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TWO-FOLD ROTATIONAL BARRIERS IN 1,1,2,2-TETRASUBSTITUTED ETHANES
A DYNAMIC NMR AND MOLECULAR MECHANICS STUDY OF SOME HIGHLY-BRANCHED SATURATED HYDROCARBONS.

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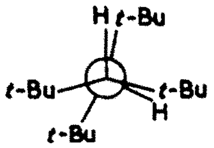
Abstract: The preferred conformation and conformational dynamics of 2,2,3,4-tetramethyl-3-*t*-butylpentane, 2,2,4-trimethyl-3-t-butyl-pentane, and its cyclic analogue cis-2,2,4,6-6-pentamethyl-*iso*-propylcyclohexane are determined by dynamic nmr spectroscopy. Molecular Mechanics calculations for each compound help to illuminate the interpretation of the experimental measurements. In each case the most significant potential minima are two stable distorted *gauche*-ones separated by about 180° of rotation, and a much less stable *trans*-one, so the rotational barrier is two-fold.

While the barrier to rotation in simple polysubstituted ethanes like, for example *1* appears to correlate reasonably well with the interactions to be expected in an eclipsed transition state[1,2], it has become apparent from studies of more highly branched compounds, and from analysis of the details of molecular mechanics calculations[5,6], that other less straight-forward factors may be important in determining the barrier. Further, in such highly-branched compounds, simple symmetrical staggered conformations may involve strong long-range



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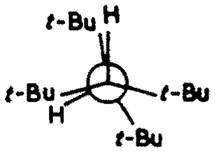

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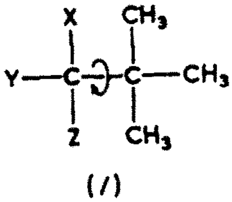

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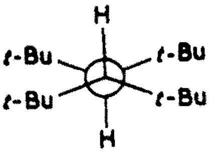

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interactions[3], so that ground-state conformations may be of unusual structure. High or low barriers to conformational interconversion may result largely as a reflection of the stability or instability of these unusual ground-state structures.

In one of the most impressive examples of this, tetra-*tert*-butylethane, 2[7,8,9,10], the typical three-fold rotational potential of ethane is greatly distorted. Two enantiomeric conformations 3 and 4 ('*gauche*-like'), are populated[9] while the third staggered one with the methine hydrogens *anti* is much more unstable. Osawa[10], has calculated that the symmetrical *anti*-conformation 5 is actually an energy maximum, and that in the total sweep from one *gauche* conformation through the *anti*-one to the enantiomeric *gauche*-one, 3 ⇄ 5 ⇄ 4 . the only minima encountered are so shallow and of so high relative energy as to be insignificant in the conformational discussion. The three-fold rotational barrier of ethane has been transformed into a two-fold barrier, and although it has not been measured it is likely to be at least 40kcal/mol[8,10] by analogy with similar compounds[11].

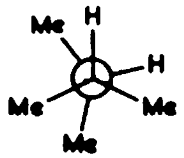
These ground-state conformations for 2 are in fact, particularly stable points in a congested rotational cycle, and a high barrier to rotation is the result. In a comparably complex molecule with no conformation in which congestion is low, rotational barriers will be small. Tri-*t*-butylmethane with a barrier of only about 8kcal/mol[12], is one example.

The steric interactions in 2 which lead to this conformational situation are worth considering.[6a] Two *t*-butyl groups attached to the same carbon atom interact strongly with each other, and with the two *t*-butyl groups at the other end of the ethane bond. The most significant distortions to accommodate these interactions are firstly the opening of the *t*-butyl - $\hat{C}$ - *t*-butyl bond angle, secondly synchronised rotation of individual *t*-butyl groups and individual methyl groups away from perfectly staggered conformations, dihedral distortions, and thirdly coupled to this, rotation away from a staggered conformation about the central ethane bond, another dihedral distortion.

These are all interrelated of course, for as diagram 5 for the *anti*-conformation emphasizes, the Newman projection of each end of the ethane becomes markedly T-shaped. The *tert*-butyl groups on adjacent carbons are thus close to each other in this conformation 5 (the one supposedly favoured by summing *gauche*-interactions), and conformations 3 and 4 represent the best ways of fitting two T-shaped Newman projections together.

As a consequence of these observations of a high two-fold rotational barrier for tetra-*tert*-butylethane and other similar ones[6b,11a,11b], Flamm-ter Meer, Beckhaus, and Rüchardt[11c] subsequently synthesized the diastereomeric 1,2-bisadamantyl-1,2-bis-*tert*-butylethanes and separated the racemic diastereomer into stable rotational isomers (atropisomers due to hindered rotation in a saturated acyclic alkane).

Compound 2 is one of several examples of tetrasubstituted ethanes HCKL—CHMN, 6, adopting unusual conformations, and similar behaviour is shown, albeit less spectacularly even in simple compounds of this kind. In 2,3-dimethylbutane (6, K=L=M=N=CH_3), the conformations 7 and 8 with two hydrogens *gauche* (and thus with formally three *gauche* methyl interactions) are of energy more or less equal to that of the *anti*-conformation 9, (with formally only two *gauche*-interactions)[13,14].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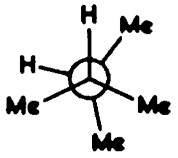
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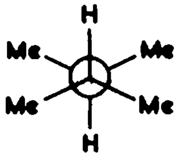
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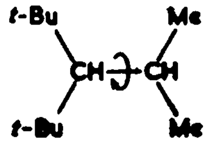
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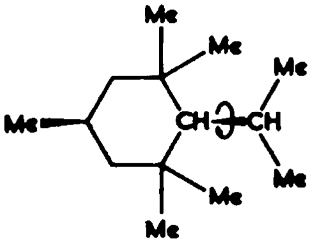
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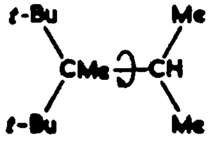
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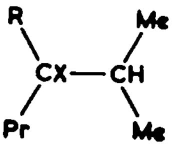
Intermediate members of the series HCKL---CMNH can be expected to show interesting behaviour. We have already investigated tri-isopropylmethane, (6, K,L,=isopropyl, M,N=methyl)[15] and we now want to report on some further examples. Each compound of this type merits discussion in detail so we will restrict ourselves here to reporting the compounds 10, 11, and 12. For compound 10, the conformation about the central bond shown, and that of each *tert*-butyl group, and the barrier to rotation of each of these bonds is of interest. 11 (with the methyl and isopropyl groups in a cis-1,4-arrangement on the ring) is a close cyclic analogue of 10 in which the conformation and rotation of the isopropyl group are the principal points of interest. The pentasubstituted ethane 12 will be compared with 10 to which it is related by addition of one methyl group.

We have also investigated compound 13, its corresponding methylated analogue 14, and compound 15, the methylated analogue of tris-*iso* propylmethane but so much of their conformational behaviour is a reflection of the interaction of isopropyl groups when attached to the same carbon atom, that we will discuss these compounds in a separate paper[16], referring to them only briefly as they are relevant to the discussion of compounds 10, 11, and 12.



(13) R = *t*-Bu , X = H

(14) R = *t*-Bu , X = Me

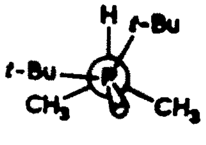
(15) R = *i*-Pr , X = Me

The evidence for the conformational situation in these heavily congested molecules comes in three forms. NMR coupling constants between the two methine protons in CHKL---CMNH should give an indication of populated conformations. Dynamic nmr measurements should allow the determination of rotational barriers, and molecular mechanics calculations should give a fairly detailed indication of the structure of the ground-state conformations, and the potential energy diagram for their interconversion.

The nature of the results which emerge from molecular mechanics calculations of crowded molecules are quite familiar now,[6,17], but general comments as introduction to the present calculations are worth-while. Bond-angle distortion and dihedral distortion are relatively less energy-expensive than bond-lengthening. For tertiary carbon atoms, bond-angle distortion will be particularly important, for C-C-C bond opening can be compensated by H-$\hat{C}$-C bond closing.[6] Dihedral distortion is likely both with tertiary and quaternary carbons; but is particularly favoured when two tertiary carbons are adjacent as in 2, 10, 11, and 18, because the near-eclipsing interactions (see 3 and 4) each involve hydrogen as one substituent and so are relatively small.

Molecular Mechanics are less generally successful in calculating rotational barriers which match experiment[18,19], often predicting enthalpies of activation which are much smaller than experimental free energies of activation. This apparent discrepancy is reduced if a negative entropy of activation for rotation is measured or can be imputed[19]. The quality of the experimental data in the present work was not good enough to allow the determination of rate constants over a wide range of temperatures, from which an entropy of activation for rotation might be derived. We have however calculated rotational potential energy diagrams for 10-12[20,21], and these are reported and discussed later in this paper.

Compound 10 is an analogue of isopropyl-di-tert-butyl phosphine 16 which has been studied by Rithner and Bushweller[22]. The substituents are similar, but since the phosphorus-carbon bonds are about 20% longer than carbon-carbon ones, the interactions we have highlighted will be considerably smaller. The barrier to rotation of the tert-butyl and iso-propyl groups is measured to be 6.7 and 4.8 kcal/mol respectively. In the ground-state conformation, the hydrogen-carbon-phosphorus-carbon dihedral angle is calculated to be 32° corresponding to a structure 17 and the anti-conformation is calculated to be about 3.8 kcal/mol less stable than the gauche ground-state one.



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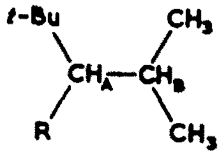

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a)	R = Me	$^3J_{AB}$ = 2.0 Hz
b)	Et	1.8 Hz
c)	iPr	1.4 Hz
d)	t-Bu	0.8 Hz

Results

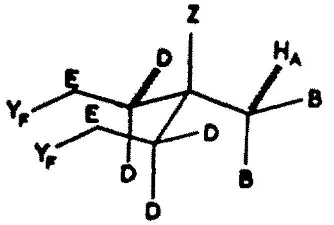
Hellmann, Beckhaus and Ruchardt[20,21] have reported some aspects of the nmr spectra of the 18a, 18b, and 18d (≡10). We have re-examined these compounds and in addition compounds 18$_c$ (≡13)[18] and 11, determining precise values of the coupling constant between H$_A$ and H$_B$ by spectral simulation. The results are reported alongside diagram 18 for these compounds. For 11 the coupling constant is 1.15 Hz, while for tetra-tert-butylethane, the corresponding coupling is 2.0 Hz[8].

NMR spectra of 10 - 12 are temperature-dependent and are described in Table 1 (proton) and Table 2 (carbon-13). The following are the significant facts.

The proton-decoupled carbon-13 spectrum of 10 at 100°C shows the expected five singlets. Figure 1 shows the upfield region of this spectrum at several

Table 1

Proton Chemical Shifts (δ) and Coupling Constants[a] (Hz) for compounds 10, 11, and 12. 'B' and 'D' represent CH_3 groups; 'E' represents a CH_2 group.

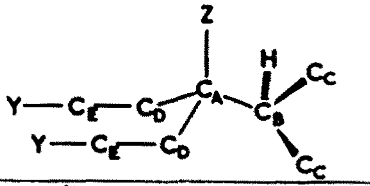


COMPOUND	TEMPERATURE	δA	δB	δz	δD	OTHER δ,J
10	Ambient	2.19	1.15	1.10	1.08	$^{3}J_{AB}$=7.5 $^{3}J_{AZ}$=0.8
Z = H	-75°	2.19	1.15	b	1.08 1.10	
Y = H					(1:1)	
	-140°	c	1.16	c	d	
11	Ambient	2.14	1.13	0.98	1.08(eq)	Y=1.75(H), 0.85(Me), J=6.4
Z = H					1.01(ax)	E=1.37(eq), 1.14(ax), J=14.0
Y = 						J_{AB}=7.4, J_{AZ}=1.15, J_{EY}=5.5, 10.6
	-150°	c	1.15	c	d	
12	Ambient	2.08	1.17	0.85	1.09	^{3}J=7.2
Z = Me	-75°	2.12	1.19	0.88	0.99 1.08 1.26	
Y = H					(1:1:1)	
	-100°	c	c	0.87	c	

Footnotes: a) Arithmetic values, sign not determined. b) covered by other signals. c) not observable at very low temperatures. d) complex.

Table 2

Carbon-13 chemical shifts (δ) for compounds 10, 11, and 12 at various temperatures (°C).



COMPOUND	TEMPERATURE	δA	δB	δC	δD	δE	OTHER δ
10	+50°	61.3	30.1	23.3	37.2	31.5	
Y = H	-50°	59.8	29.7	26.7 19.1 (1:1)	37.2 36.8 (1:1)	31.6 30.5 (1:1)	
Z = H	-125°	58.5	29.6	26.5 19.1 (1:1)	37.1 36.6 (1:1)	36.9 33.8 23.8 (1:1:1)	
						33.9 32.1 25.2 (1:1:1)	
11	35°	55.8	29.7	29.1	36.0	24.6 33.7 50.4 (CH_2)	Y=25.4(CH) 23.6
Z = H	-140°	a	28.9	26.6 30.0	36.0	21.1 28.2; 31.3 35.8 (1:1) (1:1)	24.8 23.5(CH_3)
Y = 						45.5 52.0 (1:1)	
12	25°	48.4	35.2	23.8	42.6	31.6	Z=22.4
Z = CH_3	-50°	47.6	34.8	23.7	42.5	32.3 31.7 30.5 (1:1:1)	22.5
Y = H	-100°	47.1	34.5	24.4 a (1:1?)	42.4 42.2 (1:1)	32.5 31.9 31.8 31.0 29.6 a (1:1:1:1:1:1)	22.5

Footnote: a) obscured by solvent or other peaks.

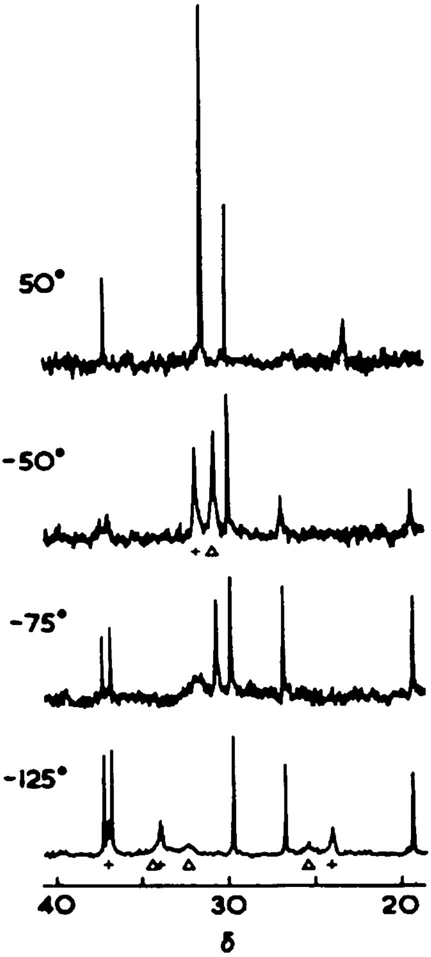


Figure 1
Upfield region of the proton decoupled carbon-13 nmr spectrum of (t-Bu)$_2$C(H)i-Pr, 10 at various temperatures. Three singlets split to doublets when isopropyl group rotation becomes slow (-50°) viz the isopropyl methyl (δ23.3) and the primary (δ31.5) and quaternary (δ37.2) t-butyl carbons. At temperatures below -75° as rotation of the two t-butyl groups becomes slow, the two t-butyl methyl singlets Δ+ split to triplets at different rates (-125°).

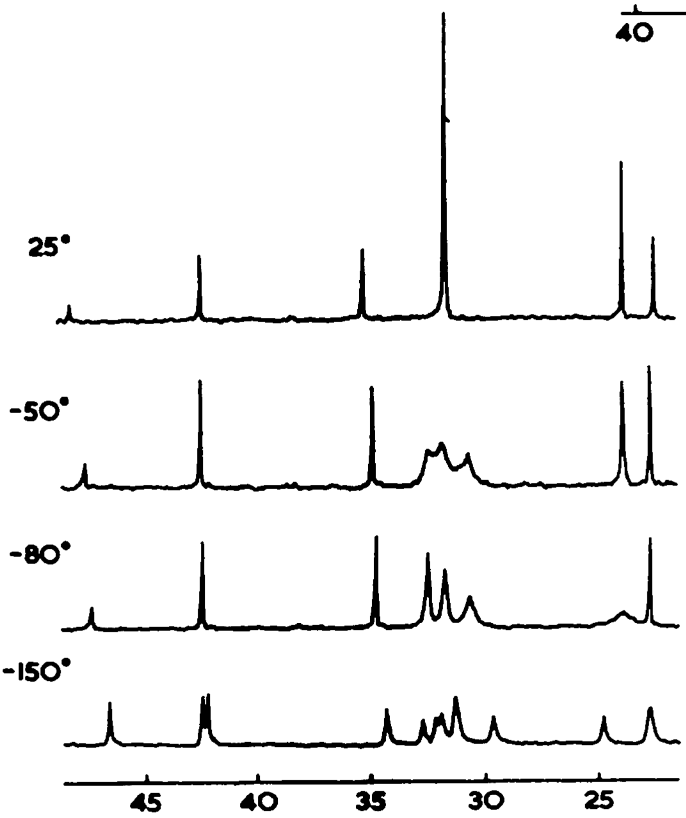
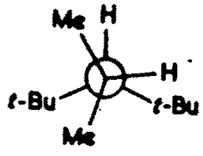


Figure 2
^{13}C nmr spectrum of 12, (t-Bu)$_2$C(Me)i-Pr, at various temperatures. The t-butyl methyl singlet at δ31.5 splits to three singlets as t-butyl rotation becomes slow (-50°). Each of these three, the isopropyl methyl carbon δ23.8 and the quaternary t-butyl carbon δ42.6 splits to a doublet when the isopropyl group rotation becomes slow (-150°

temperatures. Below about 60° the iso- propylmethyl signal, the tert-butyl methyl signal and the quaternary tert-butyl carbon signal broaden and each splits to two equal signals at slightly different temperatures below about -29°. Below about -60° the two tert-butyl signals broaden further then each splits below -79° and -99° respectively to give a 1:1:1 triplet, see Table 2.

The first changes correspond to iso-propyl group rotation ($19 \rightleftharpoons 20$) becoming slow on the nmr timescale, and from the temperature of coalescence the barrier to this process of 11.5 kcal/mol at -29°. The two tert-butyl groups in 19 (or 20) are different on the nmr timescale at this low temperature and the changes in the nmr spectrum on further cooling correspond to rotation of these tert-butyl groups becoming slow on the nmr timescale and a complete line-shape fit of spectra suggests barriers to rotation of 8.4 and 7.6 kcal/mol at -79° and -99° respectively. Analogous changes are observed in the proton nmr spectrum see Table 1, but at very low temperatures a complex overlapping set of broad signals, difficult of analysis, is observed. Nothing incongruous with the carbon-13 nmr spectrum interpretation was observed.



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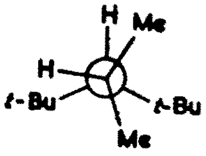

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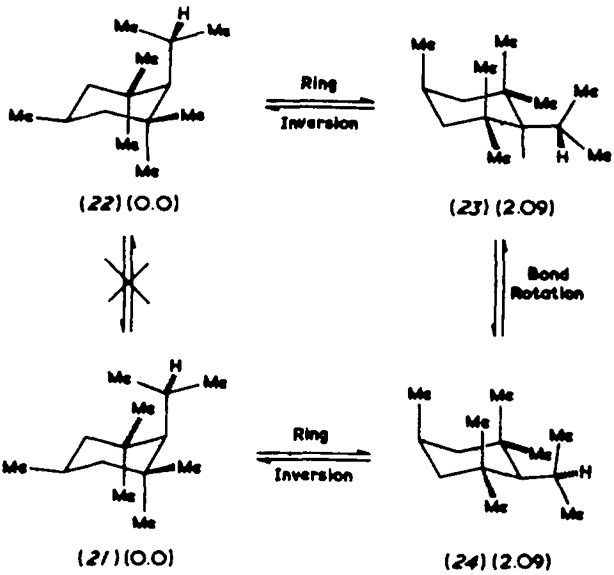
Both the proton and carbon-13 nmr spectra of 12 are temperature-dependent, and Figure 2 shows the latter spectrum with proton decoupling at a range of temperatures. Tables 1 and 2 give full details of both sets of spectra at several different temperatures of particular interest. The most striking aspect is that as the temperature is lowered, changes are first seen in the tert-butyl methyl signal without changes in the iso-propyl signal. The singlet splits into three singlets below about -41° indicating that there is a barrier of 11.0 kcal/mol to the rotation at that temperature. At slightly lower temperatures the iso-propyl methyl signal splits to a doublet, as do each of the three tert-butyl singlets indicating that rotation of the iso-propyl group is now slow on the nmr timescale with a barrier rotation of 9.0 kcal/mol at -84°.

The nmr spectra of compound 11 are reported in Tables 1 and 2. In the carbon-13 nmr there is a doubling of certain signals at temperatures below about -120°. If the cis-compound 11 can be assumed to adopt a chair conformation with the unique methyl-group equatorial and the isopropyl group axial see 21 and 22, these changes correspond to iso-propyl group rotation ($21 \rightleftharpoons 22$) becoming slow on the nmr timescale at these low temperatures. Because of the ring structure there are no complications from other rotations. The barrier to the iso-propyl group rotation is calculated to be 6.6 kcal/mol at -124°.

Molecular Mechanics Calculations

Acyclic molecules 10 and 12 and the two chair conformations of 11, viz. isopropyl—axial 21, and isopropyl—equatorial 23 have been examined. Table 3 reports molecular parameters calculated for the ground state conformations of these four structures using Allinger's MM282 program[17b]. The potential energy diagram for rotation of the iso-propyl group in each of these four structures as calculated by driving the H-C_2-C_1-Z dihedral angle (see Table 3) are shown in Figure 3.



DISCUSSION

The vicinal coupling constant between the methine hydrogens in 10 and 11, 0.8Hz and 1.15Hz respectively, indicates that the adjacent carbon-hydrogen bonds are near orthogonal. There are four commonly-used equations linking dihedral angle between two carbon-hydrogen bonds to the vicinal coupling constant[23-26] Two of these[24,26] do not admit of the coupling constant being as low as the two measured values, at any angle. The other two relations suggest that the dihedral angle is about 74° or 104° for 10, ^4J = 0.83Hz, and about 72° or 106° for 11, ^4J = 1.15Hz. The citations[23-26] of these references give the relation used and specific values of dihedral angles and corresponding calculated coupling constant.

Application of these four equations to compounds 10 and 11 thus sheds no clear light on the question of their conformation, and serves as a caution against seeking to derive much detail from the proposed relations. Conformations with unusual dihedral angles near to 90° are suggested, but nothing more precise than that.

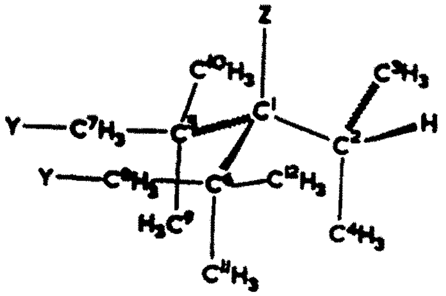
The source of the problems may be that in 10 and 11, there are large distortions from ideal ethane-like conformations, not only dihedral distortions, but others involving bond angles and bond lengths which may affect the applicability of these equations. In any case, these equations are derived from experimental measurements on compounds with their own particular distortions (e.g. bicyclic compounds), or with the modifying influence of electropositive or electronegative substituents, so lack of general applicability is hardly surprising.

It is interesting that in the compound 2 the coupling constant of 2.0Hz is not as small as in 10 and 11. This is best taken as an indication that the dihedral angle is even more distorted away for 60°, beyond the angle around 90° which gives a minimum coupling constant, into the region where the coupling constant is increasing again. In the bis-1,2-adamantyl-bis-1,2-tert-butylmethane analogues of 2, the dihedral angle is 108.8° and 106.6° respectively[11]c. From these values the various equations relating coupling constant to dehedral angle would predict couplings of 1.80-2.17Hz[23], 2.35-2.56Hz[24], 1.34-1.67Hz[25], and 3.38-3.67Hz[26] respectively.

The set of barriers for iso-propyl group rotation reported in this work is quite remarkable as the collation in Table 4 indicates. The barrier in 10 is strikingly large when compared with less-substituted and more-substituted

TABLE 3

Molecular Mechanical Calculations of Conformational Enthalpies, and structures for compounds 10, X = Z = H; 21, 23, Y = —C(H)CH_3—, Z = H; and 12, Y = H, Z = CH_3. Three bond angles at C^1 (and C^2) are greater than 109.5°,'opened up', and three are less than 109.5°,'closed down'. The Bond angle entries are the mean values of three such angles in each case. Δ Dihedral angle is the arithmetic difference between calculated values and 60° (or 180°).



ENTHALPY TERMS (kcal/mol)	10	21	23	12
Total Steric Energy	32.07	34.34	36.43	45.57
Bond Length Distortion	4.27	4.04	3.51	8.59
Bond Angle Distortion	10.10	9.17	11.10	11.91
1-4 van der Waals	8.15	10.61	11.47	9.21
Other van der Waals	2.30	1.11	-0.85	6.88
Torsional strain	6.20	8.41	10.30	7.49
BOND LENGTHS				
C^1--C^2	1.571	1.568	1.561	1.594
C^1--C^5	1.584	1.581	1.570	1.622
C^1--C^6	1.578	1.572	1.567	1.609
BOND ANGLES (°)				
Mean opened-up bond angle at C^1	116.2	115.2	116.3	113.3
Mean closed-down bond angle at C^1	101.5	102.8	101.3	105.3
Mean opened-up bond angle at C^2	114.6	114.5	113.8	114.8
Mean closed down bond angle at C^2	103.6	103.7	104.6	103.3
DIHEDRAL ANGLES				
Mean Δ, Z-C^1-C^5-C	11.0	22.8	3.90	15.0
Mean Δ, Z-C^1-C^6-C	18.1	24.4	8.70	16.8
Mean Δ, Z-C^1-C^2-C/H	27.8	9.5	34.0	21.9
H-C^2-C^1C^5	21.0	43.2	14.2	31.2
H-C^2-C^1-C^6	164.7	179.1	156.8	163.8
H-C^2-C^1-Z	86.5	67.0	93.0	80.8

TABLE 4

Barriers (kcal/mol) for *iso*-Propyl Group Rotation in Compounds of the type $R_1R_2R_3C$——*i*-Pr.

	R_1	R_2	R_3	Barrier	Reference
	CH_3	CH_3	H	4.5	13
	CH_3	CH_3	CH_3	6.9	28, 27
	i-Pr	*i*-Pr	H	6.6	15
	i-Pr	——C(Me)$_2$. CH_2——		6.5	29
10	*t*-Bu	*t*-Bu	H	11.0 8.98(calc)	This work
11	2,2,4,6,6-pentamethylcyclohexyl			6.5 6.22(calc)	This work
12	*t*-Bu	*t*-Bu	CH_3	8.9 6.60(calc)	This work

compounds. The barrier in 11 contrasts with that in 10, and is of the same order as that in much less substituted compounds. The barrier for the most highly-substituted compound 12 is not particularly large.

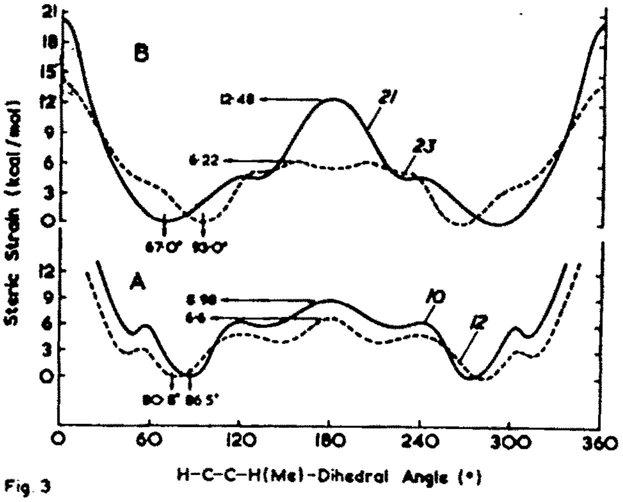


Fig. 3

The rationalisation of such a set of results, as is often the case in crowded molecules, is best done in terms of the stability of the ground state. For a set of such molecules with a similar rotation process, it seems somehow that the transition states, which are equally important of course in determining barrier size, are nonetheless more homogeneous in their total strain. Consider 10 and 12 in the light of molecular mechanics calculations (see Table 3 and Figure 3).

Increasing methyl/*tert*-butyl torsional angles to reduce their ground-state interactions must lead to a reduction of other torsional angles. In 10, the two torsional angles which are particularly small both involve an undemanding hydrogen atom. As a result, rotation away from 60° to diminish strain is as much as 26.5° (if the H--C--C--H dihedral angle of 86.5° is taken as criterion). In 12 compared with 10, one of the undemanding hydrogens has been replaced by a methyl group and the corresponding ground-state dihedral angle is only ± 80.8°. Overall torsional interactions in 12 are thus less reduced in the ground state, and there is in addition a new methyl-methyl torsional interaction at only 31° dihedral angle. This last interaction actually diminishes in the transition state with a dihedral angle of 60° and so favours a lower barrier.

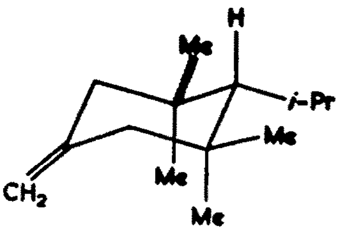
A second important feature of 10 (and of 11 as it happens) which is absent in 12 is the hydrogen atom substituent at each end of the bond. Opening of C--Ĉ--C bond angles at both ends of the bond in 10 relieves strain between geminal substituents but must be accompanied by closing of H--Ĉ--C bond angles. In 12 the additional methyl group will destabilise the ground state by resisting this closing, and the calculated bond angles for 10 and 12 reflect this point.

The third significant feature emerging from the calculations is the much greater total steric strain in the ground state of 12 compared with 11, 45.57 kcal/mol compared with 32.07, even although there is only one additional CH_2-group. Part of this difference arises from the first two features as discussed, but without looking at the total strain in any more detail, these three features make it easy to assign the low barrier to increased strain in the ground state. The calculated barriers (See Table) while not reproducing magnitudes to agree with the experimental values, do find the difference in strain between transition states to be less than that between ground states, i.e. the barrier is calculated to be lower in 12.

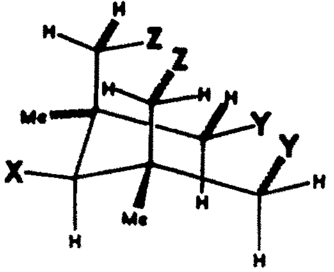
Rotation between the two enantiomeric ground states of 10 and 12 is calculated to take place more easily through the *anti*-conformation rather than through the 0° eclipsed one, see Figure 3. In both compounds, the perfectly staggered 180° anti conformation is calculated to be the high-energy point in rotation, reflecting the large destabilising parallel-1,3-interactions associated[3] with such staggering. The 120° eclipsed conformation is indeed an energy maximum, but the staggered 180° conformation between these two is even higher in energy. The *anti*-conformation is much higher in energy than the ground-state skewed-gauche conformations 40° or 50° on either side of perfectly staggered. The overall picture for both compounds is of two well-defined minima separated by 187° or 198.4° of rotation through a barrier whose profile includes some local minima of insignificant population, in other words, a two-fold rotational barrier with a perfectly staggered transition state.

The barriers are not high because they are two-fold--there is a low two-fold barrier in 12. Nor are the barriers high because they involve rotation through a large arc-- the larger rotational arc of 12 leads to a lower barrier than in 10.

It is particularly noticeable that the *iso*-propyl rotational barrier is much lower in the cyclic compound 11 than in 10. It is not uncommon that the rotational barrier should drop when the substitution pattern is incorporated in a five or six-membered ring[19,30,31]. This may be attributed to two causes. The restrictions of the cyclic system may prevent the ground-state conformation from relaxing to the least strained arrangement that the acyclic system achieves. This restriction must be less important in the transition state. Secondly, the acyclic compound has rotational degrees of freedom not present in the cyclic one, which are likely to be constrained in the transition state for rotation. This entropy effect will tend to produce a higher free energy of activation in the acyclic case. Larger rings with much more freedom of motion give rise to rotational barriers[30] directly comparable to acyclic analogues.



(25)



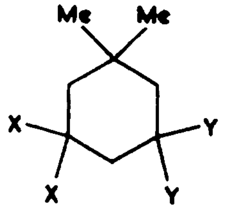
(26)

The results and calculations for the compound 11 deserve some discussion beginning with the question of its configuration and its conformation. From its synthesis by the hydride reduction of the corresponding olefin 25[32], it was expected that the compound we had prepared was the *cis*-compound 12 rather than its *trans*-epimer. The nmr spectrum showed that the ring-methine hydrogen adjacent to the methyl group has coupling of 5.5Hz and 10.6Hz to the two pairs of ring hydrogens next to it. This is consonant with that methine hydrogen's being axial and the ring-methyl group's being equatorial. A *cis*-configuration implies then that the *iso*-propyl group is axial. This is not unreasonable, for in an idealised cyclohexane ring, the preference which substituent X has for an equatorial conformation more or less *disappears* when that substituent is flanked by four methyl groups at positions 2 and 6 (see diagram 26, comparing Z = H, Y = CH_2, with Z = CH_2, Y = H).

We found from our molecular mechanics calculations that the barrier to rotation of an equatorial isopropyl group in conformation 23 of 11 should be 6.28 kcal/mol, while for an axial iso-propyl group in conformation 21 of 11 it should be 12.48 kcal/mol. The barrier we measured experimentally is 6.6 kcal/mol which agrees with an equatorial iso-propyl group. This with the demonstrated equatorial conformation of the methyl group could be taken to imply that the compound we had prepared is of the trans-configuration.

There is an alternative explanation however of the nmr observations in terms of the cis-configuration which the compound used undoubtedly has. Thus the ground-state conformation is as 21, but the route to the isomeric rotational conformation 22 involves ring inversion to an iso-propyl equatorial conformation 24, rotation by the low 'equatorial iso-propyl' path $24 \rightleftharpoons 23$, then finally reverse ring inversion to give 22.

The barrier to ring inversion $21 \rightleftharpoons 24$ is expected to be 8 kcal/mol or less as the progressively decreasing barriers 28a-28c indicate. Conformation 24 is calculated to be less stable than 21 by 2.09 kcal/mol which implies a population on only 0.1% at -120° so it is not surprising that no signs of this conformational exchange (e.g. anomalous signal broadening) are seen in the low temperature nmr.



		ΔG[#]	Reference
(*28a*)	X = Y = H	10.3	34
(*28b*)	X = H, Y = Me	8.7	35
(*28c*)	X = Y = Me	8.0	34

The rotational barrier is measured to be 6.6 kcal/mol for compound 11 (and is calculated to be 6.22 kcal/mol in conformation 24). One cannot reasonably insert a ring-inversion barrier of about 8 kcal/mol into the inversion pathway, and claim that the calculated and experimental values agree well, but if rotation and ring inversion are interdependent rather than discrete processes, and if the calculated 'axial iso-propyl' rotational barrier of 12.48 kcal/mol is kept in mind, the roundabout rotational pathway $21 \rightleftharpoons 24 \rightleftharpoons 23 \rightleftharpoons 22$ is perhaps not too improbable.

It is comparably valuable to list in Table 6, some known tert-butyl group rotation barriers. There seems to be an upper limit of about 12 kcal/mol for the barrier for a tert-group attached to a saturated hydrocarbon fragment, and this is clearly linked to increased strain in the ground state, largely associated with long-range parallel-1,3-interactions. When substituents other than alkyl

Table 5 Barriers (kcal/mol) for the tert-butyl group rotation in compounds of the type $R_1R_2R_3C$ --- $C(CH_3)_3$

	R_1	R_2	R_3	Barrier	Reference
	CH_3	CH_3	H	6.9	27, 28
	CH_3	CH_3	CH_2CH_3	9.4	5
	CH_3	CH_3	$C(CH_3)_2$.t-Bu	11.74	33
2	t-Bu	CH(t-Bu)$_2$	H	7	7
10	t-Bu	i-Pr	H	7.6, 8.4	This work
12	t-Bu	i-Pr	CH_3	11.0	This work

groups hinder rotation--for example halogen atoms, higher barriers may obtain[36]. Another strategy for high barriers is to arrange that torsional and longer range interactions are minimised in the ground state and maximised in the transition state, as in triptycyl or fluorenyl compounds, when much higher barriers result[37] the tert-butyl group rotation barriers of 8.4 and 7.6 kcal/mol for 10 are therefore not unusual in size, and it is reasonable that such chemically different groups within the same molecule show different barriers. Similar behaviour has been observed for 2[7,8]. We believe that the lower of the two barriers observed is for a tert-butyl group with a more hindered ground state, i.e. the one gauche to both iso-propyl groups. More worthy of note perhaps is the increase in barrier in going to 12 with one more methyl group, a quite uncommon sort of substituent effect in such highly-branched molecules.

It is worthwhile making some general observation on the molecular mechanics results in Table 3. Bond-lengthening in 10 and 11 is only 3 or 4 picometers but when there is the additional quaternary centre in 12, lengthening of as much as 8 picometers is calculated, and at the same time bond angle and particularly the H-C-C-C dihedral angle are less removed from ideal values than in 10 and 11. Bond-lengthening is a route to strain minimisation adopted when bond-angle distortion and dihedral distortion become energetically expensive. These two latter distortions are present however to a greater or lesser extent in all fragments of all structures. The potential energy diagrams of Figure 3 bring out well the two-fold nature of the rotation- in a 360° rotation there are two well-defined minima.

Concluding Summary

The compounds 10 to 12 indicate in their observed and their calculated behaviour, the extent to which distortion away from ideal saturated hydrocarbon structure can happen. The particular feature of the 1,1,2,2-tetrasubstituted ethanes is rotation away from 60° staggered conformations, opening of certain bond angles, and the closing of others (involving hydrogen). A two-fold as opposed to the usual three-fold potential results, and further substitution produces lower rotational barriers. A ring system as substituent leads to lower barrier to rotation than a formally-equivalent acyclic substitution pattern.

Experimental

The synthesis of 10 and 12[20,21a] and of 11[32b] have been described elsewhere. NMR spectra from a Varian XL200 spectrometer are for~0.1M solutions in~4:4:1 $CHFCl_2$:CHF_2Cl:CD_2Cl_2. Errors in the reported coupling constants arising from the assumptions made inspectral simulation and from digitisation are estimated to be ±0.1Hz. Errors in the free energies of activation quoted arise from the simulation method, and more particularly from uncertainties as to sample temperature (which was taken form the spectrometer's thermocouple calibrated by a methanol or a 2-chlorobutane thermometer), and are estimated to be ±0.3kcal/mol.

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