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A Molecular Mechanics Force Field for Conformational Analysis of Aliphatic Acyclic Amines

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An improved molecular mechanics force field for conformational and vibrational studies of aliphatic acyclic amines is developed. The resulting force field reproduces molecular structures adequately and provides a good fit for energy differences between conformers and barriers to internal rotation for a large number of amines. In addition, vibrational frequencies are calculated in good agreement with available experimental data. When compared with existent force fields for amines, the present force field is considerably more simple and gives rise to calculated properties in closer agreement with experiment.

INTRODUCTION

Molecular mechanics offers an attractive means of undertaking conformational and vibrational analysis. Therefore, we have begun to develop this technique in our laboratory with a view to applying it to the problem of model compounds used to understand the enzyme–substrate intermediates found during the catalytic action of serine and cysteine proteases [1–8]. As a starting point, we have developed a molecular mechanics force field for conformational analysis of simple acyl chlorides, carboxylic acids, and esters which can also been used to deal with alkanes, alcohols, and ethers [9]. This force field was later applied to α-chloro-substituted carbonyl compounds, mainly to assess conformational freedom involving rotation around the C—C(=O) bond [10–12] and, more recently, extended to deal with alkanethiol, thioether, and thiocarbonyl molecules [13,14].

In the present study we have extended our force field (PF1) to amines, thus initiating the nitrogen atom parameterization. This extension represents a decisive improvement for the future application of the force field to the enzyme–substrate model compounds.

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COMPUTATIONAL METHODS

The molecular mechanics calculations were carried out with the fast convergent energy minimization CFF program and Niketic and Rasmussen [15], adapted to a DG/Eclipse MV8000 computer. Detailed information on computational algorithms and the original program can be found in Refs. [15] and [16].

The potential energy function is defined as a sum of terms in bond and angle deformations (harmonic terms), torsional contributions (cosine-type), and nonbonding interactions (Buckingham potential, exp-6 type).

$$E = \tfrac{1}{2}\Sigma_i K_{b_i}(b_i - b_{0_i}) + \tfrac{1}{2}\Sigma_j K_{\theta_j}(\theta_j - \theta_{0_j})^2 + \tfrac{1}{2}\Sigma_k K_{\tau_k} \times [1 + \cos(n_k\tau_k)] + \Sigma_l[A_l \exp(-B_l r_l) - C_l/r_l^6] + \tfrac{1}{2}\Sigma_m K_{\omega_m}[1 + \cos(3\omega_m)]$$

We have used the bond torsional model, which considers all combinations of outer pairs of atoms per bond, since this model is the most appropriate for describing nonsymmetrical arrangements of atoms within

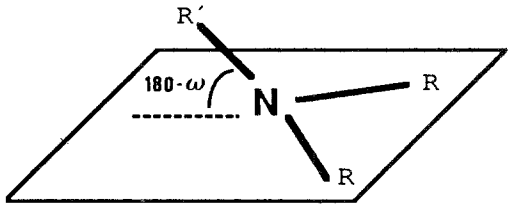

Figure 1. Definition of the dihedral angle, ω, used to account for amine group inversions.

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Table 1. Optimized Potential Energy Parameter Set (PF1) for Aliphatic Acyclic Amines[a]

Bond deformation	K_b	b_0	van der Waals	A × 10^{-4}	B × 10^2	C × 10^{-12}
C—N	3418.3	147.4	N···C	46.0	4.50	1020.9
N—H	3828.4	101.4	N···H	14.6	4.55	415.0

[a]Units are chosen so that energy is given in kJ mol^{-1}, distances in pm, and angles in radians.
[b]The symmetry of the C—C—N—H rotor in *t*-butylamine requires the derivation of a different set of C—C—N—H parameters for this molecule. Thus, in this case, K_τ and n are 1.925 and 3, respectively.

Table 2. Model Compounds and Reference Data Selected for Force Field Parameterization[a]

Molecule	Structure	Conformational energies	Vibrational spectra
Methylamine	r_o; μw [18,19]	μw [20]; IR [21]	IR (gas) [22]
Ethylamine	r_s; μw [23,24]	μw [24]; IR [25]	IR, R (gas) [26]
n-Propylamine	r_e; ab initio[b]	ab initio[b]	IR (gas) [27]; R (liq) [28,29]
Dimethylamine	r_s; μw [31]	μw [31]; IR [32]	IR (gas) [33,34]; R (gas) [34]
Ethylmethylamine	r_e; ab initio[b]	ab initio[b]	IR (gas) [35]; R (liq) [29]
Trimethylamine	r_s; μw [36]	μw [37]; IR [32,38]	IR (gas) [32,39]
n-Butylamine[c]	r_e; ab initio[b]	ab initio[b]	R (liq) [29,40]
Isopropylamine[c]	r_e; ab initio[b]	ab initio[b]; IR [41,42]	IR (gas) [41,43]; R (gas) [41]
t-Butylamine	r_g, r_α; ED [44]	ab initio[b]; IR [42]	IR (gas) [42]
Diisopropylamine[c]	r_g; ED [45]		IR (gas), R (liq) [45]
Dimethylethylamine[c]	r_α; ED [46]	ab initio[b]	IR, R (gas) [47]
	r_e; ab initio[b]		

[a]μw, microwave spectroscopy; ED, electron difraction; IR, infrared spectroscopy; R, Raman spectroscopy.
[b]This work (3–21G + d(N) basis set).
[c]Molecule used to test the force field.

a molecule. To account for amine group inversions, we have included negative threefold cosine-type terms, which depend on the value of the dihedral angle ω defined in Figure 1.

The force field parameters necessary to deal with the amine group were optimized following the general scheme referred to in Refs. [9] and [17] and are presented in Table 1. The remaining parameters were taken from our previously developed force field for alkanes [9].

In consonance with previous studies [9–14], we have not explicitely considered the lone-pair electrons in the force field parameterization, since this consideration requires an increase in the number of force-field parameters and does not seem to be necessary for a correct description of molecular properties.

The experimental data selected for parameterization and the model compounds used in this study are presented in Table 2. Ethyl- and *n*-propylamine molecules were essential to determine both the nonbonding and C—C torsional parameters, while methyl, ethyl, dimethyl, ethylmethyl, and *t*-butylamine molecules were used to evaluate C—N torsions. The nitrogen atom inversion parameters were determined using methyl, dimethyl, and trimethylamine molecules. Whenever available, microwave geometries, relative energies, and gas-phase vibrational frequencies were used for parameterization. In those cases where experimental geometries and energies are either not available or not accurate enough, SCF–MO ab initio values, calculated using the 3–21 G + d (0.8N) basis set [48,49] and the MONSTERGAUSS program package [50], were used. On the other hand, when the gas-phase frequencies were not known, spectroscopic data from solution or liquid phase were considered. This approximation does not seem to be very important considering the usual small frequency shifts accompanying the change of phase. Instead of pursuing a detailed description of the spectra that would require a strong increase in the force field complexity [16,17], our purpose is to reach a general agreement between calculated and experimental frequencies with a simple and reliable force field.

Table 1. (Continued)

Angle deformation	K_θ	θ_0	Torsional terms	K_τ	n	Inversion	K_ω
H–N–H	373.2	1.848	H—C—N—H	1.284	3	C—(H—N—H)	−2.092
C–N–H	283.2	1.956	N—C—C—H	2.427	3	H—(C—N—C)	−1.422
N–C–H	288.7	1.910	C—C—N—H[b]	−1.330	1	C—(C—N—C)	−0.628
N–C–C	577.4	1.971	N—C—C—C	3.284	1		
C–N–C	474.9	1.948	C—N—C—H	2.803	3		
			C—N—C—C	6.192	1		

RESULTS AND DISCUSSION

Molecular Structures and Relative Conformational Energies

Calculated molecular structures and energies are presented in Tables 3 and 4. When compared with experimental data our molecular mechanics results show a good general agreement (Figures 2 and 3) and improve on the literature data [29,30]. In particular, the excellent agreement between experimental and calculated values for the molecules not included in the parameterization should be noted. This agreement is a good indication of the quality and predictive power of the force field. In addition, changes in molecular geometries associated with internal rotation are also generally well predicted, especially for valence and dihedral angles (see Table 3). The exception to this general rule seems to be the N–C–C angle. In primary amines, this angle increases from ≈109.5° to ≈115.5° when the conformation around the N—C bond changes from the gauche (Lp–N–C–C dihedral angle ≈ ±60°) to the trans form (Lp–N–C–C dihedral angle = 180°) [23,24,29]. However, this increase of the N–C–C angle depends mainly on an electronic effect and so is difficult to reproduce within the molecular mechanics framework. In fact, it is associated with a greater electronic delocalization from the nitrogen lone-pair electron to the molecular skeleton in the trans conformation; this electronic transfer changes the hybridization state of the a carbon atom to closer an sp^2 state [29,51]. It should be pointed out that in the diisopropylamine molecule (Figure 4), where strong steric hindrance is present, the calculated C–C–C and C–N–C angles agree well with the experimental values (see Table 3).

The PF1 calculated minimum energy conformations of mono-, di-, and trimethylamine molecules are presented in Figure 5. The CH_3 experimental energy barriers to internal rotation in these molecules, as well as the inversion barriers of mono- and dimethylamine, are reproduced very well by calculations (see Table 4). In contrast, the inversion barrier in trimethylamine (31.4 kJ mol^{-1} [38]) is overestimated by calculations (40.9

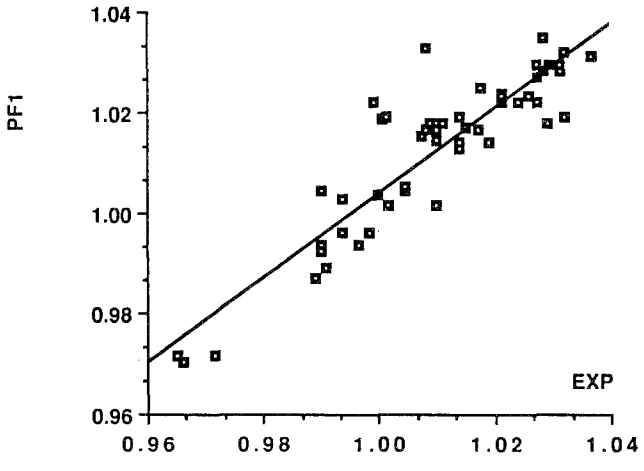

Figure 2. PF1 calculated vs. experimental geometries for amines. The plotted values correspond to reduced bond lengths and bond angles: CN/145, NH/100, CH/110, CC/150, angles/109. The straight line obeys to the equation $Y_{calc} = 0.16 + 0.85\ Y_{exp}$, the correlation coefficient being 0.90.

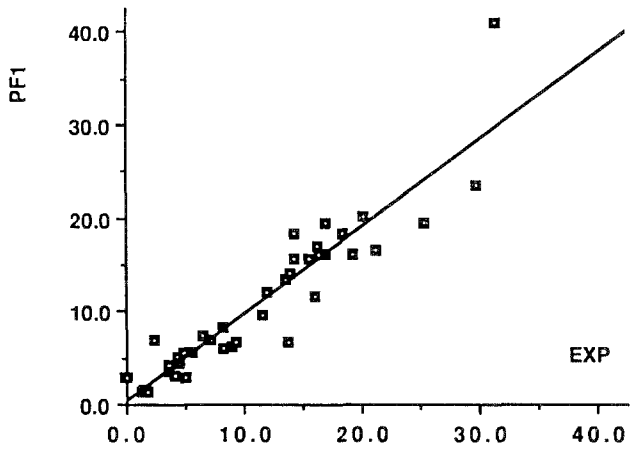

Figure 3. PF1 calculated vs. experimental conformational energies (kJ mol^{-1}) for amines. The straight line obeys to the equation $Y_{calc} = 0.37 + 0.94\ Y_{exp}$, the correlation coefficient being 0.94.

Table 3. Calculated and Reference (Experimental or ab Initio) Molecular Structures[a]

Parameter	Methylamine [18,19]	Ethylamine [23,24]		*n*-Propylamine[b]					Isopropylamine[b]	
		T	G	TT	GT	TG	GG′	GG	T	G
N—C	**147.4**	**147.4**		**147.1**	**147.2**	**147.0**	**147.3**	**147.4**	**147.4**	**147.3**
	147.4	147.5	147.5	147.5	147.5	147.5	147.4	147.5	147.5	147.5
N—H	**101.4**	**101.4**		**101.4**	**101.4**	**101.4**	**101.4**	**101.4**	**101.4**	**101.5**
	101.4	101.4	101.4	101.4	101.4	101.4	101.4	101.4	101.4	101.4
C—H	**109.3**	**109.3**								
	109.6	109.6	109.6	109.6	109.6	109.6	109.6	109.6	109.6	109.6
C(N)—C		**153.6**		**154.3**	**153.7**	**154.5**	**153.9**	**153.9**	**153.6**	**153.9**
		153.3	153.2	153.3	153.3	153.4	153.2	153.3	153.3	153.3
C—C				**154.0**	**154.0**	**154.0**	**153.9**	**154.1**		
				153.2	153.2	153.2	153.2	153.3		
H—N—H	**105.9**			**105.2**	**105.1**	**105.6**	**105.3**	**104.9**	**105.2**	**105.1**
	105.9	105.8	105.9	105.8	105.9	105.9	105.9	105.7	105.9	105.9
C—N—H	**112.1**	**112.0**		**108.3**	**108.4**	**108.7**	**108.4**	**108.4**	**108.4**	**108.1**
	112.1	112.2	112.2	112.2	112.2	112.4	112.2	112.3	112.4	112.4
C—C—N		**115.2**	**109.5**	**115.3**	**109.8**	**116.0**	**109.9**	**110.4**	**108.1**	**108.2**
		112.1	112.0	112.1	112.0	112.5	111.9	112.3	110.8	110.7
C—N—C										
C—C—C				**111.8**	**111.9**	**112.6**	**111.6**	**112.7**	**110.5**	**110.8**
				112.5	112.5	113.2	112.4	113.2	111.5	111.4
H—C—H	**109.5**	**109.5**		**107.2**[c]	**107.5**[d]	**107.1**[c]	**107.4**[c]	**107.8**[c]	**108.4**[d]	**108.4**[d]
	109.5	107.9	107.9	107.3[d]	107.3[d]	107.2[c]	107.3[d]	107.2[d]	107.9	107.9
				108.1[d]	**108.1**[d]	**108.1**[d]	**108.5**[d]	**108.2**[d]		
				107.9[d]	107.9[d]	107.9[d]	107.9[d]	107.9[d]		
C—C—H		**110.1**		**109.5**[c]	**109.6**[c]	**109.4**[c]	**109.5**[c]	**109.2**[c]	**108.7**	**108.5**[f]
		110.8[c]	110.8[c]	110.1[c]	110.1[c]	110.0[c]	110.1[c]	110.0[c]	108.9	108.9[f]
				110.8[d]	**110.8**[d]	**110.8**[d]	**110.4**[d]	**110.8**[d]	**110.3**	**110.4**[d]
		111.0[d]	111.0[d]	111.0[d]	111.1[d]	111.0[d]	111.0[d]	111.1[d]	111.0	111.0[d]
Dihedral angles				**180.0**[g]	**182.2**[g]	**57.8**[g]	**−60.9**[g]	**63.5**[g]		
				180.0[g]	180.1[g]	61.9[g]	−60.4[g]	62.7[g]		

[a] Bond lengths in pm; angles in degrees; upper values (**bold**) are reference values, lower values are calculated values.
[b] Reference values taken from ab initio 3–21 G + d(N) calculations.
[c] Average values for CH_2 groups.
[d] Average values for C—CH_3 groups.
[e] Average value for N—CH_3 groups.
[f] For the isopropyl group.
[g] N–C–C–C dihedral angle.
[h] C–N–C–C dihedral angle.
[i] C–N–C–H dihedral angle.

kJ mol^{-1}), although the molecular mechanics result agrees with the STO-3G ab initio SCF-MO value (43.1 kJ mol^{-1} [52]).

Relative stabilities of the various possible conformers of linear primary amines, including those not used during the force-field parameterization, are predicted well by calculations. In these molecules, only the energies calculated for the GG′ conformer in *n*-propylamine (Figure 6) and for the GG′T and GG′G′ conformers of *n*-butylamine (Figure 7) show large differences when compared with the reference values. Reference data show that the energy of the GG′ form of *n*-propylamine is approximately equal to that of the TT form: the GG′ form corresponds to a very stable conformer (see Table 4). However, molecular mechanics predicts an energy for the GG′ form ≈ 3 kJ mol^{-1} higher than that of the TT form and above those of the GT and TG forms. This discrepancy results from the general inability of a molecular mechanics force field to deal with hydrogen bonds, as the stabilization of the GG′ conformer of *n*-propylamine is due to the presence of an intramolecular hydrogen bond involving the formation of a H—C—C—C—N five-membered ring [28] (see Figure 6). Similar intramolecular hydrogen bonds occur in the GG′T and GG′G′ forms of *n*-butylamine (see Figure 7) [29], thus justifying the overestimation of the ΔE(GG′T–TTT) and ΔE(GG′G′–TTT) molecular mechanics calculated values. The molecular

Table 3. (Continued)

t-Butyl-amine [44]	Dimethyl-amine [31]	Ethylmethyl-amine[b]			Diisopropyl-amine [45]	Trimethyl-amine [36]	Dimethylethyl-amine[b][31]	
		T	G	G′			T	G
149.2	**146.3**	**146.5**	**146.6**	**146.7**	**147.0**	**145.1**	**146.1**	**145.2**
147.6	147.6	147.6	147.6	147.6	147.8	147.7	147.8	147.8
	101.9	**101.4**	**101.3**	**101.2**				
101.4	101.4	101.4	101.4	101.4	101.4			
	109.8					**109.5**		**110.6**
109.6	109.6	109.6	109.6	109.6	109.6	109.6	109.6	109.6
153.2		**153.7**	**154.6**	**153.9**	**153.2**		**154.8**	**153.9**
153.5		153.2	153.3	153.3	153.3		153.4	153.3
105.2								
105.9								
109.9	**108.9**	**107.6**	**108.3**	**107.5**				
112.6	111.4	111.6	111.8	111.3	111.8			
		109.9	**116.2**	**111.2**	**111.3**		**117.4**	**113.0**
109.8		111.9	112.4	112.3	111.5		113.4	112.4
					108.9			
					110.4			
	112.2	**111.6**	**113.4**	**112.4**	**120.1**	110.9	**112.8**	**111.3**
	112.2	112.4	112.6	112.5	114.3	111.7	112.9	111.8
							111.0	**111.3**
							112.3	111.4
110.1					**112.5**			
109.2					111.1			
108.0	**109.0**	**107.2**	**107.0**	**107.5**[c]		**108.3**[d]	**107.0**	**107.3**[c]
107.8	109.4	107.9	107.7	107.7[c]	107.9	109.3[d]	107.4	107.7[c]
		108.4	**108.2**	**108.5**[d]			**108.1**	**108.5**[d]
		107.9	107.9	107.9[d]			107.8	107.9[d]
		108.1	**108.0**	**108.0**[e]			**108.1**	108.2[e]
		109.4	109.4	109.4[e]			109.3	109.2[e]
		109.6	**109.1**	**109.0**[e]	**105.3**[f]		**108.8**	**109.1**[e]
111.1		110.6	110.7	110.6[e]	108.1[f]		110.4	110.4[e]
		110.4	**110.7**	**110.4**[d]	**111.0**[d]		**110.8**	**110.4**[d]
		111.0	111.0	111.0[d]	111.0[d]		111.1	111.0[d]
		178.6	**64.7**	**−76.1**[h]	**52**[i]		**−63.6**	**168.7**[h]
		181.3	66.7	−64.4[g]	59.1[i]		−64.4	172.5[h]

mechanics results also indicate that the TTT conformer of *n*-butylamine should correspond to the most stable form under conditions in which the intramolecular hydrogen bond that stabilizes the GG′T form could not subsist. On the whole, the present calculations give good theoretical support to previous vibrational spectroscopic studies [40], which had suggested that the most stable conformer of *n*-butylamine in the liquid and crystaline phases should have a trans-N—C—C—C axis.

Conformational preferences of isopropylamine have been subject to several experimental studies, which have given rise to contradictory results. An infrared spectroscopic study of the torsional modes of this molecule in the gaseous phase [53] suggested that the gauche form (see Figure 8) should predominate over the trans form, the trans–gauche energy difference being very small. On the contrary, analysis of the temperature dependence of the IR and Raman spectral bands [41,42] pointed to the reverse order of stability of the two conformers. In addition, several theoretical studies have also been carried out on this molecule. Using standard geometries and the 4–31G basis set, the ab initio calculated $\Delta E_{\text{trans-gauche}}$ was found to be −2.80 kJ mol^{-1} [54]. However, this energy difference was reduced considerably ($\Delta E_{\text{trans-gauche}}$ = −0.69 kJ mol^{-1}) when partial geometry optimization was performed and polarization functions on the nitrogen atom were used [43]. Full geometry optimization reversed the relative stabilitiy of the two conformers, the gauche form being more stable than the trans form by ≈0.15 kJ mol^{-1} (see Table 4).

The model that was proposed [41,51] to explain the greater stability of the trans form, as experimentally suggested, assumed that the trans stabilization is due to a back-donation effect from the nitrogen lone pair to the σ^* antibonding orbital associated with the trans α-CH bond. However, a similar interaction involving a trans α-CC bond, which is found in the gauche conformer, has also been recently proved possible [29]. In addition, it is now also clear that the correct prediction of the relative stabilities of amine conformers

Table 4. Barriers to Internal Rotation and Conformer Energy Differences (kJ mol^{-1})

Molecule	ΔE	PF1	Ref.	ΔE_{rot}	PF1	Ref.	ΔE_{inv} PF1	ΔE_{inv} Ref.
Methylamine					8.20	**8.20** [20]	20.2	**20.2** [21]
Ethylamine	G–T	1.32	**1.32** [24]	G→G	6.12	**8.25** [24]	19.5	**17.0** [24]
				T→G	6.69	**9.23** [25]		
				T—CH_3	15.6	**14.3**		
				G↴CH_3	15.6	**15.6**		
n-Propylamine	TG–TT	1.53	**1.53**	GT→GT	6.16	**8.86**	20.1	
	GT–TT	1.38	**1.69**	TT→GT	6.71	**13.7**		
	GG–TT	3.11	**4.11**	GG→GT	14.2	**14.0**		
	GG′–TT	2.88	**0.00**	GG→GG′	16.0	**19.2**		
				GT→GG′	16.2	**16.4**		
				TT→TG	16.0	**17.0**		
				TG→TG	16.5	**21.3**		
Dimethylamine					13.5	**13.5** [31]	18.4	**18.4** [30]
Ethylmethylamine	G′–T	4.53	**4.52**	T→G	17.0	**16.3**	16.8	
	G–T	2.95	**4.96**	T→G′	18.4	**14.3**		
				G→G′	19.5	**25.4**		
Trimethylamine					18.8	**18.4** [37]	40.9	**31.4** [38]
n-Butylamine[b]	GTT	1.38	**1.77**					
	TGT	1.52	**1.44**					
	GG′T	2.85	**−0.22**					
	GGT	3.15	**4.04**					
	TTG	4.26	**3.49**					
	TGG	5.21	**4.20**					
	GTG′	5.62	**5.48**					
	GTG	5.66	**4.90**					
	GGG	6.84	**7.06**					
	GG′G′	6.93	**2.34**					
	GG′G	7.40	**6.51**					
	TGG′	9.58	**11.6**					
	GGG′	11.7	**16.1**					
Isopropylamine	T–G	1.30	**0.15**	G→G	7.29	**13.3**	21.0	
				G→T	6.71	**12.5**		
				T↴CH_3	18.7	**16.1**		
				G↴CH_3	18.7	**16.2**		
t-Butylamine				↴NH_2	13.8	**13.8**	26.2	
				↴CH_3	22.5	**18.1**		
Dimethylethylamine	T–G	3.50	**3.63**	G→T	23.4	**29.8**	35.6[c]	
				G→G	12.1	**12.0**	39.5[d]	

[a]The reference values that do not indicate the source of data were obtained in this work, using ab initio (3–21 G + d(N)) calculations.
[b]Energies relative to the TTT form.
[c]Conformer T.
[d]Conformer G.

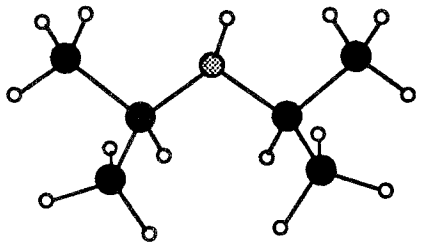

Figure 4. PF1 calculated minimum energy conformation of diisopropylamine.

at a theoretical level requires full geometry optimization [29]. Thus, good theoretical evidences point out that, at least for the isolated molecule situation, the gauche form corresponds to the most stable conformer, although the energies of the two forms are very close. In qualitative agreement with the highest level theoretical results, molecular mechanics calculations predict the gauche form more stable than the trans form by 1.3 kJ mol^{-1}.

The results obtained for the relative conformational energies of ethylmethylamine (Figure 9) are in good agreement with the reference values (see Table 4). In particular, both ab initio and molecular mechanics methods predict that a trans C—C—N—C axis is more stable than a gauche C—C—N—C axis by ≈4 kJ mol^{-1}. In addition, it is interesting to note that the

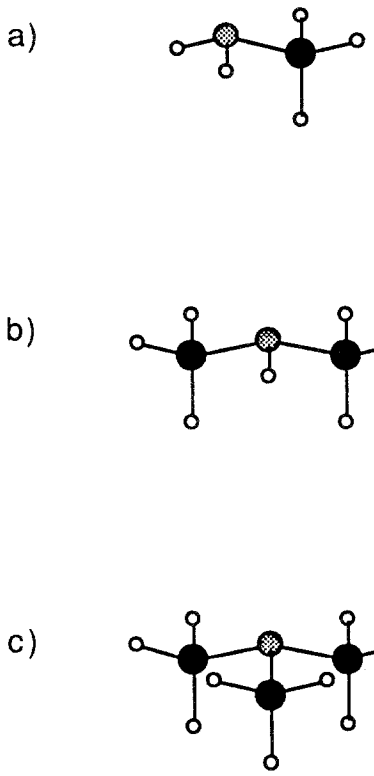

Figure 5. PF1 calculated minimum energy conformations of (a) mono-, (b) di-, and (c) trimethylamine molecules.

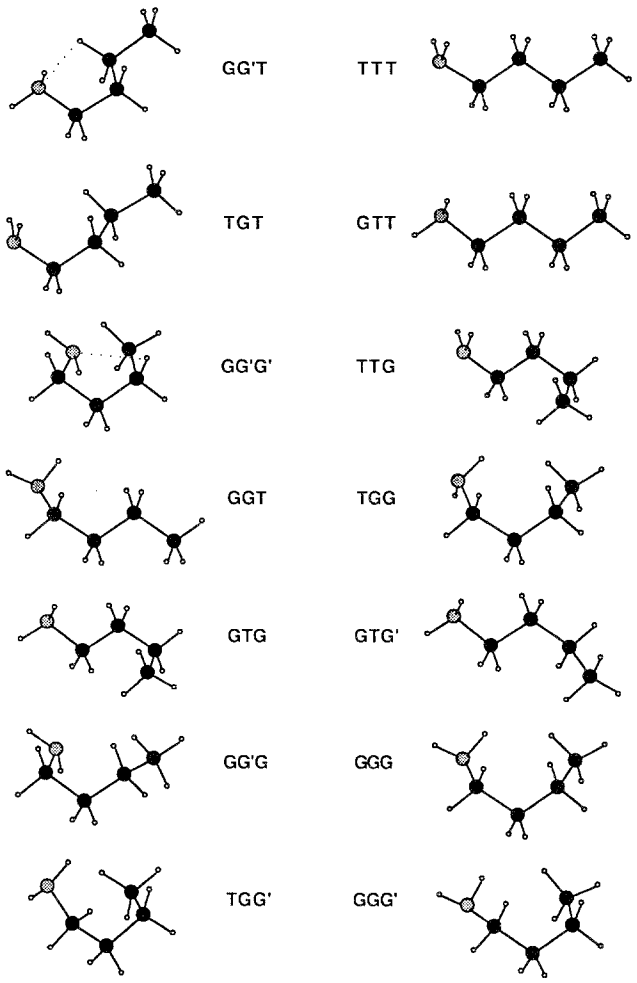

Figure 7. Conformers of *n*-butylamine.

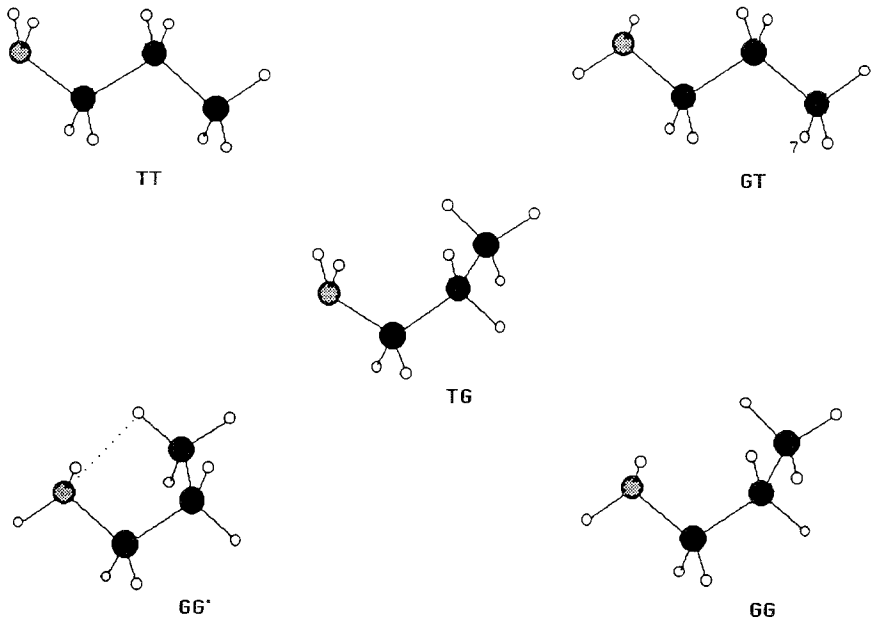

Figure 6. Conformers of *n*-propylamine.

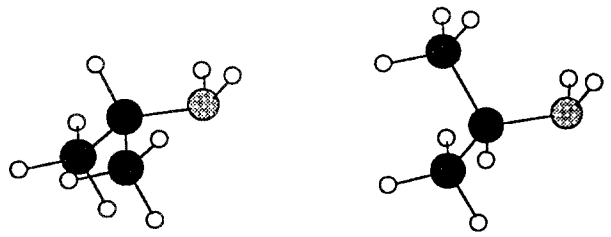

Figure 8. Conformers of isopropylamine.

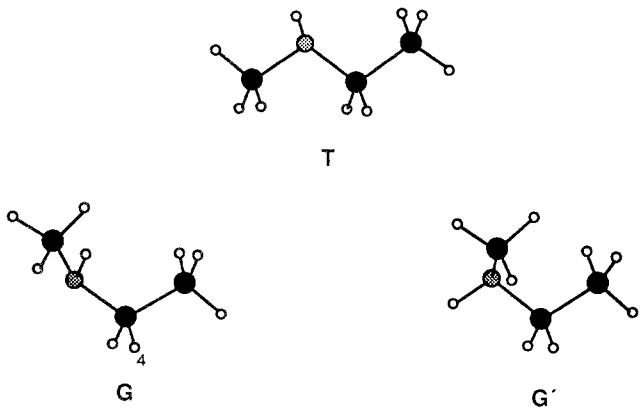

Figure 9. Conformers of ethylmethylamine.

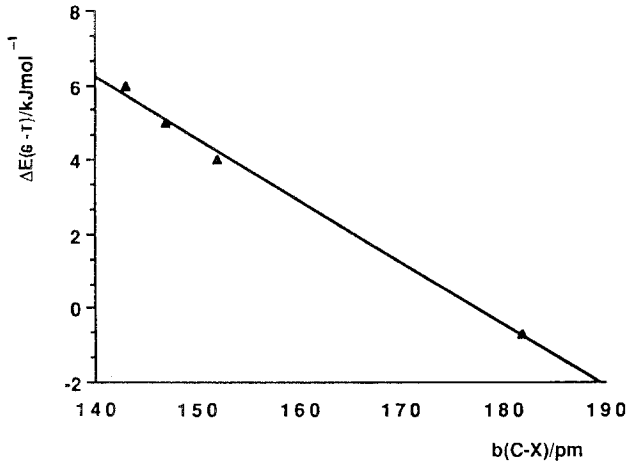

Figure 10. $\Delta E_{G-T}^{C-C-X-C}$ (X = O, CH_2, NH, S) vs. the length (b_{C-X}) of the C—X central bond. The straight line obeys to the equation $\Delta E = 29.61 b_{C-X} - 0.17$, the correlation coefficient being 1.00.

relative stability of a trans and gauche C—C—X—C axis, with X = C, N, O, or S, shows a systematic trend when it is correlated with the C—X bond length. In fact, a plot of $\Delta E_{\text{gauche-trans}}$, as evaluated from the PF1 or obtained experimentally, vs. C—X bond length (Figure 10) gives a straight line, showing that the relative stability around a C—C—X—C axis depends linearly on the length of the central C—X bond. A reduction of $CH_3 \cdots CH_3$ repulsions that accompanies the increase of the methyl–methyl distance—which, in turn, correlates with an increase in the C—X bond—can, at least in part, justify the observed trend.

Vibrational Frequencies

During the force-field parameterization, we have favored a general agreement between calculated and observed vibrational frequencies [9,13,14]. The results are summarized in Tables 5 and 6. These tables present only the results for skeletal vibrations and for the modes involving the amine group. The remaining modes show the general trends found for previously considered families of molecules [9,13,14]. Generally speaking, the agreement between calculated and experimental values is good, even when conformational dependencies of frequencies are analyzed. In particular, the remarkable agreement should be noted between calculated and experimental torsional frequencies, which are usually quite difficult to reproduce adequately at this level of calculation, due both to their usual high degree of anharmonicity and to their vibrational coupling.

CONCLUSION

The present extension of the PF1 force field to nitrogen-containing molecules allows the characterization of several imporant conformational properties of these compounds. The agreement obtained between calculated and reference data is generally very good, even in the case of vibrational frequencies which are generally quite difficult to fit by molecular mechanics. The present force field represents a decisive improvement for the future application to model compounds used in the study of the reaction intermediates resulting from the action of serine and cysteine proteases.

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Table 5. Experimental and Calculated Vibrational Frequencies (Primary Amines)[a]

Mode[b]	$MeNH_2$	$EtNH_2$		*n*-$PrNH_2$		*n*-$BuNH_2$	*iso*-$PrNH_2$		*t*-BuNH
		T	G	TT	GG′	TTT	T	G	
$\upsilon_a NH_2$	**3427**	**3411**		**3411**			**3411**	**3393**	
	3420	3420	3421	3420	3421	3420	3421	3421	3421
$\upsilon_s NH_2$	**3361**	**3345**		**3346**			**3340**	**3327**	**3320**
	3361	3362	3361	3362	3361	3362	3361	3362	3362
δNH_2	**1623**	**1622**		**1622**			**1622**		**1635**
	1623	1624	1625	1625	1625	1625	1628	1626	1628
υ NC	**1044**	**1055**	**1086**	**1024**		**1034**	**978**		**942**
	1044	1055	1053	1016	1031	1015	972	973	938
ωNH_2	**780**	**793**	**773**	**787**		**799**	**785**	**781**	**743**
	780	807	774	786	819	800	797	779	771
υ NCC		**403**		**453**	**471**	**436**	**404**		**446**
		403	404	373	435	391	396	396	406
υ CCC				**306**		**400**	**369**		**337**
				240	281	277	297	298	374
υ C—NH_2	**264**[c]	**236**	**218**	**210**	**201**		**267**	**221**	**253**
	305	221	211	227	200	235	167	179	257
υ C—CH_3		**265**	**259**	**252**	**223**		**258**		**279**
		279	272	265	234	264	275	276	298
υ C—C				129	**136** 129	128			
						115			

[a]Frequencies in cm^{-1}; upper values (bold), experimental values taken from references presented in Table 2; lower values, calculated values.
[b]υ, stretching; a, antisymmetric; s, symmetric; δ, bending, ω, wagging; τ, torsion; Me, methyl; Et, ethyl; Pr, propyl; Bu, butyl.
[c]Value obtained from normal coordinate analysis.

Table 6. Experimental and Calculated Vibrational Frequencies (Secondary and Tertiary Amines)[a]

Mode[b]	Me_2NH	EtMeNH			Di-*iso*-PrNH	Me_3N	Me_2EtN	
		T	G	G′			G	T
υ NH	**3377**							
	3393	3393	3393	3393	3393			
δ NH	**1485**				**1476**			
	1519	1532	1524	1518	1540			
υ NC	**1022**	**1013**	**989**	**1001**	**1022**	**1183**	**1173**	**1180**
	1035	1021	1000	1006	1046	1176	1191	1184
δ NH	**735**	≈**740**			**693**			
	707	740	745	724	669			
δ CCN		**447**	**363**	**355**	**487**		**481**	
		401	459	455	455		450	496
δ CNC	**384**	**277**	**336**	**330**	**193**	**366**	**383**	**397**
	383	296	342	324	189	366	377	391
δ CCC					**317**			
					305			
τ N—CH_3	**257**	**257**	**249**	**256**	**269**	**267**		
	277	253	251	257	259	286	266	271
	230					**261**[c]		
	231					269		
τ N—C		**115**	**125**		**72/43**[c]		**105**	
		111	121	117	86/42		105	149

[a]Frequencies in cm^{-1}; upper values (bold), experimental values taken from references presented in Table 2; lower values, calculated values.
[b]υ, stretching; δ, bending, τ, torsion, Me, methyl; Et, ethyl; Pr, propyl.
[c]Value obtained from normal coordinate analysis.

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