0.572	0.560	0.620	0.389	0.566	0.567	0.889
	max	17.725	17.691	20.000	16.770	16.277	16.576	19.548
torsions, deg	rms	8.925	8.979	9.036	10.042	9.533	10.611	13.324
	avg	0.222	0.232	0.225	0.286	0.457	0.576	0.256
	max	81.972	82.083	82.241	99.102	81.804	−160.083	−97.569

which are used to find the LJ parameters (R_L, D_L) for a given set of X6 parameters (R_X, D_X, ζ).

In the current studies we use options (a) and (c) for interconversions.

Nonbond interactions are not calculated between atoms bonded to each other (1,2 interactions) or atoms involved in angle interactions (1,3 interactions), since it is assumed that these interactions are included in the bond angle energy terms. Our programs allow the nonbond interactions between 1,4 neighbors to be included, excluded, or scaled. However, in DREIDING, the default is to include the full value for all 1,4 terms.

In DREIDING we require that only nuclear centers be used in defining the force field. This may reduce the accuracy for describing nonbonded interactions since there is evidence[11,12] that use of centers other than nuclear centers for (31) or (32) can lead to improved descriptions. However, omitting nonnuclear terms reduces the number of parameters to be defined and simplifies extending the force field to new atoms.

Consistent with the philosophy of DREIDING, we define the van der Waals parameters only for homonuclear cases and use combination rules to obtain the parameters for other atoms. The standard combination rules assume the following:

(a) a geometric mean for the A and B parameters

$$A_{ij} = [A_{ii}A_{jj}]^{1/2} \tag{35a}$$

$$B_{ij} = [B_{ii}B_{jj}]^{1/2} \tag{35b}$$

(b) and an arithmetic mean for the C parameters (X6)

$$C_{ij} = \tfrac{1}{2}C_{ii} + \tfrac{1}{2}C_{jj} \tag{35c}$$

For LJ (35ab) is equivalent to assuming the bond energies and bond distances combine as geometric means

$$D_{oij} = [D_{oii}D_{ojj}]^{1/2} \tag{36a}$$

$$R_{oij} = [R_{oii}R_{ojj}]^{1/2} \tag{36b}$$

The use of an arithmetic mean

$$R_{oij} = \tfrac{1}{2}(R_{oii} + R_{ojj}) \tag{36c}$$

in place of (36b), for combining vdw radii is more consistent with chemical practice, however, the geometric mean (36b) has been used in successful force fields (e.g., AMBER[3]) and is more consistent with the X6 form. Also for crystals, (35) allows a simplification in the convergence acceleration formulas for summing the vdw terms that speeds up the calculation significantly.[13] Thus, DREIDING uses (35) for X6 potentials. Our computer programs allow either form to be used for LJ cases; however, for DREIDING we use (36a) with (36c) as defaults.

The literature is replete with rather disparate values of van der Waals parameters. On the basis of ab initio calculations[14] on H_2 dimer, CH_4 dimer, and $(H_2)(CH_4)$, we concluded that the best set of empirical van der Waals parameters are those of Williams and co-workers.[11] [These were based on accurate fits to a large data base of compounds for which crystal structures and sublimation energies were available.] Consequently, for DREIDING we have adopted the Williams parameters with the following changes.

(a) Williams used the exponential-6 form, (32), whereas we also allow LJ potentials using the same D_0 and R_0.

(b) Williams used off-center locations for H (shortening the CH, NH, and OH bonds by 0.07 Å). We use nuclear positions for the H van der Waals terms and reoptimized the H parameters to fit the crystal data on *n*-hexane[15] (lattice constant and sublimation energy).

(c) We did *not* include the extra lone-pair centers that Williams used for certain N, O, and F atoms.

(d) We added other atoms for the C, N, O, and F columns by optimizing parameters to fit the structures and sublimation energies (using charges based on experimental moments or on fits to the electrostatic potentials from Hartree–Fock wave functions[16]) or by interpolation or extrapolation. We use the same van der Waals interactions independent of hybridization of the atom (e.g., C_3, C_R, C_2, C_1 all have the same parameters).

(e) Additional atoms (Na^+, Ca^{2+}, Fe^{2+}, Zn^{2+}) were added with parameters appropriate for the particular situation encountered in biological systems.

(f) Sometimes it is expedient to lump the hydrogens on carbons together with the carbons as a single effective atom (implicit hydrogens). We estimated the van der Waals parameters for such cases by calculating methane and benzene crystals and requiring that lattice spacing and heat of sublimation of 0 K match experiment (see bottom of Table II). The final values are listed in Tables II–IV.

H. Electrostatic Interactions. Electrostatic interactions are calculated by using[9]

$$E_Q = (322.0637)Q_iQ_j/\epsilon R_{ij} \tag{37}$$

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(11) (a) Williams, D. E.; Cox, S. R. *Acta Crystallogr., Sect. B* **1984**, *40*, 404. (b) Williams, D. E.; Houpt, D. J. *Ibid.* **1986**, *42*, 286. (c) Williams, D. E.; Hsu, L. Y. *Acta Crystallogr., Sect. A* **1985**, *41*, 296. (d) Cox, S. R.; Hsu, L. Y.; Williams, D. E. *Ibid.* **1981**, *37*, 293.

(12) Jorgensen, W. J.; Tirado-Rives. J. *J. Am. Chem. Soc.* **1988**, *110*, 1657.

(13) Karasawa, N.; Goddard III, W. A. *J. Phys. Chem.* in press.

(14) Brusich, M. J.; Hurley, J. N.; Lee, J. G.; Goddard III, W. A. Unpublished results. Brusich, M. J. Ph.D. Thesis, California Institute of Technology, 1988. Hurley, J. N. M.S. Thesis, California Institute of Technology, 1988.

(15) To make this conversion we first carried out calculations using the Williams scheme and verified his results for crystals of *n*-hexene and benzene.[11a] In doing these calculations we allowed the internal coordinates to respond to the fields and chose the valence force field parameters so that the observed geometries are stable (Williams calculated only intermolecular interactions). We then modified the charges in the Williams' calculations to correspond with values from more recent studies[16] (Q_H = 0.14 e) and verified that this leads to negligible changes in the results. We then centered the hydrogen van der Waals and Coulomb terms on the hydrogen nuclei and determined parameters leading to the same net stresses in the crystals (after reoptimizing valence terms to yield the observed bond distances and angles). These calculations all use the POLYGRAF program which uses periodic boundary conditions with accuracy-controlled acceleration convergence[13] for electrostatic and van der Waals terms (accuracy parameter of 0.01 kcal/mol).

TABLE IX: Errors in Calculating the Structures for 76 Organic Molecules Using the DREIDING Force Field[a]

	atoms, Å				bonds, Å				angles, deg				torsions, deg			
molecule	Natm	tRMS	Aatm	Matm	Nbnd	Rbnd	Abnd	Mbnd	Nang	Rang	Aang	Mang	Ntor	Rtor	Ator	Mtor
TOTAL	76[b]	0.235	0.221	1.953	1483	0.035	0.009	0.169	2174	3.224	0.566	17.750	2888	8.948	0.226	81.978
AAXTHP	26	0.334	0.284	0.740	26	0.039	0.002	0.088	36	5.432	1.189	12.637	41	8.399	-3.060	-20.063
ABAXES	25	0.112	0.105	0.177	28	0.036	0.012	-0.081	45	2.630	0.504	8.949	65	3.959	0.216	10.179
ABBUMO10	22	0.113	0.101	0.208	26	0.029	0.024	0.045	40	1.671	0.527	4.319	61	4.466	0.248	-10.545
ABINOR02	10	0.090	0.075	0.162	10	0.020	0.015	0.032	14	1.772	0.294	3.546	17	5.363	0.522	-8.294
ABINOS01	10	0.075	0.064	0.155	10	0.023	0.021	0.034	14	1.432	0.561	3.145	17	3.824	-0.358	6.179
ABTOET	27	0.414	0.343	1.316	30	0.028	0.011	-0.067	43	3.470	0.935	13.280	61	8.338	-1.120	-23.090
ABZTCX	20	0.351	0.287	0.915	21	0.064	0.025	0.156	33	3.404	0.394	-10.743	41	19.440	1.097	47.904
ACADOS	22	0.148	0.118	0.452	24	0.028	0.003	-0.066	35	3.728	0.742	11.893	49	5.420	-0.961	-21.874
ACAFLR	17	0.147	0.114	0.443	19	0.033	0.002	-0.082	27	1.992	0.150	4.788	36	5.386	-0.877	-22.535
ACANIL01	10	0.070	0.062	0.130	10	0.026	0.005	-0.056	12	2.055	0.328	-4.355	12	2.675	1.468	6.057
ACARAP	22	0.340	0.296	0.822	22	0.031	0.006	-0.054	30	5.510	1.849	11.947	33	10.621	-3.097	-26.447
ACBNZA01	13	0.146	0.108	0.325	13	0.042	0.007	-0.087	17	3.107	0.266	6.535	19	7.879	3.715	16.993
ACBUOL	24	0.449	0.381	0.982	24	0.035	0.009	-0.076	31	3.368	1.172	11.581	34	9.697	-1.459	25.815
ACCITR10	22	0.265	0.193	0.826	25	0.030	0.015	0.052	42	2.620	0.556	9.064	59	12.712	-0.270	-38.129
ACDXUR	19	0.141	0.126	0.294	20	0.032	0.002	-0.064	29	3.455	0.221	6.883	38	4.670	0.119	11.540
ACENAP03	12	0.023	0.022	0.033	14	0.026	0.000	0.038	20	0.856	-0.182	-1.569	29	0.475	0.001	0.853
ACFPCH	17	0.073	0.065	0.154	18	0.029	0.018	0.047	25	1.804	0.375	4.275	33	1.514	-0.041	-4.121
ACFUCN	14	0.275	0.230	0.699	14	0.034	0.005	-0.062	19	3.116	0.211	7.608	21	8.582	-1.471	-26.496
ACGLSP	25	0.341	0.287	0.763	25	0.032	0.012	0.066	34	5.043	1.793	11.280	39	6.993	-0.440	-21.170
ACGLUA11	15	0.190	0.171	0.379	15	0.024	0.011	0.039	21	2.013	0.746	4.480	26	7.300	-0.537	-22.115
ACHGAL	17	0.180	0.158	0.367	18	0.028	0.005	-0.046	26	4.416	1.298	11.487	33	5.313	0.987	15.567
ACHIST20	14	0.336	0.291	0.642	14	0.024	-0.001	-0.045	18	3.488	0.439	-9.116	19	13.314	6.693	31.175
ACHNAP10	15	0.078	0.066	0.164	16	0.036	0.035	0.055	24	3.625	0.555	10.666	32	1.798	0.026	4.231
ACHTAR10	10	0.148	0.117	0.277	9	0.024	0.007	0.046	12	4.596	1.352	10.724	7	6.675	2.637	17.029
ACIMDC	4	0.023	0.023	0.031	3	0.030	0.022	0.038	3	1.441	0.003	-1.783	0	0.000	0.000	0.000
ACINDN	14	0.072	0.067	0.111	15	0.049	0.000	-0.087	22	1.911	-0.062	-3.488	31	1.991	0.713	4.973
ACINST	26	0.244	0.207	0.605	26	0.033	0.006	-0.058	38	5.171	1.469	12.303	47	5.353	2.572	15.273
ACKYNU	18	0.391	0.338	0.852	18	0.028	0.007	-0.052	24	3.397	0.177	8.524	27	17.848	0.864	36.614
ACMBPN	24	0.259	0.206	0.716	25	0.033	0.013	0.077	39	2.634	0.666	6.547	53	9.394	-1.458	-25.839
ACMEBZ	14	0.175	0.141	0.430	14	0.038	0.012	-0.065	19	3.968	0.457	8.609	22	7.649	4.549	14.020
ACMTDE	16	0.254	0.211	0.683	15	0.029	0.008	-0.045	18	3.032	0.450	7.172	20	9.168	-1.780	-26.258
ACNORT	31	0.266	0.188	0.847	35	0.026	0.008	0.061	53	4.578	1.150	17.750	78	13.897	2.797	81.978
ACNPAC10	15	0.050	0.045	0.100	17	0.040	0.005	-0.065	25	1.826	-0.132	-5.193	36	1.687	0.779	4.686
ACNPEC	21	0.844	0.787	1.458	21	0.039	0.009	-0.092	27	3.189	0.541	9.435	29	13.905	5.504	29.653
ACONTN10	32	0.184	0.160	0.404	37	0.030	0.019	0.060	63	2.640	0.961	11.600	105	4.435	-0.442	10.753
ACPENC10	15	0.288	0.249	0.669	16	0.054	-0.016	-0.089	23	6.244	1.419	12.659	30	19.499	-0.222	-49.374
ACPPCA	12	0.225	0.165	0.509	12	0.037	0.024	0.055	16	3.674	0.331	8.881	19	11.833	-4.218	-24.082
ACPRET03	29	0.290	0.244	0.682	32	0.031	0.008	-0.053	52	2.884	0.405	13.115	76	5.488	-0.496	12.092
ACPYNS	18	0.263	0.235	0.513	19	0.040	0.018	0.076	27	4.626	1.124	12.698	35	8.989	-3.022	-23.180
ACRAMS	26	0.867	0.768	1.424	29	0.055	0.022	0.163	42	2.728	0.099	-12.551	53	15.904	-0.310	48.624
ACSALA01	13	0.097	0.086	0.191	13	0.039	0.014	-0.072	17	4.045	0.593	9.513	19	3.524	2.196	6.674
ACSESO10	23	0.211	0.169	0.608	26	0.036	0.011	0.072	42	2.942	0.391	9.973	64	6.284	1.287	21.160
ACTAND	24	0.379	0.266	1.457	27	0.039	0.018	0.064	43	1.816	0.259	5.491	62	10.152	-0.595	-48.260
ACTHBZ	22	0.297	0.223	0.864	23	0.031	0.000	-0.079	31	2.186	0.192	5.476	37	9.412	2.499	28.852
ACTHCP	10	0.093	0.077	0.202	11	0.039	-0.017	-0.070	16	2.799	0.447	7.599	22	11.087	0.032	-20.845
ACTOLD	11	0.045	0.042	0.086	11	0.031	0.012	-0.050	14	2.070	0.148	-4.471	14	1.933	0.508	-4.199
ACTYSN	16	0.774	0.650	1.953	16	0.026	0.005	-0.049	21	2.914	0.211	7.658	22	26.045	-4.720	70.212
ACURID	19	0.126	0.109	0.252	20	0.031	0.002	-0.071	29	3.358	-0.115	-7.329	38	4.716	0.790	11.713
ACVCHO	12	0.109	0.085	0.235	12	0.031	0.007	-0.046	16	1.897	0.412	3.778	20	6.019	-2.383	-14.540
ACXMOL	22	0.408	0.322	1.103	23	0.034	0.011	0.061	33	3.856	1.209	11.085	44	10.490	1.500	25.678
ACXMPR	14	0.071	0.557	1.294	14	0.038	-0.008	-0.066	20	4.172	0.389	-9.449	24	22.925	-1.103	42.963
ACYGLY11	8	0.095	0.084	0.159	7	0.034	0.012	0.059	8	4.068	0.804	7.223	5	3.335	-0.294	4.928
ACYTID	17	0.202	0.190	0.338	18	0.024	0.013	0.071	26	2.600	0.763	7.758	35	6.044	1.698	18.946
ADELOX10	28	0.127	0.109	0.300	32	0.029	0.020	-0.057	51	2.490	0.680	11.187	85	3.958	0.595	19.114
ADENOS10	19	0.088	0.077	0.168	21	0.023	0.007	-0.046	31	3.135	0.349	9.106	45	2.526	0.141	8.632
ADFGLP	11	0.059	0.056	0.079	12	0.032	0.013	0.057	18	1.984	0.358	3.529	25	4.795	-0.125	8.698
ADGSMH	29	0.340	0.284	0.976	30	0.032	0.011	0.057	45	4.699	1.451	12.574	57	9.894	3.363	28.165
ADHELA10	14	0.092	0.082	0.169	14	0.038	0.001	-0.089	19	2.855	0.332	5.443	22	4.940	0.086	-11.066
ADMANN	12	0.122	0.102	0.224	12	0.027	0.022	0.042	17	1.830	0.907	3.966	22	5.480	-0.632	-8.664
ADMHEP	14	0.080	0.072	0.176	14	0.021	0.011	0.043	21	1.642	0.512	-4.114	28	4.382	0.972	10.243
ADMINA	16	0.061	0.054	0.119	18	0.029	0.000	-0.059	27	1.011	-0.054	2.049	39	2.165	0.535	-5.464
ADMOPM	24	0.677	0.610	1.350	26	0.030	0.006	0.070	39	3.755	0.346	-10.644	52	9.020	-1.217	39.361
ADRTAR	13	0.139	0.121	0.264	13	0.024	0.006	0.039	17	2.017	0.414	5.173	20	4.775	2.039	10.617
ADYPNL	33	0.354	0.313	0.752	37	0.038	0.013	-0.083	52	1.538	0.099	4.522	73	8.416	-0.444	-21.929
AEBDOD10	22	0.256	0.210	0.597	25	0.036	0.003	0.064	41	2.344	0.084	5.613	65	10.084	2.446	22.160
AENLAN10	35	0.420	0.309	1.544	39	0.041	0.018	0.126	63	2.868	0.550	11.350	93	5.240	-0.687	-21.473
AFCYDP	24	0.413	0.332	1.098	26	0.033	-0.007	0.067	41	3.719	0.735	9.218	48	9.313	-2.233	-29.162
AFMSCY	20	0.306	0.256	0.659	22	0.026	0.005	-0.058	34	3.277	0.059	7.685	50	7.427	1.110	15.662
AFURPO10	13	0.140	0.129	0.244	14	0.040	0.001	0.078	20	3.511	0.168	-7.646	26	7.301	-0.286	-17.911
AFUTDZ10	12	0.247	0.204	0.521	13	0.081	0.025	0.169	20	2.502	0.309	-5.996	24	15.706	0.267	-32.022
AFUTHU	16	0.067	0.060	0.143	18	0.032	0.004	0.065	27	1.861	-0.091	4.288	39	2.763	0.253	-8.283
AGALAM10	15	0.109	0.097	0.194	15	0.029	0.018	0.045	21	1.658	0.449	3.459	26	3.804	0.597	8.020
AGLUAM10	13	0.328	0.281	0.680	12	0.034	0.010	0.050	15	4.206	0.321	8.847	13	17.811	9.884	37.877
AHARFU	16	0.120	0.103	0.233	18	0.036	-0.002	-0.068	27	2.701	0.673	8.506	39	4.947	0.742	-12.166

TABLE IX (Continued)

	atoms, Å				bonds, Å				angles, deg				torsions, deg			
molecule	Natm	tRMS	Aatm	Matm	Nbnd	Rbnd	Abnd	Mbnd	Nang	Rang	Aang	Mang	Ntor	Rtor	Ator	Mtor
AHCDLA	14	0.075	0.067	0.141	16	0.033	0.019	−0.051	26	1.813	0.040	−4.555	37	3.403	0.400	8.096
AHDITX	26	0.185	0.155	0.441	30	0.037	0.009	0.076	48	1.817	0.279	−5.833	71	5.588	−1.256	−22.254

[a] Cambridge notation, see Figure 1. Here NX is the number of terms, RX is the rms error, AX is the average error, and MX is the maximum error for X = atoms (atm), bonds (bnd), angles (ang), and torsions (tor). The total rms error in the Cartesian coordinates is indicated by trms. Bonds are of harmonic form (4), angles are of harmonic theta form (10), torsions are single term form (13), inversions are of spectroscopic form (29), nonbonds are of Lennard-Jones form (32), charges are not included. [b] Number of molecules.

where Q_i and Q_j are charges in electron units, R_{ij} is the distance in Å, ϵ is the dielectric constant (usually $\epsilon = 1$), and 332.0637 converts E_Q to kcal/mol. Interactions are not calculated between atoms bonded to each other (1,2 interactions) or involved in angle terms (1,3 interactions) since these are assumed to be contained in the bond and angle interactions.

A serious difficulty is how to predict the charges. For small molecules it has been possible to fit charges to the electrostatic potentials calculated from high-quality Hartree–Fock wave functions.[16] For good basis sets the results agree with observed electrical moments and should be the best choices molecular dynamics simulations. A method for predicting accurate charges of large molecules is desperately needed. Some progress has been made;[17,18] however, there is not yet a general method. In this paper we either ignore charges or use the Gasteiger[17] estimates for charges.

The calculations reported in this paper are all for molecules in a vacuum or for molecular crystals, and hence we use $\epsilon = 1$. In simulations of biological systems it is common to ignore solvent and to use $\epsilon = \epsilon_0 R_{ij}$, (where ϵ_0 is a constant, often 1.0, 4.0, or 8.0) as an approximate way to represent the effects of the solvent. This is needed in order to stabilize charged residues and phosphates and to include the proper bias toward internal hydrophobic interactions. As the simplest way to simulate solvation of charged groups by the solvent, we recommend constructing a locally neutral cluster by addition of counterions (Na^+ or Cl^-) to charged groups not involved in salt bridges. This allows us to use $\epsilon = 1$ in (37) so that local electrostatic effects can have their full effect. (Better of course is to consider the solvent explicitly.) However, in this paper we omit counterions in order to simplify comparisons between various force fields.

I. Hydrogen Bonding. Within the constraint that charges and van der Waals interactions must be centered on nuclei, it is difficult to obtain a force field that (a) correctly predicts the structure and bond energy of H_2O dimer, and (b) predicts the sublimation energy and structure of ice while (c) using the van der Waals parameters appropriate for non-hydrogen-bonded systems. As a result, DREIDING uses a special hydrogen bond term to describe the interactions involving a hydrogen atom (denoted H__HB) on the very electronegative atoms (N, O, F) associated with hydrogen bonds. When the hydrogen on such a donor is close to an electronegative acceptor atom (N, O, F), we (a) explicitly include all van der Waals and electrostatic interactions corresponding to the charges on the various atoms (including the hydrogen) and in addition, and (b) include a CHARMM-like hydrogen bonding potential[4a,9b]

$$E_{hb} = D_{hb}[5(R_{hb}/R_{DA})^{12} - 6(R_{hb}/R_{DA})^{10}] \cos^4(\theta_{DHA}) \qquad (38)$$

Here θ_{DHA} is the bond angle between the hydrogen donor (D), the hydrogen (H), and the hydrogen acceptor (A), while R_{DA} is the distance between the donor and acceptor atoms (in Å).

The values of D_{hb} and R_{hb} depend on the convention for assigning charges. Thus, Gasteiger charges lead to $Q_H = 0.21$ for H_2O, whereas Hartree-Fock calculations lead to $Q_H = 0.34$[16a] or 0.40[16b] and experiment leads to $Q_H = 0.33$. The resulting values for D_{hb} and R_{hb} (based on H_2O dimer) are given in Table V. Note in Table II that the van der Waals well depth for H__HB is different than for H_.

J. DREIDING/A. The initial stage of developing DREIDING (1984–1985) utilized somewhat simplified energy expressions. This early force field (denoted DREIDING/A) has been used for a number of calculations and leads to reasonable geometries. Differences from DREIDING are as follows.

(a) Bond stretch. Only the harmonic form (4) was used, with $K_{IJ} = 1000$ (kcal/mol)/Å^2 for all bonds. The atomic radii of Table VI are used.

(b) Angle bend. The simple harmonic angle form (11) was used with $K_{IJK} = 100$ (kcal/mol)/rad^2 for all angle terms. All X_3 bond angles were taken as tetrahedral ($\theta_J^0 = 109.471°$) except S_3 and S_31 as indicated in Table VI.

(c) Inversion. The CHARMM form (25) was used with $K_{inv} = 40$ (kcal/mol)/rad^2 for nonplanar molecules (X_3) and[19] $K_{inv} = 300$ (kcal/mol)/rad^2 for planar molecules (X_R, X_2). The X_2, X_R centers have $\phi_0 = 0$ and X_3 centers have $\phi_0 = 35.264°$ if J and K are not hydrogens and $\phi_0 = 31.4°$ if J or K is a hydrogen.

(d) Torsion. The form (13) was used but the barriers are taken as 20 kcal/mol for double bonds (J, K = X_2 or X_R), 1 kcal/mol for X_3-X_3 single bonds, and 0.2 kcal/mol for other cases. No distinction was made for the oxygen column.

(e) van der Waals. Lennard-Jones 12-6 was used (31) with the parameters in Table VII.

(f) Electrostatics. Charges based on CHARMM/EFI[4a] were used for peptides and nucleic acids. Charges were generally ignored for other sytems.

(g) Hydrogen bonds. The hydrogen atoms (H__HB) bonded to electronegative atoms (N and O) were described with the hydrogen bond form (38) (using $D_{hb} = 9.5$ kcal/mol and $R_{hb} = 2.75$ Å) when close to electronegative atoms (N and O). No explicit charges or van der Waals interactions were included for such hydrogens.

III. Discussion

We consider the DREIDING force field to be the simplest generic force field capable of providing accurate geometries for organic, biological, and main-group inorganic systems. We have deliberately used the fewest possible number of parameters and couched the choices in terms of general hybridization concepts. Thus, all geometric parameters arise from either addition of bond radii or angles of the simplest hydrides (AH_n, H_nA–BH_n). Only a single force constant each is used for bonds, angles, and inversions, and only six values for torsional barriers are used. The focus here has been on the B, C, N, O, and F columns of the periodic table, with a few other elements (e.g., Na, Ca, Zn, Fe) added that are commonly used for simulations of biological systems. The parameters have been biased toward the first-row elements (and carbon).

The valence energies calculated here can be considered as strain energies and hence one could calculate heats of formation by adding in Benson's group additivity energies.[20] We have not yet implemented this procedure.

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(17) (a) Gasteiger, J.; Marsili, M. *Tetrahedron* **1980**, *36*, 3219. (b) Extended to phosphorous by Paul Saze (parameters: $A = 7.40$, $B = 3.0$, $C = -1.0$). (c) For systems with formal charges, charges for the neutral molecule were calculated first and then the appropriate net charge was added to the affected atoms.

(18) Rappé, A. K.; Goddard III, W. A. Charge Equilibration in Molecular Dynamics Simulations. *J. Phys. Chem.* To be submitted for publication.

(19) This value must be high enough to ensure that planar centers remain planar. In previous DREIDING/A calculations, a value of 1000 (kcal/mol)/rad^2 was used.

TABLE X: Comparisons of Error (in Å) from Various Force Fields for the 76 Molecules of Figure 1[a]

molecule	standard	Morse bond	cosine angle	exponential vdw	charges $\epsilon = R$	charges $\epsilon = 1$	DREIDING/A
total	0.235	0.236	0.238	0.248	0.247	0.257	0.332
AAXTHP	0.334	0.337	0.341	0.340	0.264	0.259	0.417
ABAXES	0.112	0.119	0.117	0.087	0.111	0.110	0.109
ABBUMO10	0.113	0.115	0.116	0.079	0.112	0.112	0.107
ABINOR02	0.090	0.090	0.090	0.085	0.085	0.081	0.111
ABINOS01	0.075	0.076	0.076	0.068	0.068	0.069	0.115
ABTOET	0.414	0.420	0.427	0.273	0.404	0.403	0.557
ABZTCX	0.351	0.350	0.312	0.424	0.356	0.352	0.464
ACADOS	0.148	0.147	0.151	0.158	0.141	0.138	0.209
ACAFLR	0.147	0.150	0.174	0.292	0.148	0.152	0.319
ACANIL01	0.070	0.070	0.069	0.120	0.069	0.068	0.150
ACARAP	0.340	0.343	0.342	0.337	0.340	0.344	0.277
ACBNZA01	0.146	0.151	0.147	0.190	0.168	0.179	0.227
ACBUOL	0.449	0.491	0.465	0.523	0.536	0.681	0.786
ACCITR10	0.265	0.260	0.266	0.169	0.178	0.178	0.299
ACDXUR	0.141	0.141	0.135	0.130	0.150	0.167	0.773
ACENAP03	0.023	0.024	0.022	0.024	0.023	0.023	0.025
ACFPCH	0.073	0.077	0.075	0.056	0.072	0.072	0.277
ACFUCN	0.275	0.276	0.277	0.262	0.293	0.310	0.400
ACGLSP	0.341	0.357	0.355	0.265	0.342	0.338	0.515
ACGLUA11	0.190	0.187	0.191	0.179	0.174	0.184	0.146
ACHGAL	0.180	0.180	0.186	0.169	0.174	0.172	0.199
ACHIST20	0.336	0.336	0.339	0.329	0.463	0.221	0.537
ACHNAP10	0.078	0.080	0.086	0.064	0.078	0.078	0.089
ACHTAR10	0.148	0.151	0.149	0.144	0.148	0.173	0.151
ACIMDC	0.023	0.024	0.023	0.021	0.025	0.026	0.025
ACINDN	0.072	0.072	0.072	0.069	0.070	0.070	0.078
ACINST	0.224	0.238	0.251	0.199	0.236	0.229	0.311
ACKYNU	0.391	0.367	0.387	0.281	0.391	0.417	1.466
ACMBPN	0.259	0.262	0.263	0.250	0.189	0.243	0.310
ACMEBZ	0.175	0.176	0.177	0.210	0.154	0.153	0.487
ACMTDE	0.254	0.258	0.246	0.262	0.272	0.289	0.529
ACNORT	0.266	0.268	0.269	0.252	0.265	0.266	0.302
ACNPAC10	0.050	0.050	0.050	0.050	0.050	0.051	0.052
ACNPEC	0.844	0.853	0.856	0.784	0.830	0.810	1.083
ACONTN10	0.186	0.194	0.196	0.164	0.186	0.176	0.189
ACPENC10	0.288	0.289	0.345	0.290	0.288	0.308	0.654
ACPPCA	0.225	0.226	0.225	0.241	0.288	0.294	0.495
ACPRET03	0.290	0.285	0.291	0.243	0.294	0.290	0.845
ACPYNS	0.263	0.263	0.273	0.257	0.318	0.325	0.225
ACRAMS	0.867	0.856	0.871	0.771	0.898	1.003	0.447
ACSALA01	0.097	0.096	0.099	0.727	0.332	0.323	0.402
ACSESO10	0.211	0.214	0.215	0.220	0.208	0.208	0.178
ACTAND	0.379	0.381	0.380	0.384	0.365	0.353	0.464
ACTHBZ	0.297	0.307	0.302	0.398	0.305	0.302	0.429
ACTHCP	0.093	0.093	0.096	0.091	0.093	0.093	0.139
ACTOLD	0.045	0.047	0.054	0.070	0.044	0.045	0.160
ACTYSN	0.774	0.773	0.771	0.767	0.791	0.797	0.473
ACURID	0.126	0.128	0.125	0.130	0.128	0.130	0.161
ACVCHO	0.109	0.092	0.110	0.078	0.078	0.077	0.280
ACXMOL	0.408	0.413	0.411	0.393	0.413	0.418	0.318
ACXMPR	0.671	0.665	0.666	0.650	0.521	0.510	0.792
ACYGLY11	0.095	0.095	0.097	0.091	0.093	0.094	0.082
ACYTID	0.202	0.208	0.203	0.200	0.221	0.222	0.174
ADELOX10	0.127	0.135	0.130	0.110	0.160	0.185	0.162
ADENOS10	0.088	0.091	0.092	0.700	0.636	0.627	0.558
ADFGLP	0.059	0.060	0.058	0.054	0.052	0.054	0.061
ADGSMH	0.340	0.345	0.349	0.326	0.315	0.307	0.650
ADHELA10	0.092	0.095	0.093	0.093	0.086	0.081	0.128
ADMANN	0.122	0.120	0.121	0.118	0.147	0.151	0.156
ADMHEP	0.080	0.085	0.082	0.070	0.074	0.077	0.122
ADMINA	0.061	0.062	0.059	0.067	0.060	0.060	0.071
ADMOPM	0.677	0.671	0.666	0.910	0.608	0.614	0.447
ADRTAR	0.139	0.138	0.142	0.118	0.134	0.140	0.659
ADYPNL	0.354	0.348	0.354	0.282	0.358	0.359	0.359
AEBDOD10	0.256	0.258	0.256	0.249	0.265	0.270	0.205
AENLAN10	0.420	0.432	0.419	0.362	0.417	0.416	0.431
AFCYDP	0.413	0.415	0.420	0.397	0.518	1.325	0.351
AFMSCY	0.306	0.307	0.307	0.283	0.252	0.229	0.358
AFURPO10	0.140	0.138	0.141	0.122	0.135	0.132	0.165
AFUTDZ10	0.247	0.247	0.246	0.244	0.244	0.243	0.231
AFUTHU	0.067	0.067	0.067	0.065	0.063	0.062	0.115
AGALAM10	0.109	0.110	0.109	0.295	0.318	0.090	0.125
AGLUAM10	0.328	0.330	0.329	0.320	0.296	0.290	0.568
AHARFU	0.120	0.121	0.122	0.118	0.139	0.140	0.160
AHCDLA	0.075	0.077	0.075	0.067	0.078	0.079	0.083
AHDITX	0.185	0.192	0.185	0.166	0.186	0.185	0.199

[a] The standard force field has bonds of harmonic form (4), angles of harmonic theta form (10), torsions of single term form (13), inversions of spectroscopic form (29), nonbonds of Lennard-Jones form (32), and charges not included. Each other column is labeled with the change from the standard.

We envision a hierarchy of force fields[21] where the simple versions (DREIDING) allow rapid considerations of new structures and compositions while the more complex versions are tuned to accurately predict properties (e.g., vibrational frequencies) for particular systems. To describe vibrational frequencies accurately will certainly require more sophisticated force fields. Thus we must add angle–stretch, stretch–stretch, and angle–angle terms to the bond angle expansion (10) and additional terms to the torsion expression (13). Such terms are allowed in our programs and individual parameters have been optimized for specific molecules;[22] however, we have not yet generalized these results to obtain a more generic force field suitable for vibrational frequencies. In addition, force constants and torsional barriers generally decrease going down a column of the periodic table.

To treat main-group metals (Li, Be columns) and transition metals, the force fields must emphasize oxidation state and the interplay of attractive Coloumb interactions with short-range repulsion (van der Waals). Here the role of valence interactions, particularly the four-center terms (torsion and inversion), are less important, while the delocalization of charge characteristic of unsaturated systems becomes dominant. We leave these metallic systems to later developments.[23]

IV. Applications

A. Structures from the Cambridge Data Base. In order to provide a test of its general efficacy, we used the DREIDING force field to predict the structures of the 76 organic molecules in Figure 1 (the first 76 structures of the Cambridge Data Base[24] having R factors below 0.05). This includes a variety of bonding situations with H, C, N, O, F, P, S, Cl, and Br (many structures involve phosphates, sugars, sulfates, sulfones, nitrates, carbonates, amides, etc.). Geometry optimizations were carried out using BIOGRAF Version 2.20 on the four-processor Stardent Titan Supercomputer workstation (using Fletcher–Powell minimization) while graphics manipulations were typically carried out on the Silicon Graphics 4D/25 workstation.

In many of the 76 molecules there are strong intermolecular hydrogen bonds or salt bridges so that the structure of the free molecule might differ from that of the crystal. On the other hand, optimization of the structure of the molecule in the crystal environment is not a complete test of the force field because intermolecular packing, electrostatics, and hydrogen-bonding interactions will restrain the structures from changing. Consequently, in each case we extracted one complete molecule from the unit cell and optimized the structure in a vacuum.

We carried out calculations on the complete set of molecules for several options of the DREIDING force field. The bonds were treated either as *harmonic* or Morse, the angles were treated as harmonic in either *theta* or cosine theta. The van der Waals terms were treated either as *Lennard-Jones 12-6* or exponential-6, and the *charges* were either *ignored* or included. When included, the charges were calculated by using the Gasteiger[17] procedure and with either $\epsilon = 1$ or $\epsilon = R$. The cases in italics above were considered as the standard. In each case it is the simpler option. The results are in Table VIII. Thoreau would be happy. The simplest case leads to the most accurate result, trms = 0.235 (where trms is the total rms error for all atoms of all 76 structures). Thus, use of Morse bonds increases trms to 0.236, cosine-angle terms increase trms to 0.238, while X6 van der Waals increases trms to 0.248.

The simple DREIDING/A force field does reasonably well, with trms = 0.332. Here the error in bonds is about the same (up from 0.035 to 0.036 Å rms), but the error in angles is higher (3.683° rms rather than 3.224°) and the error in torsions is much higher (13.309° rms rather than 8.948°).

TABLE XI: Rotational Barriers (kcal/mol) about Single Bonds

	experiment		calculated
molecule[a]	periodicity[b]	barrier[c]	barrier
CH_3-CH_3	V3	2.882 (0.010)[d]	2.896
$CH_3-CH_2CH_3$	V3	3.4[e]	3.376
$CH_3-CH_2CH_2CH_3$	V3	3.4[e]	3.410
$CH_3CH_2-CH_2CH_3$	V3	3.8[e]	3.822
$CH_3-CH(CH_3)_2$	V3	3.9[e]	3.995
$CH_3-C(CH_3)_3$	V3	4.7[e]	5.071
CH_3-CH_2F	V3	3.287 (0.03)[d]	3.172
CH_3-CH_2Cl	V3	3.68[e]	3.487
CH_3-CH_2Br	V3	3.68[e]	3.345
CH_3-CH_2I	V3	3.623 (0.15)[d]	3.336
CH_3-CF_3	V3	3.16 (0.11)[d]	3.768
CH_3-CCl_3	V3	5.10 (0.3)[d]	4.851
F_3C-CF_3	V3	3.92[e]	5.562
CH_3-SiH_3	V3	1.7[e]	2.296
CH_3-GeH_3	V3	1.24[e]	2.037
$CH_3-CH_2SiH_3$	V3	2.625 (0.01)[d]	3.805
$CH_3CH_2-SiH_3$	V3	1.979 (0.007)[d]	2.517
$CH_3-Si(CH_3)_3$	V3	1.4[e]	3.191
CH_3-NH_2	V3	1.98[e]	2.085
CH_3-NHCH_3	V3	3.62[e]	2.916
$CH_3-N(CH_3)_2$	V3	4.4[d]	3.534
CH_3-PH_2	V3	1.96[e]	1.957
CH_3-OH	V3	0.373 (0.003)[d]	2.117
CH_3-SH	V3	0.445 (0.000)[d]	2.376
CH_3-SeH	V3	0.957 (0.05)[d]	2.183
CF_3-OF	V3	3.900[d]	3.608
CH_3-OCH_3	V3	2.630 (0.007)[d]	3.034
CH_3-SCH_3	V3	2.099 (0.003)[d]	2.902
CH_3-SeCH_3	V3	1.498 (0.001)[d]	2.601
$CH_3-CH=CH_2$	V3	1.995[e]	0.753
$CH_3-CH=O$	V3	1.143[d]	0.948
$CH_3-C(OH)=O$	V3	0.481[d]	1.026
$CH_3-C(OCH_3)=O$	V3	0.284[d]	1.030
$NH_2-CH=O$	V2	18 (3)[e]	24.506
$N(CH_3)_2-CH=O$	V2	19.6 (1.5)[e]	21.037

[a] The dihedral pair is indicated by the single line. [b] Symmetry assumed in experimental analysis. [c] The value in parentheses indicates estimated experimental uncertainty. [d] Reference 25. [e] Reference 26.

Using explicit charges with $\epsilon = 1$ leads to worse results (0.257) while explicit charges with $\epsilon = E$ (0.247) is worse than no charges. It appears that the major problem with charges is that intermolecular electrostatics are more important than intramolecular electrostatics. Thus, the molecules that need charges for a good description of structure need also to be treated as crystals. Thus, for these systems the *actual* error in our prediction of molecular structure (for isolated molecules) is probably much smaller than the trms quoted (which is based on the crystal structure).

In Tables IX and X we tabulate the results for DREIDING using the standard options: the harmonic form of bond stretch (5), the harmonic theta form (11) for angle bend, the single term torsional form (13), the spectroscopic inversion (29), the Lennard-Jones 12-6 nonbond form (32), and no charges.

For each molecule we list the rms error in the Cartesian coordinates (trms), the number of bond, angle, or torsion terms (nbnd, nang, ndih), the *average* error for each quantity (Abnd, Aang, Adih), the rms error for each quantity (Rbnd, Rang, Rdih), and the maximum error for each quantity (Mbnd, Mang, Mdih). The total errors over the whole set of 76 molecules are also listed. The total rms error is 0.235, while only five cases are worse than 0.5: ACNPEC with 0.844, ACRAMS with 0.867, ACTYSN with 0.774, ACXMPR with 0.671, and ADMOPM with 0.677. The first row of Table IX lists the total errors over the full data set. The average error in the bonds (out of 1483) is 0.009 Å, the average error in the angles (out of 2174) is 0.57°, and the average error in the torsions (out of 2188) is 0.23°, indicating that the general scales for these quantities are appropriate. The rms error in bonds is 0.035 Å, in angles is 3.2°, and in torsions is 8.9°.

Of the five bad cases ACNPEC, ACTYSN, and ACXMPR have intermolecular hydrogen bonds that disappear for an isolated molecule. Thus, for the crystalline form,[29] the trms drops from

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TABLE XII: Conformational Energies (kcal/mol) for Various Molecules[a]

system	exptl[b]	calcd
butane, gauche/anti	0.76	0.75
methylcyclohexane, axial/equatorial	1.8 (0.2)	1.29
phenylcyclohexane, axial/equatorial	3.00	4.51
fluorocyclohexane, axial/equatorial	0.20	0.33
chlorocyclohexane, axial/equatorial	0.40	0.82
bromocyclohexane, axial/equatorial	0.50	0.52
nitrocyclohexane, axial/equatorial	1.20	1.58
cyclohexanol, axial/equatorial	0.50	0.25
1,4-dichlorocyclohexane, axial/equatorial	0.20	1.65
methyl ethyl ether, gauche/anti	1.50	1.56
cyclohexane, twist-boat/chair	5.7 (0.3)	7.72
4,4,5-trimethyl-1,3-dioxolane, axial/equatorial	1.30	1.48

[a] The higher energy form is listed first. [b] Reference 27.

0.844 to 0.372 for ACNPEC, from 0.774 to 0.257 for ACTYSN, and from 0.671 to 0.308 for ACXMPR. For ADMOPM the experimental structure has a very short distance of 2.4 Å from a phosphate oxygen to the hydrogen on the aromatic carbon flanked by two nitrogens. This suggests a very strong electrostatic interaction (almost a hydrogen bond) that is underestimated since no explicit hydrogen bond term is included for this interaction. The crystalline form of ACRAMS has extensive intermolecular ring stacking that is lost in the isolated molecule. Thus, for the crystalline form, trms drops from 0.867 to 0.162.

We conclude from these comparisons that the DREIDING force field provides useful predictions for structures. Although, in these benchmarks, use of charges leads to slightly worse results, we recommend that charges be used in all studies involving interactions of molecules.

B. Conformations of Organic Molecules. In Table XI we show the single-bond rotational barriers calculated with DREIDING and compare with experiment.[25,26] [Experimental results from the 1982 review (ref 25, denoted as d), should be considered more reliable than results only contained in the 1968 review (ref 26, denoted as e)] DREIDING uses only one value (2.0 kcal/mol) for explicit single-bond terms, but the trends are reasonably well reproduced. For alkanes the results are quite good (errors in kcal/mol of 0.01 for ethane, 0.0 for propane, 0.0 for both torsions in butane, 0.1 for isobutane, and 0.4 for neopentane). For CH_3-CH_2X, where X s a halogen, the predicted barrier is low by 0.1 to 0.3 kcal/mol. For C–Si and C–Ge barriers, the predicted barriers are about 50% too high, indicating that the torsional barrier should be smaller than 2.0 for the Si and Ge rows of the periodic table. The rotational barriers about peptide bonds are 10–20% high (experimental 18 and 19.6 versus calculated 24.5 and 21.0, respectively).

In Table XII we show the difference in energy for various conformations of several molecules. The signs are always correct and the magnitudes are reasonably good.

In Table XIII we show the difference in energy for various stereoisomers. The signs are always correct and the magnitudes are reasonably good.

These results indicate that the torsional parameters are reasonably well-defined for organic systems and that the simple scheme of section IIE incorporates the various features required for hydrocarbons. For simplicity we have used the same parameters for all other rows and columns of the periodic table. This is oversimplified as indicated by the increased errors for these systems but consistent with the DREIDING philosophy of *not* readjusting force constants for particular combinations of elements.

TABLE XIII: Relative Energies (kcal/mol) of Various Stereoisomers[a]

system	exptl	calcd
1,3-dimethylcyclobutane, cis/trans	−0.30	−0.06
1,2-dimethylcyclohexane, cis/trans	1.86	0.98
1,3-dimethylcyclohexane, cis/trans	−2.00	−1.34
1,4-dimethylcyclohexane, cis/trans	1.90	1.28
1,1,3,5-tetramethylcyclohexane, cis/trans	−3.70	−4.13
bicyclo[3.3.0]octane, cis/trans	−6.4	−11.05
decalin, cis/trans	1.00	1.76
perhydroanthracene, cis–trans[b]	2.80	1.79
perhydroanthracene, trans–anti–trans[b]	4.10	8.79
perhydroanthracene, cis–anti–cis[b]	5.60	3.77
perhydroanthracene, cis–syn–cis[b]	8.70	6.58

[a] The energy difference is that of the first species minus the second. [b] Relative to trans–syn–trans.

C. Other Cases. To test the parameters for borons we calculated the structure of diborane (B_2H_6) where the bridging hydrogen is type H_b, and B_3 and H_ are used for the other atoms. Assuming each B_3 is bonded to four hydrogens (no formal B–B bond) leads to bond distances of 1.21 and 1.39 Å for terminal and bridging BH bonds (experimental[6b] 1.201 and 1.320 Å). The calculated bond angle at the bridging H is 81.8° (experimental[6b] 83.8°) which leads to a B–B distance of 1.82 Å (experimental[6b] 1.763 Å).

V. Conclusions

We find that DREIDING leads to accurate geometries and reasonably accurate barriers for various organic systems. As a result, we expect DREIDING to be useful in predicting structures involving new combinations of elements and should be easily extendable to new atoms. The current uncertainties in predicting the distribution of charges in molecules and in estimating the van der Waals interactions are limitations that we believe are as serious as the restricted set of parameters used in DREIDING.

The next level of sophistication in developing generic force fields is to alter the parameters (force constants, barriers) to change smoothly as a function of rows and columns. We leave this for a later study.

Acknowledgment. We thank Professor Anthony K. Rappé and Dr. Carla J. Casewit for providing stimulating discussions and carrying out tests of these force fields while on sabbatical at BioDesign. We thank Drs. Walter E. Reiher III and Paul W. Saxe for stimulating discussions and assistance in the calculations. We thank Adria McMillan and Carol Scrivnor for typing various versions of the text and Dr. Marie Ary for reformatting the text and preparing the 76 structures in the figures and the long tables (Tables VIII–XIII). Initial development of the DREIDING force field was carried out at Caltech and supported by a grant from the Department of Energy, Energy Conversion and Utilization Technologies Program (DOE-ECUT). More recent developments of the DREIDING force field were carried out at BioDesign.

Registry No. B, 7440-42-8; C, 7440-44-0; N, 17778-88-0; O, 17778-80-2; F, 14762-94-8; Al, 7429-90-5; Si, 7440-21-3; P, 7723-14-0; S, 7704-34-9; Cl, 22537-15-1; Ga, 7440-55-3; Ge, 7440-56-4; As, 7440-38-2; Se, 7782-49-2; Br, 10097-32-2; In, 7440-74-6; Sn, 7440-31-5; Sb, 7440-36-0; Te, 13494-80-9; I, 14362-44-8; Na, 7440-23-5; Ca, 7440-70-2; Fe, 7439-89-6; Zn, 7440-66-6.

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(28) This leads to $\delta E = {}^1/_2 K(\delta\theta)^2$ for θ near linear, whereas (10a) would lead to $\delta E \sim 1/8C(\delta\theta)^4$.

(29) These calculations were carried out using periodic boundary conditions with convergence acceleration[13] allowing all atoms to optimize.