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Molecular Mechanics. The MM3 Force Field for Hydrocarbons. 1

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Abstract: A new molecular mechanics force field (called MM3) for the treatment of aliphatic hydrocarbons has been developed and is presented here. This force field will enable one to calculate the structures and energies, including heats of formation, conformational energies, and rotational barriers, for hydrocarbons more accurately than was possible with earlier force fields. In addition to simple molecules, a great many highly strained molecules have been studied, and the results are almost always of experimental accuracy.

Over the last 20 years or so, molecular mechanics[1-3] has developed into a standard powerful method for studying molecular structure and related properties. When the MM2 force field was first formulated during the 1976–1977 period,[3,4] all of the heat of formation data and all of the structural data available to the author that appeared to be pertinent for alkanes were utilized in specifying the parameters in this force field. The experimental values were, on the whole, fit very well. However, it proved to be impossible at that time to fit vibrational frequencies well, and simultaneously to fit structures and heats of formation. Accordingly, we decided to let the vibrational frequencies come out as necessary in order to fit the other data as well as possible. It was found that the bending force constants utilized in spectroscopic valence force fields ordinarily had to be reduced by a factor of about 0.6 in order to fit properly the structural and energy data. (The reduction of the magnitude of the bending force *parameters* relative to the bending force *constants* has been discussed,[3] and for MM2 this factor should be larger, perhaps about 0.9, to fit vibrational spectra.)

Since that time, a large amount of additional experimental data pertinent to the problem have become available. Additionally, we eventually found that the reason we could not fit the vibrational frequency data and the other information simultaneously was because the force field used was too simple. By adding a few more parameters, we find that, in fact, we can simultaneously fit all of these things reasonably well.

We considered a revision of MM2 to take this above-described information into account. However, the revision required would be quite extensive. Accordingly, we have decided to go back to the beginning, and derive an entirely new force field, which we will call MM3. Since MM2 worked well for most purposes, MM3 is similar to it for the most part. However, it differs in several

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(4) The MM2 force field for hydrocarbons was described in ref 3a. Extensions to functionalized molecules have been described in subsequent papers, summarized in ref 3b. The original program (MM2(77)) is available from the Quantum Chemistry Program Exchange, University of Indiana, Bloomington, IN 47405, Program 395. The latest version of MM2, referred to as MM2(87), is available to academic users from QCPE, and to commercial users from Molecular Design Limited, 2132 Farallon Dr., San Leandro, CA 94577. The MM3 program is still under development, but it is intended to make it available shortly from Technical Utilization Corp., Inc., 235 Glen Village Court, Powell, OH 43065, and from Molecular Design Limited. The input format for MM3 for hydrocarbons is identical with that of MM2, so that the same input files may be used for both, except for cyclobutanes, where the atom type number of the carbon was changed from 1 to 56.

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ways; most are minor, but a few are major.

In this paper we will fully explain the types of information used to develop the force field, and we will specify the parameters and equations obtained. All of the significant errors in MM2 as they pertain to this class of compounds, insofar as they are now known to the present authors, have been examined, and most of these will be discussed in detail. Most of the known errors present in MM2 are reduced to insignificance in MM3. Those few which remain are at least reduced by a factor of 2 or more from what they were in MM2.

In 1987 we published a list of known or claimed deficiencies in MM2, which included references to 25 items or papers.[5] Of this list, some constitute specific difficulties and appear to be minor, while some others have been corrected already in later versions of MM2. But some of them describe significant systematic errors which really require substantial correction. In other cases, the error, or some of it, is apparent rather than real and results from things like comparisons between calculated values for ΔH with experimental values for ΔG when ΔS is, in fact, nonzero. We have examined all of these errors and alleged errors, but will discuss here only the ones which seem to be real, and which occur with hydrocarbons. These include (a) the underestimation of high C–C rotational barriers in congested hydrocarbons.[6,7] It was stated[6a] that MM2 barriers are on the average about 40% too low in congested molecules. Such an error could be corrected by increasing the V_3 term, and Osawa has recommended this.[7] However, much of this apparent error in the rotational barriers comes from the comparison of an experimental value for $\Delta G^\ddagger$ with a calculated value for $\Delta H^\ddagger$, on the rather poor assumption that $\Delta S^\ddagger$ is zero for these rotations. In fact, with MM3 we have calculated values for $\Delta S^\ddagger$, and we find that it is definitely not zero,[8] and it becomes, apart from symmetry, increasingly negative with increasing congestion. About half of the apparent error comes from this erroneous assumption, not from an incorrect calculation by MM2. Thus the correction used by Osawa,[7] in fact, over-corrects and gives an error in $\Delta H^\ddagger$ almost as large as was present in MM2 originally, but now of the opposite sign. Additionally, heats of formation are poorly calculated with Osawa's correction, with errors up to 4 kcal/mol. (The MM3 barriers average about 6.4% too low comparing calculated and experimental values for $\Delta G^\ddagger$.)

(b) Next, close H/H nonbonded repulsions have been found to be too strong when one gets to very short distances (less than about 2.0 Å).[9] We believe that this error is real, and it is based on data which were not available at the time MM2 was developed. This error requires a change in van der Waals' parameters from the MM2 values to correct it; this is discussed below and in an accompanying paper.[10]

(c) Bonds which are eclipsed, or nearly so, are calculated to be too short in MM2. This already shows up in ethane, where the eclipsed form has a bond length that is longer than the staggered form by only 0.003 Å. Ab initio calculations indicate that this value should be much larger.[11] Norbornane has been studied in considerable detail.[12,13] It has been found that the longest bonds in the molecule are the 2,3 and 5,6 bonds, but this is not correctly calculated by MM2, where these bonds are of only average length. Other five-membered rings, in which bonds are more or less eclipsed, have the bond lengths calculated systematically too short with MM2 by approximately 0.010 Å. This error has been overcome in MM3 utilizing a torsion–stretch interaction.[12]

(d) Of the several other items mentioned by Lipkowitz,[5] one item can be mentioned here, although it has to do with aromatic rather than aliphatic hydrocarbons. This is the crystal packing in benzene including the stability of the perpendicular benzene dimer. These were not calculated correctly by MM2, but Pettersson and Liljefors have indicated[14] how the introduction of charges on aromatic carbons and hydrogens, following earlier studies by Williams,[15] can be used to correct this. In MM3, we have used the bond dipole moment, rather than the point charge, approximation, and given a similar correction. The procedure as employed in MM3 was described earlier.[16]

(e) Another item of importance concerns the bending function. Clearly the quadratic term is the leading term, and this accounts for most of the structural information we want to fit to. However, for large deformations one expects a cubic term to be important, and possibly even higher terms. In the past, we and many others have tried to fit data on small ring compounds by using these higher bending terms. However, for the three-membered ring, it is clear that the bonding is quite different from that in a distorted propane bond angle, and one needs to describe the cyclopropane bond angle as something which is totally different.[17] There is also a difference in principle between a bond angle in cyclobutane and in an open-chain alkane.[3] For cyclopentane, it is not a priori clear whether the bond angle can be treated as a distorted alkane, or whether it needs to be something different. One of the conclusions of this work is that it is better to treat it as something different.[19] In MM2, cyclopentane was treated as an ordinary deformed alkane. In MM3, we have decided to give cyclopentane rings their own parameters, separate from those of alkanes. Of course, most of the parameters are quite similar or even identical with those in alkanes. However, if one requires that all of the parameters be identical with those in alkanes, then one has difficulties in fitting simultaneously the heats of formation, structures, and vibrational spectra for five-membered rings. Our conclusion is that a better model treats these five-membered ring parameters as different from the open chains. We, as everyone before, use the six-membered ring parameters and higher membered ring parameters to be the same as in open chains. The rationale for why cyclopentane parameters are different from open-chain alkanes is that, in a butane segment, the ends are taken to be independent of one another except for torsional and van der Waals' forces. In cyclopentane, the ends of a butane unit are certainly less independent, being bonded to a common atom. They therefore have a different and more direct interaction, in addition to the long-range one present in butane. Whatever the rationale, the model which gives cyclopentane its own parameters is superior to the model which insists upon using alkane parameters for cyclopentane, and we have therefore used this extra group of parameters in the present work. This is, of course, disadvantageous, because it means that one must deduce separate parameters for three-membered rings, for four-membered rings, for five-membered rings, and for open chains. This has been done for hydrocarbons in this work. However, every time one has a heteroatom substitution into a ring, one will again have this whole new set of parameters that will have to be deduced. Nonetheless, we feel that this amount of parameterization is the necessary minimum to fit adequately all of the things that we wish to fit.

There are other significant deficiencies in MM2, but they

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pertain to functionalized molecules and will be addressed in separate publications.[21]

The Force Field

The force field derived will be presented first, and then the details of the derivation will follow. The equations that describe the force field are similar to those in MM2, but there are some changes.

Bond Stretching. The quadratic term is adequate to describe bond stretching in all but a few cases; for those, the addition of a cubic term is sufficient to take care of all of the structural calculations. However, it was noted with the early version of MM2 that the cubic term causes the energy function to turn over and go to minus infinity as the atoms separate. If one uses a fairly poor starting geometry, where bonds are stretched beyond the energy maximum, then the molecule flies apart. This was fixed in different ways in various versions of MM2, but clearly a better fix is to simply add a quartic term, so that the energy goes up to plus infinity rather than down to minus infinity. Thus, if the starting geometry is poor, one will still end up automatically at the proper place. Knowing the value for the quadratic and cubic constants, one can derive the quartic constant needed to best represent a Morse potential; that value was used[22] in eq 1.

$$E_s = 71.94k_s(l - l_0)^2[1 - 2.55(l - l_0) + (7/12)2.55(l - l_0)^2] \tag{1}$$

Angle Bending. When the aliphatic C–C–C bond is bent to a smaller angle, the quadratic approximation seems to be adequate for most cases. However, with four-membered rings, the bending is clearly too severe for the ordinary bending constant and a quadratic formulation, from the approximately tetrahedral angle, to be used. Since different parameters are needed for four-membered rings, one cannot use them to get information on the cubic bending constant for open chains. However, some information on this point is available from a comparison of cyclobutane with the compound bicyclo[1.1.1]pentane, where the secondary carbon has a bond angle of approximately 74°.[23] In the former the bending is sufficient to bring the cubic constant into play relative to cyclobutane. One would also like to fit the heat of formation of these compounds, and these pieces of information narrow considerably the range in which the cubic bending constant must lie. There is a problem here, because the key compound is highly strained, and therefore may not be well-described the force field. Hence, while we might fit the experiment, the results may not really be as good as they look. And, in fact, there really is no experimental value for the heat of formation, but there is an ab initio value,[24] which we take to be equivalent.

On the other hand, if a secondary bond angle is opened from the tetrahedral value to some much larger value, then we have some measure of the cubic constant on the other side of the deformation, and there are several compounds that are helpful here. We also used up to a sextic constant in our preliminary optimizations. The higher constants were used to obtain the best fit to the available data, but they are not very well determined. It was considered important that they yield a monotonic function up to 180° so that no artifactual minima are introduced. The function arrived at is

$$E_\theta = 0.021914(k_\theta)(\theta - \theta_0)^2[1 - 0.014(\theta - \theta_0) + 5.6(10^{-5}) \times (\theta - \theta_0)^2 - 7.0(10^{-7})(\theta - \theta_0)^3 + 9.0(10^{-10})(\theta - \theta_0)^4] \tag{2}$$

In MM2 we had used only the quadratic and the sixth power terms, the latter having been chosen to fit the geometry of bicyclo[1.1.1]pentane. While this equation fit the data available to us at that time, with more and better data now available it is clearly not the best formulation. In MM2, part of the reason for the low values of the bending constants seems to have stemmed from the fact that the cubic term was omitted, which would have had the same effect at large bendings in the angle opening direction. It is clear that the MM3 formulation is a better representation than that used in MM2 for both small and large bendings.

Torsion. As with MM2, we use a three-term Fourier series expansion (eq 3) to represent torsional energy, where the torsional

$$E_\omega = (V_1/2)(1 + \cos\omega) + (V_2/2)(1 - \cos 2\omega) + (V_3/2)(1 + \cos 3\omega) \tag{3}$$

angles are calculated between all pairs of atoms that have a 1–4 relationship. The importance of the V_1 and V_2 terms in alkanes has been well documented.[2,3]

Stretch–Bend Interaction. As with MM2 and other force fields[3,25,26] this interaction (eq 4) has been used so as to allow bonds

$$E_{s\theta} = 2.51118K_{s\theta}[(l - l_0) + (l' - l'_0)](\theta - \theta_0) \tag{4}$$

to stretch out somewhat when the angle between them is reduced, and to shrink when that angle is increased, analogous to the effect of a Urey–Bradley term in that type of force field.[2,27] This effect is similar in MM3 to what it was in MM2. The extra stretching needed in special cases has been brought about partly with the torsion–stretch interaction, and partly by the separate adjustment of the l_0 values in four- and five-membered rings. As with MM2, this interaction is counted only when the bond being stretched and the angle being bent are centered at the same atom.

Torsion–Stretch Interaction. Bond lengths in MM2 did not stretch sufficiently upon eclipsing. Thus, for example, the 2–3 bond in norbornane, which is experimentally the longest bond in the molecule,[13] was of only average length according to MM2. Many other examples have been discussed previously.[12,13] With this torsion–stretch interaction (eq 5) added, a much better fit

$$E_{\omega s} = 11.995(K_{\omega s}/2)(l - l_0)(1 + \cos 3\omega) \tag{5}$$

to molecular geometries when bonds are other than perfectly staggered is obtained.

It might be thought that the stretch–bend interaction can be used to take care of the 2–3 bond stretching in norbornane,[25,26] but this is not the case. The 2–3 bond is definitely much longer in norbornane than the 1–7 bond, and if this stretching is brought about only with the aid of a stretch–bend interaction, the 1–7 bond length always stretches more than the 2–3 bond length does.

Torsion–Bend Interaction. This interaction has been used previously to bring about bending of cyclobutane rings.[25] However, it also caused excessive bending in five-membered rings. We accordingly revised the interactions in MM2, in which case it turned out that the torsion–bend interaction was not needed, nor has it been used in MM3. Actually, a small torsion–bend interaction might be desirable to reproduce certain observed features. In the ethane molecule, for example, the C–C bond does not stretch enough without the appropriate interaction terms, and the C–C–H angles do not open enough when the molecule eclipses. The C–C stretching has been taken into account with the torsion–stretch interaction, and the torsion–bend interaction could similarly account for the bending upon eclipsing. However, the effect is not very large,[11] and we have decided to ignore it and have left out this interaction in MM3.

Bend–Bend Interactions. Spectroscopic studies[8] indicate that bending vibrations which involve two angles centered on the same atom give calculated frequencies which are too close together if this type of interaction term is omitted. By including this interaction, these frequencies can be split apart to match better with

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experimental vibrational spectra. We have chosen only generic type constants here, where the angles either involve two carbons (or other heavy atoms) attached to the central carbon, or one carbon and one hydrogen, or two hydrogens. The equation is as given by

$$E_{\theta\theta'} = -0.021914K_{\theta\theta'}(\theta - \theta_0)(\theta' - \theta'_0) \qquad (6)$$

van der Waals' Interactions. At the time MM2 was developed, the closest approach between two hydrogens which has been experimentally measured accurately occurred in cyclodecane, and the distance between them was 1.942 Å (our estimated probable error in this value is 0.053 Å; see later under cyclodecane). MM2 fit this value marginally well, calculating 2.000 Å. More recently, three hydrocarbon structures have become available in which there are even closer approaches of hydrogen atoms. There is also one chlorinated hydrocarbon in which there is a still closer approach. The two most useful compounds for our purposes were studied by Ermer,[9] by neutron diffraction at low temperatures, and hence the positions of the hydrogens relative to one another are quite accurately known. These two compounds have the structures I and II shown later. They are derivatives of *exo,exo*-tetracyclo-$[6.2.1.1^{3,6}.0^{2,7}]$dodecane. The distance between the closest hydrogens opposing each other on the one-carbon bridges are respectively 1.748 and 1.698 Å (probable errors 0.010 Å), whereas the MM2 values calculated are 1.890 and 1.837 Å, which are clearly much too large.

We decided in view of the above that a softer van der Waals' function would be desirable, and hence reduced the exponent in the MM2 formulation from 12.5 to 12.0, as:

$$E_{\text{vdw}} = \epsilon\{-2.25(r_v/r)^6 + 1.84(10)^5 \exp[-12.00(r/r_v)]\} \qquad (7)$$

This formulation gives us only two adjustable parameters, the sum of the van der Waals' radii (r_v), and the ϵ value, or energy parameter, for the interaction between two atoms. Because MM2 worked as well as it did, we know that the values there are close to being correct, and we started from that point. We noticed that the MM2 values gave heats of sublimation for normal alkanes which were too large. This indicated that we had either to make the van der Waals' radii or the ϵ values smaller for either the hydrogens or the carbons, or some combination. From studies on graphite,[10] we were able to establish the proper parameters for aromatic carbon. We felt that the parameters for aliphatic carbon must be similar to aromatic carbon, but they did not need to be identical. We also wanted to fit the positions of the close hydrogens in compounds I and II acceptably well, and so we made some more minor adjustments in the van der Waals' parameters of carbon and hydrogen.

We recognized the above problem years ago, when Ermer's data[9] on compounds I and II were published. We did not, however, feel that an ad hoc correction of the van der Waals' parameters in MM2 was desirable, because while they could have been changed (softened) in order to accomodate Ermer's data, everything else in the force field is dependent on those parameters. If they are changed, then one would really need to go back and optimize the whole force field again; that is to say, one would need to develop a completely new force field. Otherwise, the changes brought about in unexpected places by the van der Waals' changes may do more harm than good.

After the adjustments described, it was clear that we could fit the data for Ermer's compounds and still fit the cyclodecane structure as well as previously (in fact, somewhat better than with MM2), and in addition fit acceptably well (better than MM2) the crystal packing and heats of sublimation of a number of aliphatic hydrocarbons.[10] We also fit to aromatic hydrocarbons at the same time, so that we could study compounds which contained both aromatic and aliphatic portions to make sure the balance was correct; studies on graphite have been previously mentioned.

We also examined the other two compounds which have very close hydrogens, namely, secododecahedrane (III),[12] and the chlorinated birdcage compound (IV) studied by Ermer and Anet,[28,29] which is a derivative of pentacyclo-$[6.2.1.1^{3,6}.0^{2,7}.0^{4,10}]$dodecane (V). These compounds are less useful for our purposes, the former because it was studied only by X-ray crystallography and the hydrogens were not accurately located, and the latter, which is somewhat beyond the scope of the present MM3 hydrocarbon work, because of the presence of the chlorines. The preliminary calculations that we carried out did indicate that reasonable structures for these compounds were obtained using MM3.

Electrostatics. We assumed with MM2 that a neutral molecule could have its charge distribution represented by a set of bond dipoles. Others have used point charges on atoms rather than point dipoles in bonds to represent molecular electrostatics, and from everything we know at this point, the two approximations are overall nearly equivalent.[3,123] We have not seen any convincing information that indicates that one approximation is in general conspicuously better than that other. Accordingly, we have decided to use the same approximation in MM3. However, we do wish to study molecules which contain net charges, as in proteins, and hence we have added to the program the capability for calculating not only dipole–dipole and charge–charge interactions, but also charge–dipole interactions, which must be included in this approach.[30] But for saturated hydrocarbons, as will be discussed here, these things are not pertinent.

Next comes the question: should we have bond dipoles for C–H bonds or for C–C bonds? It is certainly true that aliphatic hydrocarbons have quite small dipole moments, which can be taken as zero for our present purposes. But it is generally considered that the hydrogen has a small charge relative to a carbon.[31] The definition of quantum mechanical charge is less than straightforward, however, and it is not clear that charges in alkanes are needed in molecular mechanics. Our philosophy is therefore as previously; namely, we will take these bond dipoles to be zero unless it is convincingly shown that a nonzero value must be used to obtain desired results. In the case of benzene, it is clear that one must have charges on the hydrogens and carbons if one is to reproduce the crystal structure, the stability of the perpendicular benzene dimer, and related facts.[14,16] The magnitude of the C–H bond moment required here was not well determined but had to be equal to at least 0.6 D, above which value one obtains the qualitatively proper results. This is close to the value deduced independently by earlier workers[15] and so has been incorporated into the MM3 program.[16] But for aliphatic C–H bonds, we still see no evidence indicating that a nonzero dipole moment is necessary.[31,32] Accordingly, we have assigned a zero bond moment to the aliphatic C–H bond. The aliphatic C–C bonds in purely aliphatic hydrocarbons do not have a dipole moment in the MM3 approximation. (Bond moments need not be zero between C_{sp^2}–C_{sp^3}, etc., and are not in MM2 and MM3). Strictly, the C_{sp^3}–C_{sp^3} bond could have a bond moment if the two carbons are not identical, one primary and one secondary, for example, but we assume such values can be taken as zero to an acceptable approximation.

Rotational Barriers. In principle, one only needs to fix values for the parameters V_1, V_2, and V_3 for any given four atom linkage A–B–C–D, and then rotational barriers should be properly calculated. Note that one cannot simply transfer these constants from ab initio calculations, from spectroscopy, or from other places. One has to actually fit the experimental (or ab initio) potential curve, and the values for these constants required in molecular mechanics will not be the same as those given by the methods mentioned. The reason for this is that in molecular mechanics the van der Waals' energies also change as a function of the angular rotation, and one wants to match the total energy, not

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(30) We are indebted to Dr. J. Ponder for a copy of his subroutine for the charge–dipole interaction calculation.

(31) Wiberg, K. B.; Bader, R. F. W.; Lau, C. D. H. *J. Am. Chem. Soc.* **1987**, *109*, 1001.

(32) Charges are necessary if one wishes to calculate infrared intensities, but they are not needed in the present context, and the infrared problem will be dealt with separately.

just the part which is due to the torsional equation (eq 3).

The problem here is less than straightforward, however. In principle, one can fit the H–C–C–H V_3 constant from the known ethane barrier, the H–C–C–C constant from the neopentane barrier, and the C–C–C–C constant from the butane barrier. The results may then be checked against experimental and ab initio barriers in other molecules, or one might use some kind of weighted procedure to determine the torsional parameters from a larger amount of data. There are several problems that have to be faced. In spectroscopic measurements, the formalism usually applied does not allow for the fact that the molecule is relaxing in other internal coordinates as the rotation occurs, and therefore the spectroscopic barrier is higher than the barrier that would be calculated by molecular mechanics. Barriers observed by some methods, such as NMR, are typically determined between vibrational levels, not between the equilibrium points at the botom and the top of the barrier, and this introduces some discrepancy. Trivially, but most importantly, one must be careful about comparing values for the enthalpy, which are usually calculated, with those for the free energy, which is often observed experimentally and which may be quite different.

Specifically, we have fit ethane on the low side (experimental barrier 2.88 kcal/mol, MM3 barrier 2.41 kcal/mol. We have to fit the barrier on the low side in order to obtain a reasonably accurate value for the torsional frequency, which is calculated with the harmonic approximation. If we calculate a larger value for the barrier, the torsional frequency will also become larger, as will quantities which depend upon this frequency, such as the entropy. For neopentane, we have also chosen to calculate a somewhat low value (3.35 kcal/mol versus 4.2–4.8 kcal/mol).

The rotational barrier of butane has been a subject of much discussion, particularly the cis or 0° barrier, relative to the trans conformation. The MM2 value for this barrier was 4.7 kcal/mol for $\Delta H^{\ddagger}{}_{298}$, in agreement with the experimental (spectroscopic) value[33] of 4.6 kcal/mol for ΔE. More recent ab initio calculations have determined this energy as 5.8–6.0[34] or 6.3[35] kcal/mol for $\Delta H^{\ddagger}{}_0$, in apparently poor agreement with experiment. Our objective with MM3 is not to fit the butane value as accurately as possible, but rather to obtain a general parameter set which will fit alkane data in general as accurately as possible. These data include, in particular, the rotational barriers in congested molecules and the heats of formation of compounds which contain partly or completely eclipsed bonds, such as the twist–boat form of cyclohexane, medium-ring cycloalkanes, and bicyclo[2.2.2]octane. When the fitting is optimized over all of the available data which we have examined,[8,10] the MM3 value for the butane barrier obtained is 4.8 kcal/mol. There is some arbitrariness here, because the result obtained is dependent on the weighting scheme which is used and the particular data to which it is applied. If one chooses to weight different experiments in different ways, this value of 4.8 kcal/mol might reasonably be raised or lowered by 0.2 kcal/mol or possibly, at the outside, by 0.3 kcal/mol. However, it does not seem possible with any reasonable weighting to get a number which is very near the ab initio values (discrepancy –0.6 to –1.8 kcal/mol). One must, of course, ask why. The reason now appears to be that the basis sets used by earlier workers were too small. With a larger basis (triple ζ + 2 sets of d functions on carbon, and p functions on hydrogen), the barrier calculated[36] is quite a bit lower, 5.22 kcal/mol for $\Delta H^{\ddagger}{}_0$, or 4.89 for $\Delta H^{\ddagger}{}_{298}$.

Parametrization

The above formulation gives our force field for aliphatic hydrocarbons. It was then necessary to determine the parameters that go into the force field. This was done beginning with the necessary bending and stretching parameters, taking them to be equal to the spectroscopic force constants, and then calculating many known structures to obtain values for l_0, θ_0, etc. Having then good geometries for the molecules, the vibrational spectra were examined, and the force parameters were further adjusted so as to fit these within the limits discussed earlier.[8] Small further modifications of the structural parameters were then made to refine the calculated values for these data as well as possible. Simultaneously, heats of formation,[8] crystal structures,[10] and van der Waals' parameters were examined. The parameter set arrived at is given in Table I.

Table I. Parameter Set for Saturated Hydrocarbons[a,b]

(A) Bond Lengths and Stretching Parameters

bond	l_0	K_s
C–C	1.5247	4.49
C–H	1.112	4.74

(B) Angle Bending

atoms	K_θ	θ_0[c] type 1	θ_0[c] type 2	θ_0[c] type 3
C–C–C	0.67	109.5	110.2	111.0
C–C–H	0.59	109.8	109.3	110.7
H–C–H	0.55	107.6	107.8	109.5
Five-Membered Ring				
C–C–C	0.67	109.5	109.9	111.0
Four-Membered Ring				
C–C–C	0.192			111.0
	0.230	109.5	109.9	

(C) Torsional Parameters

atom types	V_1	V_2	V_3
C–C–C–C	0.185	0.170	0.520
C–C–C–H	0	0	0.280
H–C–C–H	0	0	0.238
Five-Membered Ring			
C–C–C–C	0.185	0.170	1.160
Four-Membered Ring			
C–C–C–C	0	0	2.300

(D) Stretch–Bend

bond	K_{sb}
C–C–C	0.13
C–C–H	0.08
H–C–H	0.00
Five-Membered Ring	
C–C–C	0.13
Four-Membered Ring	
C–C–C	0.05

(E) Torsion–Stretch

bond	$K_{\omega s}$
C–C	0.059

(F) Bend–Bend[a]

angle	$K_{\theta\theta}$
C–C–C	0.24
C–C–H	0.30
H–C–H	0.00

(G) van der Waals' Parameters

element	atom type	ϵ	R_{VDW}	at. wt
C	1	0.027	2.04	12.000
H	5	0.020	1.62	1.008

[a] Cyclopropanes will be reported on separately.[17] [b] Bond lengths in Å, angles in degrees; stretching, bending, and torsion parameters are in mdyne/Å, mdyne Å/rad^2, and kcal/mol, respectively. [c] There are three types of θ_0, 1, 2, and 3, where the central atom of the atom considered is bound to zero, one, or two hydrogens (or deuteriums), respectively, apart from the atoms that make up the angle considered. [d] The value of $K_{\theta\theta'}$ in eq 5 is the product of the two constants $K_{\theta\theta}$ in the table as appropriate for the angles involved.

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The parametrization can be broken into four parts for discussion. One part involves the internal structures of molecules, and the second part involves the heats of formation of these compounds. The third part involves the vibrational spectra of the molecules,[8] and the last part involves the interactions of molecules with each other.[10] First we will examine the structures that were utilized in the parameterization and the accuracy of the results that were obtained, and then we will discuss heats of formation. The other items will be discussed in the following papers.[8,10]

Bond Lengths. For "ordinary" hydrocarbons, these were calculated quite well with MM2. We intended to use r_g values in MM2, insofar as they were available, but the data available at the time (1976–1977) were somewhat sketchy, and r_a, r_α, r_s, r_z, etc., values were, in fact, often used, sometimes without correction. Building a force field from data of this accuracy limits the accuracy of the results that will be obtainable with the force field. Now, more and better bond lengths are available and have been used. MM3 is explicitly based on r_g values, and in cases where any other kind of value had to be used in the parameterization, it was corrected to the corresponding r_g value if possible.[37] Values which could not be so corrected were given low weight in the parameterization. Bond lengths which were well calculated with MM2 are also well calculated with MM3. Some, which suffer from special problems such as eclipsing, and were not very well calculated with MM2, are also well calculated with MM3.

Bond angles and torsion angles are generally of the r_α type, in accord with usual current conventions. We made considerable use of moments of inertia in specifying structures, and experimentally these are of the r_α type, and generally not directly compatible with our r_g structures. Rather than try to make corrections here, we simply note that the correction of a moment of inertia from an r_g to an r_α basis will generally cause the value to be reduced by an amount between 0 and 1%. Accordingly, if our calculated moments of inertia are higher than the experimental ones by amounts in that range, we regard the agreement with experiment as acceptable.

Structural Results

The organization of the following material presents in order the results for alkanes, from simple to highly congested, followed by cycloalkanes, then the substituted cycloalkanes. Next come the bicyclic and polycyclic structures, and finally a few compounds which are not strictly aliphatic hydrocarbons, but which had to be examined in connection with the hydrocarbon calculations. These are molecules which contain an ether linkage, a phenyl group, chlorine atoms, or other kinds of substitutions. The results of the hydrocarbon calculations depend to some extent on assumptions made regarding these other types of atoms. However, these substituted molecules present better, usually more severe, examples of deformations than are available in alkanes themselves, and hence need to be used here. Next, cyclobutane structures are gathered together and discussed as a unit, since they require parameterization which is separate from, and in addition to, that required for other molecules. Finally, heats of formation will be discussed.

In the interest of brevity, without sacrificing the thoroughness of the discussion, quite a few molecules have been studied in detail, but will be discussed only in the supplementary material that accompanies this manuscript. The molecules so listed are pentamethylethane (2,2,3-trimethylbutane), di-*tert*-butylmethane, tri-*tert*-butylmethane, 2,2,4,4,5,5,7,7-octamethyloctane, 5,6-di-*n*-butyl-5,6-diphenylethane, cycloheptane, cyclododecane, 1,2-dimethylcyclohexane, 1,1,3,5-tetramethylcyclohexane, decalin, perhydrophenanthrenes, pentacyclo[6.2.1.1^{3,6}.0^{2,7}.0^{4,10}]dodecane and various derivatives, [4.4.4]propellane, (*i*,*o*)-bicyclo[6.2.2]-dodec-11-ene 2,3-anhydride, 2,3-diadamantyl-2,3-dimethylbutane, ditriptycyl ether, and 1,4,7-cyclononatriene.

Methane. The calculated bond lengths are 1.112 Å, compared with 1.113 for MM2 and 1.107 (1) from electron diffraction.[38] The calculated value is thus too large by 0.005 Å, but slightly improved from MM2.

Ethane. The bond length is calculated to be 1.531 Å in the staggered conformation, and 1.544 when eclipsed (δl, 0.013) compared with the corresponding values of 1.532, 1.535, and 0.003 for MM2. The longer eclipsed bond with MM3 is mainly a result of the torsion–stretch interaction. Corresponding C–C–H angular values are 111.4 and 111.5 ($\delta\theta$, 0.1) compared with MM2 values of 111.0 and 111.5 (0.5). The rotational barrier is 2.41 kcal/mol, compared with 2.73 in MM2 and 2.88 experimentally.[39] When the experimental torsional frequency[40] from which the barrier was determined is compared with the calculated frequency, the values are 279 and 283 cm^{-1}, respectively, so the barrier height is actually well calculated by this criterion. The experimental[41] bond length is 1.534 (1) Å, and the angle is 111.0 (2)°. The calculated C–H bond lengths are 1.113 (MM3), 1.115 (MM2), and 1.112 (1) Å by electron diffraction.[41] Veillard[11] calculated Δ values of 0.019 Å and 0.3°, so our MM3 values are less than his in each case. Since our values are r_g for bond lengths, and r_α for angles, while his are r_e, they need not be exactly the same.

Propane. The MM3 values are 1.534 Å and 112.4° for the C–C bond length and C–C–C bond angle, respectively. The secondary C–H bond length is longer than the primary, with values of 1.115 and 1.113 Å, and the secondary H–C–H angle is 106.7°. The corresponding MM2 values are 1.534, 111.7, 1.117, and 107.3. The experimental values[42] are of limited accuracy, with C–C–C 112 (1)°, and an average C–H length of 1.107 (5) Å. The increase in the C–C–C angle (by 0.7°) is noteworthy in MM3 compared with MM2. A larger value was derived here earlier with MM2, but was not feasible because cyclopentane could not be adequately fit with such a value and the limited number of parameters employed.

***n*-Butane.** For the MM3 values of the anti conformation, bond lengths are 1.534 and 1.536 Å (weighted average 1.534), and the angle is 112.4°. The bond lengths are the same, and the angle is more open by 0.6°, compared with MM2. The gauche conformation has bond lengths of 1.535 and 1.538 Å (average 1.536), and an angle of 113.7°. It has an energy 0.81 kcal/mol above that of the anti form, and dihedral angle is 64.5°. The closest approach of the hydrogens on the methyls is 2.351 Å. The bond lengths here again are the same, and the angle is larger by 0.4° than with MM2. MM2 gave a dihedral angle of 65.3° and a relative energy of 0.86 kcal/mol. The calculated barriers for the two eclipsed conformations are now 3.30 and 4.83 kcal/mol, compared with the MM2 values of 3.34 and 4.73. The value at 0° is in accord with the spectroscopic value of Compton and co-workers (4.56)[33] and with the most recent ab initio value (4.89).[36] Bartell's most recent values[43] for the observed conformational mixture were 1.531 (2) Å and 113.3 (4)°, with a ΔE of 0.75 ± 0.25 kcal/mol and a gauche dihedral angle of 71 (5)°. Our overall averages are in agreement with experiment.

***n*-Pentane.** In the anti–anti conformation, the bonds on the methyl ends are calculated to be the same length as, and those for the central locations slightly longer than, for *n*-butane. The angles at the ends are also essentially the same, while that in the center is slightly larger. Since pentane also has several gauche conformations available to it, these were examined, and they have longer bonds and larger bond angles. For the anti conformation, the numbers are 1.534, 1.537 Å and 112.4, 112.5°. For the anti–gauche conformation, the corresponding values are 1.534,

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1.537, 1.538, and 1.535 Å and 112.3, 113.8, 113.8°, and the energy is 0.86 kcal/mol. The double gauche conformations have (++) 1.534, 1.538, 113.8, 115.3 (energy 1.62 kcal), and (+−) 1.535, 1.541, 1.540, 1.534, 115.1, 116.2, 115.2, (3.51 kcal). The latter structure is close to having C_s symmetry, with dihedral angles of −77.9 and +76.0°. The weighted overall averages are 1.536 Å and 113.1° for bond lengths and angles, respectively. Clearly the average bond lengths and angles increase slightly as we go from butane (1.534, 112.4) to pentane and will continue to increase as we go to larger molecules, partly because the number of shorter end groups becomes a proportionately smaller fraction of the molecule, and partly because gauche conformations generally have longer bonds and larger angles than anti conformations; there are more different gauche conformations possible, and hence a higher percentage of them as larger molecules are considered. Note the energy relationships. Whereas a single gauche conformation is slightly more costly in pentane than in butane (0.86 versus 0.81 kcal), the double gauche (++) is noticeably less than twice that value in energy (1.62 versus 1.72), while, of course, the (+−) conformation has quite a high energy.

Interesting comparisons can be made between the details of the ab initio results[44] and the molecular mechanics calculations. If we compare nonane as an example, the bonds get longer toward the center of the molecule, and the angles get bigger, by both calculations. The only discrepancy seems to be with the hydrogen on the methyl group which lies on the symmetry plane, which is bent back toward the next carbon in the MM3 calculations, but out away from it in the ab initio calculations. The wagging deformations of the methylene groups on the carbons next to the methyl group are notable. The 1–2–H angles are 109.25° while the 3–2–H angles are 109.56°. The effect persists but is diminished at the next carbon (2–3–H 109.33°, 4–3–H 109.39°) and is gone by the time C-4 is reached (3–4–H, 5–4–H 109.38°).

Bartell's study on *n*-hexadecane[45] gives an average bond length of 1.542 (4) Å, and an average angle of 114.6 (6)°, with a ΔG of 0.28 ± 0.35 kcal/unit, which corresponds to a ΔH of 0.86 kcal/mol. From butane and pentane, our values extrapolated to longer chain lengths will tend toward his experimental values, but probably will not quite reach them. The electron diffraction measurements[45] were carried out at a higher temperature (150 °C), which would contribute additionally to these increases by increasing the amounts of gauche conformations present.

Branched Chains. Isobutane. The MM3 values are 1.538 Å, 110.4°, and the tertiary C–H bond length is 1.118 Å. The corresponding values for MM2 were 1.537, 110.6, and 1.119. The experimental values[46] are 1.535 (1), 110.8 (2), and 1.112 (6).

2,3-Dimethylbutane. The symmetrical (C_{2h}) conformation is more stable (ΔH) than the C_2 conformation by 0.38 kcal/mol (MM3), compared with 0.15 kcal/mol in MM2. The electron diffraction work[47] shows a mixture which is 40% trans, which yields a ΔH of 0.17 kcal/mol favoring trans in the gas phase. Since the gauche form has more gauche interactions, it should have a smaller molecular volume, and the solution pressure[48] is expected to stabilize the double-gauche form by about 0.1 kcal/mol in the liquid phase,[49] where the experimental value is 0.0 ± 0.2 kcal/mol. The height of the smaller rotational barrier has a calculated energy ($\Delta H^{\ddagger}$) of 4.18 kcal/mol, compared with 3.07 in MM2, and 4.3 (2) experimentally.[49] [Entropy cannot contribute much to the observed rotational barrier ($\Delta G^{\ddagger}$) here, because the coalescence temperature is very low (see the following paper[8]).] So the height of the rotational barrier, which was definitely too small with MM2, is here correctly calculated. The larger barrier (experimentally unknown) has a calculated height of 6.92 kcal/mol. The reported ab initio value[49] was obtained without geometry optimization and is not regarded as accurate.

The electron diffraction work contained some assumptions that are not consistent with the MM3 calculations. For example, it is assumed that the central bond in the gauche isomer is 0.002 Å longer than that for the trans, whereas we calculate that it is, in fact, shorter by 0.001 Å. The average C–C length calculated by MM3 is 1.543 Å, compared with an experimental value of 1.540 (2).

Neopentane. The MM3 values are 1.541 Å for C–C, 111.7° for the C–C–H angle, and 1.113 Å for the C–H bond length. (The MM2 values were 1.541, 111.3, and 1.114.) For the eclipsed form, the corresponding MM3 numbers are (Δ values) 1.557 (0.016), 112.0 (0.3), and 1.112 (−0.001). The barrier is now calculated to be 3.35 kcal/mol, compared with 3.77 by MM2. The experimental value is not very certain, being given as between 4.2 and 4.8.[50] These values assume rigid rotation, so the calculated value needs to be much smaller. The most recent electron diffraction structure[51] gives the following: 1.537 (3), 112 (3), and 1.114 (8). Bowen has carried out ab initio calculations and found that the bond-length increase upon eclipsing and the barrier height are as follows: 4-31G 0.0182 Å, 4.23 kcal/mol; 6-21G 0.0207 Å, 4.39 kcal/mol.[52] The effects of including larger basis sets, correlation energy, and thermal corrections here are unknown.

It would seem that we calculate a C–C bond length a bit (0.004) on the long side in neopentane, and a bit on the short side (0.002) in ethane, but approximately to within experimental error in each case. (A good test case is provided by the steroid 20-methyl-5-pregnene-3β,20-diol where there are many bonds which are various combinations of primary, secondary, and tertiary carbons: see below.) Our diamond bond length is 1.5431 Å [MM2, 1.5417; exptl, 1.5445 (1)]. Our biggest C–H bond-length error is in methane (0.005 Å). For C–C bonds, the MM3 values seem to be within 0.003 Å of the experimental values (after allowing for the experimental error; that value can be taken as a conservative estimate of our probable error at, say, the 90% confidence limit).

Congested Acyclic Molecules. 2,2,3,3-Tetramethylbutane (Hexamethylethane). This molecule has been studied in detail by calculations and by experimental methods. It has D_3 symmetry. MM3 gives bond lengths of 1.577 and 1.548 Å for the central bonds and the methyl groups, respectively. These give an average value of 1.552 Å (exptl[47] av 1.547 (2); MM2 1.548–1.572, av 1.551). The dihedral angles about the central bond are 66.6 (MM3), 75.0 (MM2), and 65 (5)° (Bartell). The interior bond angles are 111.7 (MM3), 112.1 (MM2), and 111.0 (3)° (Bartell). The rotational barrier has been a significant problem. The MM2 value is definitely too low ($\Delta H^{\ddagger}$ = 5.25 kcal/mol), compared with the somewhat uncertain experimental values ($\Delta G^{\ddagger}$ = 8.6–10.0[53]). The MM3 value is higher, $\Delta H^{\ddagger}$ = 8.1. The experimental value is a free energy and contains a significant contribution from the entropy. There is an R ln 2 contribution to the entropy of activation from symmetry, and there is quite a lot of restriction in the transition state in addition (see below and also the following paper[8]).

Cycloalkanes. Cyclopentane. We have previously discussed in detail our calculations on this molecule.[12] The agreement of the MM3 structures with experiment and with high quality ab initio calculations is very good.

Cyclohexane. The calculated geometry has C–C 1.536 Å, θ 111.3°, C–H 1.1145 (all), with H–C–H 106.7° and a dihedral angle of 55.3°. The MM2 values were 1.536, 110.9 (107.1), and

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56.4. The experimental values (electron diffraction, by Bastiansen and Kichitsu[58]) are 1.536 (2), 111.4 (2), 1.121 (4), 107.5 (20), and 54.9 (5).

The twist–boat form has a calculated energy 5.76 kcal/mol above that of the chair (MM3), 5.35 kcal/mol (MM2), and 5.2 (2) kcal/mol by experiment.[59] The classical boat (C_{2v}) has an MM3 energy 6.53 kcal above that of the chair. The transition-state energy is 10.82 kcal/mol above the chair in MM3 and 10.53 kcal/mol in the MM2 calculation. It has a C–C–C–C dihedral angle near planar, but actually 12.8°, on the boat side of planar. The experimental energy has been measured several times in different ways, and these are summarized by True.[60] Values for $\Delta H^{\ddagger}$ range from 10.2 to 11.5 kcal/mol and for $\Delta S^{\ddagger}$ 4.6 to 0.5 eu. In the gas phase, True gets $\Delta H^{\ddagger} = 12.1$ kcal/mol (5), $\Delta S^{\ddagger} = 5.7$ (5) eu, and $\Delta G^{\ddagger}$ 10.4 (2) kcal/mol. Our preference is to consider that the ground state has a symmetry number of 6, and the transition state has a symmetry number of 2, plus the latter is a *dl* mixture. This gives an entropy change of $R \ln 6$, which yields $T\Delta S^{\ddagger} = 0.90$ kcal/mol at 253 K. Accepting the experimental $\Delta G^{\ddagger}$ value of 10.4, this gives an experimental value of $\Delta H^{\ddagger} = 11.3$ kcal/mol for the gas phase. The MM3 value (10.8) is in agreement with this.

Cyclooctane Boat–Chair. The MM3 data give bond lengths of 1.539, 1.546, 1.539, and 1.536 Å. The corresponding angles are *117.3*, 114.9, 115.2, 117.1, and *116.5*°. These average out to 1.540 Å and 116.0°, with a C–H average of 1.115 Å. Average values of 1.540 (1), 116.8°, and 1.116 (2) are found by electron diffraction.[62] Since this compound is conformationally rather pure, the averages are well calculated. The C–C and C–C–C values for MM2 were 1.537 Å are 116.1°. The HCH angles from experiment, MM2 and MM3 are respectively 106.0 (1.1), 104.6, and 105.2°.

Cyclooctane also has two other conformations that are reasonably stable, D_2 and D_{4d}. The MM3 energies are respectively 1.12 and 1.42 kcal/mol above the C_s, while the MM2 values were lower, 0.97 and 1.16 kcal/mol. Anet[63] indicates that the amount of minor component is 0.3% of the equilibrium mixture at −123 °C. He concludes that the ΔH and ΔS from the boat–chair to the other observed conformation are respectively 1.9 ± 0.2 kcal/mol and 1 ± 1 eu. MM3 agrees poorly with the ΔH value assigned by Anet, and the value for ΔS has the wrong sign (since the D_2 conformation has a symmetry number of 4 and is a *dl* mixture, its expected entropy relative to the C_s form is −1.38 eu). The crown conformation (which is in the same NMR family as the D_2 conformation and would not be distinguished from it by NMR) is not a *dl* mixture, has a symmetry number of 8, and hence does not contribute much to the mixture. It has an entropy relative to the C_s form of −4.12 eu. However, both of these conformations have anharmonic pseudorotational motions, and it is not completely straightforward just what the entropy change, in fact, should be. The electron diffraction work[62] shows an undetectable amount of crown conformation at 59 °C (1 ± 3%). MM3 calculates 1.2% of D_2 at −123 °C and 7.0% at room temperature. The D_{4d} contributes 0.11 and 1.0%, respectively, giving a total from the crown family of 1.3 and 8.0%, while Anet's values are 0.3, and 6.3%.

Meiboom,[64] from nematic NMR experiments concludes that cyclooctane is boat–chair with a small amount of another conformation, and has C–C–C and HCH angles of 118 ± 2 and 103 ± 2°, respectively.

Cyclononane. The conformation of lowest enthalpy found experimentally[65] is D_3, but two C_2 conformations are more favorable in entropy, and one of them, in fact, should predominate slightly above room temperature. For the D_3 conformation, MM3 gives six bonds of length 1.541 Å, and three of 1.551 Å, for an average of 1.544. There are three angles 116.1°, and six have the value 114.5°, giving an average of 115.1°. The more stable of the C_2 conformations (225) is calculated to have an enthalpy 0.84 kcal above that of the D_3. At very low temperatures the D_3 conformation should predominate, but at high temperatures the $T\Delta S$ term will overwhelm the ΔH term, and the C_2 conformation will predominate. (The entropy disfavors the D_3 structure because of the high symmetry number (by $R \ln 6 - R \ln 2 = 2.19$ eu).) There is also a second C_2 conformation (144). This conformation has the same entropy as the (225) conformation, but the enthalpy is calculated to be 1.15 kcal/mol above the D_3. (This is in contrast to MM2, where the (144) conformation is only 0.02 kcal/mol above the (225).) We can thus calculate the percentage composition of mixtures of these conformations as a function of temperature. At 100 K, the MM3 percentages of (333), (225), and (144) are as follows: 94.9, 4.2, 0.9. At 298 K, the corresponding percentages are 46.4, 33.7, and 20.0. The numbers agree well with those observed by Anet at 100 K (95, 5, 0), and less well at room temperature (40, 50, 10).

The electron diffraction was carried out at 70 °C.[66] At that temperature, the mole fractions calculated by MM3 for the conformations were 0.39, 0.37, and 0.24, respectively, and the experimental values were 0.50, 0.49, and 0.01, each ±0.12. The overall average bond lengths and angles are calculated to be 1.543 Å and 115.8° at this temperature (experimental values not yet available).

Some of the characteristics of these different conformations are worthy of note. The relative strain energies here are of interest. The 333 conformation has a large torsional energy (9.9 kcal) and significant bending energy (3.1 kcal), relative to an unstrained system. The 225 conformation has less torsion (7.4 kcal) and much more bending (6.7 kcal) which explains its relative energy. The 144 conformation has higher bending than the 333 (3.5 kcal), and much higher torsion (11.7 kcal). However, its non-1,4 van der Waals' interaction energy is reduced (1.0) relative to the 333 isomer (2.3).

Cyclodecane. Some definite improvements have been forthcoming here relative to the MM2 calculation, and the results for this compound seem now acceptable. The most stable conformation is BCB (C_{2h}), as with MM2 and by crystallography[67] and electron diffraction.[68] The bond lengths calculated by MM3 for BCB average 1.543 Å, and the angles average 116.9°. Hilderbrandt and co-workers[68] found an average bond length of 1.545 (3) Å and an average angle of 116.1 (11)° by electron diffraction. They suggested that either of two situations were consistent with the experimental data. Either there was a single conformation with the physical parameters above, or there was a mixture of conformations which gave average values for the parameters as above.

There are a number of possible additional conformations for cyclodecane. We have carried out calculations on two of them, which have been found in earlier work to be reasonably stable.[68] With MM3 they are respectively 0.93 (C_2) and 2.20 (C_{2h}) kcal/mol above the stable conformation. Only the first of these contributes very much to the equilibrium mixture of cyclodecane conformations at or near room temperature. The electron dif-

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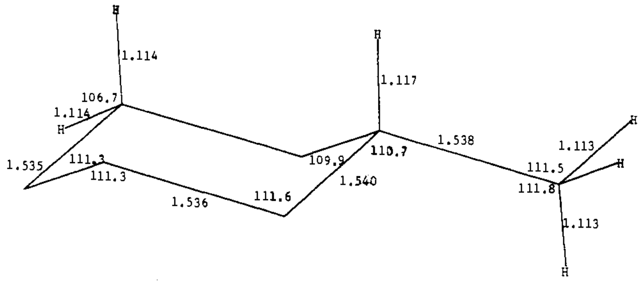
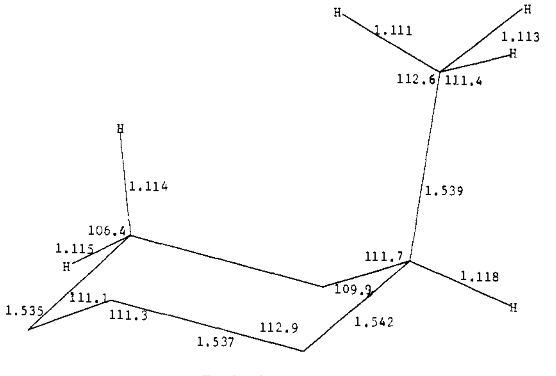
fraction study was carried out at 130 °C. The C_2 conformation has an entropy of $R \ln 2$ relative to the principal C_{2h} conformation. The value for $T\Delta S$ at 130 °C for the C_2 conformation from symmetry considerations is 0.55 kcal/mol, and hence the principal conformation is more stable (ΔG) than the C_2 conformation by only 0.28 kcal/mol at this temperature. The equilibrium mixture, excluding the minor components, is thus approximately 58% C_{2h} and 42% C_2. This appears to be consistent with the electron diffraction study, which put these percentages at 49 and 35% (with 16% of minor components). The MM3 C_2 conformation has an average C–C bond length of 1.454 Å and an average bond angle of 115.1°. The overall MM3 averages, over these two conformations, then are 1.544 Å and 116.1°, in perfect agreement with the electron diffraction values.

For MM3 the closest transannular H/H distance (in the BCB conformation) is 1.915 Å, compared with 2.00 Å in MM2, and an average experimental value[67] of 1.942 Å given by Dunitz and Ermer (neutron diffraction at room temperature). The H–C–H angle involving the crowded hydrogens is calculated to be 104.4° (MM3) and 103.2° (MM2), while the experimental value by Dunitz and Ermer is 105.7 (4)°. The X-ray values for the carbon–carbon bond lengths in this molecule (at room temperature) are systematically much too short, although the paper says thermal rigid-body corrections were applied (room-temperature data); details were not reported.

Substituted Rings. Methylcyclohexane. The conformational energy calculated by MM3 is 1.77 kcal/mol, compared with the MM2 value of 1.78 kcal/mol. Details of the geometry (MM3) are shown below (ab initio (4-21G) values corrected to r_g are given in parentheses).[71]





csc-Perhydroanthracene

The bond angle distortions are familiar and have been discussed previously.[3] Because of larger bending constants in MM3, the distortions are slightly smaller than with MM1 and MM2. The stretch–bend interaction tries to shrink the $-CH_3$ bond length axial versus equatorial, but it is longer in spite of this.

An electron diffraction study of methylcyclohexane has recently been reported.[72] The authors find an averge CC bond length of 1.536 (2) Å, and for CH 1.124 (4). The average values for C–C–C angles are 111.4 (5)° within the ring, and 112.1 (1.6)° exo to the ring. This information is limited because of the nature of the problem, but is in good agreement with our calculated values. Note the pinching of HC_3H in the axial conformation, relative to the equatorial, and other small distortions which occur in order to separate the axial methyl and the axial hydrogens at C_3 and C_5.

Table II. Relative Enthalpies of the Perhydroanthracenes (kcal/mol)

	$\Delta H_{exp}{}^{80}$	ΔH (1971)	MM3	MM3 – exp
tst	0	0	0	0
ct	2.76 (28)[a]	2.62	2.83	+0.07
tat	5.02[b] (81)	5.86	7.11	+2.09
cac	5.58 (28)	5.56	5.82	+0.24
csc	8.74 (61)	8.13	8.50[c]	–0.24

[a] The errors given are standard deviations. [b] The experimental value for ΔG is 5.02 kcal/mol at 544 °C. Using the theoretical value for ΔS (zero), ΔH is 5.02. The actual measured entropy change is -1.6 ± 1.5 eu, which would yield a ΔH of 4.15 ± 0.81 kcal/mol. [c] Will increase some when the boat conformation mixed in. If the contribution of the boat is the same as in 1971 (0.27 kcal), ΔH will be 8.77 kcal/mol.

***all-cis*-1,2,3,4,5,6-Hexamethylcyclohexane.** The crystal structure of this compound has been studied (low-temperature X-ray[74]), and one interesting feature is the distance between syn–axial carbons, which was measured to be 3.42 (2) Å. The MM2 value was 3.52 Å, noticeably too large. The MM3 value is 3.432 Å. Also of interest, the inversion barrier was measured experimentally ($\Delta G^{\ddagger}$) as 17.3 (1) kcal/mol,[75] while van de Graaf reported that $\Delta H^{\ddagger}$ here is only 11.6 kcal/mol with MM2.[76] But when the sizeable entropy was taken into account, the MM2 free energy barrier was 14.2 kcal/mol.[77] The MM3 value is 15.14 for $\Delta H^{\ddagger}$.

Also of interest are the bond lengths of the C–C bonds attached to the methyl groups in this molecule. The axial bonds might have been expected to be longer (MM3 calculates for methylcyclohexane 1.539 axial versus 1.538 equatorial). But here the axial bonds are calculated to be *shorter* (1.540 versus 1.541 for equatorial). The experimental values give 1.535 (1) ax. and 1.528 (2) eq. The ring C–C bonds are calculated, 1.552; experimental, 1.545 (3). Thus the agreement between MM3 and the low-temperature crystal data is not very good. The equatorial C–C bond lengths are calculated to be too long by 0.013 Å, the ring bonds are too long by 0.007 Å, and the axial bonds are too long by 0.005 Å. Approximate corrections for the experimental values to r_g, and for rigid-body thermal motion would reduce the discrepancies to 1 esd or less except for the axial methyl which still has a calculated bond length 0.009 Å too long. Part of this error may

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(77) The rotational barriers reported by Anderson are uniformly much larger than those calculated by MM2. But note that his barriers are determined by low-temperature NMR, and refer to values of $\Delta G^{\ddagger}$, whereas MM2 calculates values for $\Delta H^{\ddagger}$. The somewhat hopeful assumption has previously been made that the two are comparable. Certainly, in cyclohexane, where line-shape measurements have resolved the value of $\Delta G^{\ddagger}$ into values for $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, and where the latter can be calculated just from symmetry, the difference between $\Delta G^{\ddagger}$ and $\Delta H^{\ddagger}$ is small and as expected. However, when we compare all *cis*-hexamethylcyclohexane, not only do we anticipate that $\Delta G^{\ddagger}$ and $\Delta H^{\ddagger}$ will not be equal, but van de Graaf has calculated (ref 76) the values of $\Delta S^{\ddagger}$ with several force fields. Apart from symmetry considerations, the calculated entropy of activation is negative by several eu. This is because the methyl groups interfere with one another more seriously in the transition state, which raises their torsional energy levels. (The methyl torsions have very low frequencies that contribute a great deal to the entropy.) A similar effect should occur in most of the congested molecules studied by Anderson for the same reason. Namely, the restriction of the vibrational motion of the side chains (especially methyl groups) in the transition states. Using the MM3 data, the $T\Delta S^{\ddagger}$ (including symmetry) contribution to the barrier is +0.96 kcal/mol in hexamethylcyclohexane (ref 8). Similar corrections up to about 1 kcal/mol (increasing with increasing congestion, but quite symmetry dependent) are found for compounds which are as crowded as 2,2,3-trimethylbutane up to the octamethyloctane.

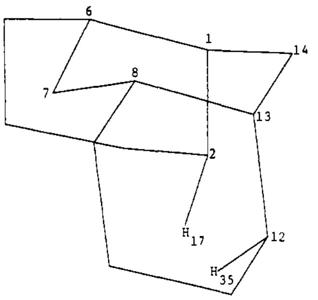
be due to neglect of the crystal packing forces.

Polycyclic Systems. Bicyclo[3.3.0]octane. The boat–chair is the preferred conformation (C_s) and seems unexceptional. The trans isomer has quite a high energy, largely due to the very open external C–C–C angle between the rings (125.3°), but is otherwise rather ordinary.

Bicyclo[2.2.2]octane. The heat of formation of this molecule has long been difficult to fit,[3,7] but the MM3 calculated value is in good agreement with the ab initio value (see later), and the geometry now looks good. The MM3 bond lengths are 1.550 (secondary), and 1.540 (tertiary), for an average value of 1.543 Å. The geometry has D_{3h} symmetry. The corresponding MM2 bond lengths and dihedral angle were 1.539, 1.540, and 11.7° (the MM2 structure had D_3 symmetry). Electron diffraction[78] has given an average C–C value of 1.543 Å, with the secondary and tertiary values being respectively 1.552 (29) and 1.538 (15). So our average values agree, and we can specify much better than the experiment can just what the individual values are. The large (0.010 Å) increase in the secondary bond length in MM3 relative to MM2 is mainly from the torsion–stretch interaction. The secondary and tertiary hydrogens have C–H bond lengths of 1.114 and 1.116 Å, respectively.

Perhydroanthracenes. There are five stereoisomers of perhydroanthracene, and the equilibrium between them has been studied as a function of temperature in the presence of palladium catalyst. The trans–syn–trans isomer is the most stable, having all of the rings in chair forms and all substituents (one ring with respect to another) in equatorial positions. Other isomers have higher energies, both by calculation and by experiment (Table II). The cis–trans and cis–anti–cis conformations are unexceptional, and their energies are calculated quite well. The unusual conformations are the trans–anti–trans (tat), in which the central ring is necessarily in a twist–boat conformation, and the cis–syn–cis (csc) conformation, in which there is a severe 1,3-syn-diaxial interaction. We find that the MM3 calculations reproduce the experimental energies less well in the case of the first of these strained conformations than did MM2. The tat conformation has a calculated heat of formation that is 2.09 kcal/mol too high. The energy calculated for the csc isomer, on the other hand, agrees with experiment.

For the latter, a crystal structure is now available,[81] and we can compare the MM3 calculations, the MM2 calculations, and experiment. Anet[82] has compared the MM2 calculations, the experiment, and calculations by several other force fields, and we can add here the MM3 results. The experimental structure is shown, and the important MM2 and MM3 results are also shown. The most notable distortions are the bond angle 1–14–13, and the distance between carbon atoms 2 and 12. Note that in the MM2 structure the repulsion between these carbons (and/or the attached hydrogens) is too strong, and the calculated distance is too great by 0.129 Å. In MM3, the repulsion between the hydrogens is considerably less, and the carbon–carbon distance is reduced considerably, but it is still larger than the experimental value by 0.068 Å. The angle 1–14–13 was calculated to be too large by 0.8° with MM2, and it is 1.2° too large with MM3. It is possible that this angle is reduced slightly in the crystal by a squashing motion due to lattice forces. A crystal packing calculation is needed here to ascertain if that is the cause of the discrepancy.



DIST./ANGLE	EXPER	MM2	MM3
2/12	3.396	3.525	3.464
17/35	-	2.025	1.906
1-14-13	116.1	116.9	117.3

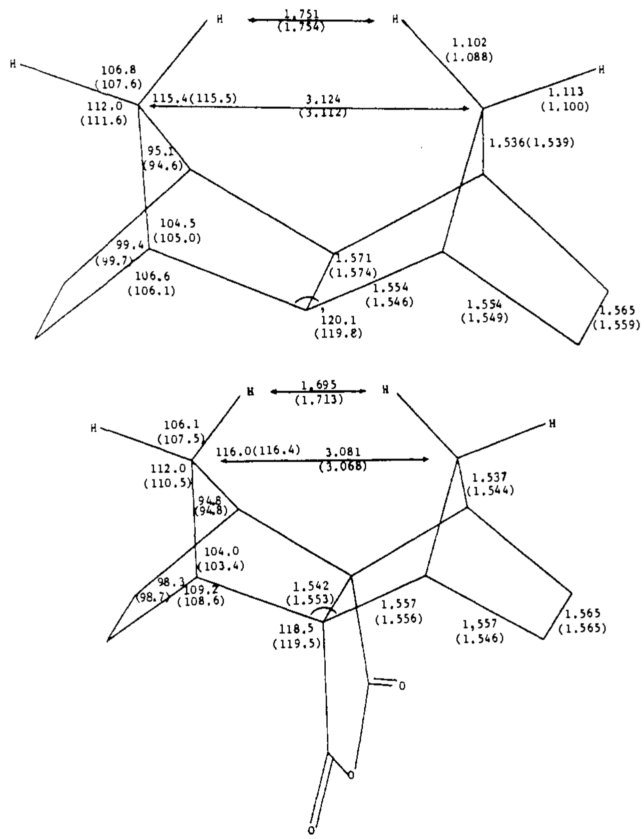


Figure 2. Structures of *exo*,*exo*-tetracyclo[6.2.1.1.$1^{3,6}$.$0^{2,7}$]dodecane (**I**) and the anhydride derivative (II).

Norbornane. The geometry of this molecule has been studied in detail, and the results were published previously. The calculated and experimental values are in good agreement.[12]

Bicyclo[3.3.1]nonane. The close H/H distance on the "bottom side" of the molecule is much relaxed in MM3 and is now calculated to be 1.922 versus 2.02 Å in MM2. The location of the hydrogens experimentally is unknown. However, the corresponding close carbons have a distance of 3.127 Å in MM3 (compared with an average value of 3.12 for various substituted compounds by crystallography,[84] and by electron diffraction,[85] whereas the MM2 value was a definitely large 3.18. The distorted bridgehead angles also become somewhat more nearly tetrahedral in MM3, in better agreement with the electron diffraction work. The bridgehead C–C–C angle on the underside is 114.3° now, versus 115.1° in MM2 and 111.9° experimentally. The peak (bridge) angle is given experimentally as 110.1 (23)°, while the MM2 and MM3 values are respectively 108.1 and 109.8°.

Adamantane. The C–C bond length is calculated to be 1.540 Å in MM3, compared to an experimental value of 1.540 (2)(r_a).[86] The calculated C–H bond lengths are 1.114 (s) and 1.116 (t), respectively, and experimental 1.112 (4) (av).

Dodecahedrane. This molecule and also some derivatives of it have been key compounds in this work and have been discussed in a previous publication in detail.[12]

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***exo*,*exo*-Tetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodecane (I).** This compound is especially interesting because of the close C/C and H/H distances, but the exact details of the distortion are of further interest. The structures of the hydrocarbon and of the corresponding anhydride derivative (II) are shown in Figure 2, along with the average experimental values (in parentheses). The H/H distance calculated by MM3 is 1.751 Å, shorter by 0.139 Å than the MM2 value of 1.890 Å. The experimental value[9] is 1.754 Å. Since the latter shows a small esd and was determined at low temperature, the probable error in this value, allowing for distortions from the lattice forces, is estimated to be 0.010 Å. For the tetracyclododecane anhydride derivative, the MM3 and MM2 values are 1.695 and 1.837 Å, respectively. The experimental[9] number 1.713 Å (estimated probable error, 0.010 Å) is somewhat larger (0.016 Å) than the MM3 value. On the other hand, the peak carbon atoms in each of these compounds are calculated to be somewhat too far apart in MM3, although much less so than in MM2. In MM3 the value for I is 3.124, compared with 3.209 (MM2) and 3.112 (experiment). With the anhydride (II), MM3 gives 3.081 which is 0.013 Å greater than the experimental value (3.068 Å). The MM2 value was 3.158. Our estimated probable errors in these carbon–carbon distances are 0.007 Å, so the MM3 values agree fairly well with experiment. Comparisons between the MM3 and experimental structures are shown. Note that the bridge angles calculated are close to the X-ray values. MM3 and (experiment) give for the hydrocarbon 95.1° (94.6°) and for the anhydride 94.8° (94.8°). These MM3 values are larger than the X-ray values by only 0.5 and 0.0°; they suggest that for norbornane itself, the discrepancy (1.9° ED, 1.0° X-ray) is likely to be more of an error in the experiment than in the calculation.

In tetracyclododecane, the "inside" hydrogens undergoing the extreme compressions have shorter MM3 C–H bond lengths (1.102) than their counterparts on the "outside" (1.113). This is mainly in response to the compression. The difference in bond lengths calculated is 0.011 Å in the hydrocarbon and 0.013 Å in the anhydride derivative. Our values (r_g) are systematically longer than those measured by neutron diffraction (r_α) as expected, but the *difference* in the diffraction values is the same as ours (0.012 Å, with the inside one being shorter).

In cyclodecane, a qualitatively similar observation is made. Here again, the inside C–H bond is shorter (1.106 versus 1.115). Both the compression and the stretch–bend interactions assist in this differential shortening. Note that the calculated bond lengths are somewhat longer in cyclodecane than in the norbornane derivative (0.002–0.004 Å). This difference is mainly a result of the stretch–bend interaction. (The average C–C–H angle is much larger in the norbornane derivative, owing to the ring constraints, which has an overall shortening effect on the C–H bonds.) Dunitz states that the neutron diffraction work on cyclodecane gives 1.081 Å as the average value for the intrannular C–H distances (r_α), uncorrected for thermal motion, while the mean value of the remaining C–H distances is 1.097 Å, with a resulting shortening of 0.016 Å (the standard deviations are 0.006 Å in each bond). His bond lengths are again systematically shorter than ours, and the errors are large, but the trend is unmistakeable.

It would appear that the C–H values determined by neutron diffraction crystallography (approximately r_α) are systematically shorter, relative to r_g values, as expected. The difference in two C–H bond lengths determined in the same experiment or calculation is an important quantity, but to relate the bond lengths from two different experiments or calculations frequently requires the use of corrections which are inexact, and which are large compared to the quantities being studied.

The current situation on molecules in which there are very close H/H approaches can be summarized as follows. At the time MM2 was developed, the only molecule of this group for which there were data was a cyclodecane derivative. The calculated distance was somewhat too great, although within experimental error of the observed value. Subsequently, two derivatives of tetracyclododecane were studied experimentally, and they provide independent measurements of similar, but different, and much closer H/H approaches than that observed for cyclodecane. While the cyclodecane number calculated was within experimental error, the values calculated for tetracyclododecane with MM2 are not within experimental error. The MM2 values here are too large by approximately 0.14 Å where the experimental errors are the order of 0.01 Å. Since the experimental numbers were determined at low temperatures by neutron diffraction, they are very good numbers. To reasonably fit these numbers, the cyclodecane distance now becomes a little too short, although within experimental error. We can now fit with MM3 all of these close H/H distances to approximately within experimental error, and we think the improvement in short H/H distances given by MM3 relative to MM2 is considerable. (The error in the case of the chlorinated birdcage compound was larger, 0.19 Å with MM2. With the MM3 preliminary calculations there is still an error, of about 0.01 Å, but until oxygen and chlorine have their parameters finalized, the exact error here cannot be assessed. In any case this is an order of magnitude improvement.) As a checkpoint, the distances between very close C/C interactions can also be examined. Molecules in which these occur which have been well studied are in the bicyclo[3.3.1]nonane system, the two norbornane dimers mentioned, secododecahedrane, and hexamethylcyclohexane. In each case except secododecahedrane, the C/C distance was calculated to be too large with MM2, and with MM3 this error has been reduced to a small value. (The MM2 value was good for secododecahedrane and remains good with MM3.[12])

Wiberg and Murcko have recently discussed the van der Waals' functions used by current and recent force fields, and that which can be derived from theoretical work on interactions between hydrogen molecules.[87] The hydrogen–hydrogen curve which they derive as the best anisotropic curve is labeled as D in his Figure 2. The MM2 curve is on the whole similar to D. Although somewhat lower in the range 3 – 2.2 Å, at 2.2 Å it crosses the D curve, but thereafter it rises much more steeply than the D curve at shorter distances and deviates markedly from the latter below 2.0 Å. Interestingly, the MM3 curve, which had been finalized long before Wiberg's work became available to us, is very slightly above the MM2 curve in the range 3.0–2.3 Å, and from 2.3 Å it approximately parallels, and stays very slightly below the D curve down to a distance of 2.0 Å, the limit of Wiberg's plot. (Actually, this is down to 1.83 Å when foreshortening is allowed for.) Since Wiberg's curve is for a hydrogen bound to hydrogen, it need not be exactly the same as a hydrogen bound to carbon, but one would expect a very strong similarity.

20-Methyl-5-pregnene-3β,20-diol. Duax and co-workers reported[92] a low-temperature crystallographic study of this compound some years ago, including neutron diffraction to locate the hydrogens. They commented that the low-temperature structure was in good agreement with the MM2 structure, while the room-temperature structure, which was also determined, showed much larger discrepancies as a result of the librational motion. There were several points of discrepancy between the MM2 structure and the low-temperature neutron structure, so that even though the overall agreement was good, these points deserve further consideration at the present time.

First, from the plot of the discrepancies between bond lengths calculated and found with MM2,[92] it is noted that there are two very large discrepancies for hydrogens, which are the O–H bonds. Since the crystal is internally hydrogen bonded, while the calculations are for the isolated molecule, these are not really discrepancies; they are different things and they should not be compared. As far as the skeletal bond length discrepancies, the major ones are the C–O bond lengths. We recognized at the time

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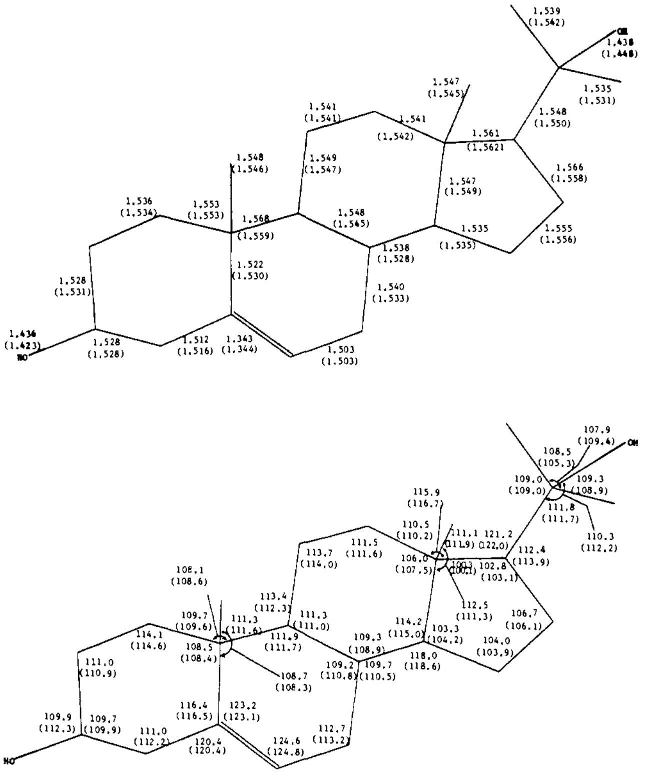

Figure 5. Structure of 20-methyl-5-pregnene-3β,20-diol.

the MM2 force field for alcohols and ethers was developed that the scheme then used could not fit accurately both alcohols and ethers with the same value for l_0 for the C–O bond. The alcohols have systematically longer bond lengths than the ethers, and because of steric effects, the reverse was necessarily calculated with MM2(77). This is another example of the electronegativity effect, discussed previously.[93] The ether has some natural bond length (l_0), but when the electropositive hydrogen replaces the carbon attached to the oxygen to give the alcohol, it has a bond lengthening effect on l_0 of about 0.015 Å. The result of this effect is to make the C–O bonds in alcohols systematically longer than the analogous bonds in ethers, in accord with experiment, but differing from MM2(77). This correction has been incorporated in MM3 (and in recent versions of MM2), and the C–O bonds here do not show this systematic error. The C–O bond lengths nonetheless show unusually large (for MM3) deviations between the calculated and experimental values, 0.009 Å, one positive and one negative, respectively. Since we have worked only on hydrocarbon parameter refinement to this point, this discrepancy may be further reduced when oxygen parameters are studied in detail.

Looking at the discrepancies in the C–C bond lengths in the steroid as calculated by MM2, we note that while the overall discrepancies were not large, the bonds in the five-membered ring were calculated to be systematically too short. With the torsion–stretch interaction now added,[12] these become longer, and the agreement with experiment here is now much improved.

When we look at the C–C bond lengths overall for this molecule as calculated by MM3 and as found experimentally, the latter are systematically shorter by about 0.004 Å. Since crystallography determines average atomic positions, rather than average bond lengths, the MM3 bond lengths (r_g) are a bit longer than the crystallographic bond lengths (approximately r_α) after the librational motion has been removed from the latter. An average correction[37] of r_α to r_g is +0.002 Å for bonds between first-row atoms. It will, of course, not be a strictly constant correction, but will be a function of the vibrational motion. Even at liquid nitrogen temperatures one may expect residual thermal motion in the crystal, and we have added 0.001 Å to each bond length to correct for this. For C–H bonds similar corrections also would be necessary, but they are usually larger and much less constant.

Table IV. Dihedral Angles in Ring D

angle	MM2	exptl	MM3
13-14-15-16	−36.7	−33.1	−35.2
14-15-16-17	11.5	4.6	8.8
13-17-16-15	17.5	25.0	20.5
14-13-17-16	−38.8	−44.0	−41.4
15-14-13-17	47.2	48.1	47.9

In Figure 5 is shown a plot of the MM3 bond lengths for each of the bonds in the molecule, together with the experimental values corrected to r_g (in parentheses). Note that after correction the carbon–carbon bond lengths are systematically too long by 0.001 Å only. The average absolute deviation in the calcd–exptl bond lengths is 0.003 Å. This value is about the same as the average ESD in the diffraction data, and the agreement is well within the expected experimental error. When the skeletal carbon–carbon–carbon bond angles calculated by MM3 are compared with the experimental values, the average absolute deviation over 42 angles is 0.61°, about 2 esd in the diffraction data, again within the expected experimental error. Other studies we have carried out[124] indicate that crystal lattice forces typically induce average distortions in rigid molecules like this of 0.001 or 0.002 Å in bond lengths, and perhaps 0.3° or so in bond angles. Hence, we conclude that the hydrocarbon skeleton for the molecule as calculated by MM3 is in good agreement with the high-quality experimental structure. While these average numbers suggest that MM3 is overall just slightly better than MM2, this interpretation is misleading. MM3 is significantly better than MM2 for the five-membered ring bonds, and for the bonds where the electronegativity effect plays a part (C–C bonds attached to oxygen, and the C–O bonds). But there is no improvement in the ordinary C–C bond, which was already calculated very well with MM2. Since there are many of these ordinary bonds present, their effect is to dilute the changes shown in the average values.

Another point worthy of mention concerns the dihedral angles found in ring D of the steroid. These are shown in Table IV The ring puckering was not reproduced too well with MM2, with discrepancies in dihedral angles of up to 7.5° being seen. There was some systematic error, with the calculated ring on the whole being too flat by a total of 3.1°. For MM3, the largest discrepancy is 4.5°, and the ring is too flat by only 0.8°. Since every angle is improved with MM3 relative to MM2, we believe this is a real improvement. Some or most of the remaining discrepancies may be due to crystal packing forces.

Ditriptycylmethane. This compound shows fairly high distortions and is of interest, especially compared with the much more distorted corresponding ether which is discussed below. The MM2 structure for the hydrocarbon is reasonably good. The crystal structure[95] is a room-temperature one, and the MM3 structure is in adequate agreement with it. A portion of the MM3 and experimental structures are shown, with a few important geometric features labeled for comparison with the corresponding ether. Note that the two C–C bonds from the CH_2 group to the trityl groups are very different in length. The one on the left is nearly eclipsed, while that on the right is nearly staggered, and the one on the left is longer by 0.032 Å. The calculated difference is 0.045 Å. The experimental bond lengths are somewhat short, owing in part to the thermal motions of the molecules in the crystal.

Cyclobutane Ring Systems. The four-membered ring needs special parameters if one is to fit the available data, as will be discussed later under the heats of formation of these compounds.

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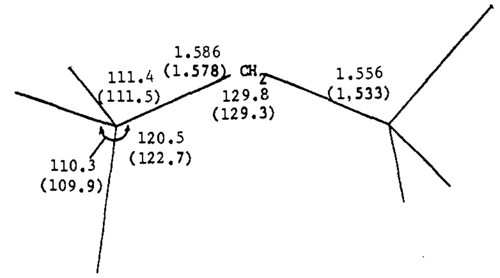


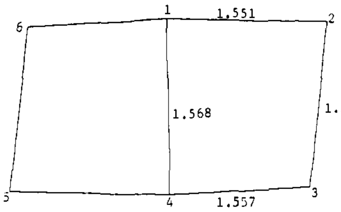
The parameters used are given in Table I.

Cyclobutane. This molecule is nonplanar, with a calculated dihedral angle of 22.5° (MM3). (This corresponds to a pucker angle (β) of 32.3°.) The C–C bond length is 1.557 Å, and the barrier to inversion is 1.37 kcal/mol, with an increase in bond length (MM3) to 1.559 at the planar transition state. MM2 gave a molecule which was a bit more flat, with a dihedral angle of 20.0° and a barrier height of 0.92 kcal/mol. The bond lengths calculated there were 1.549, going to 1.546 in the planar conformation. A structure has been recently determined by Kuchitsu.[98] The bond length (r_g) is 1.554 (1) Å. The pucker angle (β) equals 35°. The average C–H bond lengths are 1.112 (MM3) and 1.109 (3) (Kuchitsu). The calculated length is somewhat short for a secondary hydrogen (compare 1.115 in propane), largely because of the stretch–bend interaction. The earlier experimental C–C value[99] 1.548 (3), probably r_a, is now regarded by us as definitely too short.

Methylcyclobutane. There are two conformations for this molecule. The methyl can be either equatorial or axial, with the latter being higher in energy by 0.79 kcal/mol (experimental,[100] 0.96; ab initio,[101] 0.40 kcal/mol). The C–C bonds in the ring all have lengths (MM3) of 1.558 Å. Because of the stretch–bend effect, the bond to the methyl group is unusuall short, 1.530 Å. The ring pucker is close to that found in cyclobutane itself, and the ring has internal dihedral angles of 23.5°. The ab initio values are 1-2, 1.568; 2-3, 1.566; and 1-CH_3, 1.528 Å (r_e). For the axial conformer, one would expect few changes on the whole, but the ring might be expected to be flattened a bit by the repulsion between the methyl and the C_3 methylene. Indeed, the ring is flattened a bit, with internal dihedral angles of 21.6°. It might be supposed that the CCC bond angles between the methyl group and the ring would open out in the axial conformation to avoid transannular repulsion. In fact, those angles close down (from 117.2° in the equatorial to 115.9° in the axial). These deformations are consistent with a minimization of the torsion angles of the methyl with the ring, in spite of the adverse repulsion in the axial case, and are similar to what was found in the ab initio calculations.

Bicyclo[2.2.0]hexane. The cis isomer has an MM3 geometry as shown (C_2 symmetry); this does not compare very well with experiment.[102] The average MM3 bond length is 1.557 Å, while the average electron diffraction length (r_a) is given as 1.556 (2), which corresponds to 1.558 (2) for r_g. Experiment finds the rings to be flatter than in cyclobutane, and we agree qualitatively and calculate an average dihedral angle of 15.8° (MM3) versus 22.5° for cyclobutane. The experimental puckering (β) is only 11.5 (1.8°). The bond angle between the rings is calculated to be much larger than that given by experiment (117.9 versus 113.5 (1.1)). Angle 4-1-H is calculated to be only 117.9°, while a somewhat larger value would be expected (see under prismanes). The small value here seems to be connected with the large 2-1-6 angle.

Bicyclo[1.1.1]pentane. The MM3 bond length is 1.558 Å (1.566 MM2, 1.557(2) for r_a by electron diffraction[23]), which corresponds to an r_g of 1.559(2). The secondary angle, which is highly deformed, is calculated to be 71.7° in MM3 (72.9° in MM2), while the experimental value is 74.2 (2)°. The tertiary C–H bond lengths have become quite short in MM3, 1.104, with the secondary being 1.111 Å, and giving an average value of 1.109 Å. The individual experimental values are quite uncertain, but the average is 1.109 (10) Å. The reported structure has D_3 symmetry, whereas our structure is exactly D_{3h}. Wiberg[103] has discussed the bonding between the bridge carbons in this molecule, which is dependent on electron densities and hence substituents. This compound may be beyond the reach of current molecular mechanics methods.



	MM3	EXP.
2/5	3.220	3.117
2/6	2.663	2.604
3/6	2.851	2.910

Cubane. The MM3 bond lengths calculated for this molecule are 1.561 and 1.104 Å for C–C and C–H, respectively, while the MM2 values were 1.557 and 1.114. The decrease in the C–H bond length is primarily due to the inclusion of the stretch–bend interaction term in shortening the C–H bond. (No stretch–bend adjustment of C–H bond lengths was included in MM2.) The experimental values for the bond lengths are several, and variable. An X-ray value at room temperature[104] was 1.551, but one would expect this to be a good bit too short because of thermal libration. A recent report by Pine[105] assumes a C–H bond length of 1.110, and then calculates the C–C bond length from the experimental moments of inertia as 1.565 Å. Using 1.104 Å for the C–H, the C–C would increase to 1.566. The best electron diffraction (not final) r_g values[106] are 1.573 and 1.118. The disagreement here is puzzling.

Pentaprismane. This molecule has two different kinds of bonds, either within the five-membered ring or between the five-membered rings. The experimental (X-ray) bond lengths[107] of these two different types of bonds are 1.548 (8) and 1.565 (4) Å, respectively. Again, the experimental values are room-temperature values and may be assumed to be artificially shortened by libration. (The experimental values are on a carboxyl derivative, and that leads to some further distortion.) MM2 reproduced these differences adequately (1.540 and 1.566 Å).[108] The MM3 values are 1.555 and 1.567, and these appear to be improved. The C–H value is a rather short 1.107, for reasons discussed under cubane. Ab initio calculations[109] gave two different carbon–carbon (r_e) bond lengths, similar to above, but with a less pronounced difference, the values being 1.552 and 1.557 Å. Curiously, the ab initio values for the C–C–H angles are quite different from the molecular mechanics values. With respect to the angle in which the carbon–carbon bond is in between two five-membered rings, the ab initio value is 123.3°. The MM2 value is 116.6°, and the MM3 value is 120.1°.

Hexaprismane. Again, as with pentaprismane, the bonds are of very different lengths, relatively short within the six-membered ring, and much longer between the six-membered rings. MM3 calculates 1.545 and 1.571 Å, respectively. The latter value is especially long, and it will be interesting to see how this turns out experimentally. The six-membered rings are found to be planar.

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Table V. Values for Heat of Formation Parameters (kcal/mol)

parameter	H_f	strainless	parameter	H_f	strainless
C–C	2.447	3.506	Me	1.045	0.998
C–H	−4.590	−4.590	5-ring	−5.508	0.000
Iso	−2.627	−2.512	4-ring	−1.780	0.000
Neo	−6.641	−6.396	TORS	0.42	0.000

The MM2 values were 1.532, and 1.571. The C–H bond length (MM3) is 1.111 Å, compared with 1.107 and 1.104 for pentaprismane and cubane, respectively. Ab initio calculations[109] (6-31G*) give for the short and long C–C bonds respectively 1.552 and 1.558 Å (r_e). As with pentaprismane, the C–C–H angle is again substantially different from the molecular mechanics value. With respect to the C–C bond between the six-membered rings, the ab initio value for the angle is 121.5°, and the MM3 value is 116.4°.

The MM3 geometries of the prismanes are in fairly good agreement with the limited experimental data available. The agreement with the ab initio calculations[109] is less good. MM3 indicates that the C–H bond in cubane is quite short, and hence quite strong and with a high vibrational frequency, compared to an ordinary tertiary hydrogen, due to the stretch–bend interaction in MM3. As the C–C–H angles are closed and become more normal, going from cubane to the larger prismanes, the C–H bond becomes progressively longer and more ordinary. The trend is in the same direction, but the magnitude of the difference is quite small in the case of the ab initio calculations. The carbon–carbon bond lengths show similar patterns with cubane and pentaprismane when the MM3 results are compared with the ab initio calculations. However, with hexaprismane, the stretch–bend interaction in MM3 leads to an increasing elongation of the longer bond, and shortening of the shorter bond compared with the smaller homologues, while in the ab initio calculations, the bond lengths are similar in hexaprismane to what was found with pentaprismane. It is not clear why the C–C–H bond angles differ as much as they do, comparing the MM3 and ab initio results, but this might be due in part to the vibrational motion.

[2.2.2]Propellane. MM2 calculations on this compound have been reported in the literature.[110] MM3 calculates that the compound has a structure in which each of the rings is nonplanar, and the molecule is thus twisted into a C_3 conformation with the intra-ring dihedral angles of 15.5° (av). As might be guessed by extrapolating from the bicyclo[2.2.0]hexane structure, the central bond is quite long (1.628 Å), while the remaining carbon–carbon bonds are normal for four-membered rings (1.549 Å). The MM2 program has trouble with this compound, giving two minimum energy conformations with widely differing bond lengths for the central bond (1.655 and 1.900 Å). The latter is an artifact resulting from the fact that there is a cubic anharmonic stretching term in MM2 that allows the bond to stretch unrealistically if it becomes very long. (This was corrected in MM3 by the addition of a quartic term to the stretching function; eq 1.) Ab initio calculations suggest that this bond is short rather than long.[111] It may be, however, that current ab initio calculations use inadequate basis sets and/or treatment of correlation to deal properly with such nontetrahedral structures, as discussed by Dodziuk.[110]

Heats of Formation. The heats of formation of molecules may be calculated with MM3 as they were with MM2, and the necessary parameters obtained are shown in Table V. As previously, one uses a bond energy scheme, which includes also increments for methyl, secondary, and tertiary carbons, and adds these together with 2.4 kcal/mol (the PV correction + ΔE_{tr} + ΔE_{rot}) plus values for POP (from higher energy conformations) and TORS (from vibrations involving very low torsion frequencies). The TORS parameter was assigned the value 0.42 in MM3, slightly larger than previously.[3b] The parameters shown in Table V were evaluated by least-squares fitting of the data to the experimental values, as shown in Table VI. The weighting used in the least squares was initially taken as inversely proportional to the experimental error, but was then reduced for molecules in which POP and TORS have larger values, since they lead to more uncertainty. Values which were not considered reliable were weighted zero, and they were not actually used in the least-squares fitting, but are included in the table for reference purposes only. An occasional value might have had its weight increased somewhat if it was not fit well, and we considered it to be representative of

Table VI. Heats of Formation, Gas, 25 °C (kcal/mol)[a]

		H_f (0)		diff	
eq	wt	calc	exp[78]	(calc − exp)	compound
1	0	−17.89	−17.89	0.00	methane
2	6	−20.05	−20.24	0.19	ethane
3	9	−25.32	−24.82	−0.50	propane
4	8	−30.26	−30.15	−0.11	butane
5	7	−35.17	−35.00	−0.17	pentane
6	6	−40.08	−39.96	−0.12	hexane
7	5	−45.00	−44.89	−0.11	heptane
8	4	−49.92	−49.82	−0.10	octane
9	3	−54.84	−54.75	−0.09	nonane
10	9	−32.50	−32.15	−0.35	isobutane
11	7	−36.65	−36.92	0.27	isopentane
12	6	−42.03	−42.49	0.46	2,3-dimethylbutane
13	6	−47.91	−48.21	0.30	2,4-dimethylpentane
14	5	−52.57	−53.18	0.61	2,5-dimethylhexane
15	9	−41.06	−40.27	−0.79	neopentane
16	5	−56.06	−56.64	0.58	2,2,3,3–tetramethylpentane
17	5	−53.82	−53.92	0.10	2,2,3,3-tetramethylbutane
18	5	−57.85	−57.80	−0.05	di-tert-butylmethane
19	5	−54.83	−55.67	0.84	3,3-diethylpentane
20	6	−48.35	−48.95	0.60	2,3,3-trimethylbutane
21	8	−29.96	−29.43	−0.53	cyclohexane
22	7	−28.03	−28.22	0.19	cycloheptane
23	5	−29.48	−29.73	0.25	cyclooctane
24	4	−31.21	−31.73	0.52	cyclononane
25	4	−36.63	−36.885	0.25	cyclodecane
26	2	−53.65	−54.59	0.94	cyclododecane
27	9	−37.11	−36.99	−0.12	methyl-cyclohexane
28	6	−43.74	−43.26	−0.48	1,1-dimethylcyclohexane
29	6	−41.42	−41.13	−0.29	1-*ax*,2-eq-dimethylcyclohexane
30	6	−43.17	−42.99	−0.18	1-*eq*,2-*eq*-dimethylcyclohexane
31	6	−40.79	−40.45	−0.34	*cis*-decalin
32	6	−43.60	−43.54	−0.06	*trans*-decalin
33	0	−57.33	−58.12	0.78	*tst*-perhydroanthracene
34	0	−50.22	−52.73	2.41	*tat*-perhydroanthracene
35	5	−22.51	−22.58	0.07	bicyclo[2.2.2]octane
36	2	−30.41	−30.50	0.09	bicyclo[3.3.1]nonane
37	2	−32.02	−31.76	−0.26	adamantane
38	2	−67.45	−67.15	−0.30	tetramethyladamantane
39	3	−35.03	−34.61	−0.42	diamantane
40	9	−18.87	−18.74	−0.13	cyclopentane
41	2	−26.10	−26.31	0.21	methyl-cyclopentane
42	6	−33.29	−33.04	−0.25	dimethylcyclopentane
43	5	−30.79	−30.34	−0.45	ethyl-cyclopentane
44	3	−15.68	−15.86	0.18	*trans*-bicyclo[3.3.0]octane
45	3	−21.83	−22.07	0.24	*cis*-bicyclo[3.3.0]octane
46	4	−30.93	−30.41	−0.52	*cis*-hydrindane
47	4	−31.87	−31.45	−0.42	*trans*-hydrindane
48	7	−12.04	−12.42	0.38	norbornane
49	5	−30.25	−30.58	0.31	1,4-dimethylnorbornane
50	2	−19.71	−20.54	0.83	protoadamantane
51	0	−21.72	−24.46[b]	2.74	perhydroquinacene
52	(4)	6.29	6.78	−0.49	cyclobutane
53	(4)	−6.16	−6.28	0.12	ethylcyclobutane
54	(2)	148.17	148.61	−0.44	cubane
55	(1)	−4.99	−6.10	1.11	bicyclo[4.2.0]octane
56	(2)	30.66	29.90	0.76	bicyclo[2.2.0]hexane
57	(0)	51.70	50.46	1.24	bicyclo[1.1.1]pentane

[a] The standard deviation = 0.4244 based on 52 observations. The correlation coefficient = 0.9995 based on 52 observations. Statistical analysis was performed on all equations whose weight was not zero. [b] Schulman[122] has recently revised his ab initio value for perhydrotriquinacene from −24.0 to −22.7 ± 1.0, which puts it in marginal agreement with the MM3 value.

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(110) Dodziuk, H. *J. Comput. Chem.* **1984**, *5*, 571.

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an important group of molecules. Other values had their weights reduced when they were unusual (and not very important) cases.

Cyclobutane and cyclopropane rings were not included in the heat of formation fitting at the outset. The reason for this is that they constitute special situations, which for various reasons might distort the results of the least-squares fitting, so they were omitted. Subsequently, since there is a four-membered ring heat of formation parameter, it was adjusted to fit the cyclobutane derivatives. Cyclopropane has not yet been treated with MM3, but it will be handled similarly later.

Strainless heats of formation were also determined for the purpose of being able to calculate strain energies, which are useful for comparing strain in compounds that are not isomers, and the strainless parameters are given in Table V.

The heat of formation results from the present work are shown in Table VI. The calculated values are satisfactory with a few exceptions. There are some problems with the cyclobutanes, which will be discussed below. The largest discrepancies where the experimental data seem accurate are in decreasing order (kcal/mol): cyclododecane (+0.94); 3,3-diethylpentane (+0.84); neopentane (−0.79); 2,5-dimethylpentane (+0.61); and 2,2,3-trimethylbutane (+0.60).

Looking in more detail at Table VI, we see the following. The propane value (line 3) is rather low (−0.50), and definitely out of line. We could force this compound to fit better by weighting it higher, but only at the expense of a poorer fit for the larger molecules. Since the larger molecules are the more interesting ones, we accept the error in propane. The rest of the normal alkanes fit quite well, and there is no definite systematic trend. (In MM2 the larger alkanes became systematically more negative.) Neopentane (line 15), shows an error (−0.79), larger than one would like to see. But this is balanced against other neo derivatives, especially 3,3-diethylpentane (+0.84). This weighting has been judged to be optimum. Other acyclic compounds, including quite congested ones (lines 11–20), have reasonably well calculated heats of formation.

For the ring compounds, cyclododecane (line 26) was the most difficult to fit and has a heat of formation which is calculated to be too high (+0.94), but the experimental error here is also high.[112] The other middle rings (C-7 through C-10, lines 22–25) are calculated to have heats of formation which are too positive (+0.19 to +0.52), but only slightly so. Cyclohexane (−0.53, line 21) is too negative, and this error seems to carry over to other cyclohexane rings (lines 27–32, 46–47) to some extent (but see lines 29, 48, and 55).

Bicyclo[2.2.2]octane (line 35) has been a problem in the past. The three butane fragments are eclipsed here, leading to a calculated energy which is too high compared to the combustion value. Reducing the V_1 or V_3 terms in the CCCC torsional potential would help here, but would also reduce the torsional barriers in congested molecules, and in butane and cyclohexane. The possibility that the experimental heat of formation here is in error has been considered but there is no reason to think this might be the case. Ab initio calculations (6-31G*) give the heat of formation 0.73 − 1.40 kcal/mol higher than that obtained from combustion.[113] So as to avoid weighting the least-squares fitting with a value that might contain a sizable error, we have used an ab initio value here.

A few compounds shown in the table have weights of 0, for various reasons. Perhydroquinacene (line 51) shows a large discrepancy. It has been previously remarked in the literature[117] that this compound has a calculated heat of formation that is too high with MM2, and that the dodecahedrane molecule, of which this is a fragment, should similarly be too high. We would point out that dodecahedrane has the five-membered rings planar, with all bonds eclipsed, and it is quite a different kind of a structure from perhydroquinacene. The latter has ordinary (somewhat staggered) approximately C_2 conformations for the individual five-membered rings, and should be compared with cyclopentane itself (line 40), or with *cis*-bicyclo[3.3.0]octane (line 45). These latter two compounds have their heats calculated correctly; only the perhydroquinacene is very far out of line. That the calculation can be in error in this way seems improbable. We believe that the calculated number is reasonably good, and the experimental number is in error by more than the experimentalists[118] realized.

The cyclobutane rings pose additional problems. Not very many experimental data are available for these compounds, and the number of parameters to be evaluated is too large for the data set available. Cubane (line 54) was impossible to fit without introducing at least one extra parameter. After some thought, we decided to treat cyclobutane rings in the following way. First, we chose the values for θ_0 for bending to be the same as they are in open-chain molecules. Next, we adjusted the bending constants (secondary and tertiary separately) so as to give reasonable geometries and energies for molecules containing four-membered rings. The V_1 and V_2 terms were set equal to zero, and V_3 was adjusted to fit the puckering in cyclobutane. Then a constant was added for a four-membered ring to fit heats of formation. With this parameter set we were able to fit things moderately well, with some exceptions to be discussed, except for cubane, which still had much too high an energy. Also, bicyclo[1.1.1]pentane was too flat, with an angle at the secondary carbons of less than 70° (experimental, 74°) and an energy that was much too high. In principle, when one fixes some of the bonds to a carbon atom, as is demanded by the cubane cage structure, the hybridization can be regarded as changed, in which case the value for θ_0 for the C–C–H angle is no longer what it was in an open-chain compound, but has been opened out somewhat. Accordingly, we decided to let angles of this kind, where two carbons were part of the same four-membered ring, have their values for external θ_0 opened out. The opening was not much for angles where the carbons were in a single cyclobutane ring, which were opened 0.5° for C–C–H. If the two carbons were simultaneously in two cyclobutane rings as with the bridgehead hydrogen in bicyclo[2.2.0]hexane or cubane, the θ_0 values were increased 4.4°. If the external atom bound to the four-membered ring were a carbon, rather than the hydrogen, the extra angular opening of θ_0 was still different. With these values, we were able to obtain the heats of formation as given in Table VI, in addition to the geometries previously discussed. We have some trouble with bicyclo[4.2.0]octane (line 55), however, which seems pretty ordinary (but the reported experimental error is large, 1.0 kcal/mol). Bicyclo[1.1.1]pentane (line 57) is fit marginally (the only "experimental" value available is an ab initio value,[24] which is probably good to within about 2 kcal/mol). (These above changes were best brought about by assigning a carbon contained in a four-membered ring a special atom type number (56) in MM3, so as to conveniently input these parameters.)

The heats of formation of the prismanes are calculated erratically with MM2, and better with MM3. The ab initio (6-31G*) values[109] for cubane, pentaprismane, and hexaprismane are 147.1, 121.2, and 154.5 kcal/mol, while the MM2 values are

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[112] The reported error in the combustion is 0.36 kcal/mol. We used 18.7 ± 0.5 for the heat of sublimation, and we are indebted to Dr. W. Steele for this value. The error in the gas-phase heat of formation is thus approximately 0.7 kcal/mol.

[113] Using the data from ref 114 and the methods of ref 115 and 116.

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148.9, 114.7, and 129.2, respectively, so the agreement is good, fair, and poor, respectively. The MM3 values are 148.2, 129.3, and 154.9, which is some improvement.

The MM3 force field gives 1.5431 Å for the bond length in diamond (calculated with our usual model of fused adamantane rings[7]). The MM2 value is 1.5417, and the experimental value is 1.5445. The latter cannot contain rigid body motion and should be approximately an r_α value. Thus, the discrepancy may be slightly more serious than it appears.

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Supplementary Material Available: Molecular mechanics details for pentamethylethane, di-*tert*-butylmethane, tri-*tert*-butylmethane, 2,2,4,4,5,5,7,7-octamethyloctane, 5,6-di-*n*-butyl-5,6-diphenylethane, cycloheptane, cyclododecane, 1,2-dimethylcyclohexane, 1,1,3,5-tetramethylcyclohexane, decalin, perhydrophenanthracenes, pentacyclo[6.2.1.1^{3,6}.0^{2,7}.0^{4,10}]dodecane, and various derivatives, [4.4.4]propellane, (*i*,*o*)-bicyclo[6.2.2]dodec-11-ene 2,3-anhydride, 2,3-diadamantyl-2,3-dimethylbutane, ditriptycyl ether, and 1,4,7-cyclononatriene including structures in Figures 1, 3, 4, and 6 and Tables III, VII, and VIII of relative enthalpies of perhydrophenanthrenes, strainless heats of formation, and ab initio heat of formation of dodecahedrane, respectively (15 pages). Ordering information is given on any current masthead page.

Molecular Mechanics. The MM3 Force Field for Hydrocarbons. 2. Vibrational Frequencies and Thermodynamics[‡]

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Abstract: In the development of the MM3 force field, vibrational frequencies were considered for a set of eight relatively simple hydrocarbons. The 213 observed experimental frequencies over this set were fit to within a root-mean-square error of 35 cm^{-1}, of which the largest errors occur in the C–C–H bending frequencies. The torsional frequencies are generally calculated to a much higher accuracy, which allows the calculation of entropies near room temperature for a variety of alkanes and cycloalkanes with errors of less than 1%. A number of rotational barriers in hindered compounds were also calculated. The values of $\Delta S^{\ddagger}$ are usually more negative than −4 eu in congested molecules, and consequently the entropy contribution to rotational barriers can be appreciable. The largest and average discrepancies between the calculated and found values for $\Delta G^{\ddagger}$ are 2.46 and 1.02 kcal/mol, for seven examples.

Force fields can be constructed to reproduce different kinds of data. The MM2 force field was specifically constructed to fit structures and energies of organic molecules.[1-3] A few other properties were also fit, but we frankly omitted fitting vibrational spectroscopic data, because we could not see how to fit those data, and fit the other above-mentioned data at the same time, with the same parameter set. Various other force fields have been constructed along similar lines in some cases, and to fit other data, such as spectroscopic data, as well.[3,4] Such force fields have fit more things, but they have fit less well to structures and energies.[4]

With the experience now available in the design and construction of force fields, it is possible to fit both structures and energies better, overall, than was done with MM2. The previous paper[5] described the development of MM3, which does exactly that. This paper will be concerned with the fitting of some of the other kinds of data which went into the development of MM3, namely, vibrational spectra and other properties that depend on the vibrational levels (entropies, thermodynamic functions). The following paper will describe the results obtained with crystallographic data. All of this work was carried out at the same time and employs the same force field and parameter set. As discussed long ago,[6] if one can correctly calculate the unit cell constants and heat of sublimation of a crystal, one has an indication that the van der Waals' properties of the molecules are, on the whole, reasonable. Because there are many more variables in the van der Waals' parameters than there are cell constants, good fits to crystal data are required if one is to have a good van der Waals' parameter set, but such data alone do not guarantee that the van der Waals' parameter set is, in fact, accurate.

Besides the structural, energy, and crystal data mentioned above, we also wanted to fit vibrational spectroscopic data insofar as possible. Vibrational spectra have been studied in great detail

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[‡] Abstracted mainly from the Ph.D. dissertation submitted by J.-H. Lii to the University of Georgia, 1987.

(1) The MM2 force field for hydrocarbons was first described in ref 2. Extensions to functionalized molecules and other sorts of special problems have been described in subsequent papers, which are summarized in ref 3. The original version of the program (MM2(77)) is available from the Quantum Chemistry Program Exchange, University of Indiana, Bloomington, IN 47405, Program 395. The latest version of the MM2 program, which is referred to as MM2(87), is available to academic users from the Quantum Chemistry Program Exchange, and to commercial users from Molecular Design Limited, 2132 Farallon Dr., San Leandro, CA 94577. The MM3 program is still under development, but it is intended to make it available shortly from Technical Utilization Corp., Inc., 235 Glen Village Ct, Powell, OH 43065, and from MDL.

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