Tetrahedron Vol. 39, No. 17, pp 2769 to 2778, 1983
Printed in Great Britain

0040-4020/83 $3.00 + .00

A REPARAMETERIZATION OF EMPIRICAL HYDROCARBON FORCE FIELD MM2 FOR IMPROVED PERFORMANCE IN TORSIONAL ENERGY SURFACE CALCULATIONS[1]

CARLOS JAIME[2] and EIJI ŌSAWA*
Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060, Japan

(*Received in Japan* 23 *December* 1982)

Abstract—An attempt was made to improve the tendency of Allinger's latest empirical force field MM2 to underestimate barrier heights of rotation about C–C single bonds. The strategies adopted are (1) to change the smallest possible number of parameters, (2) to reproduce the experimental barrier heights of central C–C bond rotation in several substituted ethanes and the calculated *syn* barrier of n-butane (5.2 ± 0.4 kcal mol^{-1}† by *ab initio* 4-31G calculation involving structure optimization by gradient method), (3) to re-adjust the van der Waals interactions by calibrating against short intramolecular H/H distances determined by neutron diffraction analysis, and (4) to comply with the major criteria used in the original construction of MM2 including calculations of layer spacings of n-hexane crystal, C–C bond length in diamond and axial-equatorial energy difference of methylcyclohexane. The best compromise was accomplished by changing the following five parameters while keeping the other original parameters intact: V_3(C–C–C–C) 0.600, V_3(H–C–C–H) 0.350 kcal mol^{-1}, l°(C–C) 1.526, r(C) 2.000, r(H) 1.426 Å. The modified force field performed as well as the original MM2 in reproducing bond lengths, valence and dihedral angles of 21 hydrocarbons. The standard deviation between the calculated and experimental heats of formation of 44 hydrocarbons was 0.59 kcal mol^{-1}. The modified force field correctly reproduced chair–chair interconversion barrier of all-*cis*-1,2,3,4,5,6-hexamethylcyclohexane (calc. 16.7, obsd. 17.6 kcal mol^{-1}).

Empirical force field calculation has now become a popular tool for chemists as the result of wide distribution of versatile program packages.[3] Allinger's 1977 force field MM2[4] marked the arrival of the "second generation" molecular mechanics scheme and has been remarkably successful in solving numerous practical problems in diverse fields of organic chemistry.[5] Parameters for heteroatoms and functional groups are being added to the original hydrocarbon force field to facilitate the application of MM2 to wider range of compound classes.[6]

In the course of our exploitation into the application of this force field,[7] we noticed several aspects of its hydrocarbon part still needing some refinement. The most serious of these is the failure to reproduce barrier heights for internal rotation of congested C–C single bonds.[8] Also, MM2 tends to overestimate close nonbonded H...H distances.[3d] Some of the torsional parameters apparently are too small and the van der Waals parameter for H...H contact too large. While these defects may appear most clearly in rather novel congested molecules, they may accumulate themselves during the pairwise addition calculations of large molecules, where molecular mechanics should perform most advantageously, leading to large errors. In view of the remarkable merit of molecular mechanics in conformational analysis where torsional processes prevail, it is highly desirable to correct these defects. This paper describes an attempt to partially reparametrize MM2 in order to improve the performance without damaging its otherwise excellent features.

RESULTS AND DISCUSSION

Ab Initio *Calculation of n-butane*

Our previous comparison of the calculated with the observed barrier heights of internal rotation in simple to congested hydrocarbons showed almost proportional increase in the error of calculated barriers with the number of eclipsing C–C–C–C units at the torsional barrier.[8] This observation prompted us to re-examine the energy of *syn* conformation of n-butane, against which the torsional parameters of empirical force field have traditionally been determined. No experimental data is available for this energy and we must resort to the computational estimate. Previous *ab initio* calculations of n-butane have reproduced experimentally determined quantities of this molecule generally well: the relative energy of *anti* and *gauche* conformations, the height of *anti-gauche* barrier, and the C–C–C–C dihedral angle in *gauche* conformer (Table 1).[9,10] Nevertheless, these facts do not guarantee high reliability in the calculated properties of *syn* conformer.

While extensive electron correlation calculations like configuration interaction are desirable but still not feasible to us, we carried out *ab initio* calculations of the four key stationary points of n-butane (*anti*, *anti-gauche* barrier, *gauche* and *syn*) with 4-31G basis set involving full geometry optimization by the gradient method.[12,13] The results (Table 1)[14] agree well with the experimental values obtained by the direct analysis of torsional transitions in the low frequency Raman spectra in the gas phase.[11] It is interesting to note that the calculated energy of *syn* barrier *increases* from the minimal basis set on partially[9]—or molecular mechanics[10]—optimized geometries to our value of 6.13 kcal mol^{-1}. After the empirical electron correlation correction (−0.9 ± 0.4 kcal mol^{-1})[10] we obtain 5.2 ± 0.4 kcal mol^{-1} as the best estimate of the *syn* barrier height of n-butane. This value is used below as one of the criteria in the re-evaluation of torsional parameters.

Readjustment of torsional and nonbonded potential parameters in MM2 *force field*

Using the best estimate of *syn* barrier height of n-butane as well as other experimental barrier heights of

---

†1 kcal mol^{-1} = 4.184 kJ mol^{-1}.

Table 1. Relative energies of four key stationary points in gaseous n-butane (kcal mol^{-1})

Stationary point	STO-3G/PRDDO[a]	STO-3G/MM2[b]	4-31G/Gradient[c]		MM2'[d]	MM2	Exp[e]
Anti	0.0 (C_{2h})	0.0 (C_{2h})	0.0 (C_2)	(-157.07163347)[f]	0.00	0.00	0.00
AG barrier	3.41(C_2)	3.56(C_2)	3.55(C_2)	(-157.06596806)	3.29	2.49	3.63
Gauche	1.08(C_2)	0.88(C_2)	0.98(C_2)	(-157.07007300)	0.83	0.86	0.89[g]
Syn	5.68(C_{2v})	5.99(C_{2v})	6.13(C_2)	(-157.06186368)	5.42	4.73	——

[a] STO-3G calculation on PRDDO minimized geometry, ref. 9. [b] STO-3G calculation on MM2 minimized geometry, ref. 10. [c] This work, 4-31G calculation with full geometry optimization by gradient method. [d] This work. Mofified MM2. [e] Ref. 11. [f] Total energy in hartree. [g] ± 0.03 kcal mol^{-1}.

alkanes, we started to reparametrize torsional parameters of MM2. It was clear from the outset that the repulsion at the C–C–C–C eclipsing must be increased. For this purpose, we changed only the V_3 torsional parameter. Since such a change naturally disturbs the balance between torsional and nonbonded potentials, it is also necessary to modify the latter parameters. After several trial calculations using changed nonbonded potential parameters, we found it sufficient for our present purpose to change only the van der Waals radii of H and C atoms.

After a number of adjustments on the trial-and-error basis, each time followed by calculations of a large body of test molecules, we conclude that a set of only five revised parameters as given in Table 2 provides the best compromise. When used in conjunction with the remaining MM2 parameters a substantially improved force field emerged, which we call hereinafter "modified MM2" (or MM2' in Tables). The main criteria are separately mentioned below.

Rotational barriers about C–C *bond.* Relative steric energies of n-butane conformers and barriers recalculated by the modified MM2 are included in Table 1. The best *ab initio* estimate of *syn* barrier height is now well reproduced. Relative energies of other stationary points also are satisfactorily calculated. Four substituted ethanes, for which the barriers of rotation about the central bond had been calculated too low by the original MM2,[8] now gave calculated barrier heights which virtually reproduce experimental values (Table 3).

Close H...H *nonbonded distances.* White[16] previously noticed that the existing empirical force fields generally gave too large interatomic distances for short nonbonded H...H interactions. Since then several attempts have been reported trying to reduce the 'hardness' of an H atom in various molecular mechanics schemes. For example, Allinger decreased the ϵ constant of Hill equation from 0.063 to 0.047 kcal mol^{-1}, and increased the offset of the electron density center along the C–H bond toward carbon atom from 7.5 to 8.5%, in addition to transferring some part of nonbonded interactions to the torsional term in the construction of MM2 force field.[4a,17] Nevertheless, practically all of the existing force field models still overestimate the H...H distance.[3d] The problem is complicated by the fact that the experimental H...H distances are not always reliable because of technical difficulties in locating the position of protons. Table 4 illustrates the situation. Compounds **1**–**5** were analyzed by X-ray diffraction method, protons being located by using difference Fourier maps.[18–20] This

Table 2. Readjusted MM2 parameters

Parameter[a]	Original	New
V_3(C–C–C–C), kcal mol^{-1}	0.093	0.600
V_3(H–C–C–H), kcal mol^{-1}	0.237	0.350
l^o(C–C), Å	1.523	1.526
r(C), Å	1.900	2.000
r(H), Å	1.500	1.426

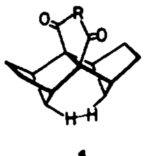
[a] V_3: Torsional constant of the third order. l^o: Natural bond length. r(X): Van der Waals radius of atom X. C: sp^3-hybridized carbon atom.

Table 3. Experimental and calculated barriers of rotation about C–C bonds (kcal mol^{-1})

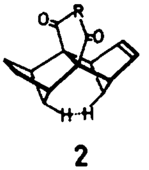
Compound	Exp	MM2'^{a}	MM2
sym-Tetramethylethane			
<u>anti</u> → <u>gauche</u>	4.3^{b}	4.81	3.09
<u>gauche</u> → <u>gauche</u>	—	6.90	5.02
(<u>anti/gauche</u> diff	0.13^{b}	0.11	0.16)
Pentamethylethane	6.97^{c}	6.98	4.1
Hexamethylethane	9.6-10.0^{c}	9.63	5.3
2,2,4,4,5,5,7,7-Octamethyloctane	13.8^{c}	11.89^{d}	9.4^{d}
		11.64^{e}	8.3^{e}
		12.25^{f}	7.8^{f}

[a] This work. Modified MM2. [b] L. Lunazzi, D. Macciantelli, F. Bernardi, and K. U. Ingold, <u>J. Am. Chem. Soc.</u>, **1977**, **99**, 4573-4576. [c] J. E. Anderson, and H. Pearson, <u>ibid.</u>, **1975**, **97**, 764-769. [d] <u>anti</u> → <u>eclipse</u>. [e] <u>gauche</u> → <u>eclipse</u>. [f] <u>gauche</u> → <u>eclipse'</u>, see ref. 8.

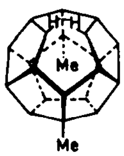
indirect technique gives large uncertainties: for example, the standard deviation for the H...H distance of **3** is 0.11 Å.[19]



1

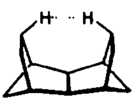


2

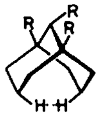


3

4



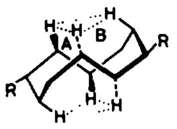
5



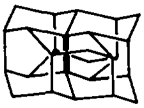
6

The observed H...H distance (1.68 Å) of **1** is too short and is supposed to represent a time average of two skewed interactions.[18] Hence, in the head-on orientation of two C–H bonds from methylene bridges, which corresponds to our calculated energy minimum, the distance should be longer.

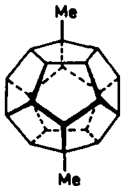
Only the neutron diffraction analysis gives sufficiently precise data. For bicyclo[3.3.1]nonane **6**, which is perhaps the most studied molecule regarding the problem of unusually short intramolecular contacts,[8,21-23] an estimate of 1.86 Å is given for the H_3...H_7 distance based on three X-ray-determined C skeletons of various bicyclo[3.3.1]nonane derivatives fitted with neutron-determined geometry of 3-methylene group in 9-thiabicyclo[3.3.1]nonane-2,6-dione.[21] Note that our modified MM2 gave a value of 1.92 Å for **6**, not exactly identical but the closest to the 'experimental' distance among all previous calculated results (Table 4). The molecular structure of flexible cyclodecane ring **7** is sensitive to the packing force in crystal, and the observed (neutron diffraction) H...H distances are subject to changes as large as 0.03 Å.[24] Nonetheless, the calculated distances are in satisfactory agreements with the observed values.



7



8



9

Hence, disregarding **1** and **3** for the reasons mentioned, we see that the modified MM2 satisfactorily reproduces short H...H distances and its hydrogen can be considered to be properly parameterized.

Table 4. Experimental and calculated short intramolecular H...H nonbonded distances (Å)

		Calcd		
Compound	Exp[a]	MM2'[b]	MM2	Other[c]
1	1.68(X)[d]	1.78[e]	1.84[e]	
2	1.80(X)[d]	1.80[e]	1.86[e]	
3	1.95(X)[f]	1.87	1.89	
4	1.82(X)[g]	1.83	1.89	1.90(CFF)[g]
5	1.85(X)[g]	1.90	1.94	1.96(CFF)[g]
6	1.86(N)[h,i]	1.92[i]	2.02[i]	2.20(A71)[i,j]
	1.85(X)[k,l]			2.15(MM1)[m]
	1.85(X)[n]			1.97(WB)[j]
7 A	1.94(N)[o]	1.93[i]	2.00[i]	2.01(CFF)[p]
B	2.08(N)[o]	2.12[i]	2.15[i]	2.13(CFF)[p]

[a] X = X-ray diffraction. N = Neutron diffraction. [b] This work. Modified MM2. [c] Other force field calculations: WB = White/Bovill force field, ref. 16b. A71 = Allinger 1971 force field, ref. 17. MM1 = Allinger 1973 force field: (a) D. H. Wertz, and N. L. Allinger, Tetrahedron, **1974**, 30, 1579-1586; (b) N. L. Allinger, and Y. H. Yuh, Quantum Chemistry Program Exchange, **1980**, 11, 318. CFF = Ermer's version of Consistent Force Field, ref. 3c. [d] R = O, ref. 18. [e] R = CH_2. Carboxylic acid anhydride cannot be handled by the present version of MM2. [f] Ref. 19. [g] Ref. 20. [h] Indirect inference from neutron diffraction analysis of a related compound. See text and ref. 21. [i] R=H. [j] Taken from ref. 21. [k] Estimated from X-ray analysis of 5-methyl-1-p-toluenesulfonyloxymethylbicyclo[3.3.1]-nonan-9-ol, ref. 22. [l] R=CH_3. [m] The present calculation. [n] The compound is 2,6-dichloro-9-thiabicyclo[3.3.1]nonane 9,9-dioxide corrected for the artefact shortening of C-H bond lengths, ref. 23. [o] R=OH. The distance given is an average of two independent molecules in the unit cell, ref. 24. [p] Taken from ref. 24.

General structural features

We now proceed to check the effects of our modified parameters on the other molecular properties at energy minima. MM2 excels in this regard and hence our primary purpose hereinafter is to see if the performance of modified MM2 remained as well as the original level. The standard set for the calibration of ground state structures is taken from those used by Schleyer[25] and Allinger,[4a] and consists of 21 hydrocarbons.[26] The standard deviations of calculated structural parameters from experimental values turned out to be essentially the same as those of the original MM2 (Table 5).[30]

Another structural criterion, used by Allinger in assessing his force fields, is to calculate the unit cell

Table 5. Standard deviations between the calculated and experimental bond lengths, bond angles, dihedral angles and nonbonded distances for the 22 hydrocarbons basis set

Structural parameter	MM2'	MM2
Bond length, Å	0.0098	0.0093
Bond angle, deg	1.7	1.3
Dihedral angle, deg	5.3	6.6
Nobond distance, Å	0.038	0.046

Table 6. Experimental and calculated spacing between chain layers along principal axes in n-hexane crystal (Å)

Principal axis	Exptl[a]	Calcd[b] MM2'[c]	Calcd[b] MM2
a	4.17	4.17	4.22
b	4.70	4.71	4.69
c	8.57	8.93	8.45

[a] Ref. 32. [b] Obtained by unconstrained relaxation of a cell containing eight n-hexane molecules. [c] This work. Modified MM2.

dimension of n-hexane crystal.[17,31] Eight n-hexane molecules (160 atoms) were packed in a space corresponding to the observed unit cell[32] and the whole assembly was relaxed without constraint. The resultant average spacings between molecular chains are again in good agreement with experiment and comparable to those obtained with MM2 (Table 6).

The modified MM2 performed slightly less satisfactory against more rigorous criterion for C-C bond lengths. As a model of diamond, we used unknown hexamantane **8**, wherein the central C–C bond (indicated with a thick line) between two quaternary C atoms is surrounded by six tertiary carbons.[33] Our modified parameter set gave 1.560 Å for this bond, 0.016 Å longer than the observed diamond value of 1.544 Å. On the other hand, like the original MM2, the modified MM2 also underestimates the bond length of eclipsed C–C–C–C unit. Differences between observed and calculated are, for examples, 0.013 Å (average) for endocyclic C–C bonds of 1,16-dimethyldodecahedrane **9**,[19] 0.020 Å for C_2–C_3 bond of norbornane and 0.011 Å for C_2–C_3 bond of bicyclo[2.2.2]octane.[30] With the original MM2 the corresponding underestimations are 0.015 (average), 0.020 and 0.014 Å, respectively.

Table 7. Experimental and calculated enthalpies (kcal mol^{-1}, gas, 25°C)

Compound	Exptl[a]	Calcd[b]	Exptl-Calcd
Ethane	-20.24	-18.88	-1.36
Propane	-24.82	-24.30	-0.52
n-Butane	-30.15	-29.46	-0.69
n-Pentane	-35.00	-34.81	-0.19
n-Hexane	-39.96	-40.03	0.07
n-Heptane	-44.89	-45.28	0.39
n-Octane	-49.82	-50.62	0.80
Isobutane	-32.15	-31.95	-0.20
Isopentane	-36.92	-36.25	-0.67
2-Methylpentane	-41.99	-41.63	-0.36
3-Methylpentane	-41.33	-40.52	-0.82
2,2-Dimethylbutane	-44.48	-44.14	-0.34
2,3-Dimethybutane	-42.49	-42.73	0.24
3,3-Dimethylpentane	-48.08	-47.86	-0.22
Neopentane	-40.27[c]	-40.27	0.00
Hexamethylethane	-53.95	-54.40	0.45
2,2,3-Trimethylbutane	-48.95	-49.24	0.29
3,3-Diethylpentane	-55.44[d]	-55.73	0.29
Cyclobutane	6.38[e]	4.34	2.04
Cyclopentane	-18.30[e]	-17.72	-0.58
Cyclohexane(chair)	-29.43[e]	-29.19	-0.24
Cycloheptane[f]	-28.22[e]	-27.44	-0.78
Cyclooctane	-29.73[e]	-29.22	-0.51

Table 7 (*Contd.*)

Compound	Exptl[a]	Calcd[b]	Exptl-Calcd
Methylcyclopentane	-25.50	-25.45	-0.05
Methylcyclohexane	-36.99	-36.90	-0.09
1,1-Dimethylcyclohexane	-43.26	-43.36	0.10
trans-1,2-Dimethylcyclohexane	-43.99	-43.60	0.61
cis-1,2-Dimethylcyclohexane	-41.39	-42.01	0.62
Norbornane	-12.48^{h}	-13.44	0.96
1,4-Dimethylnorbornane	-30.63^{g}	-31.45	0.82
2,3-Dimethylnorbornane	-25.71^{g}	-25.65	-0.06
Cubane	148.70^{g}	148.73	-0.03
cis-Bicyclo[4.2.0]octane	-6.39^{e}	-6.56	0.17
cis-Bicyclo[3.3.0]octane	-22.30^{i}	-21.26	-0.04
trans-Bicyclo[3.3.0]octane	-15.90^{i}	-15.58	-0.32
cis-Hydrindane	-30.41^{e}	-30.03	0.38
trans-Hydrindane	-31.45^{e}	-31.66	0.21
cis-Decalin	-40.45^{e}	-41.53	1.08
trans-Decalin	-43.54^{e}	-44.15	0.61
Adamantane	-31.76^{j}	-31.43	-0.33
1-Methyladamantane	-40.57^{j}	-40.19	-0.38
Tetramethyladamantane	-67.15^{j}	-66.55	0.40
endo-Tricyclo[5.2.1.0^{2,6}]decane	-14.38^{g}	-14.36	-0.02
Diamantane	-34.87^{j}	-34.66	-0.21
Di-*tert*-butylmethane	-58.16	-60.10	1.94
Cyclodecane **7**	-36.88	-39.04	2.16
Bicyclo[2.2.2]octane	-23.71^{k}	-19.57	-4.17
T-S-T-Perhydroanthracene	-58.12	-59.24	1.12
T-A-T-Perhydroanthracene	-52.73	-51.13	-1.60
Protoadamantane	-20.54	-18.12	-2.41

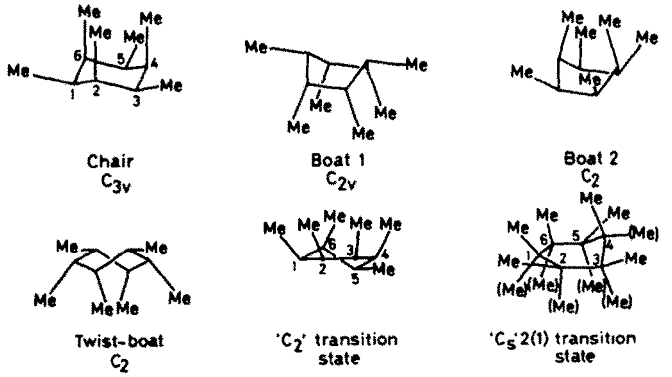
[a] Unless otherwise noted taken from F. D. Rossini *et al.* "Selected Values of Physical and Thermochemical Properties of Hydrocarbons and Related Compounds, Compiled by American Petroleum Institute," Carnegie Press, Pittsburgh, Pa., **1953**. [b] Obtained by using the modified parameter set (Table 2) and the new bond and structural heat increment parameters (Table 10) in the framework of MM2. For acyclic and cyclic alkanes, all significant conformers were taken into accounts to compute energy population according to a method similar to that described in ref. 36. However, for n-heptane and n-octane, only the all-anti conformation was calculated. [c] G. Pilcher and J. D. M. Chadwick, *Trans. Faraday Soc.*, **1967**, *63*, 2357-2361. [d] A. Labbauf, J. B. Greenshields, and F. D. Rossini, *J. Chem. Eng. Data*, **1961**, *6*, 26. [e] Taken from Table I of ref. 4a. [f] Twist- chair-twist boat. [g] Taken from Table II of ref. 25. [h] Ref. 37. [i] Ref. 38. [j] Ref. 5b. [k] Average of two determinations, refs. 38, 39.

Heats of formation. The eventual usefulness of an empirical force field is judged by its capability to reproduce heats of formation, energies being, in general, more difficult to calculate than structures.[3d,31c,34] We closely followed Allinger's method of deriving enthalpies from computed steric energies using incremental constants for various bond and structure types.[4a] Our standard hydrocarbon set is again a composite of those used by Allinger[4a] and by Schleyer,[25] consisting of 50 compounds (Table 7).[35] Two bond (C–C and C–H) and three structural (isobutane, neopentane and $C_{sp}3$-methyl types) increments were computed by the least squares method so that the errors in the calculated enthalpies for the standard hydrocarbon set were minimized. When these calculations were started, we noticed that compounds having 4- to 6-membered ring gave very poor agreements in heats of formation and decided to introduce new ring increments. The final set of eight new increments for the calculation of heat of formation is given in Table 8. Heats of formation of the standard hydrocarbon set obtained by using these increments are compared with experimental values in Table 7.

In the course of this process, we noticed that several compounds in Table 7 persistently gave large errors. Finally we removed six of them (listed under dotted line in Table 7) from the calculation of standard deviation. These are di-t-butylmethane, cyclodecane, bicyclo[2.2.2]octane, T–S–T- and T–A–T-perhydroanthracene, and protoadamantane. It is difficult to decide the reasons for the large discrepancies in these six compounds. Since the results of combustion experiments often differ significantly among different investigators,[5b,25,40] some of the reported heats of formation for these problematic molecules could well be wrong.[41] Di-t-butylmethane is certainly the most crowded molecule among the list, and it will be safe to avoid applying the modified MM2 to such an extremity.

The standard deviation of errors in the calculated heats of formation for the rest 44 compounds of various structural types is 0.59 kcal mol^{-1},[43] which is only slightly larger than that of the original MM2 (0.42 kcal mol^{-1}) but smaller than those of the first generation force fields (e.g. 0.83 kcal mol^{-1} of Schleyer force field[25] and 1.03 of Allinger's 1771 force field[17]).

Conformational energy of methylcyclohexane. We refer here only one example of conformational energy calculation. A recent accurate determination of the free energy difference between *axial* and *equatorial* methylcyclohexane by the direct low-temperature NMR method gave 1.74 ± 0.06 kcal mol^{-1} at 172 K.[34] Our modified MM2 gave an enthalpy difference of 1.74 kcal mol^{-1}.



Chair C_{3v}

Boat 1 C_{2v}

Boat 2 C_2

Twist-boat C_2

'C_2' transition state

'C_s'2(1) transition state

10

Table 8. Regular heat increments for modified MM2 (kcal mol^{-1})

C–C	1.305
C–H	-3.690
Iso	-1.941
Neo	-4.868
Methyl	-0.1016
□	-2.830
⬠	-1.242
⬡	0.0504

*Example: Torsional energy surface of all-*cis-*1,2,3,4,5,6-hexamethylcyclohexane* (**10**).

Whereas the original MM2 has performed generally well for ring processes,[3] it failed with **10**: the calculated barrier of chair-chair interconversion turned out to be much too low (11.7 kcal mol^{-1})[46] compared the observed (17.6 ± 1.0 kcal mol^{-1})[47] (Table 9). In view of the danger of artefacts in the one-bond driver calculations[5p,45] two-bond drive calculations[5p,45] were performed to cover the torsional energy surface of **10** (Fig. 1).[48]

The minimum energy reaction path of chair-chair interconversion is $C \rightarrow$ "C_2" $\rightarrow TB \rightarrow$ "C_2" $\rightarrow C$, where "C_2" corresponds to the well-known chair-chair interconversion barrier of cyclohexane where four ring carbon atoms lie in a plane.[49,50] Four such paths appear in Fig. 1 and they are all equivalent by symmetry. The highest points along this path, 16.7 kcal mol^{-1}, agree with the observed barrier height (Table 9).[51] Figure 1 clearly illustrates pseudorotational path along $\omega_{12} = \omega_{45}$ line, TB–B1–TB–B2–TB–B1–... B1 and B2 can be reached from C

Table 9. Relative energies of important conformers of all-*cis*-1,2,3,4,5,6-hexamethylcyclohexane (**10**) (kcal mol^{-1})

Conformer	Obs.[a]	Calc	
		MM2'[b]	MM2[c]
Minima			
Chair (C)	0.0	0.0	0.0
Twist-boat (TB)	—	8.5	4.8
Saddle points			
'C_2'	17.6 (±1.0)	16.7	11.7
Boat 1 (B1)	—	10.7	7.1
Boat 2 (B2)	—	13.5	10.6
Maxima			
'C_s'1	—	~23.1	—
'C_s'2	—	~16.8	—

[a] Ref. 47. [b] This work. Modified MM2. [c] Ref. 46.

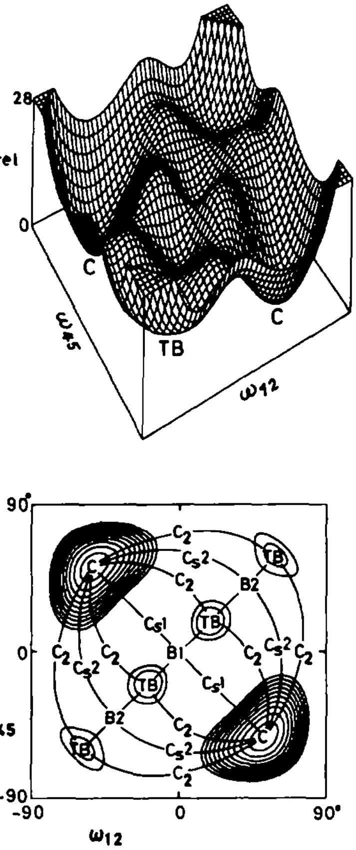


Fig. 1. Torsional energy surface of all-*cis*-1,2,3,4,5,6-hexamethylcyclohexane (**10**) obtained by using modified MM2. C = chair, TB = twist-boat, B1 = boat 1, B2 = boat 2, C_2 = transition state with four ring carbon atoms near coplanar, C_s1 = transition state with five ring carbon atoms near coplanar leading to boat 1, C_s2 = transition state with five ring carbon atoms near coplanar leading to boat 2. ω_{12} = Dihedral angle at ring carbons 6–1–2–3. ω_{45} = Dihedral angle at ring carbons 3–4–5–6. E_{rel} = relative steric energy in kcal mol^{-1}.

by way of "C_s"1 and "C_s"2 respectively, where "C_s" corresponds to the cyclohexane barrier with five ring carbons coplanar.

The reason for our success in reproducing the energy barrier is partly due to the improved van der Waals constants, leading to smaller hydrogen and larger carbon, but must be mainly due to the corrected *syn* energy of C–C–C–C unit, four nearly *syn* such units appearing in the "C_2" transition point.[53,54]

CONCLUSION

The goal of this study, to improve MM2 with regard to its performance in calculating torsional processes of hydrocarbons without sacrificing other characteristics of the original MM2, can be considered to have been fulfilled. The presently modified version of MM2 is expected to perform well not only in the region near the energy minima but also near the conformational transition states. Our modification includes decreased "size" of H atom and increased "size" of C atom, which improved the evaluation of van der Waals interactions. Further results of application of the modified force field to various aspects of dynamic conformational analysis[55] will be reported shortly.

Acknowledgements—We thank Profs. N. L. Allinger and K. Morokuma for helpful comments. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education and by a fund from Kureha Chemical Industries Co. Computations have been carried out at the Computing Centers of Hokkaido University and the Institute for Molecular Sciences.

REFERENCES

[1] Part 18 of a Series, *Application of Potential Energy Calcalculations to Organic Chemistry*. Part 17: E. Ōsawa, G. Szalontai and A. Tsurumoto, *J. Chem. Soc.*, Perkin Trans. II. in press. Part 16: E. Ōsawa, P. M. Ivanov and C. Jaime, submitted for publication in *J. Org. Chem.*

[2] Recipient of Postdoctoral Fellowship from Commissió Interdepartamental de Recerca i Innovació Tecnològica, Generalitat de Catalunya (Spain), 1981–1983.

[3] Reviews: [a]N. L. Allinger, *Adv. Phys. Org. Chem.* **13**, 1 (1976). [b]M. B. Hursthouse, G. P. Moss and K. D. Sales, *Ann. Rept. Sect. B, Org. Chem.* **75**, 23 (1978); [c]O. Ermer, *Aspekte von Kraftfeldrechnugen.* Wolfgang Baur Verlag, München (1981); [d]E. Ōsawa, and H. Musso, *Top. Stereochem.* **13**, 117 (1982).

[4a] N. L. Allinger, *J. Am. Chem. Soc.* **99**, 8127 (1977); [b]N. L. Allinger and Y. H. Yuh, *Quantum Chemistry Program Exchange* **13**, 395 (1981).

[5a] M. G. Newton, N. S. Pantaleo, S. Kirbawy and N. L. Allinger, *J. Am. Chem. Soc.* **100**, 2176 (1978); [b]T. Clark, T. McO. Knox, M. A. McKervey, H. Mackle and J. J. Rooney, *Ibid.* **101**, 2404 (1979); [c]D. W. Rogers. O. A. Dagdagan and N. L. Allinger, *Ibid.* **101**, 671 (1979); [d]E. Ōsawa, K. Aigami and Y. Inamoto, *J. Chem. Soc.* Perkin Trans. II. 172 (1979); [E]E. Ōsawa, *J. Am. Chem. Soc.* **101**, 5523 (1979): [f]E. Ōsawa, A. Furusaki, N. Hashiba, T. Matsumoto, V. Singh, Y. Tahara, E. Wiskott, M. Farcasiu, T. Iizuka, N. Tanaka, T. Kan and P. v. R. Schleyer, *J. Org. Chem.* **45**, 2985 (1980); [g]R. Huisgen, P. H. J. Ooms, M. Mingen and N. L. Allinger, *J. Am. Chem. Soc.* **102**, 3951 (1980); [h]N. L. Allinger, Y. Yuh and J. T. Sprague, *J. Comput. Chem.* **1**, 30 (1980); [i]N. L. Allinger, B. Gorden and S. Profeta, Jr., *Tetrahedron* **36**, 859 (1980); [j]C. Rüchardt and H.-D. Beckhaus, *Angew. Chem.* Int. Ed. Engl. **19**, 429 (1980); [k]T. Philip, R. L. Cook, T. B. Malloy, Jr., N. L. Allinger, S. Chang and Y. Yuh, *J. Am. Chem. Soc.* **103**, 2151 (1981); [l]L. Dosen-Micovic, D. Jeremic and N. L. Allinger, *Tetrahedron* **37**, 3455 (1981); [m]J. C. Tai and N. L. Allinger, *Ibid.* **37**, 2755 (1981); [n]E. Ōsawa, Y. Onuki and K. Mislow, *J. Am. Chem. Soc.* **103**, 7475 (1981); [o]K. Hirao, Y. Kajikawa, O. Yonemitsu and E. Ōsawa, *Heterocycles* **17**, 63 (1982); [p]U. Burkert and N. L. Allinger, *J. Comput. Chem.* **3**, 40

(1982); [d]E. Ōsawa, Y. Tahara, A. Togashi, T. Iizuka, N. Tanaka, T. Kan, D. Farcasiu, G. J. Kent, E. M. Engler and P. v. R. Schleyer, *J. Org. Chem.* **47**, 1923 (1982); [e]H.-B. Bürgi, W. D. Hounshell, R. B. Nachbar, Jr. and K. Mislow, *J. Am. Chem. Soc.* in press; [f]A. Guenzi, C. A. Johnson, F. Cozzi and K. Mislow, *Ibid.* in press; [g]R. B. Nachbar, Jr., W. D. Hounshell, V. A. Naman, O. Wennerström, A. Guenzi and K. Mislow, *J. Org. Chem.* in press; [h]R. B. Nachbar, Jr., C. A. Johnson, and K. Mislow, *J. Am. Chem. Soc.* in press; [i]S. Profeta, Jr., P. A. Kollman and M. E. Wolff, *Ibid.* **104**, 3745 (1982).

[6a] S. Profeta, Jr. and N. L. Allinger, *J. Comput. Chem.* in press; [b]H. Dodziuk, H. v. Voithenberg and N. L. Allinger, *Tetrahedron* in press. [c]J. C. Tai, *J. Comput. Chem.* **2**, 161 (1981); [d]A. Y. Meyer, *Ibid.* **1**, 111 (1980); [e]N. L. Allinger, U. Burkert and S. Profeta, Jr. *Ibid.* **1**, 281 (1980); [f]A. Y. Meyer, N. L. Allinger and Y. Yuh, *Israel J. Chem.* **20**, 57 (1980); [g]N. L. Allinger, S. H.-M. Chang, D. H. Glaser and H. Hönig, *Ibid.* **20**, 51 (1980); [h]J. T. Sprague and N. L. Allinger, *J. Comput. Chem.* **1**, 257 (1980).

[7] E. Ōsawa and H. Musso, *Angew. Chem. Int. Ed. Eng.* **22**, 1 (1983).

[8] E. Ōsawa, H. Shirahama and T. Matsumoto, *J. Am. Chem. Soc.* **101**, 4824 (1979).

[9] S. Scheiner, *Ibid.* **102**, 3723 (1980).

[10] N. L. Allinger and S. Profeta, Jr., *J. Comput. Chem.* **1**, 181 (1980).

[11] D. A. C. Compton, S. Montero and W. F. Murphy, *J. Phys. Chem.* **84**, 3587 (1980).

[12] A program package IMSPAK by K. Morokuma, S. Kato, K. Kitaura, I. Omine, S. Sakai and S. Obara, was used.

[13] A. Komornicki, K. Ishida, K. Morokuma, R. Ditchfield and M. Conrad, *Chem. Phys. Lett.* **45**, 595 (1977).

[14] All previous calculation of this fundamental molecule assumed C_{2h} and C_{2v} point group for *anti* and *syn* conformations, respectively.[10] We avoided the oversymmetrization by imposing lower symmetry of C_2 to these conformers, intending to simulate the torsional process more naturally.[15] Although the effect of such reduced constraints proved minimal for n-butane, they should certainly be more evident in large and branched molecules.[8] Under this relaxed constrain, the highest point at the *anti-gauche* barrier occurred when the C–C–C–C dihedral angle reaches 119°. The calculated dihedral angle of *gauche* conformer (64.5°) is smaller than any previous *ab initio* results,[10] and closest to the latest experimental value of 62°. Both the stretch of central C–C bond (0.025 Å) and the opening of C–C–C angle (3.8°) in going from *anti* to *syn* conformer turned out to be less pronounced than in the previous calculations.[9] For other recent but more or less simple *ab initio* calculations of n-butane: [a]J. A. Darsely and B. K. Rao, *Macromol.* **14**, 1575 (1981); [b]M. R. Peterson and I. G. Csizmadia, *J. Am. Chem. Soc.* **100**, 6911 (1978).

[15] W. D. Hounshell, D. A. Dougherty and K. Mislow, *Ibid.* **100**, 3149 (1978).

[16a] D. N. J. White and M. J. Bovill, *J. Mol. Struct.* **33**, 273 (1976); [b]*J. Chem. Soc.* Perkin Trans. II, 1610 (1977).

[17] N. L. Allinger, M. T. Tribble, M. A. Miller and D. H. Wertz, *J. Am. Chem. Soc.* **93**, 1637 (1971).

[18] P. D. Bartlett, A. J. Blakeney, M. Kimura and W. H. Watson, *Ibid.* **102**, 1383 (1980).

[19] G. G. Christoph, P. Engel, R. Usha, D. W. Balogh and L. A. Paquette, *Ibid.* **104**. 784 (1982).

[20] O. Ermer, *Angew. Chem.* **89**, 833 (1977); *Ibid.* Int. Ed. Engl. **16**, 798 (1977).

[21] M. J. Bovill, P. J. Cox, H. P. Flitman, M. H. P. Guy, A. D. U. Hardy, P. H. McCabe, M. A. Macdonald, G. A. Sim and D. N. J. White, *Acta Cryst.* **B35**, 669 (1979).

[22] G. A. Sim, *Ibid.* **B35**, 2455 (1979).

[23] P. H. McCabe and G. A. Sim, *Ibid.* **B37**, 1943 (1981).

[24] O. Ermer, J. D. Dunitz and I. Bernal, *Ibid.* **B29**, 2278 (1973).

[25] E. M. Engler, J. D. Andose and P. v. R. Schleyer, *J. Am. Chem. Soc.* **95**, 8005 (1973).

[26] Methylcyclohexane and 1,1-dimethylcyclohexane were excluded because of the doubt on the reported[27,28] C–C bond lengths (1.527 and 1.533 Å). The same research group had reported abnormally short C–C bond length of 1.528 Å of cyclohexane[27] which was later found wrong.[29] Compounds adopted for our calibration are ethane, propane, isobutane, neopentane, hexamethylethane, tri-t-butylmethane, cyclobutane, cyclopentane, cyclohexane, bicyclo[2.2.0]hexane, *trans*- and *cis*-decalin, bicyclo[3.1.1]heptane, norbornane, bicyclo[2.2.2]octane, *anti*- and *syn*-tricyclo[4.2.0.0^{2,5}]octane, [4.4.4]propellane, adamantane, diamantane and 1,1′-diadamantane. Some of the standard structural parameters used by Allinger and Schleyer are replaced by more recent experimental values: r(CC_m) of neopentane, 1.534 Å, L. S. Bartell and W. F. Bradford, *J. Mol. Struct.* **37**, 113 (1977); r(C_qC_q) of hexamethylethane, 1.582 Å, L. S. Bartell and T. L. Boates, *Ibid.* **32**, 379 (1976); r(CC) of cyclobutane, 1.548 Å, A. Alemenningen, O. Bastiansen and P. N. Skancke, *Acta Chem. Scand.* **15**, 711 (1961); CCCC pucker angle of cyclobutane, 35°, quoted in A. C. Legon, *Chem. Revs.* **80**, 231 (1980); r(CC) of cyclopentane, 1.546 Å, W. J. Adams, H. J. Geise and L. S. Bartell, *J. Am. Chem. Soc.* **92**, 5013 (1970); r(CC) of cyclohexane, 1.536 Å, Ref. 29; r(C_1C_2) of norbornane, 1.536 Å, Ref. 5*a*.

[27] H. J. Geise, H. R. Buys and F. C. Mijlhoff, *J. Mol. Struct.* **9**, 447 (1971).

[28] H. J. Geise, F. C. Mijlhoff and C. Altona, *Ibid.* 13, 211 (1972).

[29] O. Bastiansen, L. Fernholt, H. M. Seip, H. Kambara and K. Kuchitsu, *Ibid.* **18**, 163 (1973).

[30] A Table comparing experimental, MM2 and MM2′ structural parameters of the standard set is available from the authors upon request.

[31a] N. L. Allinger, M. A. Miller, F. A. Van-Catledge and J. A. Hirsch, *J. Am. Chem. Soc.* **89**, 4345 (1967); [b]N. L. Allinger, J. A. Hirsch, M. A. Miller, I. J. Tyminski and F. A. Van-Catledge, *Ibid.* **90**, 1179 (1968). [c]D. H. Wertz and N. L. Allinger, *Tetrahedron* **35**, 3 (1979).

[32] N. Norman and H. Mathisen, *Acta Chem. Scand.* **15**, 1755 (1961).

[33] The use of adamantanoid structures to model diamond was suggested by Professor N. L. Allinger, private communication.

[34] D. A. Dougherty and K. Mislow, *J. Am. Chem. Soc.* **101**, 1401 (1979).

[35] Methane, experimental ΔH_f −17.89 kcal mol^{-1}, was not included in the list since its C atom type is not defined in MM2 (neither primary, secondary, tertiary nor quaternary).

[36] D. F. DeTar, *Computers & Chem.* **1**, 35 (1976).

[37] D. W. Rogers, L. S. Choi, R. S. Girellini, T. J. Holmes and N. L. Allinger, *J. Phys. Chem.* **84**, 1810 (1980).

[38] R. H. Boyd, S. N. Sanwal, S. Shary-Tehrany and D. McNally, *Ibid.* **75**, 1264 (1971).

[39] S. S. Wong and E. F. Westrum, Jr., *J. Am. Chem. Soc.* **93**, 5317 (1971).

[40] E. Ōsawa, G. Szalontai and A. Tsurumoto, *J. Chem. Soc.* Perkin Trans II, in press.

[41] For example, the largest error occurred with bicyclo[2.2.2]octane. Despite two independent and close experimental heats of formation reported for this compound (−23.75[38] and −23.67[39] kcal mol^{-1}), not only the modified MM2 but also previous major force fields[4a,25] never calculated this molecule correctly. Redetermination of this important molecule[42] appears desirable.

[42] P. v. R. Schleyer, J. E. Williams and K. R. Blanchard, *J. Am. Chem. Soc.* **92**, 2377 (1970).

[43] Inclusion of all 50 molecules in Table 7 gave a standard deviation of 1.01 kcal mol^{-1}.

[44] H. Booth, and J. R. Everett, *J. Chem. Soc.* Chem. Commun. 278 (1976).

[45] E. Ōsawa, *J. Comput. Chem.* **3**, 400 (1982).

[46] B. van de Graaf, J. M. A. Baas and H. A. Widya, *Recl. Trav. Chim. Pays-Bas* **100**, 59 (1981).

[47] H. Werner, G. Mann, M. Mühlstädt and H.-J. Köhler, *Tetrahedron Letters* 3563 (1970).

[48] One fourth of the whole area of Fig. 1 is unique and contains 76 data points, each point representing relaxation calculation with two constrained dihedral angles. For technical details of surface drawing see Ref. 45.

[49] J. Dale, *Stereochemistry and Conformational Analysis*, p. 147, Verlag Chemie, New York (1978).

[50] Because of Me groups, the "C_2" transition state of **10** may not

necessarily have four atoms in exactly coplanar positions. The present version of our modified MM2 lacks the facility for halting the geometry optimization at the saddle point and does not allow us to evaluate exact structure of "C_2" conformer. However we give here approximate values of ring and Me–Me dihedral angles for "C_2" transition state: C_1–C_2–C_3–C_4 = −3°, C_2–C_3–C_4–C_5 = −10°, C_3–C_4–C_5–C_6 = −18°, C_4–C_5–C_6–C_1 = 56°, C_5–C_6–C_1–C_2 = −70°, C_6–C_1–C_2–C_3 = 43°, Me–C_1–C_2–Me = 41°, Me–C_2–C_3–Me = −19°, Me–C_3–C_4–Me = 7°, Me–C_4–C_5–Me = −23°, Me–C_5–C_6–Me = 63°, and Me–C_6–C_1–Me = −73°. In the case of "C_s"1 transition state corresponding values are: 16°, −30°, 29°, −15°, 4°, −4°, −40°, 50°, −56°, 56°, 50°, and 40°. Similarly, "C_s"2 transition state has the following values: −24°, 50°, −50°, 25°, 3°, −4°, 30°, −40°, 66°, −65°, 39°, and −29°. C_1–C_2–C_3–Me dihedral angle is −177° in "C_s"1 and −76° in "C_s"2.

[51] Calculated structural parameters of chair conformation of **10** agree well with those obtained by X-ray analysis.[52] For example, endocyclic C–C–C–C dihedral angle: calc. ±52.3°, obs. ±53.2°; Axial methyl . . . methyl nonbonded distance: calc. 3.47 Å, obs. 3.42 Å. For MM2 results see Ref. 52.

[52] H. van Koningsveld, J. M. A. Baas, B. van de Graaf and M. A. Hoefnagel, *Cryst. Struct. Commun.* **11**, 1065 (1982).

[53] In contrast, van der Graaf and others[46] emphasize the possible inadequacy in the van der Waals parameters of MM2.

[54] A torsional energy surface of cyclohexane was similarly prepared using MM2′. A chair-chair interconversion barrier of 11.7 kcal mol^{-1} thus obtained compares well with the observed barrier of 12.1 ± 0.5 kcal mol^{-1} by B. D. Ross and N. S. True, *J. Am. Chem. Soc.* **105**, 1382 (1983).

[55] C. Jaime, E. Ōsawa, Y. Takeuchi and P. Camps, submitted for publication to *J. Org. Chem.*

[56] The tendency of MM2 to underestimate rotational barriers has also been noted recently by other workers. [a] H.-D. Beckhaus, C. Rüchardt and J. E. Anderson, *Tetrahedron* **38**, 2299 (1982). [b] V. Sackwild and W. G. Richards, *J. Molec. Struct.* **89**, 269 (1982).

[57] Neutron diffraction analysis of **1** at low temperature gave the closest intramolecular nonbonded H . . . H distance of 1.713(3) Å: O. Ermer and S. A. Mason, *J. Chem. Soc.* Chem. Commun. 53 (1983). This result confirms Watson's interpretation[8] and is close to the MM2′ result.