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APPLICATION OF FORCE FIELD CALCULATIONS—III†

CONFORMATIONAL ISOMERISM AND DYNAMIC GEARING IN ETHANES WITH MANY ALKYL SUBSTITUENTS. EFF CALCULATIONS AND DYNAMIC NMR MEASUREMENTS

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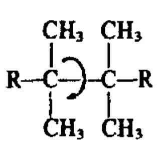
Abstract—Force-field calculations and dynamic NMR measurements of symmetrical 1,2-dialkyl-1,1,2,2-tetramethylethanes where the alkyl group is methyl, ethyl, isobutyl, neopentyl, isopropyl, cyclohexyl, or t-butyl are reported. There is usually slightly less than one third of the population in the anti-conformation, slightly more than two thirds in gauche conformations but the t-butyl compound adopts only the anti-conformation. Barriers to rotation vary markedly between 8.1 and 13.8kcal/mol, being *lower* for secondary alkyl groups than for primary alkyl groups. Calculations suggest that rotation about the central bond and rotation of the secondary alkyl group, by taking place in a concerted fashion, produce several rotational itineraries of similar energies. The low barrier is thus due to a favourable entropy effect.

Internal rotation about carbon–carbon bonds in alkanes has been much studied experimentally.[1] The most useful technique at least for relatively highly substituted ethanes, has been dynamic NMR spectroscopy,[2] where the temperature dependence of the NMR spectrum leads to quantitative results. At the same time, calculations of the energies of conformations of substituted ethanes have been made with considerable success.[3] This paper discusses experimental and calculated results for a related series of hydrocarbons **1** (2,3-dialkyl-2,3-dimethylbutanes) where R has been varied systematically.



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(a) R = CH_3
(b) = CH_2CH_3
(c) = $CH(CH_3)_2$
(d) = CH_2–$C(CH_3)_3$
(e) = $C(CH_3)_3$
(f) = cyclo–C_6H_{11}
(g) = CH_2–$CH(CH_3)_2$

Dynamic NMR (when it can be applied) provides a quantitative measure of the populations and relative energies of conformations such as gauche and anti, but tells nothing about conformations which are not populated. It also allows the measurement of the rate of interconversion of stable conformations (and thence the barrier to rotation) but tells little or nothing about the detailed structures of the transition state.

In previous work on highly substituted ethanes the barrier heights measured by NMR have been related in certain cases to the size of the substituents in the α-position[4] that is, directly attached to the carbons of the ethane fragment. Secondary effects[5] caused by different branching in the β-position have also been pointed out and may operate by compressions similar to buttressing effects.[5,6]

Well-based calculations of conformational energies should likewise predict populations and barriers, but in addition should indicate the precise structures of conformations and transition states, that is they should show distortions from idealised gauche-, anti-, and eclipsed conformations. The empirical force field (EFF)-method[7–10] accounts in a quantitative manner for the steric interactions operating in organic molecules. The method is well established for the study of the static stereochemistry of highly congested alkanes,[11–13] like the 2,3-dialkyl-2,3-dimethyl-butanes **1**. However, the energies of the transition states for internal rotations calculated by this method seem to be less reliable,[3,6] at least as to the absolute values predicted. The particular usefulness of such calculations is that they show how the molecule may accommodate steric crowding by calculating the detailed geometric structure and energy of conformations, whether stable populated ones, or not.

The conformational questions one might hope to answer about compounds such as **1** are questions both of statics and of dynamics.

Statics

The major question of statics is the relative energies and the population of gauche conformations **2** and **3** and the anti conformation **4** about the central bond, but one may further wonder whether the symmetrical representations **2**, **3** and **4** with dihedral angles θ of 60° are in fact the minimum energy gauche and anti conformations. A gauche conformation with θ different from the 60° value of the stylised representations **2** and **3** might better

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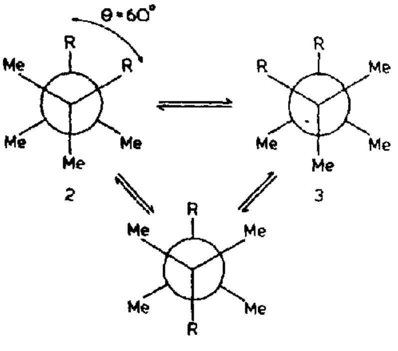
†Paper II, see Ref. 12b; Paper I: H.-D. Beckhaus, *Angew. Chem.* **90**, 633 (1978); *Angew. Chem. Int. Ed. Engl.* **17**, 593 (1978).

accommodate interactions between the groups R for example.[12,13d]

The position of the gauche-anti equilibrium is the classical problem of conformational statics of substituted ethanes but there are others. There may be possibilities for conformational isomerism about the bond joining the group R to the central carbon, and this may effect the conformation about the central bond, and there is a more subtle problem of considerable current interest. This involves concerted rotation away from an apparently stable symmetrically-staggered conformation, which is best illustrated by the example of tri-t-butylmethane **5**.[14]

It might seem that the preferred conformation of a t-butyl group in **5** should be as in **6** with most particularly, one methyl group A symmetrically placed with respect to two gauche t-butyl groups, and undoubtedly interacting strongly with them. It has been observed however, on the basis of both experiment[15,17] and calculations,[13b,16] that if each of the three t-butyl groups is rotated in the same sense, these methyl-t-butyl interactions are reduced, in conformations which look like **7** and **8**. It may be easier to understand this reduction in interactions by looking at a slightly different representation of **6**–**8**. The representation **9** is of compound **5** viewed more or less along an axis joining two of the quaternary t-butyl carbons. Some of the particularly destabilising interactions of methyl groups are clearly seen, and these are reduced in a conformation **10** which is obtained by rotating the two t-butyl groups in a clockwise direction. Simultaneous clockwise rotation of the third t-butyl group will likewise reduce interactions involving it. The conformation **11** is of similarly low energy and is obtained by simultaneous *anticlockwise* rotation.



2 3 4

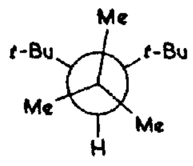
Thus, even when substituents are symmetrical like methyl or t-butyl perfect staggering of substituents (i.e. dihedral angles of 60°) may not be the preference of the molecule, and a classical conformation like **6** may be an unstable transition state between skewed conformation **7** and **8**. Thus tri-t-butyl methane, **5**, is best considered as undergoing a concerted libration between conformations like **7** and **8** or **10** and **11**.

In fact, changes have been observed[17] in the NMR spectrum of **5** which show that libration of the type illustrated $7 \rightleftharpoons 8$ (i.e. $10 \rightleftharpoons 11$) is taking place, with a barrier of about 7 kcal/mol, but the NMR spectrum gives no indication of the extent to which each t-butyl group rotates away from the symmetrically staggered conformation **6**. Calculations[13b,16] agree with the electron diffraction determination[15] of the structure of **5**, and show that the twisting away from the staggered position is by 11–20° depending on the assumptions which necessarily have to be made.

How this libration might be encountered in compounds like **1** can be seen by considering the most highly substituted example, **1e** (R = t-butyl) and considering the anti conformation, which as we shall show later is the only one populated. If there is symmetrical staggering about all bonds the structure will be as represented in **12** where methyl groups are represented by the letters V to Z, and the quaternary carbons are labelled C_2–C_5. The particular unfavourable interactions (parallel-1,3-interactions in fact[18]) between the pairs V_1 and V_2, W_1 and W_2, X_1 and X_2, and Y_1 and Y_2 are obvious.

Rotation by a few degrees in a clockwise direction about each of the C_2–C_3, C_4–C_3, and C_5–C_4 bonds leads to a structure **13** in which these pairwise interactions are diminished. As a specific example the X_1–X_2 parallel-1,3-interaction is considerably reduced, without too great an increase in the compensating X_1–C_4 and X_2–V_1 eclipsing interactions.

Rotation about the same bonds in an anticlockwise direction would lead to a structure **14** (not shown) of equal energy to **13**. Thus for **1e** libration will be between structures **13** and **14** by way of a transition state presumably like the symmetrical structure **12**.



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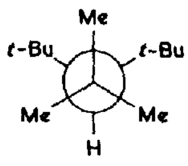

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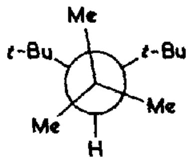

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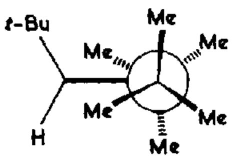

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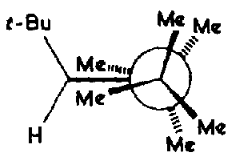

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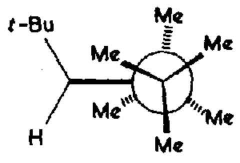

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Concentrating on the C_2–C_3 bond, structures **12**, **13** and **14** can be represented by structures **15**–**17**.

Another aspect of conformational statics which is of current interest and is particularly suitable for study by EFF calculations is the distortion of bond lengths and bond angles in crowded molecules. NMR tells nothing about this directly, and this aspect of the conformational analysis of compounds **1a**–**1g** which has been considered previously[12,13d] is not further discussed here.

Dynamics

The questions of dynamics are those of the rates of interconversion of those conformations which are populated and the associated barriers. In the series **1**, there are therefore barriers to *rotation* and barriers to *libration* about the ethane bond.

There are two rotational barriers, that to interconversion of two gauche conformations $2 \rightleftharpoons 3$ and that to interconversion of a gauche and the anti conformations $3 \rightleftharpoons 4$ or $2 \rightleftharpoons 4$, and the elucidation of such a problem is not straightforward.[19] Since for the compounds **1b**–**1f**, the populations of each of the conformations **2a**, **2b**, and **3** are nearly equal, it has been assumed that the barrier heights are equal when deriving these from changes in the NMR spectra. The calculations of barrier heights suggest that this is a reasonable assumption. Similar treatment of results for **1b** can be found elsewhere.[3]

NMR suffers from the disadvantage that if the barrier under investigation is less than about 5 kcal/mol it cannot be measured, since the process involved is too fast on the NMR timescale at accessible temperatures. Since barriers to libration are expected to be small, NMR may often give no indication of unsymmetrical staggering with its associated concerted libration processes, and this turns out to be the case here.

EFF calculations on the other hand can be made of the complete rotational itinerary in compounds like **1**, and the succession of eclipsing and libration barriers can be estimated by searching for the lowest energy transition state between stable conformations.

Thus the dynamic NMR method and force-field calculations are complementary. Experimentally, particularly high barriers and the relative energies of particularly stable conformations can be measured, and some general idea of the structure of stable conformations, and perhaps transition states can be obtained. Calculations allow a more precise estimation of the structure of stable conformations, of the relative energy of unstable unpopulated conformations, and of the structure and relative energy of transition states. In fact calculations determine a potential energy diagram for the complete rotational cycle. The NMR results are complementary to the calculations by providing an experimental verification or calibration of several points in the diagram.

RESULTS

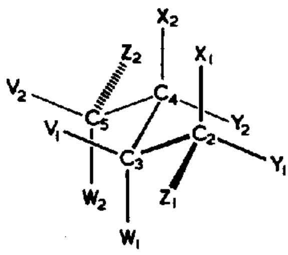
Dynamic NMR spectroscopy

The proton and carbon-13 NMR spectra of compounds **1b**–**1g** are temperature-dependent. At ambient temperatures an averaged spectrum derived from gauche and anti isomers interconverting rapidly on the NMR timescale is observed. At a suitably low temperature separate but overlapping spectra for gauche and anti conformations are observed. Complete spectral details are given in the experimental section but a typical example is the 400 MHz proton NMR spectrum of **1f**, R = cyclohexyl (Fig. 1). At ambient temperature it shows one singlet for the four methyl groups and discrete multiplets for the various cyclohexyl protons (Fig. 1). At −115°, the methyl group signal comprises three lines, a doublet (relative intensity 2.23) for the methyls in gauche conformations **2** and **3** and a singlet (relative intensity 1.0) for the methyls in the anti conformation **4**. The spectrum of the cyclohexyl protons shows small differences due mainly to changes in chemical shifts. Corresponding changes are seen in the proton-decoupled carbon-13 NMR spectrum of **1f**.

The 270 MHz proton NMR spectrum of **1b** at various temperatures is illustrated in Ref. 3. **1b**, **1c**, **1d** and **1g** have similar temperature dependent spectra.

Populations of gauche and anti conformations were most conveniently derived from the proton or carbon-13 (with proton decoupling) signals of the central geminal dimethyl groups. The singlet signal at ambient temperature became a doublet (from the gauche conformation) and a singlet (from the anti-conformation) at low temperatures, see Experimental for details.

The spectrum of **1e** (R = t-butyl) showed changes only



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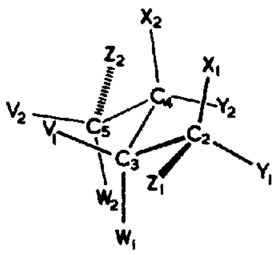

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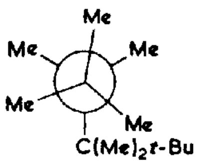

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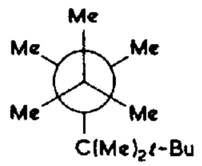

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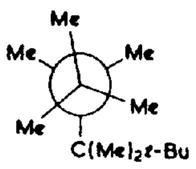

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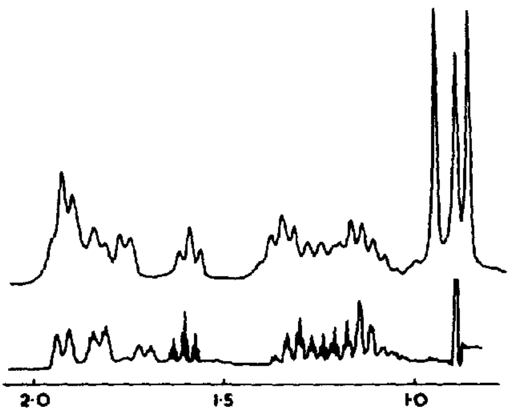


Fig. 1. 400 MHz proton NMR spectrum of **1f** at ambient temperature (lower trace) and at −115° (upper trace).

in the t-butyl signal which can be interpreted in terms of a barrier to rotation of the t-butyl group of 11.74 kcal/mol. There is no sign of other changes (in for example the geminal methyl signal) which could be interpreted in terms of slow interconversion of gauche and anti conformations about the central bond. If it is assumed that the low limit of detection of signals from the gauche conformation is 5%, then the failure to detect signals from the gauche conformation at 200°K suggests that the anti-conformation is more stable than the gauche by at least 1.2 kcal/mol.

We looked further for evidence of gauche conformations of **1e** at higher temperatures by observing the temperature-dependence of its carbon-13 chemical shifts which, being less sensitive to medium effects than those of protons, can be expected to change with changes in the position of the gauche-anti conformational equilibrium. In fact over a 150° temperature range, the two methyl carbon signals moved little, and in fact by about the same amount *in the same sense*, which does not suggest interchange of environments due to conformational exchange, but rather some medium effect. Chemical shift measurements thus offer no evidence of the gauche conformation even at 100°.

The spectra of **1d** and **1e** were examined at very low temperatures down to −150°C to look for changes which could be associated with the slowing down of libration of the type illustrated above, e.g. **16** ⇌ **17**, these being the two compounds predicted by calculations as most likely to have a measurably high libration barrier, but no such changes were observed. The barrier to libration is thus probably less than 5 kcal/mol which does not disagree with calculated values.

FORCE-FIELD CALCULATIONS

Ground state enthalpy

The heats of formation ΔH_f^0(gas) calculated for the anti and gauche conformers of **1a–e** which are minima on the hypersurface (see Fig. 2) are given in Table 2 along with the values of their torsional angles of (R–C_q–C_q–R).

According to these results, compounds **1** with R = primary and secondary alkyl (**1b–d**) are slightly more stable in the gauche conformations than in the anti. In the case of R = i-C_3H_7 (**1c**) the gauche form is favoured by as much as 0.4 kcal/mol. The intuitive prediction, that repulsion between the gauche groups R in the gauche conformation of **1** should increase the energy in comparison to the anti conformation, is only valid for **1e** (R = t-butyl). The differences ΔH_f^0(gas) (anti-gauche) calculated by the EFF method are in good agreement with the conformational populations determined experimentally by NMR (see Table 1). In particular, for every primary and secondary substituent, the calculations suggest and the NMR observations show that there is slightly less than one part in three of the anti conformation. While we note that the calculations are of

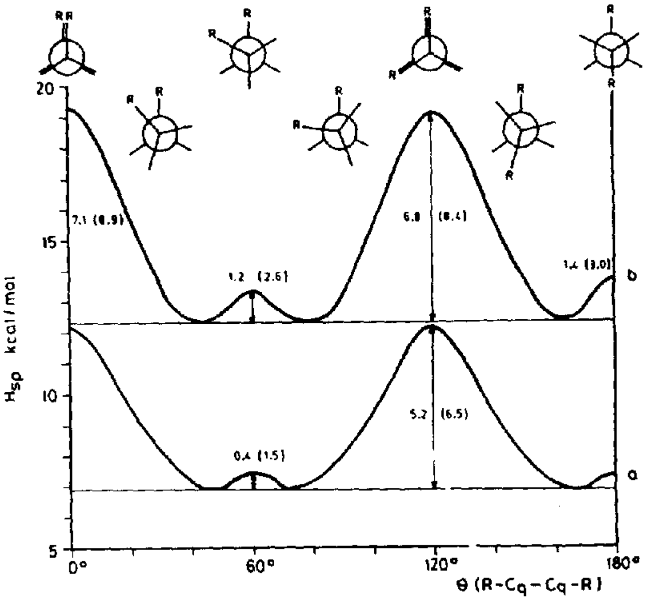


Fig. 2. Strain energies of 2,2,3,3-tetramethyl-butane **1a** (trace a) and of 3,3,4,4-tetramethyl-hexane **1b** (trace b) calculated by MM2-force field as a function of the torsional angle ϕ (R–C–C–R). All other internal coordinates are optimized. Minima and saddle points are sketched by their Newman projection along their central C_q–C_q-bond. For the energy differences results of MM2-calculations as well as MM1-calculations (in brackets) are given.

enthalpies, and observations are of free energies, we conclude that there is agreement between calculations and experiment that the anti conformation is slightly less stable than a gauche conformation by a few hundred calories.

Further, calculations and NMR observations agree that for the t-butyl-compound **1e**, the anti-conformation is much more stable than the gauche. A secondary remarkable result suggested by the calculations is that in the most stable conformation of each compound in the series **1** there is substantial deviation of the dihedral angles (R–C_q–C_q–R) from the "normal" values of 60° in gauche **1** and of 180° in anti **1**. In addition, all other torsional angles between any four adjacent carbon atoms in **1** and not only those along the central bond, differ from the normal values. This seems to be a general phenomenon[12b] for the whole series **1** and other hexaalkylated ethanes[11–13] with one exception.[20] As described in the introduction, this torsion away from the symmetrical reduces the overall repulsion between the hydrogens attached to the α-position of vicinal alkyl groups in a gauche-arrangement, in other words it reduces parallel 1,3-interactions of primary and secondary alkyl groups (i.e. 1,6-interactions of α-hydrogen atoms).

Barriers to rotation

The activation enthalpies calculated for the interconversion of the two conformations are also presented in Table 2. Compared with the experimentally-determined ΔG^*_{rot}-values, the calculated ΔH^*_{rot}-values seem to be too low, especially those calculated with the MM2 force field. It is generally accepted[4,7,21] that both force fields produce too low enthalpies for transition states of bond rotations. But surprisingly the ΔH^*_{rot}-values as obtained by the improved MM2 force field deviate even more[22] than those of the older force field MM1. If this deviation is a systematic one then the correct barrier heights can be reasonably estimated based on the MM2 calculated values.

There are striking features of the experimentally measured barriers given in Table 1. The barriers in **1c** and **1f** where the alkyl substituent is secondary (isopropyl and cyclohexyl respectively) are markedly lower than in the primary examples **1b** (R = ethyl) and **1g** (R = isobutyl). Secondly, the barrier is particularly high in **1d** where the alkyl substituent is the neopentyl group, once again primary.

The substantial decrease in the barrier (ΔG) measured by NMR, on changing R from a primary to a secondary group is not reflected in the calculated ΔH^* values. It is desirable to know the relative importance of ΔH^* and ΔS^*, the enthalpy and entropy contributions to the barrier to rotation but it is notoriously difficult to obtain these from temperature-dependent NMR spectra, since systematic errors are rather large. Detailed EFF calculations were therefore carried out in an attempt to deduce at least some trends in the variation of ΔS^* for the rotation, and they suggest that for the isopropyl compound in its transition state for rotation, there are indeed several conformations of very similar energy, (i.e. several rotational pathways). This high concentration of transition states of similar energy, should manifest itself as a positive entropy of activation for rotation, and thus as an uncommonly low free energy of activation.

It is possible to devise a qualitative explanation of this effect, based on a consideration of the conformations involved. A primary substituent R, for example the ethyl group, can adopt a conformation where the CH_3 of the ethyl group is anti to the rest of the molecule (see the idealised structure **18**) and remote from the substituents at the other end of the central bond. A secondary substituent R, for example an isopropyl group must have additional methyl–methyl interactions across the central bond in its ground state (asterisked in idealised structure **19**), and since the molecule is in a ground state energy well, distortion to accommodate this additional interaction is not easy. In the transitional state for rotation about the central bond, however the additional inter-

Table 1. Conformational populations, free energy differences ΔG^0, and barriers to rotation ΔG^* for the compounds **1a–1g** as determined by dynamic NMR spectroscopy. For conveninet comparison *calculated* enthalpies (MM2, see Table 2) are shown in parentheses

$[R\text{-}C(Me)_2]_2$ R =		$\%_{anti}$[a]	$\Delta G^0_{gauche} - \Delta G^0_{anti}$ kcal/mol[a]		Rotational Barrier[b] ΔG^* kcal/mol		Temperature and Nucleus[c]
1a	CH_3	33.3[d]	0		8.4 -10.0	(5.2)	-
1b	CH_3CH_2	27	-0.11	(-0.10)	10.6	(6.8)	188,^{13}C,209,^{13}C.
1c	iso-C_3H_7	28	-0.08	(-0.39)	8.1	(6.7)	153,^{13}C,166,^{13}C.
1d	neo-C_5H_{12}	25	-0.18	(-0.12)	13.8	(9.5)	223,^{1}H,254.5,^{1}H.
1e	tert-C_4H_9	100	>1.2	(2.95)	-	(9.6)	-
1f	cyclo-C_6H_{11}	31	-0.03		9.2		159,^{1}H,176,^{1}H.
1g	iso-C_4H_9	27	-0.10		10.3		175,^{1}H,191,^{1}H.

[a] The temperature at which this value was measured is given in the last column. [b] See discussion of the meaning of this term in the text. [c] Temperature at which population was determined, °K, nucleus used, temperature at which quoted barrier was determined, °K, nucleus used. [d] By definition. [e] See discussion in text. [f] See Ref. 4 for other work on 1b. [g] A preliminary report of this compound has been given in Ref. 6 and is corrected as described in the text.

Table 2. Conformational enthalpies ΔH_f°(gas) and barrier heights $\Delta H^{\neq}_{rot}$ of internal rotation about the central C_q–C_q-bond in **1a**–**e** from EFF calculations (torsional angles ϕ (R–C_q–C_q–R) are given in brackets)

$[R-C(Me)_2]_2$		$\Delta H_f^\circ(gas)^{a)}$ /[kcal/mol] (ϕ)				$\Delta\Delta H_f^\circ$[kcal/mol]		$\Delta H^{\neq}_{rot}{}^{b)}$/[kcal/mol]	
		anti		gauche		H_f°(gauche)- H_f°(anti		anti ⇌ gauche (ϕ - 120°)	
		MM2	MMI	MM2	MMI	MM2	MMI	MM2	MMI
1a	CH_3	-53.99 (166°)	-54.72 (162°)	-53.99 (74°)	-54.72 (78°)	-	-	$5.2^{c)}$	6.5
1b	C_2H_5	-58.77 (162°)	-60.20 (161°)	-58.87 (79°)	-60.32 (79°)	-0.10	-0.12	6.8^{d}	8.4
1c	i-C_3H_7	-62.81 (166°)	-60.90 (165°)	-63.20 (71°)	-61.32 (74°)	-0.39	-0.42	6.7	8.5
1d	neo-C_5H_{11}	-86.63 (163°)	-	-86.75 (43°)	-	-0.12	-	$9.5^{c,e)}$	-
1e	tert-C_4H_9	-60.53 (162°)	-58.60 (163°)	-57.58 (87°)	-55.44 (85°)	2.95	3.16	9.6	9.8

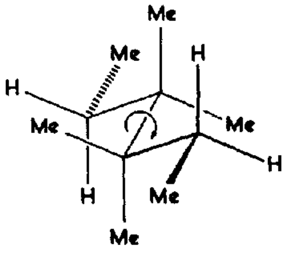
[a] According to the formalism of the MM2 force field[9] a value of 0.36 kcal/mol is added for each C–C-bond excluding C-CH_3-bonds and bonds with hindered rotation (see experimental part). [b] Given is the difference in steric energy between the highest transition state in the energetical preferred rotation process (trans ⇌ gauche) and the most stable conformation. Therefore the $\Delta H^{\neq}$-MM2-values do not include any correction term for internal rotation (see footnote a). [c] See Ref. 7. [d] See Ref. 4. [e] Barrier of rotation about the CH_2-t-C_4H_9-bond in **1d** is calculated to be 6.3 kcal/mol (MM2).

action may be accommodated by distortion which, since the molecule is at a high point on its potential energy surface, need not necessarily lead to an increased energy. In this sense unusually low barriers to rotation in **1c** and **1f** are further examples of steric acceleration of conformational processes,[23] since at a potential energy minimum, distortions in one of *several* directions may reduce interactions comparably well, entropy and enthalpy contributions to lowering that barrier are likely to be associated, so there is a similarity between this picture of the transition state and that described above based on calculations.

We will now consider the molecules **1a** to **1g** individually in some detail.

Hexamethylethane (**1a**). It has often been reported,[4,24] that EFF calculations for **1a** predict a ground state structure with D_3 symmetry, i.e. dihedral angles different from 60°. A gas phase electron diffraction study[25] confirmed this surprising fact. The fully symmetrical conformer (D_{3d}) with normal dihedral angles of 60° corresponds to a saddle point on the enthalpy surface of **1a**. Figure 2(a) shows a section of this hypersurface with the enthalpy as a function of the torsional angle ϕ. The barrier heights of the saddle point relative to the flanking energy minima is calculated to be 0.4 kcal/mol and 1.5 kcal/mol respectively by the MM2 and the MM1 force field. At this saddle point one finds a particularly close approach of two hydrogens per gauche pair of methyl groups. In the calculated (MM2) with reduced symmetry these distances are increased due to alternation of a small (ϕ = 46°) and a large (Q = 74°) torsional angle along the central bond. The same general features of the plot of enthalpy against torsional angle ϕ (R–C–C–R) are calculated for each of the compounds **1a**–**1e** (see Fig. 2–4 and 6). The differences among the plots should help elucidate the factors determining the different rotational behaviour.

The barrier to rotation in hexamethylethane cannot be



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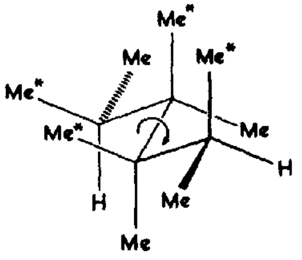

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determined by NMR spectroscopy due to the symmetry of the molecule, but is of interest as a reference point in view of the large number of barriers to rotation in substituted poly-methyl ethanes that have been measured.[6,23,26]

On the basis of the known barrier in the diethyl compound **1b** and in 2,2,3,3-tetramethylhexane, Bushweller, Mislow and their co-workers[4] suggest a value of 8.4 to 8.8 kcal/mol for this barrier. Our calculations and NMR measurements, treated in a similar way would support this value. Higher values of 9.6 kcal/mol[6] and 10.0 kcal/mol[27] have been suggested by other extrapolations of experimental results.

3,3,4,4-*Tetramethylhexane* (**1b**). The conformational behaviour of **1b–d** is more complex than that of **1a** because of reduced symmetry of the groups R. Apart from the gauche-anti isomerism about the central bond which is one of the principal topics of this paper, there are three possible conformations about the C-2–C-3 bond in **1b** (CH_3–CH_2 ⟳ CMe_2–CMe_2Et), two in which the methyl and the CMe_2Et groups are gauche, and one in which they are anti. For all conformations about the central bond, the anti-conformation about the C-2–C-3 bond idealised in structure **18** is of lowest enthalpy by at least 3 kcal/mol (see Ref. 4), so gauche conformations about the C-2–C-3 bond should not be populated. Under the assumption of anti-conformations for both ethyl groups, the plot of enthalpy vs torsional angle at the central bond ϕ (R–C_q–C_q–R) is shown in Fig. 2b. Increasing the size of R from methyl to ethyl increases the strain enthalpy of all conformations, but to a larger extent at the saddle points than at the minima. This causes higher barriers of rotation than in **1a**, in agreement with intuitive predictions. The transition state with two eclipsed pairs of methyl groups and an eclipsed ethyl pair ϕ (R–C_q–C_q–R) = 0°, the gauche to gauche transition state, is slightly higher than the other one ϕ (R–C_q–C_q–R) = 120° with one methyl pair and two ethyl-methyl combinations eclipsed, the gauche-anti transition state. In general the regular shape of the energy function of **1b** (Fig. 2a) predicts normal entropic behaviour of **1b** and **1a**. For both gauche conformations and for the anti-conformation double minima are found with the perfectly staggered 60° or 180° conformations as saddle points between these minima. The double minima of each conformation are nearly equally populated and possess the same symmetry. Therefore, no significant difference in ΔS_f° between the gauche- and anti-conformers of **1b** should exist.[28]

2,3,3,4,4,5-*Hexamethylhexane* (**1c**). In the case of **1c** (R = *i*-C_3H_7) the conformation of the isopropyl groups relative to the rest of the molecule plays a dominating role. The torsional function around the central bond for three possible conformations of the isopropyl side chain (a+, a−, and g) was calculated and is shown in Fig. 3. Due to crossing of the three traces, the torsional itinerary of **1c** around the central bond is more complex than for **1a** and **1b** and indeed the gauche- and anti-form of lowest energy have different conformations of the isopropyl group. Therefore, the rotational interconversion around the central bond must be combined with a rotation around the two C_q-R-bonds (concerted rotation). However, the pathway of lowest energy between these two main minima (see Fig. 3, thick lines) involves more than one simple rotation of the groups R, as suggested by the crossings of the curves in Fig. 3a. The jump from one curve to the other may involve an additional activation enthalpy. Therefore, the rotation process of both groups R was checked carefully near ϕ (R–C_q–C_q–R) = 120°, in order to ensure that the correct height of the barrier was calculated. The saddle point in this region corresponds to a structure with eclipsed C_q-methyl and C_t-methyl bonds and ϕ (C_q–C_q–C_t–H) = 0°, in both groups. The symmetry of the whole molecule at this saddle point ($\Delta H^* = 6.7$ kcal/mol, MM2) remains C_2. The rotation of both groups R occurs simultaneously.

The more complex enthalpy hypersurface of **1c** should have consequences for the entropy of formation of **1c** and for its free enthalpy. Again a double minimum for the anti-form is found, corresponding to two enan-

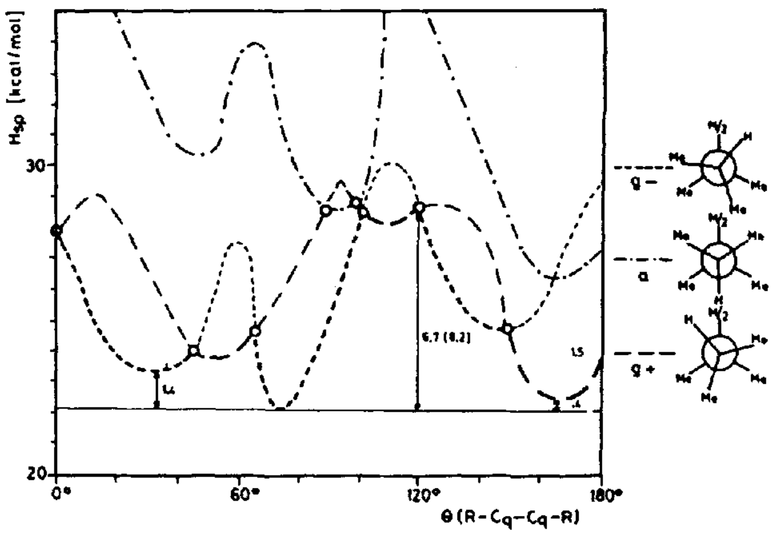

Fig. 3. Strain enthalpy of 2,3,3,4,4,5-hexamethyl–hexane (**1c**) calculated by MM2-force field as a function of the torsional angle ϕ (R–C_q–C_q–R) (R = iC_3H_7) for the three possible conformations of the isopropyl side chain as sketched by their Newman projections along their R–C_q-bonds. The bold-type lines correspond to the pathway of lowest energy between the minima, i.e. all internal coordinates, excluding ϕ (R–C_q–C_q–R), are optimized. Given energy differences for the barrier heights are MM2-results as well as MM1-values (in brackets).

tiomeric structures with ϕ (R–C_q–C_q–R) = 166° and −166°. But the two minima of each gauche conformation differ significantly in their enthalpy, by 1.4 kcal/mol (MM2). The minima with the smaller torsional angle ϕ (R–C_q–C_q–R) = 30° must be populated to a considerably smaller extent therefore than the more stable ones with ϕ (R–C_q–C_q–R) = 70° and −70°. NMR-measurements cannot differentiate between these two gauche-structures. Hence the experimentally determined total population of the gauche conformations should be decreased in favour of the anti-conformations. This "entropic" effect cancels partly the preference of the gauche form **1c** as expected for enthalpy reasons: ΔH_f° (gauche) − ΔH_f° (trans) = 0.4 kcal/mol. The observed population of 28 ± 10% anti is therefore a compromise of opposing enthalpy and entropy effects.

Additional conclusions concerning the entropy may be drawn from the enthalpy curves in Fig. 3. Near the highest transition state for rotation of **1c** (between 80° and 120°) about the central bond, all conformers with different conformations of the group R have nearly the same enthalpy. The interconversion of these seems to be little hindered. This additional freedom of rotation in the transition state compared to the ground state will increase the activation entropy of rotation about the central bond by an amount of about 4–8 e.u.[28] This is a very reasonable explanation of the comparable low $\Delta G^\ddagger_{rot}$ value of **1c** (see Table 1).

2,2,4,4,5,5,7,7-*Octamethyloctane* (**1d**). The conformations of the neopentyl groups in **1d** are very similar to those of the ethyl groups in **1b**. They adopt a torsional angle ϕ (C_q–C_q–C_s–C_q) of 162–170°. A rotation about this bond requires considerable energy and therefore does not effect the dynamic stereochemistry at moderate temperatures. For the other secondary rotation about the CH_2–tC_4H_9 bond a barrier of 6.3 kcal/mol has been calculated (MM2 force field). This threefold degenerate rotational potential has no consequences for the function of enthalpy vs torsional angle ϕ (R–C_q–C_q–R) of the central bond, which is shown in Fig. 4. Surprisingly **1d** (R = neopentyl) is the only structure in the series **1**, which adopts clearly that gauche conformation in which the geminal groups are closest together ϕ (R–C_q–C_q–R) = 43°. Another gauche minimum with ϕ (R–C_q–C_q–R) > 60° is not observed. Only a point of inflection still remains in this region of the curve. The fact that each gauche arrangement has now only one single energy minimum while there exists a double minimum for the anti-structure has entropic consequences. It corresponds to a lower entropy of formation of the two enantiomeric gauche structures compared to the anti one. Consequently the conformational population should be shifted from the normal value gauche: anti = 2.1 towards a 1 : 1 mixture on account of this entropic effect, but the experimental values does not confirm this point.

Additionally surprising is the calculation that the barrier with the two eclipsing neopentyl groups ϕ (R–C_q–C_q–R) = 0° the gauche–gauche barriers, is somewhat lower than the gauche-anti barrier (see Fig. 4).

2,2,3,3,4,4,5,5-*Octamethylhexane* (**1e**). The t-butyl groups R in **1e** with their threefold symmetry axis, simplify the torsional itinerary of **1e** in comparison to **1b–d**. However, in some cases the calculations of the lowest enthalpy for each torsion angle ϕ (R–C_q–C_q–R) (see Fig. 5) involves some difficulties. They arise from the fact that there are two conformations possible at the C_q–$C(CH_3)_3$-bond (see Fig. 5). They possess a different enthalpy of up to 4 kcal/mol. This is so because the methyl groups at the central carbon labelled A and B in Fig. 5, are diastereotopic. There is an energy barrier between the two conformations (Fig. 5) and this causes some difficulties in finding the structures of lowest energy for all points on the curve of Fig. 5.

The resulting curve (Fig. 5) shows an effect not met with for the other compounds. The repulsion between the two t-butyl groups R is decreased by increasing ϕ (R–C_q–C_q–R), overwhelming the "normal" torsional functions like those of **1a** and **1b** (see Fig. 2).

The repulsion between groups R here dominates the conformational equilibrium. The anti-conformations with

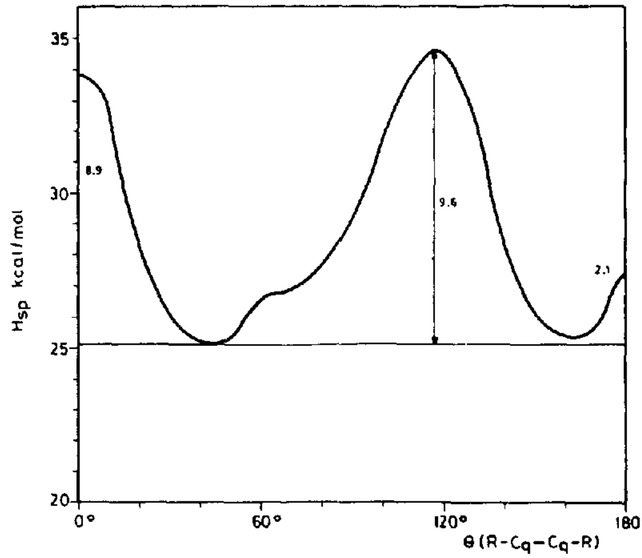

Fig. 4. Strain energy of 2,2,4,4,5,5,7,7-octamethyl-octane (**1d**) as a function of the torsional angle ϕ (R–C_q–C_q–R) calculated by the MM2-force field with all other internal coordinates optimized. Numerical values for the heights of the saddle points are included.

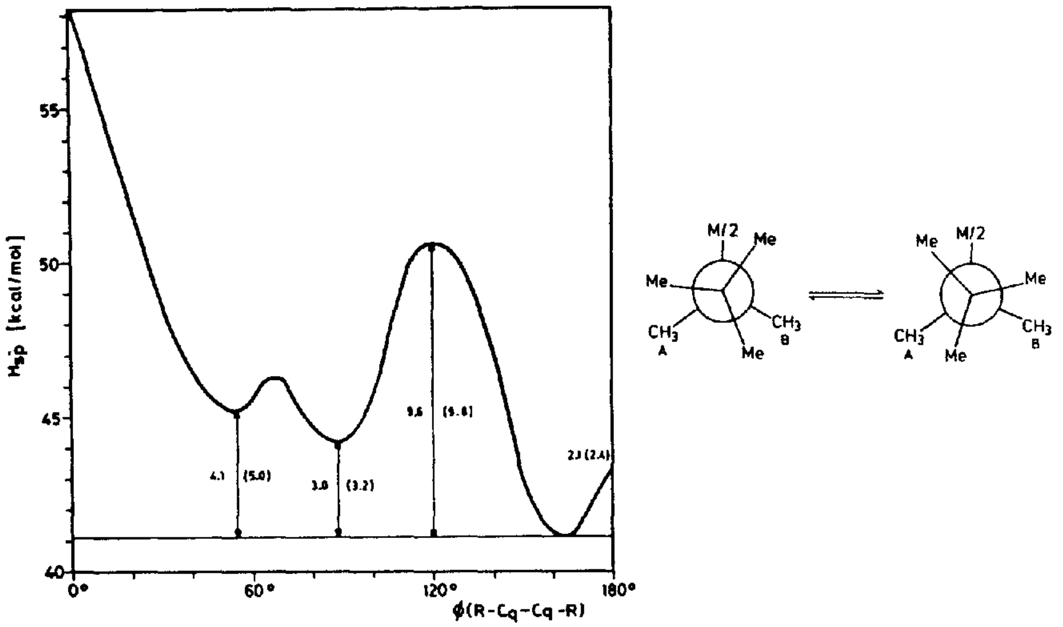

Fig. 5. Strain energy of 2,2,3,3,4,4,5,5-octamethyl-hexane (1e) as a function of the torsional angle ϕ ($R–C_q–C_q–R$) (R = tert-butyl) calculated by the MM2-force field with all other internal coordinates optimized. For the energy-differences MM2- as well as MM1-results (in brackets) are given.

ϕ ($R–C_q–C_q–R$) of about 162° or −162° are the only ones populated to a measurable amount at all temperatures at which **1e** is thermally stable.[12a] **1e** undergoes thermal cleavage of the central bond with a half life of 1h at 195°C.[13d] The barrier of rotation for **1e** is calculated to be nearly the same height as for **1d**, but due to insufficient population of the gauche-conformation of **1e** its experimental determination is impossible.

1,2-Dicyclohexyl-1,1,2,2,-tetramethylethane **1f** *and 2,4,4-5,5,7-hexamethyloctane* **1g**. EFF calculations were not carried out for these compounds, but **1f** where the R group is cyclohexyl has a conformational equilibrium and a barrier to rotation close to those in **1c** which it formally resembles and can reasonably be expected to mimic.

The isobutyl compound **1g** is intermediate between **1b** (R = ethyl) and **1d** (R = neopentyl), in the sense that each of these substituents is primary, i.e. CH_2X, where X is either methyl (**1b**), isopropyl (**1g**) or t-butyl (**1d**). It is striking that the barrier in **1g** is much closer to that in **1b** than to that in **1d**. Populations of conformations are similar in all three compounds.

CONCLUSIONS

The experimentally determined conformational populations of the 2,3-dialkyl-2,3-dimethylbutanes **1a–e** are reproduced very satisfactorily by the EFF calculations. The experimentally determined barriers to gauche-anti interconversion are consistently greater by about 40% than those calculated. Allowing for this error of scale, rotation about the central bond can be followed from the variation of the calculated enthalpy with the torsional angle along that bond. Furthermore some general features for the rotation about $C_q–C_q$-bonds are recognized from these results: The possibility of secondary bond rotations *within the groups attached to the central bond* must be considered in addition to their size and their shape, in explanations of the rotational behaviour. These secondary rotations may lead to a multiplicity of similar energy transition states to rotation which, in the form of a high entropy of activation for rotation, offer an explanation for low experimentally-determined barriers to rotation.

EXPERIMENTAL

NMR spectra were recorded on several spectrometers viz Varian HA100, Varian CFT20, Varian XL200, and Bruker SP400. Barriers were calculated by matching experimental spectra with those computed using a three site exchange programme with two sites isochronous or a two-site exchange programme, where appropriate[29] and free energies of activation reported in Table 1 are considered to be accurate to ±0.3 kcal/mol. Peak intensities were measured by planimetry, and are accurate to ±3%. The population of the anti conformation in **1b–1d**, **1f** and **1g** is certainly less than 33.3%.

The results reported for the neopentyl compound do not agree with those reported by us earlier,[5] recent 200 MHz spectra indicating that the earlier peak assignments were wrong. The earlier report of two singlets of relative intensities 644 to 356 for the methylene proton signal should be replaced by an AB quartet with two weak outer lines, and a singlet overlapping one of the central lines. Our earlier report[5] noted that such an AB quartet should be observed.

Table 3 records proton NMR data for compounds studied and Table 4 records carbon-13 NMR data. The preparation of the compounds **1a–e** has been described elsewhere [13d] along with the physical and spectroscopic data.

EFF-calculations

The calculations were performed by the two available Allinger programs.[9,10b] The formalism of the MM2-force field[9] involves a correction term of the calculated ΔH_f°-value (accounting for internal rotations). According to this arbitrary formalism[21] the ΔH_f°(gas) values (MM2-force field) in Table 1 contain the following correction terms: **1b** 0.72, **1d** 1.44.

The strain enthalpies shown for **1a–d** were calculated from the H_f(gas)-values by subtraction of the following strain-free group increments[3]: CH_3, 10.05; CH_2, 5.13; CH, 2.16; C_q, 0.30 kcal/mol^{-1}.

For comparison the results from Allinger's improved MM2

Table 3. Proton chemical shifts, δ, in the compounds **1b–1g**[a]

		Central geminal methyls		H_α		H_β		
$[R-C(Me)_2]_2$	R =	Room Temp	Low Temp[b]	Room Temp[b]	Low Temp[b]	Room Temp	Low Temp[b]	Other Signals
1b	CH_3CH_2	0.79	0.74(2) 0.79(1)	1.37,m	1.36,m	0.84,m	0.83,m	
1c	iso-C_3H_7	0.86	0.77(2) 0.86(1)	2.03,m	1.98,m	0.94,d	0.92,d	
1d	neo-C_5H_{12}	0.99	0.914(1) 0.920(1) 0.927(1)	1.39	1.43,d 1.29 1.23,d J=14.6	1.04	1.02	
1e	tert-C_4H_9	1.04	1.03	-	-	1.02	1.13(2) 0.84(1)	
1f	cyclo-C_6H_{11}[c]	0.84	0.775(1) 0.84 (1) 0.945(1)	1.55		1.10 1.86		1.29,1.77 both H_δ 1.16,1.65, both H_δ
1g	iso-C_4H_9	0.82	0.85(1) 0.815(1)	1.18,d J=4.7	1.15,m	1.63(m)1.60,m		0.96,d, J=6.6, H_δ

[a] Peaks are singlets unless otherwise stated. The molecules are labelled $[C_\delta–C_\gamma–C_\beta–C_\alpha–C(Me)_2–]–$ and hydrogens are designated by the subscript of the carbons they are attached to. [b] The figures in parentheses give approximate relative intensities, see Table 1 for precise values, and for the temperature for low temperature measurements. [c] The cyclohexyl protons have a complex spectrum, see Fig. 1.

Table 4. Carbon-13 chemical shifts in the compounds **1b–1g**[a]

		Central geminal methyls		Ethane Carbons		C_α		C_β	
$[R-C(Me)_2]_2$	R =	Room Temp	Low Temp	Room Temp	Low Temp	Room Temp	Low Temp	Room Temp	Low Temp
1b	CH_3CH_2	20.87	20.93(1) 20.07(2)	38.84	38.26	29.06	28.72(1)	9.33	9.36
1c	iso-C_3H_7	21.43	21.68(2) 20.91(1)	42.22	41.33(2) 41.59(1)	33.14	32.43(2) 30.79(1)	22.08	22.18
1d	neo-C_5H_{11}[c]	22.62	22.62(5) 21.97(3) 21.44(4)	42.05	41.31(2) 40.92(1)	49.19	48.23(2) 47.70(1)	33.02	32.57
1e	tert-C_4H_9	22.51	22.32	46.26	45.64	41.21	41.10	29.78	28.69(2) 31.60(1)
1f	cyclo-C_6H_{11}[d]	22.53	22.5	42.18	42.10	43.63	43.60	31.36	31.3,m
1g	iso-C_4H_9[e]	21.38	20.93(2) 21.59(1)	39.47	39.21	45.22	44.58	24.98	24.75

[a] The molecules are labelled $[C_\delta–C_\gamma–C_\beta–C_\alpha–C_{ethane}–C(Me)_2–]–_2$. [b] The figures in parentheses give approximate relative intensities, see Table 1 for precise values and for the temperature for low temperature measurements. [c] The γ-carbon is at 32.81, 32.57 at low temperature. [d] The γ- and δ-carbons are at 28.44 and 27.45, and at 28.38 and 27.38 at low temperatures. [e] The γ-carbon is at 26.50, and at 26.56 at low temperature.

force field[8,9] and in most cases from the earlier MM1-force-field[10] are given in Table 1. The improvement in ΔH_f° values produced by the more recent MM2 field results from expressing the torsional potentials of saturated molecules by truncated Fourier series, consisting of one- to threefold cosine functions, instead of only using the familiar threefold cosine function in the MM1-force field. The only other field known to us providing the additional one- and two-fold cosine functions for torsional potentials in alkanes is the MUB-2 force-field.[13b] As already mentioned, the improved MM2 force field is highly reliable[13a] in calculating structures and heats of formation of congested alkanes, even of those possessing substantial strain enthalpies.[12]

EFF-calculations of the hydrocarbons 1 were carried out with full relaxation techniques and all input structures were optimised[9] without symmetry constraints. In order to reduce the large number of possible *input structures* to a manageable number, we considered only such conformations of 1 as have both groups R adopt the same conformation, i.e. have roughly the same dihedral angles. After the minimisation procedure all resulting structures possess at least one twofold axis of symmetry. In test calculations, structures with two different conformations of R ended up in the point groups C_1 or C_i. These structures always had enthalpies between those of the two corresponding symmetrical structures.

The energy profiles for the rotations about the central $C_q–C_q$ bonds of the compounds 1 were calculated using the Wiberg–Boyd bond drive techniques[13c] on the torsion angle of $(R–C_q–C_q–R)$.

REFERENCES

[1] *Internal Rotation in Molecules* (Edited by W. J. Orville-Thomas). Wiley, New York (1974).

[2] S. Sternhell, *Dynamic Nuclear Magnetic Resonance Spectroscopy* (Edited by L. M. Jackman and F. A. Cotton), Chap. 6. Academic Press, New York (1974).

[3] C. H. Bushweller, W. G. Anderson, M. J. Goldberg, M. W. Gabriel, L. R. Gilliom and K. Mislow, *J. Org. Chem.* **45**, 3880 (1980). This paper cites recent work and useful reviews of the subject.

[4] Reference 2 cites original work. For compounds with two functional groups, electronic interactions may also be important.

[5] J. E. Anderson and H. Pearson, *J. Am. Chem. Soc.* **97**, 764 (1975).

[6] E. Osawa, H. Shirahama and T. Matsumato, *Ibid.* **101**, 4824 (1979).

[7] For reviews of the EFF method see footnote 2 in Ref. 3 and Ref. 6.

[8] N. L. Allinger, *J. Am. Chem. Soc.* **99**, 8127 (1977).

[9] N. L. Allinger and Y. H. Yuh, *QCPE*, No. 395.

[10a] D. H. Wertz and N. L. Allinger, *Tetrahedron* 30, 1579 (1974); [b] N. L. Allinger, *QCPE*, No. 318.

[11a] H.-D. Beckhaus, K. J. McCullough, H. Fritz, C. Rüchardt, B. Kitschke, H. J. Lindner, D. A. Dougherty and K. Mislow, *Chem. Ber.* **113**, 1867 (1980); [b] S. G. Baxter, H. Fritz, G. Hellmann, B. Kitschke, H. J. Lindner, K. Mislow, C. Rüchardt and S. Weiner, *J. Am. Chem. Soc.* **101**, 4493 (1979).

[12a] C. Rüchardt and H.-D. Beckhaus, *Angew. Chem.* 92, 417 (1980); *Angew. Chem. Int. Ed. Engl.* **19**, 429 (1980); [b] H.-D. Beckhaus, *Fresenius Z. Anal. Chem.* **20**, 240 (1980).

[13a] H.-D. Beckhaus, G. Kratt, K. Lay, J. Geiselmann, C. Rüchardt, B. Kitschke and H. J. Lindner, *Chem. Ber.* **113**, 3441 (1980); [b] S. Fitzwater and L. S. Bartell, *J. Am. Chem. Soc.* **98**, 5107 (1976)' [c] K. B. Wiberg and R. H. Boyd, *Ibid.* **94**, 8426 (1972); [d] R. Winiker, H.-D. Beckhaus and C. Rüchardt, *Chem. Ber.* **113**, 3456 (1980).

[14] **5** has been investigated by electron diffraction methods,[15] by calculations[13b,16] and by dynamic NMR spectroscopy.[17]

[15] H. B. Burgi and L. S. Bartell, *J. Am. Chem. Soc.* **94**, 5236 (1972).

[16a] E. M. Engler, J. D. Andose and P. V. R. Schleyer, *Ibid.* **95**, 8005 (1973); [b] A. T. Hagler, P. S. Stern, S. Lifson and S. Ariel, *Ibid.* **101**, 813 (1979).

[17] R. J. Wroczynski and K. Mislow, *Ibid.* **101**, 3980 (1979). The barrier to libration is not reported.

[18] A. B. Dempster, K. Price and N. Sheppard, *Spectrochimica Acta* **25A**, 1381 (1969).

[19] Examples in compounds similar to **1** are discussed in some detail in J. E. Anderson and H. Pearson, *J. Chem. Soc. Perkin II* 960 (1973).

[20] The only known hexa-alkyl ethane which does not adopt a conformation with alternating small and large torsional angles along the central bond is the C_1-structure of 3,4-dicyclohexyl-3,4-dimethyl-hexane.[13a]

[21] N. L. Allinger, privately communicated.

[22] The other force field containing the additional one- and two-fold cosine function for torsional potential in alkanes, MUB-2,[13b] seems to overestimate the barrier heights of internal rotation in congested alkanes, see Ref. 4.

[23] J. E. Anderson, C. W. Doecke, H. Pearson and D. I. Rawson, *J. Chem. Soc. Perkin II* 974 (1978).

[24] See for example E. J. Jacob, H. B. Thompson and L. S. Bartell, *J. Chem. Phys.* **47**, 3736 (1967).

[25] L. S. Bartell and T. L. Boates, *J. Mol. Struct.* **32**, 379 (1976).

[26] S. Hoogasian, C. H. Bushweller, W. G. Anderson and G. Kingsley, *J. Phys. Chem.* **80**, 643 (1976) and earlier work cited therein.

[27] C. H. Bushweller, W. J. Dewkett, J. W. O'Neil and H. Beall, *J. Org. Chem.* **36**, 3782 (1971).

[28] For the estimation of entropy by the statistical thermodynamic method see for example S. W. Benson, *Thermochemical Kinetics*. Wiley, New York, 1976.

[29] J. E. Anderson and H. Pearson, *J. Chem. Soc. B* 1209 (1971).

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