

The Consistent Force Field. 2. An Optimized Set of Potential Energy Functions for the Alkanes

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Engelsen, S. B., Fabricius, J. and Rasmussen, Kj., 1994. The Consistent Force Field. 2. An Optimized Set of Potential Energy Functions for the Alkanes. – Acta Chem. Scand. 48: 553–565 © Acta Chemica Scandinavica 1994.

A systematic approach for development of potential energy functions has been used on the alkanes. The alkane force field contains 21 parameters, 16 of which are optimized on 180 individual experimental data of five different types: internal molecular structure, unit cell dimensions, lattice energy, dipole moment and vibrational frequency. The database used covers 19 gas phase structures and 8 crystal structures. Morse potentials are used to model covalent bonds, and Lennard-Jones and Coulomb potentials for non-bonded interactions. Force field performance on substances and properties not included in the optimization are checked: internal structures, rotational constants, thermodynamic functions and rotational barriers. Both strained and flexible molecules are included. The resulting optimized force field performance is broadly documented. It possesses good potentiality for extension to other classes of substances.

In the preceding paper¹ we have described a methodology for developing empirical potential energy functions (PEF) using high precision experimental data and a qualified choice of PEF terms to be used in a molecular mechanics force field suited for structural research of glycolipids. The present work on alkanes and cycloalkanes represents our first parametrization efforts using this approach, resulting in an optimized force field for the functional groups methine, methylene and methyl.

The alkanes, just containing sp³-hybridized carbon and hydrogen, are basic components in a majority of organic compounds, including many molecules of biological interest such as the lipids. For this reason the alkanes constitute a fundamental group of model compounds when parametrizing potential energy functions for modelling organic molecules.^{2–9}

In contrast to some modern force field developments¹⁰ but similar to a recent one,¹¹ the parameter set described here, PEF91L, has been developed by use of the Consistent Force Field.^{7,12,13} The advantage of this method is that it allows for systematic least squares refinement of force field parameters on experimental data.

No *ab initio* calculated properties are used, since ideally the use of calculated properties in optimization of an empirical force field should be avoided. This implies that no optimization is done on energy differences of rotational isomers, and that the rotational barriers will be calculated

after the optimization, with the intention to probe the force field. In contrast to recent force fields^{8–11} where experimental and calculated rotational barriers have been used as the fundament in the force field fitting process, the rotational barriers in PEF91L are calculated indirectly from vibrational data.

Parametrization

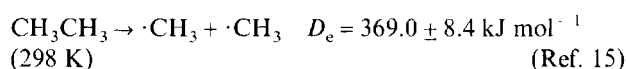
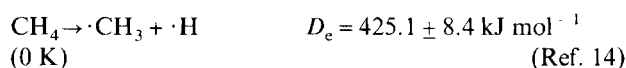
Program. Development of the new parameter set was carried out with the Lyngby version¹³ of the Consistent Force Field (CFF) program.³ The CFF, the algorithm used to optimize the potential energy function parameters and the recently implemented interactive graphical application to guide the progress of the optimization, are described elsewhere.^{1,7,13}

Constraints in conformational space are not applied to any of the model substances to be optimized; all degrees of freedom are allowed to relax. The only constraints used during the optimization process are fixing those unit cell angles which are necessary to maintain the observed unit cell symmetry during minimization with poor initial parameter sets. This means that the other unit cell angles and the unit cell lengths are relaxed in crystal simulations.

Initial parameter values. Several initial alkane parameter sets were built up and subjected to extensive optimization. The initial Morse parameters were obtained from the force field of Lifson and Stern,⁶ and the dissociation

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energies D_e from the literature.^{14,15} For this purpose the first bond dissociation energy was selected:



However, the D_e soon appeared to be completely insensitive to the optimization process, and accordingly both values of D_e were considered constant in the further development. Valence angle and torsional angle parameters were obtained from the previous work of Niketić and Rasmussen,¹² and fractional charges were initiated by using values from earlier work.^{7,16}

In order to keep the force field simple, the same parameters are used for all sp^3 -hybridized carbon atoms regardless of the number of attached hydrogen atoms and the ring context, realizing that highly angle-strained molecules such as cyclopropane and cyclobutane cannot be modelled correctly.

Experimental data. Experimental data for the following alkane crystals were used: ethane,¹⁷ *n*-pentane,^{18,19} *n*-hexane,^{18,20} *n*-heptane,²¹ *n*-octane,^{18,19} cyclohexane,²² *cis,syn,cis*-perhydroanthracene²³ and 3,4-dicyclohexyl-3,4-dimethylhexane.²⁴ Gas phase structural data of the following alkane molecules were included: methane,²⁵ ethane,²⁶ propane,²⁷ isobutane,²⁸ neopentane,²⁹ *n*-butane,^{30,31} tris(*tert*-butyl)methane,³² 1,1,2,2-tetramethylethane,³³ hexamethylethane,³³ cyclopentane,³⁴ cyclohexane,³⁵ methylcyclohexane³⁶ and all-*cis*-1,2,3,4,5,6-hexamethylcyclohexane.³⁷ Vibrational data of the following molecules were used: methane,³⁸ ethane,³⁸ propane,³⁸ isobutane,³⁹ isobutane- d_1 ,³⁹ *n*-butane,³⁸ cyclopentane⁴⁰ and cyclohexane.³⁸ Finally, dipole moments for propane⁴¹ and isobutane⁴¹ were included. The crystal structure of hexamethylcyclohexane³⁷ contains four molecules in the asymmetric unit, and in order to avoid expensive crystal simulations and the ensuing averaging problems, we reduced the system and treated it as one isolated molecule.

In an attempt to stabilize the super-iterative optimization process,¹ dividing the optimizations into gas phase and condensed phase simulations, we included data for both the internal structure and the unit cell dimensions of the *cis,syn,cis*-perhydroanthracene crystal²³ in the 'gas phase' optimizations.

Actual procedure. It proved very difficult to parametrize the Lennard-Jones A (i.e. the r^{-12} -term) parameter for carbon, and it was decided to fit it initially by the following approach. Using a single crystal, *n*-octane, and fixing the Lennard-Jones parameters of hydrogen to zero, made the carbon parameters fill out the empty space according to the observed crystal packing. After this was done, hydrogen parameters were added just to be in power, i.e. the Lennard-Jones radius for H (-H) was ini-

tiated at a value corresponding to the radius of the C (-C) atom plus the C-H bond length. The Lennard-Jones parameters for carbon and hydrogen obtained using this procedure resulted in slightly controversial van der Waals parameters for hydrogens. A conversion to the equivalent ϵ, r^* -Lennard-Jones form gives values of 0.9184 kJ mol⁻¹ and 364.6 pm for C···C interactions and 0.00615 kJ mol⁻¹ and 352.2 pm for H···H interactions. Thus the hydrogen contribution to the overall van der Waals potential is smaller than usually seen in molecular mechanics, and certainly smaller than in PEF303,⁷ where the corresponding hydrogen values were 1.469 kJ mol⁻¹ and 308.1 pm. However, the hydrogens are not far in energy from the recent force field by Smith and Karplus,⁹ which uses hydrogens of the 'size' 0.0188 kJ mol⁻¹ and 293.6 pm. The result is that these parameters performed better than any of the trial and error sets which had been tried previously. Thus they became the initial guess of choice to which the parametrization mentioned above was applied. The importance of the availability of lattice energies¹⁸ when parametrizing Lennard-Jones parameters cannot be overestimated, since these observables depend on Lennard-Jones parameters. There is, in fact, a need for a standard work on lattice energy and its derivation from experiment.

Parametrizing the bond torsional potential¹ created problems even for a simple alkane force field because of its highly correlated nature. The problem was overcome by fixing the torsional parameters at arbitrary values of 4 kJ mol⁻¹ for chain (C-C-C) torsions and 0.4 kJ

Table 1. Final parameters for the hydrocarbon force field.^a

Bond parameters	D_e	α	b_o
C-C	369.0	0.022545	151.85
C-H	425.1	0.018139	109.50
Valence angle parameters		K_θ	θ_o
C-C-C		110.8551	T_d
C-C-H		111.0844	T_d
H-C-H		94.4058	T_d
Torsion angle parameters			K_ϕ
C-C-C-C			6.7224
C-C-C-H			1.0493
H-C-C-H			0.9272
van der Waals and Coulomb parameters			
	A	B	q
C-	71174.935	2076.96	0.0934
H-	4742.736	153.495	0.1627

^aUnits: D_e , kJ mol⁻¹; α , pm⁻¹; b_o , pm; K_θ , J mol⁻¹ °⁻²; θ_o , °; K_ϕ , kJ mol⁻¹; A , (J mol⁻¹ pm¹²)^{0.5} × 10⁻¹²; B , (J mol⁻¹ pm⁶)^{0.5} × 10⁻⁶; q , elementary charge; T_d is the tetrahedral angle [=arccos(-1/3) ≈ 109.5°].

Table 4. Comparison of experimental and calculated unit cell volumes of alkane crystals.^a

Compound	Ref.	Exp.	PEF91L			PEF303 ⁶³		
			Calc.	Abs. error	Rel. error	Calc.	Abs. error	Rel. Error
Ethane	17	138.89	132.6	-6.3	-4.5	138.3	-0.6	-0.4
<i>n</i> -Pentane	19	552.93	528.9	-24.0	-4.3	570.3	17.3	3.1
<i>n</i> -Hexane	20	161.1	152.5	-8.6	-5.3	164.5	3.4	2.2
<i>n</i> -Heptane	21	372.4	352.2	-20.8	-5.6	380.2	7.9	1.9
<i>n</i> -Octane	19	212.9	194.6	-18.3	-8.6	210.7	-2.2	-1.0
Cyclohexane	22	561	547.3	-13.7	-2.4	597.1	36.1	6.4
Hexamethyl- cyclohexane	37	1110.4	1087.0	-23.4	-2.1	1199.9	89.5	8.1
<i>csc</i> -Perhydro- anthracene	23	565.5	562.2	-3.3	-0.6	620.3	54.7	9.7
3,4-Dicyclohexyl- 3,4-dimethylhexane	24	872.6	875.9	3.3	0.4	899.9	27.3	3.1
Mean				-12.8	-3.7		25.9	3.7
σ				9.63			30.4	

^aUnits are 10^6 pm^3 . Relative errors are in percent.

force field is very accurate even at those equilibrium distances which show large deviations from the parameter values b_0 . The highly strained C_q-C_t bond in tris(*tert*-butyl)methane, measured to 160.9(1.5) pm, is reproduced as 161.8 pm. The C_q-C_q bond in hexamethylethane, calculated as 158.7 pm, compares well with the experimental value 158.3(9) pm. The figure reveals that the C-C bond lengths of cyclopentane and *n*-pentane are not reproduced to within 3σ , whereas all other C-C bond lengths are neatly reproduced.

The C-H bonds (Table 5) are less well reproduced, all being close to the parameter value b_0 . This is probably caused by a very strong dependence on the structures and vibrations of methane and ethane; both structures are very accurately measured and therefore given high weight in the optimization. The two calculated data which differ

most from the experimental are C_t-H in tris(*tert*-butyl)methane and C_t-H in methylcyclohexane, indicating that the methine group would profit from having a hydrogen atom type of its own.

In his optimization procedure Dillen¹¹ could not devise a remedy for improving the average reproduction of C-C-C angles with his more complex type of force field. In this work the geometrical mean value of the C-C-C angles in propane, *n*-butane (a), *n*-pentane (aa), *n*-hexane (aaa) and *n*-heptane (aaaa) is calculated to 111.2° , which is 1.5° lower than the experimental mean of 112.7° .⁴² In *n*-butane we calculate an opening from 111.1 to 113.5° when going from the *anti* to the *gauche* conformations.

Frequencies. Analysis of normal modes is a most important part of the optimization process. It is our experience that, without normal modes (frequencies) included in the experimental data, the parameter 'hyperspace' is less restricted and the optimization process occasionally diverges. Significant improvement in the normal mode calculation was expected due to the use of Morse potentials, but the simple form of the correction potentials limited the expected success. Table 6 lists the frequency observables used. We find a numerical mean error in the calculated frequencies of 40 cm^{-1} for PEF91L (48 observables), compared to 57 cm^{-1} for the PEF303 force field (42 observables). The special cases methane and ethane show the worst calculated vibrational frequencies in PEF91L. For both molecules the symmetric C-H stretch frequencies are significantly lower than measured. In ethane one H-C-H deformation is more than 200 cm^{-1} too high.

The CFF is able to deliver a force field capable of reproducing frequencies to high precision when more complicated potential energy functions are used.⁶ As mentioned before, this is not the aim of the present work. Employment of various types of cross terms would in-

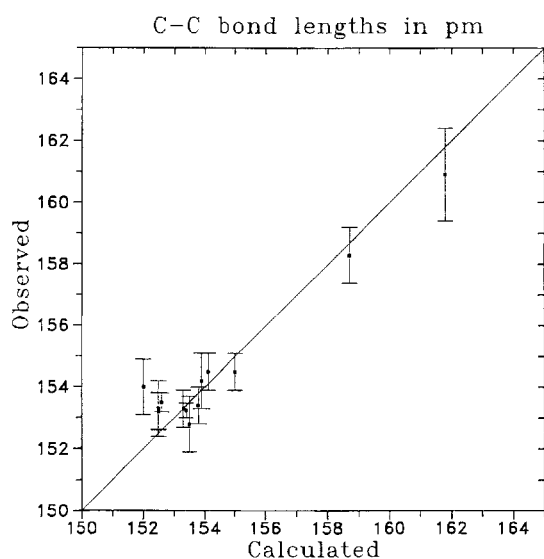


Fig. 1. Experimental versus calculated C-C bond lengths.

Table 5. Gas-phase structures of alkanes.^a

Compound	Ref.	Coord.	Exp.	PEF91L	PEF303 ⁶³
Methane (CH ₄)	25	1 CH	109.91(36)	109.5	109.9
Ethane (CH ₃ CH ₃)	26	1 CC 2 CH 19 HCH	153.23(60) 110.17(60) 107.51(92)	152.5 109.7 108.9	152.9 110.1 108.7
Propane (CH ₃ CH ₂ CH ₃)	27	1 CC 2 CH ₃ 7 CH ₂ 14 CCC 27 HCH	153.3(9) 109.7(1.5) 109.6(1.5) 112.0(3.6) 107.9(9.2)	152.5 109.7 109.9 110.7 108.6	153.3 110.1 110.3 111.3 108.4
Isobutane (CH(CH ₃)(CH ₃)(CH ₃))	28	1 CC 2 CH _t 5 CH ₃ 14 CCH _t 15 CCC 17 CCH 19 CCH 29 HCH 31 HCH	153.2(6) 110.9(2.1) 109.2(9) 108.1(6) 110.9(6) 111.4(1.2) 110.2(9) 108.7(3.3) 106.5(5.1)	153.8 110.1 109.6 108.9 110.1 110.1 110.6 108.3 108.8	152.5 110.6 110.1 108.5 110.5 110.5 110.7 108.0 108.5
Neopentane (C(CH ₃)(CH ₃)(CH ₃)(CH ₃))	29	1 CC 5 CH 20 CCH	153.5(3) 109.4(8) 112.2(2.8)	152.6 109.6 110.4	154.3 110.0 110.8
<i>n</i> -Butane <i>gauche</i> (CH ₃ CH ₂ CH ₂ CH ₃)	30,31	47 CCCC	-72 (46)	-68	-62
Tris(<i>tert</i> -butyl)methane (CH ₃ C(CH ₃)(CH ₃)(CH ₃) CH(C(CH ₃)(CH ₃)(CH ₃)) CH(C(CH ₃)(CH ₃)(CH ₃))	32	6 C _q C _m 7 C _t C _q 15 CH 42 C _t C _t H _m 50 C _m C _q C _m 55 C _m C _q C _t 59 C _q C _t C _q 60 CCH H _t C _t C _q C _m H _m C _m C _q C _t	154.5(6) 160.9(1.5) 111.1(9) 114.2(3.0) 105.7(6) 113.0(6) 116.0(1.2) 101.6(1.2) 10.8(1.5) 18.0(18.0)	154.1 161.8 109.4 113.3 104.2 115.9 115.7 102.1	155.7 163.2 109.2 115.2 106.0 112.9 116.5 101.0
Tetramethylethane (CH(CH ₃)(CH ₃)CH(CH ₃)(CH ₃))	33	80 CCCC	65 (52)	65	
Hexamethylethane (C(CH ₃)(CH ₃)(CH ₃) CH(CH ₃)(CH ₃)(CH ₃))	33	4 CC 14 CC 28 CCC	158.3(9) 154.2(9) 111.0(5)	158.7 153.9 113.2	159.3 155.3 111.6
Cyclopentane (&CH ₂ CH ₂ CH ₂ CH ₂ &CH ₂)	34	1 CC	154.0(9)	152.0	152.3
Cyclohexane (&CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ &CH ₂)	35	1 CC 21 CCC	153.3(6) 111.4(6)	153.3 110.9	153.3 110.6
Methylcyclohexane (&CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ &CH(CH ₃))	36	1 CC 2 CH 16 CC _{ex} 18 CH _{ex} 22 CCH _{ex} 24 CCC 51 CCC _{ex}	153.24(23) 110.7(5) 153.15(23) 110.4(5) 109.3(6) 111.4(6) 112.1(1.8)	153.4 109.8 152.7 109.6 109.2 110.9 110.5	153.3 110.2 153.8 110.1 109.5 110.6 110.6
Hexamethylcyclohexane (&CH(CH ₃)CH(CH ₃)CH(CH ₃) CH(CH ₃)CH(CH ₃)&CH(CH ₃))	37	1 CC _a 3 CC _r 7 CC _e 38 CCC _a 42 CCC _a 45 CCC _e 47 CCC _r 48 CCC _r 53 CCC _e	153.4(6) 154.5(6) 152.8(9) 115.4(3) 115.4(3) 112.9(3) 114.8(3) 109.2(3) 112.9(3)	153.8 155.0 153.5 115.0 116.5 113.3 115.4 108.5 113.5	154.9 155.3 154.5 113.5 116.5 112.9 115.0 110.3 113.7

^aUnits: pm and °. Numbers before the internal coordinate designations shown the internal numbering of the CFF program, interpreting from the input formulae shown. Ref. refers to experimental data.

Table 6. Vibrational frequencies (in cm^{-1}) of alkanes.^a

Compound	Ref.	Coord.	Exp.	PEF91L	PEF303 ⁶³		
Methane	38	1 CH _{ST}	3019	2956	2959		
		4 CH _{AI}	2917	2797	2800		
		5 HCH _E	1534	1473	1474		
		7 HCH _T	1306	1315	1316		
Ethane	38	1 CH _{EG}	2969	2944	2966		
		3 CH _{EU}	2985	2940	2965		
		5 CH _{AG}	2912	2844	2870		
		6 CH _{AU}	2912	2824	2841		
		8 HCH	1472	1436			
		10 HCH	1468	1422			
		7 HCH	1388	1606	1571		
		12 HCH	1379	1406	1431		
		13 CCH	1206	1064	1109		
		15 CC	995	1039	1003		
		16 CCH	882	912	1001		
		18 HCCH	289	278	282		
		Propane	38	22 CC	1054	972	947
				23 CC	869	924	872
24 rock	748			812	871		
25 CCC	369			393	473		
26 CCCH	268			263	284		
27 CCCH	216			217	199		
8 tCH	2871			2898	2841		
Isobutane-d ₁	39	10 tCD	2149	2139			
<i>n</i> -Butane <i>anti</i>	38	32 CCC	425	404	457		
		33 CCC	262	302	370		
		34 CCCH	225	254	257		
		35 CCCH	206	226	240		
		36 CCCC	121	148	117		
<i>n</i> -Butane <i>gauche</i>	38	32 CCC	429	446	534		
		33 CCC	318	349	405		
		34 CCCH	255	293	358		
		35 torsion	197	214	207		
		36 CCC	116	139	107		
Cyclopentane	40	36 skeleton	617	504			
		37 bend.	545	498			
		38 torsion	283	303			
		39 pseudorot.		16			
Cyclohexane	38	1 CH _{AIGA}	2936	2943	2973		
		2 CH _{EUA}	2914	2938	2971		
		3 CH _{A2UA}	2934	2938	2968		
		5 CH _{EGA}	2924	2936	2967		
		7 CH _{A2US}	2863	2882	2921		
		8 CH _{EUS}	2863	2876	2912		
		10 CH _{EGS}	2895	2867	2893		
		12 CH _{A1GS}	2853	2860	2883		
		43 CCC	522	565	681		
		44 CCC	427	464	483		
		46 CCCC	384	414	440		
		47 CCCC	241	266	263		

^a Numbers before the internal vibration designations show the internal numbering of the CFF program. Ref. refers to experimental data.

crease the number of parameters beyond what can reasonably be handled when heteroatoms are introduced. Rather, the intention is to obtain small errors for groups of frequencies, such as C–H stretchings and the deformation region, and good individual accuracy in the low frequencies. The first consideration secures a good zero

point energy, and the second safeguards accuracy in statistical mechanical calculations, as the low frequencies dominate the Einstein sums.

Dipole moments. Two dipole moments, measured by microwave spectroscopy, are available for the alkanes: prop-

Table 7. Lattice energies of alkanes.

Compound	Exp. ¹⁸ /kJ mol ⁻¹	PEF91L /kJ mol ⁻¹	Error (%)
<i>n</i> -Pentane	-46.4	-42.2	9
<i>n</i> -Hexane	-55.2	-51.6	7
<i>n</i> -Octane	-72.4	-69.1	5

ane, 0.083(3) debye, and isobutane, 0.132(3) debye.⁴¹ Although numerically small they are well reproduced by PEF91L: propane is calculated to 0.084 debye and isobutane to 0.117 debye, the latter being the worst case with an error of -11%.

Lattice energies. The only thermodynamic quantities used in the optimization of alkane parameters were lattice energies for the three substances, *n*-pentane, *n*-hexane and *n*-octane calculated by Shipman *et al.*¹⁸ A comparison between calculated lattice energies and values derived from experimental data is shown in Table 7. All calculated values are larger than the experimental values; however, the error decreases when the calculations proceed towards larger systems, which is encouraging, as the scope of the work is to be able to simulate large systems.

Properties and substances not included in the optimization. We consider it essential to conduct some investigation of the predictive capability of a newly developed force field by applying it to molecules and experimental data not used in the optimization process. If it has to have any value in future work, it is necessary to assess the credibility of its results. We have selected a few cases.

Charges. Table 8 collects the fractional charges of the alkanes used in this work, as obtained by the program

using the optimized parameter value and the charge allocation algorithm.

Rotational constants. Moments of inertia are easily obtained with high precision from the corresponding rotational constants. It is technically rather easy to optimize on either, but very little improvement will result. It turns out that fairly correct values may be obtained even with rather bad geometries, as the errors sometimes tend to cancel neatly. An example will serve as illustration. For the *r_z* structure of cyclohexane the rotational constant *B* is⁴³ 0.143429 cm⁻¹. The value calculated with PEF91L is 0.143945 cm⁻¹, an error of 0.000516 or 0.4‰. A precise value for *B* of the *r₀* structure of ethane was measured⁴⁴ to 0.6631 cm⁻¹; the calculated value is 0.6738 cm⁻¹, an error of 0.0106 cm⁻¹ or 1.6‰.

Thermodynamic functions. In the CFF, approximations in the statistical mechanical calculations are the same as those used by most other authors. The actual formulae are shown in a recent review.¹³

As was done previously¹⁶ for a parameter set fitted by trial-and-error, we compare calculated results with correlated data,⁴⁵ since an individual datum of this compilation supposedly is more reliable than an individually measured datum. The comparison, which includes also data for the previously optimized PEF303 and PEF401,⁷ is shown in Table 9. In the cases of *n*-alkanes, the calculated data are averaged using Boltzmann distributions calculated from Gibbs' free energies.

We find that the new PEF91L gives better performance than PEF303 but that PEF401 is better in this respect. Entropy for straight-chain alkanes is less well reproduced than for the less flexible compounds. This shows that the approximations of stiff rotor for rotational contributions and harmonic low-amplitude motion for vibrational con-

Table 8. Fractional charges of hydrocarbons calculated with PEF91L.^a

Compound	Atom type	<i>q</i> (<i>e</i>)	Compound	Atom type	<i>q</i> (<i>e</i>)
Methane	C	-0.5761	Tetramethylethane	C _t	-0.0973
	H	0.1440		C _m	-0.4227
Ethane	C	-0.4181	Hexamethylethane	H	0.1347
	H	0.1394		C _q	0.0647
Propane	C _s	-0.2575	C _m	-0.4234	
	C _m	-0.4202	H	0.1340	
	H	0.1372	Cyclohexane	C	-0.2631
<i>n</i> -Butane	C _s	-0.2587		H	0.1316
	C _m	-0.4214	Methylcyclohexane	C _m	-0.4258
	H	0.1372		C _t	-0.1004
<i>n</i> -Pentane	C _s	-0.2595		C _s	-0.2631
	C _m	-0.4222	H	0.1316	
	H	0.1352	TTBM	C _q	0.0639
Isobutane	C _t	-0.0960		C _t	-0.0989
	C _m	-0.4214		C _m	-0.4243
	H	0.1360		H	0.1331
Neopentane	C _q	0.0659			
	C _m	-0.4222			
	H	0.1352			

^a Suffixes for carbon: *m*=methyl, *s*=methylene (secondary), *t*=tertiary, *q*=quaternary.

Table 9. Thermodynamic functions at 200, 300 and 400 K calculated with PEF91L, compared with other force fields⁷ and correlated values⁴⁵ unless otherwise noted.

Compound	T/K	Corr.	PEF91L	PEF303	PRF401
Entropy, $S_r^\circ / \text{J mol}^{-1} \text{K}^{-1}$					
Methane	200	172.6	166.8	—	—
	300	186.5	180.7	—	—
	400	197.4	191.6	—	—
Ethane	200	210.5	210.1	—	—
	300	229.5	228.5	228.2	228.1
	400	246.5	245.0	—	—
Propane	200	245.1	243.8	—	—
	300	270.4	268.4	267.4	268.7
	400	294.3	291.4	—	—
isobutane	200	261.5	259.0	—	—
	300	295.1	290.9	289.1	293.5
	400	326.9	320.9	—	—
Neopentane	200	258.4	261.2	—	—
	300	306.6	300.7	297.7	307.9
	400	347.5	337.9	—	—
<i>n</i> -Butane	200	276.1	266.4	—	—
	300	311.0	297.7	296.7	—
	400	342.5	327.2	—	—
<i>n</i> -Pentane	200	307.5	290.1	—	—
	300	350.3	329.4	327.9	—
	400	389.2	366.1	—	—
<i>n</i> -Hexane	200	338.9	312.6	—	—
	300	389.6	358.5	—	—
	400	436.1	401.7	—	—
Cyclohexane ⁴⁶	300	298.2	281.8	291.5	297.0
Cyclopentane ⁵⁶	300	295	258	278	281
Heat capacity, $C_{p,r}^\circ / \text{J mol}^{-1} \text{K}^{-1}$					
Methane	200	33.5	33.5	—	—
	300	35.8	35.8	—	—
	400	40.6	40.7	—	—
Ethane	200	42.3	41.2	—	—
	300	52.8	51.0	50.1	50.9
	400	66.2	64.2	—	—
Propane	200	52.9	53.7	—	—
	300	73.4	70.2	68.7	70.5
	400	94.0	90.3	—	—
isobutane	200	70.5	68.2	—	—
	300	97.3	91.6	89.4	92.7
	400	123.9	118.0	—	—
Neopentane	200	80.5	83.0	—	—
	300	121.5	114.0	111.2	116.1
	400	156.0	146.7	—	—
<i>n</i> -Butane	200	76.8	67.8	—	—
	300	97.9	90.0	87.8	—
	400	123.2	116.7	—	—
<i>n</i> -Pentane	200	93.6	82.0	—	—
	300	120.6	109.9	106.4	—
	400	152.5	143.1	—	—
<i>n</i> -Hexane	200	110.6	96.3	—	—
	300	143.3	129.8	—	—
	400	181.5	169.5	—	—
Cyclohexane ⁴⁶	300	106.3	101.3	98.7	105.6
Cyclopentane ⁵⁶	300	96	78	—	—
Enthalpy function, $(H_r^\circ - H_0^\circ) / t / \text{J mol}^{-1} \text{K}^{-1}$					
Methane	200	33.2	33.3	—	—
	300	33.6	33.6	—	—
	400	34.7	34.8	—	—

Continued.

Table 9. Continued.

Compound	T/K	Corr.	PEF91L	PEF303	PRF401
Ethane	200	36.3	36.1	—	—
	300	39.9	39.3	—	—
	400	44.8	43.8	—	—
Propane	200	42.7	41.4	—	—
	300	49.5	48.1	—	—
	400	58.1	56.1	—	—
isobutane	200	49.0	46.7	—	—
	300	60.6	57.6	—	—
	400	73.2	69.4	—	—
Neopentane	200	56.2	51.5	—	—
	300	78.1	67.1	—	—
	400	95.1	82.9	—	—
<i>n</i> -Butane	200	56.1	48.4	—	—
	300	66.2	58.3	—	—
	400	77.4	69.5	—	—
<i>n</i> -Pentane	200	68.9	56.0	—	—
	300	81.3	68.9	—	—
	400	95.1	83.2	—	—
<i>n</i> -Hexane	200	81.8	64.2	—	—
	300	96.6	79.9	—	—
	400	113.0	97.1	—	—

tributions work less well for PEF91L than for PEF401. These approximations are too simple for accurate work on highly flexible compounds although they are used almost universally.

A few data for cyclohexane⁴⁶ are included. The results conform to those obtained for alkanes. Cyclopentane is a special case because of the pseudorotation; see the discussion below.

Rotational barriers. Calculations of rotational barriers in gaseous as well as in liquid phase are, to the best of our knowledge, controversial. The reason for this controversy originates in the experimental difficulties involved in deriving detailed information on rotational barriers and the tempting acceptance of high level *ab initio* calculations as being definite. The information provided by spectroscopic studies is limited to calculated statistical population ratios assuming only pure rotamers (usually two) and thus neglecting the shape of the potential energy well. The population ratio, which is often determined with large uncertainty, is directly related to Gibbs' free energy and not to potential energy. Both of these considerations complicate further the reproduction of rotational barriers by modelling with potential energy functions.

Ethane. The rotational barrier between eclipsed and staggered conformations around the cylindrically symmetric $\text{sp}^3\text{-sp}^3$ bond in ethane is calculated as 9.9 kJ mol^{-1} (Table 10), of which more than 80% originates from the torsional potential. The calculated barrier height is approximately 20% on the low side when compared to the experimental values of 12.05 and $12.26 \text{ kJ mol}^{-1}$.⁴⁷⁻⁴⁹ In the strained eclipsed conformation the C-C bond length is calculated to expand by 0.23 pm when compared to the staggered conformation, and the H-C-C angles are expanded by 0.25° , both results in reasonable accordance with an *ab initio* calculation⁵⁰ which finds the

Table 10. Rotational barriers of alkanes obtained from this work and compared with MM3,⁸ Smith and Karplus⁹ and experimental values (in kJ mol⁻¹).

Compound	Ref.	Exp.	PEF91L	PEF91L (<i>D</i> =80)	MM3 ⁸	Smith & Karplus ⁹
Ethane	48	12.26 (0.08)	9.9	9.9	10.08	12.34
	47	12.05				
Propane <i>V</i> ₁	52,53	13.05 ^a	12.1	11.7	—	12.93
Propane <i>V</i> ₂	52,53	16.07 ^a	13.8	13.0	—	13.93
<i>n</i> -Butane <i>g</i> : <i>a</i>	31	2.9–4.2	6.3	3.43	3.39	2.93
	65	2.1–2.5				
	4	3.14				
<i>n</i> -Butane 120: <i>a</i>	65	13.0–13.8	20.1	19.3	13.81	13.89
<i>n</i> -Butane 0: <i>a</i>	54	19.08	33.1	28.0	20.21	21.3
	66	20.46				
	55	26.53				
Isobutane	67	16.3	15.1	18.4	—	—
Neopentane	68	18.0	18.4	18.0	14.02	—
Tetramethylethane <i>C</i> ₂ : <i>C</i> _{2h}	33	0.71	0.59	2.47	1.59	—
Tetramethylethane	69	18.0(0.8)	40.2	38.1	17.49	—
Tetramethylethane	69	33	56.5	51.9	28.95	—
Hexamethylethane	70	42.7	90.8	89.5	33.9	—
Cyclohexane <i>tb</i> : <i>ch</i>	32	20.1–24.7	49.4	42.7	24.10	28.5
	71	21.8				
	72	29.2				
Methylcyclohexane <i>ax</i> : <i>eq</i>	73	7.1	10.0	5.9	—	—
All- <i>cis</i> Hexamethylcyclohexane <i>tb</i> : <i>ch</i>	74	73.6	79.9	79.1	—	—
Dodecamethylcyclohexane <i>tb</i> : <i>ch</i>	75	69.9	107.5	110.0	—	—

^a Assumes rigid rotation.

bond stretch to be 1.0 pm and the C–C–H angle expansion to be 0.4°. It is interesting to notice that the rotational barrier of ethane is optimized primarily from the torsional normal mode with the experimental value³⁸ of 289 cm⁻¹. The value calculated with PEF91L is 278 cm⁻¹ in almost complete accordance with the older estimate of 279 cm⁻¹.⁵¹

Propane. Two rotational barriers are available for propane: the *V*₁ barrier having one C–C–C–H eclipsed and one staggered and the more strained *V*₂ barrier having two C–C–C–H torsions eclipsed. The calculated values are, respectively, 12.1 and 13.8 kJ mol⁻¹, in good agreement with the experimental ones (calculated from measured data assuming rigid rotation): 12.93 and 13.93 kJ mol⁻¹.^{52,53}

***n*-Butane.** If the *anti*:*gauche* population ratio of *n*-butane originated from the difference in number of states only, it would be 33:67, independent of temperature. Experimental evidence shows that the *gauche* conformer is more strained than the *anti* conformer,^{30,54} which seems logical, since the two end methyl groups are farther apart in the *anti* conformation. Those studies have determined the *anti* fraction at room temperature to be, respectively, 68 and 64%. Using PEF91L we calculate a Gibbs' free energy difference between the rotational isomers of 6.11 kJ mol⁻¹ at 300 K, resulting in an *anti*:*gauche* ratio of 85:15, which is somewhat overestimated. The calculated rotational potential of *n*-butane is shown in Fig. 2, having the highest energy at 0° (Me eclipses Me) and the lowest energy at 180° (*anti*) with local maxima at ±120° (H eclipses Me) and local minima at ±68° (*gauche*), in

good agreement with experiment.³⁰ The energy difference between the *gauche* and *anti* conformations is calculated as 5.7 kJ mol⁻¹, which is on the high side of the experimental values of 3.14 ± 1.05 kJ mol⁻¹.^{30,31,54} The 0 – *anti* energy difference, which has been in some dispute lately, is calculated as 33.2 kJ mol⁻¹, and is much overestimated when compared to the experimental value of 19.08 kJ mol⁻¹.⁵⁴ Wiberg and Murcko⁵⁵ have recently determined the enthalpy difference (at zero Kelvin) of the *cis* and *anti* conformations to be 26.4 kJ mol⁻¹; however, this higher value has been attributed to the use of too small basis sets by Allinger *et al.*⁸

Electrostatic influences. An interesting detail (Table 10) is that we find a strong quantitative dependence on the

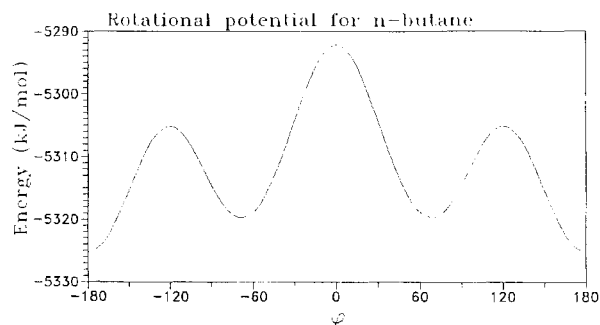


Fig. 2. Rotational potential of *n*-butane. All degrees of freedom are allowed to relax except the torsional angle of interest. The calculations were done with an as yet unpublished PC-based molecular mechanics program named MoleCast, using a simple harmonic torsional constraint potential.⁶²

electrostatic potential for the *n*-butane *g:a* barrier, the tetramethylmethane (2,3-dimethylbutane) $C_2:C_{2h}$ barrier and the cyclohexane *tb:ch* barrier, while other barriers are more independent. Increasing the dielectric constant to 80 results in a 55% lowering of the *n*-butane *g:a* barrier. This implies that the common habit of changing charges and dielectric constants in practical applications can change the fundamental properties of the models. A similar strong electrostatic dependence was observed by Smith and Karplus⁹ when they tried to scale 14 electrostatic interactions. In the generalized force field MM3⁸ the problem is overcome by assigning zero values to bond dipole moments of C–C and C–H bonds, thereby neglecting electrostatic interactions for saturated hydrocarbons.

Cyclopentane. This molecule presents some problems with a potential energy function as simple as PEF91L, as do five-membered rings in general.¹⁶ The calculated rotational constants for the *T* conformer are $A = 0.22173 \text{ cm}^{-1}$, $B = 0.22123 \text{ cm}^{-1}$ and $C = 0.12959 \text{ cm}^{-1}$. This means that the geometry is 0.2% from a symmetric top. When the *E* conformer is initiated, the modified Newton minimizer invariably changes it into the *T* conformer. The Dennis–Moré minimizer finds a well defined (energy gradient $< 10^{-4} \text{ J mol}^{-1} \text{ pm}^{-1}$) planar saddle point at 28.3 kJ mol^{-1} above the minimum. The pseudorotational frequency is calculated to 16 cm^{-1} , which compares with earlier calculations using optimized force fields:⁷ 4, 6, 8 and 22 cm^{-1} for PEF302, -303, -304 and -401. Low-frequency skeletal bendings and torsions are compared in Table 6. Calculation of thermodynamic functions requires a modified procedure: summation over internal degrees of freedom runs over N-7 rather than N-6. Otherwise the low-frequency pseudorotation will dominate the Einstein sums and distort the result. Few experimental data are available;⁵⁶ the reproduction (Table 9) is not satisfactory. The better result obtained before¹⁶ may be due to the lower value of the pseudorotation frequency.

Cyclodecane. Cyclodecane conformers were used in earlier work⁷ to assess hydrocarbon parameter sets. In the present work two of them were checked: the *BCB* which is well known in the solid state,⁵⁷ and the *TCCC*, which has been subjected to calculation⁵⁸ and which previously⁷

showed an unexpected low energy and Gibbs free energy. As stated before,⁷ the earlier non-optimized parameter sets used in this group failed to produce a reasonable geometry, whereas those optimized on simple alkanes gave good reproductions.

The results obtained in the present work are shown in Table 11. In the case of *BCB* a slight improvement over the previous calculations is seen; for *TCCC*, the results are closer to those of Engler *et al.*⁵⁸ than found before.⁷ The energy difference seems more reasonable.

Short non-bonded distances. Non-bonded distances are probably the most difficult geometrical entities to model by molecular mechanics force fields, because small errors in the internal geometry tend to add up in the non-bonded description. In order to improve this, optimization on non-bonded distances was implemented in the CFF program, but has so far been used sparingly. The complex dependence on the different parameters and the simple model used for non-bonded interactions in PEF91L has limited the results of this effort.

The shortest H···H non-bonded distance ever measured, 175.4 pm, has been observed in the highly strained *exo-exo*-tetracyclododecane structure.²³ This structure has been tested in PEF91L, where the short H···H distance was calculated to be 191.7 pm and the corresponding C···C non-bonded distance as 323.9 pm, the experimental value being 311.2 pm. When comparing the values, it must be emphasized that the values are calculated for the gas phase, whereas the measured values are from a X-ray crystal structure determination of a derivative. MM3⁸ calculates the C···C distance to be 312.4 pm, and the force field of Dillen¹¹ gives 312.8 pm, both using a Buckingham-type van der Waals potential.

Another relative close contact is found in the X-ray structure of *cis-syn-cis*-perhydroanthracene,²³ where the C(1)···C(8) distance was measured as 339.6 pm. For this structure Dillen¹¹ calculated a difference of almost 5 pm between gaseous and crystalline phase, supporting our strategy of avoiding implicit environment variables in the force field development. In PEF91L we calculate the C(1)···C(8) distance to be 344.3 pm in the crystal and 348.1 pm in the gas phase, a similar difference, but somehow underestimated when compared to the experimental value of 339.6 pm.

Bicyclohexyl. The structure of this compound was published recently.⁵⁹ Bicyclohexyl has six possible conformers,⁶⁰ of which the two diequatorial (*ee anti* of C_{2h} and *ee gauche* of C_2 symmetry) and one axial–equatorial (*ea anti* of C_s symmetry) are most stable.⁵⁹

Calculated with PEF91L, the ratio $C_{2h}:C_2:C_s$ is 12.5:86.6:0.9 at 112°C, from differences in Gibbs free energy of 3.97, 0.0 and 12.44 kJ mol^{-1} . This is a considerably higher population of the C_2 conformer compared to the electron diffraction experiment, which observed approximately equal populations of the two diequatorial conformers: $C_{2h}:C_2:C_s = 53(9):47(9):0$.

Table 11. Conformers of cyclodecane.

	BCB		TCCC	
	PEF91L	Ref. 57	PEF91L	Ref. 58
$\theta_1\theta_4\theta_7\theta_9$	119	118	114	—
$\theta_2\theta_5\theta_6\theta_{10}$	115	114	117	—
$\theta_3\theta_8$	119	118	114	—
$-\phi_1\phi_4\phi_6-\phi_9$	56	55	83	83
$-\phi_2\phi_3\phi_7-\phi_8$	65	66	145	144
$-\phi_5\phi_{10}$	151	152	66	68
$\Delta E/\text{kJ mol}^{-1}$	0.00		4.19	

The bond length of the pivot C–C has been calculated as 155.3, 154.7 and 155.5 pm for C_{2h} , C_2 and C_s , respectively. The electron diffraction experiment observed 155.9 ($3\sigma = 1.6$) pm and 160.1 (1.5) pm (r_z , converted from r_a) for C_{2h} and C_2 . The torsional angle C–C–C–C around the pivot bond is calculated as 65° , which is smaller than the value 75° found by electron diffraction.

Conclusion

In this work we have applied a systematic approach of optimizing a set of empirical energy functions to develop a new combination of potential energy functions for modelling the alkanes.

The performance has been broadly tested and compared with the performance of more complex types of force fields including Buckingham-type van der Waals potentials with foreshortening factor for hydrogen position and several cross-term potentials. The force field performance on crystals and on gas phase structures is very good. For other properties such as vibrational frequencies and thermodynamic functions it is satisfactory.

When PEF91L is applied to substances and properties not included in the optimization, very good reproduction of structure is found for e.g. cyclodecane. For substances with extremely close contacts agreement is less good. We must conclude that in this respect the parametrization of the Lennard-Jones 12–6 potential in PEF91L, and perhaps also the repulsive character intrinsic to the potential, is too crude to model extremely close contacts.⁶¹

All rotational barriers show good qualitative agreement with experiment, but in some cases they are increased when compared to state of the art experimental and *ab initio* calculations. In future refinement work optimization facilities on relative energies of rotational isomers is needed, but before embarking in such direction there is an urgent need for new and accurate experimental data on appropriate model systems.

Acknowledgements. The work reported in this paper was part of the Ph.D. studies of S. B. E. and J. F. The following funds and organizations contributed to the financing: The Technical University of Denmark, The Danish Academy of Technical Sciences, The Danish Computing Center for Science and Education, The Danish Research Academy, The Carlsberg Foundation, The Jorck Foundation, Julie Damms Foundation, Thomas B. Thriges Foundation and The COWI Foundation. All contributions were essential and are gratefully acknowledged.

We would also like to thank Professor Jaroslav Koča (Brno, Czech Republic) for useful comments on the manuscript. Mrs. Birgit Rasmussen set up the first version of the database of experimental data used in the optimizations.

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Received December 23, 1993.