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CALCULATION OF CONFORMATIONS OF ORGANIC MOLECULES*

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Abstract—The most stable conformation of the molecule has a minimum of potential energy that arises due to the competition between the tendency of the valency angles to take ideal values and that of non-bonded atoms to be situated at an equilibrium distance. The equilibrium distance is equal to the sum of intermolecular radii determined by measuring the distances between atoms of adjacent molecules in the crystal. This idea is suggested as underlying a method of computation that enables to solve two problems. Firstly, the structure of the molecule being known, it becomes possible to ascertain the points of the interaction curve of the non-bonded atoms and secondly, with the interaction curve known, one can calculate the optimal configuration of the molecule.

To illustrate the suggested theory the conformation of molecules of some cyclic hydrocarbons has been calculated. It is to be stressed that the investigation of the conformation of strained molecules affords the main means of studying the interaction of non-bonded atoms.

INTRODUCTION

THE theoretical calculation of geometrical parameters and the energy of conformation of molecules is of great interest. To this end it is necessary to possess information concerning some characteristic constants and functions that, in turn, can be derived by analyzing geometrical parameters and the energy of molecules whose structure has been determined.

This work aims at demonstrating the possibility of determining the interaction energy of non-bonded atoms by the molecular structural analysis. The empirical information thus obtained permits us the evalutation of the optimal conformation of molecules with unknown structure.

The following general considerations are underlying the suggested method of calculation. In the process of temperature vibrations the atoms of the molecule undergo complex movements without breaking the bonds. Thus there is a continuous series of conformations possible for a molecule. Various conformations differ in energy and therefore possess different probability.

The variation of conformation results, generally speaking, in the change of all its geometrical parameters such as the length of the bonds (or the equilibrium distances between the bonded atoms), the valence angles and the distances between the non-bonded atoms.

This investigation is based on the assumption of the addivity of the molecular energy, that is the overall energy can be separated into three additives responsible for the energy of the bonds, of the angles and of the non-bonded atoms. The issue is strongly facilitated by the fact that the chemical structure pre-determines the length of the bonds to as high a precision as 0·01–0·02 Å. The changes in conformation

* Translated by A. L. Pumpiansky, Moscow.

(e.g. the change of "boat → chair" cyclohexane conformation) does not lead to noticeable stretching of the bond length. This conclusion has been derived from structural investigations that show little difference in the bond length in highly strained structures and that of non-strained molecules (though bond stretching caused by the interaction of non-bonded angles up to 0·01 Å seems to be a real effect).

Thus, for example, the C—C bond lengths in cyclobutane and normal alkanes differ by about 0·02 Å.

There is no difficulty in showing that in the mechanical system of points linked by springs of different rigidity the deformation energies are in an inverse ratio to the forces constants. The rigidity of the bond is markedly higher than that of the angle or that of the interaction between the non-bonded atoms.

Any change of configuration is therefore connected with the change of both the valence angles and distances between the non-bonded atoms. Let the conformation strain energy be the sum of two additives

$$U = V + \Phi$$

where the energy V is connected with the value of the valent angles and energy Φ with the distance between the non-bonded angles.

The optimum configuration is that with the minimum value. Therefore it is of importance to determine the geometrical parameters that lead to the minimum U value.

The energy of the angle

An ideal valence angle can be said to be such an angle that could exist in the absence of interaction between non-bonded atoms (as well as, of course, in the absence of bonds imposed by the added atoms). With sp^3 bonds such an angle is known to be the tetrahedrical angle at 109° 28′, with pure p bonds the angle at 90°, etc. The deviation of the angle from its ideal value leads to a decrease of the orbital over-lapping and corresponding energy increase. For the deviations α from the ideal value which we met in practice the angle energy can be written down within the precision of the constant additive as $\frac{1}{2}C\alpha^2$ with C being the coefficient that can be, in principle, calculated by resorting to quantum chemistry.[1]

This not being practically the case we shall consider the coefficient C as an empirical coefficient and, in addition, as a constant value for the atom that is in the apex of the angle and not depending on the type of the bonded atoms. We shall refer of coefficient C as the ideal angle force constant. Its relation to the force constant of the angle k_β deduced from the analysis of the molecular vibration will be discussed below.

The energy connected with the value of angles is $V = \Sigma\frac{1}{2}C\alpha^2$, the summation embracing all valence angles.

The interaction between the non-bonded angles

Investigating different problems due to steric interaction a number of authors attempted to formulate the interaction energy–distance ratio. The first attempt dealing with the interaction between hydrogen atoms seems to be due to Eyring[2]

[1] e.g. C. A. Coulson, *Valence*. Oxford (1953).
[2] H. Eyring, *J. Amer. Chem. Soc.* **54**, 3191 (1932).

who evaluated the repulsion energy as $Q_{HH} - \frac{1}{2}T_{HH}$, with Q and T being the Coulomb and exchange integrals and the attraction energy taken from the well known work by London as A/r^6. The recent calculations of this type are those by Hirschfelder and Linnett[3] that have been used by Mason and Kreevoy[4] as well as by Adrian.[5]

The calculations used in the works cited above cannot be regarded as correct as they lead to the minimum interaction energy lying at the value 4·5 Å. It is at the same time a well established fact that the equilibrium distance for two non-bonded hydrogen atoms is 2·35 Å. Within the limits of precision not less than 0·1 Å this distance is realized for hydrogen atoms in molecules possessing quite different properties. There is no reason to believe that this figure, deduced from the analysis of inter-molecular contacts in the crystal, may be substantially different for hydrogen atoms of the same molecule.* The constancy of intermolecular radii, their negligible dependance on the dipole moments and chemical properties[6] gives us a definite knowledge of an important point on the interaction curve of the non-bonded atoms, namely that of the co-ordinate of its minimum. The theoretical methods available do not result in the necessary value of the curve minimum, this being due to the imperfection of calculations.

The main thesis of our work is the assertion that: *the non-bonded atoms of the molecule at a distance greater than the sum of their intermolecular radii are only negligibly attracted to each other, those at a distance smaller than that sum being repelled from each other to a considerable extent.*

This fact, though not clearly formulated, is taken into account in the works of Dostrovsky *et al.*,[7] as well as Westheimer and Mayer[8] who chose their interaction curves so that their minimum would correspond to the sum of the intermolecular radii. This adjustment is effected by varying the coefficients in the formulae such as $(a/r^m) - (b/r^n)$ or $Ae^{-\alpha r} - (b/r^n)$.

In this work we decided not to make use of any analytical expressions. It must however be stressed that the interaction curve of the non-bonded atoms must not be calculated but found experimentally (see below). It is thereby neither necessary nor possible to take the physical factors, affecting the interaction, separately. The same considerations apply to the electro-static field that, by the way, is of little effect on the changes in energy owing to the electric potential being slow, as indicated in the work cited above.[4]

The interaction curve is steeply rising over the range of repulsion and extremely gently sloping over that of attraction (the minimum of the interaction curve, as judged by the heat of sublimation per the pair of interacting atoms, is as small as tens of parts of kcal/mole). Therefore, in most conformation problems attraction can be easily dispensed with, and the interaction energy of non-bonded atoms can

* There is no doubt about the dependence of the atom radius on the direction of the radius depending on the direction of the bond. This dependence is however not yet sufficiently investigated and therefore not taken into consideration though it could have been easily allowed for in the approach under study. One must also bear in mind the influence of the crystal field on the atom interaction curve. Therefore the equilibrium distances of non-bonded atoms can be said to be different, depending on the aggregate state.

[3] J. O. Hirschfelder and J. W. Linnett, *J. Chem. Phys.* **18**, 130 (1950).
[4] E. A. Mason and M. M. Kreevoy, *J. Amer. Chem. Soc.* **77**, 5808 (1955).
[5] F. J. Adrian, *J. Chem. Phys.* **28**, 608 (1958).
[6] A. I. Kitaygorodsky, *Organic Crystal Chemistry*. Moscow (1955), London Engl. transl. Infosearch (1960).
[7] I. Dostrovsky, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.* 173 (1946).
[8] F. H. Westheimer and J. E. Mayer, *J. Chem. Phys.* **14**, 733 (1946).

be accounted for as $\Phi = \Sigma f(\Delta r/r_0)$ extending the summation to all pairs of atoms at a distance less by Δr than the equilibrium distance r_0. It is more convenient to write the interaction energy of a pair of atoms as the function of the relative decrease $\Delta r/r_0$ of the distance between them.

The conditions for the optimum conformation

The conformation of a molecule is characterised by a definite number of independent parameters ε_i, that can be expressed in terms of some valence angles, or the distances between the non-bonded atoms, or other geometrical parameters. When the molecule consists of n atoms linked by m bonds the number of parameters is $3n-6-m$. The symmetry of the molecule decreases the extent of freedom. To arrive at the optimum conformation it is necessary to differentiate the energy expression

$$U = \tfrac{1}{2}\Sigma C\alpha^2 + \Sigma f\left(\frac{\Delta r}{r_0}\right)$$

by all independent parameters ε_i,
Equations

$$\frac{\partial U}{\partial \varepsilon_i} = \Sigma C\alpha \frac{\partial \alpha}{\partial \varepsilon_i} + \Sigma f'\left(\frac{\Delta r}{r_0}\right)\frac{\partial(\Delta r)}{r_0\,\partial \varepsilon_i} = 0$$

allow to arrive at the value f'/C for definite values of arguments provided the structural values of the molecule in question are available. On the other hand, the curve f'/C being known, one can determine the optimum conformation of the molecule.[9] We shall refer to the value $\eta = f'/C$ as *the relative force of the interaction of atoms.*

The shape of the relative force curve

The constant C must depend on the central atom whilst $\eta(\Delta r/r_0)$ characterizes the interaction of definite atoms. To solve our problem it is therefore necessary to acquire structural information about a rather great number of molecules of the same atoms but with different valence angles and spacing of the non-bonded atoms. Unfortunately at present this information is scarce.

To demonstrate the possibility of the suggested approach to the conformational problem we have, however, attempted to calculate a number of conformations. The curve η that we have decided to make use of is shown in Fig. 1, the points obtained by calculating η for simple molecules. It will be seen that the points referring to the interaction between carbon and hydrogen atoms bound to different atoms are situated on the same curve. It is of interest, that the energy interaction curve for carbon and bromine atoms, as reported by Dostrovsky *et al.*[7] and recalculated in terms of the values of the relative force η is rather similar to our mean curve.

Whether this coincidence is occasional, how great are the changes of the curve f' for different atoms and coefficients C for central atoms can be shown only by further practical investigations of the molecular structure. It is however at present safe to say that the interaction curve for the halogen atoms is markedly steeper.

Calculation of conformations

In the table the conformational calculations for a number of hydrocarbons are given. It is quite possible that in the future the shape of the curve η we have

[9] A. I. Kitaygorodsky, *Dokl. Akad. Nauk SSSR* **124**, 1267 (1959).

used will have to be substantially changed. This will, however, not seem to affect the general character of the calculated distortions.

From the data obtained it is above all to be noted that the tetrahedral angles in normal alkanes and cyclohexane are increasing up to about 111·5°; and that the HCH angle in cycloalkanes is steadily decreasing (Fig. 2).

In addition to these simple systems three bridge structures have been calculated, only for one of which experimental data were available (Fig. 3).

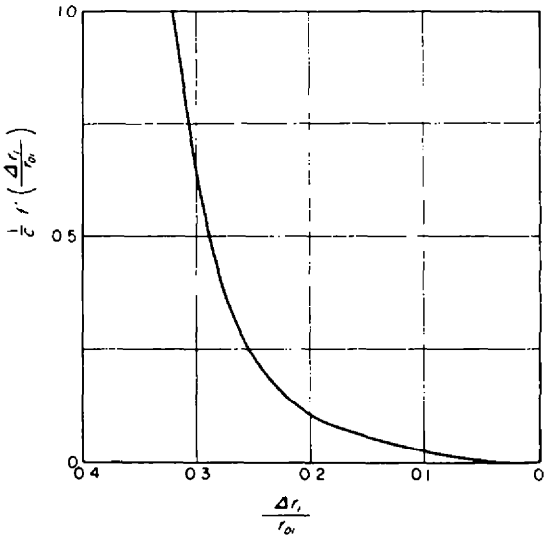


FIG. 1. Relative force of interaction of non-bonded atoms.

In Fig. 4 are listed data for acenaphtene, the calculation having been made for the values of the ideal angles (120°) and the tetrahedral value of the angle at atom 7. The calculations were compared with experimental data recorded by Ehrlich[10] (two mean values obtained from two independent measurements).

To exemplify the numerical calculation method let us take the simplest case of the conformation of the methylene group.

Let us denote ∠CCC as α, ∠HCH as β, and ∠HCC as γ with α and β being independent parameters. If their value deviate by $\Delta\alpha$ and $\Delta\beta$ from the ideal value (109° 30′); then from the correlation $\cos\gamma = -\cos(\alpha/2) \cdot \cos(\beta/2)$ it follows with reasonable precision that $\Delta\gamma = -\frac{1}{4}(\Delta\alpha + \Delta\beta)$. The interatomic distances are represented by expanding trigonometrical functions about the ideal value of the angle.

Hence

$$r_{CC} = 2{\cdot}50 + 0{\cdot}88\Delta\alpha, \qquad r_{HH} = 1{\cdot}76 + 0{\cdot}62\Delta\beta$$

and

$$r_{CH} = 2{\cdot}15 - 0{\cdot}18(\Delta\alpha + \Delta\beta).$$

The relative contractions are found by applying intermolecular radii $R_C = 1{\cdot}8$ and $R_H = 1{\cdot}2$ Å.

[10] H. W. W. Ehrlich, *Acta Cryst.* **10**, 699 (1957).

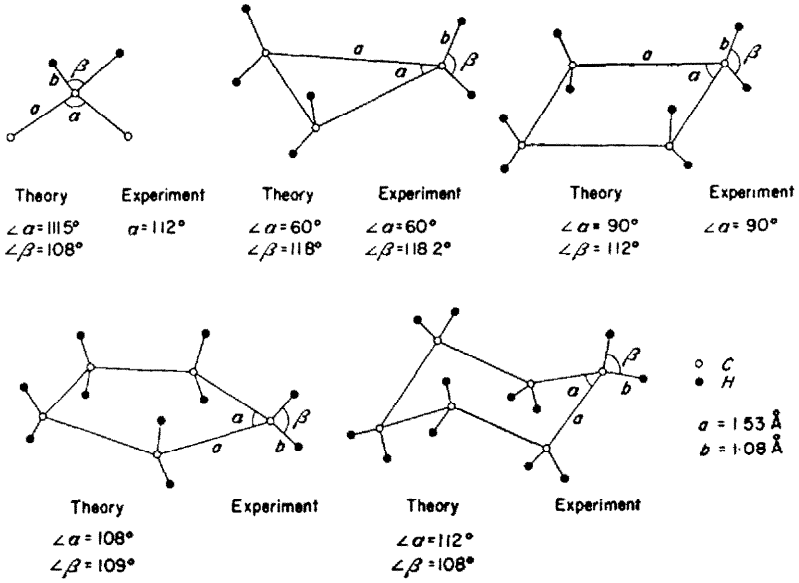
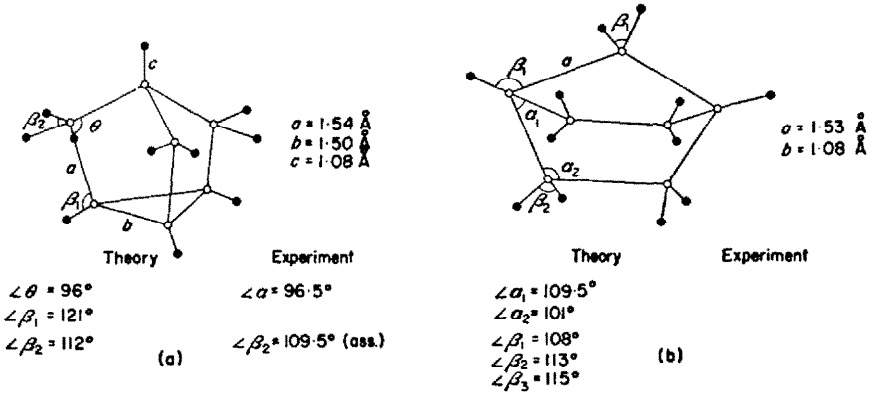


FIG. 2. Conformations of cycloalkanes.



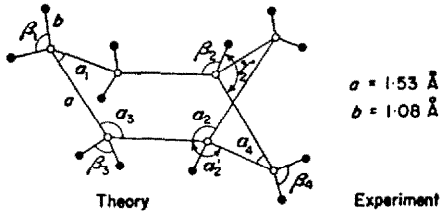


FIG. 3. Conformations of (a) nortricyclene C_7H_{10}, (b) norcamphane C_7H_{12}, (c) norpinane C_7H_{12}.

Thus, the expression for the strain energy of the methylene group can be represented as

$$U = \frac{C}{2}[(\Delta\alpha)^2 + (\Delta\beta)^2 + \tfrac{1}{4}(\Delta\alpha + \Delta\beta)^2] + f(0{\cdot}306 - 0{\cdot}245\Delta\alpha) + f(0{\cdot}267 - 0{\cdot}26\Delta\beta) + 4f(0{\cdot}283 + 0{\cdot}06(\Delta\alpha + \Delta\beta))$$

Differentiating by $\Delta\alpha$ and $\Delta\beta$, equating the value of derivatives to zero and expanding $\eta(\Delta r/r_0)$ into the Taylor's series neglecting the second and higher powers of increments

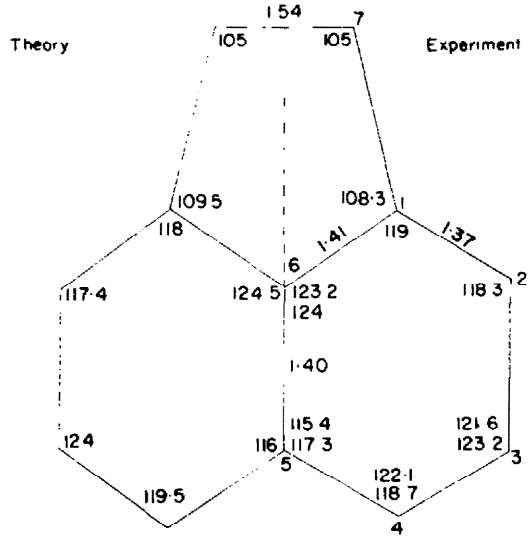


FIG. 4. Comparison of experiment and calculation for acenaphtene.

(values η and η' being taken from the above curve), one obtains two equations with two unknown quantities

$$\Delta\alpha + \tfrac{1}{4}(\Delta\alpha + \Delta\beta) - 0{\cdot}245(0{\cdot}75 - 5{\cdot}2\Delta\alpha) + 0{\cdot}24[0{\cdot}43 + 0{\cdot}64(\Delta\alpha + \Delta\beta)] = 0$$

$$\Delta\beta + \tfrac{1}{4}(\Delta\alpha + \Delta\beta) - 0{\cdot}26(0{\cdot}285 - 1{\cdot}3\Delta\beta) + 0{\cdot}24[0{\cdot}43 + 0{\cdot}64(\Delta\alpha + \Delta\beta)] = 0$$

whose solution leads to $\Delta\alpha = 0{\cdot}033$ and $\Delta\beta = -0{\cdot}025$. That is, the equilibrium values of the angles are 111·5° for $\angle$CCC and 108° for $\angle$HCH.

The same approach is applied to solve other cases, more complicated ones necessitating more than two equations.

Deviations from coplanarity in aromatic systems

At present there are well known instances of marked deviations from coplanarity in aromatic systems [e.g. see ref. (11)].

There is no need to exemplify this phenomenon by complex aromatic systems for non-planarity in aromatic nuclei appears to occur in all benzene derivatives. Indeed, the spacings of all substituents in the benzene ring are smaller than the sum of intermolecular radii. This results in repulsion that leads not only to the substituents being eliminated from the plane of the nucleus but also "dragging" carbon

[11] E. Harnik, F. H. Herbstein and G. Schmidt, *J. Chem. Soc.* 3288 (1954).

atoms with them and thereby making the benzene ring devoid of planarity. Conformational studies show that for the "triangular edge" of the benzene ring to be bent no great effort is required. Fig. 5 shows the conformation in the di-*p*-xylelene molecule. The above formulas were used to calculate the derivatives by independent parameters, in that case the deviations from the ideal angles $\Delta\alpha_1$, $\Delta\alpha_2$, and $\Delta\beta_1$. The fourth parameter was represented by angle ε, formed by the bent edge and the plane of the four central atoms. It was thereby noted that substituting experimental data in expressions for derivatives $\partial U/\partial(\Delta\alpha_1)$, $\partial U/\partial(\Delta\alpha_2)$ and $\partial U/\partial(\Delta\beta_1)$ converts them with reasonable precision to zero. At the same time $\partial U/\partial\varepsilon = 0{\cdot}3C$.

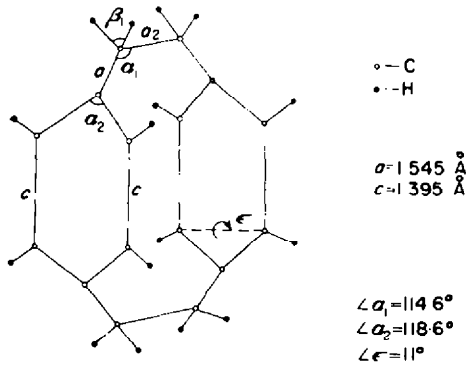


FIG. 5. Molecule of di-*p*-xylylene $C_{16}H_{16}$.

This points to the necessity of introducing into the energy member the energy due to the bending of the benzene ring. If this additive be substituted as $4(\gamma\varepsilon^2/2)$ and the experimental value of ε is $\sim$0·20 rad, then $\gamma = 0{\cdot}4C$. It will be thereby seen that the force constant of the edge bending is two and a half times less that of the ideal angle.

Of course the force constant of the edge bending cannot be regarded as established, being calculated only in one instance. It is moreover quite possible that such a strain energy characteristic of a distorted aromatic system is not strictly valid. We have, however, made use of these approximate data to estimate the distortions in such a structure as that of hexamethylbenzene. The strain energy expression is as follows

$$U = 6\frac{C}{2}[(\Delta\alpha)^2 + 2(\Delta\beta)^2] + 6f_{C_1C_3} + 12f_{Me_1C_2} + 6f_{Me_1Me_2} + \\ + 3f_{C_1C_4} + 3\frac{0{\cdot}4}{2}C(\Delta x)^2$$

with $\alpha = \angle$CCC, $\beta =$ MeCC, and Δx being the bending angle of the benzene ring edge. The molecule is believed to have a boat conformation. The drawing apart of two methyl groups proceeds at the expense of the bending of the edge bending and, in addition, at the expense of the expulsion of the methyl group from the plane of the respective carbon atom triangle, the latter deviation being due to that of the angle β from 120°.

The minimum potential energy proved to be at the angle value $\Delta x = 8°$. The adjacent methyl groups are drawn thereby further apart at the expense of the deviation

of the C—CH_3 bond by the angle 6° from the plane of the respective benzene nucleus triangle.

Such example of a similar, highly distorted system can be provided by the structure of a benzene derivative determined by Struchkov[12] at our Institute (see Fig. 6). The

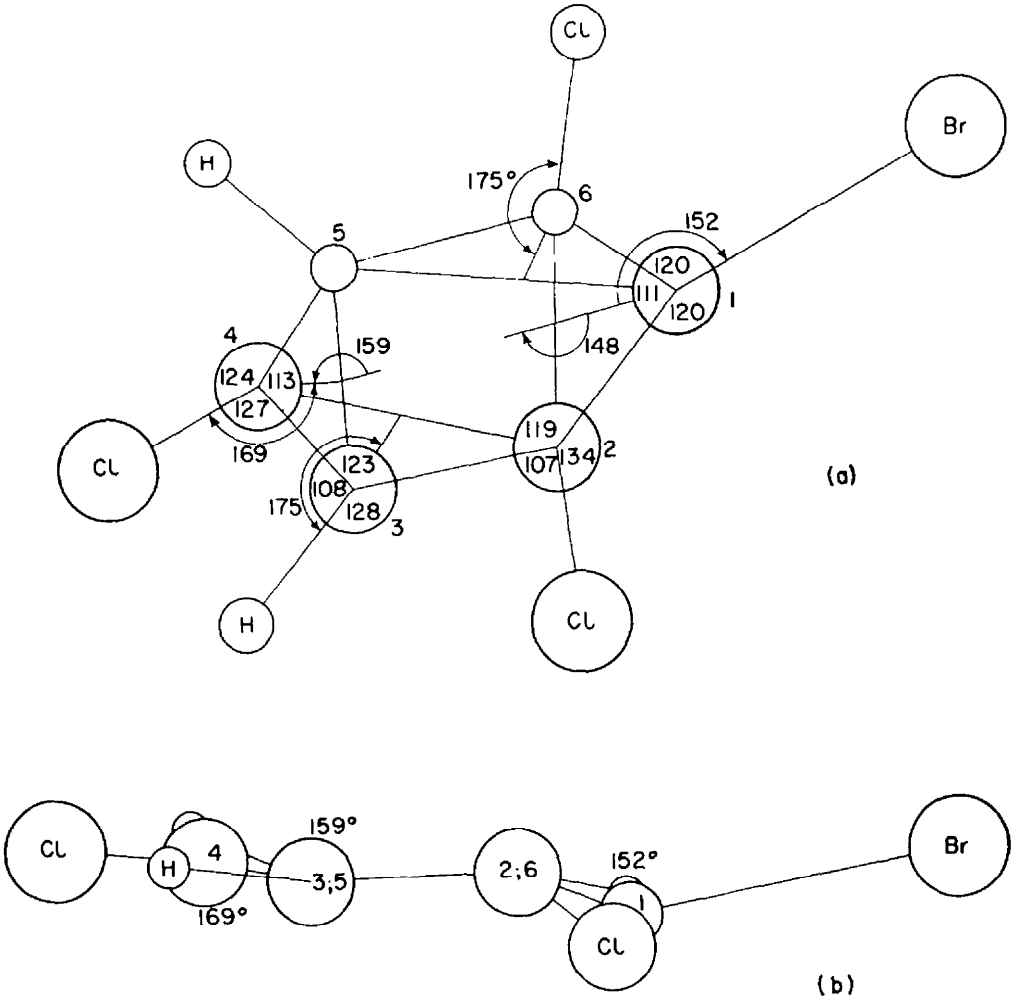


FIG. 6. Experimental data of molecule of 1-bromo-2,4,6-trichlorobenzene:
(a) perspective view,
(b) view in the direction perpendicular to the symmetry plane.

distortion of the ring is very strong, the benzene ring conformation being near to that of the boat conformation in cyclohexane.

The evaluation of the coefficient C (see below) allowed us to compute the difference in the energy of optimal and flat configurations. It proved to be less than 0·1 kc/m. Thus the influence of the crystal field can lead to the molecule becoming flat. In other instances, however, the crystal molecules can also deviate from the flat form.

[12] J. T. Struchkov and S. L. Solenova, *Proc. Moscow State Univ.* **12**, 1228 (1959).

Evaluation of strain energy and rigidity coefficients

Conformational analysis leads us to the estimation of the relative interaction force $\eta = f'(\Delta r/r_0)/C$ value. The estimation of the absolute force value and the calculation of the interaction energy is therefore possible only by taking into account other physical considerations as well.

Coefficient C can be, as already mentioned above, calculated in terms of quantum chemistry. These calculations being extremely rough, it seems of greater importance to determine C from the optical force constant $k_\beta = \frac{1}{N}\left[\frac{\partial^2 U}{\partial \beta^2}\right]_{\beta=\beta_0}$ where β_0 is the equilibrium value and N the number of equivalent angles.

Having established k_β and the relative force η curve we can determine the constant C. This correlation allows us also to check the degree of precision of our assumption on the coefficient C being dependent only upon the central atom properties. Indeed, if the apexes of the β and γ angles are in the same atom, then k_β and k_γ can be expressed by the same ideal angle force constant C.

Denoting the HCH and HCC angles in cyclopropane through β and γ, respectively and bearing in mind that the deviations $\Delta\beta$ and $\Delta\gamma$ of these angles from the tetrahedral values are related by the correlation

$$\Delta\gamma = 0{\cdot}175 - 0{\cdot}374\Delta\beta$$

one obtains

$$k_\gamma = \frac{1}{12}\frac{\partial^2 U}{\partial \gamma^2} \quad \text{and} \quad k_\beta = \frac{1}{3}\frac{\partial^2 U}{\partial \beta^2}$$

As $\dfrac{\partial^2 U}{\partial \beta^2} = \dfrac{\partial^2 U}{\partial \gamma^2}\left(\dfrac{\partial \gamma}{\partial \beta}\right)^2 = 0{\cdot}15\,\dfrac{\partial^2 U}{\partial \gamma^2}$, then $\dfrac{k_\gamma}{k_\beta} = 1{\cdot}7$,

in agreement with the experiment

$$\left(k_\gamma = 0{\cdot}5 - 0{\cdot}6\,\frac{\text{erg}}{\text{rad}^2}, \quad \text{and} \quad k_\beta = 0{\cdot}30 - 0{\cdot}35\,\frac{\text{erg}}{\text{rad}^2}\right).$$

The potential energy expression for cyclopropane is as follows

$$\tfrac{1}{3}U = \frac{C}{2}/(\Delta\beta)^2 + 4(0{\cdot}175 - 0{\cdot}374\Delta\beta)^2/ + f(0{\cdot}267 - 0{\cdot}26\Delta\beta) + 4f(0{\cdot}243 + 0{\cdot}086\Delta\beta)$$

Twice differentiating and dividing both sides of equality by C one obtains $k_\beta/C = 2{\cdot}0$.

Thus, the approximate value of the ideal angle constant of the tetravalent carbon atom can be taken as equal $C = 0{\cdot}1_7.10^{-11}$ erg/rad^2.

Having ascertained C one finds $f'(\Delta r/r_0) = C\eta(\Delta r/r_0)$ and through graphical integration determines the repulsion energy of non-bonded hydrogen and carbon atoms. Our averaged curve Λ is rather similar to the interaction curve of carbon and bromine atoms reported by Dostrovsky *et al.*[7] but markedly different from those of Mason and Kreevoy. The latter interaction curves have been construed without allowing for the intermolecular radii and represent repulsion of even those atoms (in a molecule) that are not immediately adjacent to each other.

The interaction potential of non-bonded atoms seems to drop much faster and,

within a fair approximation, the conformation in the molecule and the strain energy appear to be determined only by the interaction of adjacent neighbouring atoms that are in immediate contact with each other.

It is to be recalled that the aim of the present paper is primarily to suggest a definite method to deal with the problem in question. As to the quantative approach it is thought to be subject to changes.

At present very little is known about the structure of strained molecules and the distortion of valence angles caused by the interaction of non-bonded atoms. The accumulation of experimental evidence will enable to determine more exactly the interaction curves for various pairs of atoms and to calculate *a priori* the optimum conformation in any molecule of a known chemical structure.

The author wishes to express his gratitude to Mrs. K. Myrskaya for computational assistance.