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Exploratory Calculations of Medium and Large Rings

Part 1. Conformational Minima of Cycloalkanes

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A novel approach to the semiquantitative calculation of the conformational energy of C_9-C_{16} cycloalkanes is based on simple summation of the energy in all CC-bonds, as read off from their dihedral angles on the complete potential curve for internal rotation about the central bond in butane. All 1,2-, 1,3- and 1,4-hydrogen interactions are thereby included. Valency angles are kept constant and such strain neglected. The selection of conformations is based on a scheme for joining together three, four, or five straight-chain side-units; even-membered rings have quadrangular conformations, odd-membered the more strained triangular and quinquangular conformations.

Computer calculations of cycloalkane conformations by minimization of both valency-angle strain, torsional strain and non-bonded interactions have been carried out systematically only for rings up to and including cyclononane.[1–4] For ten-, eleven-, and twelve-membered rings a few sporadic calculations [1–4] have been reported. For higher cycloalkanes no attempts seem to have been made, but a qualitative analysis [5] led to the conclusion that for C_{14} as well as for C_{16} a single strainfree diamond-lattice conformation is possible, whereas odd-membered rings have none. However, nothing at all is known about which conformations odd-membered rings above C_9 adopt, or what is the nature of the other conformations of cyclohexadecane known [6] to be present above its solid-solid transition temperature.

The methods used to calculate conformations of normal and medium rings have the general limitation of increasing complexity as ring size increases, and no satisfactory systematic method for selecting the types of conformations to be tested has been proposed. Thus, only conformations with symmetry elements are handled by Hendrickson's method,[1] and in the steepest-descent method of Wiberg [2] and of Bixon and Lifson [3] further and lower minima may not be detected and false minima may appear.

In the same way as variation of bond length is energetically expensive and produces small geometric changes and therefore has been neglected in those calculations, it seemed justified in large rings to neglect also valency-

angle deformation, since this is more expensive and produces much smaller changes than variation of torsional angles. Furthermore, if instead of using the ethane torsional potential, the complete potential curve for internal rotation about the central bond in butane is applied, this will automatically take care also of non-bonded interactions between hydrogens in 1,2-, 1,3-, and 1,4-relationship. (Of course, such a procedure cannot be used for normal rings where the 1- and 4-carbon atoms are not repelled at short distances, but linked by one or a few bonds.) Other hydrogen interactions (1,5- and higher) can usually be avoided by adjusting the conformation so that these hydrogen distances are kept above a minimum value. This limit was chosen as short as 1.8 Å since the Fieser-Dreiding molecular models [7] used to construct the conformations and obtain dihedral angles, have tetrahedral valency angles instead of a more realistic value of 112°. Conformations which cannot be physically constructed without shorter H – H distances are rejected, except in medium rings; their calculated energies are therefore obviously too low. It should be noted that computer calculations on medium rings, especially those of Bixon and Lifson,[3] reveal that a substantial part of the strain is in fact torsional strain, and that similar total energies and geometries result from rather different distributions of the strain on valency-angle strain, torsional strain and non-bonded interaction. This suggests that a considerable part of the non-bonded interactions can be traded into torsional strain by small adjustments of dihedral angles and justifies the simplified procedure used here for the larger rings.

CONSTRUCTION OF POTENTIAL CURVE FOR BUTANE

The enthalpy difference between *anti* and *gauche* butane has been determined by several experimental methods, and the chosen value of 0.8 kcal/mol is also in agreement with theoretical values.[8,9] The dihedral angle for the *gauche* minimum was placed at 65°, close to the electron-diffraction value [10] of 67.5°, while theoretical values [8,9] are around 70°. Good experimental values for the barriers have only recently become available. Ultrasonic relaxation of butane [11] gives a barrier height between *anti* and *gauche* of 3.8 kcal/mol in enthalpy terms, and a relaxation value for methylbutane,[11] involving the passage of two methyl groups past each other, allows the adoption of an enthalpy value of 6.9 kcal/mol for the *syn*-barrier in butane. Both values are in surprisingly good agreement with recent *ab initio* calculations.[8,9]

These points are then connected with sine-shaped curves (Fig. 1). For the present exploratory calculations on mechanical models, with dihedral angles manually adjusted to minimize the energy, it was considered unrealistic to read off angles to an accuracy better than a couple of degrees. Only values for every five degrees were therefore taken from this curve and tabulated for ready use in the calculation.

SELECTION OF CONFORMATIONAL CANDIDATES

In large rings there is sufficient freedom of choice that the best conformations have only relatively staggered bonds, and as many as possible are *anti*. For rings to be formed, a certain number of *gauche* bonds must be accepted,

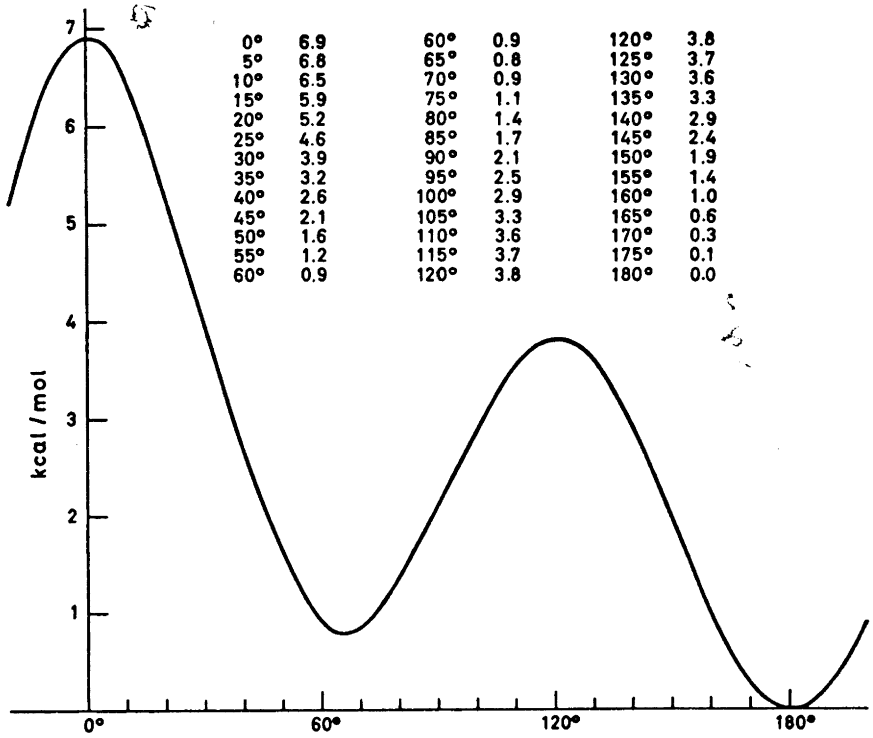


Fig. 1. Potential energy curve for butane.

and the problem is to find the smallest possible number and the best distribution as regards relative position and sign of their dihedral angles.* In Fig. 2 are shown the various possibilities when one or a sequence of *gauche* bonds are in an *anti* environment. A "wedge" representation of the CC-bond is introduced already here, since it had to be used for top-view perspective drawings of the larger rings; such drawings were found much more convenient than the familiar side-view perspective drawings. As an illustration, top-view representations of the diamond-lattice conformations of C_6-, C_8-, and C_{10}-rings are included in Fig. 2, a-c.

An isolated *gauche* bond (Fig. 2d) is defined as "allowed", since it has only the strain of one *gauche*-butane interaction. This arrangement is not very efficient for chain bending and becomes of interest only for rings larger than the 16-membered; it can in fact be used six times with alternating sign to produce one of the diamond-lattice conformations of cyclooctadecane.[5]

A sequence of two *gauche* bonds of the same sign (Fig. 2e) is also allowed; in fact, the two sets of 1,4-hydrogen interactions are essentially unperturbed

* Looking along the axis of a bond, a + sign means clockwise rotation of the rear ring-bond away from the front ring-bond, a − sign counterclockwise.

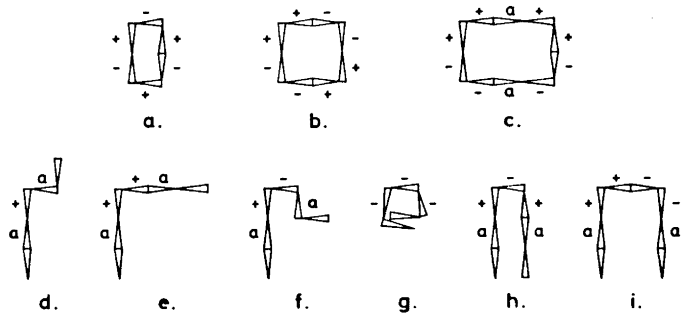


Fig. 2. "Wedge" representation for the CC-bond in some carbon ring skeletons (a – c) and some folded open chains (d – i). a = *anti*, + = + *gauche*, – = – *gauche*.

by one another.[12] This sequence is efficient for chain bending and is used four times in unstrained diamond-lattice conformations of large rings as well as in the established conformation of cyclododecane.

A sequence of two *gauche* bonds of opposite sign (Fig. 2f) is excluded by a prohibitively large steric interaction in open chains [12] (the so-called 1,5-pentane interaction). It is little efficient for ring formation and therefore not even encountered in medium rings.

A sequence of three (or more) *gauche* bonds of equal sign (Fig. 2g) is allowed, as there will be no interactions more serious than 1,4-*gauche*; however, only a helix-structure will result.

A sequence of three *gauche* bonds of alternating sign (Fig. 2h) leads in principle to a formidable steric conflict (1,6-hexane interaction). A systematic deviation from 60° dihedral angles may nevertheless relieve the interaction sufficiently to allow the acceptance of this element in the inherently strained medium rings and odd-membered large rings, since this double chain-bend is particularly efficient for ring formation.

A sequence of four *gauche* bonds is of interest only when two equal signs are followed by two equal opposite signs (Fig. 2i). This is actually nothing else than a combination of two chain bends of the allowed type (e), but involves a considerable strain (1,5- and 1,7-interactions). Again, a systematic deviation from 60° dihedral angles may relieve much strain so that this element may become of interest even for odd-membered larger rings; for medium rings it is an indispensable element.

It is easy to show that the best chain-bend element (+ *gauche*, + *gauche* or – *gauche*, – *gauche*) is perfectly suited to join together, at right angles in a projection on the main molecular plane, four side-units, each consisting of straight all-*anti*-chains, to give diamond-lattice conformations of rectangular or square shape. Also less regular conformations can be formed in this way, but only for even-membered rings. This general type of conformation will here be called "quadrangular". If the ring is to remain even-membered, there can be only four types of quadrangular conformations (Fig. 3): all four sides contain an odd number of bonds; two adjacent or opposite sides are odd and the others even; or all sides are even.

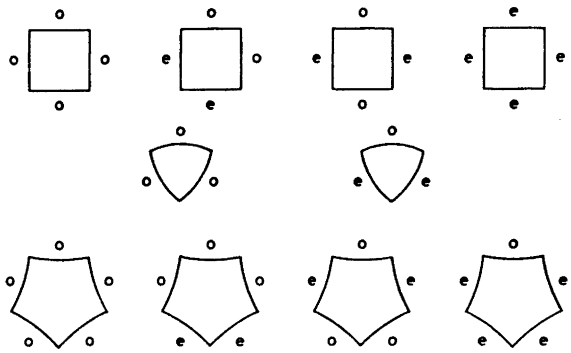


Fig. 3. Allowed combinations of ring "sides" having an odd or even number of bonds.

For odd-membered rings it can be similarly shown that it is impossible to fit together four sides so as to form the above type of "corners". Either three- or five-corner conformations will be the best alternatives and give least deformation at the corners, ideally at right angles in the ring projection. The former type will be called "triangular" and must have one or more "convex" sides (Fig. 3). The latter type will be called "quinquangular" and must have one or more "concave" sides (Fig. 3). Being odd-membered, these rings will have only two types of triangular conformations (Fig. 3): all three sides contain an odd number of bonds; or two sides are even and one odd. Similarly, there are four types of quinquangular conformations (Fig. 3): all sides contain an odd number of bonds; two adjacent or next-to-adjacent are even and the other three odd; or one is odd and four even.

It may be noted that the present scheme for selecting conformations will include conformations of odd-membered rings having a two-fold axis of symmetry, and their isoclinal position [1] is in fact nothing else than a + +(or − −)*gauche*, *gauche* corner. On the other hand, the corresponding [1] conformations having a plane of symmetry are all left out. This is entirely logical, since a C_s-conformation must have one *syn*-bond and so be on a potential maximum rather than in a minimum. It is therefore not classified as a conformation, but as a symmetric barrier separating two equivalent unsymmetric conformations (see Part 2).

Before setting up the formally possible conformations according to the present scheme, which by the way is independent of symmetry, the restriction was placed on 14-membered and higher rings that one- and two-bond sides be used not more than twice, so as to avoid the handling of an excessive number of non-competitive conformations.

STRAIN CALCULATION ON MOLECULAR MODELS

About half of the formally derived conformations could be eliminated in the model-building step, since they could not be made without prohibitively short hydrogen-hydrogen distances. The remaining possibilities were then

constructed with commercial Fieser-Dreiding models,[7] which had their bond rotation sufficiently braked by putting thin paper strips between tubes and sticks so as to allow the "freezing" of any chosen conformation. The energy minimization was carried out manually by trying to improve the most eclipsed bonds without creating worse problems elsewhere, in particular by keeping all 1,5- and higher hydrogen interactions above 1.8 Å, or as little below this value as possible in medium rings. It was encouraging that this procedure gave the

Table 1. Calculated conformational strain enthalpies of cycloalkanes.

	Conf.	$\sum H$	H_0	ΔH		Conf.	$\sum H$	H_0	ΔH
C_9:	[234]	18.5	11.3	1.4	C_{10}:	[1243]	25.4	18.2	12.2
	[333]	17.1	9.9	0		[1324]	17.9	10.7	4.7
	[12222]	19.9	12.7	2.8		[1333]	14.6	7.4	1.4
						[1414]	14.0	6.8	0.8
						[2233]	14.6	7.4	1.4
						[2323]	13.2	6.0	0
C_{11}:	[155]	22.5	15.3	6.1	C_{12}:	[1335]	19.0	11.8	9.4
	[227]	27.8	20.6	11.4		[1344]	17.1	9.9	7.5
	[245]	18.7	11.5	2.3		[1434]	21.3	14.1	11.7
	[335]	16.6	9.4	0.2		[2235]	21.7	14.5	12.1
	[344]	16.4	9.2	0		[2325]	21.3	14.1	11.7
	[12323]	16.1	9.5	0.3		[2334]	14.1	6.8	4.4
	[13223]	17.0	9.8	0.6		[2343]	14.0	6.8	4.4
						[2424]	17.2	10.0	7.6
						[3333]	9.6	2.4	0
C_{13}:	[247]	26.9	19.7	13.0	C_{14}:	[2345]	20.7	13.5	13.5
	[256]	23.7	16.5	9.8		[2435]	15.2	8.0	8.0
	[337]	21.7	14.5	7.8		[2444]	14.4	7.2	7.2
	[346]	18.3	11.1	4.4		[2525]	20.4	13.2	13.2
	[355]	16.1	8.9	2.2		[3335]	13.0	5.8	5.8
	[445]	15.6	8.4	1.7		[3344]	9.8	2.6	2.6
	[12433]	13.9	6.7	0		[3434]	7.2	0	0
	[13333]	15.0	7.8	1.1					
C_{15}:	[357]	16.1	8.9	4.6	C_{16}:	[2446]	17.2	10.0	10.0
	[366]	15.8	8.6	4.3		[2455]	20.9	13.7	13.7
	[447]	15.8	8.6	4.3		[2464]	16.2	9.0	9.0
	[456]	15.1	7.9	3.6		[2536]	13.8	6.6	6.6
	[555]	15.0	7.8	3.5		[2545]	10.8	3.6	3.6
	[12534]	14.1	6.9	2.6		[3346]	16.0	8.8	8.8
	[13344]	19.3	12.1	7.8		[3355]	13.8	6.6	6.6
	[13353]	14.0	6.8	2.5		[3436]	13.6	6.4	6.4
	[13434]	14.2	7.0	2.7		[3445]	10.4	3.2	3.2
	[13443]	13.0	5.8	1.5		[3454]	10.6	3.4	3.4
	[14334]	12.7	5.5	1.2		[3535]	8.4	1.2	1.2
	[23334]	15.9	8.7	4.4		[4444]	7.2	0	0
	[23343]	17.7	10.5	6.2					
	[33333]	11.5	4.3	0					

$\sum H$ = total calculated strain enthalpy (kcal/mol).
H_0 = strain enthalpy relative to best conf. of cyclotetradecane.
ΔH = strain enthalpy relative to best conf. of the same cycloalkane.

same results when repeated from different starting points. All dihedral angles were then read off to the nearest 5° value, again with no problem of reproducibility, and the total conformational enthalpy calculated from the tables in Fig. 1.

This procedure cannot of course give numerical values reliable to more than ± 1 kcal/mol. Nevertheless, the results are given in Table 1 with one decimal, and for the only reason that these represent the lowest values actually obtained for each conformation.

A shorthand notation for conformational type is used in Table 1, consisting of a series of numbers within brackets, each giving the number of bonds in one "side", starting with the shortest. The direction around the ring is so chosen that the following number is smallest possible. A triangular conformation is thus uniquely defined by three numbers, a quadrangular by four, and a quinquangular by five; the sum gives the ring size.

In Table 1 the conformational enthalpies are compared with that of the lowest conformation of the least strained ring, taken to be the diamond-lattice conformation of cyclotetradecane. In addition, all conformers of each ring are compared with the one among them which is of lowest enthalpy. Finally, the actual geometries with dihedral angles indicated are shown in Figs. 4 – 11 for all conformers calculated to be less than 6 kcal/mol higher than the best conformer of each set, except in the case of cyclopentadecane where only the six lowest out of twelve are given. It may be noted that the sign of the dihedral angle alternates along all convex sides, whereas in a concave portion a near-*anti* bond gets the same sign as neighboring bonds.

GENERAL DISCUSSION OF RESULTS

The listing order of tested conformations in Table 1 follows the shorthand notation and therefore implies that the most regular conformations come last. It is immediately seen, and might have been intuitively expected, that these are of lowest enthalpy in even-membered rings and among the triangular conformations in odd-membered rings. For quinquangular conformations, however, this is true only in the case of the largest ring considered, cyclopentadecane. The best of all cyclotridecane conformations is in fact a completely irregular quinquangular one having one single-bond side, and several conformations of this type are of lower enthalpy than any of triangular type also in cyclopentadecane, and of equal energy in cycloundecane. In general, the potential minimum is not well-defined in such cases, and the enthalpy may vary smoothly from that of a very irregular triangular conformation [*abc*], where c is much larger than a and b, to that of a quinquangular conformation [*1xaby*], where $1+x+y=c$. This is formally acceptable, since dihedral angle signs are alternating in the same way along a convex side of c bonds as through the two corners adjoining a one-bond side. It is also energetically acceptable, since in both forms many of the bonds in question will have to be very high up on either sides of the 120° barrier, and it is merely a question of continuous redistribution of strain on these bonds. Sometimes there is even a problem of classification, since a definition based on whether the ring projection "looks" triangular or quinquangular, and a definition based on whether the relevant dihedral angles are above or below 120°, may lead to different results.

If the dihedral angles of the outer two bonds are considerably above 120° in sufficiently large rings, the strained *+gauche, −gauche, +gauche* sequence will effectively degenerate to a strain-free *anti,gauche,anti* system (Fig. 2d).

It is interesting to note that a given quinquangular conformation having one single-bond side is closely related to a quadrangular conformation of the even-membered ring immediately below and immediately above its ring size, and it can be derived from these by insertion of one bond at a corner "ring expansion") or by cutting off a corner ring-atom ("ring contraction"), respectively. Thus, in cases where such quinquangular conformations have lower energies than their triangular partners, it is clearly more favourable to keep the main part of the ring skeleton diamond-lattice-like and concentrate the inherent strain at a few bonds, rather than to distribute the strain over many bonds in a more symmetric fashion.

A comparison of the calculated lowest enthalpies for the different ring sizes is shown graphically in Fig. 12, where also experimental strain energies from combustion calorimetry [13,14] are given. The deviation of calculated from experimental values is clearly systematic and larger than the reproducibility of the method. First of all, the calculated values are too low for all medium rings, and this is obviously due to the necessity of accepting too short 1,5- and 1,6-hydrogen interactions (marked in Figs. 4 – 7). Secondly, the odd-even alternation is too strong, which may be due to the use of fixed tetrahedral valency angles. If the experimentally established value close to 112° for the CCC-angle had been used, clearly this would have led to less favourable dihedral angles in the near-diamond-lattice conformations of even-membered rings and raised their enthalpy, whereas the inherent bond-eclipsing in odd-membered rings would be reduced and their enthalpy lowered (compare Hendrickson's calculations [1] of normal rings with tetrahedral and 112° angles as "normal" value).* On the other hand, the enthalpy order among individual conformations within those medium rings for which more rigorous calculations have been made, comes out the same, and the lowest-enthalpy conformations of larger rings are those found experimentally wherever information is available.

It is interesting to note in Fig. 12 that the enthalpy of the lowest conformation of each type (triangular, quadrangular or quinquangular) decreases very regularly with increasing ring size.

The number of low-enthalpy conformations of the types considered here increases very much in the 15- and 16-membered rings (Table 1), and the increase must be expected to continue exponentially in higher rings. For this reason, and because other conformational types having also isolated *gauche* bonds will start to be competitive in the 17- and 18-membered ring, the number of conformations with low and close-lying enthalpies would be so large that this type of exploratory calculation is hardly worthwhile.

* A further systematic error is introduced by the energy summation procedure, since each 1,3-interaction in the ring is actually counted twice (1,2- and 1,4-interactions are correctly counted once). This is, however, only of importance at the 120° barrier, where a double 1,3-interaction in butane contributes 0.8 kcal/mol, the barrier in propane and ethane being 3.4 and 3.0 kcal/mol, respectively. This again will tend to accent the alternation, since odd-membered rings have more dihedral angles approaching 120° and come out too strained from the calculation.

DISCUSSION OF INDIVIDUAL RINGS

Cyclononane (Fig. 4). The lowest-enthalpy conformation is of triangular type [333] and identical with the D_3 conformation found by more rigorous methods,[1–3] and also established experimentally [15] by low-temperature ^{13}C

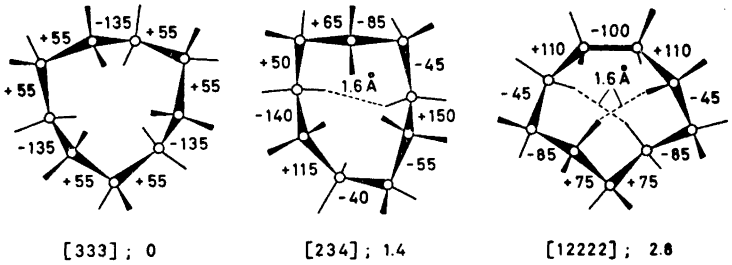


Fig. 4. Lowest minima for cyclononane.

NMR. It is of particular interest that an asymmetric triangular conformation [234], never considered before, is found to be only 1.5 kcal/mol less stable; it may be thought of as being formed by ring contraction of the diamond-lattice conformation [2323] of cyclodecane. The third may be defined both as quinquangular [12222] and as triangular [225], and can be derived by ring expansion of the diamond-lattice conformation [2222] of cyclooctane (Fig. 2b). It is identical with the ring conformation found for crystalline cyclononyl ammonium bromide,[13] and its relative enthalpy is calculated by Hendrickson [1] to be 2.2, by Bixon and Lifson [3] 3.9, while the present value of 2.8 kcal/mol is intermediate.

Cyclodecane (Fig. 5). The lowest conformation is as expected the "rectangular" diamond-lattice [2323] established for a number of derivatives.[13] Only 1.4 kcal/mol higher are two conformations [2233] and [1333], identical with the two found as a mixture in the crystal of 4,4,8,8-tetramethylcyclodecanecarboxylic acid and then calculated to have relative enthalpies of 2.1 and 3.1 kcal/mol, respectively.[13] Unexpectedly, the very low relative enthalpy of 0.8 kcal/mol was obtained for the *trans*-decalin-like conformation [1414], which can also be considered as a deformed crown conformation. Another type of deformation, the stretched crown, has sometimes been discussed,[1] but would be classified as a barrier in the present scheme and is of much higher enthalpy (see Part 2). The [1414] conformation has already been proposed [16] for the solution conformation of cyclodecane-1,6-dione.

Cycloundecane (Fig. 6). For this ring as many as four conformations have about equally low enthalpies, the two most regular triangular, [344] and [335], and two irregular quinquangular, [12323] and [13223]. The [344] conformation comes out lowest also in the calculations by Bixon and Lifson.[3] The [335] conformation is an example of a set where a clear triangular type is of much lower enthalpy than the corresponding quinquangular [12332]; both can be thought of as being formed by ring contraction from the [3333] cyclododecane conformation. The opposite situation is represented by [13223] which is clearly

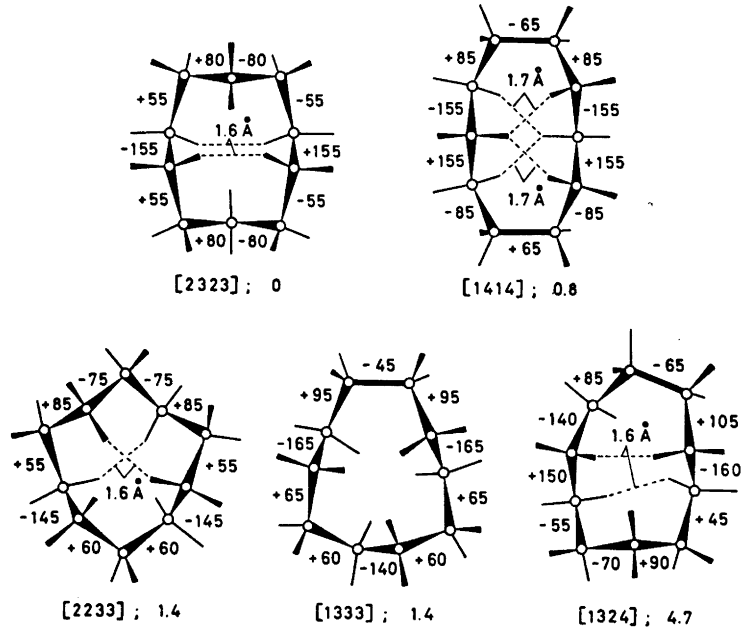
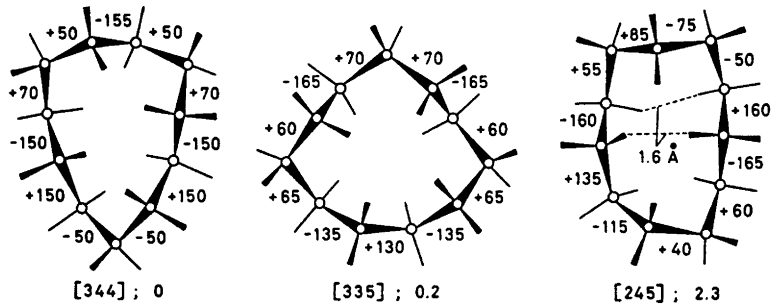


Fig. 5. Lowest minima for cyclodecane.



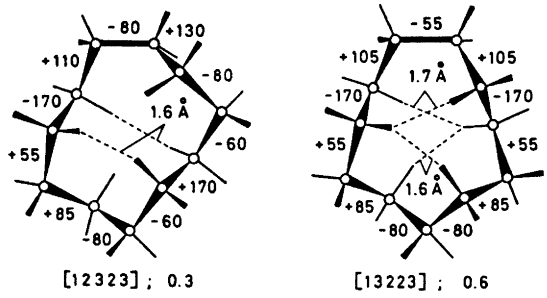


Fig. 6. Lowest minima for cycloundecane.

quinquangular of type and of much lower enthalpy than is triangular partner [227]; these can both be derived by ring expansion from the [2233] cyclodecane conformation. The ill-defined conformation marked [12323] is intermediate of character since it results on attempts to minimize both a quinquangular and a triangular type [236]; it is derivable by ring expansion from the [2323] cyclodecane conformation.

Somewhat higher in enthalpy is the unsymmetric triangular conformation [245].

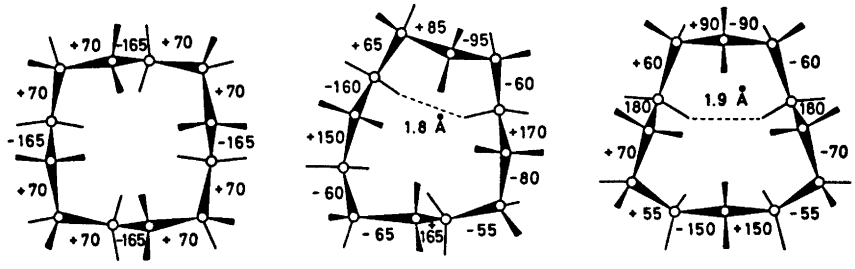
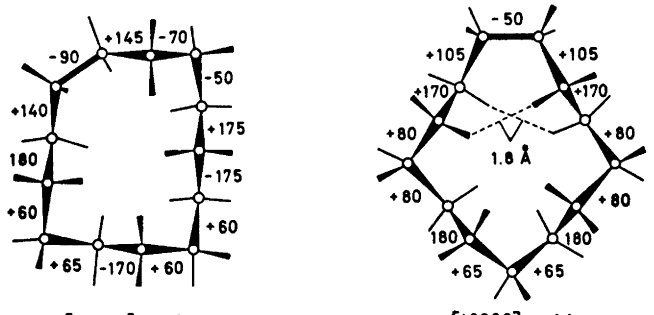


Fig. 7. Lowest minima for cyclododecane.



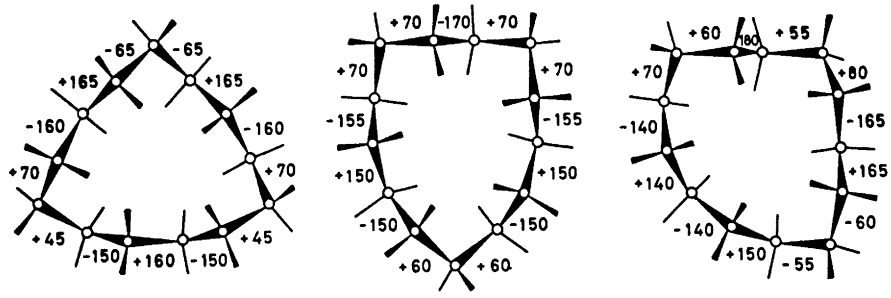


Fig. 8. Lowest minima for cyclotridecane.

Cyclododecane (Fig. 7). This is the conformationally most homogeneous ring of all studied, although its favoured "square" [3333] conformation is not of diamond-lattice type. It is identical with the one found experimentally in the crystalline state,[13] and is also the one calculated to be of lowest enthalpy by Wiberg [2] and by Bixon and Lifson.[3] The two next lowest, [2334] and [2343], are of so much higher enthalpy (4.4 kcal/mol) as to be unobservable in the equilibrium.

Cyclotridecane (Fig. 8). Both lowest conformations are here of quinquangular type. This is the only ring for which the most stable conformation, [12433], is asymmetric; it may be derived by ring contraction from the diamond-lattice conformation [3434] of cyclotetradecane and has a triangular partner [346] which is 4.4 kcal/mol higher. The next lowest conformation [13333] is at 1.1 kcal/mol and should therefore be quite important in the equilibrium; it is derivable from the [3333] conformation of cyclododecane by ring expansion, and has a much less stable triangular partner [337] at 7.8 kcal/mol. The two most regular triangular conformations [445] and [355] are of sufficiently low enthalpies (1.7 and 2.2 kcal/mol) so that they should also be detectable in the equilibrium.

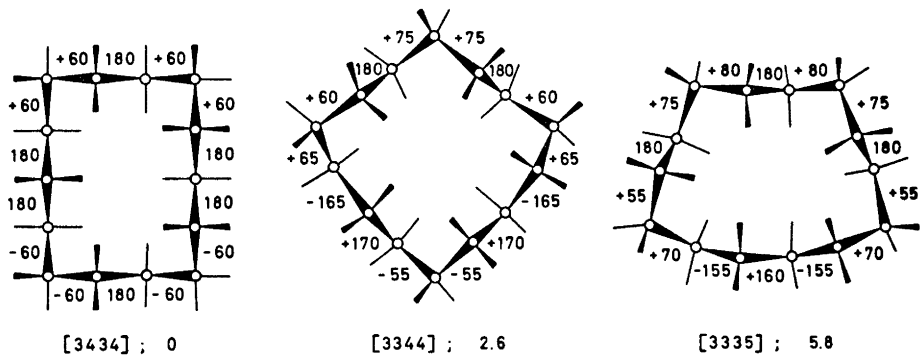


Fig. 9. Lowest minima for cyclotetradecane.

Cyclotetradecane (Fig. 9). As expected, this ring is conformationally very homogeneous with the "rectangular" diamond-lattice conformation [3434] favoured. This is also the observed conformation in the crystal,[17] liquid and solution.[6] The [3344] conformation is calculated to be 2.6 kcal/mol higher, corresponding to 1 % in the equilibrium, and none else is below 5.8 kcal/mol.

Cyclopentadecane (Fig. 10). This odd-membered ring turned out to have one clearly enthalpy-preferred, highly symmetric and regular quinquangular conformation [33333], a kind of homologue of the preferred C_9 and C_{12} conformations. The next five lowest conformations are also quinquangular, but of the type having a very irregular triangular partner of higher enthalpy. Thus, [14334] at 1.2 kcal/mol and [13434] at 2.7 kcal/mol, the latter derivable by ring expansion from the [3434] conformation of cyclotetradecane, have the very strained triangular counterparts [339] and [348], while [13443] at 1.5

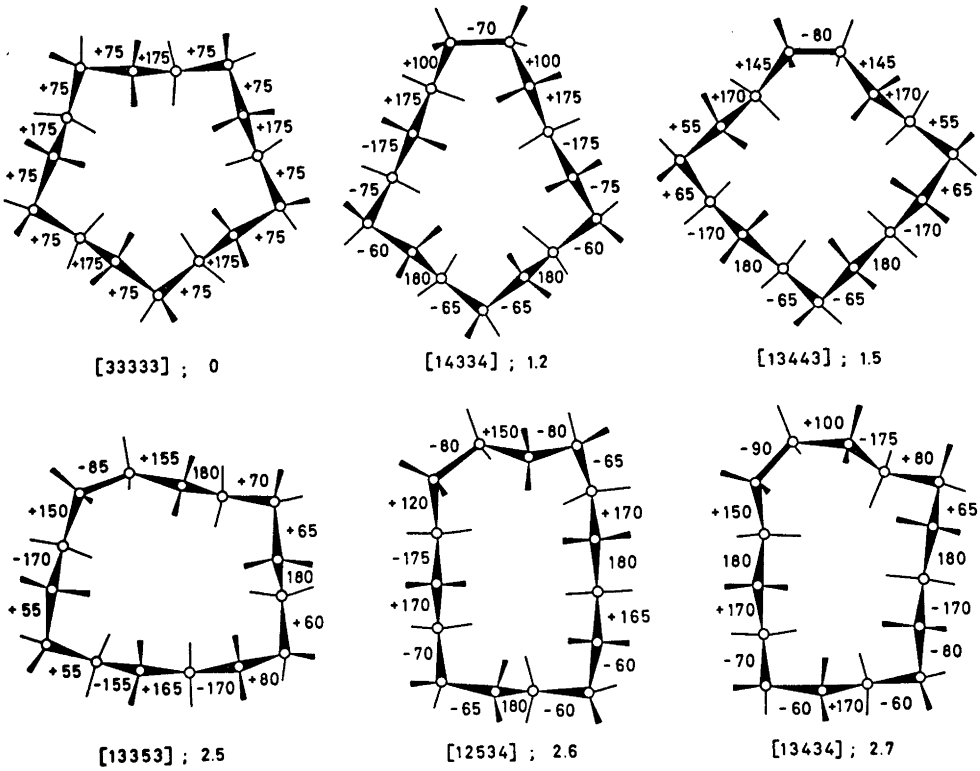


Fig. 10. Lowest minima for cyclopentadecane.

kcal/mol, derivable by ring contraction from the [4444] conformation of cyclohexadecane, is related to [447] at 4.3 kcal/mol, and [13353] as well as [12534], both at 2.5 kcal/mol, are related to [357] at 4.6 kcal/mol. The lowest triangular conformations are the regular [555] and next-most regular [456], both at 3.5 kcal/mol.

A consideration of entropy terms due to symmetry, so that free-energy differences might be used to estimate more accurate equilibria, seemed in most cases unjustified because such terms would be smaller than expected errors in the present enthalpy calculation. However, the lowest cyclopentadecane conformations have so very different symmetries, that the symmetry number of 10 for [33333], compared to only 2 for [14334] and [13443] (all are *d,l-pairs*), gives an entropy term at 300 K of 1.0 kcal/mol favouring the two latter. Their free energies are therefore only 0.2 and 0.5 kcal/mol higher, and conformational homogeneity is not to be expected.

Cyclohexadecane (Fig. 11). The "square" [4444] conformation, being of diamond-lattice type, has the lowest enthalpy. This is also the one indicated by infrared spectroscopy of the low-temperature crystal.[6] The next-lowest is the compact "rectangular" [3535] envisaged earlier.[5] Since it is

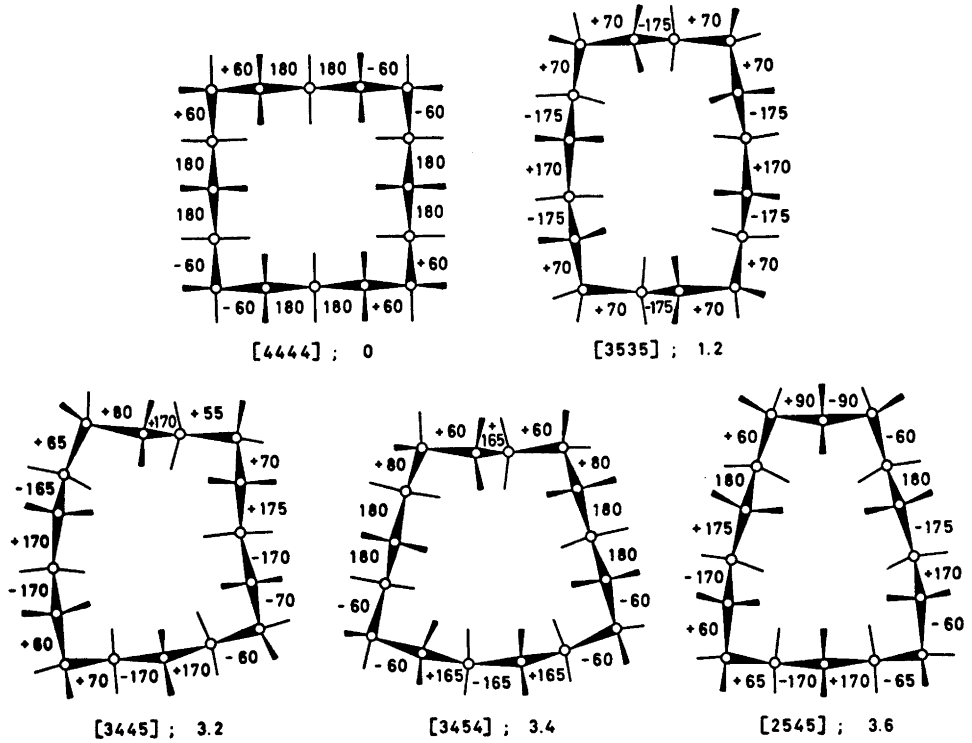


Fig. 11. Lowest minima for cyclohexadecane.

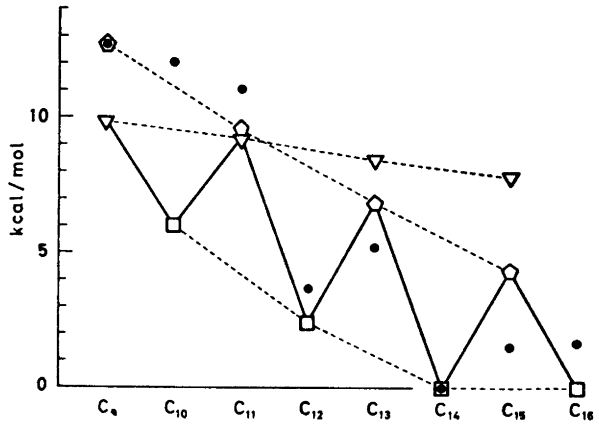


Fig. 12. Calculated enthalpy of the best conformation for each cycloalkane relative to that of cyclotetradecane.
□ = quadrangular type, △ = triangular type, ⬠ = quinquangular type,
● = experimental heat of combustion values.

only 1.2 kcal/mol higher, entropy terms must also be considered. The symmetry number is 4 for both, but only [3535] is a *d,l*-pair, thus giving an entropy term at 300° K of 0.4 kcal/mol in its favour. With a resulting free-energy difference of only 0.8 kcal/mol, it becomes understandable that the liquid is conformationally heterogeneous.[6]

Three other less symmetric conformations [3445], [3454], and [2545] are as high as 3.2 – 3.6 kcal/mol in enthalpy, and symmetry-determined entropy contributions could hardly make them important in the equilibrium. On the other hand, vibrational entropy terms might perhaps modify this picture, but cannot be considered here.

A NOTE ON CYCLOOCTANE

Obviously, the present method cannot be used for numerical calculation of cyclooctane conformations, since the very serious transannular interactions [1] are not taken properly into account; their neglect would therefore strongly favour the only diamond-lattice conformation [2222]. Nevertheless, it seemed of interest to try the present scheme for selection of conformational candidates, accepting that "non-*gauche*" bonds might in reality be very far away from *anti;* in fact quite close to the 120° barrier.[1,13] This leads to only four conformational minima: [2222], which corresponds to the boat-boat (saddle), including the twist-boat; [1223], which is a deformed boat-chair; [1232], which corresponds to the twist-boat-chair; and [1313], which is the twist-chair-chair, the lowest member of the crown family.[1] Thus, all the energetically impossible forms included in Hendrickson's symmetry-based selection scheme [1] are here automatically eliminated.

It is of particular interest that the symmetrical boat-chair, which in all numerical calculations [1–4] has the lowest energy, is not classified as a minimum in the present scheme, but as a barrier (Part 2) separating two enantiomeric [1223] conformers.

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