

## CONFORMATIONAL EQUILIBRIA IN SIX-MEMBERED RINGS

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### ABSTRACT

CNDO/2 calculations have been carried out on cyclohexane, 1,4-piperazine and 1,4-dioxane. Trends in the calculated results compare well with experimental data. The following order in steric effects has been found:  $\text{CH}_3 > \text{H} > \text{electron pair}$ .

### INTRODUCTION

During the course of our studies on chelate formation between a carbonium ion and the heteroatoms of the chair form of 1,4-heterosubstituted cyclohexanes [1, 2] it was necessary to examine the performance of the CNDO/2 method with geometry optimization [3] in the conformational analysis of six-membered rings. We report here CNDO/2 results on the geometries and relative energies of chair and boat forms of cyclohexane (1), 1,4-piperazine (2) and 1,4-dioxane (3) and the relative steric effects of a hydrogen atom and a pair of electrons.

### METHODS

It has been shown that the CNDO/2 method [4] yields best results when experimental or standard [5] geometries are used [6], but the lack of knowledge of the geometries of most of the structures studied renders this approach impossible. Instead, the energies of the species studied were minimized through successive optimization of each of the geometrical parameters involved [3]. More efficient methods of geometry optimization are now available [7].

### RESULTS AND DISCUSSION

The gas-phase geometries of six-membered rings have been determined by electron diffraction [8, 9]. The experimental values are shown together with the CNDO/2 results in Table 1. The calculated bond lengths are shorter than

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the experimental values in bonds to heavy atoms, and longer in bonds to hydrogen. On the other hand, the calculated bond angles are in general larger than the experimental ones. These effects have already been observed [3, 10] and the CNDO/2 parameters have consequently been redetermined to obtain calculated structures closer to the experimental ones [11, 12]. However, the parallelism observed between experimental and calculated results confirms the validity of the theoretical predictions for a series of molecules.

Different methods have given a large range of values for the energy difference between the chair and boat forms of cyclohexane, as shown in Table 2. Our result ( $4.9 \text{ kcal mol}^{-1}$ ) lies very close to the experimental value. The boat-chair energy difference is smaller for heterosubstituted rings:  $4.1 \text{ kcal mol}^{-1}$  for 2 and  $2.6 \text{ kcal mol}^{-1}$  for 3. The differences arise mainly from flagpole-flagpole interactions in the boat form and they show that a hydrogen atom exhibits a larger steric effect than an electron pair on a heteroatom.

The relative size of a methyl group, a hydrogen atom and a pair of electrons has been the subject of a long debate in the literature. Results based on the determination of molecular polarizabilities [19] suggest the order  $\text{CH}_3 > \text{electron pair} > \text{H}$ , but this has been criticized [20]. More recent theoretical [21] and experimental [22] results show that the preference for an equatorial position in a six-membered ring follows the order  $\text{CH}_3 > \text{H} > \text{electron pair}$ . We have calculated the energies for all chair and boat isomers of compound 2, and the results show that H always prefers the equatorial position (Fig. 1). The same preference has been calculated in morpholine with less sophisticated CNDO and INDO methods [23].

The main effects responsible for the energy differences shown in Fig. 1 are the 1,3-interactions with the hydrogen atoms that become axial in the series a-c and g-i, and the 1,4-interactions in the series d-f. The energy needed for the epimerization of the group bearing the hydrogen atom is proportional to the number of 1,3-interactions present in the product. As expected from a normal steric effect, the epimerization flattens the cycle on the side of the H atom that becomes axial, as shown by the angles in Fig. 1.

## CONCLUSION

The CNDO/2 method with geometry optimization does not reproduce experimental geometrical parameters well. However, trends in energies and geometries are well reproduced within a series of related molecules.

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TABLE 1

Geometries of 1,4-diX-cyclohexanes<sup>a</sup>

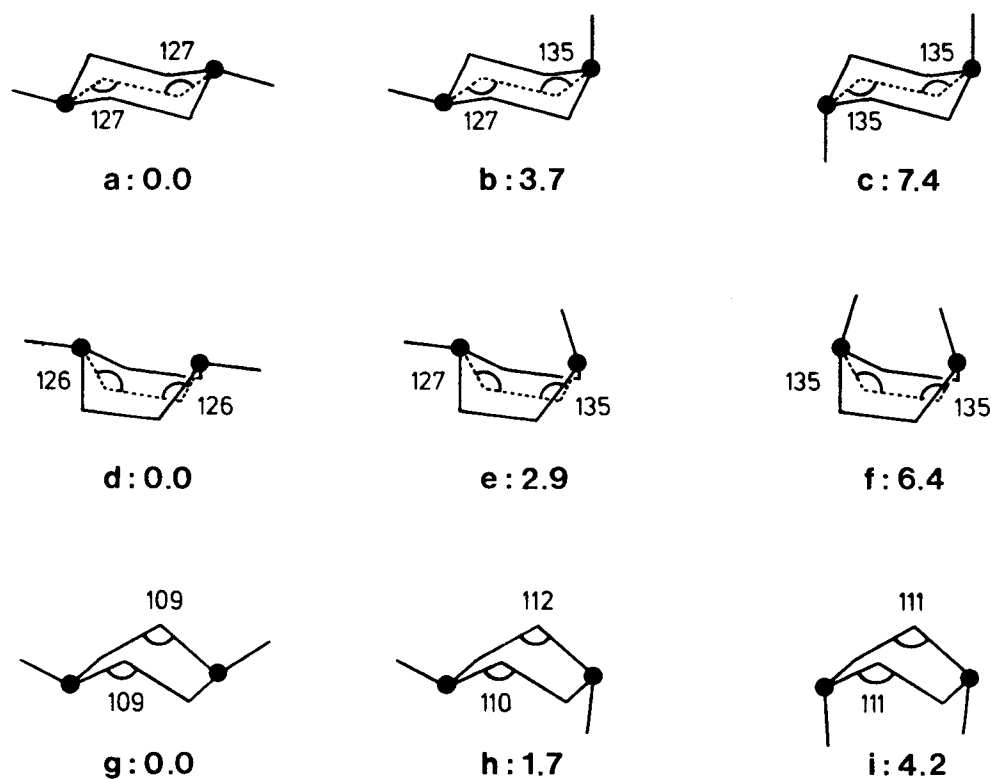
	X = CH <sub>2</sub>	NH	O
C—C	1.477 (1.528—1.536)	1.477 (1.527)	1.475 (1.523)
C—X	1.477 (1.528—1.536)	1.423 (1.471)	1.379 (1.423)
C—H	1.126 (1.09—1.121)	1.127 (1.112)	1.126 (1.112)
∠CCX	112.7 (111.1—111.6)	113.2 (109.8)	111.5 (109.2)
θ <sub>av</sub> <sup>b</sup>	112.7 (111.1—111.6)	112.6 (110.7)	110.3 (110.3)
φ <sub>av</sub> <sup>b</sup>	51.1 (54.5—55.9)	56.4 (56.8)	57.9 (57.9)

<sup>a</sup>Experimental values in parentheses [8, 9]. Bond lengths in Å, angles in degrees. <sup>b</sup>Ref. 13.

TABLE 2

ΔE (boat—chair) for cyclohexane

Method	ΔE (kcal mol <sup>-1</sup> )	Ref.
Experimental	5.3	14
Molecular mechanics	6.6	15
Ab initio MO (GTF 5.2/2)	7.2	16
Simulated ab initio MO	9.4	17
Vibrational and geometrical data	8.5	18
CNDO, Wiberg parameters, partial geometry optimization	5.0	10
CNDO/2, complete geometry optimization	4.9	This work

Fig. 1. Energies (kcal mol<sup>-1</sup>) and angles for boat and chair forms of 2.

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