Journal of Molecular Structure, 144 (1986) 199—213
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

A MOLECULAR MECHANICS FORCE FIELD FOR CONFORMATIONAL ANALYSIS OF SIMPLE ACYL CHLORIDES, CARBOXYLIC ACIDS AND ESTERS

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(Received 29 July 1985; in final form 30 October 1985)

ABSTRACT

A molecular mechanics force field for conformational and vibrational studies on acyl chlorides, carboxylic acids and esters is developed. The resulting force field can also be applied to alkanes, alcohols and ethers. Chlorine atoms and alkyl groups are considered as α-substituents.

INTRODUCTION

The work presented in this series of papers (this paper and refs. 1—3) was motivated by an effort to understand structural and vibrational properties of dithioesters used as resonance Raman probes of enzyme mechanisms [4, 5]. While our understanding of some of these probes has reached a sophisticated level, it is apparent that additional approaches are required to reinforce and interpret spectroscopic data. Since molecular mechanics offers an attractive means of undertaking conformational and vibrational analysis, we have begun to develop this technique in our laboratory with a view to eventually applying it to the problem of model compounds used in the study of enzyme substrate complexes. As an initial study we have undertaken a conformational analysis of simple α-substituted carbonyl compounds by combined molecular mechanics and vibrational studies.

In the present paper, we build a molecular mechanics force field for conformational and vibrational studies on acyl chlorides, carboxylic acids and esters. Yet, this force field is sufficiently general to deal with alkanes, alcohols and ethers. Both chlorine atoms and alkyl groups are considered as α-substituents.

As the main objective of this series of papers is to assess conformational freedom through rotation around the C_α—C(=O) bond, the following papers deal in succession with CH_3—C(=O) [1], $CClH_2$—C(=O) [2], and $CHCl_2$—C(=O) and CCl_3—C(=O) [3] molecules. General trends observed along this series of compounds are discussed in ref. 3.

0022-2860/86/$03.50

EXPERIMENTAL

Computer programs

We have used the fast convergent energy minimization CFF program of Niketić and Rasmussen [6], adapted to a DG/Eclipse MV8000 computer. Detailed information on computational algorithms and the original program can be found in refs. 6 and 7.

In order to obtain a reasonable initial set of non-bonding and torsional parameters, preliminary calculations were performed under the rigid rotor approximation, using a FORTRAN 77 program written for an Apple IIe microcomputer, and based on the Scott—Scheraga method [8].

Features of the general force field and molecules selected for parameterization

The final set of force field parameters, hereafter referred to as PF1 (Table 1), reproduces molecular structures adequately and fits energy differences between conformers as well as barriers of internal rotation very well. In addition, PF1 yields vibrational frequencies in good general agreement with experimental values.

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

$$E = \frac{1}{2}\sum_i K_{b_i}(b_i - b_{O_i})^2 + \frac{1}{2}\sum_j K_{\theta_j}(\theta_j - \theta_{O_j})^2 + \frac{1}{2}\sum_k K\tau_k(1 + \cos(n_k\tau_k)) + \sum_l (A_l \exp(-B_l r_l) - C_l/r_l^6)$$

We have used the bond torsional model, which considers all combinations of outer pairs of atoms per bond. This model is more appropriate for describing nonsymmetrical arrangements of groups.

The torsional terms of PF1 perform an important role in determining conformer energy differences and barriers of internal rotation. In particular, we have included two-fold torsional terms to account for restricted rotation around partial double bonds.

Non-bonding interactions are also quite relevant especially when involving chlorine atoms.

The molecules used in the force field parameterization (see Table 2) have fairly abundant experimental data available (structural, energy and vibrational data), and their properties resemble those of the compounds we intend to study. Alkanes are included in the PF1 parameterization for obvious reasons. The inclusion of ethers and alcohols is justified by their sensitivity to non-bonding interactions involving H, C, and O atoms.

TABLE 1

Potential energy function with parameter set PF1

Bond deformation $1/2\ K_b(b - b_0)^2$

	K_b	b_0
C—C	510.0	1.532
C—Cl	455.0	1.782
C—H	710.0	1.096
C—C_{sp^2}	520.0	1.506
C—O	689.0	1.437
C=O[a]	1710.0	1.186
C=O[b]	1420.0	1.200
C=O[c]	1365.0	1.200
C_{sp^2}—Cl	377.0	1.797
C_{sp^2}—H	669.5	1.101
C_{sp^2}—O	703.0	1.334
O—H	1015.0	0.970

Angle deformation $1/2\ K_\theta(\theta - \theta_0)^2$

	K_θ	θ_0
C—C—C	50.0	2.050
C—C—H	71.0	1.970
C—C—C_{sp^2}	60.0	1.994
C—C=O	85.0	2.224
C—C_{sp^2}—Cl	170.0	1.959
C—C_{sp^2}—O	195.0	1.902
C—O—C	143.0	1.925
C—O—H	127.0	1.889
Cl—C—Cl	200.0	1.950
H—C—Cl	100.0	1.891
H—C—H	75.0	1.913
H—C—C_{sp^2}	74.0	1.926
H—C—O	75.4	1.889
H—C=O	97.0	2.179
H—C_{sp^2}—O	87.5	1.908
C_{sp^2}—C—Cl	190.0	1.970
C_{sp^2}—O—C	127.0	2.003
C_{sp^2}—O—H	95.0	1.848
O—C—C	120.0	1.900
O—C=O	380.0	2.197
O=C—Cl	190.0	2.100

Torsional terms $1/2\ K_\tau(1 + \cos n\tau)$

	$K\tau$	n
C—C=O—Cl	70.0	1
C—C=O—O	50.0	1
H—C=O—O	80.0	1
C—C—C—C	1.700	1
C—C—C—C_{sp^2}	1.700	1
C—C—C—O	0.650	1
C—C—C_{sp^2}—Cl	4.400	3
C—C—C_{sp^2}—O	3.200	3
C—C—C=O	—1.800	1
C—C—O—C	2.000	1
C—C—O—C_{sp^2}	0.700	1
C—C_{sp^2}—O—C	5.850	1
C—C_{sp^2}—O—H	4.740	1
Cl—C—C=O	0.050	1
Cl—C—C_{sp^2}—Cl	2.400	1
Cl—C—C_{sp^2}—O	0.150	1
H—C—C—C	0.500	3
H—C—C—H	0.300	3
H—C—C—C_{sp^2}	0.100	3
H—C—C—O	0.500	3
H—C—C=O	0.033	3
H—C—C_{sp^2}—Cl	0.290	3
H—C—C_{sp^2}—O	0.080	3
H—C—O—C	0.750	3
H—C—O—C_{sp^2}	0.215	3
H—C_{sp^2}—O—C	4.520	1
H—C_{sp^2}—O—H	4.550	1
H—O—C—C	0.180	1
H—O—C—H	0.300	3
O=C—O—C	—12.000	2
O=C—O—H	—7.000	2

Non-bonding interactions $Ae^{-Br} - C/r^6$

	$A \times 10^{-4}$	B	C
C•••H	4.19	4.43	121.1
H••=O	3.46	4.57	122.0
H•••C_{sp^2}	2.98	4.52	180.5
H•••Cl	9.50	4.12	189.0
O•••C	21.21	4.44	244.0
Cl•••Cl	31.40	3.90	2570.0
C•••C	14.20	4.37	297.8
C••=O	19.40	4.45	323.4
C•••C_{sp^2}	14.20	4.37	297.8
H•••H	0.88	4.55	45.2
Cl•••O	13.70	4.28	740.5
Cl•••C	15.10	3.88	775.0
O•••H	2.68	4.57	90.4
Cl••=O	17.00	4.30	956.0

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[a] Acyl chlorides. [b] Carboxylic acids. [c] Esters.

TABLE 2

Molecules selected for parameterization, and derived parameters

Molecule	Derived parameter
Alkanes	
Ethane	H—C—C—H torsion and H•••H non-bonding (by fitting essentially the torsional energy barrier and its frequency)
Propane	C—C—C angle
Isobutane	
n-Butane (*anti* and *gauche* conformers)	C—C—C angle, C—C—C—C torsion, and C•••H and C•••C non-bonding
n-Pentane	C•••H and C•••C non-bonding
Cyclohexane	
Methane	Used to judge the quality of PF1 in alkanes
Neopentane	
Cyclopentane	
Alcohols and ethers	
Methanol	C—O—H angle and conformational energy differences of structures correlated through rotation around C—O bonds (ethanol is also used to fit C—C—O angle)
Ethanol	
n-Propanol	C—C—C—O torsion
Dimethyl ether	C—O—C angle and methoxy energy barriers of rotation
Ethylmethyl ether	C—C—O angle and conformer energy differences
Isobutylmethyl ether	Conformer energy differences
2-Propanol	Used to judge the quality of PF1 in alcohols and ethers
Cyclohexanol	
Diethyl ether	
Propylmethyl ether	
Carbonyl compounds	
Formic acid (s-*cis* and s-*trans* conformers)	C_{sp^2}—O torsions, and O—C=O and C_{sp^2}—O—H angles in both conformations
Acetic acid (s-*cis*)[a]	C—C_{sp^2}—O and C—C=O angles and conformer energy differences
Propionic acid	C—C—C=O and C—C—C_{sp^2}—O torsions and C—C—C_{sp^2} angle
Butyric acid	C—C—C—C_{sp^2} torsion
Acetyl chloride	C—C_{sp^2}—Cl and O=C—Cl angles, and H•••Cl non-bonding interactions
Propionyl chloride	O—C—C—Cl torsion and C—C—C_{sp^2} angle
Methyl formate	C_{sp^2}—O—C angle and energy barriers of rotation around C—O bonds
Ethyl formate	C_{sp^2}—O—C—C torsion
Chloroacetic acid (*syn* s-*cis* form)	Were used to fit parameters related with angles defined by chlorine atoms, and non-bonding interactions involving this element
Chloroacetyl chloride (*syn* form)	
Dichloroacetyl chloride (*syn* form)	

[a] There is no structural or vibrational experimental information for the s-*trans* conformer of acetic acid despite its existence having been confirmed previously [9]. Thus, this conformer was not included in the force field parameterization. Our results for this molecule are presented in ref. 2.

All the structural experimental data used in the PF1 parameterization were taken, whenever available, from microwave results (r_0, r_z or r_s).

RESULTS AND DISCUSSION

Structures

The results are presented in Tables 3—5. Generally speaking, the agreement between calculated and experimental values is very good. The most relevant features are discussed in the following subsections.

Alkanes (Table 3)
Methane [10], Ethane [11, 12] and Propane [13] structures are reproduced very well. The calculated C—C—C angle in propane (112.5°) is in excellent agreement with the experimental value (112.4° [13]). It is interesting to note that the calculated value of this angle increases to 113.1° when one of the methyl groups is in the eclipsed position.

The structures of n-butane conformers, isobutane, and neopentane, are also in good agreement with experimental data. In particular, the excellent agreement between calculated and experimental [16] C—C—H angles in isobutane should be mentioned.

PF1 results for cyclohexane in the chair conformation are very good. The calculated C—C—C—C dihedral angles are 57.8°, in good consonance with the experimental value (54.9°) [21]. The structure for the twist—boat conformer is also calculated. It is interesting to note that C—C—C angles are larger in this case.

Our calculations on cyclopentane yield an approximately symmetric-top structure in agreement with the results presented by Melberg and Rasmussen [50].

Alcohols (Table 4)
The structure of the methanol molecule [25, 26] is well reproduced. The calculated structure shows a small —CH_3 tilt (angle of the C—O bond axis with the axis of rotation of the CH_3 group) towards the lone electron pairs of the oxygen atom, in agreement with experimental data [26]. The large value obtained for the C—O bond length is also observed in other alcohols and is a consequence of simultaneous optimization of esters which have a somewhat larger C—O bond than the alcohol molecules.

Both conformers of ethanol [27] are reproduced quite well although large discrepancies appear in the C—C—O angle of the *gauche* conformer (108.8°, calculated; 112.4° experimental) and in the torsional angle of this form (66°, calculated; 54 ± 6°, experimental).

Generally, the structure of the 2-Propanol molecule [30] is well reproduced. The calculated H—C—O—H dihedral angle of the asymmetric conformer is 50.4°, as compared with the value found by Meyer (58°) using his

TABLE 3

Experimental and calculated structures and rotational constants for alkanes[a]

Parameter	Methane [10]	Ethane [11, 12]	Propane [13, 14]	n-Butane [15] (*a*)	n-Butane [15] (*g*)	Isobutane [16, 17]	Neopentane [18, 19]	n-Pentane (*a*, *a*)	Cyclopentane [20]	Cyclohexane [21, 22] (chair)	Cyclohexane [21, 22] (t-boat)
C—C		153.2	153.1	153.1		153.2	153.9		153.9	153.2	
		153.2	153.2	153.2	153.3	153.4	153.6	153.2	153.4	153.3	153.5
C—H	109.4	109.6	109.6	111.7		109.2[b]	112.0		109.5	110.4	
	109.4	109.6	109.6	109.6		109.6	109.6	109.6	109.6	109.6	
C—C—C			112.4	113.8		110.8				111.4	
			112.5	112.6	113.3	110.7		112.6	103.5	110.3	110.9
						111.0[c]					
C—C—H		111.5		111.0		111.0[c]	110.0				
		111.0		111.0		108.1[d]	111.1	111.0	111.3		
						108.2[d]					
			107.0[c]								
H—C—H		107.3	107.9[c]	107.9[c]		107.2	109.0	107.9[c]		107.5	
		107.9	106.1[d]			107.9	107.8		107.8	106.9	106.8
			106.7[d]	106.7[d]				106.7[d]			
C—C—C—C					65.0					54.9	
					64.2					57.8	31.5, 65.5
A	157122	80075[e]	29207			7789	4707			4299	
	157091	79805[e]	29325	23274	13101	7769	4437	169	6604	4326	4429
B		19876[e]	8446								
		19936[e]	8394	3624	4806			1939	6559		4189
C			7459					1839			
			7433	3401	4081	4510			3858	2488	2573

[a] Bond lengths in pm; angles in degrees; rotational constants (*A*, *B*, *C*) in MHz; upper values are measured, lower are calculated. [b] In CH_3; in CH_2, 110.9°. [c] In CH_3. [d] In CH_2. [e] Refs. 23, 24.

TABLE 4

Experimental and calculated structures and rotational constants for alcohols and ethers[a]

Parameter	Methanol [25, 26]	Ethanol [27—29]		n-Propanol	2-Propanol[b] [30, 31]		Cyclohexanol	Dimethyl ether [32, 33]	Ethylmethyl ether [34, 35]		Diethyl ether [36]	
		(*a*)	(*g*)	(*a*, *a*)	(*g*)	(*a*)			(*a*)	(*g*)	(*a*, *a*)	(*a*, *g*)
C—C		153.0			152.3				153.0		151.7	
		153.1	153.3	153.2	153.2	153.3	153.4		153.1	153.3	153.1	153.3
C—H	109.5	109.4						110.8	109.5		109.5	
	109.6	109.6		109.6	109.6		109.6	109.6	109.6		109.6	
C—O	142.8	142.5	142.7		144.1	144.0		141.3	141.0		141.1	
	143.8	143.8		143.8	143.8	143.9	143.8	144.0	144.0	144.1	144.0	144.1
O—H	96.0	94.5										
	97.0	97.0		97.0	97.0	97.1	97.0					
C—C—C					112.9							
				112.4	113.7	114.1	110.3					
C—C—H									110.4[c]		110.2[c]	
		110.4		111.0[c]					111.0[c]		111.0[c]	
		112.0	111.8		111.0		109.9		110.9[d]		110.4[d]	
				109.4[d]					111.7[d]		111.7[d]	
H—C—H									110.2[c]			
		108.5[c]							107.9[c]		108.9[c]	
	109.5	107.9[c]						109.2	107.2[d]		107.9[c]	
	110.1	109.0[d]			107.9		107.0	110.9	108.9[d]	108.3[d]	107.6[d]	
		108.9[d]	108.7[d]						109.9[e]		108.9[d]	108.3[d]
									109.9[e]			
C—C—O									108.2		108.5	
				108.4	107.8	108.1	108.3		108.2	109.3	108.1	108.3
O—C—H									109.8[c]			
									109.4[c]		111.0	
				107.8	106.8	106.1	107.3		109.9[d]	109.2[d]	108.2	
									108.9[d]			
C—O—X	108.5	108.5						111.8	111.8		112.1	
	108.4	108.5		108.3	108.7	108.9	108.6	111.6	111.7	112.4	111.8	112.5
Tilt	3.3							3.6	2.2			
	1.0							1.0	1.0			
			54.6[f]		58.0[g]					84.0[h]		
			66.2		50.4		51.6[f]			78.0		78.3[h]
A	123334	34892	34693		8566	8489		38789	27992		17873	
	125413	35092	32468	26422	8706	8736	4265	38216	27762	15435	17818	12958
B	24204	9350	9193		7993	8042		10057	4159		2244	
	24438	9138	9398	3741	7823	7754	2244	9773	4058	5186	2193	2501
C	23356	8135	8102		4715	4765		8887	3891		2100	
	23559	7979	8188	3492	4714	4780	1620	8651	3797	4532	2054	2350

[a] Bond lengths in pm; angles in degrees; rotational constants (*A*, *B*, *C*) in MHz; upper values are measured, lower are calculated. X = H or C. [b] Upper values are taken from ab initio and/or molecular mechanics calculations. [c] In CH_3. [d] In CH_2. [e] In OCH_3. [f] H—O—C—C dihedral angle. [g] H—O—C—H dihedral angle. [h] C—O—C—C dihedral angle.

TABLE 5

Experimental and calculated structures and rotational constants for carbonyl compounds[a]

Parameter	HCOOH [37—39] (*cis*)	(*trans*)	CH_3COOH [40] (*cis*)	CH_3CH_2COOH [41, 42] (*syn*)	$CH_3CH_2CH_2COOH$[b] [43]	$HCOOCH_3$ [44] (*cis*)	$HCOOCH_2CH_3$ [45] (*a*)	(*g*)	CH_3COCl [46, 47]	CH_3CH_2COCl [48, 49]
C_{sp^2}—Y	134.3	135.2	135.7	135.2	132.9	133.4	133.4		179.8	179.5
	133.6	133.7	133.7	133.7	133.7	133.8	133.7	133.9	180.2	180.2
C_{sp^2}—X	109.7	110.5	149.4	150.9	151.2	110.1	110.1		150.8	152.2
	110.0	110.2	150.6	150.8	150.8	110.1	110.1		151.0	151.2
C=O	120.2	119.5	120.9	121.0	120.1	120.0	120.0		118.7	118.7
	120.1	119.9	120.1	120.1	120.1	120.1	120.1		118.6	118.6
O—X	97.2	95.6	97.0	97.0	97.2	143.7	143.7			
	97.0		97.0	97.0	97.0	143.8	143.8			
C—H			109.0	109.2		108.6	108.6		110.7	110.7
			109.6	109.6	109.6	109.6	109.6		109.6	109.7
C—C			152.3	153.3			152.8			152.6
			153.1	153.2			153.1			153.1
O=C—Y	124.9	122.1	121.8	122.4	123.3	125.8	125.9		120.3	120.9
	126.1	125.7	125.8	125.7	125.7	126.3	126.3		120.1	119.8
X—C=O	124.1	123.2	126.2	125.8	125.5	124.5	124.8		127.4	127.0
	124.7	124.2	125.9	126.2	126.2	124.6	124.6		126.9	127.2
C—O—X	106.3	109.7	105.9	105.8		114.8	114.8			
	106.9	107.1	106.9	106.9	106.9	116.2	116.3	116.7		
				106.4[c]						
H—C—H			109.5	107.6[c]		110.7	108.9[c]		108.6	105.3
			109.1	108.6[d]		110.2			108.6	107.7
				108.0[d]			107.9[d]			
				107.7[c]						
C—C—H			109.5	110.3[c]	110.0[c]		112.1[c]		110.4	
			109.9	110.0[d]					110.4	
				111.0[d]	111.0[d]		111.0[d]	111.8		
O—C—H						108.2				
						108.6	107.5	107.9		
O—C—C							109.0	133.0		
							108.4	108.5		
C—C—C_{sp^2}				112.7	113.7					112.7
				111.9	111.9					111.3
				110.0[e]	68.5[f]			85.0[g]		117.5[e]
				112.0	68.3			76.1		113.7
A	77512	86461	11335	10188		19986	17955	10133	10162	8855
	79417	93034	11212	9971	8879	20394	18179	9563	10140	8968
B	12055	11689	9479	3819		6915	2908	3852	4947	2378
	12013	11465	9732	3916	1862	6760	2845	4041	4836	2399
C	10416	10284	5325	2871		5304	2581	3220	3393	1919
	10435	10207	5389	2914	1585	5249	2539	3310	3344	1900

[a] Bond lengths in pm; angles in degrees; rotational constants (*A*, *B*, *C*) in MHz; upper values are measured, lower are calculated. Y = O or Cl; X = H or C. [b] Upper values are taken from molecular mechanics calculations. [c] In CH_2. [d] In CH_3. [e] C—C—C=O dihedral angle. [f] C—C—C—C dihedral angle. [g] C—C—O—C dihedral angle.

molecular mechanics force field for alcohols [31]. Considering the sensitivity of our potential energy function to variation in torsional angles, this agreement can be considered as good.

For n-propanol the calculated C—C—C—O and C—C—O—H dihedral angles for the five expected conformers are (180°, 180°), (180°, 66°), (63°, 180°), (62°, 64°), and (—65°, 74°). The bond lengths and valence angles were found to be very similar for these conformers.

Ethers (Table 4)

The PF1 force field yields good structural results for dimethyl ether [32]. However, due to the inclusion of ester molecules in the simultaneous parameterization, the calculated C—O bond lengths of each ether studied are too long. The methyl groups are tilted by a few degrees towards the lone electron pairs of the oxygen atom, in agreement with experimental results [32]. A similar tilt is observed for the methoxy methyl group in ethylmethyl ether and propylmethyl ether [34, 35]. Generally speaking, the calculated structure of the *anti* conformer of ethylmethyl ether (C—C—O—C dihedral angle = 180°) reproduces the experimental data well [34, 35]. Also, the calculated C—C—O—C dihedral angle of the *gauche* form (78°) is near the experimental value (84 ± 6°) [35].

Carbonyl compounds (Table 5)

The calculated structures of acetic acid, propionic acid and the s-*cis* form of formic acid (O=C—O—H dihedral angle = 0°) are in good agreement with experimental results [37, 40, 41, 51]. The s-*trans* conformer of the latter molecule [38] is reasonably reproduced. It would be necessary to include other s-*trans* structures in the parameterization to improve results in this case. Unfortunately, there are no such experimental results for these conformations.

The structures of acetyl and propionyl chlorides [46, 48] and methyl formate [44] are reproduced very well by PF1. It is interesting to note that, for the s-*trans* conformer of the ester, a larger value of the H—C—O angle (110.6°) has been found than for the s-*cis* form. This suggests steric repulsion between the hydrogen atom attached to the carbonyl group and the methoxyl group, in this conformation.

The experimental structure of the *anti* conformer of ethyl formate [45] is also well reproduced. The calculated torsional angle of the *gauche* form (76.1°) is near the experimentally determined value (85°) [45]. The observed increase of the O—C—C angle in the latter conformer (113°) [45] was not reproduced in our calculations.

Agreement between calculated and experimental results is very good for the α-chloro substituted molecules. Detailed results on these molecules will be shown in refs. 2 and 3.

Conformer energy differences and barriers of internal rotation

In this section the results of calculations on conformer energies, presented in Table 6, are summarized.

Generally, the calculated values for alkanes, alcohols, and ethers, are in good agreement with experimental values.

The barriers of internal rotation of ethane [52], propane [53] and the *anti* → *gauche* barrier of n-butane [54] are very well reproduced, and improve on existing literature values. On the other hand, our result for the *gauche* → *gauche* barrier in the latter molecule is smaller than the experimental value [56].

The calculated methyl barriers of rotation of isobutane and *anti* n-butane are in good agreement with experiment.

The calculated energy differences between the (*gauche*, *anti*) and (*gauche*, *gauche*) forms of n-pentane and the more stable (*anti*, *anti*) conformer show reasonable agreement with experimental values. In addition, we have determined the energy difference between the fourth conformer of n-pentane (the inside-(*gauche*, *gauche*) form) and the more stable one.

Experimental energy barriers in methanol and ethanol (methyl, and *gauche* → *gauche*) are well reproduced by PF1. The calculated *anti* → *gauche* barrier for ethanol is somewhat smaller than the value reported in [54], but it seems more reasonable than the latter in view of steric effects.

Energy differences between various conformers of n-propanol [62] are quite difficult to fit. This difficulty had already been encountered and explained by Meyer [31] during the development of his molecular mechanics force field for alcohols. Our results are qualitatively similar to Meyer's values (1.26, 1.38, 1.80 and 2.09 kJ mol^{-1}). However, they depart somewhat from experimental values. PF1 results for energy differences between *gauche* and *anti* forms of 2-propanol (0.63 kJ mol^{-1}) and cyclohexanol (0.67 kJ mol^{-1}, for equatorial OH) are also similar to those of Meyer (0.71 and 1.13 kJ mol^{-1}, respectively).

To fit energies well by molecular mechanics in carbonyl compounds is not easy as one needs to compromise between good results and the simplicity of the potential energy function. Notwithstanding, our relatively simple force field reproduces energies for these molecules well. In particular, energy differences between conformations related through rotation around C—O bonds are in excellent agreement with experience.

The value found for the s-*trans*/s-*cis* energy difference in propionic acid is in good agreement with ab initio STO-3G results presented in ref. 43.

Generally, structures related through rotation around C_{sp^3}—C_{sp^3} bonds have a calculated energy in good agreement with experimental data for all the studied carbonyl compounds. Our result for propionic acid ($\Delta E_{gauche-syn}$ = 5.9 kJ mol^{-1}) agrees with the value obtained from consideration of the results of population analysis in this compound [42] (ca. 6.3 kJ mol^{-1}). On the other hand, the calculated C—C_{sp^2} energy barrier for acetic acid is somewhat

TABLE 6

Barriers of internal rotation and conformer energy differences[a]

Compound	Barriers of rotation				Conformer energy differences			
	Trans-formation	Calc.	Exp.	Ref.	Conformer	Calc.	Exp.	Ref.
Ethane		11.7	11.7	52				
n-Propane		14.8	14.9	53				
n-Butane	$a \rightarrow g$	16.5	16.2	54	*g-a*	4.318	4.042	55
	$g \rightarrow g$	21.2	29.0	56				
	$-CH_3$	14.8	14.2	54				
Isobutane		15.1	16.3	17				
n-Pentane					*ga-aa*	4.322	2.510	57
					gg-aa	8.050	5.314	57
					gg-aa	13.175		
Cyclohexane					tw-ch	29.9	20.1—33.1	58
Methanol		4.24	4.48	59				
Ethanol	$a \rightarrow g$	3.1	5.4	54	*g-a*	0.5	0.4	60
	$g \rightarrow g$	5.02	5.02	54				
	$-CH_3$	13.59	13.93	54				
n-Propanol[b]					*ag-aa*	0.46	0.0	61
					ga-aa	2.38	—1.2	61
					gg-aa	2.68	—1.2	61
					gg′-aa	2.84	—1.2	61
2-Propanol					*g-a*	0.63		
Cyclohexanol					*g-a*	0.67		
Dimethylether		11.02	10.90	62				
Ethylmethyl ether	$-CH_3$	11.04	10.67	44	*g-a*	5.9	6.3	63
Isobutylmethyl ether					*ga-aa*[c]	2.18	2.09	64
Diethyl ether	$-CH_3$	14.6			*ag-aa*	5.86	5.9	64
					gg-aa	12.2		
HCOOH		38.6	41.8	9	*t-c*	19.7	19.7	9
CH_3COOH	C—O	44.3	44.4	9	*t-c*	24.9	25.0	9
	$-CH_3$	1.2	2.0	65				
CH_3CH_2COOH	$-CH_3$	10.2	9.8	51	*t-c*	25.06	24.27[d]	43
					g-a	5.9	6.3[e]	
$CH_3CH_2CH_2COOH$	$-CH_3$	3.9	2.1	43[d]				
$HCOOCH_3$	C—O	58.0	43—63	66	*t-c*	19.9	19.9	66
	$-CH_3$	4.96	4.98	44				
$HCOOCH_2CH_3$					*g-a*	0.799	0.778	67
CH_3CH_2COCl	$-CH_3$	10.3	10.4	68	*g-a*	5.7	6	48

[a] Energies in kJ mol^{-1}; symbols *a*, *g*, *t*, *c*, tw, and ch, refer to *anti*, *gauche*, s-*trans*, s-*cis*, twist-boat, and chair conformations, respectively. [b] First letter refers to the methyl conformation; second, to the alcohol group. [c] First letter refers to the isopropyl conformation; second to the methoxy group. [d] Ab initio STO-3G calculation. [e] Calculated from the results of population analysis reported in [42].

smaller than the experimentally determined value. In fact, it was impossible to reproduce this and the C$-$C$_{sp^2}$ barriers simultaneously in the other molecules studied.

The results on α-chlorinated molecules will be discussed in refs. 2 and 3.

Vibrational frequencies

During parameterization, we emphasised chiefly a general agreement between calculated and observed vibrational frequencies. An additional difficulty in fitting frequencies is faced for symmetric groups, as symmetry is accompanied by reduction of force field parameters. Generally, vibrational fitting in the molecular mechanics approach becomes poorer with increasing molecular symmetry. In particular, the largest errors are apparent with methyl vibrations.

In this section and in Table 7, only general trends of the results are presented.

In alkanes, C—H stretching frequencies are quite acceptable (max. error 115 cm^{-1}, mean error 39 cm^{-1}; based on data for methane [69], ethane [69] and cyclohexane [70, 71]). The calculated frequencies of CH symmetric deformations are generally larger than those observed (mean error, 70 cm^{-1}). On the other hand, CH rockings, C—C—C deformation and C—C stretching frequencies are too small in the majority of cases.

The calculated C—C torsional frequencies agree well with experimental values. The pseudo-rotation frequency of cyclopentane, which should be 0, was calculated as 25 cm^{-1} by our molecular mechanics force field.

In alcohols and ethers, the PF1 results are reasonable for C—O stretching frequencies while O—H stretching are poorly reproduced.

In general terms, the calculated C—C—O frequencies are lower than the observed values. On the other hand, the C—O—C deformations and C—O torsions are very well reproduced (mean errors, 18 and 19 cm^{-1}, respectively, based on data for methanol [69], ethanol [74, 75], dimethyl ether [69, 77] and diethyl ether [78]).

The frequencies related to the carbonyl group are in good agreement with experimental data.

Simultaneous fitting of the C=O force field parameters in acyl chlorides, acids and esters was not possible. Thus, we were led to different sets of parameters, one for each type of compound, in order to reproduce experimental values well.

The torsions around C—O and C—C bonds are also in good general agreement with experimental data.

As has already been mentioned, the results of calculations on the α-chloro-substituted molecules are presented in refs. 2 and 3.

TABLE 7

Experimental and calculated vibrational frequencies[a]

Mode	Ethane [69]	Propane [70]	n-Butane [69, 71]		Isobutane [72]	Cyclohexane [70, 73]
			(a)	(g)		
νC—C	841/995	900/1054			830/918	895/1057
		761/869			707/797	889/1029
						889/862
						768/802
δC—C—C		283/369	298/427	343/469	367/426	428/522
			215/267	241/320	257/367	317/427
τC—C	306/275	278/268	280/254	302/201	286/280	332/403
		244/216	241/223	236/197	267/225	217/248
			128/155	121/101		

Mode	Methanol [69]	Ethanol [74, 75] (a)	2-Propanol [76]	Dimethyl ether [69, 77]	Diethyl ether [78]
νO—H	3555/3681	3555/3658	3555/3655		
νC—O	943/1033	967/1051		1045/1102	1060/1119
				1030/928	955/845
δC—O—X	1346/1345	1365/1241		427/418	371/440
δC—C—O		376/419			398/377
					197/245
τC—O	292/270	221/201	233/227	269/241	103/—
				206/202	94/—
τC—C			283/277		272/245
			266/237		256/235

Mode	$HCOOH$ [79]	CH_3COOH [79]	CH_3CH_2COOH [51]	$HCOOCH_3$ [80]	CH_3COOCH_3 [79]	CH_3COCl [81]	CH_3CH_2COCl [48]
νC=O	1770/1774	1793/1779	1790/1770	1747/1745	1766/1771	1842/1822	1820/1805
νC—O	1136/1103	1330/1280		1202/1205	1400/1378		
				859/921	993/1058		
νC—C		769/847	772/851		771/842	1101/1109	1039/1089
			623/794				919/926
νC—Cl						610/608	432/441
δC—O—X	1207/1218	1200/1181		312/308	298/295		
γC=O		618/639			603/603	505/514	507/505
δX—C=O	1393/1380	448/428	424/530	1369/1372	410/427	360/348	657/689
δC—C—C			223/270				215/229
δC—C—Cl						440/436	322/359
τC—O	522/638	397/535	401/547	321/337	163/—		
				137/—	129/136		
τC—C		69/—	205/190		68/73	145/—	206/196
			116/64				127/71

[a] Frequencies (cm^{-1}) are presented as calc./exp.; X = H or C.

ACKNOWLEDGEMENTS

The authors thank Prof. K. Rasmussen, Technical University of Denmark, 2800 Lyngby, for providing them with his Consistent Force Field program used in these calculations. J. J. C. T. D. gratefully acknowledges his hospitality during a short stay in Copenhagen, March 1983.

The authors also thank Prof. J. E. Valença for allowing them to use the University computer in Braga, where most of the computation work was performed, and Prof. H. Burrows, Chemical Department of Coimbra and Dr. P. R. Carey, Division of Biological Sciences, NRCC, Ottawa, for their helpful criticism.

The research project which included the present work was financially supported by Instituto Nacional de Investigação Científica, Portugal.

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