Tetrahedron, 1967, Vol. 23, pp. 769 to 784. Pergamon Press Ltd. Printed in Northern Ireland

POTENTIAL FUNCTIONS AND CONFORMATIONS IN CYCLOALKANES

M. BIXON and S. LIFSON
Weizmann Institute of Science, Rehovoth, Israel

(*Received* 4 *July* 1966)

Abstract—Energy functions of bending of the C—C—C angle and of twisting of the CH_3—CH_3 torsional angle have been examined through their effect on calculations of stable conformations and excess enthalpies of all the cycloalkane molecules from C_4H_{18} to $C_{15}H_{24}$.

The total strain energy was expressed as a function of the internal coordinates—bond lengths, bond angles and torsional angles. H—H distances were derived by matrix algebra, and the method of steepest descent was applied. Energy parameters like the bending force constant, the zero-strain value of bond angles, torsional potential barrier, were varied one at a time, and their effect on conformation and strain energy examined. Results have been compared with calorimetric measurements and with X-ray and electron diffractions. Enthalpy of translation-rotation-vibration was also considered and found to be significant. Best agreement between calculations and experiment was obtained when the energy parameters were derived from n-alkanes. Thus, the n-alkane bond angle value of 112·7° is preferable to the tetrahedral angle as the zero-strain value; the torsional potential barrier of propane, 3·4 kcal/mole, is preferable to the corresponding value for ethane, 2·8 kcal/mole.

INTRODUCTION

SPECTROSCOPIC and chemical evidence indicate that the potential energy of large or medium sized molecules is approximately composed of energies localized in various parts of the molecule. Thus, it has been customary to consider separately the harmonic forces of bond stretching, bond angle bending, the energy of twisting the torsional angles of rotation around C—C single bonds, and the energies of interactions between nonbonded atoms (nonbonded interactions). The selection and refinement of the appropriate energy functions through a quantitative correlation between conformations and energies is of great importance in the various branches of organic chemistry, as well as in the study of the native structure of proteins.

Valuable information about the various energy functions can be obtained from the conformational analysis of ring structures, and here cycloalkanes are of particular interest because of their simplicity. It is well known that the ring structure of medium size cycloalkanes requires the bending of the C—C—C bond angles out of the minimum energy value and the twisting of the torsional angles of internal rotation around the C—C bonds from their staggered position. The enthalpies of medium ring cycloalkanes have been measured.[1–3] The excess enthalpy per CH_2 group relative to the cyclohexane molecule exhibits a remarkable trend of increasing to a maximum of about 1·3 kcal/mole CH_2 in cyclononane and cyclodecane, and decreasing towards

[1] R. Spitzer and H. M. Huffman, *J. Amer. Chem. Soc.* **69**, 211 (1947).
[2] S. Kaarsemaker and J. Coops, *Rec. Trav. Chim.* **71**, 261 (1952).
[3] J. Coops, H. Van Kamp, W. A. Labregts, B. J. Visser and H. Dekker, *Rec. Trav. Chim.* **79**, 1226 (1960).

about ⅓ of this value in cyclododecane. The X-ray crystallography of several medium rings of cycloalkanes, or some of their derivatives,[4–7] verifies in detail this trend of bond angle bending and torsional twisting.

The quantitative theoretical conformational analysis of medium ring molecules has been considerably advanced in the last few years.[8–12]

The present contribution gives the calculated potential energies for *all* rings from n = 6 to n = 12 based on the *same* energy functions. Moreover, we examined some of the potential functions in common use in a systematic manner, varying these functions and their parameters—*one at a time*, and suggest some correction which definitely improve the agreement between experiment and calculation for *all* medium rings simultaneously. It is significant, though hardly surprising, that the agreement between calculated and measured conformations of n-alkanes is also improved by the same energy functions.

It was assumed by the investigators in the fields of conformational[8–12] and spectroscopic[13] analysis that the C—C—C zero strain bond angle is the tetrahedral one (109°28′) and that the observed deviations are all due to nonbonded interactions.[14] We found that the nonbonded interactions cannot explain these deviations while by the choice of the C—C—C bond angle of n-alkanes (112·7°)[15] as the zero strain angle, considerable improvement is achieved in the calculation of the conformations of all medium cycloalkanes. This is particularly evident in the case of the cyclohexane chair conformation.

Another substantial improvement of the agreement between calculated strain energies and measured excess enthalpies of cycloalkanes is obtained when one uses the potential barrier of internal rotation in propane,[16] instead of the potential barrier in ethane,[16] used by other authors.

The translational-rotational-vibrational contributions to enthalpy can be calculated from spectral analysis. Unfortunately, the only complete normal mode spectral analysis available is that of cyclohexane,[17,18] and cyclododecane.[19] The corresponding contribution to the excess enthalpy of cyclododecane is approximately 1·35 kcal/mole,

[4] R. F. Bryan and J. D. Dunitz, *Helv. Chim. Acta* **43**, 3 (1960).
[5] [a] E. Huber-Buser and J. D. Dunitz, *Helv. Chim. Acta* **43**, 760 (1960); [b] E. Huber-Buser and J. D. Dunitz, *Ibid.* **44**, 2027 (1961); [c] J. D. Dunitz and K. Venkatesan, *Ibid.* **44**, 2033 (1961); [d] J. D. Dunitz and H. P. Weber, *Ibid* **47**, 951 (1964).
[6] J. D. Dunitz and H. M. Shearer, *Helv. Chim. Acta* **43**, 18 (1960).
[7] M. N. Mladeck and W. Nowacki, *Helv. Chim. Acta* **47**, 1280 (1964).
[8] N. L. Allinger, *J. Amer. Chem. Soc.* **81**, 5727 (1959).
[9] R. Pauncz and D. Ginsburg, *Tetrahedron* **9**, 40 (1960).
[10] J. B. Hendrickson, [a] *J. Amer. Chem. Soc.* **83**, 4537 (1961); [b] *Ibid.* **86**, 4854 (1964).
[11] J. Rosen, Thesis, Technion-Israel Institute of Technology (1962).
[12] K. B. Wiberg, *J. Amer. Chem. Soc.* **87**, 1070 (1965).
[13] R. G. Snyder and J. H. Schachtschneider, *Spectrochim. Acta* **21**, 169 (1965).
[14] There is one exception, namely Hendrickson's suggestion in reference 10b that his results on cyclodecane can be improved by using the C—C—C bond angle in n-alkanes instead of tetrahedral angle.
[15] L. S. Bartell and D. A. Kohl, *J. Chem. Phys.* **39**, 3097 (1963).
[16] K. S. Pitzer, *Disc. Faraday Soc.* **10**, 66 (1951).
[17] H. Takahashi, T. Shimanouchi, K. Fukushima and T. Miyazawa, *J. Mol. Spect.* **13**, 43 (1964).
[18] D. A. Dows, *J. Mol. Spect.* **16**, 302 (1965).
[19] H. Fuhrer and Hs. H. Gunthard, *Helv. Chim. Acta* **48**, 236 (1965).

Assuming that the excess enthalpy of other medium rings is of the same order, one should expect the calculated values of excess strain energies to be somewhat below the experimental values of vapor phase excess enthalpies.

Our mathematical procedure in calculating the conformations of minimum energy is that of steepest descent. If differs from Wiberg's[12] in that we use internal coordinates to represent molecular conformations. Interatomic distances are expressed as functions of the internal coordinates by matrix algebra and this makes it possible to obtain analytic expressions for both the energy and the energy gradient.

METHOD OF CALCULATION

The cycloalkane molecule C_nH_{2n} is considered in the present calculations as a ring of n carbon atoms connected by straight bonds. The ring is characterized by 3n—6 independent parameters which can be chosen from the 3n internal coordinates, namely bond lengths, bond angles and torsional angles. The independent variables chosen here are the n—1 bond lengths, $b_2, b_3, \ldots, b_n$, the n—2 supplementary bond angles $\theta_2, \ldots, \theta_{n-1}$, and the n—3 torsional angles $\phi_3, \ldots, \phi_{n-1}$.

We assume that the two hydrogens bonded to a carbon are symmetrically located on both sides of the C—C—C plane,[10] and the H—C—H angle varies linearly with the C—C—C angle, according to the relation:

$$\beta - \beta_0 = 0{\cdot}3\,(\theta - \theta_0) \tag{1}$$

β is the H—C—H bond angle and β_0 chosen as 109·47°, is its zero strain value; θ and θ_0 are the supplementary CCC bond angle and its zero strain value respectively.

In order to find the stable conformations of minimum potential energy, we used the method[11,12] of steepest descent by which the independent variables are changed step-by-step in the direction of the lowest molecular potential energy. Rosen[11] used this method to minimize the energy of an open cycloalkane ring in which the bond lengths have a constant value, and a fictitious force is applied between the ends to ensure the ring closure. Wiberg[12] used cartesian coordinates of the C and H atoms to minimize the cycloalkane potential energy.

The general scheme of our computations is as follows:

1. The geometry of the molecule is computed from the 3n—6 independent internal coordinates in the following way: cartesian coordinate systems are defined on each carbon atom. The transformation matrix from one coordinate system to another is expressed as a function of the bond angles and torsional angles. The vectors connecting any two atoms are then calulated by using these matrices, and their absolute values give the desired interatomic distances. A concise presentation of these calculations is given in Appendix 1.

2. The molecular potential energy is a function of the 3n—6 internal coordinates and the interatomic distances. It is computed from the results of the geometric calculations using potential energy functions which will be discussed in the next section.

The energy gradient is calculated by differentiating the expression for the total molecular potential energy with regard to the 3n—6 independent variables. Here the application of matrix algebra appears to be particulary useful since it leads to convenient formulas for the derivatives of interatomic distances. Details are given in Appendix 1.

3. The conformation of minimum energy is given by solving the system of

3n—6 equations grad E = 0, as follows: an initial conformation is chosen and its interatomic distances, energy, and energy gradient are computed. The 3n—6 independent coordinates are changed in the negative direction of the energy gradient (steepest descent) by a small amount, the average of which is determined in advance and changes during the calculation (Appendix 2). Again, interatomic distances, energy, and energy gradient of the new conformation are computed, and this cycle of computations is iterated until the energy ceases to decrease. Then the choice of dependent and independent variables is changed and the same cycle of computations is repeated until the minimum is reached.

The energy drops fast at the beginning of the calculation, when it differs from the minimum energy by several kilo-calories. As this difference becomes smaller the rate of convergence slows down, because some small deformations may leave the energy almost unchanged. For medium rings our computations are precise within 1°. The uncertainties in the experimental conformations of medium rings are somewhat larger. The precision in the case of chair cyclohexane is within 0·1°.

RESULTS AND DISCUSSION

Potential energy and enthalpy

The potential energy of a cycloalkane molecule may be considered as the sum of a number of independent contributions.[8–12] While some of these contributions are known to a reasonable degree of accuracy, others are of semi-quantitative nature and their functional form as well as the numerical values of the parameters involved are of empirical rather than theoretical origin.

Bearing this in mind we adopted the guiding principle that an elaborate model of interaction energy is advantageous over a simpler one only if there is a good reason to believe that it agrees better with experiment. Otherwise, the simpler model is preferred, particularly if it depends on a smaller number of energy parameters.

Another guiding principle adopted is that comparison between different sets of potential functions is instructive only if the functions and their parameters are varied one at a time. This made it possible to improve systematically the agreement between the calculated and the measured conformations, and between the calculated strain energies and the related measured enthalpies in the gas phase.

Enthalpies

It is customary to present the cycloalkane enthalpies relative to cyclohexane, i.e. H(n) − (n/6)H(6) where H(n) is the enthalpy of a n-membered ring. The enthalpies have to be measured in the gas phase to eliminate contributions of intermolecular interactions. Such measurements are available for the rings up to cyclononane.[2] The enthalpies of cyclodecane and cycloundecane[3] were measured in the liquid phase and there are no measurements of the heat of evaporation. However, the heat of evaporation per CH_2 unit was found to be a constant (1·34 kcal/mole CH_2) in the lower cycloalkanes.[2] We may assume that this is true also for higher rings, and compare their enthalpies in liquid state to the enthalpy of cyclohexane in the liquid state. The case of cyclododecane, whose enthalpy was measured in the solid state[3] is more difficult. No information is available on its heat of melting, and it cannot be extrapolated safely from the heat of melting of the lower cycloalkanes because of their irregular nature.[3]

The estimated experimental error is about 0·5 a kcal/mole of excess enthalpy in all medium rings except cyclododecane where the uncertainty is about 1·5 kcal/mole.

Vibrational enthalpies. In comparing the calculated strain energies with the measured enthalpies, we take cognizance of the fact that the enthalpy of the cycloalkane ring includes the vibrational-rotational-translational contribution as well as the strain energy. Vibrational enthalpies may be obtained from the analysis of available spectral data and supplementary information derived from normal mode calculations. Such information is available only for cyclohexane[17,18] and cyclododecane.[19] Using the equations H(translation) + H(rotation) = 3kT and

$$H(\text{vibration}) = h\sum_{i}[(\nu_i/2 + \nu_i \exp(-h\nu_i/kT)[1 - \exp(-h\nu_i/kT)]^{-1}] \qquad (2)$$

we obtained, at T = 300°K the values 107·36 kcal/mole and 107·17 kcal/mole for the two sets of data for cyclohexane,[17,18] and the value 215·69 kcal/mole for cyclododecane. The contribution to the excess enthalpy for cyclododecane is therefore $215{\cdot}69 - 2 \times 107{\cdot}17 = 1{\cdot}35$ kcal/mole, using the more recent value for cylcohexane.[18] Our estimate for the degree of accuracy, which is based on the different results for cyclohexane and on the difference between IR and Raman frequencies for cyclododecane,[19] is of the order of 0·5 kcal/mole. The corresponding values for other medium cycloalkane rings might be expected to be within the same range which is, incidentally, the same as that of the inaccuracies of experimental enthalpies. Thus, one should expect the calculated strain energies to be just within or somewhat below the experimental values. It will be seen from Fig. 1 that the results of our calculations are quite close to this expectation.

Energy functions

1. *Bond stretching.* The energy of the C—C bond as a function of its length is the best known among all contributions to the potential energy. The combination of X-ray and electron diffraction measurements and of spectroscopic data gives the C—C length and its stretching force constant with a relatively high degree of accuracy. Bartell and Kohl[15] presented an extensive study of the C—C bond lengths in n-alkanes and obtained an average value of 1·533 ± 0·002 Å. The recent study of the force constant by Snyder and Schachtschneider[13] gives the value $k_b = 4{\cdot}55$ mdyn/Å. Using these values we have

$$E(b) = 300\,(b - 1{\cdot}533)^2 \text{ kcal/mole} \qquad (3)$$

The energy associated with bond stretching is very small. This is due to the fact that the stretching force constant is large as compared with the other force constants.

Intramolecular interactions affect the equilibrium bond length up to about 0·03 Å. The uncertainties in the results of X-ray diffraction analysis are of similar magnitude,[5] therefore it is impossible to examine the significance of the calculated variations in bond lengths.

It is nevertheless convenient to consider bond lengths as variable internal coordinates for computational reasons. The alternative assumption that bond lengths are fixed requires the introduction of the conditions for ring closure either in the form of Lagrange multipliers[20] or by introducing fictitious forces[11] between the ends of an

[20] R. Pauncz, S. Lifson, J. Rosen and D. Ginsburg, unpublished work.

equivalent open chain. These methods, appeared to be computationally inconvenient.

2. *Bond angle equilibrium value.* The C—C—C bond angles of the four n-alkanes n-butane to n-heptane, have also been studied in detail.[15] A value of $112{\cdot}6 \pm 0{\cdot}3°$ was found for the *trans* conformation; for the *gauche* conformation the authors gave the value $112{\cdot}7 \pm 1{\cdot}0°$. It has been common to assume that the zero strain angle is the tetrahedral angle, and that the observed values are the result of equilibrium between bond angle strain and other interactions. This assumption is not justified. Firstly, the tetrahedral angle has no theoretical justification when the central carbon atom is not bonded to four identical groups. Secondly, starting from the tetrahedral angle, nonbonded interactions cannot extend it to the observed value in n-alkanes. The deviations from the tetrahedral angle, as estimated from functions of nonbonded interactions, have always been less than half a degree.

In view of these considerations it seems more plausible to choose the experimental value of the C—C—C bond angle of the n-alkanes as the zero strain angle, and assume that the deviations from this angle, as found in cycloalkanes, are imposed by the closing of the ring. The above considerations have indeed been borne out by our calculations as this choice has considerably improved the agreement between theory and experiment in general. It has been particularly successful in predicting the correct bond angles of the chair conformation in cyclohexane to a fraction of a degree (Fig. 3 and Table 2).

3. *Bond angle force constant.* Hendrickson[10] used the force constant values for the H—C—H, H—C—C and C—C—C bond angles reported in Westheimer's review.[21] i.e. 0·32, 0·55 and 0·8 mdynÅ/rad^2 respectively. He obtained a single equivalent force constant of 0·90 mdynÅ/rad^2 (65 kcal/mole), assuming that the changes in the H—C—H and H—C—C angles accompanying the bending of the C—C—C angle make the energy change minimal. Wiberg[12] used the values[21] in one set of calculations and the value 0·5 mdynÅ/rad^2 for all three angles in another set, permitting a change of the H—C—H and H—C—C angles independent of the C—C—C angle.

Some other values of bending force constants are available in the literature. M. Larnaudie[22] obtained 0·68, 0·53, 0·97 mdynÅ/rad^2 for the above mentioned angles respectively, from normal mode analysis of cyclohexane. Snyder and Schachtschneider[13] in their recent extensive normal mode analysis of n-alkanes, obtained 0·55, 0·67 and 0·90 mdynÅ/rad^2 for the above mentioned angles respectively.

All these values for force constants were derived from normal mode analysis of spectroscopic data. This analysis considers only harmonic forces between atoms, and includes a large number of cross terms, while conformation analysis includes torsional energies and nonbonded interactions in addition to harmonic forces of bending and stretching. The two are thus not compatible and are not expected to agree in detail with respect to the values of the C—C—C, C—C—H and H—C—H force constants.

If one considers, in addition, the fact that the zero-strain values of the C—C—H and H—C—H angles are not known and that all force constants hitherto calculated are based on the assumption that the zero strain angle is tetrahedral, while the zero

[21] F. H. Westheimer, *Steric Effects in Organic Chemistry* (Edited by M. S. Newman) Chap. 12. Wiley, New York, N.Y. (1956).

[22] M. Larnaudie, *J. Phys. Rad.* **15**, 365 (1954).

strain C—C—C angle used in the present study is larger, one may hesitate to go into the detailed calculation involved in using separate force constants for the C—C—C, C—C—H and H—C—H angles. Consequently, we follow Hendrickson, using a single equivalent force constant, and try several values for it, to find which fits better the enthalpy measurements.

Fortunately, the calculated potential is not very sensitive to variations in the equivalent C—C—C bending force constant. The normal mode analysis recent value for C—C—C bending force constant[13] being 65 kcal/mole rad,[2] we tried several values for the equivalent force constant, all larger than 65, keeping all other parameters unchanged. It is found that results improve with increasing the value up to 80 kcal/mole rad.[2] Further increase to 90 kcal/mole rad,[2] namely from 23% to 38% above the normal mode value, amounts to 150 and 250 cal increase in strain energy in cyclooctane and cyclododecane respectively, and considerably less in the other cycloalkanes. These differences are smaller than the inaccuracies in enthalpy measurements and cannot affect our results.

The potential energy function for the bond angle bending is thus taken, in view of the discussion in this and the previous subsections, as

$$E(\theta) = A\left(\frac{\pi}{180}\right)^2 (\theta - 67{\cdot}3)^2 \tag{4}$$

where θ is the supplementary bond angle and A the equivalent force constant of the C—C—C angle bending, whose value is anything between 80 and 90 kcal/mole.

4. *Torsional strain.* The torsional potential function in the ethane molecule is according to Pitzer[16]

$$E(\phi) = 1{\cdot}4\,(1 + \cos 3\phi) \text{ kcal/mole} \tag{5}$$

Pitzer also suggested a potential for propane of the same form as Eq. (5) but with a potential barrier of 3·4 instead of 2·8 kcal/mole in ethane. The three-fold symmetry of the torsional potential ethane and propane is due to the CH_3 group, and is therefore not necessarily applicable to rotation about the CH_2–CH_2 bond in higher n-alkanes. An experimental indication of a possible asymmetry in the rotational potential of higher n-alkanes is the enthalpy difference between the *trans* and *gauche* isomers. This difference has the values 760 ± 100, 450 ± 60, 520 ± 70, and 470 ± 60 cal/mole[23] for butane, pentane and the two *gauche* isomers of hexane all in the liquid state. However, the asymmetry may arise, at least in part, from the nonbonded interactions and the packing of the molecules in the liquid state. Calculations of the nonbonded interactions (see next subsection) give about 250 cal/mole for the energy difference between the *trans* and *gauche* isomers.

Hendrickson[10] used Pitzer's potential function for ethane with a potential barrier of 2·8 kcal/mole in his cycloalkane calculations, Wiberg[12,24] used the same function with a barrier of 3 kcal/mole.

We first applied the ethane torsional potential due to Pitzer[16] in all our calculations. The results as shown in Fig. 1 indicate clearly that the calculated values are consistently below experimental value by a margin which is too large to be accounted for by

[23] G. J. Szasz and N. Sheppard, *J. Chem. Phys.* **16**, 704 (1948); **17**, 86 (1949).

[24] Wiberg[12] also used the function $\cos^2 1{\cdot}5\,\phi$ in his first set of potential functions, but the two functions are equivalent since $2\cos^2 1{\cdot}5\,\phi - 1 + \cos 3\phi$ is a trigonometric identity.

the unknown vibrational enthalpy. Furthermore, we noticed that in cyclononane and cycloundecane, where the deviations are the largest, the torsional angles are twisted most. By applying the propane torsional energy function[16] the agreement between calculated and observed values improved significantly as shown in Fig. 1. These changes of the potential energy functions leave the calculated conformations almost unchanged.

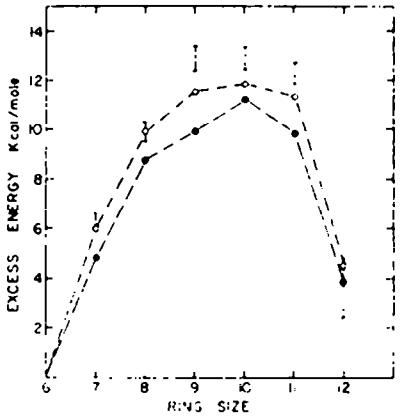

FIG. 1. Comparison between experimental excess enthalpies[8,9] (represented by segments) and the calculated excess energies. (●) with the ethane torsional barrier 2·8 kcal/mole; (○) with the propane barrier 3·4 kcal/mole. The bending force constant is 90 kcal/mole.

If we were able to account for the residual effect of asymmetry in the rotation of of the CH_2—CH_2 bond, a still better agreement could have been obtained. Unfortunately, too little is known at present on the nature of this asymmetry to justify its numerical consideration.

It will be noted that the torsional potential energy being the softest of all the energy terms, tends to account for a significant part of the total strain energy as may be seen from Table 1. The conformational strain energy is therefore more sensitive to changes in the value of the torsional potential barrier than to changes in other force constants.

5. *Nonbonded interactions.* A detailed discussion of the potential functions for nonbonded interactions is given by Hendrickson,[10] who concludes that the H—H interactions, and their repulsive part in particular, are the most significant for conformational analysis. The available knowledge of these functions is at present inconclusive, and there is not enough supporting evidence for considering the H—C and C—C interactions as independent of the H—H interactions. We have, therefore, chosen the simplest among Hendrickson's alternatives, namely we represent nonbonded interactions by H—H interaction potential (in kcal/mole)

$$F(r) = 10^4 \exp(-4{\cdot}60\, r) - 49{\cdot}2/r^6 \qquad (6)$$

We do not count as nonbonded interactions those between atoms attached to the same carbon or to adjacent carbons. In the preceeding sections the zero strain value of the C—C—C bond angle, its force constant and the torsional potential barrier were

TABLE 1. ENERGY CONTRIBUTIONS OF THE VARIOUS POTENTIAL FUNCTIONS IN KCAL/MOLE. THE BENDING FORCE CONSTANT IS 90 KCAL/MOLE RAD^2, THE TORSIONAL BARRIER IS 3·4 KCAL/MOLE

	E (stretching)	E (deformation)	E (torsional)	E (H—H)	E (total)
Cyclohexane					
Chair	0·00	0·26	0·39	−0·92	−0·27
Boat	0·02	0·25	6·99	−0·70	6·56
Skew Boat	0·01	1·04	6·36	−0·89	6·52
Cycloheptane					
Skew Chair	0·05	0·31	6·28	−1·09	5·55
Chair	0·15	0·75	6·31	−0·99	6·22
Boat	0·13	0·38	7·02	0·42	7·95
Skew Boat	0·18	0·26	6·80	0·95	8·19
Cyclooctane					
I	0·22	1·42	7·42	0·37	9·43
II	0·06	0·62	11·62	−0·98	11·32
III	0·20	0·36	11·94	−0·16	12·34
IV (crown)	0·15	1·58	12·50	−1·18	13·05
Cyclononane					
I	0·16	0·68	9·90	0·37	11·11
II	0·10	1·08	14·05	−1·01	14·22
III	0·68	2·49	9·89	1·96	15·02
Cyclodecane					
I	0·44	2·78	4·28	3·91	11·41
II	0·45	1·59	12·82	1·07	15·93
Cycloundecane	0·10	0·78	9·50	0·39	10·77
Cyclododecane	0·05	0·17	4·25	−0·51	3·96

taken from experimental observations on n-alkanes. Interactions between hydrogens attached to the same carbon or to adjacent carbons also exist in n-alkanes and contribute, among other factors, to the observed values of the above mentioned parameters.

Table 1 represents the contribution of the various energy potential functions to the total molecular strain energy. A comparison between the calculated excess potential energies (related to the cyclohexane chair conformation) and the experimental excess enthalpies is given in Fig. 1. A comparison with the results of Hendrickson and Wiberg is given in Fig. 2.

Conformations

Experimental data on conformations of medium cycloalkane rings are available from electron diffraction analysis of cyclohexane,[25] and from the extensive X-ray diffraction analysis[3] of cyclododecane[6] and of a number of derivatives of cyclooctane,[26] cyclononane[4] and cyclodecane.[6,7]

The electron diffraction results are the most suitable for our present discussion, as they are not affected by intermolecular interactions, being performed in the gas phase.

[25] M. Davis and O. Hassel, *Acta Chem. Scand.* **17**, 1181 (1963).
[26] J. D. Dunitz and A. Mugnoli, *Chem. Communications* 166 (1966).

Unfortunately, electron diffraction results on cycloalkanes other than cyclohexane are not yet published, except for a preliminary discussion of cyclooctane.[27]

In correlating our calculated results with the results of X-ray diffraction, we have to consider the fact that most measurements were made on substituted rings and that even in crystals of nonsubstituted rings intermolecular interactions may distort to some extent the equilibrium conformation. Moreover, the medium ring cycloalkane

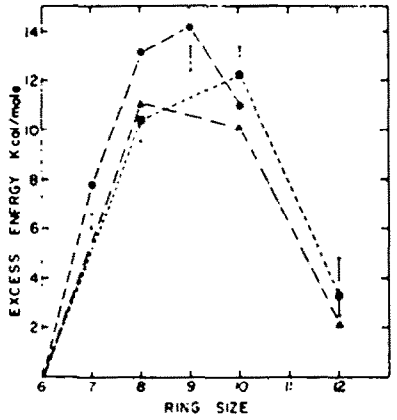

FIG. 2. Comparison between experimental excess enthalpies[3,8] (represented by segments) and the calculated excess energies by Hendrickson[10] (●) and Wiberg's[18] two sets of parameters (■, ▲).

molecules seem to possess a poor regularity of orientation in the crystalline state, and it is quite difficult to obtain satisfactory conformational parameters from X-ray diagrams. Thus, for example, Dunitz and Shearer[28] note that the cyclododecane crystal contains "two kinds of molecules randomly distributed with respect to statistical mirror planes". Similarly, Sands and Day[29] find it impossible to obtain a sufficient number of reflections from the cyclooctane crystal to determine its molecular structure, and they attribute this difficulty to a disordered orientation of the molecules in the crystal. Substituted cycloalkanes, which from ionic crystals, are superior to the cycloalkanes themselves in this respect.

We present here calculated conformations of rings with a relatively low strain energy from cyclohexane to cyclododecane. Among these, two conformations are new: cyclooctane III and cycloundecane. The others are similar to conformations calculated by Hendrickson[10] (n = 6, 7, 8, 9, 10) and by Wiberg[12] (n = 8, 10, 12), but differ in details. Five among these conformations correspond to experimentally known conformations, while the others may be considered as possible conformations due to their low strain energy.

As a measure of agreement between calculated and measured results we use the standard deviation of bond angles, $\sigma(\theta)$, defined by

$$\sigma^2(\theta) = \sum_{i=1}^{n} [\theta_i \text{ (calculated)} - \theta_i \text{ (experimental)}]^2/n$$

[27] A. Almeningen, O. Bastiansen, A. Haaland and H. M. Seip, *Angew. Chem.* (Internat. Edit.) **4**, 819 (1965).

[28] J. D. Dunitz and H. M. M. Shearer, *Proc. Chem. Soc.* 268 (1959).

[29] D. E. Sands and V. W. Day, *Acta Cryst.* **19**, 278 (1965).

and the similarly defined $\sigma(\phi)$. These are given in Table 2. The standard deviations related to the present calculations are generally in better agreement with experiment than those of previous ones. One may also note that $\sigma(\theta)$ and $\sigma(\phi)$ of 1,6-*trans*-diaminocyclodecane dihydrochloride are significantly smaller for the more accurate X-ray results of Ref. 5*b*, than those of Ref. 5*a*. On the other hand, part of the standard deviation is inherent in the fact that the calculated values do not account for the effect of substituents and intermolecular interactions. For example, two forms appear together in the same crystal of cyclononyl amine hydrobromide as twisted forms of the calculated conformations cyclononane III. The standard deviations between the two forms are $\sigma(\theta) = 3{\cdot}6$ and $\sigma(\phi) = 7$, namely of the same order of magnitude as the standard deviation of each form from the calculated conformations.

The calculated conformations are presented in Figs. 3–9 in a coordinate system coinciding with the three principal inertial axes. The numbers inside the rings represent bond angles and torsional angles. The Cartesian coordinates of the carbon atoms in the plane of the figure are in Angstroms according to scale while the perpendicular coordinate is given by numbers outside the ring.

Cyclohexane. The three conventional conformations, (Fig. 3) differ significantly from those calculated by other authors who assumed tetrahedral angles for zero strain bond angles.

The electron diffraction analysis[25] gives the value $111{\cdot}55° \pm 0{\cdot}15°$ for the bond angle in the chair conformation. The departure by 2·0° from the tetrahedral angle gives rise to a flattened chair, and[30] explains several experimental facts, such as the IR and NMR spectra of cyclohexane diols and chemical reactivities of several substituted cyclohexane.

The present calculation gives the values 111·5° for the bond angle and 54·7° for the torsional angle, which are in excellent agreement with experiment, while previous calculations, starting with tetrahedral angle as the zero strain angle, obtain the final equilibrium value within a fraction of degree from the initial value. In fact this observation was our main motivation for taking the observed C—C—C bond angles of n-alkanes as the initial zero strain value for the bending harmonic force.

Cycloheptane. No experimental results are available for comparison with the four conformations given in Fig. 4. They correspond to Hendrickson's calculated conformations, but differ by up to 4° in bond angles and 20° in torsional angles.

Cyclooctane. Among the four conformations represented in Fig. 5, the cyclooctane I corresponds to that given for 1,2-*trans*-dicarboxyl cyclooctane.[26] Electron diffraction study of cyclooctane "shows that at the temperature of . . . 40° a large number of conformations occur with approximately the same probability".[27] This is in quantitative agreement with the calculation of the strain energies of conformations I–IV given in Table 1.

Cyclononane. It will be noted that cyclononane III (Fig. 6) which corresponds to the X-ray results on cyclononylamine hydrobromide has a strain energy higher than that of cyclononane I by 3·9 kcal. This excess strain energy is apparently compensated by the crystal forces which are responsible for the existence of the A and B forms and for the relatively large σ values.

Cyclodecane. The conformations of four different derivatives of cyclodecane were

[30] R. A. Wohl, *Chimia* **18**, 219 (1964).

TABLE 2. STANDARD DEVIATIONS FOR BOND ANGLES θ AND TORSIONAL ANGLES ϕ. THE CALCULATED CONFORMATIONS FROM THE PRESENT WORK AND FROM THE LIT.[10-18] ARE COMPARED WITH THE EXPERIMENTAL ONES

Cycloalkane	standard deviation of θ in degrees				standard deviation of ϕ in degrees				Refs to the experimental conformation
	Present work	Hendrickson[10]	Wiberg[18] I	Wiberg[18] II	Present work	Hendrickson[10]	Wiberg[18] I	Wiberg[18] II	
Cyclohexane chair	0·0	1·6	—	—	0·0	5·3	—	—	25
Cyclononyl amine hydrobromide									
A	3·9	3·7	—	—	5·9	5·7		—	4
B	3·3	2·7	—	—	10·2	10·2	—	—	4
Cyclodecane 1,6-*trans*-diamino	1·9	5·1	3·6	3·4	6·2	13·6	8·0	7·3	5a
1,6-*trans* diamino	1·0	4·0	3·6	2·6	2·6	9·1	4·6	3·4	5b
1,6-*cis*-diamino	2·1	4·4	3·1	2·9	4·3	10·3	5·1	4·8	5c
1,6-*trans*-dibromo	3·3	5·7	5·0	4·4	3·9	9·4	4·6	4·2	5d
Cyclododecane	3·2	—	2·3	2·8	2·4		2·3	2·5	6

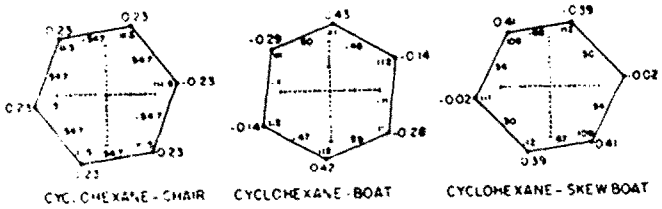

FIG. 3

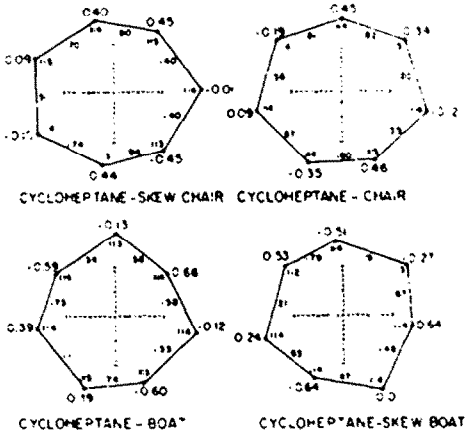

FIG. 4

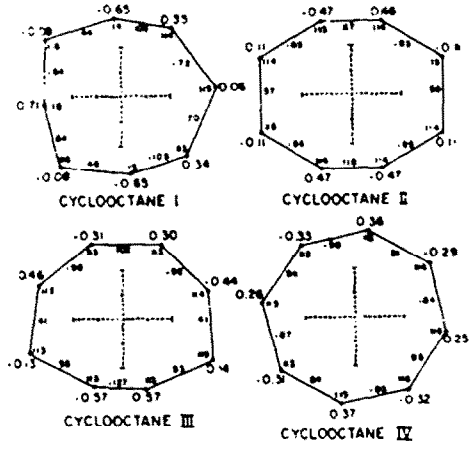

FIG. 5

studies by X-ray diffraction and all four correspond to the calculated cyclodecane I which has the lower strain energy among the two conformations given in Fig. 7. The analysis of 1,6-*trans*-diaminocyclodecane dihydrochloride was the subject of two studies.[5a,b] For the first,[5a] the standard deviations are 0·032 Å in bond length, 1°50′ in bond angle and 2° in torsional angle. In the second study,[5b] a larger number of reflections were measured and a more refined mathematical procedure was used. The estimated standard deviations in this case are 0·013 Å, 40′ in bond angle and 1° in

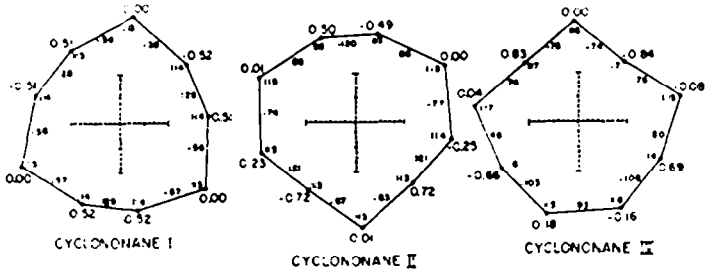

FIG. 6

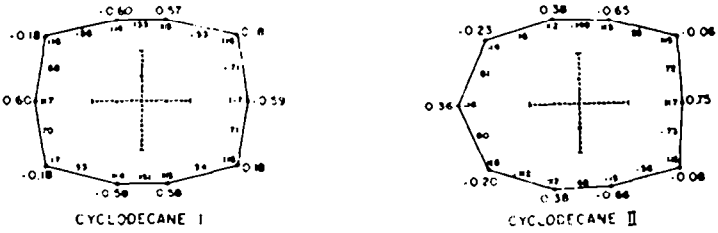

FIG. 7

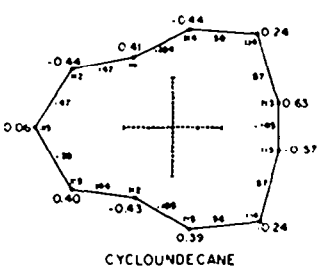

FIG. 8

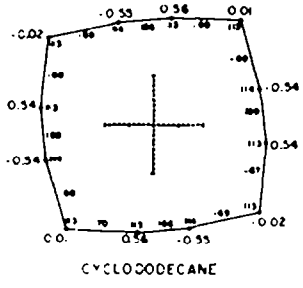

FIG. 9

torsional angle. The difference in torsional angles between the two evaluations are between 1° and 9°. These figures indicate the magnitude of uncertainties in the conformational determinations. Three more cyclodecane derivatives which were investigated[5c,d,7] give similar but not identical ring conformations.

Cycloundecane. There is no experimental check of the conformation suggested here for cycloundecane, except that its strain energy is in agreement with calorimetric measurements, particularly with the possible correction due to enthalpy of vibration-rotation-translation.

Cyclododecane. The conformation of this ring was first calculated by Wiberg[12] using two sets of energy functions. Our calculations agree reasonably with the X-ray analysis,[6] as well as with those of Wiberg.

In conclusion, we believe to have shown that comparison of calculated potential energies and experimental enthalpies, as well as comparison of calculated and measured conformations, can serve as a source of information on intramolecular interaction parameters.

With the accumulation of more information on the normal modes of the cycloalkanes, the comparison betweeen potential energy and enthalpy will permit more

accurate potential energy functions, especially for nonbonded interactions. The present approach may be used for the determination of other force constants by studying molecules containing other atoms.

APPENDIX I

Figure 10 gives a schematic sketch of the molecule and represents the following geometric parameters

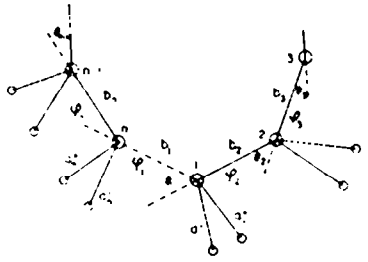

FIG. 10. Schematic sketch of the cycloalkane molecule geometry.

b_k—bond length between carbons k—1 and k.
θ_k—supplementary angle to the bond angle on atom k
ϕ_k—Torsional angle around the bond b_k, it is defined as positive by rotating the vector b_{k+1} anticlockwise around b_k.
The independent parameters are $b_3, \ldots, b_n$; $\phi_3, \ldots, \phi_{n-1}$; $\theta_3, \ldots, \theta_{n-1}$. On each carbon atom k a coordinate system is defined as follows:

$$k_k = b_{k+1}/b_{k+1}$$
$$i_k = b_{k+1} \times b_k/(b_{k+1} b_k \sin \theta_k)$$
$$j_k = k_k \times i_k$$

The transformation matrix from the kth coordinate system to the (k − 1)th coordinate system is:

$$T_k = \begin{pmatrix} \cos \phi_k & \sin \phi_k & 0 \\ -\cos \theta_k \sin \phi_k & \cos \theta_k \cos \phi_k & \sin \theta_k \\ \sin \theta_k \sin \phi_k & -\sin \theta_k \cos \phi_k & \cos \theta_k \end{pmatrix}$$

The distance between the carbon i to the carbon k in the coordinate system i is

$$b_{i,k} = b_{i+1} I + b_{i+2} T_{i+1} + b_{i+3} T_{i+2} T_{i+1} + \ldots + b_k T_{k-1} \ldots T_{i+2} T_{i+1}$$
$$= (0,0,1)[b_{i+1} I + b_{i+2} T_{i+1} + \ldots + b_k T_{k-1} \ldots T_{i+2} T_{i+1}]$$

Two hydrogen atoms are attached to each carbon. In the coordinate system of the carbon atom their positions are defined by the vectors a^σ where σ stands for either + or −; a = 1·108

$$a_k^\sigma = a(\sigma \sin \tfrac{1}{2}\beta_k, \cos \tfrac{1}{2}\beta_k \cos \tfrac{1}{2}\theta_k, -\cos \tfrac{1}{2}\beta_k \sin \tfrac{1}{2}\theta_k)$$

where β_k is the angle between the two hydrogen-carbon bonds.
The distance between the hydrogen atoms on carbons i and k are

$$r_{i,k}^{\sigma,\rho} = -a_i^\sigma + b_{i,k} + a_k^\rho T_k \ldots T_{i+1}$$

The six dependent internal coordinates are determined as follows

$$\mathbf{b}_1 = -\mathbf{b}_{n+1} = -(0,0,1)[\mathbf{b}_2\mathbf{I} + \mathbf{b}_3\mathbf{T}_2 + \ldots + \mathbf{b}_n\mathbf{T}_{n-1}\mathbf{T}_{n-2}\ldots\mathbf{T}_2\mathbf{T}_2]$$

$$\cos\theta_1 = \frac{\mathbf{b}_1 \cdot \mathbf{b}_2}{b_1 b_2}$$

$$\cos\theta_n = \frac{\mathbf{b}_n \cdot \mathbf{b}_1}{b_n b_1}$$

$$\cos\phi_1 = \frac{(\mathbf{b}_n \times \mathbf{b}_1)\cdot(\mathbf{b}_1 \times \mathbf{b}_2)}{|(\mathbf{b}_n \times \mathbf{b}_1)|\cdot|(\mathbf{b}_1 \times \mathbf{b}_2)|}$$

$$\cos\phi_2 = \frac{(\mathbf{b}_1 \times \mathbf{b}_2)\cdot(\mathbf{b}_2 \times \mathbf{b}_3)}{|(\mathbf{b}_1 \times \mathbf{b}_2)|\cdot|(\mathbf{b}_2 \times \mathbf{b}_3)|}$$

$$\cos\phi_n = \frac{(\mathbf{b}_{n-1} \times \mathbf{b}_n)\cdot(\mathbf{b}_n \times \mathbf{b}_1)}{|(\mathbf{b}_{n-1} \times \mathbf{b}_n)|\cdot|(\mathbf{b}_n \times \mathbf{b}_1)|}$$

The derivatives of the distances and the dependent variables according to the independent variables are computed using the usual laws on differentiation of products. The derivatives of the transformation matrix according to x where x is one of the 2n − 5 independent parameters θ_1, ϕ_1 is

$$\frac{\partial \mathbf{T}_k}{\partial x} = \begin{pmatrix} -\sin\phi_k\,\delta_{\phi_k x} & \cos\phi_k\,\delta_{\phi_k x} & 0 \\ -\cos\theta_k\cos\phi_k\delta_{\phi_k x} + \sin\theta_k\cos\phi_k\delta_{\theta_k x} & -\cos\theta_k\sin\phi_k\delta_{\phi_k x} - \sin\theta_k\cos\phi_k\delta_{\theta_k x} & \cos\theta_k\delta_{\theta_k x} \\ \sin\theta_k\cos\phi_k\delta_{\phi_k x} + \cos\theta_k\sin\phi_k\delta_{\theta_k x} & \sin\theta_k\sin\phi_k\delta_{\phi_k x} - \cos\theta_k\cos\phi_k\delta_{\theta_k x} & -\sin\theta_k\delta_{\theta_k x} \end{pmatrix}$$

where $\delta_{\phi_k x} = 1$ if $x = \phi_k$ otherwise $\delta_{\phi_k x} = 0$; $\delta_{\theta_k x} = 1$ if $x = \theta_k$, otherwise $\delta_{\theta_k x} = 0$

The total potential energy of the molecule is a function of the interatomic distances and the 3n internal coordinates. By using the derivatives of the distances and the dependent internal coordinates with respect to the independent variables, the derivatives of the energy with respect to the 3n − 6 independent variables can be computed. These derivatives are the 3n − 6 components of the energy gradient vector.

APPENDIX II

There are several possible methods to compute the vector of corrections $\Delta\mathbf{x}$ to the vector of independent parameters $\mathbf{x} = (b_2, b_3, \ldots, b_n, \theta_2, \ldots, \theta_{n-1}, \phi_2, \ldots, \phi_{n-1})$. One possibility is to compute $\Delta\mathbf{x}$ in such a way that this correction in the linear approximation will lower the energy by ΔE[11].

$$\Delta\mathbf{x} = -[\text{grad } E/(\text{grad } E)^2]\Delta E$$

This method can cause difficulties when the linear approximation is invalid and $(\text{grad } E)^2$ is small. In this case the calculated corrections will be too large and the new conformation will be worse than the preceeding one.

To eliminate the possibility of too large corrections we determine in advance $\overline{\Delta x}$, the average correction, instead of ΔE. The average correction is defined as

$$\overline{\Delta x} = \sum_i |(\Delta x)_i|/3n - 6$$

and by using it the vector of corrections is computed as

$$\Delta\mathbf{x} = -(3n - 6)\overline{\Delta x}\,\text{grad } E/\sum_i |(\text{grad } E)_i|$$