Structural and Strain-energy Consequences of "Intra-annular" Substitution in the Cyclodecane Ring

By M. BIXON,[a] H. DEKKER,[b] J. D. DUNITZ,[c] H. ESER,[c] S. LIFSON,[a] C. MOSSELMAN,[b] J. SICHER,[d] and M. SVOBODA[d]

([a] *Department of Chemical Physics, The Weizmann Institute of Science, Rehovoth;* [b] *Chemical Laboratory, The Free University, Amsterdam;* [c] *Laboratory of Organic Chemistry, Swiss Federal Institute of Technology, Zurich;* [d] *Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Science, Prague*)

X-RAY studies of various crystalline cyclodecane derivatives,[1] supplemented by strain-energy calculations based on semiempirical potential functions,[2–4] have shown that there is one favoured conformation of the cyclodecane ring (Figure 1). It is clearly of interest to have experimental data on the possible modes of deformation of this conformation, and on the corresponding strain-energy increments.

In the stable cyclodecane conformation, one may discern two kinds of C–H bonds: those that point out of the ring (extra-annular) and those that point into the ring (intra-annular). Groups other than hydrogen in intra-annular positions would clearly be in a highly strained situation.[5] It is obviously possible to substitute cyclodecane in such a way that one—or more—substituents would, in the stable conformation, have to occupy intra-annular positions. Such substitution is likely to enforce a deformation of the ring so as to alleviate the excessive intra-annular strain. The compound selected for our study was 1,1,5,5-tetramethylcyclodecane, in which at least one of the methyl groups would have to be intra-annular in the undeformed stable conformation (*cf.*, Figure 1).

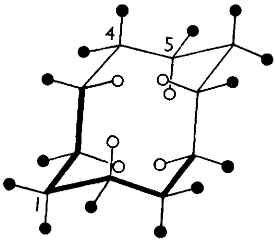

FIGURE 1. *Schematic representation of conformation of cyclodecane.* ○ *Intra-annular positions;* ● *Extra-annular positions.*

X-Ray analysis of crystals of 1,1,5,5-tetramethylcyclodecane-8-carboxylic acid leads to the structure shown in Figure 2 with bond angles and torsion angles indicated for the ring.* It is clear that the pattern of torsion angles, and hence the conformation of the ring as a whole, is distinctly different from that previously observed in five other cyclodecane derivatives,[1] which all contain approximately the same cyclic sequence of torsion angles (150°, −55°, −65°, 65°, 55°, −150°, 55°, 65°, −65°, −55°.) Neglecting the carboxyl group, the molecule appears to have an approximate

---

* The structure was determined by the symbolic addition method (W. H. Zachariasen, *Acta Cryst.*, 1952, **5**, 68; I. L. Karle, K. Britts, and P. Gum, *ibid.*, 1964, **17**, 496) and has been refined by full-matrix least-squares with anisotropic temperature factors for all atoms except hydrogen (contributions of hydrogen atoms in calculated positions have been included in the calculated structure factors but not refined). The *R*-factor is about 9%, based on the 900 most reliable *F*-values recorded with a linear diffractometer.

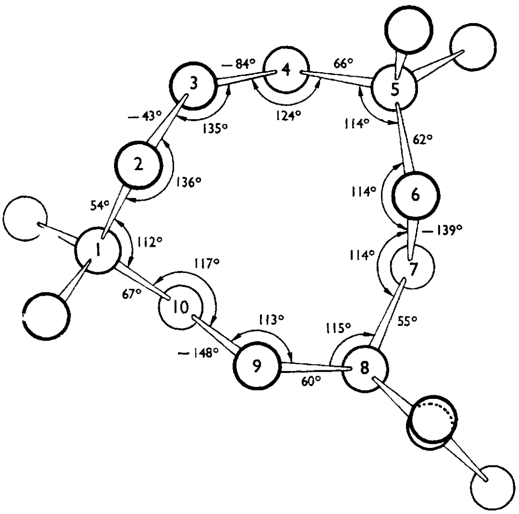

FIGURE 2. *Observed conformation of* 1,1,5,5-*tetramethylcyclodecane*-8-*carboxylic acid with bond angles and torsion angles indicated for the ring.*

2-fold rotation axis passing through atoms 3 and 8 as its only element of symmetry.

Although the observed bond lengths and angles in the segment of the ring 1, 10, 9, 8, 7, 6, 5 (with the four methyl groups) are in good agreement with expected values (range of C–C distance, 1·50—1·55 Å), the distances and angles observed in the shorter segment 1, 2, 3, 4, 5 show large systematic deviations from expected values. The bond lengths 2—3 and 3—4 of 1·33 Å and 1·45 Å, respectively, appear far too short, and the angles at 2, 3, and 4, 136°, 135°, and 124°, respectively, far too wide. We believe that these deviations are not real, and that they arise as a result of disorder in this part of the structure. In support of this, the temperature factors for the atoms 2, 3, 4 (and of the methyl groups) are unusually large and anisotropic, compared with those of the remaining atoms. We imagine that different molecules in the crystal do not have quite identical partial conformations in this region. A somewhat similar, although less marked, effect of disorder has been noted previously.[6]

When this structure is used as a starting-point for a strain-energy minimization calculation,† convergence occurs to a model with reasonable bond lengths and angles and with torsion angles as indicated in the Table [Conformation (I)]. The calculated strain-energy of conformation (I) (relative to cyclohexane) is 14·0 kcal.mole^{-1} compared with 11·9 kcal.mole^{-1} for the strain-energy of the stable conformation, as calculated under the same assumptions and using the same potential functions: the strain-energy difference due to the "deformation" is thus calculated to be 2·1 kcal. mole^{-1}. An only slightly larger strain-energy, about 15 kcal.mole^{-1}, is calculated for a second conformation (II) characterized by an approximate 2-fold axis passing through the centres of two opposite bonds (1—2, 6—7) as described in the Table. To a good approximation, the relative positions of the atoms in the "observed" ring lie between those of corresponding atoms in the two calculated rings, suggesting that the crystal contains a mixture of these two calculated conformations. This is supported by the good correlation between the directions and magnitudes of the main axes of the observed thermal motion ellipsoids and the directions and magnitudes of the vectors joining corresponding atoms in the two calculated molecules (including the attached methyl groups). It would appear that conformation (II) is present to about 20%, in keeping with its calculated excess of strain-energy of 1 kcal.mole^{-1} relative to conformation (I).

Additional experimental information on the strain-energy difference between the stable and the "deformed" conformations of the cyclodecane ring is obtained from the heats of combustion of highly purified samples of 1,1,5,5- and 1,1,4,4-tetramethylcyclodecane; in the latter all the four methyl groups can exist in extra-annular positions in the stable conformation. The value of $-\Delta H_R^{25}$ (liquid) is found to be 2194·63 ± 0·4 kcal. mole^{-1} for the 1,1,5,5-isomer and 2192·37 ± 0·3

TABLE

Torsion angles (in degrees)

Bond	1—2	2—3	3—4	4—5	5—6	6—7	7—8	8—9	9—10	10—1
Observed	+54	−43	−84	+66	+62	−139	+55	+60	−148	+67
Conformation (I)	+82	−74	−69	+80	+58	−139	+54	+56	−142	+60
Conformation (II)	−44	+101	−159	+53	+62	−134	+63	+50	−154	+104

---

† In these calculations (ref. 4) the strain-energy of a trial conformation is expressed as a function of the internal co-ordinates (bond lengths, bond angles, and torsion angles) and minimized by the method of steepest descent. In contrast to the assumptions made by Hendrickson[2] and by Wiberg,[3] the zero-strain value of the ∠CCC is taken as 112·7° rather than as tetrahedral, and the torsional potential barrier is taken as 3·4 kcal.mole^{-1} rather than 2·8 kcal.mole^{-1}. The molecular parameters and strain energies corresponding to minimum strain conformations of cyclo-octane, cyclodecane, and cyclododecane agree extremely well with the experimental values.

kcal.mole^{-1} for the 1,1,4,4-isomer. The difference in the enthalpies of combustion, $\Delta\Delta H_R^{25}$, and hence the strain-energy difference is $2{\cdot}3 \pm 0{\cdot}3$ kcal.mole^{-1}, in strikingly good agreement with the values obtained by the computation procedure.

Attempts have already been made, by Prelog and his colleagues[7] as well as by the Prague group,[8] to interpret the reactivity behaviour of cyclodecane derivatives by conformational analysis in terms of the stable conformation (Figure 1). The present results suggest that the conformational approach is basically sound and also help to indicate its scope and limitations: reactions for which the steric requirements cannot be fulfilled in the stable conformation are nevertheless capable of taking place; the energy increment of 2·3 kcal. mole^{-1} for the particular deformation now studied affords an indication of the magnitude of the effects likely to be encountered.

The synthesis of the compounds examined in this study and the details of the *X*-ray structural determination, the heat of combustion measurements as well as strain-energy computations will form the subjects of separate communications.

(*Received, February 20th,* 1967; *Com.* 159.)

---

[1] E. Huber-Buser and J. D. Dunitz, *Helv. Chim. Acta*, 1960, **43**, 160; 1961, **44**, 2028; 1966, **49**, 1821. J. D. Dunitz and K. Venkatesan, *ibid.*, 1961, **44**, 2033; J. D. Dunitz and H. P. Weber, *ibid.*, 1964, **47**, 951; M. H. Mladeck and W. Nowacki, *ibid.*, 1964, **47**, 1280.

[2] J. B. Hendrickson, *J. Amer. Chem. Soc.*, 1964, **86**, 4854.

[3] K. Wiberg, *J. Amer. Chem. Soc.*, 1965, **87**, 1070.

[4] M. Bixon and S. Lifson, *Tetrahedron*, 1967, **23**, 769.

[5] J. D. Dunitz and V. Prelog, *Angew. Chem.*, 1960, **72**, 896.

[6] C. K. Prout and T. J. Wiseman, *J. Chem. Soc.*, 1964, 497.

[7] V. Prelog, W. Küng, and T. Tomljenovic, *Helv. Chim. Acta*, 1962, **45**, 1352.

[8] J. Sicher, *Chimia (Switz.)*, 1962, **16**, 300; J. Sicher, M. Svoboda, J. Závada, R. B. Turner, and P. Goebel, *Tetrahedron*, 1966, **22**, 659; M. Svoboda, J. Závada, and J. Sicher, *Coll. Czech. Chem. Comm.*, in the press.