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Exploratory Calculations of Medium and Large Rings

Part 2. Conformational Interconversions in Cycloalkanes

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The mechanistic steps in conformational interconversions have been analysed and the enthalpy of the barriers calculated. These come out relatively low for the medium rings, but surprisingly high for cyclododecane and the largest rings studied ($C_{14}-C_{16}$). The critical step in all these rings is the passage of one ring bond through a torsional *syn* barrier. An alternative mechanism involving the passage of only 120° barriers becomes almost competitive in cycohexadecane; larger rings should therefore have lower barriers.

Computer calculation of conformational barriers should be as straightforward as of conformational minima when the nature of the barrier can be geometrically defined *a priori*. A search for the lowest interconversion barriers by the method of steepest descent would on the other hand seem difficult, since one is not looking for an absolute minimum. The type of approach used in Part 1 to find the geometries and calculate the enthalpies of potential minima seems therefore even more appropriate in a search for barriers, provided the various mechanistic possibilities can be satisfactorily analysed.

INTERCONVERSION MECHANISMS

The common distinction between ring inversion and pseudorotation in normal rings seems arbitrary and misleading if the mechanisms involved are implied. Thus, the observation of the exchange of non-identical axial and equatorial substituent positions on all identical ring positions in cyclohexane has given rise to the term inversion, although the mechanism is of course passage to the boat-forms and back again in two distinctly separate steps.[1] Strictly, the only cycloalkane for which inversion through total ring flattening must occur, is cyclobutane. The real barrier in cyclohexane involves the geometrical feature of a flattened four-carbon atom system,[1] but this is also the case for the pseudorotational barrier (the envelope form) of cyclopentane.[2] Energetically, the two situations are of course very different; in cyclohexane the four-

carbon flattening induces strain also in the rest of the ring, while in cyclopentane it relieves about the same amount of strain elsewhere in the ring.

In medium and large rings the conformations are generally of such high symmetry that it is inconceivable that the nearest barrier is also symmetric, since this would imply a synchronous change in two or more parts of the ring, hence the added energy of several changes. It is more likely that the least expensive conformational changes may be rather localized. In fact "elementary processes" can be devised involving the movement of a "corner" by one or two steps, which when repeated will produce any desired effect: the passage to other conformational minima and return to an equivalent conformation with exchange of ring-atom sites and/or substituent sites. These elementary processes are equivalent to the migration of *gauche* bonds in *anti* surroundings

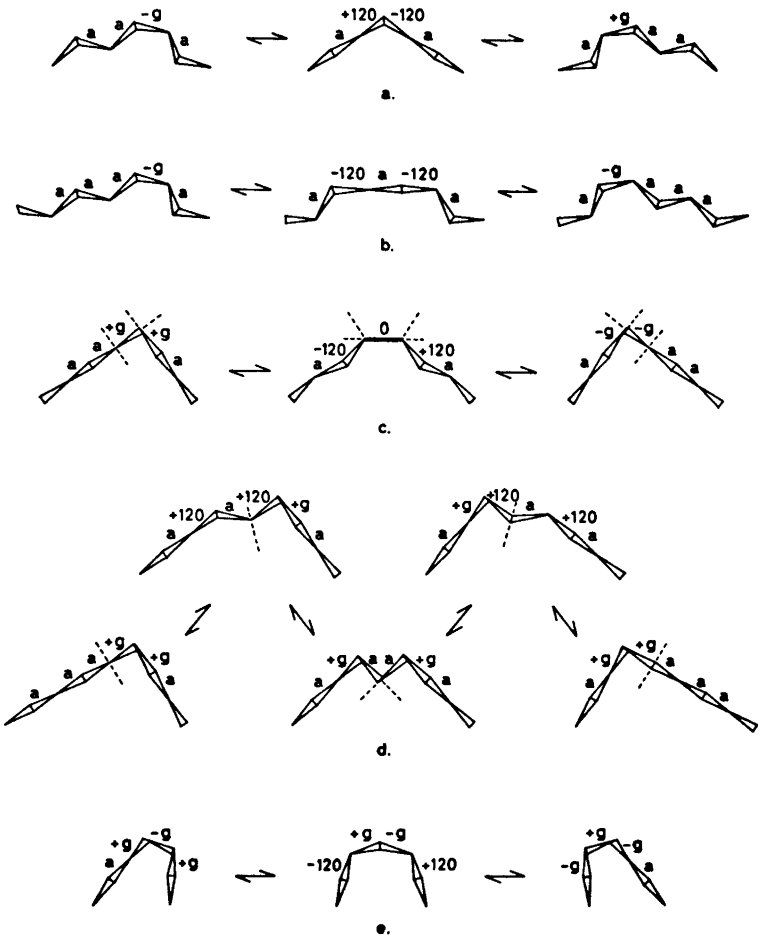

Fig. 1. Different types of barriers to the movement of *gauche* bonds or "corners".

along a chain. In an open chain, or infinitely large ring, the ends of the chain are unrelated to each other, and a *gauche* bond can be "moved" by turning it to *anti* and then the neighbouring or any other *anti* bond to *gauche*. In medium and moderately large rings the constraints of the ring may lead to partial eclipsing also in other bonds than the one just passing through a barrier. Extreme situations, obtained when a bent chain preserves as much as possible its overall shape during the whole process, are illustrated in Fig. 1.

An isolated *gauche*-bond can move by one step (Fig. 1a), changing sign, through a transition state with two adjacent bonds passing over the lower butane barrier (120°); in actual rings the eclipsing need not be totally synchronous. An isolated *gauche*-bond can move also by two steps (Fig. 1b), with unchanged sign, through a transition state having now two non-adjacent bonds on the lower butane barrier; again the two barriers must not necessarily be passed synchronously. These two mechanisms will be needed only in rings larger than C_{16} where conformations having isolated *gauche*-bonds play a role.

The more common corner element, two adjacent *gauche*-bonds of the same sign, can be moved by one step (Fig. 1c), with both signs changed, through a transition state having one bond passing the higher (*syn*) and two adjacent bonds passing the lower (120°) butane barrier; in most actual rings the three bonds may of course become eclipsed considerably out of phase. This process is particularly attractive for medium rings, since "inner" substituents will become "outer" in the transition state and transannular interactions thereby relieved. The same element can also be moved by two steps with unchanged sign (Fig. 1d), but the process involves then an intermediate conformation of low stability in the rings considered here, as well as higher-energy transition states, since "outer" substituents have to become "inner"; a methylene group is actually rotating "through" the ring. This mechanism should become of interest in rings larger than cyclohexadecane, because the transition state requires the eclipsing of only two bonds, both in low-barrier positions, and the eclipsing may not even need to be synchronous.

SEARCH FOR LOWEST BARRIERS

The procedure adopted was to define a transition state as being the situation the moment the bond between the old and the new corner atom becomes exactly eclipsed on the high-energy *syn*-barrier, as in Fig. 1c. The adjacent bonds, however, were generally hardly more than half-eclipsed (on the slopes of the low-energy 120° barrier), since these bonds, as well as the remainder of the bonds, were adjusted manually to minimize the strain in the same way as in the calculation of conformational minima (Part 1). It turned out in most cases to be energetically advantageous to keep one of these two dihedral angles above 120° (the one having the shortest adjoining side) and the other below 120° (the one having the longest adjoining side). Thus, the eclipsing rolls like a wave through the three contiguous bonds (from right to left as the models are oriented in the figures).

The notation introduced for the minima in Part 1 can be used also for the barriers if the *syn*-eclipsed bond is defined as a one-bond side; it is marked in italics. As an example, the conversion of [333] to [234], and *vice*

versa, proceeds over a barrier defined as [*1*233]. In general, triangular conformations have quadrangular barriers, and quadrangular conformations have quinquangular barriers. The quinquangular conformations may have both sexangular and quadrangular barriers, the latter *via* triangular partners.

A particular type of barrier is encountered when two corners are adjacent, since they cannot then be changed independently; passage over this barrier will shift a *+gauche, −gauche, +gauche* sequence by one step with all signs changed (Fig. 1e). The transition state has two eclipsed bonds of low-torsional-barrier type and looks like a conformation with a "forbidden" type of corner; such conformations were neglected in the search for minima (Part 1). Quad-

Table 1. Calculated strain enthalpies of conformational barriers of cycloalkanes.

	Notation	$\sum H$	H_0	ΔH		Notation	$\sum H$	H_0	ΔH
C_9	[*1*224]	26.3	19.1	9.2	C_{10}	[*1*2133]	27.4	20.2	14.2
	[*1*233]	25.7	18.5	8.6		[*1*2232]	21.1	13.9	7.9
	[*1*242]	26.1	18.9	9.0		[*244*]	19.8	12.6	6.6
	[*1*323]	22.7	15.5	5.6		[*334*]	19.4	12.2	6.2
						[**55**]	23.2	16.4	10.0
C_{11}	[*1*22312]	28.3	21.1	11.9	C_{12}	[*1*2333]	23.6	16.4	14.0
	[*1*235]	26.9	19.7	10.5		[*1*2342]	21.7	14.5	12.1
	[*1*244]	28.2	21.0	11.8		[*1*2423]	26.0	18.8	16.4
	[*1*253]	30.8	23.6	14.4		[*1*3233]	23.2	16.0	13.6
	[*1*334]	19.9	12.7	3.5		[*444*]	18.2	11.0	8.6
	[*1*343]	22.1	14.9	5.7					
	[*1*424]	27.7	20.5	11.3					
C_{13}	[*1*21333]	26.5	19.3	12.6	C_{14}	[*1*2443]	24.3	17.1	17.1
	[*1*336]	24.9	17.7	11.0		[*1*3334]	20.2	13.0	13.0
	[*1*345]	23.0	15.8	9.1		[*1*3343]	21.0	13.8	13.8
	[*1*354]	26.4	19.2	12.5					
	[*1*363]	30.0	22.8	16.1					
	[*1*435]	21.6	14.4	7.7					
	[*1*444]	21.1	13.9	7.2					
C_{15}	[*1*23333]	24.9	17.7	13.4	C_{16}	[*1*3444]	19.8	12.6	12.6
	[*1*23342]	21.8	14.6	10.3		[*1*3453]	22.7	15.5	15.5
	[*1*23432]	18.7	11.5	7.2		[*1*3534]	20.7	13.5	13.5
	[*1*31343]	28.7	21.5	17.2		[*1*4344]	19.2	12.0	12.0
	[*1*31433]	28.0	20.8	16.5		[*1*3264]	23.7	16.5	16.5
	[*1*347]	31.1	23.9	19.6		[*1*3246]	23.2	16.0	16.0
	[*1*356]	21.6	14.4	10.1		[*1*3444]	16.5	9.3	9.3
	[*1*365]	26.8	19.6	15.3		[*2*3344]	21.6	14.4	14.4
	[*1*437]	26.6	19.4	15.1		[*2*3344]	23.8	16.6	16.6
	[*1*446]	21.9	14.7	10.4		[*2*4334]	24.9	17.7	17.7
	[*1*455]	23.7	16.5	12.2					
	[*1*464]	24.6	17.4	13.1					
	[*1*536]	24.2	17.0	12.7					
	[*1*545]	21.2	14.0	9.7					

$\sum H$ = 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.

rangular conformations having a one-bond side therefore get triangular transition states, quinquangular get quadrangular. The two sides which meet at such a corner with opposite dihedral angle signs become italicized in the notation (underlined in the figures). As an example, the conversion of [1333] to [1234], and *vice versa*, proceeds over a barrier defined as [3*34*].*

Only barriers between the lowest conformational minima and those less stable minima which serve as intermediate conformations on low-energy interconversion paths have been calculated. The results are listed in Table 1 and the geometries and dihedral angles are given for the most important ones in Figs. 2 – 9.

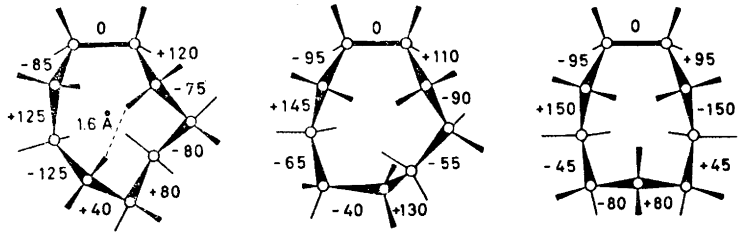

Fig. 2. Barriers for cyclononane.

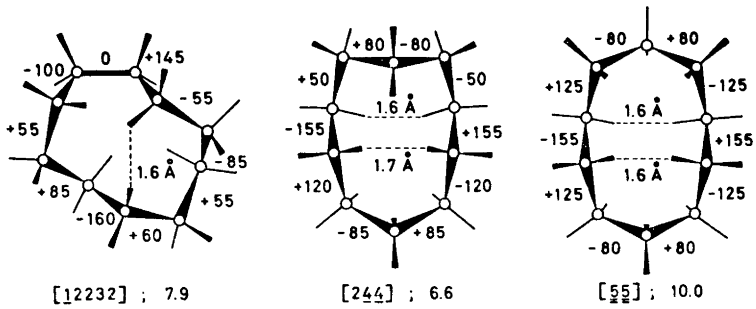

Fig. 3. Barriers for cyclodecane.

GENERAL DISCUSSION OF RESULTS

One general comment to make is that the spread in enthalpy is smaller for the barriers than for the minima. This may be related to the fact that all barriers must be strained by definition, whereas some minima are unstrained, others strained. It would, however, seem without interest to compare lowest

* The distinction between the triangular barrier [3*34*] and the quadrangular conformations [1333] or [1234], and even their biangular partner [37], becomes rather vague, in the same way as the distinction between triangular and quinquangular conformation partners and their intervening barrier (Part 1).

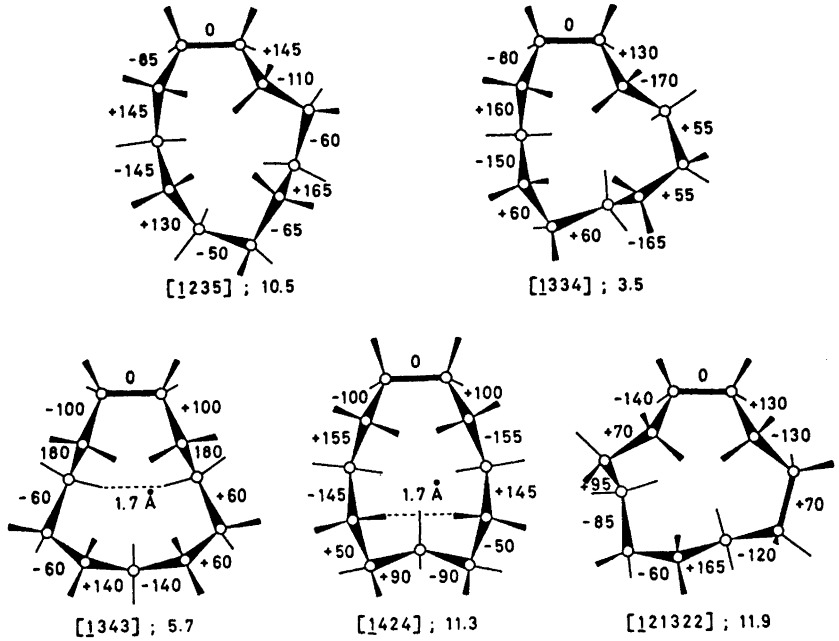

Fig. 4. Barriers for cycloundecane.

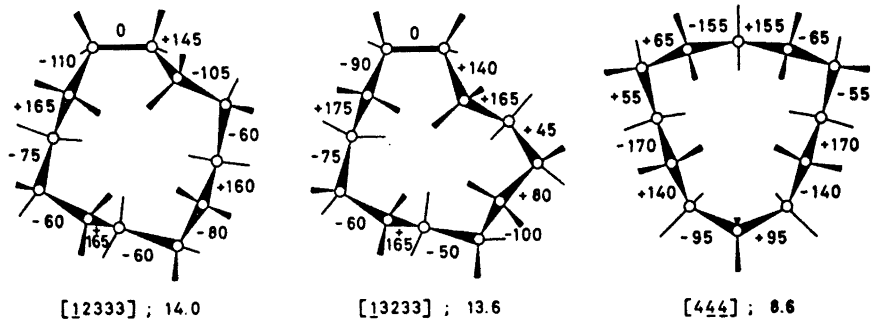

Fig. 5. Barriers for cyclododecane.

absolute values of barriers for different ring sizes, as they have meaning only in relation to the minima they connect. The barriers will therefore be discussed only in connection with the interconversion processes for each individual ring.

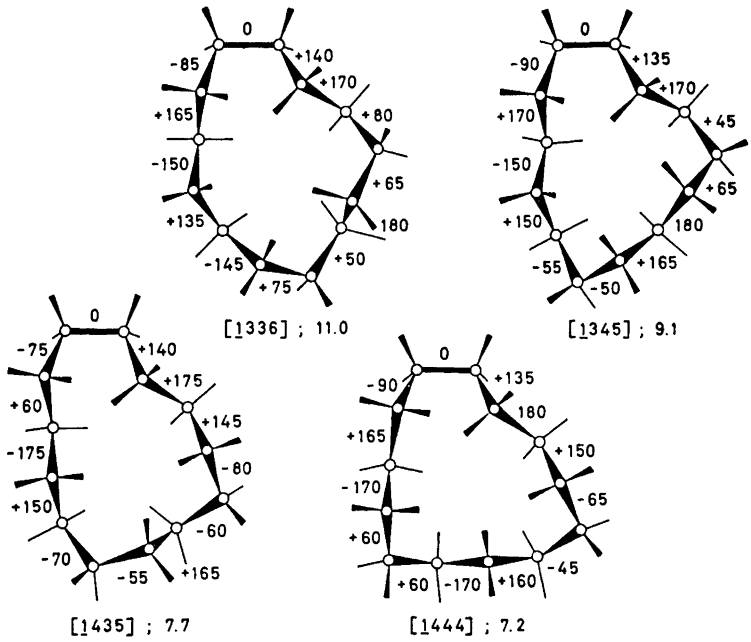

Fig. 6. Barriers for cyclotridecane.

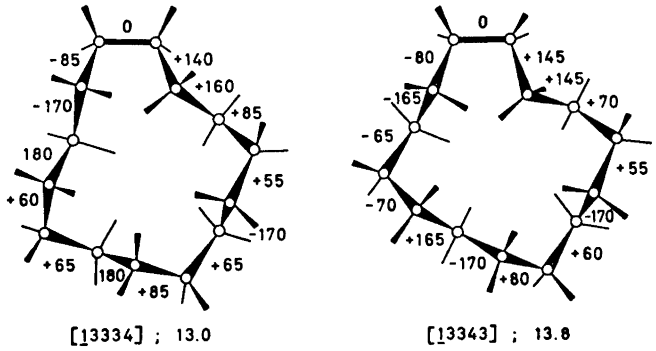

Fig. 7. Barriers for cyclotetradecane.

As to the possible systematic errors in the calculation, they will most likely produce too high barriers, and the more so the larger the rings. There are three reasons for this:

1. The search for the lowest enthalpy value of stable conformations is more easy because these represent absolute minima and have a relatively well-defined symmetry. The barriers, on the other hand, are generally less symmetric and may conceivably be further minimized by better timing of the

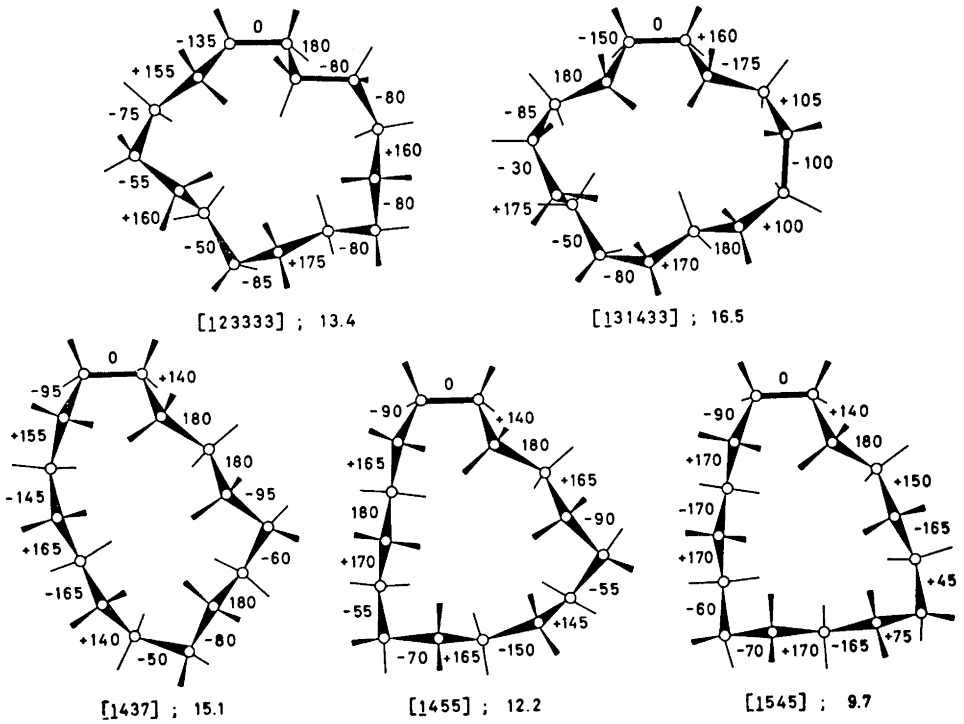

Fig. 8. Barriers for cyclopentadecane.

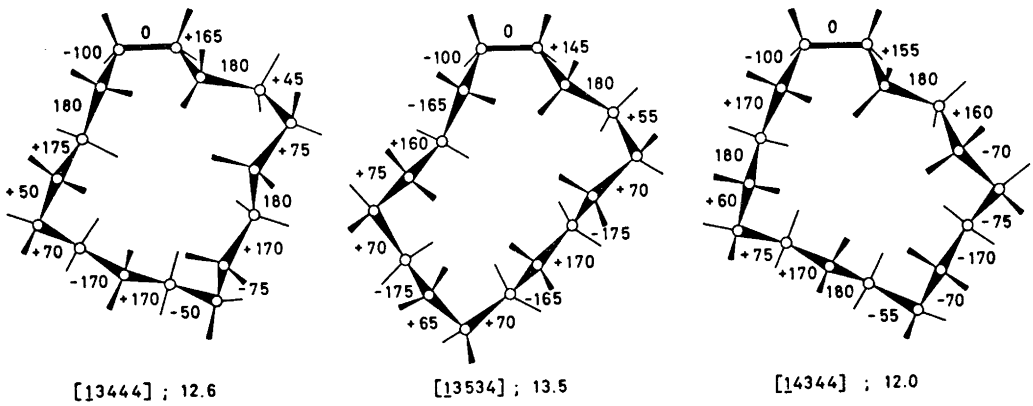

Fig. 9. Barriers for cyclohexadecane.

"eclipsing wave" through the three bonds and by better adjustment of the dihedral angles in the remainder of the ring. Of course, an asymmetric minimum may well have nearest barriers that are more symmetric, but these cases are relatively rare.

2. If the tetrahedral CCC-angle of the models were replaced by a more realistic 112°, the calculated enthalpy of the diamond-lattice-like conformational minima of the larger rings would be raised (*cf.* Fig. 12 of Part 1), whereas the enthalpy of the barriers would probably be lowered considerably because of relieved interactions in the flattened part of the ring.

3. The double weight of the 1,3-interactions inherent in the calculation procedure (see Part 1) leads to overemphasis of strain in bonds having dihedral angles near 120°, and the barriers have generally more such bonds than the minima.

Within each ring the error in relative barrier heights is likely to be small, and therefore the use of the calculated barriers to clarify the qualitative nature of the lowest-energy interconversion paths becomes the most important feature of the present work, not the absolute numerical values of the barriers.

DISCUSSION OF INDIVIDUAL RINGS

Cyclononane. The first step in any interconversion of the [333] conformation, and decisive in the site exchange process, is its passage to the [234] conformation; the relevant barrier [*1*233] is asymmetric (Fig. 2) and calculated at 8.6 kcal/mol, which value is to be compared with the free-energy value of $\approx$ 6 kcal/mol observed by ^{13}C resonance.[3] Before being able to return to an alternative [333] conformation, the [234] conformation must change to its mirror image by passing one of the symmetrical barriers [*1*242] or [*1*323]. Of these, the latter is by far the lowest and seen to be identical with the boat-chair of Hendrickson, classified by him as a conformation.[1,4] After the last passage over the [*1*233] barrier, the [333] conformation produced is not only the mirror image of the starting conformation, but all ring atoms have moved by one step around the ring. The complete cycle is illustrated in Fig. 10. Repetitions of this cycle will lead to interchange of all ring-atom sites so that the result will appear like a pseudorotation, although mechanistically it is not. Focusing the attention on outer and inner substituents of a "side" carbon-atom, these remain outer and inner until the ring-atom arrives at a corner position, where they become identical (iso-clinal),[4] then exchange roles on the next side. The result will thus appear like a ring inversion, although the mechanism is the same.

Finally, it should be noted that also the [12222] (=[225]) conformation, if it had been the stable one, might have had its sites exchanged by passing to the same [234] conformation over a similar barrier [*1*224].

Cyclodecane. The lowest conformation [2323] of this ring must go through several steps to exchange all ring-atom and substituent sites. The first step is the passage over the [*1*2232] barrier (Fig. 3) leading to the intermediate conformation [2233] (the other conceivable barrier [*1*1323] is extremely high having two adjacent one-bond sides). Repetition of this process at the diametrically opposite corner leads over the same barrier to the starting con-

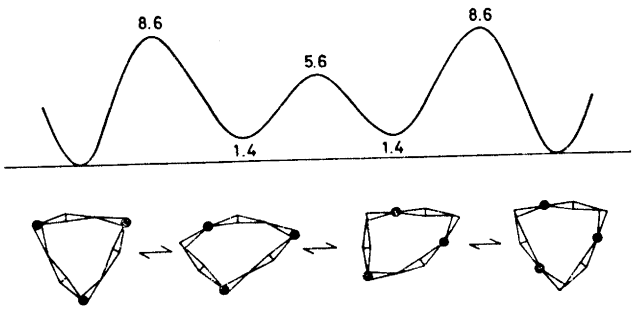

Fig. 10. Interconversion cycle for cyclononane.

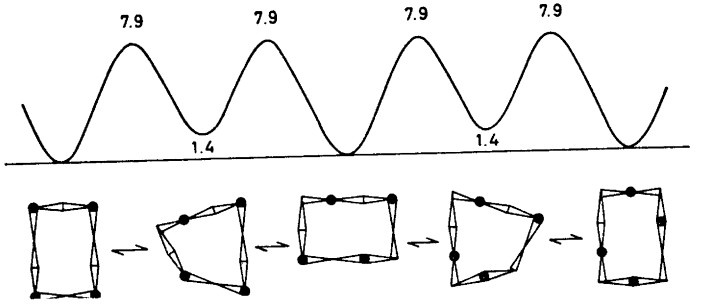

Fig. 11. Double interconversion cycle for cyclodecane.

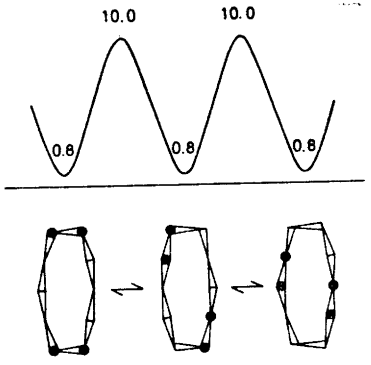

Fig. 12. Two interconversion steps for cyclodecane.

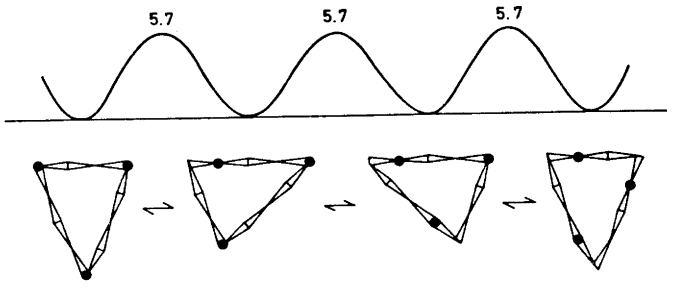

Fig. 13. Triple interconversion cycle for cycloundecane.

formation, but the ring atoms at the remaining two corners are unchanged (Fig. 11). However, if attention is focused on the substituents on each of these, they have undergone site exchange, so that the result has already the appearance of a ring inversion. The calculated value for the two identical barriers is 7.9 kcal/mole, in good agreement with the activation enthalpy value of 6.7 kcal/mol observed [5] by ^{19}F resonance for fluorine site exchange in 1,1-difluorocyclodecane (activation free energy 5.7 kcal/mol at $-135°$).

In order to get a result with the aspect of pseudorotation, the process must be repeated at the remaining corners so that all ring atoms are moved by one step. Exchange of all substituents is obtained by repetitions of the complete cycle; outer substituents become inner, and *vice versa*, each time a corner is passed (Fig. 11). The same exchanges might in principle have been effected by passing through an alternative [1333] intermediate in the middle of each complete cycle, but the necessary [*I*1332] barrier turned out to be forbiddingly high.

It may be of interest to note that the asymmetric [1324] conformation at 4.7 kcal/mol can be converted to its mirror image by passing over the symmetric [*244*] barrier at only 6.6 kcal/mol (Fig. 3), identical with the chair-chair-boat classified by Hendrickson [4] as a conformation. The enthalpy difference is so small (1.9 kcal/mol) that if the NMR-spectrum of this pair of conformers could be observed, it would reflect the symmetry of the barrier.

The other low-enthalpy conformation [1414] is seen from the regular alternation of dihedral angle sign to belong to the crown family and can best undergo ring-atom exchange (Fig. 12) over a particular [**55**] double barrier (Fig. 3) identical with Hendrickson's chair-chair-chair [4] or "stretched crown". Mechanistically, this resembles a pseudorotation, since only one barrier and one minimum are involved, but not energetically, the enthalpy difference being as high as 9.2 kcal/mol. All ring sites become exchanged, but on each carbon one substituent remains inner or "axial", the other outer or "equatorial". To exchange also these, the ring has to pass into some of the other conformations, although a barrier of the type [1*I*314] must be exceedingly high.

Cycloundecane. Of the four low-enthalpy conformations of this ring the two of triangular type interconvert particularly easily. In fact, the lowest conformation [344] can pass over the symmetric [*I*343] barrier at 5.7 kcal/mol (Fig. 4) to its own mirror image, and after three such passages all atoms will have moved by one step around the ring (Fig. 13). After further repetitions, all substituent sites will be exchanged. Mechanistically, this comes closest to a pseudorotation process. However, an even lower barrier [*I*334] at 3.5 kcal/mol (Fig. 4) separates [344] from the [335] conformation, and by switching systematically three times back and forth over only this low barrier, all ring atoms will have moved by two steps around the ring (Fig. 14). After a number of repetitions, all sites will be exchanged.

The interconversion of the two low-lying quinquangular conformations is much more difficult. They can be transformed one to the other over the [*I*21322] barrier at 11.9 kcal/mol, but this will not lead to full exchange of all sites. The [12323] conformation can, however, change slightly uphill to its triangular partner [236], which communicates over the [*I*235] barrier at 10.5 kcal/mol with the [335] conformation; from this point full exchange can be effected through the scheme given in Fig. 14 before return occurs by the same route.

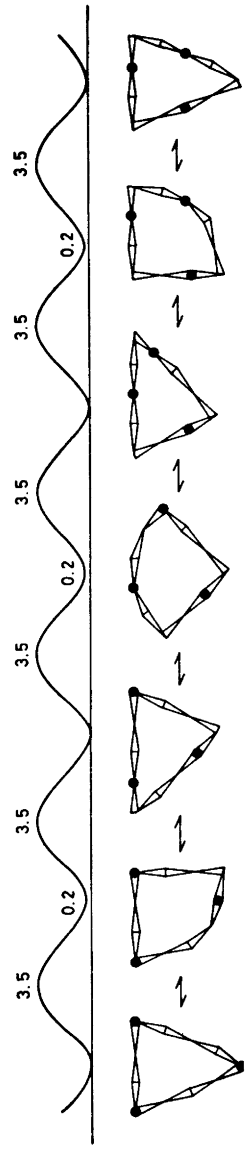

Fig. 14. Complex triple interconversion cycle for cycloundecane.

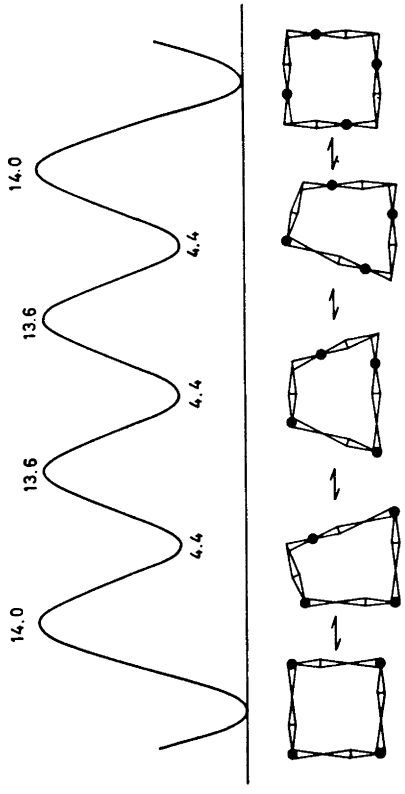

Fig. 15. Interconversion cycle for cyclododecane.

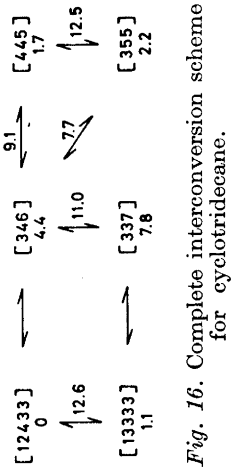

Fig. 16. Complete interconversion scheme for cyclotridecane.

The asymmetric triangular conformation [245] at 2.3 kcal/mol is also isolated by relatively high barriers, both from [344] and [335] by barriers at 11.8 and 14.4 kcal/mol, respectively (Table 1), and from its own mirror image by the symmetric [*1*424] barrier at 11.3 kcal/mol (Fig. 4).

Cyclododecane. The first barrier to pass on any route from the most stable [3333] conformation is [*1*2333], which lies as high as 14.0 kcal/mol (Fig. 5). The most economical route for effecting complete exchange of all sites, is to continue from the resulting [2334] conformation over a slightly lower [*1*3233] barrier to [2343] and then in a reversed fashion, operating at the remaining corners (Fig. 15). An alternative "central" intermediate might have been [2424], but the barrier [*1*2423] which must then be passed is much higher (16.4 kcal/mol).

The lowest calculated barrier [*44*4] at 8.6 kcal/mol (Fig. 5) is of symmetric type and can only serve to interconvert the enantiomers of the asymmetric [1344] conformation, which is nearly as high in enthalpy (7.5 kcal/mol).

Cyclotridecane. The two lowest quinquangular conformations of this ring can interconvert directly over a [*1*21333] barrier at 12.6 kcal/mol. A better path is available if both go smoothly uphill to their triangular partners, [12433] to [346] and [13333] to [337], which communicate over a lower [*1*336] barrier at 11.0 kcal/mol (Fig. 6).

The [346] conformation, although at 4.4 kcal/mol, plays a central role in the dynamics of this ring (Fig. 16), since it is not only the direct partner of the lowest-enthalpy conformation, but is also separated by a single barrier from the other three lowest conformations, notably by the [*1*345] barrier at 9.1 kcal/mol from the most regular triangular conformation [445] needed for complete site exchange. In fact, [445] can be converted to its own mirror image by passing the lowest calculated barrier ([*1*444] at 7.2 kcal/mol) in this ring, and repetition of this process therefore comes closest to a pseudorotation mechanistically. Fig. 17 shows how the lowest conformation [12433] transforms to [445], which then pseudorotates and goes back again to the mirror image with all ring atoms moved by one step.

Also the [355] conformation needs to transform to [346] over a [*1*435] barrier at 7.7 kcal/mol, and further to [445], to effect complete site exchange. The critical barrier will therefore be 9.1 kcal/mol also here, while [13333] has its critical barrier in the earlier step at 11.0 kcal/mol (Fig. 16).

It is important to note that the [*1*444] barrier (Fig. 6), as well as the [*1*363] barrier, which notation-wise are both symmetric, had to be made asymmetric to lower their energy.

Cyclotetradecane. Conversion of the favoured diamond-lattice conformation [3434] to [3344] goes over the rather high [*1*3343] barrier at 13.8 kcal/mol (Fig. 7). Systematic passage over the same barrier three more times (Fig. 18) gives one complete cycle for moving the ring atoms around the ring, and repetitions lead to complete site exchange, exactly as for cyclodecane. Also as for cyclodecane, only half a cycle is needed for substituent site exchange at the two untouched corners. In contrast, however, there is now an alternative and competitive path for the middle part of each cycle over a slightly lower [*1*3334] barrier to a less stable intermediate conformation [3335] and back again (Fig. 18). It may be noted that if this were the only path, it would have led to

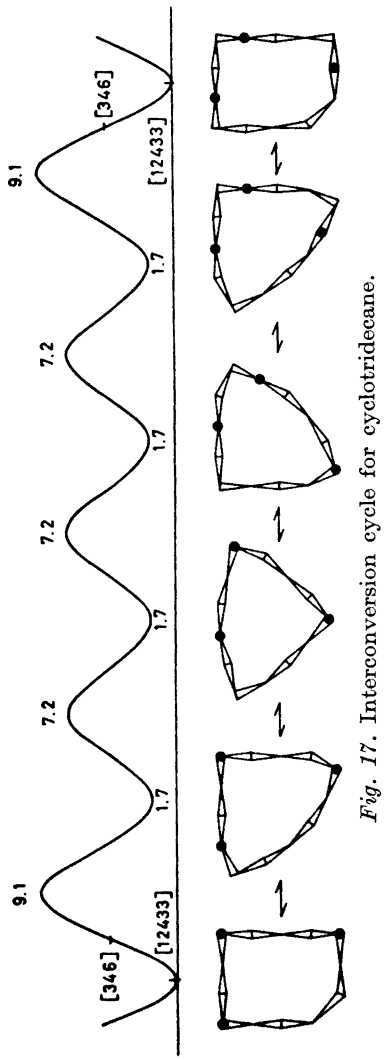

Fig. 17. Interconversion cycle for cyclotridecane.

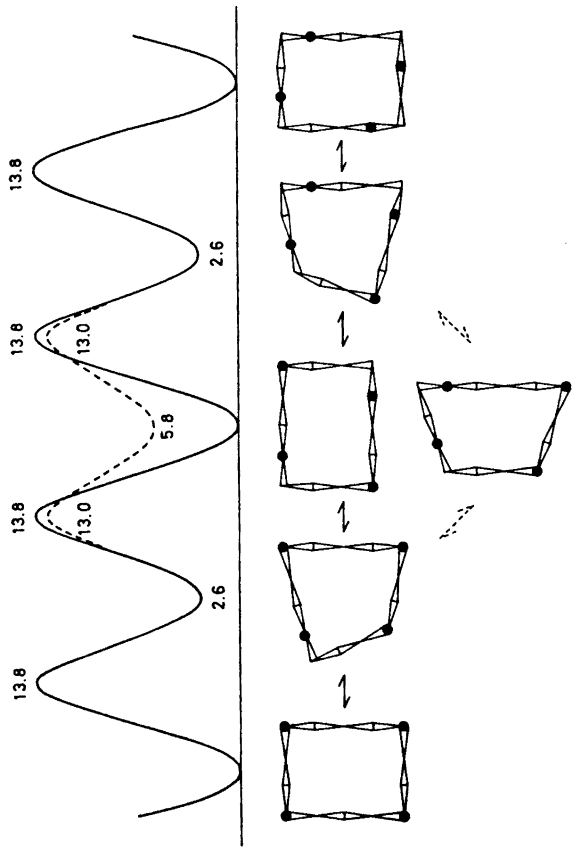

Fig. 18. Double and single interconversion cycles for cyclotetradecane.

exchange of all ring sites, but not to exchange of geminal substituents on each ring atom; outer substituents on long sides would become inner on short sides, and *vice versa*.

Cyclopentadecane. In this ring the lowest-enthalpy conformation [33333] cannot interconvert over any reasonably low and calculable barriers with the other five lowest conformations, which are all of one-bond-side quinquangular type, nor with the triangular counterparts of these latter. Higher-lying conformations [23334] and [23343] must therefore serve as intermediates, and the barriers [*1*23333] (Fig. 8), [*1*23342] and [*1*23432] must be passed to effect inter-

change of all sites. It is noteworthy (Fig. 19) that the decisive barrier, as high as 13.4 kcal/mol, is closest to the stable conformation, and that the highest minimum is surrounded by the lowest barriers.

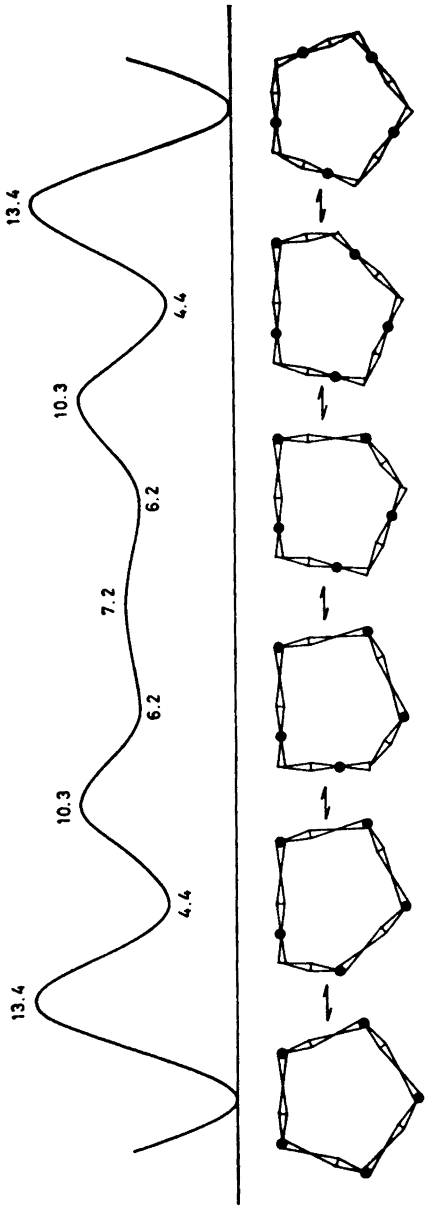

Fig. 19. Interconversion cycle for cyclopentadecane.

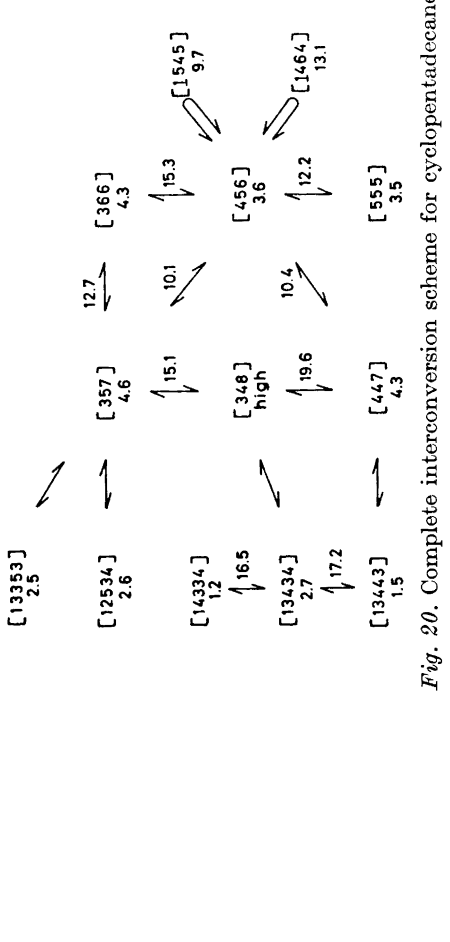

Fig. 20. Complete interconversion scheme for cyclopentadecane.

The direct interconversion of the five next-lowest conformations *via* sexangular barriers is either impossible or requires barriers higher than 16 kcal/mol. Much easier paths are available for four of them *via* their triangular partners and over the corresponding quadrangular barriers, as best clarified in the complete interconversion scheme in Fig. 20. For the dynamics of this ring, the [456] conformation, although itself high in enthalpy, plays a central

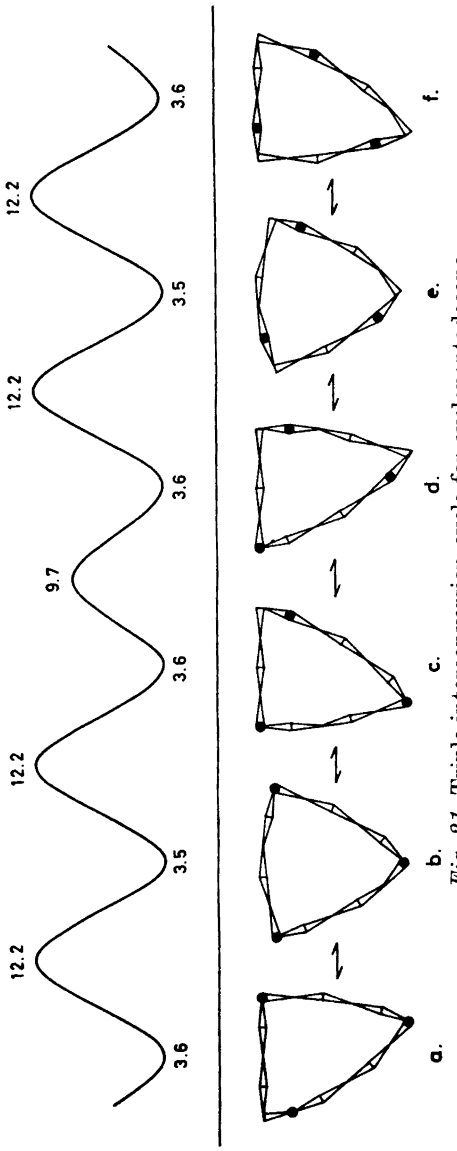

Fig. 21. Triple interconversion cycle for cyclopentadecane.

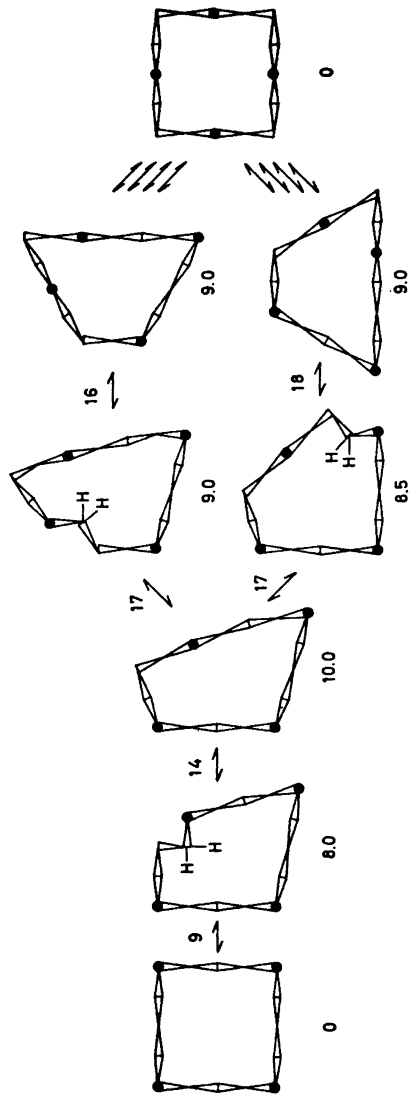

Fig. 23. Complex interconversion cycle for cyclohexadecane (numbers give enthalpies of minima and barriers).

role, as full site exchange must go through it. In fact, passage over either of two notation-wise symmetric, but in reality unsymmetric barriers, the higher [*1*464] or the lower [*1*545], converts this asymmetric conformation to its own mirror image. This is, however, not sufficient, and for full exchange also the [555] conformation is needed as an intermediate. The lowest path is shown in Fig. 21 (a – d or c – f), which also shows the lowest interconversion path for the [555] conformer as such (b-e); the decisive barrier is in both cases [*1*455] at 12.2 kcal/mol. From Fig. 20 it can be concluded that this is also the highest of the barriers in the complete site exchange process for the three conformations [13353], [12534] and [13443], whereas [14334] and [13434] have first to pass the [*1*437] barrier at 15.1 kcal/mol. The lowest of these two, as well as of this whole group of conformations, [14334], must pass even a higher sexangular barrier [*1*31433] at 16.5 kcal/mol (Fig. 20).

Cyclohexadecane. The dynamic situation in this ring is much easier to survey than the foregoing, especially since the intermediate conformations needed on the simplest route to effect complete site exchange of the lowest-enthalpy diamond-lattice conformation [4444] are exactly the three next-lowest conformations (Fig. 22). The [*1*3444] barrier at 12.6 kcal/mol (Fig.

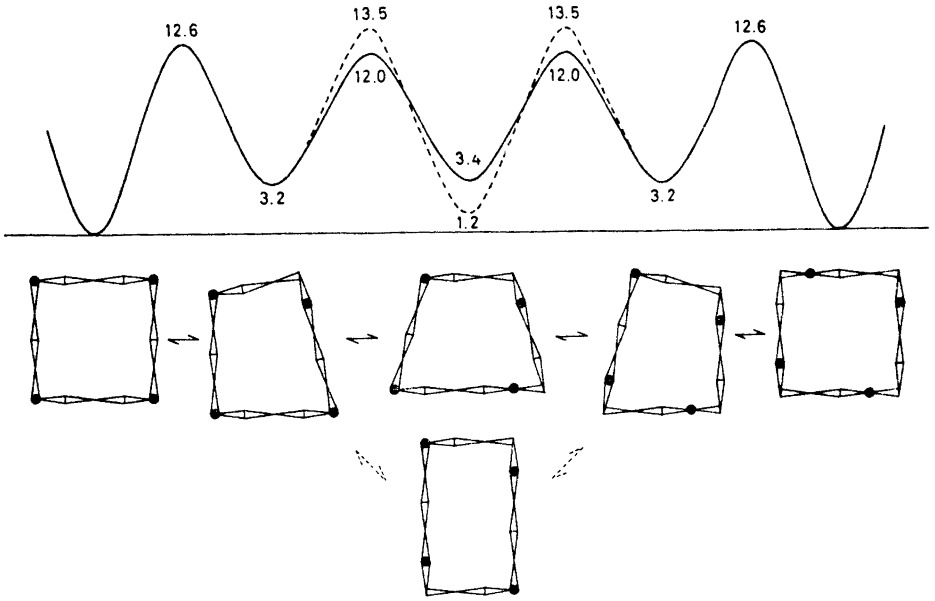

Fig. 22. Two interconversion cycles for cyclohexadecane.

9) is the only possible one for the first step, whereas two paths are available for the second step (Fig. 22). Again, it is a situation where the higher barrier [*1*3534] leads to the lower minimum [3535], and the lower barrier [*1*4344] to the higher minimum [3454].

For this largest ring studied, the elementary conformational process consisting in the rotation of a CH_2-group "through" the ring (Fig. 1d) had to be examined and was found to be a possible mechanism, although requiring the passage of somewhat higher barriers than in the classic "outwards flattening" mechanism (Fig. 1c) considered so far. The transition states are here much more difficult to define, and for simplicity have been assumed to have two synchronously eclipsed bonds. The strained sequence of three bonds at 120°, 180°, and 120° is defined as a "side" and underlined in the notation (Table 1). The calculated enthalpies are thus maximum values and may well be several kcal/mol too high. A complete cycle is now much more complex and includes not only two intermediate quadrangular conformations of high enthalpy, but requires in addition two intermediate conformations of a novel type having isolated *gauche* bonds (Fig. 23) which are also quite high in enthalpy. A most interesting aspect of this particular mechanism in this particular ring is that, if it had been of lowest overall activation enthalpy, only corner positions and central side positions would have been exchanged, while ring atoms next to corner positions would be left unaffected.

A NOTE ON PSEUDOROTATION

Free pseudorotation as defined by Pitzer for cyclopentane [2] is strictly a description of a particular thermodynamic situation rather than of a particular process. This situation is caused by the accidental, and not inherent, absence of an energy barrier between the two non-planar forms of defined symmetry (the envelope and the twist-envelope (half-chair)), and manifested by an increased entropy. Pseudorotation in cyclopentane is also intimately connected with degeneracy; in fact, the two symmetry-defined conformers correspond exactly to the deformations produced by the two symmetry-defined components of the doubly degenerate normal vibration perpendicular to a planar five-membered ring.[6]

An extended definition of pseudorotation was introduced by Hendrickson,[1] based on the analysis of various *mechanistic schemes* for conformational interconversions, and applied even for processes involving rather high barriers. A somewhat different meaning of the word is implied by Anet [7] in his distinction between pseudorotation and inversion in connection with the observation by dynamic NMR spectroscopy of a low-barrier and a high-barrier process in cyclooctane and derivatives. Strictly, this use relates to *the observed result*, the exchange of ring atom positions and geminal substituents respectively, and is independent of the actual mechanisms involved.* As shown earlier in this paper, both types of exchange may in higher cycloalkanes often result from one and the same mechanism.

* The formalism and the type of barriers used in this paper permit deduction of interconversion paths also for cyclooctane, which, although only qualitative, are in perfect correspondence with those proposed by Anet.[7] Thus, the [1223] conformer (boat-chair) may pass over a low barrier to [1232] (twist-boat-chair) and back again to exchange ring sites only, and over a medium barrier to [2222] (boat-boat) and back again to exchange also geminal substituents. The [1313] conformer (twist-chair-chair) meets very low barriers going to a symmetric crown and back again to effect ring-site exchange, but must pass a high barrier to [1223] and further to [2222] and back again to exchange also geminal substituents.

The objections to the use of the term "pseudorotation" to describe the mechanism of ring-atom site exchange (topomerization) in larger rings may therefore be several:

1. The ring is very far from planar.
2. The barriers are not negligible, so that the criterion of high entropy is not met.
3. The ring conformation is not close enough to a regular polygon.
4. The dynamic process is not a simple one with one type of minimum and one type of barrier.

Of the rings examined here, two have a conformation against which only the first two objections can be raised. These are the [344] conformation of the 11-membered ring and the [445] conformation of the 13-membered ring. Both are characterized by being closest possible to regular and by having two equal sides and the third side one bond shorter or longer. This allows a single corner-movement-step of relatively low activation enthalpy to transform it into itself. A similar situation would next arise in the [566] conformation of the 17-membered and the [667] conformation of the 19-membered ring.

It is interesting to note that when the present notation is stretched to include smaller rings, the only formally similar cases would be the [122] conformation of the 5-membered and the [223] conformation of the 7-membered ring. These are easily identified with the two most perfect examples of pseudorotation, both formally and energetically, namely the twist-envelope of cyclopentane,[2] with the symmetrical barrier [1*1*12] corresponding to the envelope, and the twist-boat of cycloheptane,[1] with the symmetrical barrier [*1*222] corresponding to the boat.

Also quinquangular conformations provide examples of possible genuine pseudorotation, at least formally: the [12222] conformation of cyclononane and the [22223] conformation of cycloundecane; the relevant barriers are [1*1*1222] and [*1*22222].

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